RMRCT UPDATE

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JABALPUR

EDITORIAL

It gives us a great pleasure to publish the second issue of RMRCT Update. The Centre saw a lot of developments in last six months. Extramural grants of more than 4 million rupees were received. The boundaries of RMRCT are increasing as it has also started work in Orissa, Chhattisgarh, Maharashtra and Uttar Pradesh in addition to Madhya Pradesh.

The Centre hosted a workshop on quality control of HIV testing. Recreational activities have also been initiated in the campus.

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FLUOROSIS AND HUMAN HEALTH

T. Chakma and P.Vinay Rao

Introduction

The effect of fluoride on human health has long been of interest to medical researchers. Fluorosis is an important clinical and public health problem in several parts of the world (Singh and Jolly, 1970). The global prevalence of fluorosis has been reported to be about 32% (Mella et al., 1994). There are several million people in India exposed to drinking water sources with high fluoride content. Excess fluoride ingestion is a major health problem, 20 of the 30 states and Union territories in India being endemic for fluorosis (Susheela, 1993). Fluoride concentration upto 38.5 ppm has been reported in drinking water (Susheela and Ghosh, 1990). Teotia and Teotia (1984) have reported dental and skeletal fluorosis in residents of rural areas consuming water containing 0.6 ppm fluoride. Skeletal fluorosis has been observed in areas having 2.4 ppm fluoride while crippling fluorosis in areas with mean fluoride levels of 3 ppm (Jolly et al., 1969).

The presence of excessive quantities of fluoride in drinking water is accompanied by a characteristic sequence of changes in teeth, bone and periarticular tissues. These changes lead to a variable degree of locomotor disability, ranging from simple mechanical back pain to severe, crippling, combined locomotor and neurological impairment. In endemic areas, a substantial proportion of the population may be affected, posing a severe public health problem. In some areas, the hazards to human health are not fully appreciated and are under-reported. The maximum impact is felt in communities engaged in physically strenuous activities, either agricultural or industrial. The need of these often-isolated communities in economically restructuring countries, for the provision of low-fluoride drinking water remains a hope rather than an expectation at the present time.

Global scenario

Fluorosis is endemic in 22 countries around the world. Drinking water containing fluoride is the major source of fluorosis due to geological crust contamination. The guidelines followed for fluoride content in drinking water in most of the countries are based on the WHO norms. According to the WHO, the desirable upper limit for fluoride in drinking water is 1.5 mg/L. Senegal is the first country to reduce the upper permissible limit of fluoride in drinking water from 1.5 mg/L to 0.6 mg/L. The reason for such drastic change is due to the high prevalence of dental fluorosis in children with 1.5 mg/L fluoride in drinking water. India has reduced the upper limit of fluoride in drinking water from 1.5 mg/L to 1.0 mg/L.

Magnitude of the problem in India

In India, around 66.6 million people including 6 million under 14 children are at risk of acquiring fluorosis. The number 66.6 million was arrived at by reviewing the data related to fluoride contamination of drinking water from different locations of various endemic states. It has revealed that the quantitative information mostly pertains to the number of water tests carried out and the levels of contamination at different points of time over a particular time frame. Some states have extremely good data, whereas some states have very scanty information. Thus the estimation of the population, which is at risk, had to be assessed within the limitations of the available data.

The health survey data available for fluorosis (1987-1992) as well as from field experience implies that the population could be broadly grouped into symptomatic and asymptomatic but may be at risk. The health survey data reported from 9 states during 1987-1992, fall under the above categories. It is also observed that a large population of children is affected by dental fluorosis. The data suggests that children between the age of 8-14 years are victims of dental fluorosis and it has been estimated that up to 20% children of this age group are staying in areas endemic for fluorosis.

Studies in Madhya Pradesh

Studies carried out by the Regional Medical Research Centre for Tribals, Jabalpur in Mandla district of Madhya Pradesh revealed a high prevalence of Genuvalgum (51.1%) and Dental fluorosis (74.4%). Water analysis revealed a high fluoride content (9 to 13 ppm) in few villages (Chakma et al., 2002).

A follow up study was undertaken after 5 years of intervention in these villages and reversal of bony deformities was noted. Considering the improvement in clinical and radiological findings it is concluded that the changes over a period were due to intervention of safe drinking water.

Types of fluorosis

Fluorosis mainly manifests in three forms - skeletal, dental and non-skeletal.

Skeletal fluorosis

The effect of fluoride on bones and skeletal system depends on the type of bone and its inorganic and organic constituents. A fluorosed bone shows characteristic structural changes like increased bone mass and density, exostosis, increased osteoid scam and resorption surfaces, increased trabecular bone volume, cortical porosity and periosteocytic lacunar surface. The osteon diameter and mottling of osteon are increased and there is formation of unmineralized cartilaginous loci within the trabeculae of the cancellous bone.

There are biochemical changes in the fluorosed bone in the form of reduction in collagen content and collagen cross-link precursors. The glycosaminoglycan and proteoglycan content are altered in cancellous bones.

Skeletal fluorosis is characterized by severe pain and stiffness in the neck, backbone and joints. The individual can not touch the toes without bending the knees. X-ray shows increased girth, thickening and density of bone. There is constriction of vertebral canal and intervertebral foramen exerting pressure on nerves and blood vessels.

Dental fluorosis

Ingestion of fluoride is the cause of dental fluorosis. Fluoride in drinking water, toothpaste, mouth rinses and sodium fluoride tablets administered on prescription, can contribute to the fluoride burden of the body leading to dental fluorosis. Dental fluorosis occurs in children during the developmental stages when the teeth are exposed to fluoride.

The discoloration of the teeth may progress from white, yellow, brown and black. The discoloration may be in spots, or as streaks invariably horizontal in orientation, since new layers of the matrix are added on horizontally during tooth development. The discoloration due to dental fluorosis should be seen in teeth in pairs based on developmental pattern and never in a single isolated tooth.

Calcium rich constituents of teeth, viz. enamel and dentin have strong affinity for fluoride during the formation of teeth. Fluoride combines with calcium forming calcium fluoroapatite crystals during the mineralisation of teeth. Tooth commonly affected are (a) central incisor (b) lateral incisors (c) molar of the permanent dentition. Fluorosis affects both the inner and outer surfaces of the teeth.

Non-skeletal fluorosis

The conventional belief that fluoride affects only bone and tooth has been negated in recent years as the evidences on the involvement of the soft tissues/organs/systems of the body are convincing. Investigations have demonstrated that there is involvement of soft tissues like skeletal muscles, red blood cells, gastro-intestinal mucosa, ligaments, spermatozoa and thyroid gland in human fluorosed patients. There are evidences on involvement of other organ and systems of animal models viz. kidney, liver, adrenal gland and reproductive organ.

Non-ulcer dyspeptic complaint is the earliest manifestation of fluoride poisoning. Hence, it is possible to diagnose fluoride poisoning at early stages.

Module for detection of fluorosis

A module has been developed for early detection of fluorosis. Following guidelines may help to detect fluorosis at an early stage. Pain in the joints without visible signs of fluid accumulation may be due to fluoride toxicity. Non ulcer dyspepsia characterized by nausea, vomiting, pain in abdomen, constipation followed by diarrhea may be due to fluoride toxicity manifestations beside other reasons. Muscle weakness, fatigue, anaemia with very low hemoglobin level may be seen in fluoride toxicity. Polyurea and polydipsia may also be due to fluoride toxicity. Complaints of repeated abortions/still birth in patients from endemic area may be due to fluoride toxicity, as fluoride is known to calcify/harden blood vessels, and thereby hamper blood flow to the growing foetus. Complaints of male infertility with abnormality in sperm morphology and low testosterone levels in patients from endemic area should lead one to suspect fluoride toxicity beside other reasons.



Pre intervention (1996)



Post intervention (2003)

Any discoloration of the enamel surface in the front row of teeth of the patients away from the gums and seen as horizontal streaks or spots is invariably due to dental fluorosis. Children with short stature, funny face, deformed bones, knock-knee, bowed leg, rickets, low IQ, deaf-mutism may be due to fluoride toxicity besides other reasons.

Removal of fluoride from drinking water

Several methods have been suggested from time to time for removing excess fluoride from water and several models were developed. Various defluoridating methods available include chemical reactions (Nalgonda technology & activated alumina technology), ion exchange process and reverse osmosis.

Nalgonda technology

Nalgonda technique involves addition of two chemicals, lime and alum to water, followed by flocculation, sedimentation and filtration. Bleaching powder can be added simultaneously for disinfection. The quantities of alum and lime required depend on dissolved solids, alkalinity and fluoride content of raw water.

Activated alumina technology

The activated alumina procedure essentially involves removal of fluoride by adsorption of the ion on the surface of the activated alumina.

Ion exchange resin based approach

Resin based ion exchange process for removal of fluoride from ground water is also available in India. It is commercially available but is expensive. Reverse osmosis

Reverse osmosis is a process wherein water is forced through a semi-permeable membrane by applying strong pressure, there by allowing only fine water molecules to pass through it. All contaminants including heavy metal and chemical poisons are removed.

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BIOLOGY OF ADULT FILARIAL PARASITE

The filarial nematodes infect man, animals, rodents and even birds. There are about seven species of filarial worms which complete there life cycle in man. Though the pathology produced by them is dissimilar, their basic biology is alike. The filarial worms, which infect animals, resemble the human filarial worms closely in morphology and biology. Three types of filarial parasites which cause lymphatic filariasis, are *Wuchereria bancrofti, Brugia malayi, Brugia timor*i.

The filarial worms have a complex life cycle. Infective larvae (L3) are transmitted to the definitive host by an arthropod vector. After 10 to 11 days of the entry of L3, third moult occurs and the larvae develop to the L4 stage. The fourth moult occurs after 35-40 days and the larvae develop to L5 stage or juvenile adult. Maturation of adult worm occurs over a period of several months (3-18 months). In contrast to the larval stages, adults are long lived about 10-12 years.

The infective larvae do not settle at the site of entry into the host but migrate to their preferred places. These parasites are very specific in their site requirements. Probably this is a directed event involving the active participation of the parasite.

Morphology

The adult worms are slender, long, white and threadlike; the males are approximately half of the females in size. The worm has a lipless mouth, cylindrical esophagus and a simple intestine. The alimentary canal is divided in to three distinct regions, the stomodeum, intestine and proctodeum. Stomodeum consists of the mouth, labia, buccal cavity and pharynx. The intestine is a straight tube. Proctodeum includes the rectum and anus. A collagenous material the cuticle covers the surface of the filarial worms. An underlying epidermal tissue, the hypodermis, elaborates this. It is composed of three zones basal, median and cortical. The cuticle is modified with the development of infective larvae to the adult stage. The filarial parasites are bisexual in nature. The males are armored with two unequal spicules and the female reproductive system contains paired ovaries, oviduct, uteri which connect with a single vagina opening via the vulva.

In contrast to the intestinal nematodes, filarial parasites possess a cuticle which is permeable to a wide range of low molecular weight substances such as hexose, amino acids etc. Cuticle does not play an active role in uptake but movement across the cuticle occurs by diffusion.

Metabolism

Although free-living parasite worms are capable of utilizing a variety of energy generating pathways (Saz, 1981), filarial parasites depend primarily on breakdown of carbohydrates to lactate. In addition to enable the parasites to obtain energy rapidly, this suits their low oxygen environment in which these organisms generally live. Thus, glycolysis has evolved in these parasites as the major route of carbohydrate metabolism rather than an emergency source of energy. Compared to glycolytic enzymes, the activities of Tricarboxylic acid cycle (TCA) enzymes in the parasites are reported to be rather low. However, complete sequence of TCA cycle enzymes have been demonstrated (Middeleton and Saz, 1970). The presence of glucose 6-phosphate dehydrogenase enzyme (Barrett et al., 1986) in some filarial parasites suggest the pentose phosphate pathway operating in filariids. But it is an insignificant pathway in these worms.

Reproduction

The males and females of filarial parasites often found coiled together at specific sites in the host body. During copulation the males used their spicules to open the vulva of the female. After fertilization, the eggs embryonate within the uterus of the female worm and develop to microfilariae. These microfilariae once hatched came out of the uterine canal and emerge from the vagina. The microfilariae production is cyclical in Onchocerca volvulus a human filarial parasite prevalent in Africa. In *Dirofilaria immitis* (a canine filarial worm) oogenesis is cyclical but spermatogenesis is continuous. The microfilariae produced by the adults finds their way to the specific sites like blood, skin etc. In these sites they are picked up by the vector to undergo the development to the infective larvae. A gravid female of *Setaria digitata*, a cattle filarial worm can lay as much as about 10^5 microfilariae at a time.

Dr. Dasarathi Das
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(April - October 2004)

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Revised Manuscripts Submitted

1. Rao V.G., Agrawal M.C., Vohra S., Singh B.K., Singh K.P. CHR as a tool for assessing human schistosomiasis in India. **American Journal of Tropical Medicine & Hygiene.**
2. Das D., Gyanchand, Kumar S., Das S.K., Sahare L.K., Sahoo P.K. Dash A.P. Bancroftian filariasis : A 11-year follow up study of endemic normals and microfilariae carriers in Panna district, India. **Transactions of Royal Society of Tropical Medicine Hygiene.**
3. Das D., Kumar S., Sahoo P.K., Dash A.P. Bancroftian filariasis in two villages of Madhya Pradesh: a survey of Microfilaraemia and circulating antigenemia. **Indian Journal of Medical Research.**

Papers Communicated

1. Rao V.G., Sugunan A.P., Murhekar M.V., Sehgal S.C. Malnutrition and high childhood mortality among Onges - A primitive tribe of A & N islands. **Public Health & Nutrition.**
2. Rao V.G., Yadav R., Bhondele M.K., Uike M., Dolla C.K., Kumar S. Undernutrition and childhood mortality among tribal preschool children of M.P. **Indian Journal of Medical Research.**
3. Gupta R.B., Solanki S.S., Singh N. Splenic infarction in an Indian youth - A brief report. **Acta Haematologica.**
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5. Saha K.B. Rethinking on ethical restrictions and relaxations in social science researches. **The National Medical Journal of India.**
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8. Kumar D., Joshi N., Roy J., Jain D.C. Continuity of infertility among Khairwar tribe of Central India : A test of multivariate hypothesis. **Journal of International Family Planning Perspective.**



PARTICIPATION OF RMRCT SCIENTISTS IN CONFERENCES / WORKSHOPS / MEETINGS

(April - October 2004)

Prof. A. P. Dash attended a meeting on task force for hepatitis in tribal areas of India at ICMR, New Delhi on 24th August 2004.

Prof. A. P. Dash attended the scientific advisory committee meeting at RMRC Bhubaneswar from 16th to 18th September 2004.

Prof. A. P. Dash attended the International Symposium on Emerging Viral Infections at NIV Pune from 11th to 13th October 2004.

Dr. V. G. Rao attended the 59th annual conference of Association of Physicians of India held at Hyderabad from 18th to 21st January 2004 and presented a paper entitled 'Short term effects of lifestyle modification, stress management and dietary changes in coronary artery disease patients'.

Dr. V. G. Rao and Dr. Deepali Savargaonkar (S.R.F.) attended the 28th National Conference of Society for STD and AIDS at Jabalpur from 2nd to 4th November 2004 and also presented papers.

Mr. Gyanchand, Dr. Anup Anvikar, Dr. Dasarathi Das and Dr. Deepali Savargaonkar (S.R.F.) attended the International Symposium on Emerging Viral Infections at NIV Pune from 11th to 13th October 2004 and also presented papers.

Dr. Anup Anvikar was program coordinator in the workshop for Medical Officers External Quality Assurance Scheme on 10th and 11th June 2004.

Dr. Anup Anvikar attended a meeting on task force for hepatitis in tribal areas of India at ICMR, New Delhi on 24th August 2004.

Dr. C.K. Dolla and **Dr. Surendra Kumar** attended a training program on Biomedical Information Retrival at NIC, New Delhi from 27th to 30th July 2004.

Dr. Ujwala Das attended a Training Programme on Reverse Dot Blot Temporal Temperature Gradient Electrophoresis at CMC, Vellore from 13th to 17th September 2004

NATIONAL TECHNOLOGY DAY



Dr. Rukhsana Ahmed, delivering seminar

The National Technology Day was celebrated at the Centre on 14th May 2004. On this occasion, Dr. Rukhsana Ahmed, Research Scholor, Liverpool School of Tropical Medicine & Hygiene delivered a seminar on Malaria in Pregnancy. She talked about malaria in pregnancy and its effects on the nutritional status & growth of newborn.

The scientists as well as staff members of RMRCT attended the seminar.

RAJBHASHA FORTNIGHT CELEBRATIONS



Prize distribution ceremony on Rajbhasha day

Rajbhasha Fortnight was celebrated at RMRCT from 1st to 15th September 2004. On this occasion, an appeal was made to all the officers and staff members of the Centre to do their official work in Hindi. On this occasion, different competitions were organized for staff members like Hindi typing, noting / drafting, extempore essay writing and slogan writing competitions were also organized. Dr. V. G. Rao, Assistant Director of the Centre distributed prizes under the Incentive scheme for doing official work originally in Hindi. All the staff-members participated enthusiastically in the programs.

RMRCT
UPDATE

WORKSHOP
ON
EXTERNAL QUALITY ASSURANCE SCHEME



EQAS workshop in progress

A training program on External Quality Assurance Scheme for HIV testing was organized at RMRCT in association with the M.P. State AIDS Control Society, Bhopal on 10th & 11th June 2004. Fourteen medical officers and 20 laboratory technicians attended the training program.

The training program was inaugurated by Dr. V. G. Rao, Assistant Director, RMRCT, Jabalpur. The faculty members were Dr. Brajendra Mishra, Joint Director, MPSACS, Bhopal, Smt. Shrutika Chipkar from Institute of Immunohematology, Mumbai, Dr. Sharad Jain, Officer-in-Charge, Blood Bank, NSCB Medical College, Jabalpur, and Dr. Anup Anvikar, RMRCT, Jabalpur.

A hands on training was given to the participants as regards the HIV testing and its quality control.

RECREATIONAL
ACTIVITIES

Recreation club was revived at RMRCT in August 2004. Facilities for outdoor games like cricket, volleyball, and badminton were developed in addition to those for various indoor games.





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