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FLUORIDE IN DRINKING WATER IN RAJASTHAN AND ITS ILL EFFECTS ON HUMAN HEALTH

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Fluorine is the ninth element of the periodic table. Nevertheless, its applications and biological significances were known only in the decades of 1920's. It is the lightest member of the halogen family and the most electronegative among all chemical elements (Hodge and Smith, 1965). Fluorine has both notable chemical qualities and physiological properties, which are of great interest and significance to human health. Fluorine is rarely or never found free in the nature in elemental form. It has strong affinity to combine chemically with other elements to form compounds called 'fluoride'. Many workers and reviewers used the word 'Fluoride' to donate the ionized, physiologically available form of the element. The chemical activity of the fluoride ion (E^0 = -2.8 Volts) makes it physiologically more active than other elemental ion. Therefore, fluoride ions play an important role in human physiology. Its presence in low concentration may either inhibit or stimulates enzymatic process and its interaction with other organic and inorganic body components may cause disruption in normal physiological functions of human body. The extent of caries reduction by various methods is influenced by the initial caries prevalence and the standard of health care in the community. Fluoride has been used in the treatment of osteoporosis for two decades and, though beneficial effects have been reported, the dose-response relationships and efficacy need further clarification. Fluoride containing compounds are still used to increase the fluidity of metals and slugs in the glass and ceramic industries, fertilizer industry. The fluoride tablets are effective as anticarcinogenic agent. Anhydrous hydrogen fluoride is used in the production of most fluorine-containing chemicals and in the production of refrigerants, herbicides, pharmaceuticals, high octane gasoline, alu-

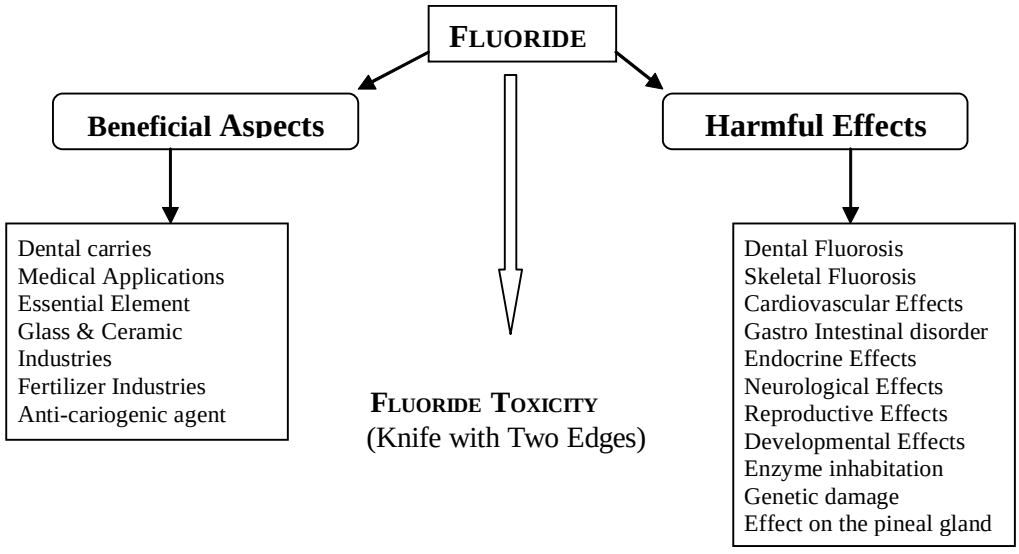

Fig. 1: Some beneficial and harmful effects of fluoride

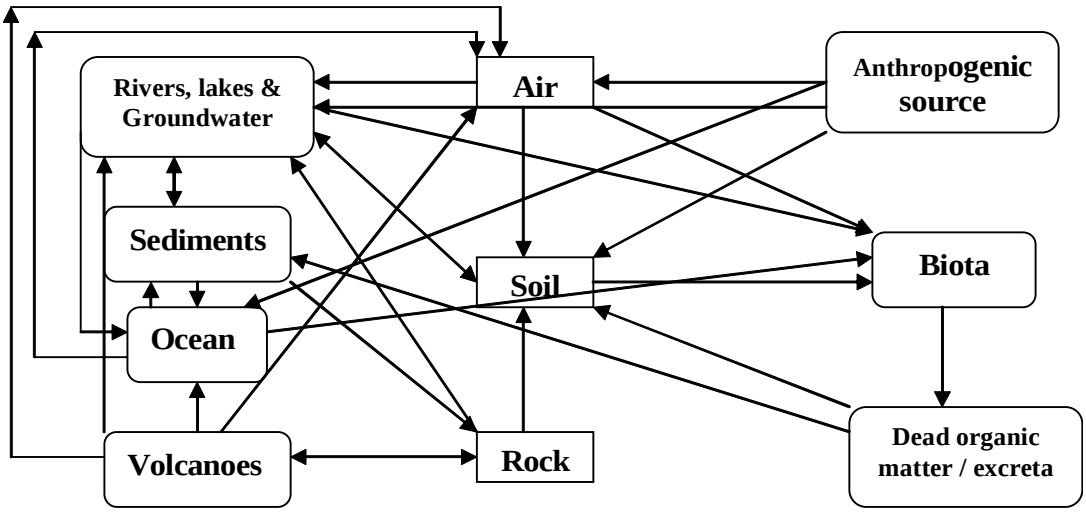

Fig. 2. Accumulation of fluoride in water (Biogeocycle)

minum, plastics, electrical components, and fluorescent light bulbs. Aqueous hydrofluoric acid is used in stainless steel pickling, glass etching, and metal coatings. Volcanoes are the major natural source of hydrogen fluoride. Sodium fluoride has been used as an insecticide, rodenticide, and fungicide.(Figure 1)

1. SOURCES OF FLUORIDE IN ENVIRONMENT:

The Cycle of fluoride through the biogeosphere is summarized in Figure 2

2. SOURCE OF FLUORIDE IN WATER:

Fluorine always occurs in combined form of minerals as fluoride. It is high reactivity and represents about 0.06 to 0.09% of the earth crust (WHO, report 1994). The presence of fluorine in ground water is mainly a natural phenomenon, and mainly influenced by local and regional geological conditions, as the fluoride minerals are nearly insoluble in water. Hence fluorine is present in ground water only when the conditions favor their solution. The main source of fluorine in groundwater is basically from the mafic minerals shown in table 1 and concentration of fluoride in these rocks given in table 2. These minerals are commonly associated with the country rocks through which the ground water percolates under variable temperature conditions.

Besides these minerals, alkali rocks, hydrothermal solutions may also contribute to higher concentration of fluoride in groundwater. Robinson and Edington (1946) reported that the main source of fluorine in ordinary soil consists of clay minerals. The weathering and leaching process, mainly by moving and percolating water, play an important role in the incidence of fluoride in groundwater. The features related to the release of fluoride into water by fluoride bearing minerals may be due to i) The chemical composition of water ii) The presence and accessibility of fluoride minerals to water or iii) The contact time between the source minerals.

Fluoride rich minerals, which are present in rocks and soil, when come in contact with water of high alkalinity they release fluoride into groundwater through hydrolysis replacing hydroxyl (OH) ion. The degree of wreathing and leachable fluoride in a terrain is more important in deciding the fluoride bearing minerals in the bulk rocks or soil. Due to weathering of rocks the Ca-Mg / carbonate concentration which form in arid and semi arid areas appears to be good sink for the fluoride ion (Jack et al., 1980). The factors that control the leachability to fluoride from carbonate concentration from carbonate concentration or from the topsoil horizon may be (1) pH of the draining solution (2) Alkalinity and (3) the dissolved CO_2 in water and in features in the soil. Besides these factors, the topographic features also play an important role in the control of fluoride content as suggested by Rameshan and Rajagopalan (1985). The existence of some of the basis dykes such as doleritic intrusions normally acts as natural barriers against the flow of underground water making the groundwater stagnated in fractures and pores. If the groundwater is more alkaline and stagnant for longer time, all the fluoride minerals in basic dyke rocks, and the overlying soil that are rich in mafic minerals undergoes greater ionization facilitating the ground water to get enriched with fluoride. The degree of ionization increases with

Table 1: Source of fluoride in ground water

Minerals	Chemical Composition	Rocks of these minerals
1. Fluorite (Fluorspar)	CaF_2	Pegmatite Pneumatolitic deposits as vein deposit
2. Fluorapatite (Apatite)	$Ca_5(F,Cl)PO_4$	Pegmatite & metamorphosed limestone.
3. Micas		
a. Biotite	$K(MgFe^{+2})_3(AlSi_3)O_{10}(OHF)_2$	Basalts
b. Muscovite	$KAl_2(AlSi_3O_{10})(OHF)_2$	Permatites, Amphiboites,
4. Amphiboles		
a. Hornblende	$NaCa_2(MgFe^{+2})_4(AlFe^{+3})(SiAl)_8O_{22}(OHF)_2$	Gneisses, schists, shales,
b.Tremolite Actinolite	$Ca_2(MgFe^{+2})_5(Si_8O_{22})\ (OHF)_2$	Clay, Alkaline rocks etc.
5. Topaz	$Al_2SiO_4(OH.F)_2$	Acid Igneous rocks, Schists, gneisses etc.
6. .Rock Phosphate	$NaCa_2(MgFe^{+2})_4(AlFe^{+3})(SiAl)_8O_{22}(OHF)_2$	Limestone, Fossils etc.

Table 2: The value of fluoride in various rock types.

Rocks	Fluoride range (in ppm)	Average (in ppm)
Basalt	20-1060	360
Granites & Gneisses	20-2700	870
Shales & Clay	10-7600	800
Lime stones	0-1200	220
Sandstones	10-880	180
Phosphorite	24000-41500	31000
Coals(ash)	40-480	80

Fig. 3: Categorization of fluoride affected districts of Rajasthan Category A: 50% and above villages have excess of fluoride (very serious). Category B: 25-50 % villages having excess fluoride (serious). Category C: 10-25 % villages having excess fluoride (less serious). Category D: Below 10% villages having excess fluoride (insignificant).

Table 3: Fluoride concentration and affected population of villages in Rajasthan

S. No.	Fluoride concentration mg/l	Number of affected Village	Total population under threat
1.	1.2 to 2.9	1467	1643542
2.	3.0 to 4.9	668	719309
3.	5.0 to 9.9	255	238447
4.	Above 10	43	35477
	Total	2433	

depth resulting an increase in total dissolved salts and alkalinity. The rocks are the natural aggregation of minerals and contain fluoride in abundant quantity. Soil is also rich in fluoride bearing minerals (Keller, 1976). Rameshan and Rajagopalan (1985) summarized the ingestion of fluoride concentration in the arid and semi arid drought prone areas of Karnataka.

3. FLUORIDE DISTRIBUTION IN RAJASTHAN:

Rajasthan is the largest state, which covers 10% of the country area but receives only 1/100 of the total rains. It shares only 1/10 of the average share of water than rest of the country. The geographical and geological setup leads to deterioration of water quality. Therefore, state faces acute water crisis. The great Indian Thar Desert covers most of the area affected by fluoride. Thus extremely arid and dry climate conditions prevail, receiving 5 mm to 20 mm annual rainfall. Groundwater is deeper and contains high mineral concentrated chemicals which makes the water unfit to drink. The eastern part of the state is semi desert and hilly, therefore the water availability in this region is also limited (Fig.3).

Due to arid and semi arid climate and insufficient surface water resources, Rajasthan is indebt heavily on ground water for drinking and for agriculture purpose. Unfortunately, the groundwater quality in a large number of districts is not according prescribed standards. Rajasthan is the only state where almost all the districts are affected by high fluoride (beyond the permissible limit). In 23 districts the fluorosis problem can be visualized at various intensity level i.e. Dental fluorosis, skeletal fluorosis, nonskeletal manifestation etc. The studies made by Rajasthan Voluntary Health Association in 1994 has showed that the total number of villages having fluoride problem in Rajasthan is 2433 covering nearly 2.6 million population. Moreover, nearly 30,000 people are drinking water with concentration of 10.0 mg/l of fluoride. Data on number of population in affected villages and fluoride concentration is shown in Table 3.

In order to actuate the proper coverage of water supply schemes in rural area and to identify the quality of water a survey was conducted in the year 1973-74. Public Health Engineering Department conducted the district wise surrey under a program Rajeev

Table 4. Detail of Fluoride Affected Villages in Rajasthan

S.No.	Name of District	Total Number of			No. of Villages/ Habitation Where F> 1.5			No. of Villages/ Habitation Where F> 3.0		
		Villages	Habitation	Total	Villages	Habitation	Total	Villages	Habitation	Total
1	Ajmer	985	952	1931	654	371	1025	352	232	584
2	Alwar	1946	2449	4395	537	342	879	155	68	223
3	Banswara	1431	3175	4606	293	551	844	35	60	95
4	Bharatpur	1345	549	1894	529	81	610	152	11	163
5	Barmer	1623	2780	4403	597	221	818	181	68	249
6	Bhilwara	1566	963	2534	678	318	996	392	227	619
7	Bikaner	580	366	946	84	2	86	7	0	7
8	Bundi	826	332	1158	42	9	51	3	0	3
9	Chittorgarh	2173	904	3077	115	48	163	14	9	23
10	Churu	926	199	1125	240	8	248	27	1	28
11	Dholpur	551	983	1534	142	157	299	22	18	40
12	Dungarpur	846	681	1527	127	225	362	30	55	85
13	S. Ganga nagar /Hanumangarh	4437	4190	8627	425	418	844	149	129	273
14	Jaipur/ Dausa	3140	7518	10758	1187	1795	3172	491	739	1230
15	Jaisalmer	518	1172	1690	300	184	484	96	65	161
16	Jalore	666	823	1489	369	107	476	115	45	160
17	Jhalawar	1448	124	1572	42	5	47	15	3	18
18	Jhunjhuinu	824	208	1032	96	3	99	15	1	16
19	Jodhpur	860	2801	3661	314	99	413	59	8	67
20	Kota / Baran	1881	288	2169	44	0	44	17	0	22
21	Nagaure	1374	1972	3346	778	147	925	322	42	364
22	Pali	904	651	1555	242	83	330	69	34	103
23	Swaimadhopur/ Karoli	1464	2191	3655	452	263	725	121	69	190
24	Sikar	931	2401	3332	331	471	792	125	144	269
25	Sirohi	446	92	544	176	5	181	43	1	44
26	Tonk	1019	881	1900	516	209	724	199	71	270
27	Udaipur/Raj Samand	3179	5561	8740	431	497	923	74	81	155
	Total	37889	45311	8200	9741	6619	16560	3280	2181	5461

Source: Public Health Engineering Department Rajasthan, (1991) and Hussain et al. (2002)

Gandhi National Drinking Water Mission. The permissible limit is 1.5 mg/l according to the CPHED, Government of India and the World Health Organization. The district wise number of villages and other habitations having excessive concentration of fluoride (> 1.5 & 3.0 mg/l) is shown in table 4. Total 9741 villages and 6819 other habitations are having fluoride level over 1.5 mg/l in groundwater. Similarly 3280 villages and 2181 habitations are having fluoride concentration more than 3.0 mg/l. A district wise categorization is shown in the following Map -1. The survey indicates that the degree of fluoride problem is very serious in 7 districts (Ajmer, Bhilwara, Nagaure, Dausa, Jaipur, Tonk, Jalore) and a serious in 10 districts (Alwar, Barmer, Bharatpur, Dungarpur, Jaisalmer, Sikar, Pali, Swaimadhopur, Karoli, Sirohi), less serious in 9 districts (Banswara, Jhunjhuinu, Udaipur, Churu, Dholpur, Ganga nagar, Raj Samand, Jodhpur, Hanumangarh) and insignificant in 6 districts (Baran, Bundi, Bikaner, Chittorgarh, Jhalawar and Kota,). Fluoride level in ground water is spread in all the 32 districts and become a health hazard in 25 districts.

4. EFFECT OF FLUROIDE ON HUMAN HEALTH:

Fluoride contamination is a major health hazard in many parts of the world. Fluoride is considered beneficial to human health if taken in limited quantity (0.5 to 1.5 mg/l). Fluoride prevents tooth decay by enhancing the remineralization of enamel that is under attack, as well as inhibiting the production of acid by decay causing bacteria in dental plaque. Fluoride is also a normal constituent of the enamel itself, incor-

Table 5. Concentration of fluoride and Biological effects

S. No	Fluoride in drinking water mg/l	Effect
1.	0.002 mg/l in air	Injury to vegetation
2.	1 mg/l in water	Dental caries reduction
3.	2 mg/l or more in water	Mottled enamel
4.	3.1 to 6.0 mg/l in water	Osteoporosis
5.	8 mg/l in water	10%osteoporosis
6.	20 – 80 mg/day or more in water or air	Crippling skeletal fluorosis
7.	50 mg/l in food or water	Thyroid change
8.	100 mg/l in food or water	Growth retardation
9	More than 125 mg/l in food or water	Kidney change
10	2.5 – 5.0 gm in actual dose	Death

porated into the crystalline structure of the developing tooth and enhancing its resistance to acid dissolution. But it is also known to cause dental, skeletal fluorosis, osteosclerosis, thyroid, kidney changes and cardiovascular, gastrointestinal, endocrine, neurological, reproductive, developmental, molecular level, immunity effects. If concentration is higher than 1.5 mg/l in drinking water (WHO, 1996). Smith and Hodge, (1959) have shown the correlation between fluoride and biological effect (Table 5).

Effect on dental enamel: Dental fluorosis is a condition that results from the intake of excess levels of fluoride during the period of tooth development, usually from birth to approximately 6–8 years of age. It has been termed a hypoplasia or hypomineralization of dental enamel and dentine and is associated with the excessive incorporation of fluoride into these structures. The severity of this condition, generally characterized as ranging from very mild to severe, is related to the extent of fluoride exposure during the period of tooth development. Mild dental fluorosis is usually typified by the appearance of small white areas in the enamel; individuals with severe dental fluorosis have teeth that are stained and pitted ("mottled") in appearance. In human fluorotic teeth, the most prominent feature is a hypomineralization of the enamel. In contrast to many animal species, fluoride-induced enamel hypoplasia (indicating a severe fluoride disturbance of enamel matrix production) seems to be rare in affected human enamel. The staining and pitting of fluorosed dental enamel are both post eruptive phenomena (i.e., acquired after tooth eruption and occur as a consequence of the enamel hypomineralization). The incorporation of excessive amounts of fluoride into enamel is believed to interfere with its normal maturation, as a result of alterations in the rheologic structure of the enamel matrix and/or effects on cellular metabolic processes associated with normal enamel development (WHO, 1984; Aoba, 1997; Whitford, 1997). Experimental animal studies suggest that this hypomineralization results from fluoride disturbance of the process of enamel maturation (Richards et al., 1986).

In India, Viswanathan (1951) first reported a disease similar to mottled enamel, which is prevalent in human beings in Madras presidency. Mahajan (1934) reported a similar disease in cattle in certain parts of old Hyderabad state. However, Shortt et al. (1937) was the first to identify the disease as fluorosis. Subsequent to these findings, cases of fluorosis were reported from several other parts of the country. Dental fluorosis is caused in human being consuming water containing 1.5 mg/l or more of fluorides, particularly from birth to the age of eight. Mottled enamel usually takes the shape of modification to produce yellow brown stains or an unnatural opaque chalky white appearance with occasional striations patting. The incidence and severity of mottling was found to increase with increasing concentration of fluoride in drinking water. In extensive studies, Dean and coworkers (Dean, 1942; Dean and Elvove, 1937) have correlated the appearance and severity of dental fluorosis to different fluoride levels in the drinking water with the aid of a special classification and weighing of severity of the lesion (Table 6).

Distribution of dental fluorosis at different levels of fluoride in drinking water may be assessed by a mottled enamel index of the community, which is defined in terms of the degree of severity of mottled enamel observed clinically. Since no such data available in India to evaluate community index of fluorosis and in the absence of this permissive or excessive limits of fluoride in drinking water are only arbitrary.

Osteoporosis: Fluoride above 4 mg/l in drinking water may cause a condition of dense and brittle bones known as osteoporosis. It affects tens of million of

Table 6. Dental fluorosis categorization (Dean, 1942)

Normal	The enamel presents translucent, semi-vitriform type of structure. The surface is smooth, glossy and usually pale creamy white colour.
Questionable	Seen in area of relatively high endemicity, occasional cases are borderline and one would hesitate to classify them as apparently normal or very mild.
Very Mild	Small, opaque paper-white area seen, scattering irregularly over the labial and buccal tooth surfaces.
Mild	The white opaque areas involve at least half of the tooth surface and faint brown stains are sometimes apparent
Moderately	Generally all tooth surfaces are involved and minute pitting is often present on the labial and buccal surfaces. Brown stain is frequently a disfiguring complication.
Moderately Severe	Pitting is marked, more frequent and generally observed on all tooth surfaces. Brown stains if present are generally of greater intensity.
Severe	The severe hypeoplasic affect the form of the teeth and stains are wide spread, and vary in intensity from deep brown to black.

people worldwide and is responsible for as many as 75% of all fractures in people over the age of 45. Costly and disabling fractures of spine, hip, wrist and other bones can be preceded by years of undetected bone loss. It is found that as many as 20% of those who suffer from osteoporosis related hip fractures die within 6 months. Women are at four times greater risk of developing osteoporosis than males (Bezerra et al., 2003).

Skeleton fluorosis: The chronic toxic effects of fluoride on the skeletal system have been described from certain geographical regions of the world where drinking water contains excessive quantities of natural fluoride. This form of chronic intoxication was first described in India from the state of Madras as early as 1937 (Shortt et al., 1937). Subsequently cases of endemic fluorosis have been reported from other parts of India, particularly from Punjab (Singh et al., 1962a,b, 1963) and sporadically from other parts of the world, notably Ceylon (Clark, 1942), China (Lyth, 1946), Japan (Hamamoto et al., 1954), Saudi Arabia (El, Tannir, 1959), USA, (Leone et al., 1954; Zipkin et al., 1958) Canada (Kilborn et al., 1950) and Europe (Odenthal and Wieneke, 1959). Besides endemic fluorosis, chronic toxic effects of fluoride on the skeletal system have also been observed in relation to industrial exposure to fluorides such as cryolite and in fact it is the pioneer studies of Roholm (1937) that have paved the way for further contributions on the subject.

At higher levels of ingestion from 2 to 8 mg daily when signs of fluorosis appear in teeth mineralized during the ingestion period, certain other factors (climatic conditions, malnutrition, age, storage, other constituents of water and possibly individual variations in absorption) may be involved. Under such conditions and over a number of years, skeletal fluorosis may arise characterized by an increased density of bone and demonstrated in adults radiographically (Yildiz et al., 2003). The data put forward by McClure et al. (1945), although no longer regarded as accurate indicate that the limit of total fluoride which may be ingested daily without hazardous body storage is of the order of 4-5mg daily.

Fluoride replaces hydroxides and deposited in bones causing chronic effect known as skeleton fluorosis. The dental and skeletal changes in endemic fluorosis provide important clinical diagnostic criteria. Whereas dental fluorosis is easily recognized but the skeletal involvement is not clinically obvious until the advanced stage of crippling fluorosis. However, radiological changes are discernible in the skeleton at a much earlier stage and provide the only means of diagnosing the early and relatively asymptomatic stages of fluorosis (Connett, 2002; Lavy, 2003).

Such early cases are usually in young adults whose only complaints are vague pains noted most frequently in the small joints of the hands and feet, in the knee joints and in the joint of spine. These cases are frequent in the endemic areas and may be misdiagnosed as rheumatoid or osteoarthritis. In later stages, there is an obvious stiffness of the spine with limitation of movements and still later, the development of kyphosis. There is difficulty in walking due partly to stiffness and limitation of the movements of various joints and partly to the neurological lesions of advanced cases. Similarly, some of the patients complain of dyspnoea on exertion because of the rigidity of the thoracic cage. In Roholm's series of industrial fluorosis cases, the gastrointestinal symptoms of lack of appetite, nausea and constipation were as frequent as the symptoms of stiffness of joints, but the former have not been described in the different studies of endemic fluorosis.

According to an early estimate, the number of persons at risk of developing skeletal fluorosis was 5 million in Punjab and more in Andhra Pradesh and Madras, India (Siddiqui, 1970). The frequency of skeletal fluorosis (as identified by the clinical picture) among children 3–10 years of age was 39% (18/46) in a village in India, where the fluoride concentrations in the three wells were 0.6, 4.0 and 1.34 mg/l (Shivashankara et al., 2000). It was not possible to discern, from the information available, the contribution of each well to the drinking water of the residents.

In a clinical survey for fluorosis in a random sample of residents in five areas in Tamil Nadu, South India, the drinking-water fluoride concentration was directly related to the prevalence of dental fluorosis in children (8–15 years of age) and adults. Among children, no skeletal fluorosis (no information on diagnostic criteria provided) was observed; among adults, the prevalence of fluorosis was 34% (157 individuals surveyed) in the area with the highest drinking-water fluoride concentration (summer month average 6.8 mg/l, non-summer month average 5.6 mg/l) (estimated total daily fluoride intake 20 mg), while no skeletal fluorosis was observed in the other areas, where the mean fluoride concentrations were 2.2 (summer

months) and 1.8 (non-summer months) mg/l or lower, with estimated total daily fluoride intakes less than 10 mg (Karthikeyan et al., 1996).

A correlation between average water fluoride concentration and prevalence of skeletal fluorosis (assessed by X-ray) was found among adults in 15 villages in Dungapur district in Rajasthan, India (Choubisa et al., 1997). The prevalence ranged from 4.4% at a water fluoride level of 1.4 mg/l to 63.0% at the level of 6.0 mg/l. Crippling fluorosis was consistently observed in villages with fluoride concentrations of >3 mg/l. In a survey carried out by Hussain et al. (2004) in Bhilwara district of Rajasthan, 825 individual were examined for fluorosis due to intake of fluoride above 5.0 mg/l in drinking water. In the skeletal fluorosis positive individuals maximum individual (194 no's, 23.52%) have Grade I skeletal fluorosis, which is characterized by bone and joint pain. Only 4 individual (0.48%) have Grade III type of skeletal fluorosis in which bone and joint pain, stiffness and rigidity of dorso-lumber spine and restricted movements at spine and joints are general symptom inclusive deformities of spine and limbs, knock knees, crippled or bed ridden state, kyphosis, invalidism, genu-varum and genu-valgum. Prevalence and severity of skeletal fluorosis were found also increasing with increasing fluoride concentration.

Deformities and crippling fluorosis: The advanced stage of fluoride intoxication results from the continuous exposure of an individual to 20-80 mg of fluoride ion daily over a period of 10 - 20 years. Such heavy exposure is associated with a level of at least 10 mg/l in the drinking water supply. The crippling fluorosis is seen in such numbers in endemic areas of Rajasthan, Punjab and Southern India. The Crippling deformities are due partly to mechanical factors and partly to the immobilization necessitated by pain and paraplegia. The commonest deformities are kyphosis, flexion deformity of the hips, flexion deformity of the knees and fixation of the chest in the position of inspiration due to calcification of cartilages. The quadriplegic patient bent with kyphosis and with restricted movements of his spine, with contractures of hips and knees (Kaminsky et al., 1990)

Cardiovascular effects: The cardiovascular effects of fluoride have been attributed to hypocalcemia and hypercalemia caused by high fluoride levels. Fluoride can bind with serum calcium if the dose is sufficient and cause hypocalcemia. Calcium is necessary for the functional integrity of the voluntary and autonomic nervous systems. Hypocalcemia can cause tetany, decreased myocardial contractility, and possibly cardiovascular collapse (Bayless and Tinanoff, 1985). Hyperkalemia has been suggested as the cause of the repeated episodes of ventricular fibrillation and eventual death that are often encountered in cases of fluoride poisoning (Baltazar et al., 1980).

Gastrointestinal effects: The primary gastrointestinal effects following both acute and chronic oral exposure to fluoride consist of nausea, vomiting, and gastric pain. The irritation of the gastric mucosa is attributed to fluoride (as sodium fluoride) forming hydrofluoric acid in the acidic environment of the stomach (Hoffman et al., 1980; Waldbott, 1981). The uncharged hydrogen fluoride molecule can then penetrate cell membranes and enter the neutral environment of the cytoplasm.

A study by Susheela et al. (1993) assessed the prevalence and severity of gastrointestinal disturbance in an area of endemic skeletal and dental fluorosis in India. The highest prevalence (52.4%) of non-ulcer dyspeptic symptoms was found among 288 individuals (69 families) living in a village where the mean fluoride concentration in the 36 separate water sources was 3.2 ppm (range 0.25 to 8.0 ppm). Eleven of these water sources were defined by the authors as safe (i.e., with fluoride levels of 1.0 ppm or less). The authors noted that in patients who reverted to safe water, dyspeptic symptoms and complaints disappeared within 2-3 weeks.

Endocrine effects: In the endocrine system where the intermediary metabolism and synthesis of highly sensitive hormones involves enzymatic action, it is expected that interferences with the mechanism by chemical agents would produce early and pronounced clinical effects. Considerable attention has consequently been given of recent years to the behavior of fluoride in hormone chemistry and to the possible and to the possible clinical disturbances of endocrine function, particularly the thyroid gland Robinson et al., 2002). Significant increases in serum thyroxin levels were observed in residents of North Gujarat, India with high levels of fluoride in the drinking water (range of 1.0–6.53 mg/L; mean of 2.70 mg/L) (Michael et al., 1996). No significant changes in serum triiodothyronine or thyroid stimulating hormone levels were found. Increases in serum epinephrine and norepinephrine levels were also observed. It is unclear if nutritional deficiencies played a contributing role to the observed endocrine effects.

Immunological and lymphoreticular effects: A request to the American Academy of Allergy was made by the U.S. Public Health Service for an evaluation of suspected allergic reactions to fluoride as used in the fluoridation of community water supplies (Austen et al., 1971). The response to this request included a review of clinical reports and an opinion as to whether these reports constituted valid evidence of a hypersensitivity reaction to fluoride exposure of types I, II, III, or IV (Austen et al., 1971), which are, respectively, anaphylactic or reaginic, cytotoxic, toxic complex, and delayed-type reactivity. The Academy reviewed the wide variety of symptoms presented (vomiting, abdominal pain, headaches, scotomata [blind, or partially blind areas in the visual field], personality change, muscular weakness, painful numbness in extremities, joint pain, migraine headaches, dryness in the mouth, oral ulcers, convulsions, mental deterioration, colitis, pelvic hemorrhages, urticaria, nasal congestion, skin rashes, epigastric distress, and hematemesis) and concluded that none of these symptoms were likely to be immunologically mediated reactions of types I–IV. No studies were located that investigated alterations in immune response following fluoride exposure in humans. No studies were located that investigated alterations in immune response following fluoride exposure in human. In a study with rabbits administered 4.5 mg fluoride/kg/day as sodium fluoride for 18 months, decreased antibody titers were observed (Jain and Susheela, 1987). These results were observed after 6 months of treatment; the authors hypothesized that a threshold level is reached at which time the immune system is impaired. However, as only one dose level (4.5 mg fluoride/kg/day) was tested, no dose-effect.

Neurological effects: The neurological manifestations have been exclusively reported from India. Credit for the earliest description of neurological complications in fluorosis must be given to Shortt et al. (1937), who reported ten such cases from the Nellore district of Madras. A few sporadic cases have also been described from other parts of India (Chuttani et al., 1962; Janardhanan and Venkaswamy, 1957; Murthi et al., 1953). Fluoride has been shown to interfere with glycolysis. Because the central nervous system relies heavily on this energy source, hypotheses have been advanced as to a mechanism for fluoride effects on the central nervous system. Although effects on glycolytic enzymes could explain the neuromuscular symptoms seen frequently in cases of fluoride poisoning (e.g., tetany, paresthesia, paresis, convulsions), studies tend to indicate that hypocalcemia caused by fluoride binding of calcium causes these symptoms (Eichler et al., 1982). The decreases in intelligence were reported in children living in areas of China with high levels of fluoride in the drinking water, as compared to matched groups of children living in areas with low levels of fluoride in the drinking water (Li et al., 1995; Lu et al., 2000), but these studies are weak inasmuch as they do not address important confounding factors.

Reproductive effects: There are limited data on the potential of fluoride to induce reproductive effects in humans following oral exposure. A meta-analysis found a statistically significant association between decreasing total fertility rate and increasing fluoride levels in municipal drinking water (Freni, 1994). Annual county birth data (obtained from the National Center for Health Statistics) for over 525,000 women aged 10–49 years living in areas with high fluoride levels in community drinking water were compared to a control population approximately 985,000 women) living in adjacent counties with low fluoride drinking water levels. The fluoride-exposed population lived in counties reporting a fluoride level of 3 ppm or higher in at least one system. The weighted mean fluoride concentration (county mean fluoride level weighted by the 1980 size of the population served by the water system) was 1.51 ppm (approximately 0.04 mg fluoride/kg/day), and 10.40% of the population was served by water systems with at least 3 ppm fluoride. The mean weighted mean fluoride concentration in the control population was 1.08 ppm (approximately 0.03 mg fluoride/kg/day). However, this meta-analysis relied on a comparison of two quite disparate data sets, inasmuch as the fluoridation population often did not correlate well with the population for whom health statistics was available. Furthermore, other studies have not found a similar correlation. Another study found significantly decreased serum testosterone levels in 30 men diagnosed with skeletal fluorosis and in 16 men related to men with fluorosis and living in the same house as the patient (Susheela and Jethanandani, 1996). The mean drinking water fluoride levels were 3.9 ppm (approximately 0.11 mg fluoride/kg/day), 4.5 ppm (0.13 mg fluoride/kg/day), and 0.5 ppm (0.014 mg fluoride/kg/day) in the patients with skeletal fluorosis, related men, and a control group of 26 men living in areas with low endemic fluoride levels. No correlations between serum testosterone and urinary fluoride levels or serum testosterone and serum fluoride levels were found. One limitation of this study is that

the control men were younger (28.7 years) than the men with skeletal fluorosis (39.6 years) and the related men (38.7 years). In addition, the groups are small and potentially confounding factors are not well addressed (Mychreest et al., 2002).

Developmental effects: Fluoride crosses the placenta in limited amounts and is found in fetal and placental tissue (Gedalia et al., 1961; Theuer et al., 1971). The available human data suggest that fluoride has the potential to be developmentally toxic at doses associated with moderate to severe fluorosis. The human and animal data suggest that the developing fetus is not a sensitive target of fluoride toxicity. Analysis of birth certificates and hospital records for over 200,000 babies born in an area with fluoridated water and over 1,000,000 babies born in a low fluoride area found no difference in the incidence of birth defects attributable to fluoride (Erickson et al., 1976). Exposure to high levels of fluoride has been described together with an increased incidence of spina bifida (Gupta et al., 1995). The occurrence of spina bifida was examined in a group of 50 children aged 5–12 years living in an area of India with high levels of fluoride in the drinking water (4.5–8.5 ppm) and manifesting either clinical (bone and joint pain, stiffness, and rigidity), dental, or skeletal fluorosis. An age- and weight-matched group of children living in areas with lower fluoride levels (#1.5 ppm) served as a control group. Spina bifida was found in 22 (44%) of the children in the high fluoride area and in six (12%) children in the control group. This study did not examine the possible role of potentially important nutrients such as folic acid, however, and had other study design flaws.

Effect at molecular level: The acceleration of the aging process by fluoride occurs at the bio-chemical level through enzyme inhabitation, collagen break down, genetic damage or disruption of the immune system. Fluoride damage enzymes, and results in a wide range of chronic disease. Fluoride as low as 1 mg/l causes breakdown of collagen, the most abundant of the body protein at 30%. It leads to irregular formation of collagen, which serves as a major structural component of skin, ligaments, tendons, muscles, cartilage, bone and teeth. A number of studies revealed that fluoride causes genetic damage. The mechanism cannot be exactly pinpointed because fluoride interferes with a number of physiological processes. Most evidence indicates that it acts on the DNA Repair Enzyme system. It may also interfere with DNA synthesis. If the unprepared DNA damages occur in a cell, producing a sperm or egg it will be replicated in every cell of the offspring body and leads to birth defects. Irreparable damage of a segment of DNA is responsible for control of cell growth and may cause tumors or cancer.

Effect on immune system: Fluoride interacts with the bonds of protein molecular required to maintain the normal shape of proteins. The fluoride effect the immune system by i) Damage the immune system by inhibiting the migration rate of white blood cells to infected means, ii) Interferes with phagcytosis (destruction of bacteria and other foreign agents by white blood cells or iii) Induces the release of super oxide free radicals in resting white blood cell. The fluoride-induced interference leads to an increased and more prolonged exposure of the body to foreign materials and releases free radicals damaging the body.

Fluoride as carcinogen: Fluoride was found to be an equivocal carcinogen by the National Cancer Institute. Toxicological effects due to excess of fluoride is 6.9 fold and cause bone cancer in young males. Several epidemiological studies are available on the possible association between fluoride in drinking water and cancer rates among the population IACR evaluated these studies on fluoride and carcinogenticity in humans. (IARC, 1987; Maurer et al., 1990). Numerous epidemiological studies have examined the issue of a connection between fluoridated water and cancer. The weight of evidence indicates that no such connection exists. However, all of the investigations were ecologic studies, and the sensitivity limit of even the most sensitive analysis in these studies appears to be a 10–20% increase. Since any carcinogenic effect of fluoride at the levels found in water supplies would probably be below this level of sensitivity, a National Toxicology Program (NTP) cancer bioassay was conducted to assess the effect of fluoride on cancer incidence in animals (Bucher et al. 1991; NTP report, 1990). The NTP study found equivocal evidence of a fluoride-related increase in osteo-sarcomas in male rats, and no evidence of any fluoride-related neoplasm in female rats or male or female mice. A study sponsored by Proctor and Gamble (Maurer et al., 1990) found no evidence of fluoride carcinogenicity in either male or female rats. Both studies contain limitations that preclude strong conclusions. The NTP is presently carrying out additional experiments on the relationship, if any, between fluoride and cancer. The International Agency for Research on Cancer (IARC) reviewed the literature on fluoride carcinogenicity in 1982. It concluded that

Table 7. Defluoridation Techniques

Technique	Description	Limitations
Using bone Char	Water is filtered through crushed bone char in column. Fluoride is taken up by the bone char.	Material is costly & continued availability is not guaranteed, not accepted by Hindu population
Contact	Precipitation of fluoride with Ca & PO_4^{-2} in contact with an appropriate surface.	
Nalgonda techniques	Aluminum sulphate and lime are mixed slowly then left for setting. Fluoride is removed with precipitates	Fluoride removed as CaF_2, but the solubility of CaF_2, is such that fluoride below 8 mg/l remains in drinking water.
Yttrium Loaded Poly (hydroxamic acid) resin	Yttrium loaded Poly (Hydroxamic acid) ion exchange resin absorbs fluoride ion in the pH range of 2.8 to 4.2	It absorbs only in the pH range of 2.8 to 4.2, but the drinking water range is generally 6.5 to 7.5
Reverse osmosis	Membrane filtration based technology, which removes all dissolved solids including fluoride.	Costly and requires electricity which is not available all the time in rural areas
Marble Slurry	Marble slurry is mixed slowly then left for settling. Fluoride is removed with precipitates	-
Activated Alumina	Fluoride can be removed by adsorption on alumina. This method is widely used.	Alumina should be pretreated

there is no evidence from epidemiological studies of an association between fluoride ingestion and human cancer mortality, and the available data are inadequate for an evaluation of the carcinogenicity of sodium fluoride in experimental animals (IARC, 1982). Several major cancer bioassays of fluoride have been conducted since the IARC review.

5. DEFLUORIDATION METHODS:

Wide range of treatment systems have been reported for controlling excess fluoride in water. Some are very expensive, where as some are ineffective with certain type of water quality and only laboratory studies are available for some systems. Defluoridation methods can be broadly divided into three categories i) precipitation, ii) adsorption / ion exchange or iii) electrochemical methods and membrane technique. Several reviews are available on the various defluoridation methods (Balusu, 1979; Killedar and Bhargava, 1988). Precipitation methods involve the addition of a soluble chemical to the water, which leads to the fluoride precipitation or adsorption of fluoride on formed precipitate. In adsorption methods the raw water is passed through the bed containing defluoridating material. Some of these defluoridation methods along with their merits and demerits are given in Table 7.

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