



## HEALTH EFFECTS OF GROUND WATER FLUORIDE CONTAMINATION IN BANKURA DISTRICT OF WEST BENGAL, INDIA.

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### ABSTRACT

India is a subcontinent country with large amount of resources, though many places in India people uses ground water as only the sources for drinking and domestic purpose. But ground water is not safe in most of the places. Arsenic and Fluoride are the major concern of ground water pollution in these days. The Indian Ministry of Water Resources informs that several districts of nine states (*i.e.*, Bihar, Haryana, Jharkhand, Karnataka, Maharashtra, Madhya Pradesh, Orissa, Tamil Nadu and Uttar Pradesh) of India are affected by high Fluoride concentrations (greater than 1 mg/l) in groundwater. Fluoride has beneficial effects on teeth at low concentrations of 1mg/l by preventing and reducing the tooth decay. Fluorosis is a common disorder it occurs due to entry of fluoride in the body, which affects every organ, tissue, cells in the body, and results in health complaints having overlapping manifestations with several other diseases like gout and osteoporosis. In short, it also causes dental fluorosis, musculo-skeletal fluorosis. Fluoride damages the Pineal Gland and affects the reproductive systems and intelligence.

**KEYWORDS:** *Fluoride, Groundwater, osteoporosis, dental fluorosis and musculo-skeletal fluorosis.*



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## INTRODUCTION

Water is essential for all physiological activities associated with animal kingdom as well as the plant kingdom. However, the nature and the quality of surface and ground water are widely variable and are determined by the local geological history. Fluoride is known to contaminate groundwater reserves globally. The most electronegative of all chemical elements fluorine is so violently reactive chemically, that it is rarely or never encountered in nature as elemental fluorine. Fluoride is an ion of fluorine (F), which belongs to the halogen family. Fluoride ion is an ionic form of the element fluorine, which is found in abundance in nature, primarily in water and soil. Fluorine is never found in nature in its elemental form as its extreme reactivity. It is found only in the form of compounds known as fluorides. All living organisms are exposed to inorganic fluorides mainly through food and water. The most relevant inorganic Fluorides are Hydrogen Fluoride (HF), Calcium Fluoride (CaF<sub>2</sub>), Sodium Fluoride (NaF), Sulfur Hexafluoride (SF<sub>6</sub>) and Silicofluorides which are present naturally in the environment. They are mainly the focus of this digest. There are many natural products such as tea and fish contain significant quantities of fluorides.<sup>1</sup>

## SOURCES OF FLUORIDE

### NATURAL

Fluoride as an element is found in the environment and it constitutes about 0.06-0.09% of the total earth's crust. Most of the fluoride found in groundwater is naturally occurring from the breakdown of rocks and soils or weathering and deposition of atmospheric volcanic particles and gases emitted from earth's crust.

### HUMAN ACTIVITIES

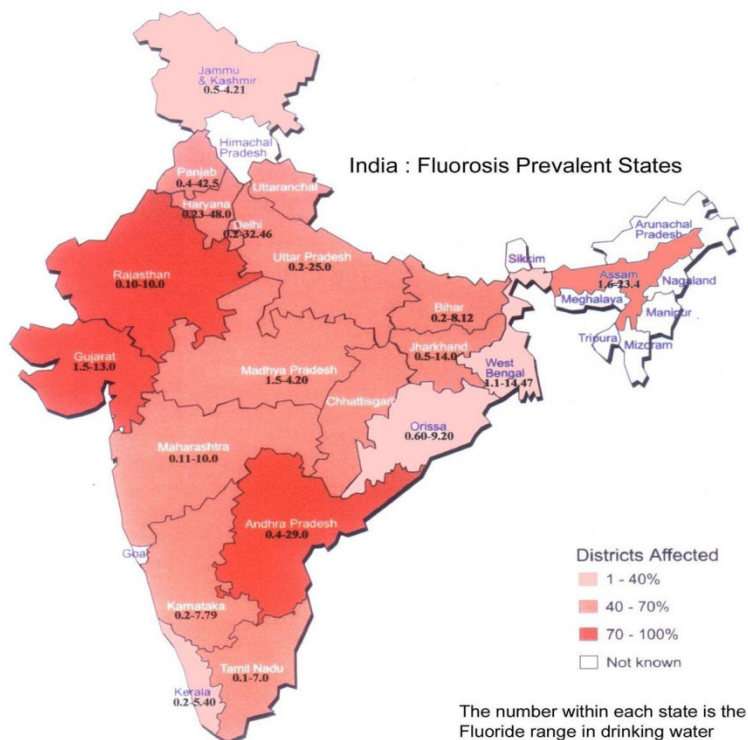
Fluorides are released into the environment are mainly the mining and processing of phosphate rock. It also uses as agricultural fertilizer, as well as the manufacture of aluminium. The other sources include the combustion of coal and other manufacturing processes such as steel, copper, nickel, glass, brick, ceramic, glues and adhesives. In addition, small amount comes from the use of fluoride-containing pesticides in agriculture.

## FLUORIDE CONTENT IN GROUND WATER

85% of rural population of our country uses groundwater for drinking and domestic purposes. According to World Health Organization (WHO), the guideline value and the permissible limit of fluoride as per guidelines of Bureau of Indian Standard (BIS) is 1.5 mg/L. It becomes toxic when the drinking water beyond the maximum permissible limit of 1.5 mg/L<sup>2</sup>. Chronic exposure to fluoridated ground water in drinking creates a health problem in human beings as well as diverse species of domestic animals in the form of osteo-dental fluorosis.<sup>3-6</sup>

## FLUORIDE AFFECTED AREAS

In India sixty millions of people, including six millions of children who are highly affected with fluoride related health disorders. The problem of high groundwater fluoride concentration resources has become one of the most important toxicological and geo-environmental issues in India. In India, about 20 states out of the 35 states and Union Territories of the Indian Republic are highly affected with high ground water fluoride (Figure 1). Highest natural level concentration reported being 38.50 mg/l in Haryana. Almost 40-70% districts are affected in Bihar (6-endemic districts), National Capital Territory of Delhi (7-endemic districts), Haryana (12-endemic districts), Jharkhand (5-endemic districts), Karnataka (16-endemic districts), Maharashtra (10-endemic districts), Madhya Pradesh (14-endemic districts), Orissa (18-endemic districts), Tamil Nadu (9-endemic districts) and Uttar Pradesh (7-endemic districts). In India 10-40% affected districts are Assam (2-endemic districts), Jammu & Kashmir (1-endemic district), Kerela (3-endemic districts), Chattisgarh (2-endemic districts) and West Bengal (7-endemic districts). While the endemicity for the remaining states are not known. In West Bengal fluoride contamination of ground water was first detected during 1997 at Nasipur area of Nalhati-I Block in the district of Birbhum. In west Bengal, 225 villages in 49 blocks of 7-districts were found to contain fluoride in ground water beyond permissible limit (Including 7-districts- Birbhum, Bankura, Malda, Purulia, 24-South Parganas, Dakshin Dinajpur and Uttar Dinajpur), were identified as endemic for fluorosis and people in these regions are at risk of fluoride contamination (Table 1).<sup>7</sup> It was also observed that in West Bengal at South 24-Pargana, Baruipur is a place where both arsenic and fluoride has found in ground water.<sup>8</sup>



**Figure1**  
**UNICEF state of art report, 1999 (Sources information)**

**Table 1**  
**Blocks of West Bengal affected with Fluoride > 1.5 mg/l (Sources from Public Health Engineering Department, Government of West Bengal)**

Sl. No	District	Fluoride Affected Blocks	No of Blocks
1	Purulia	Jaipur, Purulia-I &II, Para, Raghunathpur-I &II, Neturia, Santuri, Kashipur, Hura, Pancha, Arsha, Jhalda- I& II, Bagmundi, Balarampur, Arabazar	17
2	Bankura	Saltora, Gangajalghati, Chhatna, Mejia, Khatra, Ranibandh, Sarenga, Indpur, Bankura-I & II, Barjora, Taldangra, Simlapal, Hirbandh, Raipur & Sonamukhi.	16
3	Birbhum	Nalhati-I, Rampurhat-I, Mayureswar-I, Rajnagar, Suri- II, Sainthia, Khoyrasol,	7
4	South 24-Parganas	Baruipur	1
5	Malda	Ratua-II, Bamangola	2
6	Uttar Dinajpur	Itahar	1
7	DakshinDinajpur	Kushmundi, Gangarampur, Kumarganj, Tapan, Bansihari	5
<b>TOTAL NO OF BLOCKS</b>			<b>49</b>

According to Public Health Engineering Department, Government of West Bengal shows that the ground water quality and percentage of fluoride content (Table 2 & 3). Results show that Purulia district with 15 blocks (out of 17 blocks) having fluoride contamination is the

worst affected. As the problem spreads day by day, a scientific inquest to find out the source and cause of fluoride in groundwater of Purulia has become the need of the hour. In Bankura Total 16blocks- are affected with fluoride contamination.

**Table 2**  
**Water quality statuses of the spot sources in the Fluoride affected district of West Bengal (Sources from Public Health Engineering Department, Government of West Bengal)**

District	Percentage of tube wells having Fluoride content (in mg/l)					Max Fluoride (ppm)	Total	
	>=0 to <1	>=1 to <=1.5	>1.5					
	%	Count	%	Count	%	Count		
Bankura	92.17	7854	4.88	416	2.95	251	10.80	8521
Purulia	88.88	9525	7.71	826	3.42	366	8.28	10,717
Birbhum	97.91	8842	1.16	105	0.93	84	20.40	9031
South 24 Parganas	98.85	1120	0.79	9	0.35	4	1.81	1133
Uttar Dinajpur	97.33	3897	2.27	91	0.40	16	1.87	4004
DakshinDinajpur	77.34	11254	15.54	2261	7.13	1037	7.58	14552
Maldah	96.05	2333	2.18	53	1.77	43	4.53	2429

Table 3

**Water quality status of the spot sources in the Fluoride affected different blocks of Bankura district, West Bengal (Sources from Public Health Engineering Department, Government of West Bengal)**

Bankura	Percentage of tube wells having Fluoride content (in mg/l)						Max Fluoride (ppm)	Total
	>=0 to <1		>=1 to <=1.5		>1.5			
	%	Count	%	Count	%	Count		
Saltora	96.32	497	2.33	12	1.36	7	3.41	516
Gangajalghati	86.12	732	11.53	98	2.35	20	2.32	850
Chhatna	96.07	1,419	2.91	43	1.02	15	4.25	1,477
Indpur	94.20	779	5.44	45	0.36	3	1.63	827
Bankura - II	93.41	893	4.71	45	1.88	18	5.10	956
Barjora	93.59	788	5.23	44	1.19	10	2.51	842
Taldangra	95.52	939	2.85	28	1.63	16	3.65	983
Simlapal	79.23	698	3.52	31	17.25	152	2.00	881
Hirbandh	79.23	525	8.70	51	1.71	10	10.80	586
Raipur	96.85	584	3.15	19	0.00	0	1.50	603
<b>Total</b>	<b>92.17</b>	<b>7,854</b>	<b>4.88</b>	<b>416</b>	<b>2.95</b>	<b>251</b>		<b>8,521</b>

## ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE OF FLUORIDE

Fluoride is widely distributed in the lithosphere mainly in the form of fluor spar, fluorapatite and cryolite, and is also recognised as the thirteenth most common element in the earth's crust. The principal sources of entry of fluoride to the physiology of human are: a) Water, b) air (dust), c) some species of vegetations, d) certain edible marine animals and e) certain industrial processes. It is also found in seawater at a concentration of around 1.2 – 1.4 mg/litre, in ground waters at concentrations up to 67 mg/litre, and in most surface waters at concentrations less than 0.1 mg/litre.<sup>9</sup> Fluoride is also found in foods particularly fish and tea.<sup>10</sup> While almost all foodstuffs contain at least traces quantity of fluoride. Water and non-dairy beverages are the main sources of ingested fluoride, accounting for 66 to 80% of fluoride intake in US adults according to the concentration of fluoride in the public drinking water. Other significant sources of ingested fluoride are toothpaste in very young children (who tend to swallow most of their toothpaste), tea in tea-drinking communities, and inhaled fluoride in some communities in China where coal containing very high levels fluoride is burned indoors. Absorption of ingested fluoride is via the stomach and small intestine.<sup>10</sup>

## ABSORPTION OF FLUORIDE ON HUMAN BODY

Fluoride absorption in human body is mainly occurs due to chronic exposure. The absorption mainly occurs in mucosal and enteral, inhalational and dermal part of the body.

## MUCOSAL AND ENTERAL ABSORPTION

The currently accepted theory on fluoride absorption is that inorganic fluoride in the form of the undissociated molecule, hydrofluoric acid (HF), is absorbed by rapid passive diffusion along the entire gastrointestinal tract (stomach and intestine), without any apparent active transport mechanisms being involved.<sup>11-13</sup> Since soluble ionic fluorides dissociate to release free F<sup>-</sup> in solution and protonate to form HF in the acid milieu of the gastrointestinal tract. In this form readily absorbed in the stomach.

## INHALATIONAL ABSORPTION

When fluorides in gaseous or particulate form are breathed in the respiratory tract, they are partially or completely absorbed depending on how soluble they are or on how big the fluoride-containing particles are.

## DERMAL ABSORPTION

Different group of researcher shows only hydrofluoric acid is absorbed through the dermis. Liquid hydrofluoric acid is either a strong or weak acid, depending on its aqueous concentration.<sup>14-15</sup> Dermal exposure to concentration of hydrofluoric acid solutions can result in severe chemical burns.<sup>16-17</sup>

## DISTRIBUTION OF FLUORIDE ON HUMAN BODY

Once fluoride is absorbed, either by ingestion, inhalation, or dermal absorption, it passes into the blood for distribution throughout the body and for partial excretion. In plasma, fluoride exists in two distinct forms: a non-ionic form covalently bonded to carbon-containing, lipid-soluble molecules and in an unbound ionic form.<sup>18</sup> Fluoride is then rapidly distributed in tissues. From plasma, fluoride complexes with calcified tissues and is distributed to either the extracellular or intracellular spaces of the soft tissues or is excreted. Most of the ionic fluoride retained in the body enters into the calcified tissues (bone and dentition), either by substituting for the hydroxyl ion (OH<sup>-</sup>) or bicarbonate ion (HCO<sub>3</sub><sup>-</sup>) in hydroxyapatite in bone. or enamel to form fluoroapatite, or as an ionic exchange within the hydration shell of the crystalline surface.<sup>19-20</sup> In humans fluorides mostly build up in bones and teeth, which retain about 99% of the total fluoride body burden. It is eliminated from the body primarily through the urine. Infants retain 80 to 90% of fluoride ingested, while adults retain approximately 60%.

## EXCRETION OF FLUORIDE ON HUMAN BODY

Renal excretion is the predominant route for removal of inorganic fluoride from the body. Approximately 50% of the daily intake of fluoride is cleared by the kidneys.<sup>21</sup> Renal excretion and deposition in calcified tissues account for almost 100 percent of the clearance of inorganic fluoride from plasma.<sup>22</sup> As fluoride deposition in bone decreases with age, fluoride levels in plasma

increase.<sup>23</sup> However the fluoride content in the body (i.e. the difference between the amount of fluoride ingested and the amount excreted) can be positive or negative. This physiological balance is determined by earlier fluoride exposure in the body, the degree of accumulation in bone, the rate at which it is released from bone and the efficiency of the kidneys in excreting fluoride. When fluoride intakes are low excretion through urine can exceed the quantity of intake. Fluoride can be transferred from mother to foetus through the foeto-placental unit.

### **EFFECT OF GROUND WATER FLUORIDE ON HUMAN HEALTH**

India is among 23 Nations where health problems occur due to consumption of fluoride contaminated ground water. Fluorine has been found to be an essential nutritional element for animal species. A large number of organizations around the world have studied the effects of fluoride on human health. It has both beneficial and detrimental effects on human health. Generally the prevalence of dental caries is inversely related to the concentration of fluoride in drinking water. There also observed a dose-response relationship between the concentration of fluoride in drinking water and the prevalence of dental fluorosis.<sup>24</sup>

### **BENEFICIAL EFFECTS OF FLUORIDE ON HUMAN HEALTH**

Fluoride is not considered to be essential for human growth and development but it is considered to be beneficial micronutrient for the proper development of teeth and bones. It has beneficial effects on teeth at low concentrations of 1mg/l by preventing and reducing the dental caries (tooth decay).<sup>25-27</sup> Dental caries occurs when sugar-containing foods are metabolised by oral bacteria in the mouth, resulting in acid production on the tooth surface. It causes the removal of minerals from the tooth enamel and ultimately produces dental caries. As a local effect, fluoride in saliva interacts with the minerals on the tooth surface and replaces all the lost enamel and so prevents dental caries. Fluoride at an optimal level (as per WHO permissible range) in the water supply provides the ideal, constant "repair kit" for teeth. Since the early 20th century in several parts of the world as a public health protective measure against tooth decay, intentionally fluoridation of drinking water (it is the adjustment of the natural concentration of fluoride in drinking water to the optimal recommended level for the prevention of dental caries) and the development of fluoride containing oral care products (toothpastes and mouth rinses), foods (fluoridated salts) and supplements (fluoride tablets) have been employed. Additional amount of exposure to fluoride comes from naturally occurring water (tap and mineral), beverages, food, and to a lesser extent, from other environmental sources.

In 1993, the results of 113 studies in 23 countries were reported.<sup>28</sup> The most frequent reported decay reduction were-

- a. 40-49% for primary teeth or baby teeth; and
- b. 50-59% for permanent and adult teeth.

### **ADVERSE HEALTH EFFECTS OF FLUORIDE**

Depending on the level of exposure of fluoride, it has two effects. The effects are acute effects (i.e., short term effects) and chronic effects (i.e., Long term effects) on human body.

#### **SHORT-TERM (ACUTE) EFFECTS**

Acute toxicity of fluoride is quite rare and has occurred principally as a result of exposure to excess fluoride in accidental poisonings.<sup>29</sup> The symptoms of acute toxicity include severe nausea, vomiting, excess saliva production, abdominal pain, and diarrhoea. Severe cases of exposure can result in convulsions, irregular heartbeat, and coma. Young children are potentially at risk for acute effects because of the often attractive taste of fluoridated toothpaste. They should always be supervised when brushing and, as is appropriate for their age, made aware of the danger in swallowing excessive amounts.<sup>30-35</sup>

#### **LONG-TERM (CHRONIC) EFFECTS**

The major manifestation resulting from chronic ingestion of excessive amounts of fluoride. Chronic exposure of fluoride causes dental fluorosis and systemic effects such as reproductive or developmental health effects, cardiovascular system, skeletal system (i.e., structure and function of skeletal muscle), brain and spinal cord. Recent studies also shows the accumulation of fluoride in the hippocampus of the brain causes degeneration of neurons and decreased aerobic metabolism and altered free-radical metabolism in the liver, kidney, and heart.<sup>36-45</sup>

#### **DENTAL FLUOROSIS**

Excessive, chronic ingestion of the fluoride ion can cause a condition known as enamel fluorosis. Depending on the amount of fluoride exposure (the dose) and the period of tooth formation at which the exposure occurs. This causes enamel fluorosis which can range from mild discoloration of the tooth surface to severe staining, enamel loss, and pitting. Fluoride-related fluorosis usually starts appearing in children between birth and age of 3 years, most significantly on the permanent central incisors, which are the most important teeth from an esthetic standpoint. This condition is permanent after it develops in children during tooth formation (from birth until about the age of 8).<sup>46</sup> Depending on the amount of fluoride exposure it may be very mild, mild or moderate form, is not considered to be a toxic effect.<sup>47</sup> According to WHO Oral Health Surveys Manual Scores (Table 4), shows that mild or very mild fluorosis is often unnoticeable to the normal (untrained) eye, but moderate fluorosis, caused by the ingestion of large quantities of fluoride during tooth formation and affect tooth appearance.<sup>36</sup> If large quantities of fluoride are ingested during tooth formation can lead to severe fluorosis and enamel erosion, making teeth more vulnerable to decay. This undesirable effect is generally associated with water fluoride concentrations in excess of 4 mg/L.<sup>47</sup>

Table 4

**Levels of dental fluorosis (Sources from WHO Oral Health Surveys Manual Scores)<sup>48</sup>**

Level of Exposure	Dental effects
0 = Normal	Enamel surface is smooth, glossy and usually a pale creamy- white colour
1 =Questionable	The enamel shows slight aberrations in the translucent normal enamel and which may range from a few white flecks to occasional spots
2 = Very mild	Small opaque, paper-white areas scattered irregularly over the tooth but involving less than 25% of the labial tooth surface
3 = Mild	White opacities of the enamel involving more than 25% but less than 50% of the tooth surface
4 = Moderate	The enamel surfaces show marked wear, and brown staining
5 = Severe	The enamel surfaces are severely affected and the hypoplasia is so marked that the general form of the tooth may be affected. There are pitted or worn areas and brown stains are widespread; the teeth often have a corroded appearance

**SKELETAL FLUOROSIS**

In chronic exposure of fluoride also causes it readily incorporated into the crystalline structure of bone, and accumulates during the course of time. Fluoride ions are readily incorporated into bone by substituting hydroxyl groups in the carbonate-apatite structure to produce fluorohydroxyapatite. Therefore it alters the mineral structure of the bone. As the bone strength is thought to derive mainly from the interface between the collagen and the mineral, alteration in mineralization affects bone strength.<sup>49</sup> Such condition is called skeletal fluorosis. It is extremely rare, and this condition is characterized by increased bone brittleness and a greater risk of fractures. Usually occurs when exposure to fluoride in drinking water exceeds 4 mg/L over a lifetime.<sup>50</sup> Skeletal fluorosis is categorized into a preclinical stage and stage I, II, and III and the last of which is referred to as the "crippling" stage because mobility is affected. At stage II, mobility is not significantly affected, but it is characterized by sporadic pain, stiffness of joints, and osteosclerosis (bone thickening) of the pelvis and spine.

**OSTEOSARCOMA**

Researchers have been found that there is a potential link between fluoride and cancer-osteosarcoma. Since fluoride is deposited in the bones during bone formation, some researchers hypothesized that this phenomenon may induce osteosarcoma in growing children.<sup>51</sup> But this hypothesis is still on debate, whether fluoride might be associated with bone cancer or not. Some researcher, on animal studies has suggested the possibility of increased risk of osteosarcoma (a bone cancer) in male rats, but no new animal bioassays have been performed to evaluate this further. Overall, the results obtained were mixed, as some studies reporting a positive association and others no association. The National Toxicology Program concluded that the evidence to date is tentative and mixed as to whether fluoride has the potential to initiate or promote cancers, particularly of the bone.

**DEVELOPMENTAL AND REPRODUCTIVE TOXICITY**

Few research on human studies have reported that fluoride might be associated with alterations in reproductive hormones and fertility, but limitations in the

study design make them of limited value for risk evaluation. Many researchers worked on animal studies and observed no reproductive toxicity. Effects of fluoride on the morphology of reproductive organs and reproductive function have been reported in male and female rabbits and mice, where given doses of greater than 4.5 mg kg<sup>-1</sup> body weight per day for varying periods, either orally or by injection. However, in recent studies on laboratory animals, there was no effects have been observed on reproduction, reproductive organs or the development of the foetus.<sup>52</sup>

**NEUROTOXICITY/IQ EFFECTS**

Different group of researchers from China and other areas where fluoride levels in groundwater are naturally very high (fluorosis endemic regions) claiming that an association between high water fluoride levels and slightly reduced intelligence (measured as IQ) in four- to seven year-old children.<sup>53</sup> Afterwards, reviewed and meta-analysed by Choi *et al*, who concluded that the results supported a possibility of adverse neuro-developmental effects of high fluoride intake.<sup>54</sup>

**ENDOCRINE EFFECTS**

Fluoride has suppressive effect on the thyroid function, and is more severe when iodine is deficient. Mostly fluoride is associated with lower levels of iodine. Different studies on animals with iodine deficiency showed effects on thyroid function at fluoride doses of 3-6 mg/kg/day and in one study, at doses in the range of 0.4- 0.6 mg/kg/day.<sup>55-57</sup> The levels of thyroid hormones T<sub>3</sub>, T<sub>4</sub>, and TSH are altered in response to excess fluoride in rodents.<sup>58</sup> Thyroid effects in humans were observed when fluoride levels 0.05–0.13 mg/kg/day when iodine intake was adequate and also 0.01–0.03 mg/kg/day when iodine intake was inadequate. The mechanisms and effects of fluoride on the endocrine system are still remaining unclear.

**EFFECT ON PHAGOCYTOSIS**

Fluoride also plays an important role in the breakdown of phagocytosis process. It depletes the energy reserves and the ability of white blood cells to properly destroy foreign agents by the process of phagocytosis. It was observed that as little as 0.2 ppm fluorides stimulate free radical production (superoxide) in resting white blood cells, virtually abolishing phagocytosis. Even micro-

molar amounts of fluoride, <1ppm, may seriously depress the ability of white blood cells to destroy pathogenic agents.

## **EFFECT ON CARDIOVASCULAR SYSTEM**

Fluoride has also found to accumulate the cardiovascular system. This causes in increased blood pressure (i.e., hypertension), arterial calcifications, arteriosclerosis, and myocardial damage.<sup>59-64</sup> Electrocardiogram abnormalities observed on chronic exposure of fluoride on both human and animals.<sup>65-66</sup> Recent research shows that patients with cardiac failure have significantly elevated levels of fluoride in their blood, even more than patients with kidney disease.

## **EFFECT ON OTHER ORGAN SYSTEM**

Different Scientific organization also considered the effects of fluorinated ground water on human body such as the gastrointestinal system, kidneys, liver and immune system. Still today there were no research findings shows that the effect of fluoride at 4 mg/L on human studies on GI tract, renal system, hepatic, or immune system.

## **CONCLUSION**

Preventive and curative measures against pollution and contamination of groundwater may continue to receive low priority for many years. The major reasons which contribute to elevated concentration of fluoride in

## **REFERENCES**

1. Environmental Health Criteria 227. Fluorides [Internet]. International Program on Chemical Safety. World Health Organization, Geneva 2002, Available at: <http://www.inchem.org/documents/ehc/ehc/ehc227.htm>
2. World Health Organization [Internet]. Guidelines for drinking water quality, Geneva: World Health Organisation; 1984. Available at: [www.who.int/water\\_sanitation\\_health/dwq/fulltext.pdf](http://www.who.int/water_sanitation_health/dwq/fulltext.pdf)
3. Choubisa SL. Endemic fluorosis in southern Rajasthan, India. *Fluoride*; 2001, 34(1):61-70.
4. Choubisa SL. Fluoride in drinking water and its toxicosis in tribals, Rajasthan, India. *ProcNatlAcadSci India Sect B BiolSci*; 2012; 82(2):325-30. doi: 10.1007/s 40011-012-0047-8.
5. Choubisa SL. Some observations on endemic fluorosis in domestic animals of Southern Rajasthan (India). *Vet Res Commu*; 1999, 23(7):457-65.
6. Choubisa SL. Fluoridated ground water and its toxic effects on domesticated animals residing in rural tribal areas of Rajasthan, India. *Int J Environ Stud*; 2007, 64(2):151-9.
7. Gupta S, Banerjee S, Saha R, Datta JK, Mondal N. Fluoride geochemistry of ground water in Nalhati -1 block of the Birbhum district, West Bengal, India. *Fluoride*; 2006, 39:318-20.
8. Central Ground Water Board ministry of water resources Government of India, "Bhu-Jal News", Quarterly Journal Volume No.24 , Number 1, Jan-March 2009.
9. Smith FA, Ekstrand J. The occurrence and the chemistry of fluoride. In: *Fejerskov O, Ekstrand J, Burt BA, eds. Fluoride in dentistry, 2nd ed. Copenhagen: Munksgaard, 1996, 20-21.*
10. IPCS. Environmental Health Criteria 227 Fluorides. *Geneva: World Health Organisation; 2002.*
11. Singer L, and Ophaug R, "Ionic and Nonionic Fluoride In Plasma (or Serum)". *CrcCrit Rev Clin Lab Sci*; 1982, 8(2): 111-40.
12. Barbakow F, "Intake, Absorption, and Excretion of Dietary Fluoride". *Int J VitamNutr Res Suppl*; 1983, 25:83-94.
13. Whitford GM, and Pashley DH, "Fluoride Absorption: The Influence of Gastric Acidity," 1984, *Calcif Tissue Int*; 1984, 36(3):302-7.
14. Leech HE, "The Physical and Chemical Properties of Fluorine and the Physical and Chemical Properties and Uses of Hydrogen Fluoride". *Mellor's Comprehensive Treatise on Inorganic and Theoretical Chemistry, London; Longmans, Green, (Suppl II); 1956 1:46-146.*
15. Rudge AJ, "The Manufacture of Fluorine and Its Compounds," 1962, Oxford Univ Press, London.
16. Dale RH, "Treatment of Hydrofluoric Acid Burns". *Br Med J*; 1951, 1:728-32.

## **CONFLICT OF INTEREST**

Conflict of Interest declared none.

17. Greco RJ, Hartford CE, *et al.*, "Hydrofluoric Acid-Induced Hypocalcemia". *J Trauma*, 1988, 28(11):1593-9.
18. Guy WS, "Inorganic and Organic Fluorine in Human Blood," in Continuing Evaluation of the Use of Fluorides, AAS Selected Symposium 11, 1979, Johansen E, Taves DR, and Olsen TO, Eds., Boulder, CO; Westview Press, 124-47.
19. McCann HG, and Bullock FA, "The Effects of fluoride Ingestion on the Composition and Solubility of Mineralized Tissues of the Rat". *J Dental Res*; 1957, 36:391-8.
20. Neuman WF, and Neuman MW, "The Chemical Dynamics of Bone Mineral". University of Chicago Press, Chicago: 1958, 75-100.
21. Whitford GM, "The Physiological and Toxicological Characteristics of Fluoride". *J Dent Res*; 1990, 69:539-57.
22. Jamberg PO, Ekstrand J, *et al.*, "Renal Excretion of Fluoride During Water Diuresis and Induced Urinary pH-Changes in Man". *ToxicolLett*; 1983, 18(1-2):141-6.
23. Parkins FM, Tinanoff N, *et al.*, "Relationship of Human Plasma Fluoride and Bone Fluoride to Age". *Calcif Tissue Res*; 1974; 16(4):335-8.
24. McDonagh M, Whiting P, Bradley M, Cooper J, Sutton A, Chestnut I, Misso K, Wilson P, Treasure E, Kleijnen J. A systematic review of public water fluoridation. *York: The University of York NHS Centre for Reviews and Dissemination*; 2000.
25. Jha SK, Mishra VK, Sharma DK, Damodaran T. Fluoride in the environment and its metabolism in humans. *Rev Environ Contam Toxicol*. 2011;211:121-42. doi: 10.1007/978-1-4419-8011-3\_4.
26. Slooff W *et al.*, eds. (1988) Basisdocument fluoriden. Bilthoven, Netherlands, National Institute of Public Health and Environmental Protection (Report No. 758474005).
27. Newbrun E. Systemic benefits of fluoride and fluoridation. *J Public Health Dent*, 2004: 64 (Spec Iss): 35-9.
28. Murray JJ. Efficacy of preventive agents for dental carries. *Carries Research* 1993: 27 (Suppl 1): 2-8.
29. Leland, D.E., Powell, K.E. and Anderson, R.S. 1980 A fluoride overfeed incident at Harbour Springs, Mich., *Journal of the American Water Works Association*, 72(4), 238–243.
30. Casarett and Doull's Toxicology: The Basic Science of Poisons, Fifth Edition. Klaassen, C.D., ed. McGraw-Hill Publishing Co., Inc., New York, 1995.
31. Toxicological information on Fluorine (Soluble Fluoride). Integrated Risk Information System (IRIS). U.S. EPA, Office of Health and Environmental Assessment. Last significant revision 1/87.
32. Toxicological Profile for Fluorides, Hydrogen Fluoride, and Fluorine (Update). Agency for Toxic Substances and Disease Registry (ATSDR). Atlanta, GA. September, 2003.
33. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Standing Committee on the Scientific Evaluation of Dietary reference Intakes. Institute of Medicine. 1997.
34. Health Effects of Ingested Fluoride. Commission on Life Sciences. National Research Council. 1993.
35. Fluoride in Drinking Water: A Scientific Review of EPA's Standards. Board on Environmental Studies and Toxicology. National Research Council. 2006.
36. Jolly SS, Prasad S, Sharma R. Review of 25 years research on fluoride. *Journal Association of Physicians of India*; 1970, 18:459-71.
37. Kaul RD, Susheela AK. Evidence of muscle fibre degeneration in rabbits treated with sodium fluoride. *Fluoride*; 1974, 7(4):177-81.
38. Shashi A, Singh JP, Thapar SP. Protein degradation in skeletal muscle of rabbit during experimental fluorosis. *Fluoride*; 1992, 25(3):155-8.
39. Shashi A, Singh JP, Thapar SP. Effect of long-term administration of fluoride on levels of protein, free aminoacids and RNA in rabbit brain. *Fluoride*; 1994, 27(3):155-9.
40. Mullenix PJ, Denbesten PK, Schunior A, Kernan WJ. Neurotoxicity of sodium fluoride in rats. *Neurotoxicology and Teratology*; 1995, 17(3):169-77.
41. Spittle B. Comments on the finding of toxin-induced blood vessel inclusions and alterations in neuronal and cerebrovascular integrity following the chronic administration of aluminum fluoride and sodium fluoride. *Fluoride*; 1998, 31(2):89-90.
42. Sharma A, Chinoy NJ. Role of free radicals in fluoride-induced toxicity in liver and kidney of mice and its reversal. *Fluoride*; 1998, 31(3):S26.
43. Patel D, Chinoy NJ. Influence of fluoride on biological free radical reactions in ovary of mice and its reversal. *Fluoride*; 1998, 31(3):S27.
44. Chinoy NJ, Patel D. Influence of fluoride on biological free radicals in ovary of mice and its reversal. *Environmental Sciences*; 1998, 6(3):171-84.
45. Sun G, Qiu L, Ding G, Qian C, Zheng Q. Effects of  $\beta$ -carotene and SOD on lipid peroxidation induced by fluoride: An experimental study. *Fluoride*; 1998, 31(3):S29.
46. Hong, L., Levy, SM., Broffitt, B., *et al.* Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. *Community Dent Oral Epidemiol*; 2006 Aug; 34(4): 299-309.
47. Fluoride in Drinking Water: A Scientific Review of EPA's standards: National Research Council of the National Academies. The National Academy Press. Washington, D.C. March 2006.
48. World Health Organization [Internet]. Oral Health Surveys: Basic Methods. Fifth ed. 2013, Geneva: World Health Organization. Available at: [www.who.int/oral\\_health/publications/9789241548649/en/](http://www.who.int/oral_health/publications/9789241548649/en/)
49. Catanese J, Keavney TM. Role of collagen and hydroxyapatite in the mechanical behaviour of bone tissue. *J Bone Miner Res*; 1996, 11:S295.
50. Fluoride in Drinking Water: A Scientific Review of EPA's standards: National Research Council of the National Academies. The National Academy Press. Washington, D.C. March 2006.
51. Morry, D.W. and C. Steinmaus, Evidence on the carcinogenicity of fluoride and its salts, 2011,



- Office of Environmental Health Hazard Assessment's Reproductive and Cancer Hazard Assessment Branch, California Environmental Protection Agency.
52. IPCS. Fluorides—Environmental Health Criteria 227. International Programme on Chemical Safety. Geneva, Switzerland: World Health Organization; 2002.
  53. Guojian Wang, Delong Yang, FenggeJia, Huiqin Wanga Shehezi, Xinjiang. A study of the IQ levels of four- to seven- year-old children in high fluoride areas. *Fluoride*; 2008 41(4)340–343.
  54. Choi, A.L., *et al.*, Developmental fluoride neurotoxicity: a systematic review and meta-analysis. *Environ Health Perspect*; 2012. 120(10): p. 1362-8.
  55. Bobek, S., S. Kahl, and Z. Ewy, Effect of long-term fluoride administration on thyroid hormones level blood in rats. *EndocrinolExp*; 1976. 10(4): 289-95.
  56. Guan, Z.Z., *et al.*, Synergistic action of iodine-deficiency and fluorine-intoxication on rat thyroid. *Chin Med J (Engl)*; 1988. 101(9): 679-84.
  57. Zhao, W., *et al.*, Long-term Effects of Various Iodine and Fluorine Doses on the Thyroid and Fluorosis in Mice. *EndocrRegul*; 1998. 32(2): 63-70.
  58. International Programme on Chemical Safety. World Health Organization, Fluorides. Environmental Health Criteria 227, 2002, World Health Organization: Geneva.
  59. Amini H, *et al.* Drinking water fluoride and blood pressure: an environmental study. *Biol Trace Elem Res*; 2011, 144:157-63.
  60. Tuncel E. The incidence of Moenckeberg calcifications in patients with endemic fluorosis. *Fluoride*; 1984, 17(1):4-8.
  61. Varol E, *et al.* Impact of chronic fluorosis on left ventricular diastolic and global functions. *Sci Tot Environ*; 2010, 408: 2295-8.
  62. Song AH, *et al.* Observations on fluoroticaortosclerosis by two-dimensional echocardiography. *Endemic Diseases Bulletin*; 1990, 5(1): 91-94.
  63. Basha MP, Sujitha NS. Chronic fluoride toxicity and myocardial damage: antioxidant offered protection in second generation rats. *Toxicollnt*; 2011, 18(2):99-104.
  64. Cicek E, *et al.* Effects of chronic ingestion of sodium fluoride on myocardium in a second generation of rats. *Human ExperToxicol*; 2005 24:79-87.
  65. Ji F, *et al.* Study on the cardiovascular damage of skeletal fluorosis patients. *Chin J Ctrl Endem Dis*; 2004, 19(6):321-3 (Abstract).
  66. Xu RY, Xu RQ. Electrocardiogram analysis of patients with skeletal fluorosis. *Fluoride*; 1997, 30(1):16-8.

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