Fluoride is a naturally occurring trace element whose health effect of essentiality and toxicity in humans still remains controversial. Its compounds are extraordinary high strategic chemicals with unique physico-chemical properties that make them indispensable in recent high technology industries. Thus, fluoride related health problems appear in various situations of our clinical, nutritional, industrial and environmental activities.

In the past 15 years, the author’s group analyzed fluoride concentrations of fluid samples obtained from healthy adults, patients undergoing hemodialysis, fluoride-exposed animal models, workers suffered hydrofluoric acid exposure, commercial bottled mineral water and groundwater by means of a fluoride ion selective electrode.

This review article describes urinary fluoride reference value, insufficient fluoride removal during dialysis session, fluoride induced renal toxicity, occupational fluoride exposure, fluoride content in commercial bottled water and endemic dental fluorosis in India including recent work from the first author’s laboratory. In addition, the article discusses the potential health risk of fluoride, particularly in industrial workers, young children and elderly people.

**Keywords**: fluoride, hemodialysis, hydrofluoric acid, bottled water, endemic fluorosis

**Introduction**

Fluoride is a ubiquitous element widely distributed in natural environment in the form of fluorite (calcium fluoride, CaF₂) [1]. People may be exposed to fluoride through mainly following three routes: 1) impaired or diminished kidney function that cause fluoride retention in the body [2]; 2) consumption of fluoride contaminated groundwater [3]; 3) inhalation of and dermal contact with fluoride compounds during industrial processing [4,5].

Fluoride may be an essential element for animals and humans. For humans, however, the essentiality has not been demonstrated unequivocally, and no data indicating the minimum nutritional requirement are available [6]. Thus, health effect of fluoride in humans has been controversial [7,8].

The kidney is the main pathway for the elimination of absorbed fluoride and serum fluoride is excreted rapidly via urine [9]. Chronic kidney disease often seen in recent aging society shows the gradual reduction of kidney function that may lead to permanent kidney failure, or end-stage renal disease. Dialysis is a life-sustaining medical technology used with increasing frequency in the elderly population [10]. Although dialysis involves removal of fluid and waste products from the blood when kidneys fail, the dialysis system by itself cannot reduce serum fluoride to normal. Thus, abnormal high fluoride imbalance profiles are reported among patients undergoing long-term hemodialysis [11].

Hydrofluoric acid popularly used to etching glass, alu-
aluminum production, petroleum alkylation, fluorocarbon production and pharmaceuticals is a dangerous aqueous solution of hydrogen fluoride because of its extremely corrosive and easily vaporized nature. Despite the occupational fluoride exposure prevention controls and measures, fluoride exposure still continues to affect the health of industrial workers [4,12,13].

Kidney is reported to be the primary target organ for fluoride toxicity [14,15]. Urine levels of alpha glutathione S-transferase (α-GST) [16,17] and N-acetyl-β-D-glucosaminidase (NAG) [18] are reported to be useful biomarkers for the diagnosis of fluoride-induced acute nephrotoxicity along with the monitoring of urinary fluoride excretion.

Water is the main source of fluoride in humans and its intake is strongly dependent on the source the water is obtained from [19], however, the information on the fluoride concentration of bottled water products is limited and their levels mentioned on the labels are reported to be inaccurate [20,21].

Endemic fluorosis is a water-related disease and one of the major public health problems in the developing world (China, India, the Middle East, North Africa and the Ethiopian rift valley) [22-25]. It’s typical clinical features include dental and skeletal fluorosis (mottling of the teeth, bone sclerosis, osteomalacia, bone fractures and extraperiosteal soft tissue calcification) related to fluoride accumulation caused by excessive fluoride intake when fluoride contaminated groundwater is used for drinking water [26-28].

The common approach to analyze these fluoride related health problems is the determination of fluoride concentrations in fluid samples by means of a fluoride ion selective electrode (FISE) [29]. Since the development of FISE in 1966 by James Ross and Martin Frant of Orion Research (now, Thermo Fisher Scientific), it has become an important method for determining fluoride in a wide variety of environmental and industrial samples because of its excellent performance, speed, and general convenience [30]. In this review, we summarize the fluoride analysis and fluoride related health problems in above mentioned clinical, experimental, occupational and environmental aspects.

Materials and Methods

**Subjects**

1. **Urinary fluoride reference value (Healthy subjects)**

Spot urine samples were collected from 167 healthy Japanese adults (141 men, 26 women; mean age was 32 ± 9 years old, ranging from 19 to 59 years). The specific gravity of the urine samples was determined using a clinical refractometer (Erma, Tokyo, Japan). Urinary fluoride concentration was corrected to a specific gravity of 1.024 by multiplying the analytical result by 24/SG, where SG is the last two digits of the specific gravity of the urine sample.

Urinary fluoride concentration was adjusted to normal urine density using Eq. 1:

\[
\{F\} = \left[ \frac{\text{F}}{24} \right] \times 10^\text{SG}
\]

where \{F\} is the specific-gravity-corrected fluoride concentration and [F] is the observed fluoride concentration [31]. Obtained urinary fluoride reference value of the geometric mean (GM) with 95% confidential interval (CI) was compared to reported values.

2. **Fluoride removal in patients during dialysis session (Clinical subjects)**

Serum fluoride were determined in 29 patients (10 men, 19 women; mean age was 59 ± 11 years old, ranging from 41 to 83 years) under hemodialysis treatment. The serum samples were collected before (from the inlet tube of dialyzer at the beginning of dialysis) and after hemodialysis (from the outlet tube of dialyzer at the end of dialysis) [32].

3. **Fluoride induced renal toxicity (Laboratory fluoride-exposed animal models)**

An excess of sodium fluoride (135 mg F/kg body weight; 63.3% of the 48-hour LD50) was given in a single oral dose to 8-week-old SPF male Wistar rats weighing 180-200 g (n = 5) and twenty-four-hour urine samples were collected into test bottles of metabolic cages avoiding facial contamination to determine urinary fluoride, α-GST, NAG and creatinine. NAG was determined by the Shionogi NAG test (Shionogi Co., Osaka, Japan). α-GST was determined by Nephtkit-Alpha (Biotrin International, Dublin, Ireland). Creatinine was determined by the Wako creatinine test (Wako Pure Chemical Ind., Osaka, Japan) [33].

4. **Hydrofluoric acid exposed worker (Occupational subjects)**

Case study was conducted on a 52-year-old reinforcing rod worker who exposed to hydrofluoric acid vapor and showed a rapid onset of severe dyspnea [34].

5. **Commercial bottled water (Nutritional subjects)**

Thirty-three brands of commercially available bottled water in Osaka, Japan were selected at random to determine fluoride, calcium and magnesium concentration.
The samples were divided into three lots depending on their origin: Group A (Japan, n = 20); Group B (Europe, n = 7) and Group C (All other areas, n = 6) [35].

6. Groundwater of India (Environmental subjects)

Precedent survey for Japanese Official Development Assistance (ODA); Hogenakkal Water Supply and Fluorosis Mitigation Project was conducted in 2008 by the Japan Bank for International Cooperation (JBI, now JICA; Japan International Cooperation Agency). In this survey, groundwater samples from the Indian state of Tamil Nadu (Dharmapuri and Krishnagiri) where severe endemic dental fluorosis is prevalent were collected for fluoride and other mineral (calcium, magnesium, zinc, manganese, strontium and boron) analysis [36].

Fluoride and other element analysis

The analytical standards for elemental analysis were prepared by dilution of a commercial stock solution. Ultra-pure water of 18 MΩ cm was used to prepare samples and standards.

For fluoride analysis, one milliliter of sample was injected in a mixer bowl with magnetic rotating rotor on magnetic stirrer (Yamato MAG mixer MD-21, Yamato scientific Co., Ltd., Tokyo, Japan). To each of sample, 100 µL of total ionic strength adjustment buffer was added. Then, electrode potential of the sample was determined with FISE (Orion, Thermo Fisher Scientific, Inc.). When the electrode was stable, fluoride concentration was automatically calculated by memorized calibration slope which yields the calibration line with -57 mV/ decade of concentration change within the range of 10 to 10,000 µg/L [31-36].

Other elements (calcium, magnesium, zinc, manganese, strontium and boron) were determined by means of a Hitachi inductively coupled plasma-argon emission spectrometry (ICP-AES) system (P-5200-3600/1200; Hitachi, Ltd., Tokyo, Japan) [35, 36].

Results

Fig. 1 shows the log-normal distribution of corrected urinary fluoride concentrations with the geometric mean (GM) of 613.8 µg/L and 95% confidential interval (CI) of 241.0-1633.1 µg/L [31]. A literature review of urinary fluoride values for fluoride exposed and non-exposed population are presented in table 1 [37-46].

Table 2 shows the mean serum fluoride of the patients before dialysis (F1) and after dialysis (F2). As shown in this table, both F1 and F2 are significantly higher than reference value (Fr) (p < 0.001). Significant reduction of serum fluoride of F1>F2 (p < 0.001) was observed [32].

Table 3 shows the correlation coefficients and P-values

<table>
<thead>
<tr>
<th>Reported values (µg/L)</th>
<th>Subjects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>320 ± 210</td>
<td>non exposed workers</td>
<td>Irwbeck et al. [37]</td>
</tr>
<tr>
<td>390</td>
<td>Brazilian population in non-fluoridated areas</td>
<td>Heintze et al. [38]</td>
</tr>
<tr>
<td>470 ± 240</td>
<td>Swisslander population in fluoridated (250 µg/L) areas</td>
<td>Guindy et al. [39]</td>
</tr>
<tr>
<td>500</td>
<td>Malaysian population in non-fluoridated (140 µg/L) areas</td>
<td>Foo and Chong [40]</td>
</tr>
<tr>
<td>500 ± 270</td>
<td>Children in non-fluoridated areas of Trinidad and Tobago</td>
<td>Ramsanphag et al. [41]</td>
</tr>
<tr>
<td>590</td>
<td>Japanese population in non-fluoridated areas</td>
<td>Toyota [42]</td>
</tr>
<tr>
<td>640 ± 240</td>
<td>Swisslander population in fluoridated (1000 µg/L) areas</td>
<td>Guindy et al. [39]</td>
</tr>
<tr>
<td>740</td>
<td>Occupationaly non exposed German population</td>
<td>Massmann [43]</td>
</tr>
<tr>
<td>800–890</td>
<td>Preschool children in Mexico City</td>
<td>Juárez-López et al. [44]</td>
</tr>
<tr>
<td>880</td>
<td>Brazilian population in fluoridated (640 µg/L) areas</td>
<td>Heintze et al. [38]</td>
</tr>
<tr>
<td>900</td>
<td>Malaysian population in fluoridated (710 µg/L) areas</td>
<td>Foo and Chong [40]</td>
</tr>
<tr>
<td>1,310</td>
<td>Brazilian population in fluoridated (900 µg/L) areas</td>
<td>Heintze et al. [38]</td>
</tr>
<tr>
<td>1,480–1,580</td>
<td>Indian population in fluoride-rich groundwater</td>
<td>Yadav and Lata [45]</td>
</tr>
<tr>
<td>2,260–2,480</td>
<td>Indian population in fluoride-rich groundwater</td>
<td>Singh et al. [46]</td>
</tr>
<tr>
<td>4,800 ± 2,900</td>
<td>exposed workers</td>
<td>Irwbeck et al. [37]</td>
</tr>
</tbody>
</table>
of urinary fluoride compared to the other measured values in rat urine after fluoride administration. Of these markers studied, α-GST showed the strongest (r = 0.86, p < 0.001 in the first half of the experimental time course) and more durable (r = 0.70, p < 0.001 in the second half of the experimental time course) relationship with urinary fluoride [33].

Table 4 shows the serum and urine fluoride concentration of 52-year-old worker at small iron works who inhaled hydrofluoric acid vapor. Elevated fluoride concentrations were found up to 48 h after hospitalization in those specimens. He had widespread wheezing and crackles in his lungs on arrival at the emergency medical center. Chest radiograph showed a fine diffuse veiling over both lower pulmonary fields. The arterial blood gas monitor (PaO₂) showed a remarkable low of 46.6 mmHg and an arterial CO₂ tension (PaCO₂) of 30.0 mmHg, with pH 7.36 even on 100% O₂ supply by mask. He was intubated immediately with an oral endotracheal tube and given 5% calcium gluconate solution by intermittent positive pressure breathing (IPPB), utilizing a nebulizer. On the 5th hospital day, his respiratory faction had improved and the treatment was discontinued. On the 21st hospital day, chest film and CT scan were normal, and he was discharged very much improved on the 22nd hospital day [34].

Table 5 shows the fluoride, calcium and magnesium concentrations of commercial bottled mineral water. As seen in this Table, the geometric means of fluoride, calcium and magnesium were 79.8 µg/L, 19.1 µg/L and 2.8 µg/L, respectively. The fluoride content of Japanese and European brands was significantly higher than that of other brands. The calcium and magnesium concentrations were higher in the European brands than in all other brands [35].

Table 6 shows the concentration of fluoride and other minerals in groundwater samples obtained in the Indian state of Tamil Nadu. The fluoride concentrations were 3-7 times higher than the world health organization (WHO) guide line value of 1.5 mg/L. The calcium and magnesium concentrations were 2-5 times that of the Japanese standard of 300 mg/L. The strontium, manganese and bo-

Table 2  Serum fluoride in patients before and after hemoialysis [32]

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Fluoride (µg/L)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients before dialysis (F1)</td>
<td>65.9 ± 28.3</td>
<td>&lt;0.001 vs. F2 and Fr</td>
</tr>
<tr>
<td>Patients after dialysis (F2)</td>
<td>46.7 ± 26.7</td>
<td>&lt;0.001 vs. Fr</td>
</tr>
</tbody>
</table>

Fluoride values are given as the arithmetic mean ± SD.
The reference value of human serum fluoride (Fr) 12 ± 8 µg/L (arithmetic mean ± SD, n = 2656) is from a previous report by our group [29].
*Asterisks are used to indicate significant differences to Fr; 95%, p < 0.001.

Table 3  Correlation between urinary fluoride and other parameters in rats given a single excess dose of fluoride (n = 5) [33].

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Experimental time-course, days</th>
<th>r</th>
<th>P value</th>
<th>r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine volume</td>
<td>0-5 (First half)</td>
<td>0.58</td>
<td>&lt;0.01</td>
<td>Not significant</td>
<td></td>
</tr>
<tr>
<td>NAG</td>
<td>0.84</td>
<td>&lt;0.001</td>
<td>0.45</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>GST</td>
<td>0.86</td>
<td>&lt;0.001</td>
<td>0.70</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>-0.61</td>
<td>&lt;0.01</td>
<td>Not significant</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NAG; N-acetyl-β-D-glucosaminidase
GST; alpha glutathione S-transferase
r and P-values are obtained by linear regression analysis

Table 4  Changes is serum and urinary fluoride after hydrofluoric acid inhalation [34]

<table>
<thead>
<tr>
<th>Hospital day</th>
<th>1st Time</th>
<th>2nd Time</th>
<th>3rd Time</th>
<th>4th Time</th>
<th>21st Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum (µg/L)</td>
<td>74.6</td>
<td>37.8</td>
<td>19.4</td>
<td>21.3</td>
<td>10.7</td>
</tr>
<tr>
<td>Urine (mg/L)</td>
<td>0.33</td>
<td>-</td>
<td>0.70</td>
<td>0.48</td>
<td>0.35</td>
</tr>
</tbody>
</table>
ron levels were also high, indicating that groundwater presently in use is hard and unsuitable for human consumption [36].

Fig. 2 shows dental fluorosis prevalent among the children in the Indian state of Tamil Nadu. As shown in this figure, child with severe dental fluorosis shows pitting of the enamel and serious brown staining.

Table 5 Concentration of elements in bottled water obtained from various supermarkets in Osaka, Japan [35]

<table>
<thead>
<tr>
<th>Element</th>
<th>Group</th>
<th>GM</th>
<th>Median</th>
<th>Observed Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoride (µg/L)</td>
<td>A</td>
<td>96.6**</td>
<td>120.5</td>
<td>15.2-571</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>201.8*</td>
<td>205</td>
<td>30.4-1700</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>14.2</td>
<td>19.9</td>
<td>0.5-245.0</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>79.8</td>
<td>111</td>
<td>0.5-1700</td>
</tr>
<tr>
<td>Calcium (mg/L)</td>
<td>A</td>
<td>12.6###</td>
<td>12</td>
<td>2.2-48.5</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>161.8</td>
<td>254.5</td>
<td>14.4-580.4</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>6.3###</td>
<td>8</td>
<td>0.8-29.3</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>19.1</td>
<td>13.4</td>
<td>0.8-580.4</td>
</tr>
<tr>
<td>Magnesium (µg/L)</td>
<td>A</td>
<td>1.2###</td>
<td>1.8</td>
<td>0.07-13.7</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>30.3</td>
<td>29.9</td>
<td>7.4-92.3</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>2.8###</td>
<td>4.8</td>
<td>0.1-12.7</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>2.8</td>
<td>2.6</td>
<td>0.07-92.3</td>
</tr>
</tbody>
</table>

GM: geometric mean
*p < 0.05 and **p < 0.01 as compared with group C.
###p < 0.001 as compared with group B.

Groups: A – Japanese Brands; B – European Brands; C – Brands from other countries

Table 6 Element Concentration of Groundwater in the Indian State of Tamil Nadu [36]

<table>
<thead>
<tr>
<th>Source</th>
<th>*Fluoride (mg/L)</th>
<th>**Manganese (µg/L)</th>
<th>**Calcium (mg/L)</th>
<th>**Magnesium (mg/L)</th>
<th>**Zinc (µg/L)</th>
<th>Strontium (mg/L)</th>
<th>**Boron (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dharmapuri</td>
<td>5.43</td>
<td>46</td>
<td>938</td>
<td>340</td>
<td>422</td>
<td>14</td>
<td>38</td>
</tr>
<tr>
<td>Krishnagiri</td>
<td>9.82</td>
<td>5</td>
<td>525</td>
<td>200</td>
<td>330</td>
<td>2.9</td>
<td>38</td>
</tr>
<tr>
<td>Krishnagiri Elementary School</td>
<td>5.69</td>
<td>250</td>
<td>1219</td>
<td>400</td>
<td>384</td>
<td>9.2</td>
<td>51</td>
</tr>
</tbody>
</table>

*p < 0.05 and **p < 0.01 as compared with group C.
***p < 0.001 as compared with group B.

*The WHO guideline for fluoride is given as 1.5 mg/L.
**Japanese Ministry of Health, Labor and Welfare set the level of elements in drinking water below 0.05 mg/L for Manganese, 300 mg/L for Calcium and Magnesium, 1.0 mg/L for Zinc and 1.0 mg/L for Boron.

Discussion

1. Urinary fluoride reference value (Healthy subjects)

Urinary trace element concentrations including fluoride have been reported to show log-normal distribution pattern because of their elimination phases described by the negative exponential function of time (nonlinear process of overflow into urine with time) [47-50]. Taking reported values into consideration, it can be assumed that mean urinary fluoride value is ≈ 500 µg/L. It also can be estimated that mean urinary fluoride value of fluoride-exposed population shows ≈ 2,000 µg/L. As Osaka prefecture, Japan is free from fluoridation, GM of 613.8 µg/L with CI of 241.0-1633.1 µg/L compares well with the literature and can be regarded as reference values of urinary fluoride of normal unexposed individuals [31].

2. Fluoride removal in patients during dialysis session (Clinical subjects)

As fluoride is mainly eliminated from human body via the kidney, renal failure impairs the fluoride clearance.
The elevated serum fluoride can be explained by the accumulation of fluoride in patients with long-term hemodialysis. Taking into consideration the reported value of 117.3 ± 8.4 µg/L in F1 and 113.3 ± 8.5 µg/L in F2 by Canturk et al. [51] and 28.4 ± 5.9 µg/L in F1 and 17.9 ± 4.9 µg/L in F2 by Chaleil et al. [52], serum fluoride cannot be reduced to normal, although the significant difference of F1 > F2 shows the fluoride filtration from serum to dialysate. The existence of plasma proteins or macro constituents binding fluoride that makes free diffusion unavailable across the dialysis membrane is suggested. Thus, the high serum fluoride at the completion of the hemodialysis session was thought to originate from the fraction of unfilterable binding fluoride [53].

3. Fluoride induced renal toxicity (Laboratory fluoride-exposed animal models)

Urinary NAG activity is a marker of the proximal convoluted tubule (PCT) cell necrosis [54-57] and used as the indicator of the S1 or S2 segment injury. α-GST is a marker of the proximal pars recta of proximal straight tubule (PST) and S3 injury [58-60]. As α-GST proved to be a useful marker for the early detection and long-term observation of fluoride induced proximal renal tubular injury, fluoride induced renal toxicity may be more pronounced in the proximal tubule than the glomeruli region, and that the disorder of the proximal tubule is more serious in the S3 (see Fig.3 [61]) segment than S1 or S2 segment.

4. Hydrofluoric acid exposed worker (Occupational subjects)

Fluoride ions from hydrofluoric acid can penetrate tissues and absorbed into the body. They rapidly bind to calcium to form insoluble fluoride salts that can cause calcium depletion and hypocalcemia. With the onset of clinical hypocalcemia, heart function is impaired and the heartbeat becomes abnormal, resulting in cardiac dysrhythmia. Calcium gluconate is very effective and the only hydrofluoric acid poisoning detoxication drug. The theory behind this is that as the calcium can complex with the fluoride anion and precipitate out as a salt thus preventing the fluoride from scavenging the body’s own calcium stores. Hydrofluoric acid is one of the most corrosive acids known. It is necessary to use personal protective equipment, which are effective to protect against hydrofluoric acid exposure. The present case indicates that an adequate method of emergency treatment for accidental hydrofluoric acid poisoning is necessary [62].

5. Commercial bottled mineral water (Nutritional subjects)

The results we obtained show that 94% of the analyzed samples contained fluoride at concentrations lower than WHO guideline value of 1.5 mg/L. The geometric mean of 14.2-96.6 µg/L and median value of 19.9-205.0 µg/L indicate that most of the waters analyzed have fluoride levels that are less than 10% of the WHO guideline value. Two samples from France and Italy surpassed that

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**Fig. 3** Schemea of a nephron with indication of the segments distinguished for dissection [61]
level at 1.69 and 1.70 mg/L, respectively. In general, European brands contained twice as much fluoride as Japanese brands. Those from other countries had fluoride at levels 1% that of the WHO value.

According to the Mineral Water Association of Japan, the average individual annual consumption in Japan was 18.4 L in 2006. This is less than the 2007 consumption in the United States (80.6 L), France (156.2 L), Italy (168.3 L) and Spain (168.7 L). Taking these values as reference, the amount of fluoride intake per year would be about 4.9 µg/day/person for Japanese brands, 10.2 µg/day/person for European brands, 0.72 µg/day/person for other brands and, if the highest-content water were considered, the intake would be 85.7 µg/day/person.

Our results show that Japanese and other brands do not contain high levels of fluoride and that the intake from drinking mineral water reaches only 0.018-0.123% of the Food and Nutrition Board, National Research Council (NRC) upper limit. Considering the European brands that are highest in fluoride, the intake would be 0.26-2.14% of the NRC upper limit. Since water is consumed in the US and Europe at about 4-9 times that of the Japanese consumption level, then the fluoride intake from mineral water could reach 8-18% of the NRC upperlevel if the highest fluoride content brand is consumed [35].

6. Groundwater of India (Environmental subjects)

Endemic fluorosis due to excessive fluoride in groundwater is a serious health problem in the rural districts in India. The supply of fluoride-free drink water from surface water is an urgent matter in these regions. The government of Japan provided official development assistance (ODA) in the amount of 22,387 million yen for a project entitled “Hogenakkal Water Supply and Fluorosis Mitigation Project.” The project was undertaken to use the Cauveri River as a stable water supply to the population, reducing their exposure to fluoride.

In a recent trend of ODA, recognition of the importance of combating extreme poverty in India is key to attain the Millennium Development Goals (MDGs), so India has become the biggest recipient of ODA from Japan in the last five years.

It should be stated that India does not accept international interference in domestic issues of poverty and the gap among different strata of the population as part of ODA programs or activities. In divergence to most other developing countries, India’s approach to international assistance embraces the concept of self-help or autonomous ownership that Japan needs to respect and explore forms of assistance that take full advantage of the strengths of this policy concerning acceptance of ODA.

It is necessary for us to offer the best aid package that we can within the concept of self-help or ownerships valued by the Indian government in cooperation with the local inhabitants, non-governmental organizations and the United Nations’ offices in the region [36].

Conclusion

Global aging is presently ongoing process to present unprecedented challenges in the 21st century. In the setting of an aging global population, the burden of chronic diseases is rapidly increasing worldwide. Hemodialysis is the most common health-sustaining treatment for chronic kidney failure designed to remove impurities from blood, however, patients undergoing hemodialysis show abnormally high serum fluoride concentrations. As the fluoride chemicals are important material used in the production of numerous high performance commercial applications, industrial workers are at great risk of fluoride exposure. Although most bottled waters contain fluoride less than WHO guideline value of 1.5 mg/L, groundwater in underdeveloped countries is found to contain fluoride in excess of WHO guidelines and rural inhabitants especially children are at great risk of fluorosis. We conclude that there is a wide variability in human individual sensitivity to fluoride by various factors of clinical, occupational and environmental conditions.

References

6) World health organization sustainable development


32) Usuda K, Kono K, Yoshida Y: The effect of hemo-


