



# INDIAN JOURNAL OF PRACTICAL PEDIATRICS



- IJPP is a quarterly subscription journal of the Indian Academy of Pediatrics committed to presenting practical pediatric issues and management updates in a simple and clear manner
- Indexed in Excerpta Medica, CABI Publishing.

**Vol.13 No.1**

**JAN.-MAR. 2011**

**Dr. K.Nedunchelian**  
Editor-in-Chief

**Dr. S. Thangavelu**  
Executive Editor

## CONTENTS

### INFANT AND CHILD NUTRITION

<b>Current concepts on nutritional requirements in infants and children</b>	<b>5</b>
- Elizabeth KE	
<b>Principles and problems of complementary feeding</b>	<b>12</b>
- Panna Choudhury	
<b>Feeding of low birth weight babies</b>	<b>18</b>
- Naveen Jain	
<b>Total parenteral nutrition in neonates</b>	<b>23</b>
- Giridhar S	
<b>Treatment of common nutritional deficiencies</b>	<b>32</b>
- Prema A	
<b>Food Fortification: Present and future</b>	<b>40</b>
- Sushil Madan	
<b>Ready to use therapeutic food: A review</b>	<b>50</b>
- Dubey AP, Malobika Bhattacharya	
<b>Zinc in child health: A mineral that means a lot!</b>	<b>57</b>
- Pawan Rawal, Thapa B R	
<b>Newer iron preparations: Advantages and limitations</b>	<b>65</b>
- Sudhir Vinod Sane	

**Journal Office and address for communications:** Dr. K.Nedunchelian, Editor-in-Chief, Indian Journal of Practical Pediatrics, 1A, Block II, Krsna Apartments, 50, Halls Road, Egmore, Chennai - 600 008. Tamil Nadu, India. Tel.No. : 044-28190032 E.mail : [ijpp\\_iap@rediffmail.com](mailto:ijpp_iap@rediffmail.com)

**GENERAL ARTICLES**

- Skin manifestations in pediatric HIV infection** **71**  
 - Sandipan Dhar, Raghubir Banerjee
- Preventive dentistry in pediatrics** **75**  
 - Aruna Mohan

**DRUG PROFILE**

- Aminoglycosides in pediatric practice** **83**  
 - Jeelson C. Unni

**DERMATOLOGY**

- Childhood psoriasis - A challenge to all** **91**  
 - Jayakar Thomas, Parimalam Kumar

**RADIOLOGIST TALKS TO YOU**

- Brain tumors - 1** **97**  
 - Vijayalakshmi G, Malathy K, Elavarasu E, Venkatesan MD

**CASE STUDY**

- Children eating pan masala-Beware of oral submucous fibrosis** **100**  
 - Vishal Mehrotra, Tandon VK, Paravathi Devi,  
 Thimmarasa VB, Manas Gupta
- A rare case of intracranial and intramedullary tuberculomas** **105**  
 - Ravisekar CV, Lakshmi S, Kumarasamy K, Luke Ravi Chelliah,  
 Sujatha S

**CLIPPINGS****11, 17, 39, 49, 56, 64, 70, 99****NEWS AND NOTES****82, 96****FOR YOUR KIND ATTENTION**

\* The views expressed by the authors do not necessarily reflect those of the sponsor or publisher. Although every care has been taken to ensure technical accuracy, no responsibility is accepted for errors or omissions.

\* The claims of the manufacturers and efficacy of the products advertised in the journal are the responsibility of the advertiser. The journal does not own any responsibility for the guarantee of the products advertised.

\* Part or whole of the material published in this issue may be reproduced with the note "Acknowledgement" to "Indian Journal of Practical Pediatrics" without prior permission.

**- Editorial Board**

Published by Dr.K.Nedunchelian, Editor-in-Chief, IJPP, on behalf of Indian Academy of Pediatrics, from 1A, Block II, Krsna Apartments, 50, Halls Road, Egmore, Chennai - 600 008. Tamil Nadu, India and printed by Mr. D. Ramanathan, at Alamu Printing Works, 9, Iyyah Street, Royapettah, Chennai - 14.

## INSTRUCTIONS TO AUTHORS

### General

Print the manuscript on one side of standard size A4, white bond paper, with margins of at least 2.5 cm (1") in double space typescript on each side. Use American English using Times New Roman font 12 size. Submit four complete sets of the manuscript.

They are considered for publication on the understanding that they are contributed to this journal solely.

All pages are numbered at the top of the right corner, beginning with the title page.

All manuscripts should be sent to: The Editor-in-Chief, Indian Journal of Practical Pediatrics

### Manuscript

#### 1<sup>st</sup> Page –

Title

Name of the author and affiliation

Institution

Address for correspondence (Email, Phone, Fax if any)

Word count

No. of figures (colour / black and white)

No. of references

Authors contribution

#### 2<sup>nd</sup> Page –

Abstract (unstructured, not exceeding 100 words) with key words (not exceeding 4)

#### 3<sup>rd</sup> Page -

Acknowledgement

Points to remember (not more than 5 points)

Text

References

Tables

Figures – should be good quality, 4 copies black & white / colour, (4 x 6 inches – Maxi size) Glossy print.

(Each colour image will be charged Rs.1,000/- separately)

Legends

### Text

Only generic names should be used

Measurements must be in metric units with System International (SI) Equivalents given in parentheses.

### References

Recent and relevant references only

Strictly adhere to Vancouver style

Should be identified in the text by Arabic numerals in parentheses.

Type double-space on separate sheets and number consecutively as they appear in the text.

Defective references will entail rejection of article

### Tables

Numbered with Roman numerals and typed on separate sheets.

Title should be centered above the table and explanatory notes below the table.

### Figures and legends

Unmounted and with figure number, first author's name and top location indicated on the back of each figure.

Legends typed double-space on separate sheet. No title on figure.

## Article Categories

### *Review article*

Article should be informative covering the recent and practical aspects in that field. Main articles can be in 1500 – 2000 words with 12 – 15 recent references and abstract not exceeding 100 words.

### *Case report* (covering practical importance)

250 – 600 words, 8 – 10 recent references

### *Clinical spotters section*

100 – 150 words write up

With 1 or 2 images of clinically recognizable condition

(of which one could be in the form of clinical photograph / specimen photograph / investigation)

### *Letters to the Editor*

200 – 250 words pertaining to the articles published in the journal or practical viewpoints with scientific backing and appropriate references in Vancouver style.

### **Check List**

Covering letter by corresponding author

Declaration (as enclosed) signed by all authors \*\*

Manuscript (4 copies)

Accompanied by a copy in CD / or submit as an email attachment in addition to hard copy.

Failing to comply with the requirement at the time of submission would lead to the rejection of the article.

### **Author's contribution / Authorship Criteria**

All persons designated as authors should qualify for the authorship. Authorship credit should be based on substantial contributions to i) concept and design, or collection of data, and interpretation of data; ii) drafting the article or revising it critically for important intellectual content; and iii) final approval of the version to be published. All conditions i), ii) and iii) must be met.

### **\*\*Declaration by authors**

I/We certify that the manuscript titled ‘.....’ represents valid work and that neither this manuscript nor one with substantially similar content under my/our authorship has been published or is being considered for publication elsewhere. The author(s) undersigned hereby transfer(s), assign(s), or otherwise convey(s) all copyright ownership, including any and all rights incidental thereto, exclusively to the Indian Journal of Practical Pediatrics, in the event that such work is published in Indian Journal of Practical Pediatrics. I / we assume full responsibility for any infringement of copyright or plagiarism.

Authors' name(s) in order of appearance in the manuscript

Signatures (date)

**All manuscripts, which are rejected will not be returned to author. Those submitting articles should therefore ensure that they retain at least one copy and the illustrations, if any.**

### **Selection procedures**

All articles including invited articles will be peer reviewed by two masked reviewers. The decision of the Editorial Board based on the reviewers' comments is final.

## INFANT AND CHILD NUTRITION

### CURRENT CONCEPTS ON NUTRITIONAL REQUIREMENTS IN INFANTS AND CHILDREN

\* **Elizabeth K E**

**Abstract:** *Infant and young child feeding (IYCF) practices lay the foundation of the health of the future citizens. Nutritional requirements of infants and young children can be met by optimum breast feeding and complementary feeding practices with a smooth transition to family pot feeding supported by a safety net in the form of supplementary feeding and extra feeding during illness. Currently complementary feeding is considered as the bottle neck in IYCF. Hence, this should be improved keeping the energy, protein, essential fat and micronutrient content of the diet should be kept optimum. Kitchen based multimixes should be popularized.*

**Keywords:** *Infant and young child feeding, Breast feeding, Complementary feeding, Family pot feeding, Supplementary feeding, Group eating, Safety net, Multimixes*

Infant and young child feeding (IYCF) practices are very important as these lay the foundation of nutritional status and health of future citizens. Initial exclusive breast feeding followed by smooth complementary feeding and empowerment to family pot feeding and balanced diet are the steps involved. Complementary

feeding is the bottle neck in IYCF practices pushing millions of children into the pit of malnutrition.<sup>1</sup> The diet of young children should be wholesome and should contain all food groups as depicted in the 'food square' (Fig.1.). Simple messages like; one year old should be eating half of what the mother eats, a toddler should be eating half of what the father eats etc.' should reach the grass root level.

#### 1. Exclusive breast feeding

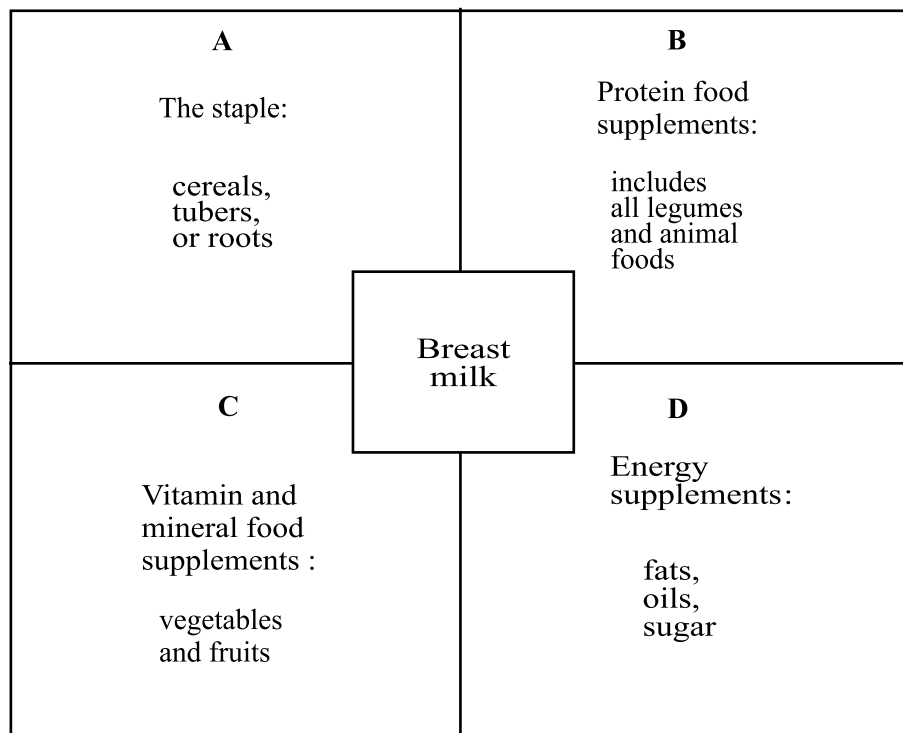
Exclusive demand feeding is ideal up to 6 months of age. Employees in the public and organized sector are eligible for 6 months leave with pay for the promotion of breast feeding. Even though the BFHI initiative is commendable in this context, there are gap areas like abrupt stoppage of breast feeding, dual feeding using breast milk and cow's milk, bottle feeding and early and late introduction of complementary foods. Exclusively breastfed infants of mothers who do not have any vitamin deficiency are protected against various vitamin deficiencies. Breast milk increases up to 6 months and then it plateaus off. WHO recommends exclusive breastfeeding until 6 months of age and continued breastfeeding for at least 2 years to support brain growth and myelination. Together with the introduction of adequate amounts of complementary foods of suitable nutritional and microbiological quality WHO growth curves for breastfed children are recommended for monitoring. The nutritional requirements in the various age groups are given in Table 1.

#### 2. Complementary feeding

After the period of exclusive breastfeeding,

---

\* Professor of Pediatrics and  
Consultant in Nutrition and Genetics,  
SAT Govt. Medical College,  
Thiruvananthapuram.



**Fig.1. Food square for the young child**

the diet undergoes a change, from a single liquid food - breast milk, to a variety of complementary foods plus breast milk, to meet infant's nutritional requirements. Complementary feeding is defined as 'the systematic process of introduction of suitable food at the right age in addition to mother's milk in order to provide needed nutrients to the baby' (UNICEF 1984). It is a bridge that the mother has to make during liquid to solid transition (Fig.2.). This term is preferred than 'weaning'. To wean is understood as to abruptly take off breast milk by some. As this is a period of rapid growth and development, poor nutrition during this critical period of life may result in growth faltering and micronutrient deficiencies, and adverse effects on health and mental development. Improved complementary feeding is a cost-effective public health tool.<sup>2</sup>

At 6 months of age, breast milk may not provide adequate calories and nutrients for the child's growth. At this period, infants enjoy 'mouthing and gumming', and also new tastes. Teeth eruption follows, baby can do chewing and grinding movements, intestinal amylase increases and the 'tongue extrusion reflex' which pushes out solid food disappears. Thus, the infant is ready to accept semi-solid foods. Mothers also realize that babies are not satisfied with breast milk alone and frequently cry after feed.

Foods that complement breast milk, sustain growth, development and health should be made available.<sup>3</sup> The aim is to introduce smoothly a soft digestible diet containing adequate calories, proteins and micronutrients, free of contamination, without much salt or

**Table.1. Nutritional requirement (ICMR recommendations of RDA 1998)**

Age Group	Energy (Kcal/d)	Protein (g/d)	Iron (mg/d)	Vitamin A (µg/d)	
				Retinol	β-carotene
0-6 months	118/kg	2.05/kg		350	1200
6-12 months	108/kg	1.65/kg			
1-3 years	1240	22	12	400	1600
4-6 years	1690	30	18	400	

spices, easy to prepare from family foods, easy to eat and easily accepted by the infant, in an appropriate amount, and at a cost that is acceptable by most families.<sup>4</sup>

When starting complementary foods, breastfeeding has to be continued as often as before keeping the length of each breastfeed the same as before. However, as the infant gets used to complementary foods and begins to take it in adequate quantities, baby would suckle less and breast milk secretion would proportionately decrease. Usually, around 2 years, breast milk is entirely replaced by family foods, although a child may still sometimes suckle for comfort.<sup>5</sup>

Complementary feeding is the bridge the mother has to make between liquid and solid diet, at the right time supported by three pillars namely continuation of breast feeding, introduction of vegetarian food and nonvegetarian items (Fig.2). Mothers are also expected to make a safety net in the form of supplementary feeding from the ICDS or group eating in preschools or akshayapatra to give small frequent foods in the home setting.<sup>1</sup>

When exclusively breastfed infants younger than six months do not develop properly, a careful assessment should be made to verify whether they are getting too little breast milk due to a poor breastfeeding technique, which leads to inadequate emptying of the breasts and,

consequently, to a low milk production. In these cases, the usual recommendation is that mothers receive instructions and support so that the baby can increase the intake of breast milk and complementary feeding is not introduced early unnecessarily. The ideal age for complementary feeding is 24 months but with arrange of 17–27 months in special circumstances.

### 1) Energy content of complementary foods

The current view is that inadequate intake of energy, and not protein, is the main etiological factor in infantile malnutrition. The reduced stomach size (30-40 ml/kg) of infants may prevent them from meeting their energy requirements on a low-energy diet. The recommended energy intake of complementary foods varies according to the age of the infants, and depends on how much breast milk they ingest. For infants with an average breast milk intake and who eat at least three meals a day of complementary foods, the recommended energy intake ranges from 0.6 kcal/g at 6-8 months of life to 1 kcal/g at 12-23 months. Oil, butter, ghee, jaggery and honey supply extra energy.

### 2) Protein content of complementary foods

The recommended protein content for complementary foods is of 0.7 g/100 kcal, from 6 to 24 months. The protein requirements are

usually met when the energy intake is appropriate. It is of paramount importance that infants eat high quality and easily digestible proteins, like animal products that are expensive. Hence affordability should be considered during nutrition advice. Often mothers are advised to use locally available and affordable food items. The protein in all staples is not as well balanced as in animal foods. That is one reason why continuing with breast feeding during weaning is so important. All legumes have a protein content of 18% in the uncooked form. However, the quality of protein is not as good as animal protein, but legumes contain amino acids that are less plentiful in cereals. Hence a mixture of the cereals and legumes makes a balanced form of protein. To this, limited amounts of animal foods may be added.<sup>6</sup>

### **3) Micronutrient content of complementary foods**

To meet the micronutrient requirements of infants, a variety of foods should be offered,

#### **a) Iron**

Exclusive breastfeeding provides iron requirements in the first 6 months in full-term normal weight babies, if mothers are iron sufficient. After 6 months, iron stores become depleted and iron has to be supplied. In developing countries, due to low iron intake and low bioavailability, iron requirements cannot be totally met. Infants aged 6-12 months, usually do not eat enough iron-rich foods to meet their requirements. Affordability is yet another constraint. Foods of animal origin have a better iron bioavailability (up to 22%) than those of vegetable origin (1 to 6%). Meats, especially red meat and liver have high iron content and bioavailability. Foods like egg yolk, beans, lentils, soybean and dark green vegetables contain iron. The iron absorption can be enhanced by adding

meat, fish, fructose and ascorbic acid (orange, guava, lemon, mango, papaya, melon, banana, passion fruit, peach, tomato, capsicum, green leaves, cabbage, broccoli, cauliflower) in the same meal. Raw and fresh foods should be preferred, as vitamin C is destroyed during cooking. Avoid concurrent intake of eggs, milk, tea or coffee that hamper iron uptake, since they form insoluble precipitates with iron. The inhibitory effect of whole cereals is due to the presence of phytates. WHO/UNICEF recommends ferrous sulfate supplementation at the dose of 12.5 mg of elemental iron for infants 6-24 months, who do not have access to iron-fortified foods. Low birth weight babies should receive iron supplementation earlier.

#### **b) Vitamin A**

If the mother's diet has adequate vitamin A content, breast milk shall meet the requirements in infants. The major food sources of vitamin A are liver, egg yolk, milk products and green, yellow, orange, red (GYOR) vegetables and fruits like carrots, pumpkin, red peppers, yellow peppers, mango, passion fruit and papaya. Cultivation and consumption of GYOR vegetables and fruits rich in micronutrients and antioxidants is called as 'rainbow revolution'.<sup>1</sup> Vitamin A administered at intervals of 6 months during immunization/ campaigns is an effective measure to tackle vitamin A deficiency.

#### **c) Others**

Micronutrients such as riboflavin, niacin, thiamin, vitamin C, vitamin E, calcium, zinc may be low in some, but further evidence is necessary before specific recommendations are made available. Exposure to sunlight is recommended for the young children and also nursing mothers to meet the requirements of Vitamin D. Folate deficiency is already addressed by the iron and folic acid (IFA) tablets and liquid available



in the RCH Kits. Iodine deficiency is being covered by iodine fortified salt (IFS). Iron and iodine double fortified salt (DFS) is also undergoing field trials.

#### 4) Multimixes

Multimixes, suitable for feeding are double (cereal pulse), triple (2 cereal pulse) or quadrimix. Examples are given below:

a) SAT Mix (Precooked and Ready to use Therapeutic Food - RUTF)

Rice: Wheat: Black gram: Sugar 1:1:1:2

100 g provides 350 kcal and 8g protein.

b) Quadrimix (Precooked and Ready to use)

Wheat: Bengal gram: Groundnuts: Jaggery 6:3:1:2

100g gives 9 g of protein; 260 kcal, 500 mg of sulphur amino acids and 400 mg of lysine.

### 3. Family pot feeding

Infants and young children can be fed family foods, provided the consistency and energy content are appropriate. Usually, from the 8<sup>th</sup> month onwards, various foods and balanced mixtures containing cereals, tubers, and foods of animal and vegetable origin, and fat can be offered. Only variety guarantees the supply of micronutrients, enhances good eating habits and prevents the development of anorexia caused by monotonous foods. Children and adults later on, tend to prefer the foods, the way they were initially introduced. Infants should be initially offered foods containing low sugar and salt contents. Avoid offering sugary beverages like soft drinks, as they reduce the appetite for more nutritious foods and may soften the stools. It is not advisable to give infants younger than 6-12 months, unmodified cow's milk because its use is associated with blood loss in the stools, iron deficiency and allergy.

There are two kinds of complementary foods: specially prepared foods and usual family foods that are modified to make them easy to eat. For example: to mash the foods to modify the consistency and to add oil or butter for extra energy or a piece of mango or carrot to give extra vitamin A.<sup>7</sup> Malted grain is more easily digestible and binds less water. The gruel prepared from such grain is more fluid in consistency, more easily digestible, has more micronutrients and are less bulky on cooking. This is also known as 'Amylase rich food.'

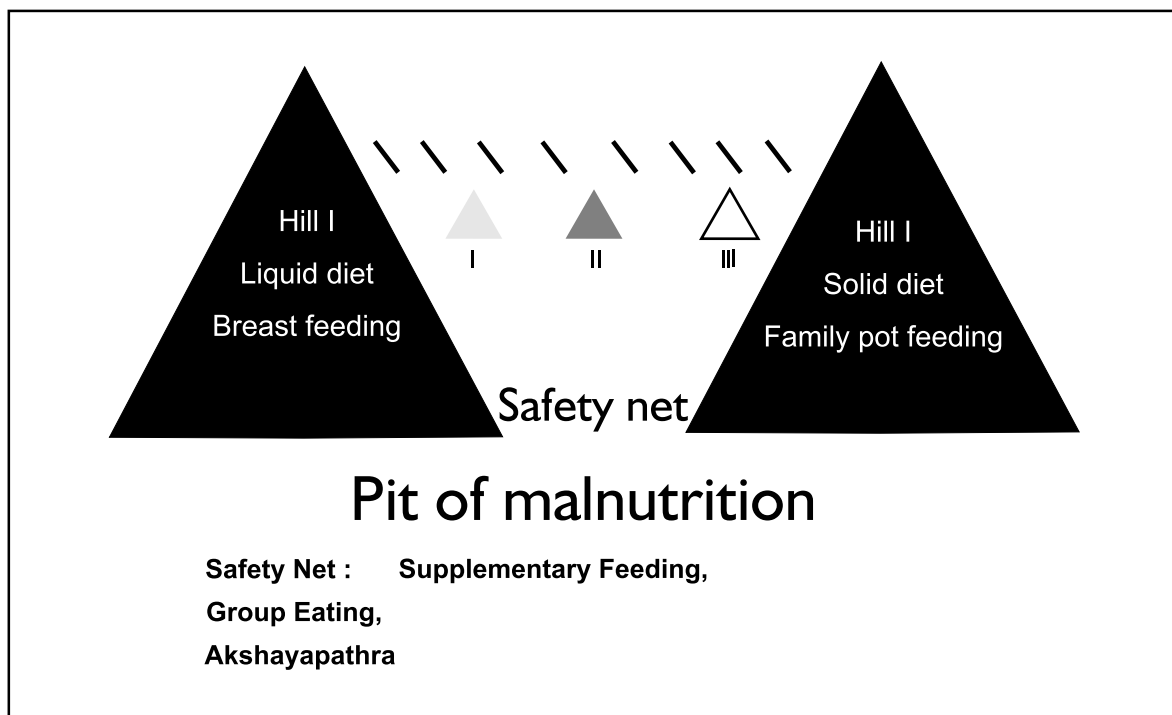
### 4. Extra feeding during illness

Growth is a highly sensitive process depending on the body's physiological processes and supply of nutrients. Any illness, mild or severe upsets the delicate balance and growth falters. Under normal circumstances, growth accelerates during recovery of an illness. This catch-up growth requires additional nutrients. Studies on malnutrition have shown that such infants gain weight 2-3 times higher compared to normal infants of the same size. Protein synthesis is very expensive in terms of energy requirement. It is realized that for glucose and fat, the maximum energy convertible to ATP is 38-40%. The remainder is released as heat. The energy needs of catch-up growth are heavy and there should be more energy and protein.<sup>8</sup>

### 5. Safety net

Extra care is needed in bridging the energy gap in young children by the safety net (Fig.2). Providing 300 kcals and 10-15g protein/day/child for 300 working days a year through ICDS is a big leap. Group eating and small frequent feeds with the 'Akshayapatra' concept are also good for children, while staying at home (Fig.2).

Appropriate breastfeeding and complementary feeding practices are the foundations of infant's nutrition, health, and



**Fig.2. The bridge of complementary feeding and the safety net**

**Table.2. Ten steps to healthy feeding of infants younger than 2 years**

<p>Step 1: Feed the infant exclusively with human milk up to 6 months. Do not offer water, tea or any other kind of food.</p> <p>Step 2: After 6 months, gradually introduce other kinds of food. Keep providing human milk up to 2 years or longer.</p> <p>Step 3: After 6 months, give complementary food (cereals, vegetables, fruits, meat) three times a day if the child is being breast fed, and five times a day if the child is no longer breastfed.</p> <p>Step 4: Complementary food must be offered on demand, always respecting the child's appetite.</p> <p>Step 5: Complementary food must be thick and it must be offered with a spoon; in the beginning it should have a pasty consistency (porridge/</p>	<p>mashed food) and, gradually, it should get thicker up to the time when the child is able to eat a family meal.</p> <p>Step 6: Offer the child with different kinds of food throughout the day. A varied diet is colorful and better accepted.</p> <p>Step 7: Stimulate the daily intake of fruits and vegetables.</p> <p>Step 8: Avoid sugar, coffee, canned food, fried food, soft drinks, candies, and treats in the first years of life. Use a moderate amount of salt.</p> <p>Step 9: Make sure to wash your hands before handling food; make sure the food is appropriately stored.</p> <p>Step 10: Stimulate the sick child to eat. Offer the usual and favorite meals and respect the child's appetite.</p>
--	---

survival. Hence, the key objective is to provide optimum nutrition as per the 'ten steps' given in Table 2. The linear growth retardation in early infancy cannot be reversed after the second year of life. Nutritional adequacy is essential for the prevention of morbidity and mortality, including malnutrition and overweight.

## Points to Remember

- *In infancy, initial exclusive breast feeding should be complemented by complementary foods by six months of age.*
- *Later, empowerment for family pot feeding and continuation of breast feeding are most important.*
- *A safety net of supplementary feeding, group eating and extra feeding during illness is ideal to support IYCF practices.*
- *Kitchen based multimixes should be popularized in IYCF.*
- *Stress should be on energy, protein, essential fat and micronutrient content of the diet.*

## References

1. Elizabeth KE. Feeding of infants and children In: Nutrition and Child development. 3<sup>rd</sup> Edn, Paras, Hyderabad, 2004;p1-29.
2. Ebrahim G. J. Mother and Child Nutrition in the Tropics and Sub-Tropics. 2<sup>nd</sup> Edn, of Nutrition in Mother and Child Health. Book Aid, London, 2005 (electronic edition). Available at: [www.oxfordjournals.org/tropej/online](http://www.oxfordjournals.org/tropej/online)
3. Daelmans B, Martines J, Saadeh R. Special Issue based on a World Health Organization Expert Consultation on Complementary Feeding. Food and Nutrition Bulletin 2003; 24:1-139. Available at [www.ruandi.org.uy/lecturasexpert\\_consultation\\_on\\_complementary\\_feeding\\_2003](http://www.ruandi.org.uy/lecturasexpert_consultation_on_complementary_feeding_2003)
4. Ebrahim G. J. Practical Mother, Newborn and Child Care in Developing Countries. Book Aid, London, 2007 (electronic edition). Available at: [www.oxfordjournals.org/tropej/online](http://www.oxfordjournals.org/tropej/online)
5. Monte C, Gigliani ERJ. Recommendations for the complementary feeding of the breastfed child. Jornal de Pediatria 2004; 80: S131-S141. Available at [www.jped.com.br/conteudo/04-80-S131/ing.asp](http://www.jped.com.br/conteudo/04-80-S131/ing.asp)
6. Pan American Health Organization/WHO. Guiding principles for complementary feeding of the breastfed child. PAHO/WHO, Division of Health Promotion and Protection/Food and Nutrition Program, Washington DC, USA, 2003. Available at: [www.who.int/nutrition/topics/complementary\\_feeding/en](http://www.who.int/nutrition/topics/complementary_feeding/en)
7. World Health Organization-WHO. Complementary feeding: family foods for breastfed children. WHO, Geneva, 1998. Available at: [www.who.int/nutrition/topics/complementary\\_feeding/en](http://www.who.int/nutrition/topics/complementary_feeding/en)
8. WHO. Complementary feeding: report of the global consultation. Summary of guiding principles for complementary feeding of the breastfed child. WHO, Geneva, 2001. Available at: [www.who.int/nutrition/topics/complementary\\_feeding/en](http://www.who.int/nutrition/topics/complementary_feeding/en)

## CLIPPINGS

***Karen Y. Kwan, Alan L. Nager. Diagnosing pediatric appendicitis: Usefulness of laboratory markers. The American Journal of Emergency Medicine, November 2010***

C-reactive protein with WBC is useful in distinguishing appendicitis from other diagnoses in pediatric subjects presenting to the emergency department. White blood cell count greater than  $12 \text{ cells} \times 1000/\text{mm}^3$  and C-reactive protein greater than 3 mg/dL increases the likelihood of appendicitis. d-Lactate is not a useful laboratory adjunct.

**INFANT AND CHILD NUTRITION****PRINCIPLES AND PROBLEMS OF COMPLEMENTARY FEEDING**

**\* Panna Choudhury**

**Abstract:** *Complementary feeding is extremely essential from six months of age, while continuing breastfeeding, to meet the needs of the growing baby. In principle it should start with small amounts of feed from the staple cereal of the family. Subsequently amount of food to be offered should be based on the principles of responsive feeding, while assuring that energy density and meal frequency are adequate to meet the child's needs. A variety of foods should be introduced gradually, one at a time. Safety of complementary food need to be ensured and hand washing before handling of the food remains mainstay for preventing contamination of food.*

**Keywords:** *Complementary Feeding, Safety.*

From the age of 6 months, an infant's need for energy and nutrients starts to exceed what is provided by breast milk, and complementary feeding becomes necessary to fill the energy and nutrient gap.<sup>1</sup> If complementary foods are not introduced at this age or if they are given inappropriately, an infant's growth may falter. In many countries, the period of complementary feeding is the time of peak incidence of growth faltering, micronutrient deficiencies and infectious illnesses.<sup>2</sup>

Complementary feeding is the process starting other foods and liquids along with breast

milk, when breast milk is no longer sufficient to meet the nutritional requirements of infants. The target range for complementary feeding is generally taken to be 6 to 23 months of age.<sup>3</sup>

Even after complementary foods have been introduced, breastfeeding remains a critical source of nutrients for the young infant and child. It provides about one half of an infant's energy needs up to the age of one year, and up to one third during the second year of life. Breast milk continues to supply higher quality nutrients than complementary foods, and also protective factors. It is therefore recommended that breastfeeding on demand continues with adequate complementary feeding up to 2 years or beyond.

Complementary foods need to be nutritionally-adequate, safe, and appropriately fed in order to meet the young child's energy and nutrient needs. However, complementary feeding is often fraught with problems, with foods being too dilute, not fed often enough or in too small amounts, or replacing breast milk while being of an inferior quality. Both food and feeding practices influence the quality of complementary feeding, and mothers and families need support to practice good complementary feeding. Principles and problems of complementary feeding are given in Table 1.<sup>2</sup>

**When to introduce complementary feeding?**

Exclusive breastfeeding is ideal for baby for the first six months and potential health benefits of waiting until six months to introduce other

\* Former Editor-in Chief, Indian Pediatrics and Consultant Pediatrician, New Delhi.

**Table.1. Guiding principles for complementary feeding of the breastfed child**

- Practise exclusive breastfeeding from birth to 6 months of age, and introduce complementary foods at 6 months of age (180 days) while continuing to breastfeed.
- Continue frequent, on-demand breastfeeding until 2 years of age or beyond.
- Practise responsive feeding, applying the principles of psychosocial care.
- Practise good hygiene and proper food handling.
- Start at 6 months of age with small amounts of food and increase the quantity as the child gets older, while maintaining frequent breastfeeding.
- Gradually increase food consistency and variety as the infant grows older, adapting to the infant's requirements and abilities.
- Increase the number of times that the child is fed complementary foods as the child gets older.
- Feed a variety of nutrient-rich foods to ensure that all nutrient needs are met.
- Use fortified complementary foods or vitamin-mineral supplements for the infant, as needed
- Increase fluid intake during illness, including more frequent breastfeeding, and encourage the child to eat soft, favourite foods. After illness, give food more often than usual and encourage the child to eat more.

*Source:* Infant and young child feeding : model chapter for textbooks for medical students and allied health professionals. WHO 2009

foods outweigh any potential risks.<sup>4</sup> One major benefit is less risk of gastrointestinal infection when breastfeeding is given exclusively upto 6 months. Gut matures between 4-6 months and allergies are less when other foods are avoided till this period. On population basis no adverse effects on infant growth have been seen when solids were started at six months.<sup>5</sup> Six months is also the age when the baby is ready to sit up with support making intake of solids easier. Baby also moves the food to the back of his mouth rather than pushing it out with his tongue as earlier. Teeth may erupt helping the baby to chew.

### **How to go about starting the complementary feeding?**

There is increasing recognition that optimal complementary feeding depends not only on what

is fed, but also on how, when, where and by whom the child is fed. It is useful to practice responsive feeding, applying the principles of psycho-social care.<sup>6</sup>

- Infants should be fed directly and assisted when they feed by themselves, being sensitive to their hunger and satiety cues.
- Feeding should be done slowly and patiently, with encouragement to eat, but not forcing them.
- One food should be introduced at one time to help the baby get accustomed to the new taste and observe any problems.
- If children refuse many foods, experiment with different food combinations, tastes, textures and methods of encouragement

- Minimize distractions during meals if the child loses interest easily
- Feeding times are periods of learning and love; talk to children during feeding, with eye to eye contact.

### **What to do when baby spits out food every time**

Baby may spit out food in the beginning as the art of taking food without sucking, that is rolling the food back and swallowing may take little time. Using a tiny spoon and holding it between the lips so that the baby opens the mouth and can suck it off can be rewarding. Once cereals are started, some liquid feed may be given to wash it down. Boiled and cooled water can be given with spoon or directly by cup. As this is the period of learning experience, utmost patience on the part of care giver is essential.

### **What food should be given in the beginning?**

The staple cereal of the family should be used to make the first food for an infant. Porridge can be made with suji (semolina), broken wheat, atta (wheat flour), ground rice, ragi, millet etc, by using a little water or milk, if available. Roasted flour of any cereal can be mixed with boiled water, sugar and a little fat to make the first complementary food for the baby and could be started on the day the child becomes six months old. In case a family can not prepare the porridge for the infant separately, pieces of half chapati could be soaked in half a cup of milk or boiled water, mashed properly and fed to the baby after adding sugar and fat. Soaked and mashed chapatti could be passed through a sieve so as to get a soft semi-solid food for the infant.<sup>7</sup>

It is important to give new food in tiny amount. New food should be given when the baby is hungry but not too hungry. If a particular food

is not liked, it should not be forced upon but can be retried after few days. It is better to give new food at day time so that the baby can be watched for reaction throughout the day.

### **What other foods can be given to the baby?**

Fruits like banana, papaya, chikoo, mango, pears etc could be given pureed. Cauliflower, carrots, spinach, potato, beet, tomatoes, beans, pumpkin, peas are all good starters. They can be boiled and mashed. Yogurt may be included. The foods that can be gradually introduced are khichdi, overboiled rice or rice kanji, upama, sujee or raw kheer, ragi porridges, poha, (flattened rice) with curds, bread puddings, vegetable broth, bread or chapatti soaked in milk, dhokla, dosa, pongal, idli, missi (mixture of wheat flour, gram flour, spices and others), roti etc. This will allow the child to learn about different tastes with adaptation to the family menu. Introduce lumpy or granular foods and most tastes by about 9 to 10 months. Missing this age may lead to feeding fussiness later. So do not use mixers/grinders to make food semisolid/pasty.

Infants could also be given commercial infant foods at this age. Though they are easy to prepare, carry and serve, they have less variability and do not help in adapting the baby to family meals and best avoided.

Non vegetarian foods like fish, chicken etc can be introduced and should be cooked and pureed before giving. However, vegetarian diet can meet all the requirements of the child if properly planned.

Foods can be enriched by making a fermented porridge, use of germinated or sprouted flour and toasting of grains before grinding. Avoid giving drinks with low nutrient value, such as tea, coffee and sugary drinks.

## **What should be the consistency of the food?**

When consistency of food is not appropriate, the child may not consume in right amount leading to reduced intake. In the beginning the consistency should be thin, meaning semisolid food that flows freely from a spoon into baby's mouth. Solids can be diluted with breast milk, milk, boiled water, vegetable or dal water. But as the child grows older the consistency has to be thicker. Gradually increase food consistency and variety as the infant gets older, adapting to the infant's requirements and abilities. A thick porridge is more nutritious than a thin one. By 8 months most infants can also eat "finger foods" (snacks that can be eaten by children alone). By 12 months, most children can eat the same types of foods as consumed by the rest of the family. Avoid foods having shape or consistency that may cause them to become lodged in the trachea and may cause choking, such as nuts, grapes, raw carrots.

## **What should be the frequency of complementary foods?**

The appropriate number of feedings depends on the energy density of the local foods and the usual amounts consumed at each feeding. For the average healthy breastfed infant, meals of complementary foods should be provided 2-3 times per day at 6-8 months of age and 3-4 times per day at 9-11 and 4-5 times per day at 12-24 months of age (Table.2). If energy density or amount of food per meal is low, or the child is no longer breastfed, more frequent meals may be required.<sup>2</sup>

However, a meal frequency that is greater than necessary may lead to excessive displacement of breast milk and may be counterproductive. In addition, preparing and feeding five meals per day requires a considerable amount of time and effort by caregivers, which

may prompt them to hold prepared food over from one meal to the next, thereby potentially increasing the risk of microbial contamination. These considerations should be borne in mind when developing messages regarding meal frequency.

## **How to ensure adequate food intake for optimum growth**

Inadequate calorie intake results from low energy density of complementary foods and low frequency of feeding. Most of the foods are bulky and a child cannot eat more at a time. Hence it is important to give small energy dense feeds at frequent intervals to the child with a view to ensure adequate energy intake by the child. If necessary, energy density of foods given to infants and young children can be increased by adding a teaspoonful of oil or ghee in every feed. Contrary to popular belief in the community a young child can digest fat easily. Energy density can be increased by adding sugar or jaggery to the child's food.

Adequate total energy intake can also be ensured by addition of one to two nutritious snacks between the three main meals. Snacks are defined as foods eaten between meals, usually self-fed, convenient and easy to prepare (such as a piece of fruit or bread). Snacks are in addition to the meals and should not replace meals. They should not to be confused with foods such as sweets, chips or other processed foods.

## **What should be the amount of complementary food?**

Start at six months of age with small amounts of food and increase the quantity as the child gets older, while maintaining frequent breastfeeding. The total energy requirements of healthy, breastfed infants are approximately 615 kcal/d at 6-8 months, 686 kcal/d at 9-11 months, and 894 kcal/d at 12-23 months of age. The energy needs from complementary foods

for infants with “average” breast milk intake in developing countries are approximately 200 kcal per day at 6-8 months of age, 300 kcal per day at 9-11 months of age, and 550 kcal per day at 12-23 months of age.<sup>5</sup> If an infant is consuming more or less breast milk than the average, the amount needed from complementary foods will differ accordingly. In practice, it may not be possible to know the precise amount of breast milk consumed, or to measure the energy content of complementary foods to be offered. Thus, the amount of food to be offered should be based on the principles of responsive feeding while assuring that energy density and meal frequency are adequate to meet the child's needs.

### **Ensuring safety of complementary food**

Careful hygienic preparation and storage of complementary foods is crucial to prevent contamination. Personal hygiene plays an important role in feeding infants. If cleanliness is not observed, complementary feeding may do more harm than good to the child by introducing infections to the infant. It is, therefore, important that all foods prepared for young infants are handled in a way that they are free from any

germs. Some of the considerations while preparing foods for infants are as under:

- Hands should be washed with soap and water before handling the food as germs that cannot be seen in dirty hands can be passed on to the food.
- Utensils used should be scrubbed, washed well, dried and kept covered.
- Cooking kills most germs. The foods prepared for infants should be cooked properly so as to destroy harmful bacteria present, if any.
- After cooking, handle the food as little as possible and keep it in a covered container protected from dust and flies.
- Cooked foods should not be kept for more than one to two hours in hot climate unless there is a facility to store them at refrigeration temperature.
- The hands of both mother and child should be washed before feeding the child.

### **Feeding during and after illness**

During period from six months to two years of age, young children are prone for infections

**Table.2. Texture, frequency and amount of complementary food**

Age	Texture	Frequency	Amount in each meal
6-8 mo	Start with porridge, well mashed home foods	2-3 meals per day in addition to breastfeeding	Start with 25 ml gradually increasing to 50 ml
9-11 mo	Finely chopped or mashed home foods	3-4 meals in addition to breastfeeding.	100to 125 ml (half a cup/katorie)
12-23 mo	Family foods; may be chopped or mashed	4-5 meals in addition to breastfeeding.	150 to 250 ml(One katorie); also depends on energy density

If baby is not breastfed, give in addition: 200 to 400 ml of milk per day or 1-2 extra meals per day to give required amount of calories.



like diarrhoea, measles, cold, cough etc. A child may lose appetite and may refuse to eat, but the child needs adequate nutrition to recover from illness. Both breastfeeding and complementary feeding should continue during illness. Restriction or dilution of food should be discouraged. Time and care must be taken to help an ill child eat enough food. The infant can be encouraged to eat small quantities of food but more frequently and by offering foods the child likes to eat. Children with measles, diarrhoea and respiratory infections should eat plenty of vitamin A rich foods. After the illness when the child is recovering, the appetite returns. It is necessary to enable him to catch up growth with a nutritious diet with sufficient energy. The nutrient intake of child after illness can be easily increased by increasing one or two meals in the daily diet for a period of about a month or so.

### Points to Remember

- *Appropriate complementary feeding is vital for normal growth and development of baby after 6 months of age.*
- *Use of family foods for complementary feeding will allow the infant to learn about different tastes with adaptation to the family menu.*

### References

1. Dewey KG, Adu-Afarwuah S. Systematic review of the efficacy and effectiveness of complementary feeding interventions in developing countries. *Maternal and Child Nutrition*, 2008;4(s1):24–85.
2. PAHO/WHO. Guiding principles for complementary feeding of the breastfed child. Washington DC, Pan American Health Organization/World Health Organization, 2002.
3. Dewey KG. Nutrition, growth and complementary feeding of the breastfed infant. *Ped Clin N Am* 2001;48: 87-104.
4. Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding (Cochrane Review). *Cochrane Database Syst Rev* 2002; 1:CD003517.
5. WHO/UNICEF. Complementary feeding of young children in developing countries: a review of current scientific knowledge. Geneva: World Health Organization, WHO/NUT/98.1, 1998
6. Engle PL, Bentley M, Pelto G. The role of care in nutrition programmes: current research and a research agenda. *Proc Nutr Soc* 2000;59:25-23.
7. National Guidelines of Infant and Young Child Feeding. Ministry of Women and Child Development. 2006.

### CLIPPINGS

***Dimitriou G, et al. Prediction of respiratory failure in late-preterm infants with respiratory distress at birth. European Journal of Pediatrics, 08/06/2010***

Composite indices, such as A-aDO<sub>2</sub>, a/A ratio, and PaO<sub>2</sub>/FiO<sub>2</sub>, can reasonably predict respiratory failure in late-preterm neonates with respiratory distress, allowing for closer monitoring, early medical intervention, or transfer to a level III neonatal unit.

**INFANT AND CHILD NUTRITION****FEEDING OF LOW BIRTH WEIGHT BABIES**

**\* Naveen Jain**

**Abstract:** *Preterm and growth restricted babies are born low birth weight. Although our country has more growth restricted babies, studies published refer mostly to preterm babies. Breast milk is surely the safest feed and is associated with less infections and NEC. Neonatal units must make an effort to support mother and encourage breast feeding. Calcium, phosphorus, iron, vitamins A and D and some other vitamins must be supplemented in preterm babies fed breast milk. There is a protein, energy and sodium gap in RDA and breast milk. Human milk fortifiers may be able to bridge this gap without losing the benefits of breast milk, but not recommended as routine practice, currently. Even in the most preterm babies, feeding is started early and in small amounts (minimal enteral nutrition). This is associated with better feed tolerance and shorter time to full feed as compared to babies fed late. Studies have demonstrated safety of advancing feeds as fast as 30- 40 ml / kg / day in stable very preterm infants, although the studies were not powered to safely exclude risk of NEC. Orogastric feeding and transition to cup are preferred methods of feeding. The classical teaching of pre-feed aspirates as pointer to NEC is now challenged and may just indicate immaturity. Abdominal girth may provide the same information in a less*

*invasive assessment. Although there are special growth charts for preterm infants, debate is unresolved on ideal growth targets.*

**Keywords:** *Low birth weight, Nutrition, Enteral.*

Exclusive breast feeding is the best. But, in preterm babies, physiological immaturity of the baby, increased nutritional needs, concerns on growth faltering and possible effect on neurodevelopment necessitates a different approach than for babies born at term. Also, overzealous nutrition is likely to set up adult onset diseases like hypertension and diabetes.

Birth weight less than 2500 grams – LBW (low birth weight) can be due to prematurity / intra-uterine growth restriction or both. Both the group of babies are likely to have increased and different need for nutrients than babies born normal. Most studies are on preterm babies. Although growth restriction is the major problem in our country, we have limited data on the same.

Although many practices are now a part of “preterm nutrition”, only few have been systematically tested and proven.

This document attempts to answer the following questions regarding feeding of LBW babies.<sup>1,2</sup>

1. What to feed ?
2. What are the recommended nutrient supplements ?
3. Schedule - When to start feeding, frequency and how to increase ?

\* Consultant Neonatologist,  
Kerala Institute of Medical Sciences,  
Thiruvananthapuram.

4. Methods of feeding
5. Feed intolerance / NEC
6. What to monitor? – Blood glucose, growth
7. Duration of exclusive breast feeding and weaning

## 1. What to feed?

**a. Breast milk** (or mother's own expressed milk) remains the feed of choice even for the very preterm and severe IUGR babies. It is the safest milk and nutrients are most bio-available when compared to available alternatives.

There is strong and consistent evidence that breast feeding reduces the risk of NEC and sepsis and is associated with better neurodevelopmental outcomes. Serum lipid profile, pro-insulin levels and blood pressure are better in young adults who were preterm babies fed breast milk.

Every neonatal unit must encourage practices that enhance breast milk availability in settings where sickness separates the infant – mother dyad and when direct breast feeding is not immediately possible.

- Educate the mother and family on the importance of breast milk
- Allow mother to visit and touch the baby
- Encourage expressing breast milk as soon as mother is medically stable, every 4 hours.
- Breast feeding support group / lactation nurse and constant counselling are associated with higher breast feeding rates.
- Breast pumps are helpful, manual expression is equally effective.
- Kangaroo mother care is advocated
- Non-nutritive sucking in premature babies (who are not ready for safe suck, swallow and breath) is beneficial.

- Care of mother is vital - Rest, fluid, protein rich diet and reassurance regarding baby's health.
- Medications to mother – metoclopramide 10 mg thrice a day (with counselling and support for breast feeding) may improve lactation.

**b. Donor milk:** If the mother's breast milk is not sufficient, then the next best alternative is donor milk (banked human milk / other mother's drip milk). It has same advantages as mothers own breast milk with regards to its anti-infective properties, feed tolerance and reducing risk of NEC. Babies fed on breast milk or donor milk tends to have lesser weight and length gain in infancy. But, these seem to be only short term differences.

**c. Formula designed for preterm babies or nutrient enriched formulas:** Short term growth and neurodevelopment benefits were noted in babies fed on preterm formula when compared to term formula. Incidence of feed intolerance and infections is higher with formula feeding. Although hydrolysed protein based formulas have been considered to aid feed tolerance, studies haven't been able to demonstrate the same. Formula milk is devoid of biologically active products that breast milk has.

Other alternatives include (in decreasing order of preference) term formula and animal milk.

## 2. What are the recommended nutrient supplements?

The preterm breast milk can vary in nutrient content over the days after birth and also from mother to mother. Certain nutrients are lower in quantity in breast milk than needed by a preterm baby and in absence of supplementation will result in biochemical / clinical deficiency states. Unlike a formula with pre-determined

constituents, the preterm breast milk may have unknown but certain gap from RDA.

**a. Calcium phosphate :** 160 – 200 mg /kg /day of calcium as a phosphate salt with Ca: P ratio of 2: 1. Start when feeding of the preterm neonate has progressed to full feed, (100 ml / kg / day) and continue till term (empirical). Since the primary process in preterm baby is renal loss of phosphate, the replaced mineral must be a phosphate preparation.

**b. Iron :** 3-4 mg / kg / day. Start at 6 weeks of life and continue till one year. Starting early by 2 weeks seems to have no increased benefit. If babies have received red cell transfusions, the ferritin levels may be very high and iron therapy can be delayed.

**c. Vitamins:** Vitamin A 750 – 1500 U till preterm baby is 2000 grams in weight, Vitamin D 400 U till preterm baby is 2000 grams in weight and certain B vitamins are essential requirements.

Vitamin E: The requirements of daily intake has been reduced from 25 IU to 10-15 units. This quantity is present in multi-vitamins and separate Vit E may not be required.

**d. Protein:** The gap between high protein needs (3.5 - 4 gm/kg/day) and amount available from preterm milk (1.1 gm x 180 ml/kg/day) is not corrected without use of human milk fortifier (HMF) or preterm formula that is higher in protein content. Low blood urea is a useful biochemical marker that protein intake may be sub-optimal. HMF has the advantage of retaining the biological benefits of breast milk (over preterm formula). Studies have shown short term benefit in linear growth, but, this advantage is not long lasting. There is an increased risk of feed intolerance, infections and hypercalcemia in babies fed expressed milk supplemented with HMF. Most units use HMF selectively when

growth is faltering in spite of optimizing nutrition. Routine use of HMF cannot be recommended.

**e. Fat:** Method of expressing breast milk can have an impact on fat content. If mothers do not empty a breast completely, only foremilk that is poor in fat content will be collected. Practice of expressing breast milk and storing in fridge also causes fat loss as it solidifies. If continuous tube feeding is required, the nozzle of the syringe must be at upper side, as fat floats and will be lost if the nozzle is in lower position.

**f. MCT oil:** Increasing calorie intake without proportionate protein consumption is not helpful.

### **3. Schedule - When to start feeding, frequency, how to increase ?**

**Start early:** It is recognized that earlier initiation of feeding is safe and beneficial even in the smallest and sickest babies, although in amounts that may not contribute to nutritional value - minimal enteral nutrition / trophic feeds. (classically described as 1 ml/kg/hr over 1<sup>st</sup> week). Most neonatal units in India start small amounts (1-2 ml) of expressed breast milk 3-4 hourly even in the extreme preterm babies as early as on the first day. We advance feeds far rapidly and most babies between 1000–1500 grams would be on full feeds by an average of 10 days. It has not been studied whether this hurried enteral regimen is superior to parenteral nutrition or is a poor man's alternative. If breast milk is not available on 1<sup>st</sup> days, formula feeding may be better than gut starvation.

**No early feeding:** When gut perfusion is compromised in – utero (abnormal dopplers suggesting fetal distress), most neonatal units are reluctant to feed for first 1-2 days for fear of NEC. Also, whether IUGR babies need a different approach than appropriately “perfused gut”

LBW babies is not studied. Babies on inotropes and extremely preterm babies may have vulnerable guts and opinion on 1<sup>st</sup> day feeding is divided.

**Frequency:** Hourly feeding is better tolerated by the smallest babies (<1000 grams). Continuous feeds may be tried in this group as an alternative, if feed intolerance doesn't allow advancing feeds. Two hourly feeds seem to have an edge over 3 hourly feeding in preterm babies. Demand feeding may be tried once the baby is stable [even in preterm babies (as 32 weeks at birth), 3 hourly / demand feeding was successful].

**Advancing feeds:** Recent studies support earlier feeding and faster increase in feed volume (35 – 40 ml / kg / day), without increase in complication rate, e.g. NEC and other complications related to low birth weight. But, NEC being a uncommon complication would require a large population to demonstrate difference in incidence of NEC in the two feeding regimes.

#### 4. Methods of feeding

Direct breast feeding is considered unsafe till suck-swallow-breath coordination is established (32 – 34 weeks). This is seen to mature earlier in stable preterm babies.

**Orogastric vs nasogastric:** Babies who are smaller and sicker are given oro-gastric feeding (tube feeding). Although nasogastric tubes are easier to fix, oro-gastric feed has an advantage of allowing a free air-way and is preferred.

**Cup vs bottle:** The methods of transition from tube feeding to full breast feeding are cup / bottle feeding

##### a. Cup feeding

- i. Special cup with pout called “paladai” or gokarnam

##### ii. Katori and spoon

- b. Bottle feeding is discouraged; it decreases the chances that the baby will breast feed later.

#### 5. Feed intolerance

Can manifest as vomiting, abdominal distension, change in abdominal girth, increased and or altered pre-feed aspirates, apnea and systemic illness. All intolerance to feeds is not due to NEC. Traditionally large volume pre-feed aspirates or bilious / bloody aspirates were considered as pointers to NEC. They may be only reflection of immaturity of gut motility. Recent studies have suggested that routine aspiration before every feed may not only be of limited value, but also “disturbing”. These studies have proposed that measurement of abdominal girth may be just as useful a pointer.

The observations of general condition of the baby especially made by an experienced NICU nurse or parents (in units that allow free parent entry) may be currently, best guides on rapidity of advancing enteral feeds. (no evidence!)

**Prokinetic agents:** In babies more than 32 weeks gestation, erythromycin has shown some benefit, not currently a routine practice.

**Probiotics:** Have demonstrated decreased risk of NEC in some studies. Again use of breast milk may still be a better choice and probiotics cannot be recommended as a practice.

The low birth weight babies may not tolerate escalation of enteral feeds due to a) NEC, b) Prematurity of gut motility, c) GERD, d) Sepsis, e) Metabolic complications like hypokalemia.

#### 5. What to monitor?

- a. **Blood glucose:** Monitor blood glucose 4 hourly before a feed for first 48 hours and then

once daily (after 2 blood sugar levels have been normal till the baby is on IVF).

### **b. Growth**

Recommendations: Weigh the low birth weight infant daily in the first week of life and then twice weekly / weekly till term, monthly for the first year. Unwell babies especially <1500 grams may be weighed more frequently. Early growth is plotted on intra-uterine or postnatal (Ehrkaranz) growth charts for preterm, WHO / IAP growth charts after the baby is term. Corrected age should be used in the first year of life.

Growth is a surrogate for good health and adequate nutrition. Most low birth weight babies fall behind their similar aged term born babies (even after correcting for prematurity). Even aggressive parenteral nutrition and enriched post-discharge formula milk have not resulted in full catch up growth in VLBW babies.

The ideal end points of growth of babies born preterm have been derived from actual weight measurements of “healthy born” preterm babies at various gestations / ultrasound assessment of weight of unborn fetuses at various gestations (in-utero growth charts). These represent the “ideal growth” of preterm babies. Since, preterm babies invariably fare poorly on these charts, they overestimate malnutrition.

The postnatal growth charts are based on linear growth monitoring of babies born preterm. They show the postnatal loss of weight in first 1-2 weeks, seen as a dip in the growth curve. They have the benefit of representing the achievable targets with the current nutritional practices. Babies failing to keep up on these charts must be investigated for feeding or other medical problems.

**Caution:** Since NEC is an uncommon occurrence, no single study can ever be powered enough to pick a difference between care giving

methods or establish superiority of a newer care giving practice. Hence, caution should be exercised when adopting new ideas like “no pre-feed aspiration”, advancing feeds at 40 ml / kg / day in small babies and increasing feed volumes beyond 180 ml / kg.

**8. Duration of exclusive breast feeding and weaning:** In late preterm babies a study done at our organization demonstrated normal growth on exclusive breast feeding till 6 months.

### **Points to Remember**

- *Breast milk is the best food for low birth weight neonates. Its availability can be enhanced by bringing mothers into NICU, KMC, non-nutritive sucking, and constant support for breast feeding and use of breast pumps. Donor breast milk / banked milk are alternatives if mother's milk is not available.*
- *Start feeding early on day 1 even in small and sick babies (minimal enteral nutrition). Exceptions may be extremely preterm babies, babies in profound shock or if fetal doppler had shown reversal of flow in umbilical vessels.*
- *There are encouraging studies to suggest faster advancement of feeds, without a definite risk of NEC. This may solve our problems of having to decide between costly and difficult parenteral nutrition and malnutrition.*

### **References**

1. King C. What is new in enterally feeding the preterm infant? Arch Dis Child Fetal Neonatal Ed 2010; 95: F304-F308.
2. Edmond K, Bahl R. Optimal feeding of low birth weight infant: technical review. Whqlibdoc.who.int/publications/2006/9789241595094\_eng.pdf

## INFANT AND CHILD NUTRITION

### TOTAL PARENTERAL NUTRITION IN NEONATES

\* **Giridhar S**

**Abstract:** *Total parenteral nutrition allows us to meet a neonate's requirement for growth and development when their size or condition precludes enteral feeding. In order to replicate in utero growth rates, early and aggressive nutritional practices are currently advocated. Dextrose is initiated at endogenous hepatic glucose production rates of 6 mg/kg/min and increased gradually. Aminoacids are started from birth at high doses of 2-3 g/kg/d and have been shown to improve nitrogen balance. Lipid emulsions are started at 1g/kg/d and administered over 24 hours to avoid complications. Meticulous attention to asepsis, good nursing care and close biochemical monitoring are absolutely essential for successful parenteral nutritional therapy.*

**Keywords:** *Total parenteral nutrition, Aminoacids, Dextrose, Lipids.*

Nutrition management of neonates, particularly very low birth weight (VLBW) infants, poses a unique challenge and is fraught with risks. The nutritional goal is to achieve a postnatal growth at a rate that approximates the intrauterine growth. However translating principle into practice is not easy and in reality

the growth of VLBW infants lags considerably after birth.<sup>1</sup>

Feeding through the gastrointestinal tract is the preferred route for nutritional management. However enteral nutrition is often precluded by the presence of various factors. VLBW infants have an immature gastrointestinal tract, are almost always critically ill during the early days and are uniquely prone to infections. The logical conclusion would be to initiate parenteral nutrition, but this is often delayed for various reasons, most importantly, concerns about "tolerance" in the first days after birth for critically ill infants. This results in a lot of heterogeneity in practice. This period of early malnutrition during a vulnerable period slows somatic growth, including brain growth, and impairs neurocognitive development.<sup>2</sup> Today there is consensus that, if this impairment is to be avoided, the provision of early parenteral nutrition is vital.

Total parenteral nutrition (TPN) is the intravenous infusion of all nutrients necessary for metabolic requirements and growth. Usage of parenteral nutrition in newborns is ever increasing. With improving survival of extremely premature infants in India, need for parenteral nutrition is being widely recognized among health care providers.

### Indications

Parenteral nutrition is indicated when infants cannot tolerate enteral feedings or when there is a need to supplement enteral intake. There

---

\* Asst. Professor,  
Department of Neonatology,  
Kasturba Gandhi Hospital,  
Madras Medical College, Chennai.

is considerable variation in institutional practices but the generally accepted indications are given below

- All infants < 1 kg (consider starting on day 1 itself)
- Infants with birth weight 1-1.5 kg and not expected to receive significant enteral nutrition for more than 3 days.
- Infants with birth weight > 1.5 kg and not expected to receive significant enteral nutrition for more than 5 days
- Infants with NEC, surgical abdominal conditions, intractable diarrhoea and short bowel syndrome

### Nutritional requirements

The nutritional goal is to provide nutrients in amounts approximating those received by the fetus in utero and thereby to provide the substrate for uninterrupted growth and development.<sup>3</sup> The protein and energy requirement for premature infants are given in Table 1.<sup>4</sup> The daily recommended allowances for the parenterally fed infant should be less overall, as intravenous feeding bypasses the gut. In addition, activity levels in these infants are often minimal; energy costs of morbidity vary and cost of thermoregulation is small as the infants are usually nursed in a thermoneutral environment.

The most important goal of parenteral nutrition is to provide sufficient energy and nitrogen to prevent catabolism and to achieve a positive nitrogen balance. The nutritional goals of parenteral nutrition are summarized below

- To achieve a postnatal growth rate that approximates the intrauterine growth rate.
- To provide 90-110 Kcal/kg/day for optimum growth from non-protein sources.
- Achieve a ratio of non-protein calories per gm of aminoacids of 24 to 32.

- Carbohydrates to provide 60% and lipids 40% of the total non-protein calories.

For example if we deliver dextrose of 12 mg/kg/min, aminoacids 3 gm/kg/day and lipids at 3 gm/kg/day, the non-protein calories will be 88.7 Kcal/kg/day (66% from carbohydrate & 34% from lipids) and there will be 25.3 non-protein calories per gm of aminoacids infused.

### Components

**Fluids:** Fluids are started and increased as per standard guidelines. Parameters considered are insensible losses, urine output, weight loss/gain pattern and electrolytes.

**Carbohydrates:** Dextrose is the main energy substrate. It is available as 5, 10, 25 and 50% substrates. Energy density of dextrose is 3.4 kcal/g. Dextrose is initiated at endogenous hepatic glucose production rates in order to maintain euglycemia. Thus dextrose is started at 6 mg/kg/min (right from birth) and increased everyday by 2 mg/kg/min if there is no hyperglycemia to a maximum of 12-14 mg/kg/min. Infants on parenteral nutrition should have blood sugar maintained between 70 and 120 mg/dL. Sick premature infants can develop hyperglycemia even at low glucose infusion rates due to insulin dysregulation. Excessive carbohydrate delivery above the amount that can be oxidized for energy and glycogen storage will result in an increase in basal metabolic rate, fat deposition, cholestasis, hepatic steatosis, or overfeeding. If blood glucose levels are > 100 mg/dL, do not increase the glucose infusion rate and if blood glucose levels are > 150 mg/dL decrease the glucose infusion rate by 2 mg/kg/min. The maximum concentration of dextrose that can be used is 12.5% and 25% in the peripheral and the central lines respectively.

**Proteins:** The fetus receives a continuous supply of aminoacids (AA) through the umbilical cord.



In the event of premature delivery, ongoing delivery of AA is necessary for growth and neurodevelopment. Provision of exogenous AA prevents protein catabolism, improves glucose tolerance and prevents non-oliguric hyperkalemia. The protein requirements of preterm newborns are given in Table 1.<sup>4</sup> In spite of the recognition of the need for early AA supplementation, the practice, till recently, was to withhold AA. This was mainly due to the frequent metabolic derangements seen with usage of older AA solutions. Then, during the early 1990s, several studies demonstrated that administration of newer AA preparations beginning in the first 24–36h of life was safe and effective. As a consequence, but with a delay of several years, early administration of amino acids was gradually adopted into clinical practice during the late 1990s.<sup>5</sup> The low starting doses and step wise increase in AA is the next practice that is likely to change. In the recent past, three randomized controlled trials have evaluated higher early AA infusion rates in VLBW infants (Table 2). The results of these studies seem to suggest that commencement of TPN at higher amounts of AA is associated with improved nitrogen balance. The optimal AA solution should contain essential (valine, leucine, isoleucine, methionine, phenylalanine, threonine, lysine and histidine) and conditionally essential (cysteine, tyrosine, glutamine, arginine, proline, glycine and taurine) AAs, should not have excess of glycine and methionine and should not contain sorbitol. Two types of crystalline AA preparations are available in market: Aminoven (6% and 10%) and Primene (10%). AA yields 4 kcal per gm but this should not be included in the calorie count as AA should be utilized only for tissue growth. The current consensus is to administer AA mixed with dextrose from day 1 of life at 2-3 g/kg/d and advance by 0.5 g/kg/d to a maximum of 3 g/kg/day in term infants and 4 g/kg/d in preterm infants. The complications of amino

acids reported are hyperaminoacidemia, hyperammonemia, metabolic acidosis and azotemia. A rise in blood urea is not an adverse effect or sign of toxicity; rather it is a normal accompaniment of increased protein intake. More often it's because of fluid deficit and fluid therapy should be optimized. Hyperammonemia and metabolic acidosis are uncommon with present day AA solutions. However, protein intake is restricted to 0.5-1 g/kg/d when there is oliguria associated with serum creatinine > 1.5 mg/dL.

**Lipids:** Lipid emulsions serve as an energy dense substrate besides preventing or reversing essential fatty acid deficiency, which can occur as early as 72 hours after fat free nutrition. Lipid emulsions are isotonic with plasma (268 mOsm/L) and suitable to administer through both the central and peripheral vein and helps maintain patency. They also ensure co-administration of fat soluble vitamins. Intralipid (10% and 20%) is the available brand. It is prepared from soyabean and safflower oil, emulsified with egg yolk phospholipid, with glycerol added to achieve an isotonic solution. 10% lipid has an energy density of 1.1 kcal/ml and 20% lipid of 2 kcal/ml. Lipids are usually started at the rate of 1 g/kg/d beginning within 24 hours of life and gradually increased by 0.5 g/kg/d in < 1 kg babies and 1 g/kg/d for babies with weight > 1 kg till a maximum of 3 g/kg/day.<sup>9</sup> Lipid emulsions are administered separately from the rest of the parenteral nutrition solution and given as continuous infusion over 24 hours. Infusion rate should not exceed 150 mg/kg/hr (i.e. 3.6 gm/kg/d). This is because free fatty acids released after lipolysis of the parenteral lipids infused at higher rates may displace bilirubin from albumin binding sites, resulting in increased unbound bilirubin and an increased risk of kernicterus. A targeted molar free fatty acid to albumin ratio < 6 prevents generation of free

**Table.1 Protein and energy requirements of premature infants**

Body weight (g)	500 – 700	700 – 900	900 – 1200	1200 – 1500	1500 - 1800
Fetal weight gain (g/kg/d)	21	20	19	18	16
<i>Protein (g/kg/d)</i>					
Inevitable loss	1.0	1.0	1.0	1.0	1.0
Growth	2.5	2.5	2.5	2.4	2.2
Required intake					
Parenteral	3.5	3.5	3.5	3.4	3.2
Enteral	4.0	4.0	4.0	3.9	3.6
<i>Energy (Kcal/kg/d)</i>					
Loss (expenditure)	60	60	65	70	70
Growth	29	32	36	38	39
Required intake					
Parenteral	89	92	101	108	109
Enteral	105	108	119	127	128

**Table.2 Summary of recently published studies on the effects of supplemented amino acids shortly after birth on nitrogen balance**

Study	No of infants	Birth weight (g)	Start of protein	Protein intake (g/kg/d)	Nitrogen balance (g/kg/d)
Thureen et al 2003 (6)	13	945 ± 187	24 hours	0.85	-41.6
	15	947±232		2.65	185.6
Ibrahim et al 2004 (7)	16	968±244	< 2 hours	0	-180
	16	846±261		3.5	400
te Braake et al 2005 (8)	69	989±252	< 2 hours	0.4	-84
	66	1039±235		2.4	145

bilirubin. 20% lipid emulsions are preferred over 10% emulsions as higher phospholipid content in 10% lipid interferes with triglyceride (TG) clearance leading to higher TG and cholesterol values. Clearance is monitored by measuring plasma TG levels. Serum TG value should be checked once lipids of 3 g/kg/d is reached and subsequently at weekly intervals. It should also be checked if the plasma looks visibly lipemic and in presence of severe sepsis. Maximal acceptable level ranges from 150 to 200 mg/dL. If the value is between 150 to 200 do not increase the dose and if it is above 200 mg/dL stop it altogether. Intravenous lipid emulsions in the recommended infusion rate (< 150 mg/kg/hr) do not seem to affect platelet number or function, or oxygenation in infants who have severe acute respiratory failure with or without pulmonary hypertension. However, in neonates with acute respiratory failure without pulmonary hypertension, lipids should be limited to 2 gm/kg/d, and in neonates with pulmonary hypertension, lipids should be avoided during critical periods with lability in oxygenation. Other concerns about lipid infusions include increased risk of coagulase negative staphylococcal sepsis, free radical stress and fat embolism. Lipid emulsion should be protected by aluminum foils or carbon sheets during phototherapy to decrease the formation of hydroperoxides. Carnitine at an intravenous dosage of 8 to 10 mg/kg to increase oxidation of fat is recommended only for low-birthweight infants who require parenteral nutrition over 2 to 4 weeks.

## Electrolytes

**Sodium:** The normal requirement is 3 mEq/kg/d. VLBW infants may need as much as 5-6 mEq/kg/day because of their poor renal tubular absorption. It should be added once the cumulative weight loss is > 5%. It is added as normal saline 0.9% (1ml= 0.15 mEq) or 3% NaCl (1ml= 0.5mEq).

**Potassium:** The normal requirement is 2 mEq/kg/d. It is provided as 15% potassium chloride solution (1ml= 2 mEq).

**Chloride:** The normal requirement is 3-6 mEq/kg/d. This amount is delivered automatically as constituent of sodium chloride or potassium chloride.

**Calcium:** Normal requirement is 36-72 mg/kg/day of elemental calcium. This is given as 10% calcium gluconate injection (1ml= 9 mg of elemental calcium) or 10% calcium chloride injection (1ml=27 mg of elemental calcium).

**Phosphorus:** Currently intravenous phosphate solutions are not available in India.

**Magnesium:** The usual dose is 1 mEq/kg/d and is given as 0.25 ml/kg/d of 50% magnesium sulphate.

**Trace elements (Zn, Cu, Mn, Se) :** Zinc is required from day 1; others are required after 2 weeks. If the baby is getting partial enteral feeds, these trace elements are not required. Currently I.V. zinc and trace elements are not available in India. In patients on TPN, giving 10 ml/kg of fresh frozen plasma every 4th day can provide these trace elements.

**Vitamins:** Multivitamin injection (MVI) pediatric is designed for pediatric use but is not available in India. The adult MVI solution is available. The dose is 1 ml/kg/d. It does not provide vitamin K, B12, biotin and folic acid. Therefore administration of a weekly dose of vitamin K (0.5-1 ml/kg I.M.) and vitamin B12 (10 µg/kg I.M.) is necessary. About 80% of vitamin A and 30% of vitamin D and E are lost during administration owing to adherence to tubings and photodegradation. By adding the vitamin preparation into fat emulsion instead of AA-dextrose mixture, fat soluble vitamin losses can be reduced.

## Preparation

TPN should be prepared only under strict aseptic precaution (wear gowns, mask and gloves) by trained staff. Use of laminar flow hoods is advisable. Dextrose, AA, electrolytes are mixed to form one solution in a glass bottle (Fig.1). Lipids are drawn in another syringe and vitamins are added. Both solutions can be administered through the same IV line by means of a 3-way connector. Use bacterial filter in the tubing coming from dextrose-AA mixture just before the 3-way connector, to prevent air bubbles and bacteria entering the venous line. Change of the tubings and bottles after every 24 hours is recommended and periodically assess the IV site for any extravasation. Avoid breakage of the line through which the TPN is infused. Use separate peripheral cannula for antibiotics, blood transfusion or other drugs. The addition of heparin (0.5 units/ml) reduces the incidence of phlebitis and thrombosis of both peripheral and central lines. Because of the effects of

heparin on stability of calcium and lipids, it should not be added as a routine. Steps for calculation of TPN are shown in Fig.2.

## Administration

TPN can be delivered through peripheral or central venous lines. Central venous access is required if need for parenteral nutrition exceeds 5 days or the osmolality of the infusate exceeds 900 mOsm/L. Osmolarity is primarily determined by the dextrose concentration. A dextrose concentration greater than 12.5% has an acidic pH and can be irritating to the peripheral veins. Use of peripherally inserted central catheters has facilitated administration of parenteral nutrition while avoiding many potential complications of surgically inserted central lines. Parenteral nutrition can be administered through the umbilical vein. Administration of lipids through same IV line offers protection against phlebitis or potential loss of the access sites.

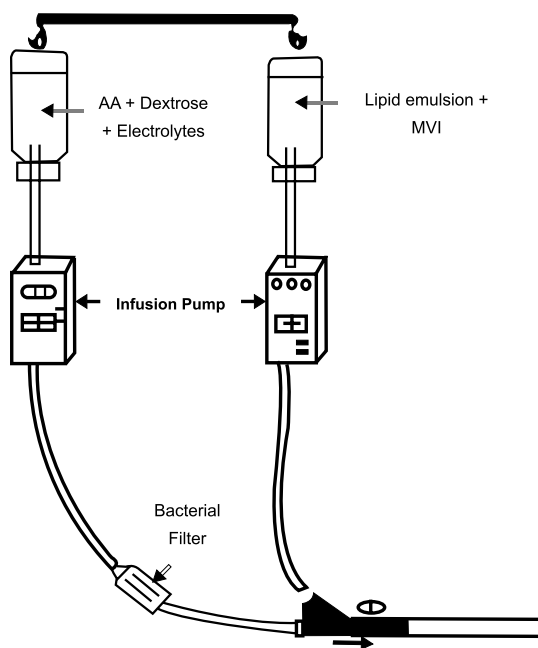
## Monitoring

Meticulous monitoring is needed in a neonate receiving TPN. Monitoring protocol is summarized in Table 3. Monitoring should be more frequent in the initial stages. Once a steady metabolic stage has been achieved, monitoring can be reduced to once a week.

## Complications

Besides infection and catheter related complications, following are the important metabolic complications of parenteral nutrition

- Hypoglycemia, hyperglycemia, glycosuria, hyperosmolality and dehydration are related to low or excessive carbohydrate infusion. If blood sugar >200 mg/dL or glycosuria: start insulin infusion @ 0.05 U/kg/h and gradually increase as required to a maximum of 0.2 U/kg/h. If blood sugar remains high, stop TPN and start isolyte-P with glucose @ 4 mg/kg/min.



**Fig.1. TPN infusion assembly**

**Fig.2. Steps for calculation of TPN**

I. Total fluid intake (TFR): \_\_\_\_ ml/kg/d x \_\_\_\_ kg = \_\_\_\_ ml/d

Total TPN volume:

I – (Feed vol+ drug vol+ arterial line vol+ blood products) = \_\_\_\_ ml/d

II. Fat volume: \_\_\_\_ gm/kg/d x \_\_\_\_ kg ÷ 0.2\* = \_\_\_\_ ml/d

(\*Lipid concentration per ml of 20% lipid, use 0.1 if using 10% lipid)

III. Glucose-AA volume: I – II = \_\_\_\_ ml/d

IV. Glucose-AA volume to be prepared: III x 1.2# = \_\_\_\_ ml

(#1.2 was multiplied to have 20% extra volume for wastage factor)

V. Additive volume:

a. Amino acids \_\_\_\_ g/kg/d x \_\_\_\_ kg x 10 x 1.2 = \_\_\_\_ ml

b. Sodium \_\_\_\_ mEq/kg/d x \_\_\_\_ kg x 6.6\$ x 1.2 = \_\_\_\_ ml

(\$ 6.6 ml of 0.9% NaCl = 1 mEq of Na, multiply by 2 if 3% NaCl used)

c. Potassium \_\_\_\_ mEq/kg/d x \_\_\_\_ kg x 0.5 x 1.2 = \_\_\_\_ ml

d. Calcium gluconate 4 ml/kg/day x \_\_\_\_ kg x 1.2 = \_\_\_\_ ml

e. MgSO<sub>4</sub> 0.25 ml/kg/d x \_\_\_\_ kg x 1.2 = \_\_\_\_ ml

Total additive volume (a + b + c + d + e) = \_\_\_\_ ml

VI. Dextrose volume: = IV-V = \_\_\_\_ ml

VII. Dextrose amount: \_\_\_\_ mg/kg/min x 60 x 24 x 1.2 = \_\_\_\_ gm/d

VIII. Calculate the volumes of 10% and 25% dextrose to make VI volume with VII dextrose amount

10% Dextrose = \_\_\_\_ ml

25% Dextrose = \_\_\_\_ ml

IX. Add 1 ml/kg/day of MVI in the fat volume= \_\_\_\_ ml

Final TPN order to infuse

Line 1: Lipids \_\_\_\_ ml/hr for 24 hours (II ÷ 24)

Line 2: Glucose-AA \_\_\_\_ ml/hr for 24 hours (III ÷ 24)

**Table 3. TPN monitoring schedule**

Parameter	Initially (1st week)	Later
<b><i>Clinical</i></b>		
Weight	Daily	Daily
Head circumference, length	Weekly	Weekly
Urine output	8 hourly	8 hourly
IV site	1 hourly	1 hourly
<b><i>Laboratory</i></b>		
Urine specific gravity/glucose	Each specimen	8 hourly
Blood glucose	6 hourly	12-24 hourly
Serum Na/K, urea, creatinine, calcium, pH, hematocrit, Inspection for lipemia	Daily	Twice weekly
Liver function tests, serum proteins, serum triglycerides, blood counts/ C-reactive protein/ urine for fungus	Weekly	Weekly

- Metabolic acidosis, azotemia, hyperammonemia are related to protein intolerance.
- Hyperlipidemia, abnormal platelet adhesion, increased risk of bilirubin encephalopathy are attributed to lipids.
- Metabolic bone disease due to phosphorus and mineral deficiency and trace elements deficiency could occur after prolonged TPN.
- Cholestasis and abnormal liver enzymes. Etiology is multifactorial.<sup>10</sup> Gamma glutamyltranspeptidase and alkaline phosphatase are initially raised followed by rise in direct bilirubin and transaminases. Management is controversial. Most institutions decrease AA to 1g/kg/day

but continue lipids and maintain triglycerides <150mg/dL. A septic work up is performed and appropriate antibiotics are started. Oral ursodeoxycholic acid at 15-20 mg/kg/day in 3 divided doses can be started. Starting minimal enteral nutrition as early as possible can prevent TPN associated cholestasis.

### **Weaning of parenteral nutrition**

It is important to start trophic feeds as soon as the baby is hemodynamically stable. Unless contraindicated, attempts should be made to administer sub-nutritive amounts of oral feeds along with parenteral nutrition. The rate of TPN is decreased in tandem with rate of advancement of enteral feed to achieve the desired total fluid

volume. When the caloric intake by enteral feeding is at least 50% of the total intake, discontinue vitamins, calcium, phosphorus, magnesium, and proteins in the TPN. Subsequently lower the dextrose concentration by 1-2% per day until glucose infusion rate of 4 mg/kg/min is reached and also taper lipid infusion rate by 1 g/kg/d. Discontinue TPN when 2/3rd of total calories can be administered through enteral route.

## Summary

TPN should be promptly instituted in any infant in whom full enteral nutrition cannot be achieved in 3-5 days. TPN should be started from day 1 and early high dose AA supplementation can reverse negative nitrogen balance. AA, dextrose and electrolytes are mixed but administered separately from lipid emulsions. Since TPN is potentially dangerous, complications should be meticulously looked for. Starting trophic feeds with TPN prevents many important TPN related complications.

## Points to Remember

- *Any very low birth infant who is not expected to receive enteral nutrition for more than three days and any other infant for more than five days is a candidate for total parenteral nutrition.*
- *Candidate infants should receive parenteral nutrition from day 1 of life*
- *Aminoacids should be instituted at starting doses of 2-3 g/kg/day.*
- *Lipid infusions should be administered separate from other solutions with multivitamins over 24 hours at doses  $\leq$  3g/kg/day.*
- *Strict adherence to aseptic precautions should be followed during preparation and administration of TPN.*

## References

1. Lemons JA, Bauer CR, Oh W, Korones SB, Papile LA, Stoll BJ, et al. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, January 1995 through December 1996. *Pediatrics* 2001;107(1):E1.
2. Cooke RW, Foulder-Hughes L. Growth impairment in very preterm and cognitive and motor performance at 7 years of age. *Arch Dis Child* 2003;88(6):482-487.
3. American Academy of Pediatrics, Committee on Nutrition. Nutritional needs of the preterm infant. In: *Pediatric Nutrition Handbook*. 5th Edn. Elk Grove Village, IL: American Academy of Pediatrics 2003;pp23-46.
4. Ziegler EE. Protein requirements of very low birth weight infants. *J Pediatr Gastroenterol Nutr* 2007;45 Suppl 3:S170-174.
5. Kashyap S. Is the early and aggressive administration of protein to very low birth weight infants safe and efficacious? *Curr Opin Pediatr* 2008;20(2):132-136.
6. Thureen PJ, Melara D, Fennessey PV, Hay WW Jr. Effect of low versus high intravenous amino acid intake on very low birth weight infants in the early neonatal period. *Pediatr Res* 2003;53(1):24-32.
7. Ibrahim HM, Jeroudi MA, Baier RJ, Dhanireddy R, Krouskop RW. Aggressive early total parenteral nutrition in low-birth-weight infants. *J Perinatol* 2004;24(8):482-486.
8. te Braake FW, van den Akker CH, Wattimena DJ, Huijman JG, van Goudoever JB. Amino acid administration to premature infants directly after birth. *J Pediatr* 2005;147(4):457-461.
9. Adamkin. Use of intravenous lipids in very low-birthweight infants. *Neoreviews* 2007;8:543-546.
10. Hsieh MH, Pai W, Tseng HI, Yang SN, Lu CC, Chen HL. Parenteral nutrition-associated cholestasis in premature babies: risk factors and predictors. *Pediatr Neonatol* 2009;50:202-207.

**INFANT AND CHILD NUTRITION**

## **TREATMENT OF COMMON NUTRITIONAL DEFICIENCIES**

\* **Prema A**

**Abstract:** *Most prevalent nutritional deficiency is iron deficiency anemia, treated with daily ferrous salt (better absorbed and cost effective). Megaloblastic anemia is less common and treated with injection vitamin B12 and oral folic acid (FA). High risk group for folate deficiency should be given FA supplementation.*

*Xerophthalmia is treated with oral vitamin A concentrate and one should remember signs and symptoms of hypervitaminosis.*

*Nutritional rickets is treated with parenteral vitamin D followed by oral calcium supplements. Eventhough specific vitamin B deficiency is diagnosed, it is advisable to treat with entire B complex vitamins.*

*Nutrition education, diet, food fortification with micronutrients play a major role in preventing nutritional deficiencies.*

**Keywords:** *Vitamins, Anemia, Iron deficiency, Vitamin A deficiency, Diet.*

Since the prevalence of gross under-nutrition (eg. Kwashiorkor) is on the decline, the attention has shifted from inadequate protein and energy, to inadequate micro nutrients. This shift of focus concerns appropriate intervention and

prevention strategies. This chapter deals with treatment of common nutritional deficiencies like vitamin A, D, B complex vitamins (especially B12 and folic acid) and iron.

### **Treatment of vitamin A deficiency**

Xerophthalmia is a medical emergency. If untreated, it can cause corneal destruction and secondary bacterial sepsis, which can result in blindness or death. Oral vitamin A concentrate is the preferred treatment as it is safe, cheap and highly effective. The underlying systemic illness and protein-energy malnutrition should also be treated.

### **Treatment schedule**

Immediately upon diagnosis and next day, 2 lakh units of oral Vitamin A (110 mg retinyl palmitate or 66 mg retinyl acetate) given. Third dose is given after 1-4 weeks in the same dosage (to replenish liver reserves).

### **Note:**

- 1) In 6 – 11 months, half the dose is given.
- 2) In <6 months, quarter the dose is given.
- 3) Parenteral (IM) vitamin A can be given as an alternate to oral Vitamin A in some related instances. Intramuscular Vitamin A is needed especially
  - a) When children with severe stomatitis (seen in severe measles), cannot swallow,
  - b) In case of persistent vomiting or
  - c) Severe malabsorption (e.g: cystic fibrosis).

---

\* Professor & HOD, Pediatrics,  
SRM Medical College Hospital and  
Research Centre, Chennai.



Oil miscible preparations of Vitamin A should never be given parenterally because they are poorly absorbed from the injection site. Water miscible preparations of Vitamin A when given intramuscularly do not serve the purpose of replenishing liver stores. So, they should always be followed with oral vitamin A concentrates.

**Keratomalacia:** Usually treated with intramuscular vitamin A 5000 IU / kg / day for 5 days followed by 2500 IU / day till recovery. In the presence of corneal involvement, broad-spectrum antibiotic eye ointment should be applied along with systemic antibiotics to reduce the risk of secondary bacterial infection, especially with staphylococci and pseudomonas. Every effort should be made to preserve the structural integrity of the eye. When cornea is weakened (keratomalacia or ulceration or thinning), protecting the eye from undue pressure examinations and application of drugs and change of dressing should be performed with utmost care. The eye should be kept covered at all other times by firm plastic / metal shield. If necessary, child's hands can be restrained.

Phrynoderma is classically thought to result from vitamin A deficiency, although deficiencies in vitamin B complex, Vitamin E and essential fatty acid have been implicated.

Treatment with Vitamin A along with B complex and fatty acid (fish liver oils, soyabean oil, salflower oil, corn oil, palm oil) unprocessed cereal grains and fats are tried.

**Treatment during pregnancy:** Vitamin A is a class X teratogen. The safe limit for oral vitamin A is 10000 IU /day. This dose can be safely administered throughout pregnancy. If there is night blindness or Bitot's spots, 10000 IU of vitamin A is given daily for at least 2 weeks. If corneal lesions are present, the risk of blindness overweighs the risk of congenital

defects and so is treated with the full therapeutic schedule.

**High risk groups:** Severe infections especially measles, malaria and chicken pox can cause acute decompensation in vitamin A status. The following high-risk groups are presumed to be vitamin A deficient regardless of their appearance.

- a) All cases of measles where measles case fatality rates are >1% or where vitamin A deficiency is a significant public health problem.
- b) Severe complicated life threatening measles.
- c) Measles in a child < 2 years of age.

These children are given the age appropriate dose of vitamin A for 2 successive days. In case of severe acute malnutrition (SAM) (defined as weight for height / length is < - 3 SD or mid – arm circumference < 11.5 cm), the complete treatment schedule is instituted. Additionally, repeat doses of vitamin A are given every 2-4 weeks till recovery.

In other risk groups like chronic or recurrent diarrhea, LRI or otitis media, the first dose alone is given. Prophylaxis trials and one trial on therapy reveal that there is neither therapeutic nor prophylactic benefit of vitamin A supplementation for childhood community acquired pneumonia.

**Diet therapy:** Even if mega doses of vitamin A are given for treatment, always initiate vitamin A rich diet, either directly as vitamin A or as provitamin A ( $\beta$  – carotenoids). Vitamin A rich foods are fish and animal liver, fish liver oil, egg yolk, dairy products, etc (Table 1).

**Health education:** The most logical and least expensive way of preventing recurrence of vitamin A deficiency is by educating the mother on diet rich in vitamin A. As a rough guide, a handful of fresh green/red varieties of amaranth

(40g) or drumstick leaves (35g) or a medium sized mango (100g) will provide the daily requirement of toddlers/ preschool children. Green leafy vegetables should be boiled until tender to increase digestibility and remove toxic substances. Green leafy vegetables should be shredded (mashed or sieved for infants) and mixed with staple food to encourage consumption. They can be combined with small amount of edible oil to increase absorption. The mothers should be stressed upon prolongation of breastfeeding and early dietary enhancement with vitamin A rich foods. Simple wall posters in clinic can help.

**Periodic supplementation:** Pulse doses of vitamin A are given every 6 months in areas where vitamin A deficiency is a significant public health problem, which is defined as the incidence of

- Night blindness >1%
- Bitot's spots > 0.5%
- Corneal scar/ ulcer > 0.05% or
- Keratomalacia > 0.01%

In India, the prevalence of vitamin A deficiency is 6%. According to the vitamin A prophylaxis program, children between 9 months and 3 years are given five age appropriate mega doses of oral vitamin A concentrate at 6 months interval. The first two doses are integrated with measles vaccination and DPT first booster.

Fortification of common food items (e.g. milk) is also an option to prevent recurrence. Fortification of sugar is practiced in Costa Rica. It has some practical difficulties due to varied consumption of the fortified food item among various economic groups and also due to its altered taste and odour.

**Hypervitaminosis A:** Some manifestations of vitamin A deficiency are not reversible, eg: Bitot's spots. If they are given frequent doses

of vitamin A, it can cause hypervitaminosis A. Also larger doses (for age) or overzealous ingestion of oil pearls can cause hypervitaminosis A (also called as Gulf syndrome). It can manifest as bulging fontanell, headache, vomiting, seizures, pseudotumour cerebri, changes in mental activity, pruritus, anorexia, hyperostosis of long bones (tender swelling of tibia), alopecia, craniotabes, desquamation of palms and soles, seborrheic cutaneous lesions and fissures in the corners of the mouth.

Excess ingestion of  $\beta$  – carotenoids can cause carotenemia, which is not toxic but manifests as yellowish discoloration of skin and plasma. It does not cause scleral discoloration. It does not result in hypervitaminosis A as the enzyme responsible for the conversion of  $\beta$  – carotenoids to vitamin A (dioxxygenase) is inducible i.e. when vitamin A stores are replete, the enzyme activity is suppressed and no vitamin A is formed from  $\beta$  – carotenoids.

### **Treatment of megaloblastic anemia due to B12 and folate deficiencies**

The megaloblastic anemias usually develop gradually. Most patients who have adjusted to low hemoglobin levels and do not require transfusions, are treated with cobalamin and folate therapy.

- Cobalamin (1000 $\mu$ g) should be given parenterally daily for 2 weeks, then weekly until the hematocrit value is normal and then monthly for life. This dose is large, but it may be required for some patients. Patients with neurological complications should receive cobalamin at 1000 $\mu$ g (more in some cases) every day for 2 weeks, then twice a week for 6 months, and monthly for life.
- Oral cobalamin (1000 $\mu$ g) can be administered to patients with hemophilia (as intramuscular injections to be avoided)

**Table.1. RDA, food sources and deficiency signs of nutrients**

VITAMIN	RDA / DAY	FOOD SOURCES	DEFICIENCY
Vitamin A	1500 IU (500 µg)	Liver, Fish, Dairy products, kidney, eggs, and green and yellow Vegetables from provitamin A carotenoids & β - carotenoids are abundant in lightly cooked green leafy vegetables especially drumstick leaves, amaranths, cassava leaves, red palm oil and red, yellow & orange coloured fruits its like papaya, mango, pumpkin, squash, etc.	Night blindness, Keratomalacia
Vitamin D	400 IU (10 µg)	Vitamin D – fortified dairy products (present as cholecalciferol from animal sources and ergocalciferol, or Vitamin D2, from plants and fungi).	Rickets
Thiamin (B1)	0.5 – 1.5 mg	Whole- grain products and refined- grain products fortified with thiamin & yeast.	Beriberi, CCF, neuritis, Encephalopathy
Riboflavin (B2)	0.5 – 1.5 mg	Milk, milk drinks, bread products, and fortified cereals, green leafy vegetables, egg.	Cheilosis, stomatitis, glossitis, neovascularisation of cornea, nasolabial dyssebacea
Pyridoxine (B6)	0.5 – 1.5 mg	Fortified ready –to- eat cereals, meat, fish, poultry, white potatoes, starchy vegetables, noncitrus fruits, beef liver, organ meats, soy-based meat, substitutes.	Neuritis, convulsion, anaemia
Niacin	5 – 15 mg	Meat, fish, poultry, enriched whole- grain breads and bread products, fortified ready –to- eat cereals, liver & nuts.	Pellagra, diarrhoea, dermatitis, dementia
Biotin		Liver	
Folate (folic acid and folacin)	50 – 150 µg	Folate – fortified cereal, grains, and vegetables such as green beans and peas, Asparagus, broccoli melons, liver, lettuce, mushrooms, spinach.	Megaloblastic anaemia
Cyanocobalamin (Vitamin B12)	0.5 – 1.5 µg	Animal products such as red meat, poultry, fish, eggs, and dairy, as well as cereals fortified with Vitamin B12	Megaloblastic anaemia, CNS degeneration
Vitamin C		Fruits and vegetables, especially citrus fruits, tomatoes juice, potatoes, broccoli, kiwi, yams, strawberries, melons.	

and to patients with severe malnutrition or those who have abnormalities in the terminal ileum. Oral dosages should be monitored for desired response, since absorption can be variable and may be insufficient in some patients.

- Folate (1-5 mg) should be administered orally. If this is difficult, comparable doses can be administered parenterally.

- Cobalamin deficiency does not respond to daily folate doses of 100-400 µg (physiological dose), but this dose results in complete response in patients with folate deficiency. Under no circumstances should therapeutic doses of folate (1-5mg/d) be administered without cobalamin. The reason is that folate therapy corrects the anemia, but folate does not correct a cobalamin-

induced neurological disorder and thus results in the progression of neuropsychiatric complications.

- **Prophylactic folate therapy** (1mg/d) should be administered during pregnancy and the perinatal period to meet the increased demand for folate by the fetus and during lactation. Folate should also be given daily to patients with chronic hemolysis. Folate therapy is currently recommended for individuals with high levels of homocysteine who have a propensity for thromboembolic disease, to prevent this complication. Multivitamins that contain folate have been recommended for elderly persons.
- Fortification of foods with folic acid has been recommended to prevent hyperhomocysteinemia-related thrombosis, folate deficiency-related neoplasia and fetal abnormalities.
- However, those not favouring the fortification plan are concerned that folate-fortified foods given to patients with unrecognized cobalamin deficiencies will increase the frequency of cobalamin-induced neuropsychiatric disorders.
- Blind loop syndrome should be treated with antibiotics.
- Patients with TCII deficiency may require higher doses of cobalamin.
- Tropical sprue should be treated with cobalamin and folate.
- Acute megaloblastic anemias due to nitrous oxide exposure can be treated with folate (5mg/d) and cobalamin (1mg/IM).
- Fish tapeworm infection, pancreatitis, Zollinger-Ellison syndrome, and inborn errors should be treated with appropriate measures.

## Treatment of iron deficiency anemia

According to third National Family Health Survey [NFHS-3 2005-06], the prevalence of anemia among under 5 children is 70%. The National Nutritional Anemia Control programme [NNACP] recommends routine supplementation with iron [20 mg] and folic acid [100 µg] to all children aged 6-60 months, for 100 days per year regardless of iron status

**Aim of therapy is to:** a) restore Hb level, b) replenish Iron stores and c) treat etiological factors

**Iron therapy :** Oral therapy 3-6 mg/day (ferrous sulfate containing 20% iron) preferably 1 hour before meals, continued for 8 weeks after normal blood values to replenish iron stores.

Concurrent administration of Vitamin C enhances absorption. Food rich in phytates (cereals) and phosphates (milk) reduce absorption. Hb rise following iron therapy is around 1g/dL/week.

Poor response to therapy can be due to a) poor tolerance/compliance, b) malabsorption state, infection, c) persistent bleeding, d) H.Pylori infection (known to reduce iron absorption).

Parenteral iron therapy is seldom indicated in children.

## Iron preparations

- Simple ferrous salts (sulphate, gluconate, fumarate)
- Iron polymaltose complex-Equal absorption, fewer side effects, very expensive.
- Prolonged release ferrous sulphate enhanced absorption with fewer side effects.
- Carbonyl iron.
- Iron orotransferins
- Ferrous sulphate is superior to others.

**Table.2. Sources and requirement of iron**

Element	Sources	Requirement	Remarks & toxicity
<b>Iron</b>	Fish, meat group, cereals, legumes, greens, jaggery, cooking in iron vessels, asafetida, turmeric, dates, watermelon etc., Infant cereal iron fortified, prune juice, liver, egg, fish, dried beans, peanut butter, soya bean, apricot, oat meal, raisine, spinach oyster, fresh corn broccoli, onion, celery cucumber, peas, bread crump's.	<b>Prophylaxis:</b> 2mg/kg/day. Older children 10 – 20mg/day. <b>Treatment:</b> Oral, 3– 6 mg/kg/day, for 3 – 4 mos. Parental: Weight in kg x Hb deficit in g/dL x 2.5+25% for stores. Packed cell transfusion: 5 –10 ml/kg. Always treat the cause.	<ul style="list-style-type: none"> <li>• Oxalates, phytates &amp; Zn inhibit absorption.</li> <li>• Vit C, cobalt and acid medium increase absorption.</li> <li>• Toxicity: GI upset, quiescent phase, metabolic derangement, acidosis, hypoglycemia, hepatic failure and strictures.</li> <li>- Management: Gastric lavage with soda bicarb. and desferrioxamine. Desferal 50 mg/kg followed by 10 mg/kg/hr x 24 hours, IV.</li> <li>- S. Iron &gt; 1800 µg% is fatal.</li> </ul>

**Prevention :** Measures that prevent iron deficiency anemia are prophylactic iron in the dose of 2mg/kg/day for premature babies from 4 weeks of age, including iron rich cereal in diet, using micronised iron and periodic deworming. Preventive measures at the National level are supplementation programs and iron fortified candies, weaning food or salt.

### **B complex vitamin deficiency**

B complex vitamins serve as co-enzymes in many metabolic pathways that are functionally closely related.

Diets deficient in one of the B complex vitamins are frequently poor sources of other B vitamins. It is advisable to treat a patient with evidence of a specific B vitamin deficiency with the entire B complex vitamins.

**Thiamine deficiency:** For Beriberi 10 mg/day oral. In CCF IM/ IV.

**Thiamine dependence :** Seen in megaloblastic anemia, maple syrup urine diseases and Leigh's encephalomyelopathy.

**Diet whole grains cereal :** Thiamine requirements depend largely on carbohydrate

intake and are calculated on the basis of energy intake 0.3mg / 1000kcal.

**Riboflavin:** Inadequate intake, faulty absorption in children with biliary atresia and drugs like phenothiazine lead to deficiency, characterised by cheilosis, glossitis, keratitis, seborrheic dermatitis. It can be prevented by intake of adequate milk, egg, cereal, dark green vegetables. The dose of riboflavin for treatment of deficiency is 3-10 mg / day. Riboflavin deficiency can cause secondary deficiency of iron, B1 and niacin. Also riboflavin deficiency is associated with resistance to malaria.

**Niacin:** Deficiency occurs in countries where corn/ maize is staple diet (Pellagra).

Sources and prevention: Meat, egg, milk, fortified cereals.

Nicotinic acid 50 - 300mg/day 100mg/oral IV may be given

No toxic effect. Sun exposure avoided during acute phase.

Nicotinic acid used in pharmacological doses to treat hyperlipidemia.

**Pyridoxine (B6):** Risk of deficiency is seen in

persons taking drugs that inhibit the activity of Vit B 6 (isoniazid, corticosteroids, anti convulsants, patients in dialysis).

B6 requirements are calculated per unit dietary protein intake.

B6 dependence syndrome seen as convulsions in newborn where large amounts of B6 needed.

### Vitamin D deficiency Rickets

Globally, there has been renewed interest and attention focused not only on the role of vitamin D status and calcium intakes in the prevention of rickets and osteoporosis, but also on the role of vitamin D in the reduction of cancer risk, immune related disorders and infectious diseases.

**Specific treatment:** Single massive dose of D3, 6,00,000 units IM(3,00,000 units up to 1 year age) with supplementation of calcium and phosphorus. Apparent healing seen in 10-14 days. Radiological evidence of healing noted after 6 weeks.

In order to achieve real consolidation of cure, desirable to give additional dose of vitamin D (6 lakh units) therapy must be supplemented with calcium.

Alternative: 60,000 units of D3 daily orally for 10 days. (or) observation 20,000 units of D3 /day orally for 30 days.

Poor response: In refractory / resistant rickets, malabsorption state, chronic renal disease, Hypophosphatemia, hypocalcemia, Fanconi syndrome, chronic liver disease, hypomagnesemia.

Preparations: Calcitriol sachets 60,000 IU/ sachet oral Inj. Arachitol (Vit D3 3lakhs/ 6L IU/ ml)

Alpha D3 – 1.25/µg

Adexoline A & D cap A 5000 IU, D 400 IU

Calciferol oral solution: 0.125 mg of calciferol (eq to 5000 IU of Vit D). Maximum 20 µg (1000 units 0.2 ml). 75 -100 µg (3000 - 4000 units/daily for rapid healing).

**Prevention:** 400 IU D through sunshine/diet/supplements. Pregnant and lactating women should be given supplementation.

### Points to Remember

- *Overzealous administration of vitamin A can cause hyper vitaminosis. During pregnancy do not prescribe high dose of vitamin A. There is no need to initiate vitamin A supplementation to newborns as core intervention.*
- *To control iron deficiency in infants and children general health measures which include exclusive breastfeeding for 6 months, control of infections / infestations.*
- *Giving nutrient dense complementary food and food fortification with iron, nutrition education and home garden.*
- *Iron therapy to be given 1 hour before meals, not to be taken with coffee /tea.*
- *Prevention of rickets is by ensuring adequate sunlight exposure.*
- *Vitamin D therapy should be supplemented with calcium.*
- *If cobalamin deficiency has not been excluded, folate must be administered with cyanocobalamin. To prevent loss of folate, food should not be cooked excessively, especially in large amount of water.*
- *To prevent cobalamin deficiency, patients who prefer vegetarian diet, should include diary products and eggs in their meals.*

## Bibliography

1. Joseph L Mathew A systematic review of Vitamin A supplementation for prophylaxis or therapy in childhood pneumonia: Indian Paediatr 2010; 47: 255-260.
2. Piush Gupta: Do we need universal neonatal vitamin A supplementation. Indian pediatr 2008; 45: 439-440.
3. Lewin M. Iyengar A, Vasdevan A. Vitamins and mineral requirements and deficiency disorders. In: Ed, Achars text book of pediatrics, Swanarekha Bhat, 4<sup>th</sup> Edn University press, Hyderabad, 2009; pp57-58.
4. Robin k Ohls, Robert D Christensen. Megaloblastic anemia. In: Nelson text book of Pediatrics, Eds, Kleigman, Jensen, Behrman, Stanton, 18<sup>th</sup> Edn, Elsevier, New Delhi. 2008; pp2012-2014.
5. Anand K, Lakshmi R, Janakiraman VN, Ritvik A, Puneet Mishra, Pandey RM, et al. Effect of consumption of micronutrient fortified candies on the iron & Vit A status of children. Indian Pediatr 2007; 44:823-829.
6. Hall berg Z Combating iron deficiency: daily administration of iron is far superior to weekly administrated AM J Clin Nutr 1998; 68: 213-217.
7. Rohnes F, Zimmermann NB, Amon RJ. Randomized controlled trial of Fe fortification. J Nutrition 2010 Feb 3(E Pub ahead of Print).
8. Ankun Vikas Bopche, Rashmi Ducivedi, Rakesh Mishra, GS Patel. Ferrous sulphate superior to iron polymaltose complex for treatment of iron deficiencies. Indian Paediatr 2009; 46: 825- 922.
9. Stanley Zlotkin, control of anemia –the time to act is now; Indian pediatr 2007; 44:84-86.

## CLIPPINGS

### ***Cahill, Alison G; Stout, Molly J; Caughey, Aaron B. Intrapartum Magnesium for Prevention of Cerebral Palsy, continuing controversy. Current Opinion in Obstetrics & Gynecology, April 2010***

The purpose of the present review is to review the literature regarding the use of antenatal magnesium sulfate (MgSO<sub>4</sub>) for fetal neuroprotection and prevention of cerebral palsy in women at risk of preterm delivery.

Cerebral palsy is a nonprogressive disorder of movement and posture and a leading cause of childhood disability. Preterm birth is a major risk factor for the development of cerebral palsy; gestational age at delivery has an inverse relationship to the risk of cerebral palsy. Observational studies over the past 15 years have suggested a possible protective role for MgSO<sub>4</sub>. In some studies, children born preterm who were exposed prenatally to MgSO<sub>4</sub> for obstetric indications such as seizure prophylaxis or tocolysis had decreased rates of cerebral palsy as compared with children born preterm to women who were not exposed to MgSO<sub>4</sub>.

## INFANT AND CHILD NUTRITION

### FOOD FORTIFICATION: PRESENT AND FUTURE

\* **Sushil Madan**

**Abstract:** *Overt effects of micronutrient deficiencies (MND) such as goitre, blindness, Iron deficiency anemia (IDA) are well known in developing countries. Short term strategy such as National nutritional anemia prophylaxis (NNAPP) and vitamin A prophylaxis program have failed to show significant impact. Food fortification (FF) is a cost effective medium term approach. Universal salt iodization (USI) and home fortification (HF) with sprinkles have established efficacy. Identification and development of fortifying agents which guarantee product quality are not only scientific and technological challenges but require proper monitoring, implementation and evaluation. Sharing expertise and resources with public private partnership is key strategy to reduce barriers in future.*

**Keywords:** *MND, FF, NNAPP, USI, HF.*

WHO defines food fortification (FF) as a process whereby nutrients are added to food in relatively small quantities to maintain or improve the quality of a diet of a group, community or population.<sup>1</sup> Attempts have been made in countries to fortify food and water so as to prevent micro nutrient deficiency (MND), specifically Vitamin A, iodine, iron and folic acid.

Currently FF encompasses a broader concept which might be done for several reasons.<sup>2</sup>

1. To restore nutrients lost during food processing, a process known as "enrichment."
2. Fortification: to add nutrients that may or may not be present naturally in food,
3. "Standardize" the contents of nutrients that show variable concentrations..
4. Preservatives or coloring agents added to food for technological purposes.

### **Magnitude of micronutrient malnutrition**

Thirty percent of the world's population is affected by Vitamin A, iron or iodine deficiency. About 700 million suffer from clinical and another 2 billion from sub-clinical forms of these deficiencies. Three quarters of the population especially women and children suffering from these deficiencies live in Asia.<sup>3</sup>

Vitamin A deficiency (VAD) is the second largest cause of global blindness next to cataract. Xerophthalmia and blindness are reduced to a great extent with Vitamin A supplementation. One third of pre schoolers still have VAD and is reported to cause 10% cases of blindness in India. Anemia due to iron and folic acid deficiency is known to affect 40-60% of pre-schoolers, 25-30% of women in child bearing age.<sup>4</sup> Neonatal chemical hypothyroidism was found in 10% of neonates in Tarai regions of U.P by Kochupillai, et.al. Further studies revealed high prevalence of cretinous and subcretinous levels

---

\* Retd. Professor of Pediatrics,  
Institute of Child Health,  
Kolkatta



of developmental damage to the brain of children in these regions. Both iron and iodine deficiencies have a negative impact on growth and psychomotor development of children leading to stunted growth, reduced IQ and lower resistance to infection.<sup>5</sup> Eliminating these deficiencies is essential to improve health and is important for sustained economic growth and national development. Keeping in view such gross impact of MND Heads of State, who gathered at the World Summit for children (WSC1990) and the International conference of nutrition (ICN1992) made a commitment to eliminate Vitamin A deficiency, iodine deficiency disorders (IDD) and substantially reduce iron deficiency anemia (IDA) by 2000. They also endorsed fortified foods aid for displaced persons and refugees.<sup>6</sup>

### **Objectives of food fortification**

1. Fortification of staple foods with idea of prophylaxis against general malnutrition.
2. Fortification of staple foods to wipe out nutritional disease such as IDD, IDA, VAD.
3. Fortification of processed foods to encourage sale and for enrichment.
4. FF also standardizes the contents of nutrients eg. Vitamin C in orange juice.
5. For technological purposes, preservatives or coloring agents are added.
6. FF can combat both macro and micro nutrient deficiencies that often co-exist.

### **Historical background**

Nutrient supplementation of foods was mentioned in the year 400 BC by Persian physician Melanpus, who suggested adding iron filings to wine to increase soldier's "potency". In 1831 the French physician Boussingault urged adding iodine to salt to prevent goitre. It was between the first and second World Wars,

(1924-1944) that supplementation was established as a measure either to correct or prevent nutritional deficiencies or to restore nutrients lost during food processing.<sup>2</sup>

During this period the addition of iodine to salt, Vitamin A and D to margarine, Vitamin D to milk and Vitamins B 1, B2, Niacin and Iron to flours and bread was established (Table.1).

### **Fortification strategy to reduce MND**

The National Action Plan of Government of India places emphasis on FF, medium to long term strategies besides short term strategies such as medicinal supplements of iron, folic acid, Vitamin A on the prevention of micro nutrient deficiencies (MND).

FF has several advantages over supplementation : 1) No change required in dietary pattern of population, 2) Does not call for individual compliance, 3) Multiple micronutrients can be given on continuous basis as per RDA and 4) Can be included in existing food production and distribution system, thus can be sustained for long period.

### **Food fortification – some experiences**

Various vehicles and fortificants have been tried making programs successful (Table.1).

There are certain criteria for selection of food vehicle, nutrient and technical considerations in FF. A number of food vehicles can be considered in case there is no single universally consumed vehicle in a country. The product's quality should not be at risk especially its stability. Iron for example may react with fatty acids in the fortified food, forming free radicals that induce oxidation (Table.2).

Alterations such as change in color, taste, odor and appearance should be avoided altogether since they affect consumer

**Table.1. Fortified foods**

	<b>Fortifying Agents</b>
Salt	Iodine, iron, flour
Flours, bread, rice	Vitamins B1, B2, niacin, iron
Milk, margarine	Vitamins A and D
Sugar, monosodium glutamate, tea	Vitamin A
Infant formulas, cookies	Iron
Vegetables mixtures amino acid, proteins	Vitamins , minerals
Soy milk, orange juice	Calcium
Ready to eat cereals	Vitamins, minerals
Diet beverages	Vitamins, minerals
Enteral and parenteral solutions	Vitamins, minerals

Criterion For Selection Of Food Vehicle, Nutrient And Technical Considerations In: Food Fortification : Food Carrier And Nutrient added should fulfill certain criterion.

**Table.2. Creterion for selection of food vehicle and technology**

<b>Criteria</b>	<b>Technology</b>
Suitable food consumed by high proportion of population	Centrally processed Legislation
Locally available- no of foods should be considered	Minimal segregation of fortificant and vehicle
	Minimal regional variation
Unrelated to social-economic status	Good masking quality
	Simple, low cost technology
Low potential for excessive intake	Good Absorption of fortificant (Nutrient), No change in color, Odor of vehicle.
No change in Consumer's acceptability	High bio-availability and stability of fortificant
	Simple and Low Cost technology
	Recurring expenses are less

acceptability of the product. In general, as solubility of compound increases, the nutrient is more bio-available but it is more reactive with fortified food making it less stable (Table.3).

Commonly used food vehicles for fortification are:

**Fortified common salt** : Iodization of salt is a time tested, effective and economical means of combating Iodine deficiency disorders (IDDs). The National Goitre Control Program (NGGC) was introduced in goitre epidemic areas of UP.<sup>5</sup> Government has now adopted the policy of universal iodization of salt.

**Iron fortified salt**: The workshop on measures to increase iron in foods and diets organized by the Food and Nutrition Board of National Academy of Science, US in 1970 observed that large-scale studies on iron fortification failed to show expected benefits because inert iron used in the compound was ineffective. Later, the acceptance of fortified salt and nutritional effects on consumers were tested in 3 urban and 1 rural centre in India. It was accompanied by improvement in hemoglobin status and reduction in prevalence of anemia. The program is now being applied project wise. Absorption and bio availability of iron increased with addition of vitamin C to vehicles such as common salt or sugar and zinc stearate and vitamin A to monosodium glutamate<sup>2</sup> (Table.3).

The high moisture content and presence of magnesium salts posed technical problems in fortifying common salt with iron. The final formulae recommended by NIN were to fortify the salt with a combination of ferric ortho phosphate and sodium acid sulphate as to contain 1 mg of iron per gram of salt.

**Double fortified salt** - DFS (Iron and Iodine Fortified common salt) : To maintain stability of iodine in DFS a polyphosphate, sodium hexa

metaphosphate (SHMP) is included. DFS has been shown to reduce the incidence of anemia and IDD in the community. This would provide 1 milligram iron and 30 microgram of iodine per gram of salt. Monosodium glutamate (MSG), fortified with vitamin A and iron is used regularly in many of the South East Asian countries.<sup>2</sup>

**Iron fortification of other foods**: Sugar fortification with iron salt of EDTA has been successfully used in Gautemala (13 mg iron / 100 gram sugar). Fortification of tea was considered by Nutrition Board of India but bio-availability of iron gets reduced by chemical constituents of tea.<sup>1</sup>

**Fortified rice**: Rice being staple diet is a good vehicle for fortification. Ultra rice is the name given to the reconstituted vitamin A or iron fortified rice where one kilogram of ultra rice is fortified with 11.4 grams of vitamin A palmitate 250-500 units. This is then blended with unfortified rice in the ratio of 1: 100 to 1:200 to provide an appropriate dietary level of micronutrients. In comparison with vitamin A, it is easier to fortify rice with chelated iron owing to the inherent stability of the iron compound. Fortifying rice with both iron and vitamin A was not possible because vitamin A gets oxidized by iron leading to discoloration of rice on storage.<sup>1</sup>

**Parboiling** of rice: It is a natural and accepted form of fortification of cereal grains. It has a higher concentration of vitamins than raw or polished rice.<sup>1</sup>

**Wheat flour for fortification** : Wheat is the staple food consumed in forms such as Suji, noodles, semolina, chapatti in India. Fortification of wheat flour is done at the mill or bakery. Forty percent of iron consumed in Sweden and 20% in North America comes from fortified wheat flour and bakery products. Incorporating sufficient iron absorption promoter (vitamin C) in wheat flour can enhance invitro bio availability

**Table.3. Bioavailability of iron with addition of additives**

Vehicle	Iron Salt	Additive	Bio-availability
Salt	Ferrous Sulphate	None	Poor
	Ferrous Sulphate	Ascorbic acid	Increased
	Ferric phosphate	None	Poor
	Ferric Phosphate	Ascorbic acid	Increased
	Ferrous Sulphate	Sodium hexa meta phosphate and sodium acid sulphate	Poor
	Ferrous Sulphate	Orthophosphoric acid	Decreased on storage
	Ferrous Sulphate	Sodium acid sulphate	Good
Sugar	Ferrous sulphate	None	Poor
	Ferrous sulphate	Ascorbic acid	Increased
	Ferric chloride	None	Poor
MSG*	Ferrous sulphate	Zinc stearate and Vitamin A	Good

Stability of the fortifying agent depends on factors such as pH, oxygen, air, light and temperature. The same is controlled during processing and storage of fortified foods.

Iron salts such as ferric orthophosphate are more inert. They are insoluble in water but soluble in diluted acids and show low reactivity with the food carrier. They are widely used as fortificants though their bioavailability is low. Similarly, several compounds of elemental iron have high bioavailability and cause no changes in foods.

It is also desirable that fortification does not significantly increase the total cost of the final product. It is necessary to have monetary evaluation and control system that guarantees adequate nutrient concentration and program compliance.

of both endogenous and exogenous iron. Egyptian wheat flour fortification indicates that the disodium salt of EDTA enhances bioavailability of ferrous sulphate by reducing the inhibitory effects of both wheat phytate and high bread baking temperatures.<sup>7</sup>

**Edible oil as a vehicle:** In India fortification of fats dates back to 1953. It was made compulsory to fortify 1 kg of vanaspati with 25000 units of Vitamin A. Vitamin A is uniformly soluble and stable in oil and its bioavailability increases in presence of oil. Retinyl palmitate is added to the refined oil with butyryl hydroxy toluene as an antioxidant. Blending of red palm oil could be a cheaper alternative instead of fortification with synthetic vitamin A. It would be reasonable to fortify 20ml of oil with 300 microgram of retinol presuming daily intake of oil is 20 ml and it would meet half the RDI of vitamin A (600 microgram/day).<sup>1</sup>

**Tea fortification:** FF of tea with vitamin A was carried out in 1943 in US and found to be stable. Vitamin A is reactive to atmospheric oxygen and hence was not adapted in India.

**Sugar as a vehicle:** FF process can be easily controlled as sugar is distributed by PDS and producing units are mostly under organized sector in India. Now it is possible to obtain quality sugar double fortified with iron and vitamin A. Successful fortification programs in Guatemala and Chile are good examples. Sugar has been fortified with vitamin A in Costa Rica, El Salvador, Guatemala, Honduras, Panama and Zambia. In India, a collaboration of the National Federation of Cooperative Sugar Factories (NFCFS) and the Micronutrient Initiative (MI) has established the stability of vitamin A fortified sugar under local conditions.<sup>4</sup> Fortified candies were used by MI to assess the efficacy of vitamin A, iron and folic acid in children aged 3-6 years in the Integrated Child Development

Scheme. It resulted in improvement of haemoglobin and serum ferritin levels of children.<sup>8</sup>

**Curry powder :** In Thailand spicy powder accompanying noodles is fortified with iron, vitamin A and iodine. Curry powder, mixture of turmeric, coriander, red chilies, black pepper and fenugreek seeds are also used in India, and the same can act as suitable vehicle for food fortification.<sup>1</sup>

**Bread :** Initially modern bakeries opted for fortification of bread with lysine, vitamins and a few minerals. Now they use soya flour to supplement wheat with lysine.

**Fortification of processed foods:** Infant foods and weaning foods are fortified with vitamins, calcium and iron as per specifications of ISI. To overcome over vitaminization Le Chance has suggested that vitaminization of foods should be based on calorie content.

**Progress in food fortification:** Several nutritional deficiencies have been eliminated. In 1900s the problem of VAD disappeared after margarine was fortified with vitamin A in Denmark. Milk was fortified with vitamin A and D for tackling vitamin D deficiencies and rickets in Europe and North America. Fortification of bread with niacin eliminated the problem of pellagra in US in 1930s. Flour fortification with B vitamins was introduced in 1944 in New Foundland. Vitamin A fortification has depended on sustained political commitment (both in country and by donors), persistence with technical development of fortificant technologies, increased awareness of health consequences of vitamin A deficiency by governments and involvement of the private sector. Amongst developing countries, many have achieved the goal of universal salt iodization (USI) since the early 1990s. In areas where households consume iodized salts evidence of

Neonatal chemical hypothyroidism, goiter and cretinism has reduced. It is essential to ensure sustainability through consumer demand. People should be made aware why their salt is iodized and what are the associated benefits. Success is due to advocacy and support from UNICEF and International Council for control of Iodine Deficiency Disorders. (ICCIDD). The MI and Heinz are working together to develop micronutrient sprinkles which can be added to supplements used in the ongoing feeding programs.<sup>9</sup>

In July 2005 fortification consultant of Global Alliance for Improvement of Nutrition (GAIN), Quentin Johnson summarized the successful fortification programs and attributed it to political and industry support, adequate legislation, consumer acceptance, low cost, sustainable easily available fortified food with micro nutrients barring any cultural or other objections.<sup>10</sup> Tables 4 and 5 summarises various fortification programs in different countries over years.

### **Current constraints and future opportunities**

Factors that constrain private investment in developing markets for fortified foods :

- High initial cost of new technology
- Low consumer demand for fortified products
- Lack of awareness of public of micronutrient malnutrition.
- Distribution, regulatory and monitory systems being not in place.
- This means higher investment for private investors.

Sharing, expertise and resources with public private partnership during product development is a key strategy to reduce barriers in future.<sup>3</sup>

**Role of Governments and NGOs :** They should create public awareness about micro nutrients and the benefit of FF through social marketing with the support of international agencies like IFM.

- Fortified food products should be used in school feeding programs
- Food purity act should be reformed to encourage food fortification.
- Fortified foods should be favorably treated in respect of direct and local taxes.
- Public health institutions should survey the prevalence of MND and monitor the result of FF program.
- Food regulations should be brought in conformity with Internationally accepted disciplines like “CODEX”.
- Government laboratories be upgraded to analyze fortified foods.

### **Role of industry, research and development institutions**

- Industry should make efforts to reach rural areas.
- Industry should support development through multiple product fortification.
- Chamber of Commerce should devise and support fortification programs.
- Micro nutrient should remain stable during cooking and processing.
- Levels of fortification should be evaluated and adjusted according to bio- availability.

### **Role of NGOs and international organizations**

- International association of Infant Food Manufacturers (IFM) with it's Global Network can focus on development of low cost fortified complementary/supplementary foods. They can collaborate with Governments at national level.

**Table.4. Successful fortification programmes**

- 1920's Switzerland Salt Iodization
- 1930's N Europe Vitamin D in Dairy Products
- 1930's Denmark Vitamin A in margarine
- 1940's N. America Vitamin B, Iron in flour
- 1953 India Vitamin A in oil
- 1974 Guatemala Vitamin A in sugar
- 1992 Universal Salt Iodization, 51 countries including India.
- 1990-2000 India Wheat Flour with iron project wise
- Eighteen nations fortify foods

**Table.5. Successful fortification programmes**

- 1996 N America Folic acid in flour
- 1996 Venezuela Vit A, B's, Iron in flour
- 1998 Philippines Vitamin A in flour
- 1999 Zambia Vitamin A in sugar
- 1999 Indonesia Iron, Folic acid, Zinc in flour
- 1999 Egypt Iron in Biscuit flour.
- 2000 Mexico Addition of Zinc to fortified flour.
- 2002 Jordan, Kuwait, Qatar Iron Folic Acid to flour.
- 2002 South Africa Wheat and Maize flour with Iron.

- “International Agencies” like UNICEF, USAID, MI are already promoting fortification programs.
- GAIN, (Global Alliance for Improvement of Nutrition) another high profile alliance of public, private and international organizations assists recipient countries in putting iron, iodine, Vitamin A folic acid, other vitamins and minerals into everyday foods like salt, flour, oil, sugar and soya sauce.
- They have to take coordinated steps to promote and facilitate food fortification by bringing funds and technology.
- They should also discuss on all food fortification issues as was done by GAIN in July, 2005 at Georgia to monitor progress and assess the impact of FF.

## Conclusion

The overt effects of micronutrient deficiencies such as goiter, blindness and anemia are known. Short term strategy such as NNAPP and vitamin A prophylaxis have failed to show significant impact.<sup>11,12</sup> Food fortification is an effective and cost effective medium term approach and will continue to be an important tool to treat or prevent specific nutritional deficiencies and also improve nutritional status and general state of well being in different populations. The identification and development of fortifying agents which guarantee product quality and high bio-availability are technological and scientific challenges.

## Options for the future are :

1. Multiple vehicles should be considered.
2. Encourage use of nutrient bio-availability stimulants such as ascorbic or other organic acid and concurrent consumption of foods rich in vitamin C (citrus fruits, guava,

mango, cabbage, cauliflower, tomatoes and lime to promote iron absorption)

3. Elimination of inhibitors of mineral absorption in the intestine for example phytates from cereals and pulses. Avoid drinking tea at meal-time.

4. Micro-encapsulation of nutrients like sprinkles should be implemented for home fortification of complementary foods.

5. Increasing production activities from pilot level to industrial scale- success more likely.

6. Strategy should be to fortify foods for all sections of the society to be addressed by public-private partnership along with the involvement of International agencies to be facilitated by GAIN and IFM.

7. Reach the vulnerable populations through special feeding programs.

## Points to Remember

- *The overt effects of micronutrient deficiencies (MND) such as goitre, blindness, anemia are well known in developing countries.*
- *Food fortification is an effective and cost effective medium term approach for eliminating MND.*
- *Universal salt iodization and home fortification with sprinkles have established its efficacy in India and other countries.*
- *The identification and development of other fortifying agents which guarantee product quality are scientific and technological challenges and also require proper monitoring, implementation and evaluation.*
- *Sharing expertise and resources with public, private partnership is the key strategy to reduce barriers in future for food fortification.*



## References

1. Anila ME, Sivakumar B, Madhavan Nair K, et al. Why Food Fortification? Nutrition 1999;133:12-22.
2. Louis MA Fortification of Foods. Historical Development and Current Practices <http://www.unu.edu/unupress/food/10/15/09>
3. Vinodini R. Food Fortification for Reducing Micronutrient Deficiencies and Public Private Partnerships, Nov'2003. Accessed on [www.ifm.net/industry/food-fortification.htm](http://www.ifm.net/industry/food-fortification.htm)
4. IIPS National Family Health Survey (NFHS-3) 2005-06 Mumbai's International Institute for Population Sciences (IIPS) and Macro International, 2007.
5. Kochupillai N National Iodine Deficiency Disorders Control Program In: IAP Textbook of Pediatrics 4<sup>th</sup> Edn 2008-p210.
6. Jan Darnton Hill - Overview :- Rationale and Elements of successful food fortification programme. [www.unu.edu/unupress/food](http://www.unu.edu/unupress/food) accessed on 11/19/2009
7. Hemlatha S, Patel K, Srinivas K, Inhibitors of Iron Absorption Zinc & Iron contents and their bioaccessibility in Cereals and Pulses consumed in India. Food Chem 2007;102:1328-1336.
8. Anand K, et al. Effect of Micronutrient Fortified Candies on Iron and Vitamin A status of children aged 3-6 years Indian Pediatr 2007;44:823-829.
9. Home Fortification with Micronutrient Sprinkles – A New Approach for the prevention and treatment of Nutritional Anemias. Journal of Pediatrics and Child Health, Feb 2003;8(2):87-90 Accessed on 11/19/2009.
10. Quentin Johnson, Fortification Consultant GAIN. International Activities on Food Fortification, Presentation to NFA Georgia July'2005.
11. Madan S. Nutritional Anemia in Adolescence. Eds. Parthasarathy A, et al In: IAP Text book of Pediatrics. Jaypee Brothers 4<sup>th</sup> Edn, 2008.
12. Madan S. Recommendations in Prevention and Control of Iron Deficiency Anemia. In: Madan S, Mukerjee KL, Khatua SP (Eds) Nutritional Anemia in Infancy and Childhood. Publication of Indian Academy of Pediatrics 1990.

## CLIPPINGS

**G. H. Rabbani, C. P. Larson, R. Islam, U. R. Saha, A. Kabir. Green banana-supplemented diet in the home management of acute and prolonged diarrhoea in children: a community-based trial in rural Bangladesh. Tropical Medicine & International Health, October 2010.**

A cluster randomized field trial was conducted among 2968 Bangladeshi rural children 6–36 months old. Wards (villages) were randomly assigned to either a standard care group or a standard care plus green banana group where mothers were instructed to add cooked green banana to the diets of diarrhoeal children. Through a village-based surveillance system, diarrhoeal morbidity data (severity, duration, compliance) were collected for 14 days. Treatment effects were determined by analysing cumulative probability of cure by testing Cox proportional hazards models and relative risk (RR). The study concluded that green banana-supplemented diet hastened recovery of acute and prolonged childhood diarrhoea managed at home in rural Bangladesh.

**INFANT AND CHILD NUTRITION****READY TO USE THERAPEUTIC FOOD: A REVIEW**

**\* Dubey AP**

**\*\* Malobika Bhattacharya**

**Abstract:** *Severe acute malnutrition (SAM) is an important health problem in developing countries like India. Until recently, it needed hospital admission and facility-based management. Ready to use therapeutic food (RUTF) is a soft and crushable food item that is calorie dense and can be fed without any preparation to a malnourished child at home. This has made it possible for uncomplicated SAM to be managed at home. Clinical efficacy trials have proved the efficacy of RUTF in the management as well as prevention of SAM. A number of commercially manufactured, imported RUTFs are available. These need to be evaluated in large multicentric trials for their efficacy and cost-effectiveness. Moreover, a number of locally produced nutrimixes are available in India which have never been fully evaluated in trials. We should transfer technology to manufacture indigenous RUTF as well as use local nutrimixes wherever possible.*

**Keywords:** *Severe acute malnutrition (SAM), RUTF, Nutrimix.*

Severe acute malnutrition is defined by a very low weight for height (less than -3 z scores

of the median WHO growth standards), visible severe wasting, presence of nutritional edema and in children aged 6-59 months, mid arm circumference less than 110mm.<sup>1</sup>

Globally, an estimated 20 million children are suffering from SAM. Most of them are living in South Asia and Sub-Saharan Africa. The National Family Health Survey-3 estimates that 8 million under-5 children in India suffer from SAM. They have a high mortality rate of 20-30%. The cause of SAM in these children is a cumulative effect of inadequate diet, paucity of health services and recurrent illnesses such as diarrhoea and pneumonia.<sup>2</sup>

In developing countries, the majority of children who have SAM are never brought to health facilities. In these cases, only a strong community management component can provide them with appropriate care. The community-based approach involves timely detection of SAM in the community and provision of dietary rehabilitation for those without medical complications. The advantages of community-based management of SAM have decreased incidence of nosocomial infection, allowing mothers to spend more time with the rest of the family and continuity of care after discharge.<sup>2</sup>

The WHO recommended starter feeds (F75) and follow-up diets (F100) are not suitable for home use as they are water-based and hence prone to bacterial contamination. In this scenario, ready-to-use therapeutic food (RUTF) is a new and promising alternative in the treatment of SAM providing a diet that is safe to use at home and ensures rapid weight gain in these children.

\* Professor and Head

\*\* Senior Research Associate

Department of Pediatrics,  
Maulana Azad Medical College and  
Lok Nayak Hospital, New Delhi.

## What is RUTF ?

RUTF are soft or crushable foods that can be easily consumed by children from the age of 6 months without adding water. RUTF have similar nutrient composition to therapeutic F100 diet used in facility-based management of SAM. However, unlike F100, RUTF are not water-based, hence, not prone to bacterial contamination. Therefore, these can be used without refrigeration and in areas where hygiene is suboptimal. Children with SAM without medical complications can be given a standard dose of RUTF as per body weight that can be consumed without any preparation with minimal supervision. A child being treated for SAM will need on an average, 10-15 kg of RUTF, given over a period of 6-8 weeks.<sup>3</sup>

RUTF should fulfil certain criteria such as, it should be calorie dense, high in proteins, vitamins and minerals, simple to store and deliver, easy to use, fast acting, affordable, culturally acceptable, not require trained staff to administer, available in single serve packets of 400-500 calories each, require little or no preparation before use, have appropriate shelf-life and stability under varied climate and temperature, resist bacterial growth and not cause addiction to the child.<sup>4</sup> WHO has recommended that such RUTF be prepared locally by each country as per international standards.<sup>5</sup>

RUTF has 5 times greater energy density than F100 formulation but a similar nutrient to energy ratio. This is obtained by replacing part of the dried skimmed milk of the F100 formulation by powdered lactoserum with peanut butter, and oil by a vegetable fat mixture including essential fatty acids. Atleast half the proteins contained in the foods should come from milk products. The resultant product tastes like peanut butter. The high fat content masks the taste of some micronutrients present in high

concentrations in the mix. It has a low water content (less than 2%) that prevents reaction between individual micronutrients, thus, increasing the shelf-life.<sup>6</sup> Table.1 summarises the nutritional composition of RUTF as recommended by WHO.<sup>3</sup>

The food should be free from deleterious substances such as heavy metals or pesticides. It should have a mineral composition that will not alter the acid base metabolism of children with SAM. In particular it should have a moderate positive non-metabolizable base sufficient to eliminate the risk of metabolic acidosis.<sup>3</sup>

Plumpy Nut is a commercially manufactured RUTF prepared as per the guidelines above by a French company called Nutriset. It has been imported and distributed in India and a few African countries by the UNICEF for community-based treatment of SAM. However, most of the studies demonstrating the efficacy of Plumpy Nut have been done in disaster situations and data on its use in the management of SAM in non-disaster situation are lacking. If produced in India, it would cost approximately US \$ 40 per child per treatment.<sup>7</sup>

Recently, a similar product named eeZeePaste NUT, manufactured in India by Compact, India Pvt Ltd, has been used by UNICEF and Medecins Sans Frontiers for the management of SAM in some Asian and African countries. It confirms to the composition recommended by the WHO and uses locally produced ingredients and equipments manufactured in India for its production. It is available in 92 gram sachets and provides 500 kJ/sachet. The product has a shelf-life of 15 months in Indian climatic conditions. Its use in India is awaiting government approval.

Many locally produced/produced, culturally acceptable and relatively inexpensive foods that are being used in India by reliable

**Table.1. Nutritional composition of RUTF as recommended by WHO<sup>3</sup>**

<b>Nutritional composition</b>	
Moisture content	2.5% maximum
Energy	520-550 Kcal/100g
Proteins	10-12% total energy
Lipids	45-60% total energy
Sodium	290mg/100g maximum
Potassium	1110-1400 mg/100g
Calcium	300-600 mg/100g
Phosphorus (excluding phytates)	300-600 mg/100g
Magnesium	80-40 mg/100g
Iron	10-14 mg/100g
Zinc	11-14 mg/100g
Copper	1.4-1.8 mg/100g
Selenium	20-40 µg
Iodine	70-140 µg/100g
Vitamin A	0.8-1.1 µg/100g
Vitamin D	15-20 µg/100g
Vitamin E	20 mg/100g minimum
Vitamin K	15-30 µg/100g
Vitamin B1	0.5 mg/100g minimum
Vitamin B2	1.6 mg/100g minimum
Vitamin C	50 mg/100g minimum
Vitamin B6	0.6 mg/100g minimum
Vitamin B12	1.6 µg /100g minimum
Folic acid	200 µg /100g minimum
Niacin	5 mg /100g minimum
Pantothenic acid	3 mg /100g minimum
Biotin	60 µg /100g minimum
n-6 fatty acids	3-10% of total energy
n-3 fatty acids	0.3-2.5% of total energy

medical institutions and non-governmental groups fulfil many of the prerequisites of RUTF. These indigenous RUTFs have a few advantages over imported RUTF. Longer shelf life ceases to be a precondition as they are produced and consumed locally. They promote local agricultural practices as most use millets and other locally grown food grains. Their production gives source of livelihood to the very families that may be harbouring children with SAM. They use existing bodies such as womens' groups for distribution. Lastly, being decentralised, it allows greater community participation.<sup>7</sup> Table.2 lists a few of these indigenous RUTFs.

### Clinical efficacy trials with RUTF

A number of randomised clinical trials have evaluated the efficacy of RUTF in the management of children suffering from SAM.

In an Indian study,<sup>8</sup> RUTF was compared with a cereal and legume based porridge (khichri). Thirty one children aged 6 to 36 months and from urban low to middle socioeconomic class neighbourhoods with malnutrition (weight for height Z scores -2 to -3) without infection or edema were recruited. The children were given unlimited offerings of weighed amounts of either RUTF or khichri and water on demand for 2 days. It was found that 58% and 77% children accepted RUTF and khichri eagerly ( $p=0.35$ ). The median energy intake over the 2 days was 305 kcal from RUTF and 242 kcal from khichri ( $p=0.02$ ). The authors concluded that both the foods had good acceptability, but RUTF, being more energy dense, provided higher energy intake.

Isanaka, et al<sup>9</sup> evaluated the efficacy of RUTF in the prevention of moderate to severe

**Table.2. Indigenous RUTFs<sup>7</sup>**

Name of mix	Chief constituents	Developed by	Locally prepared by	State
<b>Davangere Mix</b>	Groundnut, roasted Bengal gram, jaggery, ragi	Medical College, Davangere	Women's group	Karnataka
<b>Shakti Nutrimix</b>	Rice, wheat, whole gram, ground nut, vitamins, minerals	Shibpur People's Care Organisation	Women's group	West Bengal
<b>Nutrimix</b>	Wheat, rice, gram, lentil, groundnut	Development Research Communication & Service Centre	Women's group	West Bengal
<b>LAPSI</b>	Green millet, peanut, jaggery	Bharat Agro Industries Foundation & CAPART		Maharashtra
<b>SAT Mix</b>	Rice, wheat, black gram, sugar	Sree Avittom Thirumal Hospital		Kerela
<b>Satthu Maavu</b>	Wheat, maize, ragi, Bengal gram, jaggery, vitamin pre-mix	Nutrition Monitoring Programme (state programme)		Tamil Nadu

wasting. Twelve villages in Nigeria were randomised to receive either RUTF supplementation for 3 months or no intervention. All children aged 6-60 months from these villages with weight for height more than 80% were recruited. The difference in weight for height Z score between the RUTF and non-intervention groups at the beginning and after 8 months of follow-up were -0.10Z and 0.12Z respectively. The adjusted effect of intervention was thus 0.22. RUTF supplementation also resulted in 36% (95% CI, 17% to 50%,  $p < 0.001$ ) reduction in the incidence of wasting and 58% (95% CI, 43% to 68%,  $p < 0.001$ ) reduction in the incidence of severe wasting. It was concluded that short term RUTF supplementation decrease the fall in weight for height Z score and the incidence of wasting over an 8 months follow-up.

In a Malawian study,<sup>10</sup> 1178 children with moderate or severe wasting, kwashiorkor or both were randomly assigned to receive either home-based RUTF or standard therapy and their recovery rates evaluated. Children who received home-based RUTF were more likely to achieve weight for height Z score  $> -2$  (79% vs 46%,  $p < 0.001$ ), had higher rates of weight gain (3.5 vs 2.0 g/kg/day; difference: 1.5; 95% CI: 1.0, 2.0 g/kg/day) and had lower prevalence of fever, cough and diarrhoea. Hence, home-based RUTF was found to have better outcome in the treatment of malnutrition.

In another Malawian study,<sup>11</sup> 282 malnourished HIV negative children were assigned to receive either RUTF in sufficient quantity to meet their requirement for full catch-up growth or micronutrient fortified RUTF in amounts that will provide 33% of their daily nutritional requirement or maize-soy flour with micronutrients in quantity sufficient for full catch-up group. It was seen that the RUTF group was more likely to reach weight for height Z score  $> 0$  as compared to the other two groups

(95% vs 78%, RR 1.2, 95% CI 1.1 to 1.3). The average weight gain was also higher in The RUTF group (5.2g/kg/day vs 3.1g/kg/day). Hence, home-based RUTF therapy was found to be more successful than the other two modalities.

A similar study recruited 93 HIV positive malnourished Malawian children aged  $> 1$  year. They were divided into three intervention groups identical to the previous study.<sup>12</sup> The RUTF group had higher likelihood of attaining weight for height of 100% and also reported higher weight gain.

All the above trials have reported better outcome with RUTF as compared to standard treatment consisting of milk-based F100 diet and flour supplements. Preventive supplementation of non-malnourished children with RUTF also reduced the subsequent incidence of wasting. Table.3 summarises the clinical efficacy trials with RUTF.

### **Should India use commercially produced RUTF for SAM**

SAM is an important health problem of under-five children in India. Community based management of uncomplicated SAM with RUTF is an attractive alternative to facility-based management in view of the advantages mentioned earlier. However, in view of our porous administrative system there is a risk of commercial exploitation by continued high import of RUTF for the treatment of SAM and delaying the development of indigenous RUTF.

We need to first evaluate imported RUTF by multicentric efficacy and effectiveness trials. If the results of these trials are encouraging, then we should transfer technology to manufacture RUTF locally to reduce cost and simplify logistics. Also, locally available, indigenous mixes should be evaluated as effective alternatives to commercially produced RUTF.<sup>4,7</sup>

**Table.3. Clinical efficacy trials with RUTF**

Authors	Design	Population	Intervention	Outcome
Dube <i>et al</i> <sup>8</sup>	Acceptability trial with cross-over design	31 children with WHZ -2 to -3 without infection or edema	Unlimited helpings of weighed amounts of RUTF or <i>khichri</i> for 2 days	RUTF had better acceptability and provided higher energy intake due to its extra energy density
Isanaka <i>et al</i> <sup>9</sup>	Cluster randomised trial	All children of 12 Nigerian villages aged 6-60 months with wt for ht $\geq 80\%$	1 packet/day of RUTF for 3 months vs no intervention	Short term RUTF supplementation reduced decline in WHZ and incidence of wasting
Ciliberto <i>et al</i> <sup>10</sup>	Controlled comparative clinical effectiveness trial	1178 Malawian children with WHZ $< -2$ , mild edema or both with good appetite	Standard therapy vs home based therapy with RUTF	RUTF group more likely to achieve WHZ $> -2$ , greater wt gain, lower prevalence of infections
Manary <i>et al</i> <sup>11</sup>	Randomised controlled trial	Malawian children $> 12$ months discharged from Queen Elisabeth Central Hospital over 9 months	RUTF or RUTF supplement or blended maize soy flour	RUTF group more likely to reach WHZ $> 0$ , had higher wt gain
Ndekha <i>et al</i> <sup>12</sup>	Randomised controlled trial	93 HIV-positive children $> 1$ y old discharged from the nutrition unit in Blantyre, Malawi	RUTF or RUTF supplement or blended maize soy flour	RUTF group more likely to reach WHZ=100%, had higher wt gain

WHZ=weight for height z score, wt= weight, ht=height,

## Points to Remember

- *Community-based management of uncomplicated severe acute malnutrition (SAM) is preferable to facility-based management.*
- *Ready to use therapeutic food (RUTF) is the cornerstone of such management.*
- *Efficacy of commercially manufactured imported RUTF needs to be evaluated in larger trials and, if found efficacious, they should be manufactured locally.*

- *Locally produced, indigenous RUTF should be used wherever appropriate.*

## References

1. World Health Organisation. The management of nutrition major emergencies. Geneva: World Health Organisation; 2000.
2. Ashworth A. Efficacy and effectiveness of community-based treatment of severe malnutrition. Food Nutr Bull 2006;27:S24-48.
3. Community based management of severe acute malnutrition. [http://www.who.int/child\\_adolescent\\_health/documents/pdfs/](http://www.who.int/child_adolescent_health/documents/pdfs/)

- severe\_acute\_malnutrition\_en.pdf. Accessed on 14th April 2010.
4. Kapil U. Ready to use therapeutic food (RUTF) in the management of severe acute malnutrition in India. *Indian Pediatrics* 2009;46:381-382.
  5. Prudhon C, Prinzo ZW, Briend A, Daelmans BM, Mason JB. Proceedings of WHO, UNICEF, and SCN Informal Consultation on community-based management of severe malnutrition in children. *Food Nutr Bull* 2006; 27:S 99-104.
  6. Briend A. Highly nutrient-dense spreads: a new approach to delivering multiple micronutrients to high-risk groups. *Br J Nutr* 2001;85:S175-179.
  7. Should India use commercially produced ready to use therapeutic foods (RUTF) for severe acute malnutrition (SAM). Working group for children under 6. *Social Medicine* 2009; 4: 52-55.
  8. Dube B, Rongsen T, Mazumdar S, Taneja S, Rafiqui F, Bhandari N, *et al.* Comparison of ready to use therapeutic food with cereal legume-based khichri among malnourished children. *Indian Pediatr* 2009;46:383-388.
  9. Isanaka S, Nombela N, Djibo A, Poupard M, Van Beckhoven D, Gaboulaud V, *et al.* Effect of preventive supplementation with ready to use therapeutic food on the nutritional status, mortality and morbidity of children aged 6-60 months. *JAMA* 2009;301:277-285.
  10. Ciliberto MA, Sandige H, Ndekha MJ, Ashorn P, Briend A, Ciliberto MA. Comparison of home-based therapy with ready to use therapeutic food in the treatment of malnourished Malawian children: a controlled, clinical effectiveness trial. *Am J Clin Nutr* 2005;81:864-870.
  11. Manary MJ, Ndekha MJ, Ashorn P, Maleta K, Briend A. Home-based therapy for severe malnutrition with ready-to-use food. *Arch Dis Child* 2004;89:557-561.
  12. Ndekha MJ, Manary MJ, Ashorn P, Briend A. Home-based therapy with ready to use therapeutic food is of benefit to malnourished, HIV infected Malawian children. *Acta Paediatr* 2005;94:222-225.

### CLIPPINGS

***Neuman, Mark I. Scully, Kevin J. BS; Kim, Daniel BS; Shah, Sonal Bachur, Richard G. Physician Assessment of the Likelihood of Pneumonia in a Pediatric Emergency Department. Pediatric Emergency Care: November 2010***

The value of physical examination findings in the diagnosis of pneumonia in children may be limited, and the accuracy of physicians in predicting pneumonia is not known. the correlation between physicians' assessment of the likelihood of pneumonia and radiographic presence of pneumonia. This was a prospective observational study of children 21 years or younger presenting to a pediatric emergency department, who had a chest radiography performed for suspicion of pneumonia. Physicians recorded clinical findings and likelihood of pneumonia before obtaining the radiograph. Definite and probable pneumonia was defined by a radiologist's interpretation of the radiograph. With some overestimation, physicians' assessment of the likelihood of pneumonia correlates well with radiographic diagnosis of pneumonia.



## INFANT AND CHILD NUTRITION

### **ZINC IN CHILD HEALTH: A MINERAL THAT MEANS A LOT!**

**\* Pawan Rawal**

**\*\* Thapa BR**

**ABSTRACT:** *Zinc has diverse roles in maintaining human health. Low zinc status at birth, frequent diarrhea, high nutrient demands for growth, inadequate weaning practices and reliance on plant-based diets are the main factors that predispose infants and young children to zinc deficiency. There is evidence that zinc supplementation of children with poor zinc status can enhance the treatment for malnutrition, reduce the occurrence of diarrhea and pneumonia, improve growth and possibly improve psychomotor development. Improved dietary quality and intake, fortification of foods, agricultural approaches and introduction of zinc in national public health programs are some ways of mitigating zinc deficiency.*

**Keywords:** *Zinc, Child health, Zinc deficiency, Supplementation.*

Zinc has emerged as a critical nutrient factor for growth, immune function, cognitive development and normal functioning of the central nervous system.<sup>1</sup> It is well known that zinc deficiency is likely a public health problem worldwide,<sup>2</sup> especially among infants and young

children living under impoverished conditions and in areas where infection prevalence rates are high. The effects of such a deficient state in humans can be devastating because zinc is essential for normal fetal growth and development, for milk production during lactation and it is extremely necessary during the initial years of life when the body is growing rapidly.<sup>3,4</sup>

### **Zinc Metabolism**

Zinc is present in all body tissues and fluids. The total body zinc content has been estimated to be 30mmol (2g). Skeletal muscle accounts for approximately 60% of the total body content and bone mass with a zinc concentration of 1.5-3mmol/g (100-200mg/g), for approximately 30%.

Zinc is an essential component of a large number (>200) of enzymes participating in the synthesis and degradation of carbohydrates, lipids, proteins and nucleic acids as well as in the metabolism of other micronutrients. Zinc absorption is concentration dependent and occurs throughout the small intestine. Zinc administered in aqueous solutions to fasting subjects is absorbed efficiently (60–70%), whereas absorption from solid diets is less efficient and varies depending on zinc content and diet composition.<sup>5</sup>

Zinc stabilizes the molecular structure of cellular components and membranes and thus contributes to the maintenance of cell and organ integrity. Furthermore, zinc has an essential role in polynucleotide transcription and thus in the

---

\* Division of Pediatric Gastroenterology  
Hepatology and Nutrition,  
Dept. of Gastroenterology,  
Postgraduate Institute of Medical Education and  
Research, Chandigarh, India.

process of genetic expression. The major losses of zinc from the body are through the intestine by desquamation of epithelial cells, urine and in sweat. Starvation and muscle catabolism increase zinc losses in urine.

The body has no zinc stores in the conventional sense. In conditions of bone resorption and tissue catabolism, zinc is released and may be reutilized to some extent.

### **Dietary sources and available forms**

Lean red meat, whole-grain cereals, pulses, and legumes provide the highest concentrations of zinc. Processed cereals with low extraction rates, polished rice and chicken, pork or meat with high fat content have moderate zinc content. Fish, roots and tubers, green leafy vegetables and fruits are only modest sources of zinc. Saturated fats and oils, sugar and alcohol have very low zinc contents.

Phytates, which are found in whole grain breads, cereals, legumes and other products, can decrease zinc absorption.<sup>6</sup> Animal proteins improve zinc absorption from a phytate containing diet.<sup>7</sup> Zinc absorption from some legume-based diets (e.g. white beans) is comparable with that from animal protein-based diets despite higher phytate content in the former.<sup>7,8</sup> Among the commercially available forms, zinc sulfate is the most frequently used supplement. This is the least expensive form, but it is the least easily absorbed and may cause stomach upset. If zinc sulfate causes stomach irritation, another form, such as zinc citrate, should be tried. Zinc should be taken with water or juice. However, if zinc causes stomach upset, it can be taken with meals. It should not be taken at the same time as iron or calcium supplements.

### **Recommended dietary allowance (RDA)**

Recommended dietary allowance (RDA) is the average daily dietary intake level that is

sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals. WHO recommended amounts of zinc as recommended nutrient intakes (RNIs) for various age groups are given in Table.1.

### **Assessment of zinc status**

In clinical practice, it is difficult to identify zinc deficiency with certainty as there are no simple clinical indicators for zinc status.<sup>9</sup> Zinc deficiency signs and symptoms are similar to deficiencies of other essential nutrients or systemic diseases. A change in velocity of growth with faltering of height and weight measurements compared with normal standards may be one of the first clinical observations that suggest zinc deficiency.<sup>10</sup>

The measurement of plasma zinc levels has been the most widely used method for assessing zinc deficiency. It is generally assumed that a low plasma zinc concentration is indicative, in the majority of cases, of zinc deficiency. Estimates of dietary zinc intake can provide clues to underlying risk of poor zinc status in individuals and groups. The phytate- zinc ratio in a given food is thought to be a helpful qualitative index for the bioavailability of zinc from that food.<sup>11</sup> When the ratio is high; the bioavailability of zinc is low. The WHO uses the phytate- zinc ratio as one index for estimating zinc bioavailability in reference diets and calculating recommended daily zinc intakes.

### **Zinc deficiency**

A recent meta-analysis of 25 intervention trials comprising 1834 children less than 13 years of age, with a mean duration of approximately 7 months and a mean dose of zinc of 14 mg/day (214mmol/day), showed a small but significant positive effect of zinc supplementation on height and weight.<sup>12</sup>

Results from zinc supplementation studies suggest that a low zinc status in children not only affects growth but is also associated with an increased risk of severe infectious diseases.<sup>13,14</sup>

Malnutrition, especially insufficiency of micronutrients such as zinc, is identified consistently as one of the most important host factors that determine the risk and severity of diarrhea.<sup>15</sup> The role of zinc in supporting the health and functions of the gastrointestinal tract is well established. Because zinc is required for cell division, cells with rapid turnover, such as those of the intestinal mucosa, are particularly vulnerable to poor zinc nutriture. In animals, zinc deficiency causes both decreased brush border disaccharidase activities and mild villous atrophy.<sup>16-18</sup> Thus, poor zinc nutriture sets the stage for the vicious cycle of diarrhea, leading to more severe zinc depletion, resulting in more severe diarrhea, etc.<sup>19</sup> Preventing this cycle is critically important to pediatric practitioners worldwide.

Loss of appetite, poor growth, weight loss, impaired taste or smell, poor wound healing, skin abnormalities (such as acne, atopic dermatitis and psoriasis), hair loss, lack of menstrual period, night blindness, hypogonadism and delayed sexual maturation, white spots on the fingernails and feelings of depression are some other effects of zinc deficiency.

### **Role of zinc therapy**

#### **Acute and persistent diarrhea**

Development of improved oral rehydration solutions had continued in last few years and several of these more recent approaches have used zinc either with or without concomitant ORS as an adjunct therapy for acute childhood diarrhea in developing countries.<sup>20</sup> Results of many double-blind, randomized, placebo-controlled clinical trials in developing countries

have confirmed that along with oral rehydration therapy, zinc supplementation is an effective treatment for acute and persistent diarrhea.<sup>21</sup> Usual doses advised are

2 months – 6 months	10 mg/day
7 months onwards	20 mg/day

#### **Duration of treatment**

Acute diarrhea	14 days
Persistent diarrhea	4 weeks

Studies showed that zinc reduced stool output and diarrheal duration when administered as an adjunct to ORS in hospitalized children ages 3–36 months with acute diarrhea and dehydration. In a pooled analysis of 9 randomized trials, zinc supplementation was reported to decrease the incidence of diarrhea by 18%.<sup>22</sup>

Although the studies varied in design, length, number of subjects and measured outcomes, a few general observations were possible. First, zinc supplementation reduced the duration of diarrhea in almost all studies. In fact, zinc-supplemented children had a 15% lower probability of continuing diarrhea on a given day and a 24% lower probability of continuing diarrhea than those children in the placebo group.<sup>21</sup> In some studies, growth retarded children or those with initial low serum zinc values experienced the most pronounced reductions in diarrhea duration. Second, almost all studies reported reductions in the severity of diarrheal illnesses after zinc supplementation. Both the total volume of stool output and the mean number of watery stools per day were reduced with zinc supplements.<sup>21</sup>

#### **Zinc supplementation and prevention of diarrhea**

All prevention trials reported positive results with zinc supplementation. Both the incidence

and the prevalence of acute diarrhea were reduced with zinc. Some studies indicated that boys had a better response to zinc supplementation than did girls, that supplemented children with low baseline plasma zinc had the most significant reductions in numbers of diarrheal episodes. In addition, the beneficial effects of zinc on diarrhea may extend beyond the supplementation period, because several studies found benefits in reduction of morbidity for 2 to 3 months after zinc supplementation.<sup>23</sup>

Pooled analysis of zinc supplementation trials already mentioned has shown that overall, zinc-supplemented children had a 18% lower incidence and a 25% lower prevalence of diarrhea.<sup>24</sup> There were trends suggesting greater effects of supplementation in children 12–59 months of age (compared with infants), children with lower plasma zinc concentrations, and children with nutritional wasting but none of these differences was statistically significant.

### **Zinc in celiac disease**

Celiac disease (CD) predominantly affects the proximal small intestine. The small intestine has the central role in maintaining zinc homeostasis. In celiac disease patients, zinc deficiency may result from a cumulative loss of insoluble zinc complexes with fat and phosphate, exudation of zinc protein complexes into the intestinal lumen and massive loss of intestinal secretions or impaired zinc absorption because of injured intestinal epithelial cell membrane. Some of the symptoms of CD (e.g. anorexia and reduced growth rate) may be related, in part, to zinc deficiency. Henker, et al found that abnormally low values were found only in children with acute celiac disease (50% below 2 SD), but not in children receiving a gluten-free diet. They suggested to measure the serum zinc concentration in children with celiac disease and to add a zinc supplementation in patients with

diminished zinc values during a period of 2–4 weeks, because zinc deficiency could inhibit the recovery of the intestinal mucosa.<sup>24</sup> We studied the role of zinc supplementation in patients with celiac disease with gluten free diet and found that supplementation of zinc with gluten free diet in newly diagnosed patient with celiac disease did not make any difference on plasma zinc levels at 4 weeks of treatment when compared to gluten free diet alone.<sup>25</sup>

### **Zinc in respiratory infections**

Zinc supplementation enhances immune system activity and protects against a range of infections including colds and upper respiratory infections (such as bronchitis). Several important studies have revealed that zinc lozenges may reduce the intensity of the symptoms associated with a cold, particularly cough, and the length of time that a cold lingers. Few clinical trials are available to evaluate the effects of zinc supplementation on acute lower respiratory infection (ALRI) rates. Studies from Vietnam and India<sup>26</sup> found large reductions in ALRI. The recent pooled analysis incorporated data from two additional randomized controlled trials. Overall there was a 41% decrease in ALRI with zinc supplementation. Effect of weekly zinc supplements on incidence of pneumonia and diarrhea in children younger than 2 years in an urban, low-income population in Bangladesh was studied in a recent randomized controlled trial.<sup>27</sup> Authors found that among young children zinc has a substantial protective effect against pneumonia, severe pneumonia, suppurative otitis media, and most importantly, mortality secondary to pneumonia.

### **Zinc in malaria**

Zinc is essential for a variety of lymphocyte functions implicated in resistance to malaria caused by *Plasmodium falciparum* (Pf). These include production of immunoglobulins

(IgG), interferons, tumor necrosis factor, and enhancement of microbiocidal activities of macrophages. Zinc may reduce morbidity associated with Pf but not with other malaria pathogens.<sup>28</sup>

### **Zinc and acrodermatitis enteropathica (AE)**

Zinc replacement therapy should be started at 3 mg/kg/d of elemental zinc in AE. Dose of zinc should be adjusted according to serum or plasma zinc levels which should be monitored every 3 to 6 months. Patients may require a higher or lower dose than 3 mg/kg/d of zinc to normalize their genetic defect of zinc metabolism. Clinical improvement is seen very rapidly, within days to weeks, before a significant change in serum zinc levels.

### **Other uses**

There are health problems that may increase the need for zinc or affect how the body absorbs or uses this mineral. Zinc supplementation may aid the treatment of these conditions. These include Wilson's disease, cirrhosis, kidney diseases, burns, tuberculosis, attention deficit hyperactivity disorders, eating disorders, HIV/AIDS, inflammatory bowel disease (ulcerative colitis and crohn's disease), osteoporosis, high blood pressure, pancreatic conditions, herpes simplex and acne.

### **Zinc toxicity**

Zinc toxicity has been seen in both acute and chronic forms. Intakes of 150 to 450 mg of zinc per day have been associated with low copper status, altered iron function, reduced immune function, and reduced levels of high-density lipoproteins (the good cholesterol). In 2001 the National Academy of Sciences established tolerable upper levels (UL), the highest intake associated with no adverse health effects, for zinc for infants, children, and adults.

The ULs do not apply to individuals who are receiving zinc for medical treatment.

### **Prevention of zinc deficiency**

Approaches to eliminate zinc deficiency need to be implemented and evaluated. Several approaches can be used to circumvent zinc deficiency.

Supplementation may be most beneficial to children who either ingest a chronically low-bioavailable zinc diet that is not easily remedied by food-based strategies or present with severe stunting, persistent diarrhea, or a combination of these factors. The Indian Academy of Pediatrics (IAP) National Task Force on the management of acute diarrhea recommended the use of 20 mg of elemental zinc during the period of diarrhea and for 14 days after cessation of diarrhea to children older than six months based on studies in India and other developing countries.

Exclusive breastfeeding during the first six months of life should be supported because breast milk is an excellent source of bioavailable zinc during this period. Addition of nutrients to commonly eaten foods has played a major role in eliminating micronutrient deficiencies. Infant formulas, infant cereals and ready-to-eat breakfast cereals can be fortified with zinc. Zinc chloride, zinc gluconate, zinc oxide, and zinc stearate and zinc sulphate are the compounds available for use as fortificants. The choice will depend on the solubility of the compound, its effect on the taste of the final food product, shelf life and cost.

### **Field fortification**

'Field-fortification' techniques include the use of zinc fertilizers to increase the zinc content (and yield) of cereal grains, and plant breeding to produce zinc-efficient genotypes.

**Table.1 Recommended nutrient intakes for dietary zinc (mg/day) from diets differing in zinc bioavailability-WHO**

Group	Assumed body weight(kg)	High bioavailability	Moderate bioavailability	Low bioavailability
Infants and children				
0-6 months	6	1.1	2.8	6.6
7-12 months	9	2.5	4.1	8.4
1-3 years	12	2.4	4.1	8.3
4-6 years	17	2.9	4.8	9.6
7-9 years	25	3.3	5.6	11.2
Adolescents				
Females 10-18 years	47	4.3	7.2	14.4
Males 10-18 years	49	5.1	8.6	17.1

## Removal of phytates

Unrefined cereals or their flours contain greater concentrations of phytates than refined products, such as processed flour or polished rice. Most of the phytates are found in the germ of corn and in the outer layer of wheat and rice bran. Therefore, removing the bran and germ when processing corn, wheat kernels, other grains and polishing rice removes most of the phytates.

## Addition of zinc to existing public health programs

Opportunities to improve zinc status should be applied to ongoing general health and nutrition programs such as growth monitoring programs, diarrhea treatment facilities, integrated management of childhood illnesses (IMCI) interventions, and national and targeted fortification programs. Zinc can be included along with other important micronutrients, such

as vitamin A, iodine and iron in all the national activities.

## Points to Remember

- *Zinc is a micronutrient of extraordinary versatility and ubiquity in biology.*
- *Zinc deficiency has physiologic consequences because of its widespread effect on various biological functions.*
- *Positive effects of zinc supplementation on growth, cognitive development, diarrhea, and other infectious diseases have been supported by various large scale studies.*
- *Among the various strategies to improve zinc nutrition, food-based strategies hold the greatest promise. More comprehensive food fortification programs are needed, particularly those aimed at the lowest socioeconomic sectors.*

## References

1. Aggett P, Comerford J. Zinc and human health. *Nutr Rev* 1995; 53: S16-S22.
2. Sandstead H. Is zinc deficiency a public health problem? *Nutrition* 1995; 11: 87-92.
3. Fung EB, Ritchie LD, Woodhouse LR, Roehi R, King JC. Zinc absorption in women during pregnancy and lactation: a longitudinal study. *Am J Clin Nutr* 1997; 66:80-88
4. Brown JL, Pollit E. Malnutrition, poverty and intellectual development. *Sci Am* 1996;274: 38-43.
5. Sandström B. Bioavailability of zinc. *Euro Clini Nutri*, 1997, 51(Suppl. 1): S17-S19.
6. Sandström B, Lönnerdal B. Promoters and antagonists of zinc absorption. In: Mills CF, ed. *Zinc in human biology*. New York, NY, Springer-Verlag, 1989:pp57-78.
7. Sandström B, Almgren A, Kivistö B, Cederblad A. Effect of protein level and protein source on zinc absorption in humans. *Nutri* 1998, 119:48–53.
8. Petterson D, Sandström B, Cederblad Å. Absorption of zinc from lupin (*Lupinus angustifolius*)-based foods. *Br Nutri*, 1994; 72: 865–871.
9. Gibson R, Ferguson E. Assessment of dietary zinc in a population. *Am J Clin Nutr* 1998; 68(suppl): 430S–434S.
10. Gibson R. Zinc nutrition in developing countries. *Nutr Res Rev* 1994; 7: 151-173.
11. Sandström B. Dietary pattern and zinc supply. In: Mills CF, ed. *Zinc in human biology*. New York, NY, Springer- Verlag, 1989: pp350-363.
12. Brown KH, Pearson JM, Allen LH. Effect of zinc supplementation on children's growth: a meta-analysis of intervention trials. *Bibliotheca Nutritio et Dieta* 1998; 54: 76–83.
13. Black MM. Zinc deficiency and child development. *Am Clini Nutri* 1998, 68(Suppl.): S464–S469.
14. Castillo-Duran C, Heresi G, Fisberg M, Uauy R. Controlled trial of zinc supplementation during recovery from malnutrition: effects on growth and immune function. *Am J Clin Nutr* 1987; 45: 602-608.
15. Fuchs G. Possibilities for zinc in the treatment of acute diarrhea. *Am J Clin Nutr* 1998; 68(suppl): 480S–483S.
16. Roy S, Tomkins A. Impact of experimental zinc deficiency on growth, morbidity, and ultra structural development of intestinal tissue. *Bangladesh J Nutr* 1989; 2: 1–7.
17. Koo S, Turk D. Effect of zinc deficiency on the ultra structures of the pancreatic acinar cell and intestinal epithelium in rat. *J Nutr* 1977; 107: 896–908.
18. Endsley S, Galbraith A. Are you overlooking oral rehydration in childhood diarrhea? It's not just for use in developing countries. *Postgrad Med* 1998; 104: 159-171.
19. Hambidge K. Zinc deficiency in young children [editorial]. *Am J Clin Nutr* 1997; 65: 160-161.
20. Robberstad B, Strand T, Black RE, Sommerfelt H. Cost effectiveness of zinc as adjunct therapy for acute childhood diarrhea in developing countries. *Bull WHO* 2004; 82:523-531.
21. Zinc Investigators' Collaborative Group. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *Am J Clin Nutr* 2000; 75: s1516-1522.
22. Zinc Investigators' Collaborative Group. Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries: pooled analysis of randomized controlled trials. *J Pediatr* 1999; 135: 689-697.
23. Sazawal S, Black R, Bhan M, Jalla S, Sinha A, Bhandari N. Efficacy of zinc supplementation in reducing the incidence and prevalence of acute diarrhea—a community-based, double-blind, controlled trial. *Am J Clin Nutr* 1997b; 66: 413-418.
24. Henker J, Gabsch HC. Serum zinc level in children with celiac disease. *Helv Paediatr Acta* 1985; 40: 47-53.
25. Rawal P, Thapa BR, Prasad R, Prasad KK, Nain CK, Singh K. Zinc supplementation to

- patients with celiac disease - is it required?  
J Trop Pediatr 2010. Published in advanced access.
26. Sazawal S, Black R, Jalla A, Mazumdar S, Sinha A, Bhan M. Zinc supplementation reduces the incidence of acute lower respiratory infections in infants and preschool children: a double-blind, controlled trial. *Pediatrics* 1998; 102:1-5.
  27. Brooks WA, Santosham M, Naheed A, Goswami D, Wahed MA, Diener West M, et al. Effect of weekly zinc supplements on incidence of pneumonia and diarrhoea in children younger than 2 years in an urban, low-income population in Bangladesh: randomised controlled trial. *Lancet* 2005; 366: 999–1004.
  28. Shankar A, Genton B, Baisor M, Paino J, Tamja S, Adiguma T, et al. The influence of zinc supplementation on morbidity due to *Plasmodium falciparum*: a randomized trial in preschool children in Papua New Guinea. *Am J Trop Med Hyg* 2000; 62: 663-669.

### CLIPPINGS

***Van Westreenen, Mireille; Tiddens, Harm A.W.M New Antimicrobial Strategies in Cystic Fibrosis. Pediatric Drugs, 11/01/2010***

This article focuses on recent developments in the field of new antimicrobial strategies for CF. It is clear that studies on new classes of antibiotics or antimicrobial-like drugs are scarce, and that most studies involve new formulations, new routes of delivery, or analogs of existing classes of antibiotics. Studies of new antibiotic-like drugs are, in most cases, in preclinical phases of development and only a few of these agents may reach the market. Importantly, new inhaled antibiotics, e.g. aztreonam, levofloxacin, and fosfomycin, and new, more efficient delivery systems such as dry powder inhalation and liposomes for current antibiotics are in the clinical phase of development. These developments will be of great importance in improving effective treatment and reducing the treatment burden for CF patients in the near future.

***Emily T. Martin, , Tara Kerin, MS, Dimitri A. Christakis, Heidi K. Blume, et al. Redefining Outcome of First Seizures by Acute Illness. Pediatrics, Dec 2010***

Seizures are common in children, but the causes and recurrence risk for children with a nonfebrile first seizure remain poorly understood. In a prospective longitudinal study of children who presented with a first-time seizure, the viral etiology of associated infectious illnesses was investigated and sought to determine the risk of recurrent seizures stratified by fever and type of illness. Children with acute gastroenteritis at first seizure, regardless of fever, had a lower risk of seizure recurrence compared with children with other acute illnesses. The results confirm the role of gastrointestinal illness as a distinguishing feature in childhood seizures. Children with this distinct presentation have a low rate of seizure recurrence and few neurologic complications.



## INFANT AND CHILD NUTRITION

### NEWER IRON PREPARATIONS: ADVANTAGES AND LIMITATIONS

\* **Sudhir Vinod Sane**

**Abstract:** *There are various iron preparations in the market. They can be divided into three types. 1) Salts of iron either ferrous or ferric form. 2) Chelates or complexes of iron. 3) Novel forms such as pure metallic form, micronized form etc. Newer iron preparations may have some advantages over traditional iron preparations mainly in terms of lesser unpleasant effects and more palatability. Some preparations have better bioavailability. A clinician should evaluate each of these preparations on its merits and demerits factoring also the cost of these newer preparations. One needs to monitor effectiveness of therapy for the individual patient irrespective of the type of iron used.*

**Key words:** *Newer iron preparations, Absorption, Side effect profile, Acute toxicity.*

Iron deficiency is the commonest nutrient deficiency across the globe. Its impact is felt mostly in developing countries and in children less than two years of age. As many as 50 % of pregnant women and 40 % of children are afflicted with iron deficiency anemia in developing countries.

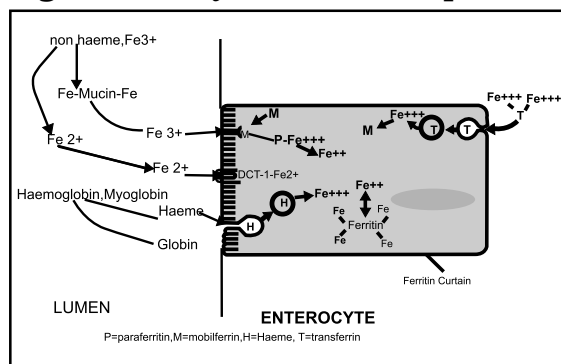
Iron deficiency is known to cause impairment of many systems including central nervous system. Some effects of this impairment may be irreversible even after treatment.

\* Consultant Pediatrician,  
Thane.

Iron preparations available can be classified as salts of iron or complexes of iron such as iron poly maltose complex (IPC), ferrous bis glycinate. There are also some novel preparations like carbonyl iron or colloidal iron. Iron salts can be either of ferrous or ferric form.

Ferrous sulfate is the oldest iron salt available for treatment and prevention of iron deficiency. However due to its side effect and toxicity potential newer iron salts are being developed. An attempt is made in the following pages to describe the rationale behind the newer iron salts, their advantages and limitations. For the purpose of this article all oral iron salts developed subsequent to initial ferrous salts are referred to as “newer” iron salts.

**Fig.1. Pathways of iron absorption**



**Intestinal iron absorption:** Food contains iron in two forms heme and non heme. There are three pathways for intestinal iron absorption. Heme form is directly absorbed in enterocyte through a process of endocytosis which is not yet completely understood. Non-heme portion of iron exists mainly in ferric form. Some amount

of ferric iron is reduced to ferrous form and then absorbed by a 'divalent cation transporter- 1' pathway (DCT-1). Rest of it is absorbed with the help of two ligands via mobilferrin-integrin pathway (Fig.1).<sup>1</sup>

### **Ferrous sulfate (FS) basic information:**

Older iron salts included ferrous sulfate, ferrous fumarate and ferrous gluconate. These salts have several advantages. FS has elemental iron of 20% in dry form. Its bioavailability in non iron deficiency states is 10%. However this can increase by 2-3 times in presence of deficiency state. Dietary inhibitors such as phytates, phosphates, polyphenols, etc. can markedly decrease iron absorption.

FS can cause teeth staining and gastrointestinal side effects due to its free radical action. All this and prolonged treatment leads to poor compliance which is reported to be up to 30-40%.

FS is not stable in liquid form and hence is available as elixir. Other ferrous salts such as gluconate, fumarate, etc are more stable in liquid form. However they do not differ much in side effects profile from FS. Claimed lesser gastrointestinal side effects are due to lesser elemental iron content.

One of the important drawbacks of FS is its acute poisoning potential. When there is no demand for iron, iron absorbed from the intestinal lumen doesn't enter circulation directly. It is stored in the epithelial cell as ferritin. When there is demand the ferritin from enterocyte is absorbed. In periods of no demand the ferritin stored in the intestinal cell is lost when the cell is shed. This process prevents excessive iron absorption. This safety mechanism is variably called as 'Ferritin curtain' or 'mucosal barrier'. Large doses of FS have the capacity to overcome this ferritin curtain and cause toxicity. Some of the newer iron compounds have advantage of more safety potential due to different mechanism of absorption (Fig.1).

## **Newer iron preparations: Preparations, advantages and limitations**

**Iron III polymaltose complex (IPC):** It is iron preparation of non ionic iron and polymaltose in stable form. The formulation is available with variable elemental iron content ranging from 25-40%.

The absorption of Iron (Ferric) III polymaltose complex is thought to resemble natural process of iron absorption from food via mobilferrin-integrin pathway. In the presence of excessive IPC the ligands get saturated thereby limiting the absorption and thus increasing the safety profile.

Because iron is in complex form, it is associated with better tolerability. As there are less free radicals, gastrointestinal side effects are less. There is lesser incidence of teeth staining.

Even from latest studies IPC is known to have good efficiency for treatment and prevention of iron deficiency.<sup>2</sup>

However a major limitation of IPC is its inability to bring up the hemoglobin consistently.<sup>3</sup> Most probably this is due to variation in IPCs of different brands due to their pharmacokinetic properties such as pH, etc. Thus a clinician should be aware that IPC preparations from different manufacturers may have different bioavailability.

**Colloidal iron:** Colloidal iron forms are very popular in India. They are economical even in syrup formulations. These are ferric hydroxide compounds which get soluble in hydrochloric acid and then absorbed. The elemental iron content is high (50%).

**Carbonyl iron:** These are very small micronized particles of pure metallic iron. The name carbonyl iron is given due to the manufacturing process. These iron forms were initially used as food fortifiers to prevent iron deficiency and are now marketed for the treatment.

This iron in pure form is made soluble by the action of hydrochloric acid from stomach and then absorbed. This is a slow process depending on gastric pH. Due to slow absorption rate acute toxicity potential is less than FS. However for the same reason there is reduction in bioavailability, which is 70% of FS.<sup>4</sup>

Side effect profile is similar to FS with lesser incidence of teeth staining. Other category of newer irons include iron molecule either complexed or chelated with absorption enhancers. Ascorbic acid, amino acids and complex molecules like EDTA are used as absorption enhancers.

**Ferrous ascorbate:** Presence of vitamin C increases the iron absorption. When ferrous ion is combined with ascorbic acid, ferrous ascorbate has increased bioavailability, reduced side effect profile due to reduced free radicals in the intestine. It also facilitates incorporation of iron into haemoglobin.<sup>5</sup> However the molecule is not totally free of GI side effects. Its safety profile is also like that of FS. It has potential to cause acute toxicity in large doses.

**Sodium feredetate:** In this molecule the iron in ferric form is chelated with EDTA. The iron bound with EDTA is released in the alkaline medium where it is absorbed by usual biophysical processes. Iron availability is less affected by presence of inhibitors. In fact, sodium feredetate works as a better food fortification agent when used with foods with high dietary inhibitors. It has excellent safety potential, reduces the teeth staining. Similarly it has less gastrointestinal side effects. The formulation is sugar free and can be mixed in milk or juice.

**Ferrous bis glycinate and other amino acid chelates:** In these compounds iron is chelated with amino acids. This process of chelation probably does not allow iron to form insoluble compounds like in presence of inhibitors. Ferrous

bis glycinate, ferric tris- glycinate are representatives of this group.

Ferrous bis glycinate is now commercially available as iron preparation both in syrup and capsule form with 20% elemental iron content. Here, iron is covalently bound with two molecules of glycine to form chelate. It has good bioavailability in presence of phytates.<sup>6</sup> There seems to be a mechanism of absorption of Iron amino acid chelate that is distinct from handling of non-heme iron by enterocyte and also a mucosal mechanism that prevents excess absorption of iron when there is no need.<sup>7</sup> The molecule has good GI tolerability.

**Micronized iron forms:** These are used as sprinklers or food fortifiers. This form of iron looks promising if consistent bioavailability can be demonstrated. Recently there have been reports of utility of micronized iron for treatment of iron deficiency anemia.<sup>8</sup> This form of iron looks exciting. In a study from India micronized fortified iron form was better tolerated than conventional iron in 'drop' form. There was also better compliance.<sup>9</sup>

**Combination of iron salts with vitamins, etc:** There is no evidence that any trace element, vitamin or other hematinic significantly increases response to iron salt. In fact, some of the iron preparations in market have calcium or zinc added which should be considered as irrational.

### **Intravenous iron preparations**

Intravenous iron is only rarely needed in clinical practice. There are mainly three salts available, iron sucrose, iron dextran, sodium ferric gluconate. Intravenous iron rapidly replenishes the iron store, however rise in the hemoglobin may not be faster than with oral iron.

**Indications:** Mainly used in patients with chronic renal insufficiency especially in adults.

These are the patients who are on long term renal replacement therapy.

Other indications might be an occasional patient with severe intolerance to oral iron, or with severe iron malabsorption like in celiac disease.

The infusion of intravenous iron, iron dextran can be given in single dose. However its use is limited by its potential to cause anaphylaxis and delayed adverse effects. It was found that absolute rates of potential life threatening adverse drug events were 0.6, 0.9, 11.3 per million for iron sucrose, sodium ferric gluconate complex and higher molecular weight iron dextran respectively.<sup>10</sup> Sodium ferric gluconate can cause rare anaphylaxis however the maximum dose at single infusion can not be more than 125mg. Iron sucrose seems to be safer with no cases of fatal anaphylaxis reported and can be given in single dose.

## Conclusion

Ferrous Sulfate is effective and preferred iron in most of the clinical conditions. Wide variety of iron preparations increases therapeutic options for the physician to choose in different clinical situations. One must evaluate the minor differences amongst them so as to increase our prescription efficiency. For example a fussy child may be given tastier preparation of iron such as IPC, whereas a child who is refusing to take medicines can be given sodium feredetate mixed with food or fruit juices. A school going child can be prescribed ferrous bis glycinate, sodium feredetate or IPC preparation which avoids teeth staining. When safety due to acute toxicity is of concern IPC or Na feredetate may score over other preparations, however these ferric molecules especially IPC may cause unreliable hemoglobin rise. Similarly sodium feredetate is a new molecule and hence

effectiveness of both needs to be monitored for the individual patient. A common problem while prescribing iron is its tendency to cause constipation, here IPC, sodium feredetate, Iron bis glycinate would score over other preparations (Table.1).

While choosing the dose, it is elemental iron content that should be calculated and not the content of iron salt e.g. each 5 ml of a sodium feredetate may have 231 mg of salt but at 14.3% of elemental iron means its elemental iron content is 33 mg.

From practical point of view oral iron preparation in some or other form and dose will almost always be effective in correcting iron deficiency anemia and hence intravenous iron preparations have a small, if at all any place in pediatric clinical practice.

Most of the times any iron preparation with reasonable bioavailability is good in treating iron deficiency and it is important not only to diagnose and treat iron deficiency but to follow up for effectiveness of treatment irrespective of any iron preparation that has been used.

A physician should take advantage of this vast array of iron preparations for effectively increasing prescription efficiency. While choosing a thought should be given to efficiency, cost, side effect profile and also safety profile (Table.2). Also look at other contents which may interfere with the bioavailability of iron. When side effects occur, most of the times they can be decreased by dividing the dose or starting with a smaller dose.

When a clinician uses any iron preparation the effectiveness should be monitored and the treatment continued for at least three months to replenish iron stores.

**Table.1. Effective elemental iron content of various iron preparations.**

Name of iron salt	Mg of salt / 5ml in the preparation	Elemental iron	Effective elemental iron /5ml#	% absorbed*
FS (excicated)	100	20%	30	10%
Ferrous fumarate	100	33%	33	10%
IPC	**	25-40%	50	10%
Colloidal	100	50%	50	
Carbonyl	50	100%	50	7.3-11.7%
Ferrous ascorbate	180	16.6%	30	30-40%
Na-feredetate	231	14.3%	33	25%
Ferrous bis glycinate	150	20%	30	30-40%

\* Percentage of iron absorbed varies depending on iron status of patient.

# Elemental iron content of different brands may vary.

\*\* mg of salt may be variable in different preparations.

**Table.2. Summary of advantages and limitations of various iron preparations.**

Name of iron salt	Affected by dietary inhibitors	Teeth staining	GIT side-effects	Toxic potential	Available in syrup form	Cost in Indian rupees.#
FS	Yes	Yes	Yes	yes	Yes	36
Ferrous fumarate	yes	yes	less	yes	yes	77
IPC	No	No	No	No	Yes	70
Colloidal	Yes	Yes	Yes	yes	Yes	47
Carbonyl	Yes	No	Yes	less	Yes	48
Ferrous ascorbate	less	Yes	Less	Yes	Yes	150
Na-feredetate	No	No	Less	No	Yes	117
Ferrous bis glycinate	less	Less	Less	Less	Yes	132

# For 1 month treatment of 10 kg child @ 6mg/kg\* of elemental iron. Cost may vary according to the brand.

\* Many authorities advocate dose of 3mg/kg/d of elemental iron for treatment of iron deficiency anemia.

## Points to Remember

- *Ferrous sulfate is cheap and effective in most cases for treatment of iron deficiency anemia.*
- *Newer irons have various advantages over FS.*
- *These advantages come at a cost and sometimes at effectiveness.*
- *Dose of iron should be calculated according to elemental iron of the preparation.*
- *Therapy should be monitored for effectiveness.*

## References

1. Conrad ME, Umbreit JN. Pathways of iron absorption. *Blood Cells Mol Dis* 2002; 29:336-355.
2. Tobli JE, Brignoli R. Iron III –hydroxide polymaltose complex in iron deficiency anaemia/review and meta analysis. *Arzneimittelforschung* 2007;57:431-438.
3. Mehta BC. Ineffectiveness of iron polymaltose in treatment of iron deficiency anemia. *J Assoc Physicians India* 2003;51:419-421.
4. Devasthali SD, Gordeuk VR, Brittenham GM, Bravo JR, Hughes MA, Keating LJ. Bioavailability of carbonyl iron: a randomized double blind study. *Eur J Haematol* 1991;46:272-278.
5. Teucher B, Olivares M, Cori H. Enhancers of iron absorption: ascorbic acid and other organic acids. *Int J Vit Nutr Res* 2004; 74:403-419.
6. Bovell-Benjamin AL, Viteri FE, Allen LH. Iron absorption from ferrous bis glycinate and ferric trisglycinate in whole maize is regulated by iron status. *Am J Clin Nutr* 2000;71:1563-90.
7. Ashmead HD. The absorption and metabolism of iron amino acid chelate. *Arch Latinoam Nutr* 2001;51:13-21.
8. Beininger MA, Velasquez-Melendez G, Pessoa MC, Greiner T. Iron fortified rice is as efficacious as supplemental iron drops in infants and young children. *J Nutr* 2010; 140:49-53.
9. Hirve S, Bhavsar S, Bavdekar A, Naik S, Pandit A, Schaffer C, Christofides A, Hyder Z, Zlotkin S. Low dose 'sprinkles' - an innovative approach to treat iron deficiency anemia in infants and young children. *Indian Pediatr* 2007;44:91-100.
10. Chertow GM, Mason PD, Vaage Nilsen O, Ahlmen J. Update on adverse drug effects associated with parenteral iron. *Nephrol Dial transplant* 2006;21:378-382.

## CLIPPINGS

### *Inhaled nitric oxide for respiratory failure in preterm infants*

Inhaled Nitric Oxide (iNO) as rescue therapy for the very ill preterm infant does not appear to be effective. Early routine use of iNO in preterm infants with respiratory disease does not affect serious brain injury or improve survival without BPD. Later use of iNO to prevent BPD might be effective, but requires further study.

Barrington KJ, Finer N. Inhaled nitric oxide for respiratory failure in preterm infants. *Cochrane Database of Systematic Reviews* 2010, Issue 12. Art. No.: CD000509. DOI: 10.1002/14651858.CD000509.pub4. This version first published online: January 25, 1999. Last assessed as up-to-date: October 13, 2010

GENERAL ARTICLES
------------------

## SKIN MANIFESTATIONS IN PEDIATRIC HIV INFECTION

\* Sandipan Dhar

\*\* Raghubir Banerjee

**Abstract :** *The commonest skin manifestation in HIV infection is a nonspecific generalized dermatitis. Other skin lesions are secondary infections and the frequency is related to the severity of immune suppression. Viral, bacterial, and fungal skin infections are more common, but also more difficult to treat than in children who are not immuno-compromised. A wide variety of clinical expressions of the acquired immunodeficiency syndrome (AIDS) has been apparent from the earliest case reports in adult patients and pediatric patients. Both human immunodeficiency virus (HIV) infection and AIDS in children are associated with an increased prevalence of several dermatologic manifestations*

**Key words :** *HIV infection, Neoplasm, Vascular lesions, Seborrhoeic dermatitis.*

HIV infection affects children causing pediatric AIDS which is manifested by loss of immunity, wasting and neurological degeneration. This RNA virus bearing tropism for CD4 surface antigen was found to progressively decrease the immune function

approximately of 3.2 million children infected by HIV.<sup>1</sup> Perinatal transmission, receiving contaminated blood products and sometimes breast feeding are relevant transmission modes in children. Apart from general features like fever, weight loss, diarrhoea, lymphadenopathy, mucocutaneous manifestations correlating with the immunosuppression are observed in children.

The most common skin manifestation of HIV/AIDS in children is a non-specific generalized dermatitis. Other skin lesions are secondary infections and the frequency is related to the severity of immune suppression. Viral, bacterial, and fungal skin infections are more common, but are also more difficult to treat than in children who are not immuno-compromised. A wide variety of clinical expressions of the acquired immunodeficiency syndrome (AIDS) has been apparent from the earliest case reports in adult patients and pediatric patients.<sup>2</sup> Both human immunodeficiency virus (HIV) infection and AIDS in children are associated with an increased prevalence of several dermatologic manifestations.

The cutaneous manifestations of AIDS in children can be divided into three categories: (1) neoplastic manifestations; (2) viral, bacterial and fungal manifestations, and (3) vascular lesions and other manifestations. Pediatricians as well as dermatologists may be the first physicians to recognize and to treat the clinical manifestations of AIDS.<sup>3</sup> Cutaneous manifestations are common in patients with HIV infection and mainly due to the immunodeficiency.

---

\* Associate Professor,  
Pediatric Dermatology Division

\*\* Lecturer, Pediatric Dermatology Division  
Institute Of Child Health, Kolkata

In the initial stage of HIV infection, macular rash is frequently observed. During the asymptomatic phase, the patients may typically show the following skin diseases: seborrheic dermatitis, acneiform folliculitis, persistent herpes simplex, and infections with the human papilloma virus. Herpes simplex and herpes zoster may develop into ulcerating and necrotising forms especially in patients with advanced immunodeficiency. Because of the obvious visibility of the integument, these lesions are often the presenting manifestation of HIV-related disease.<sup>4</sup> The cutaneous afflictions are frequently related to the sequelae of impaired immunity and include opportunistic infections and neoplasms as well as dramatic exacerbations and/or the development of rapidly progressive and severe manifestations in pre-existing, normally benign dermatoses.

In many cases of AIDS, iatrogenic cutaneous disorders associated with toxic or allergic drug reactions are seen. With the increasing incidence of pediatric HIV infection and with therapeutic prolongation of survival, certain cutaneous manifestations (especially drug reactions) are likely to become more common. Kaposi sarcoma and other neoplasms may be recognized with increased frequency in HIV-infected children. New or previously unrecognized cutaneous manifestations of pediatric AIDS are likely to emerge. More than 50% of the AIDS patients treated with trimethoprim/sulfamethoxazole developed a severe drug eruption. African and Caribbean patients with AIDS frequently suffer from pruritic skin lesions, the pathogenesis of which is not known. Aside from these cutaneous manifestations, a variety of other skin disorders have been reported in patients with HIV infection, ARC, or AIDS.<sup>(5,6)</sup>

A generalized eruption lasting for a few weeks have been observed in children with acute HIV infection. This rash is usually

papulosquamous and sometimes morbilliform in nature.

Bacterial infections as a result of immune suppression is commonly noted in HIV infected children. Folliculitis, cellulitis, impetigo, ecthyma are some of the common forms of infection mostly due to increased presence of staphylococcus aureus as a skin surface colonizer. Haemophilus influenzae, pseudomonas aeruginosa infections of the skin have been noted in children presenting with bacteraemia or cellulitis sometimes ranging to ecthyma gangrenosum. Mycobacterium marinum Listeria monocytogenes and Mycobacterium avium are some of the other pathogens causing skin infections ranging from follicular papules to pustules and petechiae. Bacillary angiomatosis, although rare in children, is manifested by purplish papulonodular lesions together with general symptoms like fever. This disorder is now found to be caused by Bartonella henselle.<sup>7</sup>

Fungal infections are very common in HIV infected children with oral thrush being the prime manifester. This feature is mostly manifested in symptomatic HIV infection with low CD4 counts. Clinically whitish plaques, atrophic patches and chelitis are commonly seen as the presenting feature. Napkin dermatitis due to candida infection may also develop sometimes spreading beyond the napkin area to the other body folds. Resistance to antifungal agents is a common cause for recurrent candidiasis in HIV infected children. Paronychia and nail dystrophy due to candidal infections may also be a presenting feature in children. Dermatophyte infections like tinea capitis, tinea corporis and onychomycosis in widespread forms have been observed. A number of uncommon fungal infection can affect children causing a bizarre pattern of skin lesions which are not commonly seen. Disseminated sporotrichosis, herpetiform lesions due to cryptococcosis and disseminated



histoplasmosis may cause a variety of cutaneous manifestations.<sup>8</sup>

Viral infections - Varicella zoster virus infection in children has a variable course with severe recurrent forms dominating the picture. Herpes zoster is severe, more painful with scarring and also recurrent episodes are not uncommon. Chronic persistent varicella leading to complications like pneumonia and central nervous system infections have also been observed. Measles in HIV infected children may present with typical or atypical exanthem sometimes warranting a skin biopsy for diagnosis. Complication like pneumonia is often fatal in these children.

Cytomegalovirus infection may present with erosions and bullae in the perineal region. In such conditions skin biopsy and CMV culture are necessary for diagnosis. Epstein - Barr virus infection of the oral mucosa leads to the classic oral hairy leucoplakia in pediatric AIDS. Whitish plaques with fissuring on the sides of the tongue is the common presenting feature in such cases. Molluscum contagiosum infection is usually present in a widespread distribution with giant lesions. Human papillomavirus in children with HIV infection present with widespread warts, resembling epidermodysplasia verruciformis. Large genital or perianal condyloma acuminata are commonly reported in these children. Gianotti- crosti syndrome has also been reported.<sup>9</sup>

## **Infestations**

Crusted scabies or Norwegian scabies are common in children with HIV infection usually presenting with widespread papulonodular lesions infested with large number of mites. papulofollicular eruption caused by Demodex infestation have been reported in HIV infected children.

**Parasitic Infection:** Pustules or deep dermal nodules due to parasitic infection with acanthamoeba has been rarely reported.

## **Inflammatory disorders**

Atopic dermatitis shows a higher incidence among HIV infected children.

HIV-infected adults commonly develop a condition that strongly resembles atopic dermatitis and is sometimes called “atopic-like dermatitis” moreover, atopic dermatitis and other atopic disorders have been described as common manifestations of pediatric HIV infection. Conditions such as sinusitis, asthma, and hyper-IgE syndrome, and laboratory abnormalities, eg, elevated IgE levels, eosinophilia, and possible Th1-Th2 imbalances, suggest a predilection for atopic disorders in these patients.<sup>10</sup> This may be due increased xerosis, viral or bacterial superantigens and epidermal barrier disruption.

Seborrhoeic dermatitis has a more severe presentation in these patients which varies from cradle cap in infants to scaly erythematous lesions on scalp and nasolabial folds in children. Psoriasis also follows a more widespread form in such cases. We have observed a peculiar skin manifestation that resembles cutis marmorata in three patients with AIDS and may be included among the several clinical aspects of AIDS in pediatric patients. One of the three patients died 4 months after the diagnosis. In another patient, the skin lesion is still present 2 years after appearance.<sup>11</sup>

Incidence of drug eruptions are higher in children with HIV infection. Iatrogenic cutaneous disorders associated with toxic or allergic drug reactions are seen. With the increasing incidence of pediatric HIV infection and with therapeutic prolongation of survival, certain cutaneous manifestations (especially drug reactions) are likely to become more common Trimethoprim-

sulphamethoxazole is found to be the prime offender in the pediatric age group. Severe forms like Stevens-Johnson syndrome and toxic epidermal necrolysis are not uncommon in these patients. Palpable purpura and leukocytoclastic vasculitis have been reported in a number of cases. Pityriasis rubra pilaris, pyoderma gangrenosum and ashy dermatosis have also been reported. Pellagra and Kwashiorkor like manifestations have been observed in chronic HIV infection.<sup>12</sup>

Neoplasms- Cutaneous Kaposi's sarcoma presenting as violaceous nodules on skin or mucosa may present in an epidemic form. Smooth muscle tumours like leiomyosarcomas have also been reported in HIV infected children.<sup>13</sup>

New or previously unrecognized cutaneous manifestations of pediatric AIDS are likely to emerge. Familiarity with the various dermatologic presentations of pediatric AIDS can result in the earlier diagnosis and treatment of the disease and, hopefully, the prolongation of the patient's life.

### Points to Remember

- *Non specific generalized dermatitis is the most common skin manifestation in HIV infection.*
- *Other cutaneous manifestations in AIDS fall in to three categories namely viral, bacterial, fungal infections, neoplastic and vascular lesions.*
- *Incidence of drug eruptions are higher in HIV infection, with prolonged survival after therapy.*

### References

1. UNAIDS Joint United Nations Update on HIV/AIDS. AIDS Epidemic Update December 2002. Dermatologic manifestations of AIDS in children.

2. Wananukul S, Deekajorndech, Panchareon C, Thisyakorn, Usha. Mucocutaneous Findings in Pediatric AIDS Related to Degree of Immunosuppression. *Pediatr Dermatol* 2003;20:289-294.
3. Torre D, Zeroli C, Fiori GP, Ferraro G, Speranza F. Dermatologic manifestations of AIDS in children. *Pediatrician* 1991;18:195-203.
4. Nance KV, Smith ML, Joshi VV. Cutaneous manifestations of acquired immunodeficiency syndrome in children. *Int J Dermatol* 1991;30: 531-539.
5. Eichmann A. Skin manifestations in patients with HIV infection. *Z Hautkr* 1990;65:640-644.
6. Wananukul S, Thisyakorn, Usha. Mucocutaneous Manifestations of HIV Infection in 91 Children Born to HIV-Seropositive Women. *Pediatr Dermatol* 1999;16:359-363.
7. Prose N, Mendez H, Menikoff H et al. Pediatric human immunodeficiency virus infection and its cutaneous manifestations. *Pediatr Dermatol* 1987; 4:67-74.
8. Prose NS, HIV infection in children. *J Am Acad Dermatol* 1990; 22:1223-1231.
9. Penneys NS, Hicks B. Unusual cutaneous lesions associated with acquired immunodeficiency syndrome. *J Am Acad Dermatol* 1985;13:845-852.
10. Rudikoff D. The relationship between HIV infection and atopic dermatitis. *Curr Allergy Asthma Rep* 2002;2:275-281.
11. Torre D, Sampietro C, Fiori GP, Dietz A, Montanari M. Skin manifestations in infants with AIDS. *Int J Dermatol* 1987 ;26:459-460.
12. Straka BF, Whitaker DL, Morrison SH, et al. Cutaneous manifestations of the acquired immunodeficiency syndrome in children. *J Am Acad Dermatol* 1988 ; 18: 1089-1092.
13. Chadwick E, Conner EG, Guerra Hanson IC, et al. Tumours of smooth muscle origin in pediatric HIV infected children: an association of AIDS and cancer. *J Am Med Assoc* 1990; 263: 3182-3185.

GENERAL ARTICLES
------------------

## PREVENTIVE DENTISTRY IN PEDIATRICS

**\* Aruna Mohan**

**Abstract:** *Preventive dentistry in children has gained prominence over the years. Unrestricted intake of sugary food and drink, especially in the very young, has resulted in an alarming increase in early childhood caries or dental decay. This contributes to pain, an inability to chew, facial and intra-oral swellings and space loss in the jaws resulting in malocclusions. Trauma causing loss of front teeth and/or dislocation injuries is common place and warrants immediate dental care. If not attended to, such trauma could eventually cause loss of front teeth thus ruining the child's self-esteem. It is therefore important that parents play an active role in the maintenance of good oral hygiene and schedule early dental visits.*

**Keywords:** *Early Childhood Caries, Prevention, Pediatric dentist.*

Oral health is an integral part of overall general health. Good dental health is essential for the comprehensive development of the child. Children's teeth play an important role in speech, nutrition and health and in aesthetics. It is therefore paramount that children's teeth are nurtured and cared for. Pediatricians have the opportunity to recognize and give valuable advice regarding good oral health.

Dental problems in children vary from the common 'decayed' tooth to dental trauma, problems with eruption and/or malocclusions. These problems are seen in children of all age groups and not just relegated to older children as previously believed. Today, pediatric dentists possess a body of scientific knowledge and technology to assist parents in raising caries-free children. Promotion of oral health and preventive dental care has become a fundamental concept in dentistry for children.

Preventive dentistry means a healthy smile and this starts with the first tooth. Daily cleaning of teeth should begin as soon as the first tooth erupts! Early visits to a pediatric dentist are the foundation for a lifetime of good oral health. The goal is to provide infants and toddlers with a pleasant, non-threatening introduction to dentistry and to establish and reinforce the foundation of sound dental habits.

### Importance of 'primary teeth'

Even though they are thought of as dispensable and unimportant, primary teeth serve several important functions in a child.

- They act as a guide for the proper eruption of the permanent teeth.
- Children with healthy primary teeth eat better and have better pronunciation compared with children who have decayed or absent teeth.
- A healthy mouth is more attractive giving children confidence in their appearance.

---

\* Professor and HOD,  
Dept. of Pedodontia and Preventive Dentistry,  
Tagore Dental College, Chennai

- Preventive dentistry can result in less extensive and less expensive – treatment for the child.

The misconception that primary teeth are not all that important since “they fall out anyway” is entirely misleading since these teeth do not begin exfoliating till the child is at least 6 years of age. This process carries on through the years up to age 12 at which time most permanent teeth have erupted. Therefore, maintenance of the primary teeth upto 12 years of age is of utmost importance. Although tremendous variability exists in the timing and sequence of normal tooth eruption, the eruption timing shown in Fig.1 can be used as a guide.

### Problems with tooth eruption

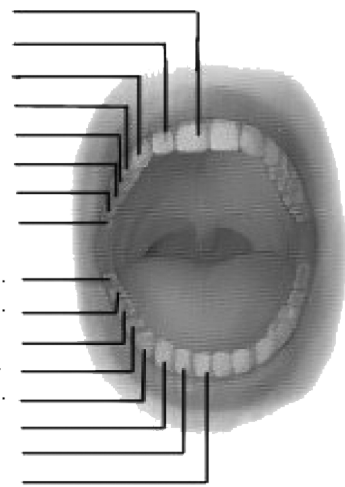
A normal infant's oral cavity will have rugae present on the palate and tooth bud bulges but no teeth present. Eruption of teeth in children may be early or late by as much as 6 months compared to the average time of eruption.

1. Premature eruption of primary teeth is not common, although 1-2 children in 6000 births are found to have natal teeth (teeth present at birth) or neonatal teeth (teeth erupting within 30 days of birth). Of these teeth, 90% are primary teeth and 10% are supernumerary (extra teeth). If highly mobile (aspiration risk) or found to be causing a nursing obstacle, these teeth require extraction.<sup>1</sup>

2. Systemic conditions causing a delay in eruption include hypothyroidism, Down syndrome and certain craniofacial syndromes.<sup>1</sup> Though most delays in eruption are not significant, systemic causes are to be ruled out if this delay persists well beyond the normal range. Additionally, teeth can fail to erupt due to developmental defects, abnormalities in the bone or jaws and the presence of cysts and tumors.<sup>2</sup>

3. Teeth may be congenitally missing with many children having a family history of missing teeth.<sup>2</sup> Most common missing teeth in the

Upper Teeth	Primary Erupt	Permanent Erupt
Central Incisor	8-12 mos.	7-8 yrs.
Lateral Incisor	9-13 mos.	8-9 yrs.
Canine (cuspid)	16-22 mos.	11-12 yrs.
First Premolar		10-11 yrs.
Second Premolar		10-12 yrs.
First Molar	13-19 mos.	6-7 yrs.
Second Molar	25-33 mos.	12-13 yrs.
Third Molar		17-21 yrs.
<b>Lower Teeth</b>		
Third Molar		17-21 yrs.
Second Molar	23-31 mos.	11-13 yrs.
First Molar	14-18 mos.	6-7 yrs.
Second Premolar		11-12 yrs.
First Premolar		10-12 yrs.
Canine (cuspid)	17-23 mos.	9-10 yrs.
Lateral Incisor	10-16 mos.	7-8 yrs.
Central Incisor	6-10 mos.	6-7 yrs.



**Fig. 1. Tooth eruption chart**

permanent dentition include the maxillary lateral incisors and the mandibular second premolars. Congenitally missing teeth may be a characteristic of some syndromes. In some instances, only a few teeth may be missing, as in Down syndrome. Ectodermal dysplasias show multiple missing teeth or a complete absence of teeth.<sup>2</sup>

A common scenario in most practices is the complaint of a normal 6-yr-old child having a 'double row' of teeth in the lower jaws. This is due to the position of the permanent lower incisors, which develop behind (lingual position) the primary teeth (Fig.2). This is more the norm than the exception and is a perfectly normal eruption pattern!



**Fig.2. Normal eruption of lower incisors**

## Dental caries

Dental caries is an infectious and transmissible disease.<sup>3</sup> Although it is multifactorial in nature, the essential factors that cause dental caries are a susceptible tooth, dietary fermentable carbohydrates, and bacterial plaque.

### The process of dental caries involves:

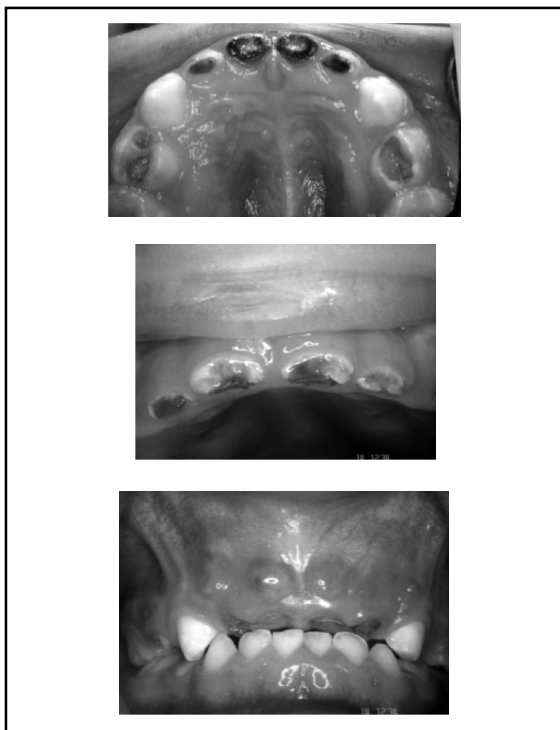
- a primary infection by mutans streptococci,
- accumulation of these microorganisms to pathologic levels as a consequence of frequent and prolonged oral exposure to cariogenic substrates (eg. sugary foods and beverages) and
- rapid demineralization and cavitation of enamel resulting in dental caries.

Although studies show a general decline in the incidence of dental caries in older children, early childhood caries or ECC (earlier termed 'baby bottle tooth decay') remains a major threat to oral health in young children (Fig.3, 4 and 5).

ECC is defined as the occurrence of any sign of dental caries on any tooth surface during the first 3 years of life.<sup>3</sup> This form of caries is associated with frequent and prolonged feeding with a bottle. It is also associated with breast feeding on demand and the use of sweetening agents on a pacifier. The clinical pattern is characteristic, first affecting the primary upper incisors followed by the first primary molars. In the earliest stage, "chalky white spots or lines" appear on the surface enamel along the gum line of the teeth.<sup>5</sup> This is an early warning sign that warrants dental attention. The condition progresses so that the 'white spots' become cavities that are discolored to brown or black. When left untreated, the decay of the incisors eventually continues to such an extent that the crowns of the teeth are weakened and fracture. This process may be so rapid that the parents often perceive the teeth as defective from the moment of eruption!<sup>3</sup>

Needless to say, children with ECC go through phases of pain causing absence at school, an inability to eat, and in severe cases, breakdown of tooth structure with development of dento-alveolar abscesses. At this time, the teeth require almost immediate and extensive management, often under general anesthesia, to help regain oral health.<sup>5</sup>

Decay also contributes to a loss of space in the jaws for the succeeding teeth, thus setting up a stage for bite problems and crowded permanent teeth (Fig.6). This further leads to crowded, mal-aligned teeth in the permanent dentition for which the child then has to undergo orthodontic correction (appliance therapy).



**Fig.3,4,5. ECC (Pictures courtesy: "The Gross, Disgusting and Totally Cool Mouth Book" by Theodore Croll, Reed Drabick Pub, 2004)**

### **Preventing ECC – How can parents help? (Fig.7)**

- DO NOT allow the baby or toddler to fall asleep with a bottle containing milk, formula, or sweetened liquids.
- If the baby needs some comfort between regular feedings or at bedtime, use only water in the bottle.
- Wean children away from night-time bottle feeds by the age of 1.
- Oral care should begin early, with wiping of the gum pads after each feed.
- Brushing of the child's teeth should begin as soon as the first tooth appears.



**Fig.6. Decay leading to loss of space**

- Check the child's teeth regularly. If white or stained areas are seen on the teeth, visit a pediatric dentist right away.
- Monitor dietary habits and restrict sugars, chocolates, sticky sweets, and fizzy beverages.
- As the child grows older, parents should continue to brush the teeth (at least till age 7).

It is indeed common practice by elders in the family or others to give children chocolates and other sweetmeats on a regular basis. In today's nuclear families, it is common to see parents giving in to tantrums by "bribing" the child with chocolates. This practice in India has taken dental caries to alarming proportions in young children.

Prevention is two-pronged. Maintenance of oral hygiene by simple brushing twice a day is essential to prevention. In the younger age group, it is advisable for parents to brush till the child demonstrates dexterity in brushing techniques (usually up to age 7). A strict restriction should be placed on the consumption of plain sugar, sugary foods and fizzy beverages by the child.

### **Dental trauma**

An injury to the teeth of a young child can have serious and long-term consequences, leading to their discoloration, malformation and possible loss. The emotional impact of such an injury can also be far-reaching.<sup>6</sup>

## Help keep decay away

### Babies

- Clean your baby's gums even before her first teeth erupt. Wipe them with a damp washcloth after feedings.
- Start brushing as soon as the first tooth appears. Wet a baby toothbrush and gently rub it back and forth on the surface of the tooth and along the gum line. If you use toothpaste, make sure it's fluoride free

### Toddlers

- Brush your child's teeth for at least 30 seconds (ideally a minute) after breakfast and before bed. Lean her head on your lap and place the brush at a 45° degree angle to the teeth.
- Start using a tiny amount of fluoride toothpaste when she's 2 or 3 years old. Begin flossing teeth when two of the teeth are touching.

### Preschoolers

- Brush your own teeth at the same time as your child brushes, and give him lots of positive feedback.
- Studies have found that manual toothbrushes are just as effective as powered ones. But if letting your kid use an electric or battery-operated one makes it easier to get her to brush, go for it.

### School - Age Kids

- Your child can start brushing and flossing on her own at around age 7. If she can tie her own shoes, chances are she's ready to brush solo. She should now brush for two minutes.
- Look for food and plaque around the gum line of her teeth to see whether she's doing a sufficient job. You can also let her chew gum with Xylitol.

**Fig.7. Keep decay away (Source: PARENTS magazine – 'truth about cavities' Oct. 2006)<sup>9</sup>**

Automobile accidents and unfortunately, increasing cases of child abuse, contribute to dental trauma. Trauma to primary teeth causes more luxation injuries (dislocation) than fractures (Figs.8-10) due to the spongy nature of the bone in young children. However, teeth that are already compromised by the presence of dental caries fracture easily and most often show involvement of the dental pulp.

To prevent complications of trauma, emergency dental intervention is necessary. This is especially true of permanent teeth that can be saved or re-implanted as the need be.<sup>7</sup>

**If there are injuries, parents should**

- Clean the mouth with water and soft cloth
- Check the soft tissues for tears or ulcers
- If the permanent tooth has fallen out, pick it up and wash under tap water. Place the tooth in tap water or a glass of milk and get to a dentist immediately. Teeth re-implanted within an hour of injury have a good prognosis
- If a primary tooth has been dislocated outwards or to the side, wash hands and reposition in the socket. Then take the child to the dentist.
- Most importantly, stay calm. This helps a child come to terms with the injury.



**Fig.8 . Extrusion and intrusion injuries in the primary dentition**



**Fig. 9 Fractured incisor**



**Fig.10 Avulsion of an incisor**

(Source : “The Gross, Disgusting and Totally Cool Mouth Book” by Theodore Croll, Reed Drabick Pub, 2004)<sup>10</sup>



**Figs. 11 and 12. Malocclusion**

### **Malocclusions**

Disturbances in eruption and jaw growth may result in significant malocclusions (Figs. 11 and 12).<sup>8</sup>

The etiology of these disturbances can include cranio-facial malformations, cleft lip and

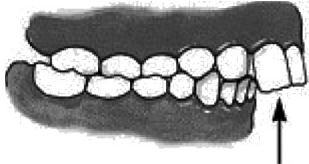
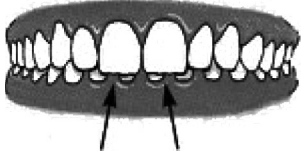
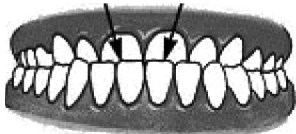
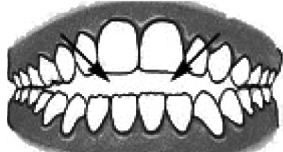
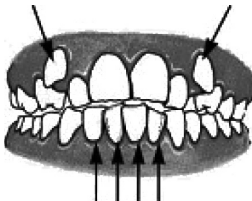
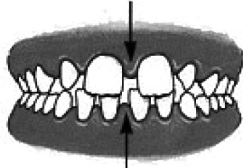
palate, inherited parental growth patterns, oral-digital habits and trauma.<sup>8</sup>

### **Management**

Management of malocclusions is done with removable and/or fixed appliances.<sup>8</sup> This constitutes what is referred to as



**Fig. 13. Five warning signs to look for in 8-year-olds<sup>11</sup>**

<p><b>1. Do the upper teeth protrude?</b></p> <p>Excessive protrusion of the upper front teeth or “buck teeth”</p>	
<p><b>2. Is there a deep bite?</b></p> <p>The upper front teeth cover the lower front teeth too much.</p>	
<p><b>3. Is there an underbite or “cross bite of the front teeth?”</b></p> <p>The upper front teeth fit inside the arch of the lower teeth.</p>	
<p><b>4. Is there an open bite?</b></p> <p>The child can stick his/her tongue between the upper and lower front teeth when the back teeth are together. This occurs mainly due to finger sucking habits.</p>	
<p><b>5. Is there overcrowding or spacing of the teeth?</b></p> <p>Too little room or overlapping teeth</p>	
<p>Too much room or large gaps between teeth.</p>	

‘orthodontic’ treatment. These appliances range from the simple ‘habit-breaking appliance’ to ‘orthodontic brackets and wires’. Depending on the severity of the malocclusion and the age of the child, dentists diagnose and plan treatment.

Early visits to a pediatric dentist would go a long way in preventing problems. Pediatric dentists counsel children and parents regarding prevention and help alleviate a child’s fear of the dentist by creating an ambience of comfort and

warmth. Good habits learned early can provide a child with a lifetime of good oral health.

### Points to Remember

- *Primary teeth are essential for proper speech development and for guidance of eruption of permanent teeth.*
- *Avoid prolonged bottle feeding.*
- *Parental supervision and brushing twice daily is important in the maintenance of oral hygiene.*
- *Accidents involving the teeth warrant immediate dental attention.*
- *Visits to a pediatric dentist in early childhood can help prevent dental problems and alleviate any phobia associated with dentistry.*

### References

1. Pinkham JR, Casamassimo PS, McTigue DJ, Fields Jr. HW, Nowak AJ, editors: Pediatric Dentistry – Infancy through Adolescence. 4th edn., Saunders, An Imprint of Elsevier, 2005; 212-215.
2. Wright TJ: Normal formation and development defects of the human dentition. In: DCNA: Pediatric Oral Health 2000, 47: 975-1000.
3. Berkowitz R: Etiology of nursing caries: A microbiologic perspective. J Pub Health Dent 1996;56: 51-54.
4. Twetman S, Garcia-Godoy F, Goepferd S: Infant oral Health. In: DCNA: Pediatric Dentistry Vol. 2000;44: 487-504.
5. Caufield PW, Griffen AL: Dental Caries: An infectious and transmissible disease. In: DCNA: Pediatric Oral Health 2000;47: 1001-1019.
6. Andreasen JO, Andreasen FM. Classification, Etiology and Epidemiology. In: Textbook and Color Atlas of Traumatic Injuries to the teeth, 3<sup>rd</sup> edn, Munksgaard. 1994; pp151-162.
7. Andreasen JO, Andreasen FM. Examination and Diagnosis of Dental Injuries. In: Textbook and Color Atlas of Traumatic Injuries to the teeth. 3<sup>rd</sup> edn, Munksgaard. 1994; pp196-215.
8. Profitt WR, Fields HW, Sarver DM. Contemporary Orthodontic Appliances. In: Contemporary Orthodontics. 4th edn, Mosby Inc. 2007; pp395-493.
9. PARENTS magazine: 'Truth about cavities', Oct 2006.
10. Croll, Theodore: "The Gross, Disgusting and Totally Cool Mouth Book". Reed Drabick Pub, 2004.
11. Michael L Stepovich DDS, 4110 Moorpark Ave, San Jose, CA 95117. Health article - "Seven warning signs in 7-yr-olds". Dr. Mike's Wire Works website.

### NEWS AND NOTES

**IAP Training Programme in Pediatric Allergy  
Conducted by IAP Allergy & Applied Immunology Chapter  
at Chennai  
21st – 27th March, 2011**

#### Contact

**Dr. Major K Nagaraju**

Senior consultant in pediatric allergy

Kanchi Kamakoti CHILDS Trust Hospital

12 A, Nageswara Road

Nungambakkam, Chennai 600 034.

Mobile: 09840230199, Email: majorknr@yahoo.co.in

<b>DRUG PROFILE</b>
---------------------

## AMINOGLYCOSIDES IN PEDIATRIC PRACTISE

\* **Jeeson C Unni**

**Abstract:** *The aminoglycoside antibiotics - netilmicin, gentamicin, tobramycin and amikacin have been widely used in pediatric practice for treating gram negative infections. They are all old agents and are now rarely considered the drugs of choice for common bacterial infections. However, new roles for this group are being coined, especially with the emergence of MDR gram-negative bacilli, studies suggesting its efficacy in single daily dose and its synergism when combined with other antibiotics in treating certain gram-positive cocci and gram-negative bacilli.*

**Keywords:** *Aminoglycosides, Children*

Aminoglycosides are a class of bactericidal antibiotics characterized by the presence of a six-carbon aminocyclitol ring, covalently bonded to multiple amino sugar groups. They are a widely used class of drugs in the treatment of various infectious diseases in pediatric patients. The extensive use of these agents, whether proper or improper, may lead to poor therapeutic outcome in terms of both health and economy. A review of these agents may serve to identify absolute indications and safety of this group of antibiotics. Aminoglycosides, as a class, possess many of the property considered by infectious

disease specialists to be inherently associated with an ideal antibacterial agent. Despite the introduction of newer less toxic, antimicrobial agents, such as cephalosporins and newer beta lactam antibiotics, aminoglycosides continue to serve a useful role in the treatment of serious enterococcal and gram negative bacillary infections.<sup>1</sup> Aminoglycosides are used commonly in neonates, in immunosuppressed individuals and children with chronic diseases such as cystic fibrosis who are at risk of developing systemic gram negative bacterial infections. The prolonged and improper use of aminoglycosides may result not only the development of resistance pathogens and also development of nephrotoxicity and ototoxicity. It is necessary to evaluate the usage of aminoglycosides in the hospital settings as reports from the West suggest that this group of antibiotics have been primarily relegated to a role as companion drugs either to broaden coverage against gram-negative aerobic bacilli or to provide synergistic killing against gram-positive cocci or certain gram-negative bacilli.<sup>2</sup> Further, with the emergence of MDR gram-negative bacilli, aminoglycosides, along with the polymyxins, may become antibiotics of last resort.<sup>3</sup> The major change in the use of aminoglycosides has been a trend toward single daily dosage, even though this is not an FDA-approved dosing regimen.

### Mechanism of Action

Aminoglycosides act in part by impairing bacterial protein synthesis through irreversible binding to the 30S subunit of the bacterial ribosome.

---

\* Consultant Pediatrician,  
Dr Kunhalu's Nursing Home, Cochin, Kerala.

## Pharmacokinetics

The aminoglycosides are rapidly bactericidal broad-spectrum antibiotics that need to be administered parenterally because it is not absorbed when given orally. After intravenous infusion of 1.7 mg/kg gentamicin (every 8 hour dosage), peak serum levels (C<sub>max</sub>) are 4 to 10 µg/mL. After infusion of 5 mg/kg (once daily dosage), peak levels are about 20 µg/mL serum. The half-life of all aminoglycosides is about 2 to 3 hours. Protein binding is low (<10%) and, because the agents are water soluble, they are distributed in the intravascular space and into interstitial fluid. The drugs diffuse into synovial, pleural, and peritoneal fluids, but penetration into CSF and bile is poor. Their CSF penetration, except in neonates, is poor and they are entirely excreted through kidney. In the absence of large effusions and edema, the volume of distribution is low. Increases in the volume of distribution tend to decrease the C<sub>max</sub> and area under the serum-concentration-time curve (AUC), and increases in clearance tend to decrease the AUC. For example, the volume of distribution tends to be elevated and peak serum levels decreased in patients who have large effusions, fever, burns, or congestive heart failure and in critically ill patients.<sup>4</sup>

## Spectrum of activity and recommended uses

Their spectrum includes Gram negatives including pseudomonas and staphylococci but they are inactive against anaerobes, streptococci and intracellular organism. However, they may exhibit synergism with beta-lactam antibiotics, especially against streptococci and enterococci. The clinical application of drug synergy is based primarily on in vitro and animal studies because there are no comparative trials showing better cure rates with addition of an aminoglycoside.<sup>5</sup> Synergy is lacking or variable when

aminoglycosides are combined with newer drugs such as daptomycin, quinupristin-dalfopristin, or linezolid.<sup>6</sup> The synergistic killing effect of beta-lactam antibiotics and aminoglycosides has been demonstrated in multiple animal models with multiple aerobic gram-negative bacilli and gram-positive cocci. In uncontrolled clinical studies, synergistic activity has been demonstrated to be important in the treatment of native valve endocarditis caused by enterococci and in prosthetic valve endocarditis due to *S epidermidis*.<sup>7</sup> Though there is a lack of clinical studies to clearly demonstrate benefits of drug synergy with aminoglycosides in serious *P aeruginosa* infections, and in infections caused by gram-negative bacilli in neutropenic patients, they remain among the most active antibiotics against *P aeruginosa*.<sup>8</sup>

Gentamicin and Netilmicin needs to be the most used among the aminoglycosides, especially for serious infections - usually in combination with beta lactams. When additional anaerobic cover is required metronidazole needs to be added to the regime. Netilmicin is probably less toxic than gentamycin, but less active against pseudomonas aeruginosa. Tobramycin has better pseudomonas cover but is less active against other gram negatives. Hence it is combined with anti-psuedomonal beta lactam in treating pseudomonal infections. Amikacin is stable to many aminoglycoside converting enzymes which confer resistance. Therefore, it should preferably be reserved for serious infections by organisms resistant to other aminoglycosides.<sup>9</sup> Though these are the recommended order of preferences for aminoglycoside usage, gentamicin and amikacin are more commonly used in India.<sup>10,11</sup>

## Pharmacodynamics

Aminoglycosides demonstrate the following well - (i) Concentration-dependent killing<sup>12</sup> - for drugs with this property, giving the total daily

dose once every 24 hours rather than in smaller divided doses would maximize the C max and possibly allow for comparable or better efficacy at greater convenience and lower cost (ii) Post antibiotic effect (PAE) has been demonstrated for both staphylococci and gram-negative bacilli - meaning that suppression of bacterial growth persists despite concentrations of antibiotic below the MIC<sup>12,13,14</sup> (iii) Postantibiotic leucocyte enhancement (PALE) - Enhanced phagocytosis of aminoglycoside-exposed bacteria by host leukocytes has been observed in vitro.<sup>15</sup>

The antibacterial effects of aminoglycosides can be impaired in a couple of settings. (i) acidic or anaerobic environment impairs the activity of aminoglycosides.<sup>16,17,18</sup> (ii) adaptive resistance - transient reduction bacterial killing rate following pre-exposure to that drug.<sup>19</sup> This phenomenon has been observed mainly when *P. aeruginosa* is treated with aminoglycosides. Reported also with other gram-negative bacilli and more recently while treating staphylococcal infection.<sup>20,21</sup> Once-daily dosing may help overcome this handicap by providing a drug-free interval.<sup>12</sup>

### **Extended-interval aminoglycoside administration for children**

All the above mentioned characteristics of aminoglycosides and the possibility of lower accumulation in renal tubules and inner ear, makes once daily dosing (ODD) of this group of antibiotics possible and probably better than multiple daily dosing. Although single trials have been small, the available randomized evidence supports the general adoption of ODD of aminoglycosides in pediatric clinical practice.<sup>22</sup> This approach is projected to minimise cost, simplify administration, and provide similar or even potentially improved efficacy and safety, compared with MDD of these drugs. However,

multiple daily dosing has remained a common strategy for both children and adults despite the fact that evidence from many dozens of randomized trials and meta-analyses has failed to show its superiority and have even suggested its inferiority.<sup>23</sup> This is because there still remains gaps in our knowledge about (i) the incidence of ototoxicity, (ii) the appropriate dose (which varied from 4 to 7.5 mg/kg per 24 hours in various trials), and (iii) the role and appropriate mode of therapeutic drug monitoring with extended-interval aminoglycoside administration; issues that are crucial to the pediatrician considering adopting this dosage schedule.<sup>24</sup> Clinicians also need to be provided with recommendations about which groups of children can receive extended-interval aminoglycoside dosing safely (newborn; children in special circumstances like cystic fibrosis, UTI, oncology; or all children?). A once-daily regimen should be avoided in children with endocarditis or burns of more than 20% of the total body surface area, or in children over 1 month of age with a creatinine clearance of less than 20 mL/minute/1.73m<sup>2</sup>.

### **Dosage**

Many dose regimens exist for aminoglycosides depending on target concentration aimed for and patient groups treated. The dose regimens shown here are generally accepted initial doses and dose adjustments should be made in the light of serum concentration measurement.

**Gentamicin** - Neonates IV/IM < 7 days  
 1200-2000 gm 2.5mg/kg once in 12-18hr and  
 >2000 gm 2.5mg/kg once in 12hr; > 7 days  
 1200-2000 gm 2.5mg/kg once in 8-12hr and  
 >2000 gm 2.5mg/kg once in 8hr.  
 Extended interval dose regimen by slow intravenous injection or intravenous infusion  
 - < 32 wks gestation 4-5mg/kg every 35 hrs; >

32wks gestation 4-5mg/kg every 24 hrs. Children - <12 yr 7.5 mg/kg/day and 12-18 yr 3-6mg/kg/day in 3 divided doses. Plasma levels done after 3-4doses to achieve pre-dose level of <2mg/l and 1 hr post dose peak of 5mg/l. Alternatively 5-7.5 mg/kg/24hr IV once daily. Plasma levels done 18-24 hr after 1st dose to achieve pre-dose level of <1mg/l and 1 hr post dose peak of 16-20mg/l. Once daily dose regimen (not for endocarditis or meningitis) by intravenous infusion - Child 1 month–18 years - initially 7 mg/kg, then adjusted according to serum-gentamicin concentration. Intrathecal/ventricular - preservative free preparation - newborn 1mg/24hr; children 1-2 mg /24 hr; 16-18 yr.

**Pseudomonal lung infection in cystic fibrosis** - By inhalation of nebulised solution - Child 1 month–2 years 40 mg twice daily; Child 2–8 years - 80 mg twice daily; Child 8–18 years - 160 mg twice daily.

**Bacterial infection in otitis externa-gentamicin 0.3% (as sulphate)** 3 times daily (avoid prolonged use). Because of reports of ototoxicity in patients with a perforated tympanic topical aminoglycoside antibiotic is contraindicated in those with a tympanic perforation. However, many specialists do use these drops cautiously in the presence of a perforation in children with otitis media and when other measures have failed for otitis externa.

**Eye** - Frequency of application depends on the severity of the infection and the potential for irreversible ocular damage; Eye drops-gentamicin 0.3% (as sulphate) - Apply 1 drop at least every 2 hours in severe infection then reduce frequency as infection is controlled and continue for 48 hours after healing. For less severe infection 3-4 times daily is generally sufficient. (1.5% eye drops for severe eye infection).

**Netilmycin** – Newborn - IV 3mg/dose 12th hrly. Increase to 8th hrly after 1 week age post

natal. Monitor after 3rd dose for 1 hr post dose peak of 8-12mg/L and a trough of <3mg/L. Prolong dose interval in PDA, prolonged hypoxia and indomethacin therapy. Children - IV/IM <12 yr 7.5mg/kg/day and > 12 yr 6 mg/kg/day in 3 divided doses or 1 month - 18 yr 7.5mg/kg as single dose daily. Intraperitoneal 7.5-10mg/L in peritoneal dialysis fluid.

**Tobramycin** - Newborn - IV <32 wks 4-5mg/kg 36 hrly and > 32 wks 4-5mg/kg once in 24 hr. PDA, prolonged hypoxia, indomethacin treatment necessitate increased dose intervals. Extended interval dose regimen by intravenous injection over 3–5 minutes or by intravenous infusion - Neonate less than 32 weeks postmenstrual age 4–5 mg/kg every 36 hours; Neonate 32 weeks and over postmenstrual age 4–5 mg/kg every 24 hours.

Child - IV/IM 2.5 mg/kg/dose 3 times daily or 7mg/kg as single daily dose. Once daily dose regimen by intravenous infusion - Child 1 month-18 years - initially 7 mg/kg, then adjusted according to serum-tobramycin concentration

Intraventricular - newborn 1mg/day, child 1-2mg/day, adolescent 2-4mg/day.

**Pseudomonal lung infection in cystic fibrosis** - Child 1 month-18 years - 8-10 mg/kg daily in 3 divided doses. Once daily dose regimen by intravenous infusion over 30 minutes - Child 1 month–18 years - initially 10 mg/kg (max. 660 mg), then adjusted according to serum-tobramycin concentration. Chronic pulmonary *Pseudomonas aeruginosa* infection in patients with cystic fibrosis - By inhalation of nebulised solution -

Child 6-18 years - 300 mg every 12 hours for 28 days, subsequent courses repeated after 28-day interval without tobramycin nebuliser solution

**Amikacin** - Neonate - loading dose of 10 mg/kg then 7.5 mg/kg every 12 hours;

Extended interval dose regimen by slow intravenous injection or intravenous infusion

15 mg/kg every 24 hours. Children (1 month to 18 years): IV/IM 7.5 mg/kg/dose 2 times daily upto maximum of 500mg/dose. Child >12 years with life-threatening infection - 1.5gm/day in 3 divided doses for upto 10 days may be given. Once daily dose regimen (not for endocarditis or meningitis) - Child 1 month–18 years - initially 15 mg/kg, then adjusted according to serum-amikacin concentration.

### **Administration rate**

The initial standard method of aminoglycoside administration was to infuse the drug over 30 to 60 minutes. Bolus administration of multiple daily doses has become common practice.<sup>25,26</sup> However, with the higher doses required for once daily administration, there has been some thought as to its safety. The only publication addressing bolus administration (2-3min) of approximately 5mg/kg once daily in children was unable to show toxicity in 123 infants, children, and adolescents using this mode of administration.<sup>27</sup>

### **Side effects**

Most side-effects of this group of antibiotics are dose-related; therefore care must be taken with dosage and whenever possible treatment should not exceed 7 days. The major adverse effects of the aminoglycosides are nephrotoxicity and oto-vestibular toxicity as they mediate toxic damage to the proximal convoluted tubules in the kidneys, and to the cochlear and vestibular bodies of the inner ear.<sup>3,12</sup>

**Nephrotoxicity** - Once proximal renal tubular cells are saturated with aminoglycoside, the higher peak serum concentrations seen with once-daily dosing should not cause greater intracellular accumulation of drug than is seen

with multiple lower doses. A randomized double-blind study of aminoglycoside use showed that once-daily administration was less likely to result in nephrotoxicity than twice-daily administration.<sup>28</sup>

**Oto-vestibular toxicity** - Most studies in infants and children from different parts of the world show that hearing loss is a rare complication of aminoglycoside therapy.<sup>29</sup> There is no significant difference in the incidence of ototoxicity between once daily dosing and multiple doses per day.<sup>29</sup> Vestibular function is much more sensitive to aminoglycosides than hearing.<sup>30</sup> Most individuals with vestibular toxicity do not develop hearing loss<sup>31</sup> and these cases are usually missed. However, vestibular toxicity appears to be rare in children and neonates.<sup>22</sup>

Aminoglycosides may impair neuromuscular transmission and should not be given to children with myasthenia gravis<sup>32</sup> large doses given during surgery have been responsible for a transient myasthenic syndrome in patients with normal neuromuscular function.

### **Renal impairment**

Excretion of aminoglycosides is principally via the kidney and accumulation occurs in renal impairment. Ototoxicity and nephrotoxicity occur commonly in patients with renal failure. If there is impairment of renal function, the interval between doses must be increased if the renal impairment is severe, the dose itself should be reduced as well. Serum-aminoglycoside concentrations must be monitored in patients with renal impairment renal, auditory, and vestibular function should also be monitored. A once-daily, high-dose regimen of an aminoglycoside should be avoided in children over 1 month of age with a creatinine clearance less than 20 mL/minute/1.73 m<sup>2</sup>.<sup>32</sup>

## Serum concentrations

Serum concentration monitoring avoids both excessive and subtherapeutic concentrations thus preventing toxicity and ensuring efficacy. In children with normal renal function, aminoglycoside concentration should be measured initially after 3 or 4 doses of a multiple daily dose regimen; children with renal impairment may require earlier and more frequent measurement of aminoglycoside concentration.

Blood samples should be taken just before the next dose is administered ('trough' concentration). If the pre-dose ('trough') concentration is high, the interval between doses must be increased. For multiple daily dose regimens, blood samples should also be taken approximately 1 hour after intramuscular or intravenous administration ('peak' concentration). If the post-dose ('peak') concentration is high, the dose must be decreased.

Serum-aminoglycoside concentration should be measured in all children and must be determined in infants, in neonates, in obesity, in cystic fibrosis, or if high doses are being given, or if there is renal impairment.<sup>32</sup>

## Resistance

Acquired resistance to the aminoglycosides is usually mediated by bacterial elaboration of aminoglycoside-inactivating enzymes. These enzymes are widely distributed in both gram-positive and gram-negative bacteria, and usually are plasmid-mediated.<sup>12</sup> Since amikacin has only one locus that is susceptible to aminoglycoside-inactivating enzymes compared with six susceptible loci on gentamicin and tobramycin, it is less likely that bacteria are resistant to it and therefore, more likely to be effective against MDR gram-negative bacilli.<sup>8</sup>

The most clinically significant resistance is that reported against enterococci which cause endocarditis. Although all enterococci are

intrinsically resistant to low concentrations of aminoglycosides, the clinical problem arises with high level gentamicin resistant (HLGR) enterococci.<sup>7</sup> Detection of HLGR requires either special susceptibility wells or screening plates with high concentrations of gentamicin or streptomycin (eg,  $\geq 500$   $\mu\text{g/mL}$  gentamicin  $\geq 1000$   $\mu\text{g/mL}$  streptomycin). HLGR is reported in various studies in India.<sup>33</sup>

## Conclusion

There have been recent changes in the recommendations for aminoglycoside use in pediatrics. This is due to evolving disease and pathogen characteristics, acquired resistance to this group of antibiotics, new dosage patterns and in turn schedules for drug level monitoring and improved understanding of pharmacokinetics and pharmacodynamics. A review of some of these features has been made in this article.

## Points to remember

- *The aminoglycoside antibiotics- netilmicin, gentamicin, tobramycin and amikacin have been widely used in pediatric practice for treating enterococcal, gram negative, including pseudomonal infections.*
- *Commonly in neonates, immunosuppressed individuals and children with chronic diseases such as cystic fibrosis who are at risk of developing systemic gram negative bacterial infections.*
- *With the emergence of MDR gram-negative bacilli, aminoglycosides, along with the polymyxins, may become antibiotics of last resort.*
- *Unique characteristics of aminoglycosides and the possibility of lower accumulation in renal tubules and inner ear, makes once daily dosing (ODD) of this group of antibiotics possible.*



- *The major adverse effects of the aminoglycosides are nephrotoxicity and oto-vestibular toxicity and both are rare in children.*
- *Reports of high level gentamicin resistant (HLGR) enterococci are emerging in India.*

## References

1. Lode H. Tobramycin: A Review of therapeutic uses and schedules. *Curr Ther Res* 1998; 58: 420-453.
2. Chen LF, Kaye D. Current Use for Old Antibacterial Agents: Polymyxins, Rifamycins, and Aminoglycosides. *Infectious Disease Clinics of North America* 2009; 23: 1053-1075.
3. Drusano GL, Ambrose PG, Bhavnani SM, et al. Back to the future: using aminoglycosides again and how to dose them optimally. *Clin Infect Dis* 2007; 45: 753-760.
4. Buijk SE, Mouton JW, Gyssens IC, Verbrugh HA, Bruining HA. Experience with a once-daily dosing program of aminoglycosides in critically ill patients. *Intensive Care Med* 2002; 28: 936-942.
5. Falagas ME, Matthaiou DK, Bliziotis IA. The role of aminoglycosides in combination with a beta-lactam for the treatment of bacterial endocarditis: a meta-analysis of comparative trials. *J Antimicrob Chemother* 2006; 57: 639-647.
6. Lentino JR, Narita M, Yu VL. New antimicrobial agents as therapy for resistant gram positive cocci. *Eur J Clin Microbiol Infect Dis* 2008; 27: 3-15.
7. Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Bolger AF, Levison ME, Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. *Circulation* 2005; 111: 394-434.
8. Cunha BA. New uses for older antibiotics: nitrofurantoin, amikacin, colistin, polymyxin B, doxycycline, and minocycline revisited. *Med Clin North Am* 2006; 90: 1089-1107.
9. Aminoglycosides. In: IAP Drug Formulary 2009. Unni JC, Nair MKC, Menon PSN, Bansal CP. Eds. Publication of Indian Academy of Pediatrics. Pixel Studio Cochin. 2009: 224-225.
10. Ramesh M, John S, Narayanappa D. Audit of aminoglycosides usage. *Indian J Pediatr*, 2002; 69(5): 385-388.
11. Blomberg M, Jensen, Henry A, Singh ST, Banipal RPS, Cunha-Bang Cd, Bygbjerg IC. Antimicrobial drug use in a small Indian community hospital. *Trop Doct* 2010; 40: 194-198.
12. Rea RS, Capitano B. Optimizing use of aminoglycosides in the critically ill. *Semin Respir Crit Care Med* 2007; 28(6): 596-603.
13. Isaksson B, Maller R, Nilsson LE, Nilsson M. Postantibiotic effect of aminoglycosides on staphylococci. *J Antimicrob Chemother* 1993; 32: 215-222.
14. Isaksson B, Nilsson L, Maller R, Soren L. Postantibiotic effect of aminoglycosides on gram-negative bacteria evaluated by a new method. *J Antimicrob Chemother* 1988; 22: 23-33.
15. McDonald PJ, Wetherall BL, Pruul H. Postantibiotic leukocyte enhancement: increased susceptibility of bacteria pretreated with antibiotics to activity of leukocytes. *Rev Infect Dis* 1981; 3: 38-44.
16. Baudoux P, Bles N, Lemaire S, Mingot-Leclercq MP, Tulkens PM, Van Bambeke F. Combined effect of pH and concentration on the activities of gentamicin and oxacillin against *Staphylococcus aureus* in pharmacodynamic models of extracellular and intracellular infections. *J Antimicrob Chemother* 2007; 59: 246-253.

17. Simmen HP, Battaglia H, Kossmann T, Blaser J. Effect of peritoneal fluid pH on outcome of aminoglycoside treatment of intraabdominal infections. *World J Surg* 1993; 17: 393-397.
  18. Harrell LJ, Evans JB. Anaerobic resistance of clinical isolates of *Staphylococcus aureus* to aminoglycosides. *Antimicrob Agents Chemother* 1978; 14: 927-929.
  19. Barclay ML, Begg EJ. Aminoglycoside adaptive resistance: importance for effective dosage regimens. *Drugs* 2001; 61: 713-721.
  20. Daikos GL, Lolans VT, Jackson GG. First-exposure adaptive resistance to aminoglycoside antibiotics in vivo with meaning for optimal clinical use. *Antimicrob Agents Chemother* 1991; 35: 117-123.
  21. Chandrakanth RK, Raju S, Patil SA. Aminoglycoside-resistance mechanisms in multidrug-resistant *Staphylococcus aureus* clinical isolates. *Curr Microbiol* 2008; 56 I, 558-562.
  22. Contopoulos-Ioannidis DG, Giotis ND, Baliatsa DV, Ioannidis JP. Extended-interval aminoglycoside administration for children: a meta-analysis. *Pediatrics* 2004; 114: 111-118.
  23. Barza M, Ioannidis JP, Cappelleri JC, Lau J. Single or multiple daily doses of aminoglycosides: a meta-analysis. *Br Med J* 1996; 312 : 338-345.
  24. Best E J, Palasanthiran P, Gazarian M. Extended-Interval Aminoglycosides in Children: More Guidance Is Needed. *Pediatrics* 2005; 115: 827-828 (doi:10.1542/peds.2004-2425).
  25. Mendelson J, Portnoy J, Dick V, Black M. Safety of the bolus administration of gentamicin. *Antimicrob Agents Chemother* 1976; 9: 633-638.
  26. Stratford BC, Dixon S, Cobcroft AJ. Serum levels of gentamicin and tobramycin after slow intravenous bolus injection. *Lancet* 1974; 1: 378-379.
  27. Robinson RF, Nahata MC. Safety of intravenous bolus administration of gentamicin in pediatric patients. *Ann Pharmacother* 2001; 35: 1327-31.
  28. Rybak MJ, Abate BJ, Kang SL, Ruffing MJ, Lerner SA, Drusano GL. Prospective evaluation of the effect of an aminoglycoside dosing regimen on rates of observed nephrotoxicity and ototoxicity. *Antimicrob Agents Chemother* 1999; 43: 1549-1555.
  29. Rao SC, Ahmed M, Hagan R. One dose per day compared to multiple doses per day of gentamicin for treatment of suspected or proven sepsis in neonates. *Cochrane Database Syst Rev*, 2006(1): p. CD005091.
  30. Seemungal BM, Bronstein AM. Aminoglycoside ototoxicity: Vestibular function is also vulnerable. *BMJ* 2007; 335: 952.
  31. Dobie RA, Black FO, Pezsnecker SC, Stallings VL. Hearing loss in patients with vestibulotoxic reactions to gentamicin therapy. *Arch Otolaryngol Head Neck Surg* 2006; 132: 253-257.
  32. Aminoglycosides. BNF for children. 2006 Section 5.1.4. <http://www.medicinescomplete.com/mc/bnfc/current/3831.htm>.
  33. Mendiratta DK, Kaur H, Deotale V, Thamke DC, Narang R, Narang P. Status of high level aminoglycoside resistant *Enterococcus faecium* and *Enterococcus faecalis* in a rural hospital of central India. *Indian J Med Microbiol* 2008; 26: 369-371.
-

## DERMATOLOGY

### CHILDHOOD PSORIASIS - A CHALLENGE TO ALL

**\* Jayakar Thomas**  
**\*\* Parimalam Kumar**

**Abstract:** *Pediatric psoriasis consists broadly of 3 age groups of psoriatic patients: infantile psoriasis, a self-limited disease of infancy, psoriasis with early onset and pediatric psoriasis with psoriatic arthritis. About one-quarter of psoriasis cases begin before the age of 18 years. A variety of clinical psoriasis types are seen in childhood, including plaque-type, guttate, erythrodermic, napkin, and nail-based disease. Like all forms of auto-immunity, susceptibility is likely genetic, but environmental triggers are required to initiate disease activity. The most common trigger of childhood is an upper respiratory tract infection. Once disease has occurred, treatment is determined based on severity and presence of joint involvement. Topical therapies, including corticosteroids and calcipotriene are the therapies of choice in the initial care of pediatric patients. Ultraviolet light, acitretin and cyclosporine can clear skin symptoms, while methotrexate and etanercept can clear both cutaneous and joint disease. Concern for psychological development is required when choosing psoriatic therapies.*

*This article reviews current concepts in pediatric psoriasis and a rational approach to therapeutics.*

**Keywords:** *Psoriasis, Autoimmunity, Streptococcus, Etanercept, Calcipotriene, Topical corticosteroids*

Twenty ninth of October is observed as “World Psoriasis Day”; for the year 2010, ‘the theme is fixed as ‘Childhood Psoriasis - a challenge to all!’.

Psoriasis vulgaris is a common dermatologic disorder seen in about 3.5% of the population.<sup>1</sup> One-third of psoriasis cases in a dermatology center are pediatric.<sup>2</sup> Psoriasis is a T-cell mediated chronic inflammatory disorder of the skin characterized by hyper-proliferation of keratinocytes and consequent red scaly skin plaques. Pediatric onset psoriasis is somewhat different than adult disease, as pharyngitis, stress, and trauma are more common triggers of disease activity than in adulthood.<sup>3,4</sup> Despite the differences in pediatric psoriasis, the therapies used for pediatric psoriasis are essentially the same as those used in adulthood, with dosage and strength reductions calculated based on age, weight, and available formulations. This article looks at a rational approach to the diagnosis and management of pediatric psoriasis, with a careful focus on those aspects of disease unique to the pediatric patient.

### Pathogenesis

The exact pathogenesis of psoriasis has not been completely elucidated; however, it is known

---

\* Senior Consultant Dermatologist,  
Apollo Children's Hospital, Chennai

\*\* Senior Assistant Professor of Dermatology,  
Government Stanley Hospital, Chennai

to have a genetic basis, as 23.4% to 71% of children will have a family history of psoriasis<sup>3,5,6</sup> The guttate psoriasis subset is linked to inflammatory focus in about two-thirds of cases, and is not caused by a specific subtype of group A beta hemolytic streptococcus, but rather by a host-specific response. Cross-reactivity of keratinocytes antigens with streptococcal antigens is thought to initiate psoriatic disease in this setting. Other infections that have been noted in psoriatic disease are presence of staphylococcal superantigens and HPV DNA.<sup>7,8,9</sup> No single gene has been found to be responsible for psoriasis vulgaris. A series of genes have been isolated in which mutations have been associated with psoriatic disease. These genes play a role in Th2 cell and Th17 cell activity and signaling, demonstrating both a role for Th2 and Th17 lymphocytes in the pathogenesis of psoriatic disease. Th17 cells have been noted in psoriatic lesions, as have collections of Th2 and Th1 cells.<sup>10</sup>

Many patients with psoriasis will have other autoimmune conditions, often of the skin, including morphea and vitiligo vulgaris (sometimes this association is familial).<sup>11</sup> Family history of psoriasis and other forms of autoimmunity can be noted in patients with psoriasis and in patients with a personal history of other autoimmune diseases such as multiple sclerosis.<sup>12</sup>

### **Clinical aspects and diagnosis**

Most children manifest with plaque-type psoriasis vulgaris (68.6%) in similar patterns to adult patients, with lesions localized to the scalp, post auricular region, elbows, and knees. Guttate disease is more common in pediatric than adult patients. Diaper involvement is very common in infancy, but involvement of the groin is uncommon in older children. Inverse psoriasis with involvement of the folds of the skin (axillae, inner thighs) represents a small minority of

children. Additionally, nail psoriasis can be noted in the setting of plaque-type psoriasis vulgaris, psoriatic arthritis, or with isolated nail disease, the last sometimes being called trachyonychia, although this is controversial. Involvement of joints with psoriatic arthritis is less prevalent in younger patients; however, it does occur in childhood disease and should be considered in the differential of pediatric arthritis.<sup>4</sup>

Psoriasis vulgaris occurs in a variety of clinical types.

A few clinical features of psoriasis that are pertinent during physical examination include

- 1) the isomorphic response or Koebner phenomenon, which is occurrence of lesions in areas of trauma,
- 2) altered pigmentation with lesional clearance,
- 3) the Auspitz sign – pinpoint bleeding at the base of scale that has been removed, and
- 4) presence of nail pitting, which can aid in diagnosis of the disease. Severity grading for psoriasis is usually based on surface area and presence and co-morbid psoriatic arthritis. The Psoriasis Area and Severity Index (PASI) can be used to assess severity (given below). Others will divide disease into mild if less than 3% body surface area, moderate 3% to 10% body surface area, and severe >10% body surface area.<sup>13</sup>

### **Psoriasis Area and Severity Index (PASI) score**

To determine PASI score, establish grade and severity and then use site-based weighting

Grade: surface area as below (0-6)

- 0% of involved area, grade: 0
- <10% of involved area, grade: 1

- 10%–29% of involved area, grade: 2
- 30%–49% of involved area, grade: 3
- 50%–69% of involved area, grade: 4
- 70%–89% of involved area, grade: 5
- 90%–100% of involved area, grade: 6

Severity: 0–4 none to severe

Erythema (redness)

Induration (thickness)

Desquamation (scaling)

**Notes:** The sum of all three severity parameters is then calculated for each section of skin, multiplied by the area score for that area and multiplied by weight of respective section (0.1 for head, 0.2 for arms, 0.3 for body and 0.4 for legs).

## Differential diagnosis

The differential diagnosis of psoriasis includes other papulosquamous disorders of childhood including lichen planopilaris, psoriasiform ID reactions, nummular dermatitis, pityriasis rosea, and pityriasis rubra pilaris. Biopsy can be helpful in differentiating psoriasis from these other illnesses.

## Treatments

The treatments of psoriasis have expanded over the past decade; however the use of topical therapy in childhood is the first line of treatment for skin-limited disease, in combination with a trial of oral antibiotics where indicated. With chronicity of illness and in more severe cases, systemic therapy and phototherapy are added to help induce remission. Significant psychological disturbances are seen in children with psoriasis, no matter what the surface area. Disease, although cutaneous, should be treated

more aggressively when it is causing psychological disturbance, to improve quality of life.

## Topical therapy

Topical therapies for pediatric psoriasis include over-the-counter agents such as tar and salicylic acid, the latter of which aids in removal of hyperkeratosis. Tar has been a controversial medication in pediatric psoriasis because of demonstrable genotoxic risk, including chromosomal aberrations in peripheral lymphocytes and release of heat shock protein. Prescription agents for psoriasis vulgaris in childhood include anthralin, topical corticosteroids, topical calcipotriene with or without topical corticosteroids and topical calcineurin inhibitors such as tacrolimus 0.3% ointment, and pimecrolimus 1% can be beneficial for pediatric psoriasis, particularly in sites where atrophy is of risk, such as the face, intertriginous areas and groin. Use in children under the age of 2 years is not recommended.<sup>13,14</sup>

## Phototherapy

Phototherapy is a safe and effective treatment for children old enough to stand still in a phototherapy booth, particularly teenagers with extensive disease. Generalized or hand foot therapy, either narrowband UVB (NBUVB) or psoralens and UVA (PUVA), can be used. Topical psoralens are preferable to oral psoralens because of the difficulty of wearing protective eyewear for a 24-hour time period after oral psoralens. As PUVA has been associated with long-term carcinogenicity in psoriatics, NBUVB is likely safer in childhood cases.<sup>15, 16</sup>

## Systemic agents

Systemic agents should be saved for severe psoriasis, disabling psychological ramifications, and psoriatic arthritis. Usage of systemic agents

is generally limited to a 6-month time period for immunosuppressants such as cyclosporine, acitretin or methotrexate. Longer usage periods have been observed to be safe in rheumatoid arthritis patients on etanercept, however usage beyond a one year time period has not been well assessed in pediatric psoriatics. Methotrexate has been used for pediatric patients for decades longer than etanercept. Oral antibiotics are the systemic therapy of choice in early disease, due to their superior side effect profile.

1. Oral antibiotics can be useful in treating psoriasis vulgaris, particularly in the setting of positive oral pharyngeal cultures, presence of perianal bacterial dermatitis, pustular psoriasis, or in guttate psoriasis of childhood (but not adult guttate disease), as these settings are linked to a bacterial precipitant of psoriasis.<sup>17, 18</sup>

2. When pediatric psoriasis becomes chronic and severe (PASI > 10), systemic therapy provides the major source of improvements in pediatric quality of life. The original psoriatic systemic therapy used for extensive psoriasis is methotrexate, which has been used for over 3 decades for pediatric psoriasis and pediatric psoriatic arthritis. Addition of folic acid supplementation helps protect against pancytopenia and macrocytic anemia.<sup>16, 19</sup>

3. Cyclosporine A, a systemic immunosuppressant used originally for prevention of transplant rejection, can be dosed for oral use at 3 to 5 mg/kg can improve cutaneous symptoms in pediatric psoriatic patients. Alterations in renal function with altered serum urea nitrogen and creatinine and high blood pressure can be observed. Therefore, close monitoring is warranted. Risks of malignancy and lymphoproliferative disorders seem to be minimal in children treated for skin diseases due to limited courses of therapy and dosages that are below 5 mg/kg/day.<sup>20</sup>

4. Retinoids: Acitretin orally 0.5 to 1 mg/kg per day has been used for disorders of cornification and psoriasis with good results. Because of teratogenicity, oral contraceptives in girls of childbearing age should be used concurrently, and for 3 years after drug discontinuation. Short-term side effects, such as elevations in lipids or alterations in blood counts, require monitoring. Long-term changes such as bony abnormalities can occur and treatment periods should be limited, using a cyclic approach. Bony evaluation may be required.<sup>20</sup>

5. Biologics: Etanercept and infliximab, injectable and intravenous, respectively, tumor necrosis factor alpha (TNF- $\alpha$ ) inhibitor therapies have been used for a decade in pediatric psoriasis. Long-term use did not increase serious side effects such as tuberculosis, opportunistic infections, malignancies, lymphomas, lupus, demyelinating disorders, or death. Long-term improvements on bony disease in arthritis of childhood have been demonstrated with etanercept.<sup>21, 22</sup>

## Natural supplements

A common question asked by parents of children with psoriasis is "What dietary changes or natural supplements can I give my child to improve their skin disease?" While natural supplements or dietary alterations cannot cure psoriasis, they can improve disease severity. The best-known supplement is fish oil, rich in omega-3 fatty acids. The ingestion of this agent for psoriasis is based upon its preventive effects in the Inuit population. Oral and intravenous supplementation of omega-3 and, less effectively, omega-6 fatty acids have been found effective in psoriatic adults, possibly through alterations in production and alterations in arachidonic acid (20:4 omega 6) and docosapentaenoic acid. Fish meals 4 to 6 times per week can mimic the effects of omega-3 supplementation.<sup>23</sup>

## Conclusion

Recent advances in genetics and the unraveling of the processes responsible for psoriatic disease are making possible considerable advancements in the treatment of pediatric psoriasis.

## Points to Remember

- *One-third of psoriasis cases in a dermatology center are pediatric.*
- *Most children manifest with plaque-type psoriasis vulgaris*
- *A few clinical features of psoriasis that are pertinent during physical examination include*
  - i. *the isomorphic response or Koebner phenomenon, which is occurrence of lesions in areas of trauma,*
  - ii. *altered pigmentation with lesional clearance,*
  - iii. *the Auspitz sign – pinpoint bleeding at the base of scale that has been removed, and*
  - iv. *presence of nail pitting, which can aid in diagnosis of the disease.*
- *The treatments of psoriasis have expanded over the past decade; however the use of topical therapy in childhood is the first line of treatment for skin-limited disease, in combination with a trial of oral antibiotics where indicated.*
- *With chronicity of illness and in more severe cases, systemic therapy and phototherapy are added to help induce remission*
- *While natural supplements or dietary alterations cannot cure psoriasis, they can improve disease severity.*

## References

1. Kurd SK, Gelfand JM. The prevalence of previously diagnosed and undiagnosed psoriasis in US adults: results from NHANES 2003-2004. *J Am Acad Dermatol* 2009;60:218–224.
2. Raychaudhuri SP, Gross J. A comparative study of pediatric onset psoriasis with adult onset psoriasis. *Pediatr Dermatol* 2000;17:174-178.
3. Seyhan M, Coskun BK, Saggılam H, Ozcan H, Karıncaoglu Y. Psoriasis in childhood and adolescence: evaluation of demographic and clinical features. *Pediatr Int* 2006;48:525-530.
4. Kumar B, Jain R, Sandhu K, Kaur I, Handa S. Epidemiology of childhood psoriasis: a study of 419 patients from northern India. *Int J Dermatol* 2004;43:654-658.
5. Fan X, Xiao FL, Yang S, et al. Childhood psoriasis: a study of 277 patients from China. *J Eur Acad Dermatol Venereol* 2007; 21:762-765.
6. Morris A, Rogers M, Fischer G, Williams K. Childhood psoriasis: a clinical review of 1262 cases. *Pediatr Dermatol* 2001;18:188-198.
7. Telfer NR, Chalmers RJ, Whale K, Colman G. The role of streptococcal infection in the initiation of guttate psoriasis. *Arch Dermatol* 1992;128:39–42.
8. Balci DD, Duran N, Ozer B, Gunesacar R, Onlen Y, Yenin JZ. High prevalence of *Staphylococcus aureus* cultivation and superantigen production in patients with psoriasis. *Eur J Dermatol* 2009;19: 238–242.
9. Simeone P, Teson M, Latini A, Carducci M, Venuti A. Human papillomavirus type 5 in primary keratinocytes from psoriatic skin. *Exp Dermatol* 2005;14:824–829.
10. Lowes MA, Kikuchi T, Fuentes-Duculan J, et al. Psoriasis vulgaris lesions contain discrete populations of Th1 and Th17 T cells. *J Invest Dermatol* 2008;128:1207–1211.
11. Leitenberger JJ, Cayce RL, Haley RW, Adams-Huet B, Bergstresser PR, Jacobe HT. Distinct autoimmune syndromes in morphea: a review of 245 adult and pediatric cases. *Arch Dermatol* 2009;145:545–550.

12. Barcellos LF, Kamdar BB, Ramsay PP, et al. Clustering of autoimmune diseases in families with a high-risk for multiple sclerosis: a descriptive study. *Lancet Neurol* 2006;5:924–931.
13. Farber EM, Nall L. Childhood psoriasis. *Cutis* 1999;64:309–314.
14. Oranje AP, Marcoux D, Svensson A, et al. Topical calcipotriol in childhood psoriasis. *J Am Acad Dermatol* 1997;36:203–208.
15. Jain VK, Aggarwal K, Jain K, et al. Narrow-band UV-B phototherapy in childhood psoriasis. *Int J Dermatol* 2007;46:320–322.
16. Kaur I, Dogra S, De D, Kanwar AJ. Systemic methotrexate treatment in childhood psoriasis: further experience in 24 children from India. *Pediatr Dermatol* 2008;25:184–188.
17. Wilson JK, Al-Suwaidan SN, Krowchuk D, et al. Treatment of psoriasis in children: is there a role for antibiotic therapy and tonsillectomy? *Pediatr Dermatol* 2003;20:11–15.
18. Dogan B, Karabudak O, Harmanyeri Y. Antistreptococcal treatment of guttate psoriasis: a controlled study. *Int J Dermatol* 2008;47:950–952.
19. Gisondi P, Fantuzzi F, Malerba M, et al. Folic acid in general medicine and dermatology. *J Dermatolog Treat* 2007;18:138–146.
20. Cordoro KM. Systemic and light therapies for the management of childhood psoriasis: part II. *Skin Therapy Lett.* 2008;13:1–3.
21. Hawrot AC, Metry DW, Theos AJ, Levy ML. Etanercept for psoriasis in the pediatric population: experience in nine patients. *Pediatr Dermatol* 2006;23:67–71.
22. Farnsworth NN, George SJ, Hsu S. Successful use of infliximab following a failed course of etanercept in a pediatric patient. *Dermatol Online J* 2005;11:11.
23. Mayser P, Mrowietz U, Arenberger P, et al. Omega-3 fatty acid-based lipid infusion in patients with chronic plaque psoriasis: results of a double-blind, randomized, placebo-controlled, multicenter trial. *J Am Acad Dermatol* 1998;38:539–547.

## NEWS AND NOTES

### PAED - ENDO 2011

#### Conference on Paediatric & Adolescent Endocrinology for Postgraduates and practicing pediatricians

**Date:** 12<sup>th</sup> February 2011 (Saturday) **Venue:** Sri Ramachandra University, Porur, Chennai.

Organized by Department of Pediatrics, Sri Ramachandra University, Porur, Chennai – 600 116.

#### Organizing chairpersons

Dr. L.N. Padmasani, MD, MRCP CH(UK)

Dr. P. Venkataraman, MD, DCH

#### Organizing Secretary

Dr. Saji James MD (Paed)

Delegate fee Rs.300/- to be drawn in favour of “Paediatric CME” payable at Chennai either as DD or Cheque and send it to Dr. Saji James, Organizing Secretary, PAED ENDO 2011, Department of Paediatrics, Sri Ramachandra University, Ramachandra Nagar, Porur, Chennai – 600 116.

**Mobile Nos.:** 98401 19237 & 98412 23038



**RADIOLOGIST TALKS TO YOU**

## **BRAIN TUMORS - I**

**\* Vijayalakshmi G**

**\*\* Elavarasu E**

**\*\*\* Venkatesan M D**

Brain tumors are a rare entity, but among malignancies, they are the commonest solid tumors in children next to lymphomas and leukemias. Upto the age of two, infratentorial tumors are common. Afterwards, both supratentorial and infratentorial tumors are equal in occurrence. The commonest supratentorial tumor is astrocytoma. Meningiomas, pituitary tumors and metastases that are more likely in adults, are rare in children.

The brain is a closed box and radiological imaging is required very early in the investigative work-up of these children. Older children can communicate better and bring to attention problems like disturbances of vision, headache and nausea, Young children should be watched for vomiting, ataxia and mental disturbances. Babies with an open fontanelle allow quiet expansion of the calvarium and are recognized quite late when the tumor is large.

The baby in Fig.1 is such an example. The open fontanelle has allowed use of ultrasound which shows a highly echogenic lesion filling and distending the lateral ventricle. This is a choroid plexus papilloma. The common

site of occurrence is the lateral ventricle and is rarely seen in the fourth and third ventricles. It shows a lobulated contour and will show flapping movement in the dilated ventricles on real time ultrasound. The hydrocephalus is due to increased formation of CSF but more due to obstruction of the foramen of Munroe by the mass.

CT will show the lesion as a uniformly and brightly enhancing mass within dilated ventricles (Fig.2). Calcification may be present. On MRI they appear as isointense or hypointense, lobulated intraventricular masses in T1 weighted images. In T2 they may appear similar to T1 or hyperintense. After administration of gadolinium there is homogenous, bright enhancement as in a meningioma. But meningiomas do not have a lobulated contour. The choroid plexus papilloma arises from the epithelium of the choroid plexus. 5% of choroid plexus papillomas can turn malignant when they will show inhomogeneity in appearance. More often, malignant choroid plexus papillomas like malignant ependymomas, arise in the parenchyma from cell rests and extend into the ventricle.

The most common supratentorial tumor is astrocytoma. They are seen in all age groups. They can attain a large size and have solid areas that homogeneously enhance on contrast (Fig.3) and non-enhancing cystic areas (Fig.4). Astrocytomas range from benign to the malignant. The most malignant glioblastoma multiforme is uncommon in children except after radiation. Astrocytoma rarely shows a diffuse infiltrating form involving large portions of the brain called gliomatosis cerebri.

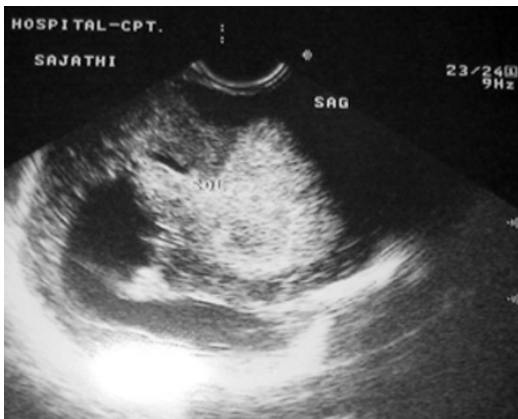
---

\* Associate Professor,

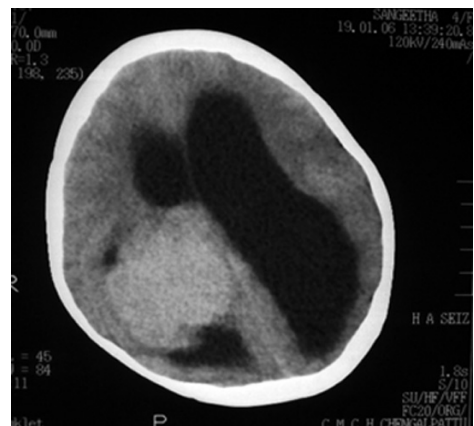
\*\*\* Asst. Professor,

\*\*\*\* Professor,

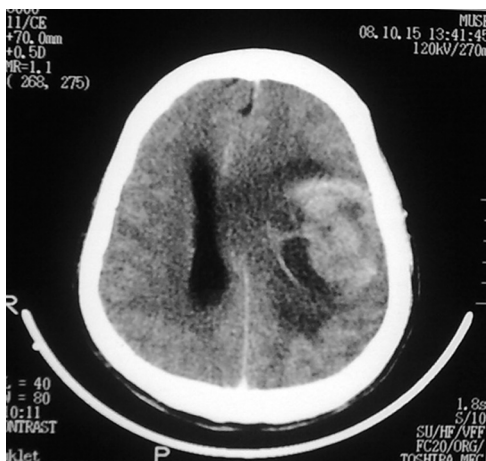
Chengalpet Medical College Hospital, Chengalpet



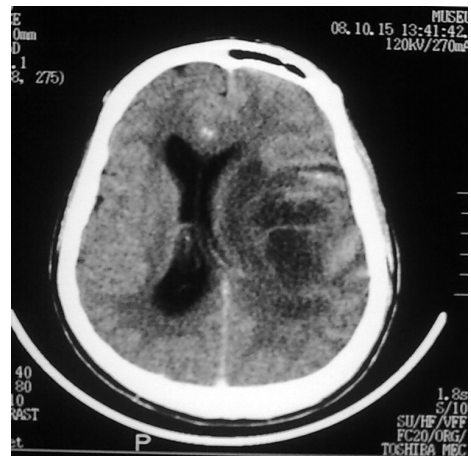
**Fig.1. Choroid plexus papilloma-  
Ultrasound**



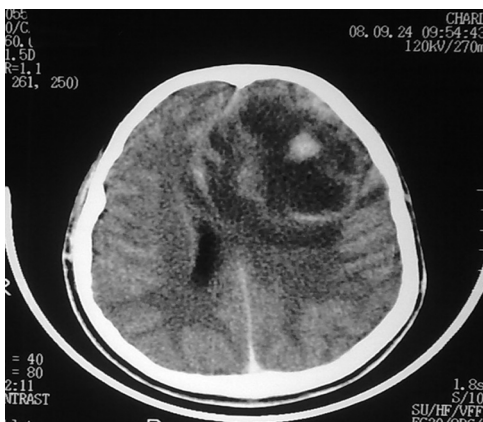
**Fig.2. Choroid plexus papilloma – CT**



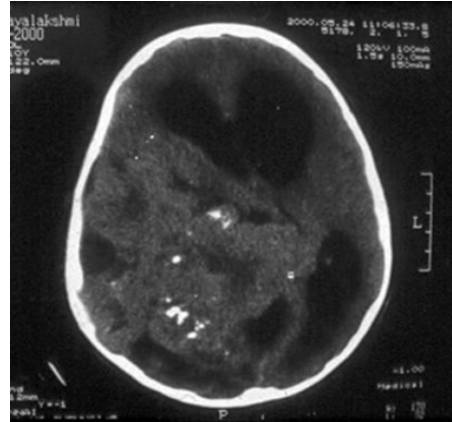
**Fig.3. Astrocytoma- CT with con-  
trast showing enhancing solid areas**



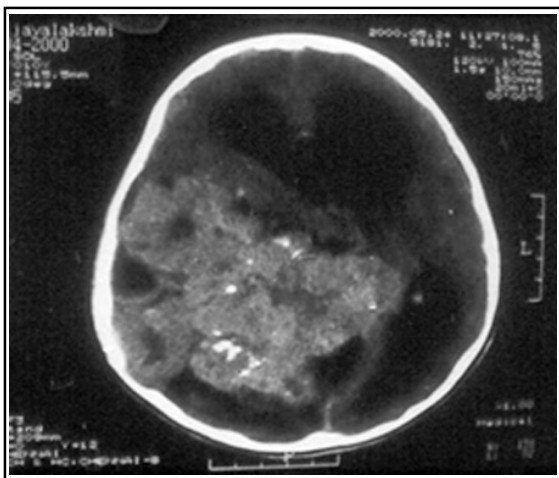
**Fig.4. Same patient as Fig 3. showing  
non-enhancing cystic areas**



**Fig.5. Oligodendroglioma**



**Fig.6. PNET- plain CT**



**Fig.7. PNET- contrast CT**

The oligodendroglioma is rare in children but can be seen between 6 and 12 years. It is the most benign glioma. The most common locations are frontal and temporal lobes.

Fig.5 is a typical picture of an oligodendroglioma. There is a hypodense lesion in the left frontal region with a nodular calcific focus. It is the commonest tumor that calcifies. With contrast there is a white enhancing rim. MRI shows hypointense solid portion in T1 weighted images and hyperintense or isointense lesion in T2. CT is essential to show

calcification. The hypodense area around the enhancing rim is edema surrounding the mass.

Younger children, typically less than one year of age, have a higher tendency to present with larger, more aggressive tumors of embryonal origin, mainly primitive neuroectodermal tumors (PNET). Fig.6 shows a large PNET occupying the whole hemisphere. The tumor is very large and solid with calcification and shows heterogeneous enhancement on contrast administration (Fig.7). The tumor arises from rests of the primitive ganglionic cell called the neuroblast which migrates from the subependymal layer to the periphery to form the cerebral cortex. Other names for this tumor are pineoblastoma, cerebral neuroblastoma, ependymblastoma and medulloblastoma. They account for 3% of all brain tumors in children and have a worse prognosis than medulloblastoma.

It should be noted that tumors are space occupying lesions that have a mass effect which is compounded by peritumoral edema. Consequently the ipsilateral ventricle is compressed and the midline is shifted to the opposite side. The opposite lateral ventricle may be dilated due to obstruction of its outflow foramen. Intracranial tension may rise so much as to cause herniations that can be fatal.

## CLIPPINGS

### ***Can venous blood gas analysis replace arterial in emergency medical care, Kelly, Anne-Maree Emergency Medicine Australasia, Dec 2010***

There is insufficient data to determine if these relationships persist in shocked patients or those with mixed acid-base disorders. For patients who are not in shock, venous pH, bicarbonate and base excess have sufficient agreement to be clinically interchangeable for arterial values. Agreement between arterial and venous pCO<sub>2</sub> is too poor and unpredictable to be clinically useful as a one-off test but venous pCO<sub>2</sub> might be useful to screen for arterial hypercarbia or to monitor trends in pCO<sub>2</sub> for selected patients.

<b>CASE STUDY</b>
-------------------

## **CHILDREN EATING PAN MASALA- BEWARE OF ORAL SUBMUCOUS FIBROSIS**

**\*Vishal Mehrotra**

**\*\*Tandon V K**

**\*\*\*Parvathi Devi**

**\*\*\*\*Thimmarasa V B**

**\*\*\*\*\*Manas Gupta**

**Abstract:** *Oral submucous fibrosis (OSMF) has been well established in Indian medical literature since the time of Sushruta (2500-3000 B.C.) This premalignant condition is commonly seen in 2<sup>nd</sup> to 4<sup>th</sup> decade of life and is extremely rare in children. This case report describes a 12 year old boy chewing pan masala developing oral submucous fibrosis and highlights the strong association of areca nut chewing as the potential etiologic factor and its treatment aspect. The case report underlines the danger that children face with products which are clearly targeted at them by the tobacco / pan masala industry and suggests public health measures for the government to enforce.*

**Keywords:** *Areca nut, Premalignant condition, OSMF, Antioxidants, Steroids.*

---

\* Senior Lecturer,

\*\* Consultant,

\*\*\* Professor & Head,

\*\*\*\* Professor,

\*\*\*\*\* Post Graduate Student,

Department of Oral Medicine & Radiology,  
Rama Dental College, Hospital & Research  
Centre. Kanpur

Oral submucous fibrosis (OSMF) was first described in the modern literature by Schwartz in 1952 and its precancerous nature reported by Paymaster in 1956.<sup>1</sup> Joshi first described the condition in India.<sup>1</sup> The occurrence of this condition in children is extremely rare.<sup>1</sup> The case reported here describes oral submucous fibrosis in a 12- year-old boy. The only etiologic factor that could be traced in this case is the habit of chewing pan masala.

### **Case Report**

A 12 year old boy reported at the outpatient department of the Dental College Hospital, Kanpur with a complaint of difficulty in opening the mouth, protrusion of the tongue and intolerance to spicy food. The history revealed that he had the habit of chewing panmasala and placing it in left buccal vestibule. He started the habit at the age of 9 years and continued it regularly since then (a minimum of 3 to 5 packets per day). The interincisal distance of maximal mouth opening was 1.8 cm with restricted tongue movements (Fig.1). The oral mucosa appeared pale, blanched and gave a marble like appearance (Fig.2) Vertical fibrotic bands were palpable in relation to left buccal mucosa resulting in decreased elasticity and a leathery consistency. Routine hematological analysis showed no abnormalities. Toulidine blue application was performed prior to incisional biopsy from left buccal mucosa. Histopathologic examination revealed atrophic epithelium and the underlying connective tissue showed moderate to intense number of chronic inflammatory cells infiltrating subepithelial zone. In deeper areas vascularity

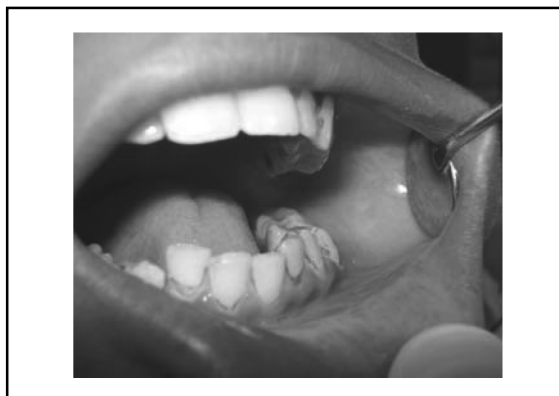


**Fig.1. Restricted tongue protrusion**

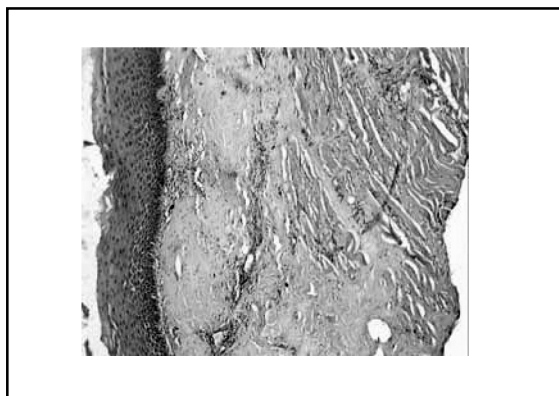
decreased, dense bundles of collagen fibers with few areas of hyalinization are seen (Fig.3). Thus a diagnosis of oral submucous fibrosis was made and the patient was advised for discontinuation of pan masala chewing habit. Oral antioxidant administered once daily and biweekly submucosal (intralesional) injections of betamethasone 4mg were given in the regions with palpable fibrotic bands for two months. Each time, 2 ml of solution was deposited around the specific regions on the left side. A remarkable improvement in the burning sensation of the mouth and moderate improvement in mouth opening was observed. Patient was followed up for 6months and there was no recurrence of the symptoms.

## Discussion

In 1966, Pindborg defined oral submucous fibrosis as “an insidious chronic disease affecting any part of the oral cavity and sometimes pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxtaepithelial inflammatory reaction followed by fibroelastic changes in the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa causing trismus and difficulty in eating”.<sup>2</sup>



**Fig.2. Blanching and Stiffening on left buccal mucosa.**



**Fig.3. H & E section showed atrophic epithelium and the underlying connective tissue showed moderate to intense number of chronic inflammatory cells infiltrating subepithelial zone.**

This disease is common among Indians, Pakistanis, and Sri Lankans. Pindborg, et al. found a prevalence of 0.2- 5% in India.<sup>3</sup> They estimated that there are no fewer than 2,500,000 cases of OSF in India.<sup>3</sup>

The etiology of this crippling condition still remains obscure but is believed to be multifactorial.<sup>4</sup> Currently, the habit of chewing

**Table 1. Therapeutic measures for oral submucous fibrosis and their mechanism of action**

Drugs	Mechanism of action
Lycopene	The antioxidant activity of lycopene is at least twice as great as that of beta-carotene. Newer studies highlight the benefit of this oral nutritional supplement at a daily dose of 8 mg twice a day for 2 months. <sup>7</sup>
Steroids	Biweekly submucosal intralesional injections or topical application of steroids are the most common mode of treatment. The mechanism of action includes its anti-inflammatory and immunosuppressant properties. <sup>5,7</sup>
Human placental extracts	Its action is essentially biogenic stimulation and increases the vascularity of tissues based on the method of tissue therapy. Due to its anti-inflammatory action, inhibits the mucosal damage. <sup>1</sup>
Hyaluronidase	Topical use has shown to improve symptoms more quickly than steroids alone. Hyaluronidase can also be added to intralesional steroid preparations. The combination of steroids and topical hyaluronidase shows better long-term results than either agent used alone. <sup>5,7</sup>
Combined therapy	Chymotrypsin (5000 IU), hyaluronidase (1500 IU) and dexamethasone (4 mg), twice weekly submucosal injections for 10 weeks. <sup>7</sup>
IFN-gamma	Also known as antifibrotic cytokines is given intralesionally because they have ability to alter collagen synthesis. Intralesional injection of interferon gamma (0.01–10.0 U/mL) 3 times a day for 6 months. <sup>5</sup>
Milk from immunized cows	It has an anti-inflammatory component that may suppress the inflammatory reaction and modulate cytokine production. 45 g milk powder twice a day for 3 months. <sup>8</sup>
Pentoxifylline	It is a drug of methylxanthine derivative that has vasodilating properties and helps to increase mucosal vascularity. The curative effect of pentoxifylline may be attributable to its properties of suppressing leukocyte function, altering fibroblast physiology, and stimulating fibrinolysis. In advanced oral submucous fibrosis given at 400 mg 3 times daily or may be used in conjunction with other therapies. <sup>5,9</sup>
Turmeric	The volatile oil of <i>Curcuma longa</i> has anti-inflammatory, anti-hyaluronidase action and antioxidative effect. Alcoholic extracts of turmeric (3 g), turmeric oil (600 mg), turmeric oleoresin (600 mg) daily for 3 months. <sup>7</sup>

areca nuts is recognized as the most important etiologic agent in the pathogenesis of this condition.<sup>1</sup> The areca nut has psychotropic and antihelminthic activity due to the presence of areca alkaloids, predominantly arecoline. These alkaloids have powerful parasympathetic properties, produce euphoria and counteract fatigue. The frequency of areca nut chewing habit reported ranges from 84 to 100% in oral submucous fibrosis cases.<sup>1</sup> Sinor, et al in a case control study, demonstrated that this condition occurred only among those who chewed areca nuts in one form or other.<sup>1</sup> Long term exposure to areca nut results in clonal selection of fibroblasts with up regulation of lysyl oxidase there by resulting in a high amount of stable collagen (type I trimer) production.<sup>5</sup>

The majority of oral submucous fibrosis cases belongs to the 20- to 40-year-old age group and is extremely rare in children. A male-to-female ratio of 1.8 to 2:1 is reported.<sup>6</sup> In the past very few cases of oral submucous fibrosis in children are reported in the literature. Hayes PA reported first case of oral submucous fibrosis in a 4-year-old girl.<sup>1</sup> Anil S and Beena VT reported a case of oral submucous fibrosis in a 12-year-old girl highlighting the strong association of areca nut chewing as the potential factor in the etiology of this condition.<sup>1</sup>

Shah B, et al reported a case of oral submucous fibrosis occurring in an 11-year-old Bangladeshi girl with the habit of areca nut chewing.<sup>2</sup>

The treatment of patients with oral submucous fibrosis depends on the degree of clinical involvement. If the disease is detected at a very early stage, cessation of the habit is sufficient. Moderate-to-severe oral submucous fibrosis is irreversible. Medical treatment provides symptomatic relief and is predominantly aimed at improving mouth opening.<sup>5</sup> The various

therapeutic measures used are shown in Table 1.<sup>5,8,9</sup>

## Conclusion

We describe a young child with the habit of chewing pan masala who developed oral submucous fibrosis. Management of OSMF is only palliative and does little to prevent the progressive nature of the disease as well as its malignant potential. Because of the significant cancer risk among these patients, periodic follow up is essential for early detection and management of high-risk oral premalignant condition and prevention of cancer. Dental practitioners can play an important role in both educating the patients about the perils of chewing betel quid/pan masala and in the early diagnosis of high-risk premalignant condition and cancer. Certain public health measures for effective and preventive education are thus needed.

## References

1. Anil S, Beena VT. Oral submucous fibrosis in a 12- year – old girl: case report. *Pediatr Dent* 1993; 16:120-122.
2. Shah B, Lewis MAO, Bedi R. Oral submucous fibrosis in a 11- year old Bangladeshi girl living in the United Kingdom. *Br Dental J* 2001; 191:130-132.
3. Khanna JN, Andrade NN. Oral submucous fibrosis. a new concept in surgical management. Report of 100 cases. *Int J Oral Maxillofac Surg* 1995; 24: 433- 439.
4. Rajalalitha P, Valli S. Molecular pathogenesis of oral submucous fibrosis- a collagen metabolic disorder. *J Oral Pathol Med* 2005; 34: 321-328.
5. Jiang X, Hu J. Drug treatment of oral submucous fibrosis: a review of the literature. *J Oral Maxillofac Surg* 2009; 67: 1510-1515.
6. Yazdanpanah MJ, Banihashemi M, Pezeshkpoor F, Famili S, Layegh P, Katebi M, et al. Oral submucous fibrosis in a young patient. *Acta Dermatoven APA* 2009; 18: 176-178.

7. Auluck A, Rosin MP, Zhang L, KN S. Oral submucous fibrosis, a clinically benign but potentially malignant disease: Report of 3 cases and review of the literature. J Can Dent Assoc 2008; 74: 735-740.
8. Tai YS, Liu BY, Wang JT, Sun A, Kwan HW, Chiang CP. Oral administration of milk from cows immunized with human intestinal bacteria. J Oral Pathol Med 2001; 30: 618-625.
9. Rajendran R. Pentoxifylline Therapy: A new adjunct in treatment of OSMF. IJDR 2006; 17: 190-198.



## TAMIRABARANI PEDICON 2011

### 36<sup>th</sup> ANNUAL CONFERENCE OF IAP – TNSC

#### HOST: IAP – CTKK CHAPTER – TAMILNADU

**Venue:** Tirunelveli

**Date:** 12<sup>th</sup> -14<sup>th</sup> August

Dates	IAP	NON IAP	P.G.	ACCOM. PERSON	
				IAP	Non-IAP
16.08.2010 – 30.04.2011	<b>3500</b>	<b>4000</b>	<b>2500</b>	<b>3250</b>	<b>3750</b>
01.05.2011 – 31.07.2011	<b>4000</b>	<b>4500</b>	<b>3000</b>	<b>3750</b>	<b>4250</b>
01.08.2011 – 14.08.2011 (SPOT)	<b>4500</b>	<b>5000</b>	<b>4000</b>	<b>4250</b>	<b>4750</b>

- \* **Mode of payment:** By cash or Cheque / DD in favor of “**Tamirabarani pedicon 2011**” payable at “**Tirunelveli**”
- \* For IAP Senior citizens above 70 yrs of age (as on 12.08.11) – Registration free. Send age proof.
- \* Children of registrants (who are IAP members) below 5 yrs (as on 12.08.11) are free
- \* Letter is required from HOD for PGs and they must be students as on 14.08.2011.
- \* Add Rs.50/- for outstation cheques. For bulk amount add necessary collection charge.
- \* Enjoy excellent tourist spots like Kanyakumari, Thiruchendur, Courtallam and Thiparapu falls with your family.

#### **Conference secretariat**

**Dr.S.Thirumalai Kolundu**

Organising Secretary, Tamirabarani Pedicon 2011

166, Kotur Road, Palaymkottai, Tirunelveli – 627 002.

Phone: 9366714700

Email ID: iap\_tvl@yahoo.co.in



<b>CASE STUDY</b>
-------------------

## **A RARE CASE OF INTRACRANIAL AND INTRAMEDULLARY TUBERCULOMAS**

**\*Sujatha S**

**\*\*Ravisekar C V**

**\*\*Lakshmi S**

**\*\*Kumarasamy K**

**\*\*Luke Ravi Chelliah**

**Abstract:** *There are very few reports of concurrent intracranial and intramedullary tuberculomas reported in literature, especially in children. We report a one year old boy who presented with intracerebral, intracerebellar and intramedullary tuberculomas. He was successfully treated conservatively with drugs alone, obviating the need for surgical intervention.*

**Keywords:** *Ring enhancing lesion, Intramedullary tuberculoma.*

With increasing use of neuroimaging in the evaluation of children presenting with seizures or focal neurological deficit, ring/ disc enhancing lesions posing a diagnostic dilemma due to a wide variety of causes are now detected on CT or MRI. The case reported here had an unusual combination of intracerebral, intracerebellar and intramedullary ring enhancing lesions in CT brain.

## **Case report**

A one year old developmentally normal boy was admitted for fever, vomiting, lethargy and right lower limb weakness for two weeks. BCG scar was present and there was no history of contact with an open case of tuberculosis. Physical examination revealed a malnourished child with meningeal signs and flaccid weakness of right lower limb. There was no evidence of spine tenderness or bladder or bowel involvement. Fundoscopy was normal.

CSF analysis revealed lymphocytic pleocytosis with elevated protein and normal glucose level, suggestive of tuberculous meningitis. CSF for acid fast bacilli was negative. Other tests for TB such as chest x-ray, mantoux, resting gastric aspirate for AFB and parental screening for TB were negative. ELISA for HIV was negative. X-ray of dorsolumbar spine was normal. ELISA for neurocysticercosis done on CSF was negative. Complete blood count and ESR were normal.

CT brain revealed multiple ring enhancing lesions over the left parietal lobe, left occipital lobe and left cerebellar hemisphere. MRI of the brain done three weeks later revealed the same lesions as seen on CT (Fig.1 and Fig.2). In view of the right lower limb weakness, MRI of the spinal cord was done, which showed two ring – enhancing lesions at the level of D1 and D12 (Fig.3 and Fig.4).

The child was started on anti-tuberculous chemotherapy. He showed good improvement on followup. A repeat MRI of the brain and spinal cord taken one year later showed complete resolution of the lesions.

---

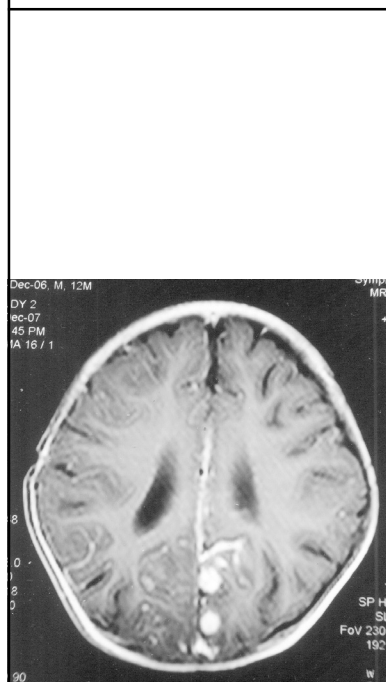
\* Postgraduate in Pediatrics,

\*\* Assistant Professor of Pediatrics,

Institute of Child Health and Hospital for Children, Chennai.



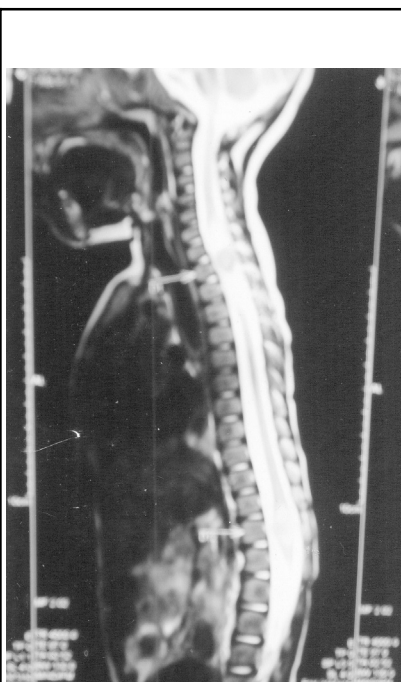
**Fig.1 MRI brain showing ring enhancing hemisphere lesions in left parietal lobe, left occipital lobe and left cerebellar hemisphere.**



**Fig.2 MRI brain. Two ring enhancing lesions in left occipital lobe.**



**Fig.3 MRI spinal cord showing ring enhancing lesion at the level of D12 vertebra.**



**Fig.4 MRI spinal cord showing two lesions at the level of D1 and D12 vertebra.**

## Discussion

Concurrent intracerebral, intracerebellar and intramedullary tuberculous granulomas are very rare, with fewer than ten cases reported in literature<sup>1</sup>. CNS tuberculous granulomas present with altered sensorium, seizures, raised intracranial pressure and focal neurological deficit. Tuberculomas in children are often infratentorial located at the base of the brain near the cerebellum.<sup>2,3</sup> Quite often, the child is already on ATT for another focus of TB, and formation of the granuloma represents good host immune response resulting in localization of the disease process.<sup>4</sup>

Intramedullary tuberculomas without Pott's spine has a reported incidence of 0.2 – 5% of neurotuberculosis.<sup>5</sup> TB of the spinal cord is classified into four types – extradural (64%), arachnoidal (20%), intramedullary (8%) and intradural- extramedullary (1%).<sup>6</sup> Intramedullary tuberculous granulomas have a predilection for the thoracic spinal cord and manifest as subacute cord compression, Brown – Sequard syndrome or total paraplegia.

In upto one third of the patients, there may be no evidence of extraneural TB and this does not exclude the possibility of tuberculoma.<sup>5</sup>

MRI is the imaging modality of choice, especially if spinal cord involvement is suspected. A hypointense lesion on T1 weighted imaging, which shows hyperintense ring with or without central hypointensity on T2 imaging is suggestive of tuberculous granuloma. Gd DTPA MRI further increases the sensitivity of detecting tuberculomas.<sup>3,7</sup>

Table.1 lists the various differential diagnoses to be considered on detecting a contrast-enhancing lesion on CT/ MRI brain. Of these, tuberculomas and neurocysticercosis are the most common.<sup>10</sup> Table.2 compares a few of the features of these two diagnoses on CT. It must be kept in mind that these findings are not specific for the disease, and other supportive evidence may be needed for definite diagnosis.

Treatment consists of ATT for 12 months with a course of oral steroids for 4 -6 weeks. If the child is already on ATT for another focus of TB, the granuloma does not indicate failure of therapy. Continuation of ATT with a brief course of steroids is recommended. Surgical intervention may be required for spinal cord lesions that do not respond to medical therapy.<sup>4,11</sup> MRI is useful to monitor the response to treatment. The patient may show complete

**Table. 1. Differential diagnosis of contrast-enhancing lesions on neuroimaging.<sup>9</sup>**

1. Tuberculosis
2. Neurocysticercosis
3. Mycosis
4. Toxoplasmosis
5. Pyogenic abscess
6. Early glioma
7. Metastases
8. Arteriovenous malformations

**Table. 2. Comparison of features of tuberculoma and neurocysticercosis on neuroimaging.**<sup>3,8,12</sup>

Feature	Tuberculoma	Neurocysticercosis
Number of lesions	Usually single	Often multiple (racemose)
Size of lesion	Larger in size (>20mm)	Smaller (<20mm)
Cyst wall	Thick, irregular	Thin-walled
Scolex	Absent	Pathognomonic if present

resolution of signs and symptoms or have residual neurological impairment secondary to gliosis.

## Conclusion

Spinal cord lesions without involvement of the bony spine may occur in tuberculosis. MRI is a valuable tool in both diagnosis and follow up of neurotuberculosis. Appearance of new lesions or enlargement of existing lesions during treatment with ATT does not necessarily indicate failure of therapy or drug resistance. Intracranial and intramedullary tuberculomas often respond to conservative management with ATT.

## References

- Shenoy SN, Raja A. Concurrent intramedullary and intracranial tuberculomas. *Neurol India* 2004;52:514-516.
- Starke Jeffrey R, Munoz Flor M. Tuberculosis In: Nelson Textbook of Pediatrics, Eds, Kleigman RM, Behrman RE, Jenson HB, Stanton BF, 18<sup>th</sup> Edn, Reed Elsevier India Private Limited, India. 2008;pp1248-1249.
- Vijayalakshmi G, Elavarasu E, Chitraranjan P, Venkatesan MD. CT brain the ring lesions 1. *Indian J Pract Pediatr* 2007;4:320-322.
- Shaharao VB, Pawar M, Agarwal R, Bavdekar SB. Intramedullary tuberculoma occurring during treatment of tuberculous meningitis. *Indian J Pediatr* 2004;71:107.
- Thacker MM, Puri AI. Concurrent intramedullary and intracranial tuberculomas. *J Postgrad Med* 2004;50:107-109.
- Arsilantas A, Faruk A, Kismet B, Esref T. Intramedullary tuberculoma of the spinal cord. *J Postgrad Med* 2002;48:54-55.
- Parmar H, Shah J, Patkar D, Varuna R. Intramedullary tuberculomas : MR findings in seven patients. *Acta Radiologica* 2000;41:572-577.
- Vijayalakshmi G, Elavarasu E, Chitraranjan P, Venkatesan MD. CT brain the ring lesions 2. *Indian J Pract Pediatr* 2008;(10) 1:81-83.
- Blanton Ronald B. Cysticercosis. In: Nelson Textbook of Pediatrics, Kleigman RM, Behrman RE, Jenson HB, Stanton BF, Eds, 18<sup>th</sup> Edn, Reed Elsevier India Private Limited, New Delhi, 2008;pp514-1516.
- Husain N, Jyotsna, Bagachi M, Husain M, Mishra MK, Gupta S. Evaluation of cysticercus fasciolaris antigen for the immunodiagnosis of neurocysticercosis. *Neurol India* 2001; 49:375-379.
- Devi BI, Chandra S, Mongia S, Chandramouli BA, Sastry KV, Shankar SK. Spinal intramedullary tuberculoma and abscess: a rare cause of paraparesis. *Neurol India* 2002;50:494.
- Garg RK. Diagnostic criteria for neurocysticercosis: Some modifications are needed for Indian patients. *Neurol India* 2004;52:171-177.



# INDIAN JOURNAL OF PRACTICAL PEDIATRICS

## SUBSCRIPTION TARIFF



### JOURNAL OFFICE

1A, Block II, Krsna Apartments,  
50, Halls Road, Egmore,  
Chennai 600 008, Tamilnadu, India.  
Phone: +91-44-28190032, 42052900.  
Email: ijpp\_iap@rediffmail.com

Enter  year  
Subscription  
for  years

**Official Journal of the Indian Academy of Pediatrics**  
**A quarterly medical journal committed to practical**  
**pediatric problems and management update**

### For office use

Ref. No.

Cash / DD for Rs.

DD No.

Receipt No. & Date

Name .....

Address .....

City ..... State .....

Pin ..... Phone (R) ..... (O).....

Mobile ..... Email .....

Designation ..... Qualification.....

I am enclosing a DD No. .... dated ..... drawn on .....  
favoring **Indian Journal of Practical Pediatrics** for Rs.....

**Signature**

### Subscription rate

Individual	Annual	Rs.400/-
	Ten Years	Rs.4000/-
Institution	Annual	Rs.500/-
	Ten Years	Rs.5000/-
Foreign	Annual	US \$ 60/-

Send your subscription, only by crossed demand draft,  
drawn in favour of **INDIAN JOURNAL OF**  
**PRACTICAL PEDIATRICS**, payable at **Chennai**  
and mail to **Dr. K. NEDUNCHELIAN**,  
Editor-in-Chief, 1A, Block II, Krsna Apartments,  
50, Halls Road, Egmore, Chennai 600 008,  
Tamilnadu, India.



# INDIAN JOURNAL OF PRACTICAL PEDIATRICS



## ADVERTISEMENT TARIFF

**Official Journal of the Indian Academy of Pediatrics - A quarterly medical journal committed to practical pediatric problems and management update**

Name .....

Address .....

.....

.....

.....

City .....

State ..... Pin .....

### FULL PAGE

	<b>B/W</b>	<b>Colour*</b>
Ordinary	5,000	10,000
Back cover	-	15,000
Second cover	-	12,000
Third cover	-	12,000

\* Positives of the advertisements should be given by the company.

Signature

Kindly send your payment by crossed demand draft only drawn in favour of  
“Indian Journal of Practical Pediatrics” payable at Chennai.

### MANAGING EDITOR

Indian Journal of Practical Pediatrics  
1A, Block II, Krsna Apartments,  
50, Halls Road, Egmore,  
Chennai - 600 008, Tamilnadu, India.  
Phone : 044-2819 0032, 42052900  
Email : ijpp\_iap@rediffmail.com