GENERAL ARTICLE

FLUOROSIS AND ASSOCIATED HEALTH ISSUES

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Abstract: *In this update the types of fluorosis affecting different tissues / organs / systems in the body, their characteristics, how fluorosis can be suspected from the symptoms and how it can be confirmed based on the diagnostic procedures are discussed. After early diagnosis, complete recovery from fluorosis, is achieved by withdrawal of fluoride consumption through diet modification. Diet counselling to promote intake of nutrients, vitamins and antioxidants has been highlighted. Drugs are less effective in the recovery process. This article also deals with associated health problems due to fluoride toxicity such as anemia in pregnancy despite iron and folic acid supplementation and anemia in adolescent girls. This article also details the approaches for addressing fluorosis in children and the commonalities with iodine deficiency disorders (IDD).*

Keywords: *Fluorosis, Diagnosis, Recovery.*

Fluorosis, was detected in 1930's both in cattle and in human beings in Nellore district, then in Madras Presidency and was reported in the Indian Medical Gazette.[1] At that time the disease did not draw the attention of health administrators and policy makers, as during the Second World War and post independent era, the priorities in health sector were different. However, the publications made significant impact on the disease characteristics in the western world. The contributions of Amarjit Singh and Jolly from Punjab were classics in the understanding of the disease.[2,3,4] Until the 1970s, the two major entities of the disease recognized and reported were dental and skeletal fluorosis and for a good number of professionals and scientists, fluorosis meant only dental and skeletal fluorosis. But the nation marched forward to find new scientific dimensions, and thus other health problems that are of immense significance for addressing the disease were identified.

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As research activities gained momentum, it was inconceivable that an environmental toxin, a powerful, corrosive chemical 'fluoride', upon entering the body would selectively attack only the teeth and bones. The concept that fluoride being a negatively charged anion (F^-) would be reacting with positively charged cations such as calcium (Ca^{++}) is acceptable; but positively charged cations are present in abundance in soft tissues as well. The major breakthrough in the understanding of soft tissue involvement in fluorosis led on to a third entity, "non-skeletal fluorosis"[5], which was considered to be the beginning of a new era. "Non-skeletal fluorosis" and its clinical manifestations led to diagnosis of fluorosis at very early onset and complete recovery from fluorosis became a reality. Unfortunately, the early manifestations are still "non-specific".

This article deals not only with classical dental, skeletal and non-skeletal fluorosis but also the recent developments in the understanding of associated health problems due to fluoride toxicity in new born, infants, children and pregnant women as more information in greater detail is available in recent years.[6,7,8]

Fluorosis and its manifestations

Dental fluorosis (DF): This affects children during development of teeth when the mother has consumed or inhaled fluoride through food, drinking water, drugs, dental products and / or industrial emission. DF may start from intra-uterine life when tooth germ erupts. When the disease sets in, it disfigures the matrix molecules of the teeth. The permanent teeth in children would then develop discoloration. The discoloration on the enamel surface is horizontal, away from the gums and bilaterally symmetrical. It is not reversible, but masking the discoloration of teeth during adolescence is done as it causes social and cosmetic problems.

Skeletal fluorosis (SkF): This afflicts the bones and major joints (excluding joints in the hand and feet) of young and old, men and women without discrimination. In advanced stages of skeletal fluorosis, it is not reversible. Severe pain in joints and rigidity or stiffness in joints would incapacitate an individual. Patients of skeletal fluorosis may also get paralysis.

Non-Skeletal Fluorosis (NSkF): This is the earliest manifestation of fluorosis. The clinical manifestations of non-skeletal fluorosis are seldom understood. Fluorosis may not be suspected based on the history and the symptoms. The manifestations that may overlap with other diseases are quite non-specific. Yet another possibility is that the health complaints are considered as non-specific and ignored. The elicitation of proper history and conduct of diagnostic tests for confirmation of the disease are of prime importance.

The questionnaire which can be used for screening fluorosis is given in Box 1.

While dealing with a suspected case of fluorosis the name of the state, district or village where the patient is/ was residing and source of water used for drinking, cooking and duration of stay, provides valuable information.

Whenever fluorosis is suspected it is necessary to confirm the diagnosis.

Diagnostic procedure for fluorosis

The diagnostic procedure for fluorosis needs the following tests done:

(1) Fluoride content of (a) drinking water (b) serum (c) urine.

(2) X-ray of forearm antero - posterior (AP)

(3) Baseline hemoglobin (would be used for impact assessment during the recovery process)

Precautions to be taken while estimating fluoride levels in blood, urine and water source

1. The drinking water, urine and serum samples for fluoride testing is collected in plastic bottles /vials and not in glass bottles. Fluoride would bind to silica in glass, resulting in erroneous results.

2. Spot samples of urine and blood: 30 ml sample volume for water and urine; 1 ml serum.

Box 1. Proforma for screening for fluorosis

A. Non-skeletal manifestations with focus on Gastro-intestinal system (tick ✓)

1. Nausea / Loss of appetite:	☐	4. Constipation:	☐
2. Flatulence	☐	5. Diarrhea (intermittent):	☐
3. Pain in the abdomen:	☐	6. Headache:	☐

B. Other Non-skeletal manifestations.

1. Polyuria	☐	4. Muscle weakness:	☐
2. Polydipsia:	☐	5. Unenthusiastic and prefers to sleep whole day:	☐
3. Fatigue (extreme tiredness):	☐	6. Allergic reaction on the skin (which may appear/ disappear)	☐

C. Skeletal manifestations

1. Pain in major joints ☐
2. Stiffness in the major joints with pain ☐
3. Immovable joints with pain ☐

D. Dental Fluorosis:

1. Discoloration on enamel surface (away from the gums) seen, irrespective of age ☐

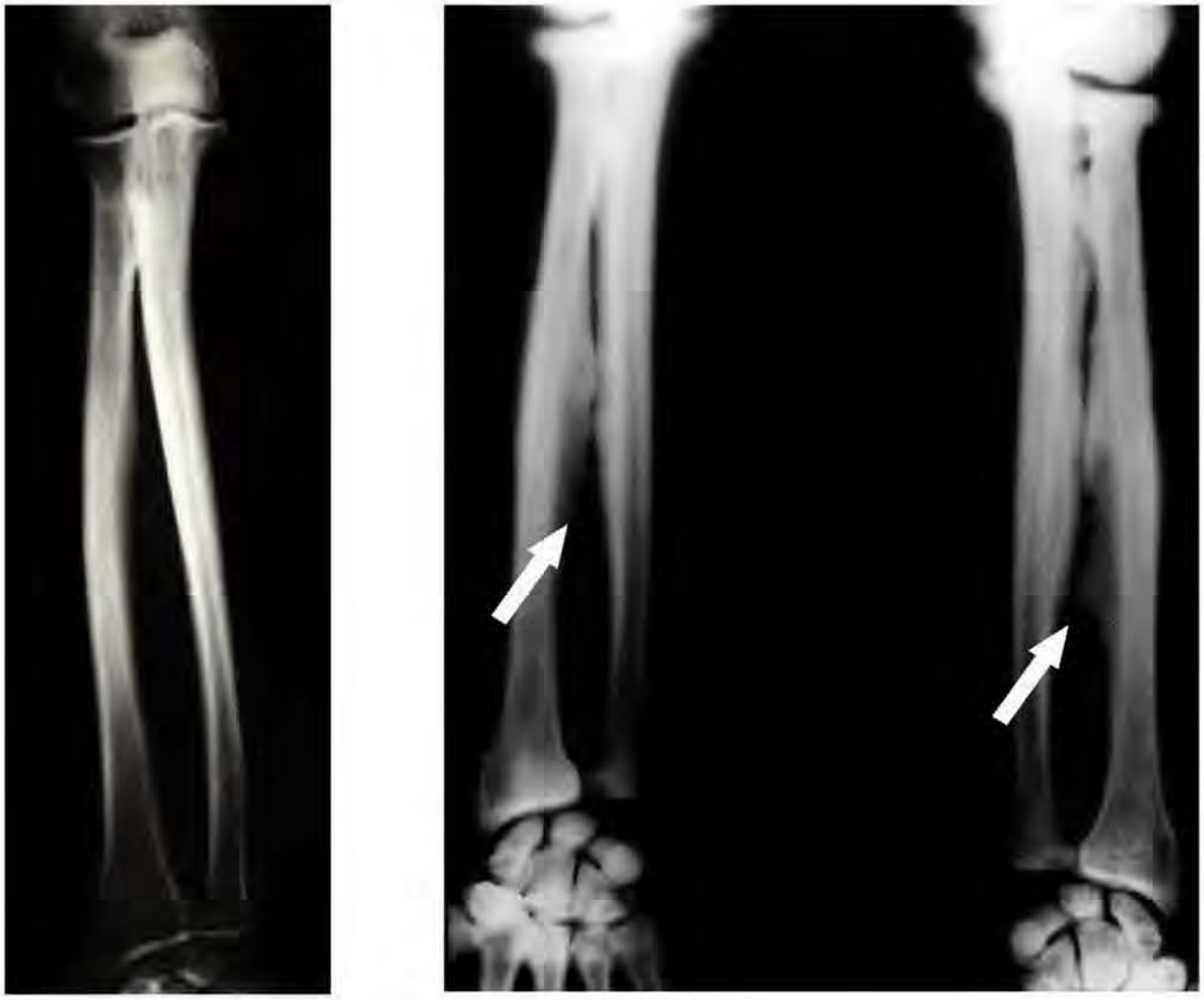
3. For assessing whether interosseous membrane covering the radius and ulna is calcified or not, an X-ray of forearm bones AP is required.

Evaluation of test results

Normal reference range for fluoride in:

- Urine: 0.1 - 1.0 mg/L
- Serum: 0.02 - 0.05 mg/:L
- Drinking water: 1.0 mg/L is the upper limit the body may tolerate; less the better as fluoride is injurious to health (Bureau of Indian Standards, 2012).[9]
- X-ray forearm AP (Fig.1): While looking at the X-ray forearm it is necessary to look for the interosseous membrane calcification. It has to be noted that the calcified interosseous membrane may be mistaken for "inflammatory reaction of the membrane" and may not be attributed any importance while reporting.

The diagnosis is confirmed on the basis of the test reports of high levels of F^- in body fluids and interosseous membrane calcification. It is possible that the drinking water F^- is within safe limits. Then it can be inferred that the source of fluoride may be food, beverages, dental products, industrial emission, chewing habit of foaming substances, viz. churans, supari or tobacco and use of black



Normal fore-arm x-ray **Fluorosed fore-arm x-ray**

(Fluorosed fore-arm x-ray radiographs, revealing calcified interosseous membrane (arrows) sticking out as thorns)

Fig. 1. Radiograph of normal and fluorosed fore-arm x-ray

rock salt as a spice (with 157 ppm F^-).[10] The markets are flooded with ready-to-cook gravy with F^- containing spices, cocktail party snacks, soft drink preparation such as jaljeera which are high in fluoride due to addition of black rock salt (CaF_2). Fluorosis afflicting a number of urban elite has been traced to consumption of high F^- salt through a variety of food items, beverages, black tea, lemon tea etc.

Management of fluorosis

The best option for the patient is to undergo counselling for diet editing for withdrawal of all fluoride sources from use/consumption. Simultaneously the patient should undergo diet counselling for promotion of intake of nutrients (essential nutrients, micronutrients, vitamins and antioxidants) through dairy products, vegetables and fruits. The concept of consumption of fruits and vegetables has considerable variation from family to family and may not be rewarding when left to the decision of the family. Diet editing and diet counselling are integral parts of the recovery process.

The regular hospital dieticians have an extremely important role and should be updated to understand the implications for offering an effective counselling for the patients of fluorosis to recover within a matter of 10 to 15 days. The issue that may confront the treating physician, is that the patient shall not be happy, if he or she does not receive a prescription for medicines. The doctor may at such times prescribe calcium and vitamin C tablets for a few days, until the dietary regime is standardized and the patient is comfortable with adequate intake of nutrients through dietary sources. The patient may be counselled that with dietary option the recovery will be in 10 to 15 days while it may take longer with tablets alone.

The recovery needs to be monitored and patient should be informed to come for review after 4 weeks post-intervention for assessing the impact of the interventions by re-testing i) urine fluoride and ii) hemoglobin along with re-assessing health complaints. Reduction in urine fluoride levels and rise in hemoglobin with disappearance of symptoms of non-skeletal fluorosis to a large extent would be the first impact on the health of the patient after interventions are practised. The need for the patient to be brought for follow up has to be re-emphasized including reassessment after 3 months and / or 6 months. There can be a recurrence of symptoms if there is contamination of drinking and cooking water with high fluoride due to industrial effluents. The ideal management for such patients would be to procure a RO water filter system so that even if industrial effluents are discharged into the ground contaminating the drinking water source, they are not affected by the fluorides.

The research and development activities in the field of fluorosis have enriched the nation with a wealth of additional information and contributed immensely for the welfare of the society. (Fig.2) highlights the four discoveries with focus on fluoride action and the strategy for prevention and control of the public health problems.

The major reasons for the delay in rectifying the important health problems confronting pregnant women and infants include the wide publicity and promotion of fluoride as an essential element for good teeth and prevention of dental caries in children and the gross unawareness among the medical fraternity and health administrators of the necessity to develop infrastructure for testing fluoride in body fluids, to diagnose fluorosis and associated health problems. The role of fluoride from that of an essential trace element to that of a toxic,

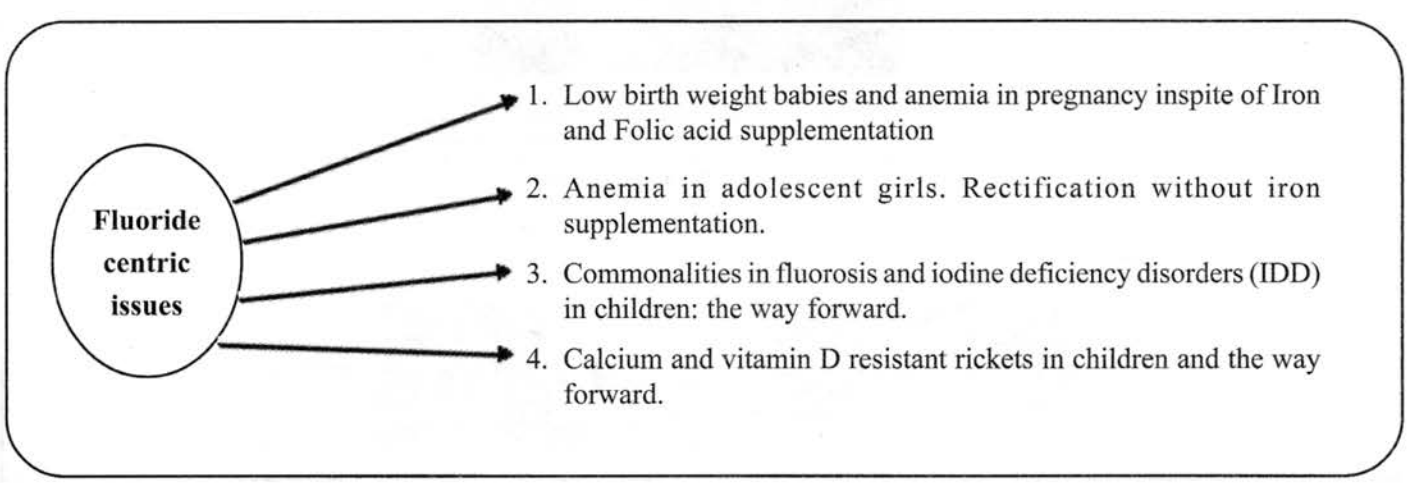


Fig. 2. Discoveries with focus on fluoride action

corrosive, poisonous element will be a major change. In the national norms for "Recommended Dietary Allowances"[11], there is no guideline for fluoride. More and more institutes in the health sector, starting from district hospitals to teaching hospitals are beginning to understand the importance of development of human resource, skills and infrastructure to address fluorosis and associated health problems. The use of fluoridated dental products, in the name of prevention of dental caries, based on the information available is unethical, unscientific and an outdated concept.

Action of fluoride in the biological system

While addressing the associated problems, it may be meaningful to provide the details on how fluoride acts essentially causing anemia in antenatal women resulting in low birth weight babies.

Fluoride consumption through food, water and use of dental products essentially destroys the gastro-intestinal mucosa (Figs.3-5). Mucus production by the goblet cells is considerably reduced and microvilli of the mucosa fall off which are the most damaging effects of fluoride consumption. The function of the microvilli is to absorb nutrients from the diet, including orally administered iron and folic acid provided to pregnant women.[12] If there is scanty mucus production, the individual would be constipated. The wide publicity that is 'on' in the country for correction of anemia, designates the condition as undernutrition and/or malnutrition. It may be more appropriate now to add the terminology "non-absorption of nutrients" for the reasons cited above.

Secondly fluoride ingestion destroys the probiotics, (the good bacteria) in the intestine which produce vitamin B12, an essential ingredient for hemoglobin biosynthesis.[13,14]

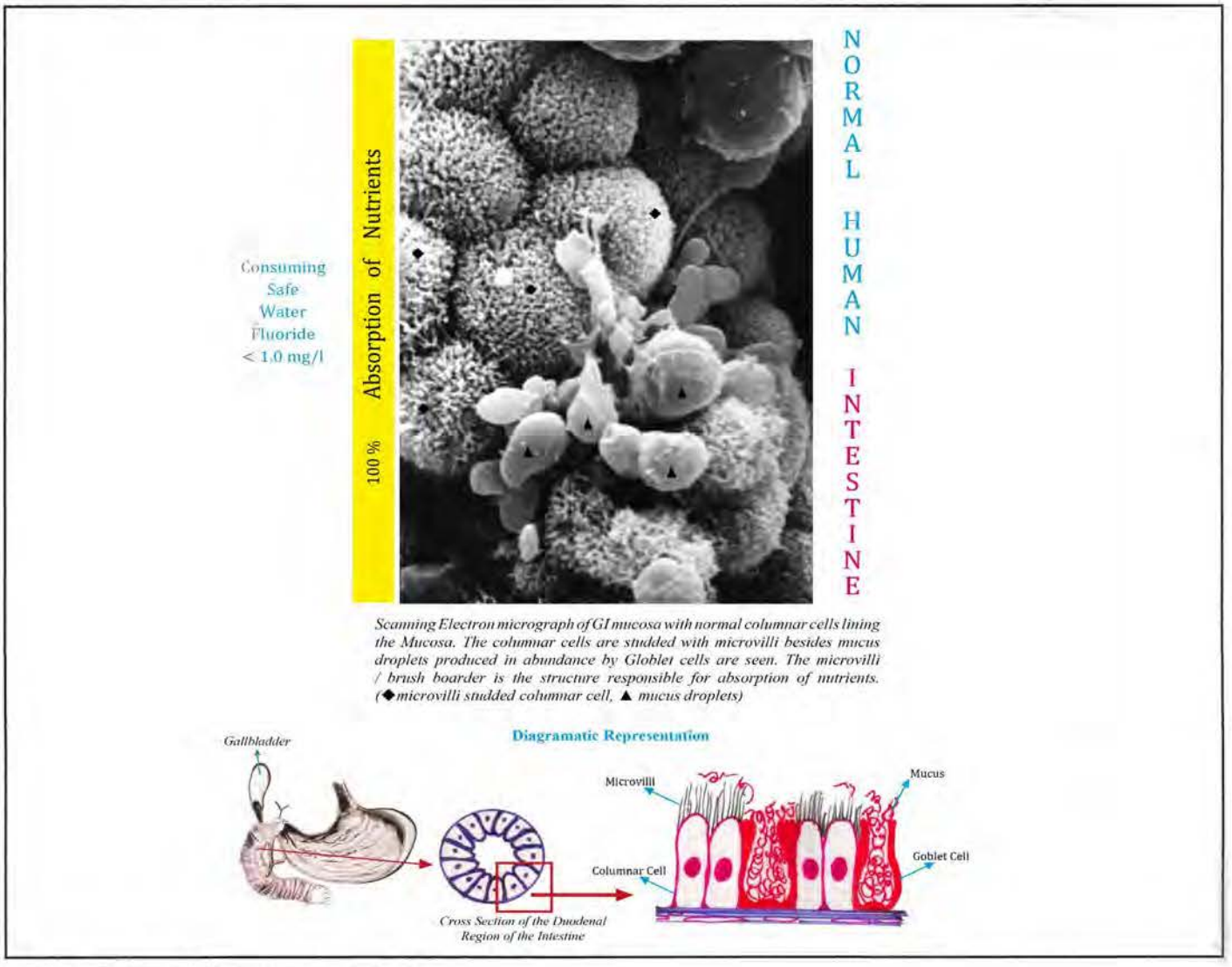


Fig. 3. Normal human intestine

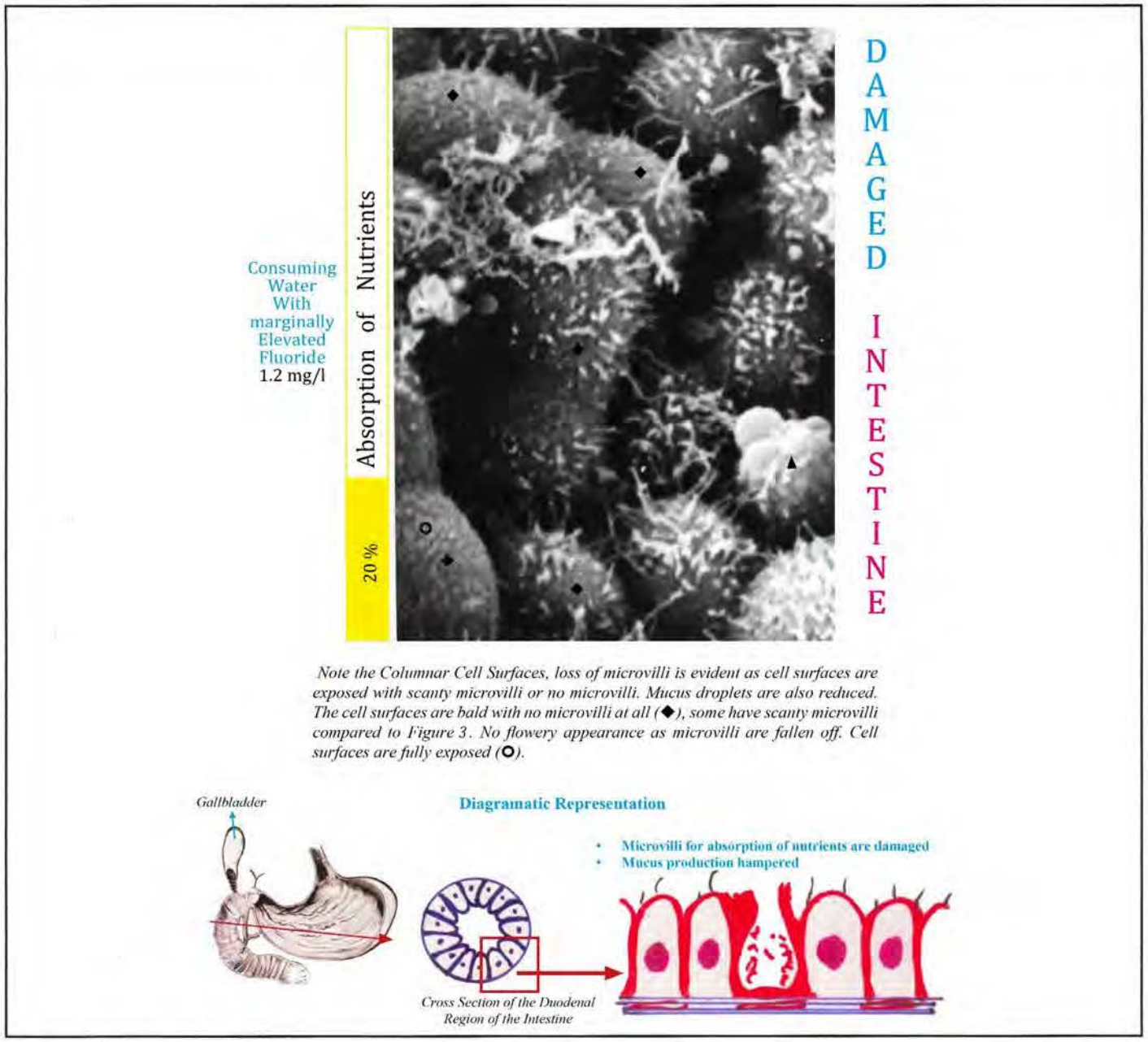


Fig. 4. Damaged intestine

Thirdly, fluoride ingestion deranges the structure and function of the thyroid gland, leading to reduction in thyroid hormone production, resulting in inadequate stimuli on erythropoietic tissues to produce erythrocytes. A high percentage of erythrocytes produced in an environment high in fluoride, are abnormal with crenations known as echinocytes. The echinocytes do not survive the normal RBC life span of 120-130 days but get phagocytosed and eliminated from blood stream.[15] Less number of erythrocytes result in low hemoglobin. The 3 major reasons for low hemoglobin production can be reversed to normal by mere withdrawal of fluoride i.e. diet editing and simultaneous diet counselling for promotion of consumption of nutrients for correction of the damages caused to the system.

There is an urgent need for the doctors handling the antenatal clinics to be sensitized on the possibility of fluorosis as a cause for anemia in pregnant women and the need to test all anemic pregnant women for fluorosis by testing 30 mL of urine collected in plastic bottles for fluoride content . All pregnant women with high urine fluoride > 1.0 mg/L are instructed to bring a sample of their drinking and cooking water in a plastic bottle (30 mL) collected from the source of the water, and the fluoride content in the water is tested. All anemic pregnant women

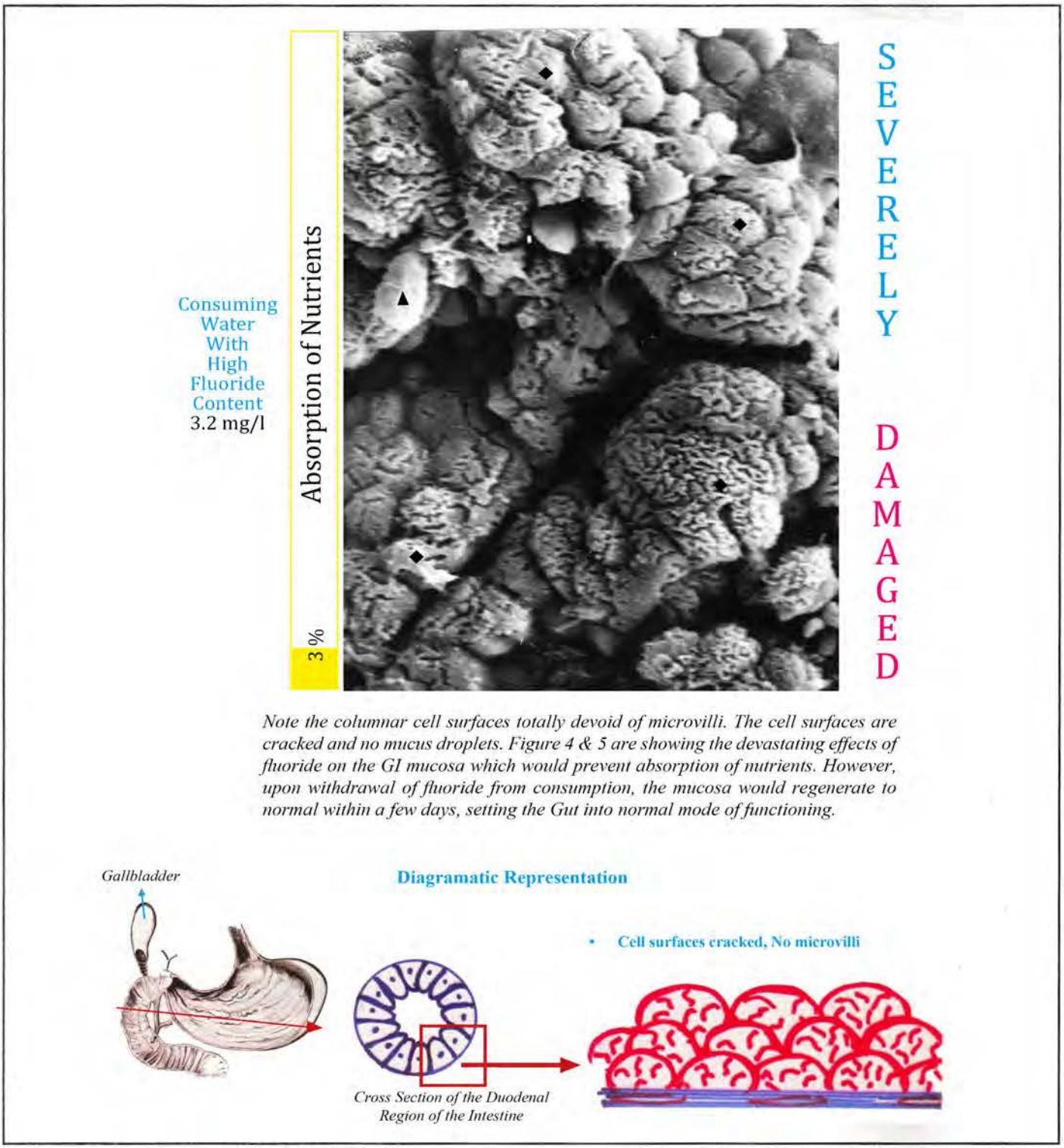


Fig. 5. Severely damaged intestine

with Hb< 12. g/dL; urine F^->1.0 mg/L and drinking water F^- > 1.0 mg/L are to be introduced to diet editing and diet counselling. If the drinking water is contaminated with F^-, they have to shift to an existing safe source of drinking water in the neighbourhood. This is considered as the best option particularly for pregnant women.

Studies have shown that iron and folic acid at the levels currently in use (100 mg iron and 500µg folic acid) are effective in reducing the risk of low birth weight babies, provided there is no increase in fluoride content in the anemic antenatal women. Studies have shown that with monitoring of urinary F^-, appropriate interventions and

dietary modifications Hb level had improved and the frequency of low birth weight babies had come down.[16] There is no short-cut way for increasing hemoglobin in pregnancy and improving birth weight of babies other than promoting non-toxic food and safe water for consumption with iron and folic acid supplementation. For the first time the nation reported fluoride as a high risk factor in production of haemoglobin.[16,17,18] The concept was validated in other anemic individuals as well. A recent review on perinatal health in India[19] emphasises that "good maternal nutrition, prevention and management of anemia and high quality antenatal care will reduce the incidence of complications and there by improve chances of survival of the mother, the foetus and the new born infants". The most essential factor missing in the above review is total elimination of consumption of fluoride by the pregnant women so that the results emerging within a span of 37- 40 weeks from the date of commencement of the programme in ANCs across the country, would be highly rewarding.

The efforts to rectify anemia in school children with withdrawal of fluoride consumption and monitoring of urine fluoride levels followed by adequate intake of nutrients through diet editing and counselling have improved the Hb levels in them and opened out very valuable and sustainable path to follow.[20,21]

Commonalities in fluorosis and iodine deficiency disorders (IDD): The way forward.

Children living in fluoride endemic regions in the country whether in Assam, Andhra Pradesh, Bihar, Gujarat, Punjab, Haryana, Delhi, Rajasthan, Karnataka, Tamil Nadu and/or West Bengal would present with health problems such as bone deformities, short stature/ cretinism, mental retardation / low IQ, the reason may be due to consumption of fluoride in excess (> 1.0 mg/L) or it may be due to deficiency of iodine in diet. The excess fluoride and/or iodine deficiency may commence during intrauterine life when the pregnant women are the victims, and the children born shall reveal the above mentioned derangements (2005).[22]

Therefore when fluoride toxicity / fluorosis is suspected in children, besides testing fluoride in urine, iodine estimation is considered necessary. In a study conducted on children in endemic areas of Delhi state with focus on children with dental fluorosis, the thyroid hormone profile led to the conclusion that testing of drinking water and body fluids for fluoride content along with FT_3, FT_4 and TSH in children living in endemic areas with and without dental fluorosis is desirable for recognizing thyroid hormone derangements.The primary cause of iodine deficiency disorders (IDD) may not always be due to iodine deficiency as it might be due to fluoride ingestion in excess. Prevention and control of fluorosis and IDD require an integrated approach for diagnosis and patient management.

If children have the deformities due to consumption of excess fluoride, it can be corrected to a large extent by diet editing and diet counselling for withdrawal of fluoride and adequate intake of all nutrients.

Calcium and Vitamin D resistant rickets in children: Protocol for correction

Assessment of serum fluoride and its association with calcium and Vitamin D resistant rickets in infants and children is the most recent revelation.[23] Children living in fluoride endemic areas in the country have overtly visible bone deformities suggestive of rickets. Infants and children are brought to the out patient department with respiratory distress and X-ray radiographs reveal that they suffer from rickets. Certain percentage of infants and children do not respond to mega dose of calcium and vitamin D and they are labelled as vitamin D resistant rickets. Assessing the serum fluoride levels and introducing diet editing and counselling with adequate calcium and vitamin D through dietary sources, as an alternate treatment option for children is recommended, if found resistant to mega-dose of calcium and vitamin D treatment.[24]

In conclusion it will be of immense value and significance both for the treating physician and the patients to consider the following: (i) Sensitize the medical fraternity to fluorosis with associated health problems and introducing the testing for fluorosis for routine patient care services. (ii) Infants and children attending pediatric OPDs with bone deformities, under-nourished with anemia and growth retardation may be considered for testing fluoride in body fluids, drinking water and thyroid hormone profile. With this approach, it may be possible to address the health problems in an effective manner than what has been experienced in the past. (iii) Finally the newly emerged scientific information in addressing anemia in pregnant women, adolescent girls and low birth weight babies due to fluoride toxicity is adding a new chapter in medical history.

Points to Remember

- ***Non-skeletal fluorosis is the earliest manifestation of fluorosis and requires a high index of suspicion for diagnosis.***

- ***Testing fluoride in body fluids and drinking water is necessary for diagnosis and management.***
- ***Fluorosis, IDD and rickets have commonalities in clinical manifestations.***

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