Journal of the Indian Academy of Paediatrics, Meghalaya Chapter

Towards Better Health of All Children

Editorial office

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From the President Desk

Dr. Palash Ranjan Gogoi, President IAP, Meghalaya State Branch

Dear fellow Academicians,

Greetings from the State Branch IAP office!

At the outset I thank all my fellow members who had given me the opportunity to work as an executive member of IAP, Meghalaya State Branch for the year of 2013.

Friends, today I am very happy & satisfied that I have tried my level best to work selflessly for Indian Academy of Paediatrics in this state.

I feel proud to acknowledge that most of the year long programs of Central IAP have been conducted with the true spirit of the programs.

As for example, the BNCRP Provider courses under IAP NRP FGM project are being conducted well in our State & so far we have conducted 10 (Ten) courses this year. We have conducted one IAP PALS course & one IAP GEM course successfully. Recently we conducted Mission Uday Resource person workshop also. IAP Undergraduate quiz 2013 has been organized as a routine activity in NEIGRIHMS. ORS Day & Week plus World Breastfeeding Week are also celebrated with great sincerity. This year we organized 3rd IAP Inter Nursing Institute quiz in Theresa House Training Centre, GDH. I must thank all the members for their kind cooperation in doing all these activities & making them a great success.

I congratulate our own Dr. M.S.Hu Dhar who has been given Shishu Shiromani Visheshagya award 2013 & Dr.Santanu Deb for receiving Purbanchal Pioneer award 2013 in East-Zone PEDICON, Tezpur, Assam.

As an outgoing President, I pledge that I shall work for the betterment of the child health in this part of our country as a common soldier for rest of my life.

I wish all my friends a happy & fruitful 2014.

Long live IAP! Long live Meghalaya State Branch!

Sincerely yours

Dr. Palash Ranjan Gogoi
President,
Meghalaya State Branch, 2013

Letter from Secretary IAP Meghalaya State Branch:

Dear fellow Academicians,

It's my pleasure & privilege to write this message for the Annual Report of IAP Meghalaya State Branch 2013 under leadership of our Honorary President, Dr. Pallash R. Gogoi. I am grateful to all the members for their love & support though out the year. It's been a year of achievements; academy has grown by leaps & bound. Let us all contribute to take it for further height.

It is the time for reporting activities done under the banner of IAP Meghalaya 2013; the report encompasses detail of our academic & social activities & they are as follows: -

- *The Memorandum of our Society was written with aim & objective to dedicate our activities entirely on New Born & Child Care. Our society got its Registration Number & PAN Card allotted for it's fund raising & carrying various academic activities.*
- *10 NRP (Neonatal Resuscitation Program) courses were held at various districts of Meghalaya to train the Nurses for better Neonatal Care.*
- *Pediatric Advanced Life Support (PALS) & Golden Hour Emergency Management (GEM) courses were conducted by imminent faculties of India in our State to uplift the knowledge & skill of practicing Pediatrician in managing a sick child.*
- *ORS & Breast Feeding Weeks were celebrated with enthusiasm at various hospitals & community levels to combat the common killer childhood disease i. e; Diarrhoea & Malnutrition. People were educated regarding the proper preparation of ORS & benefits of Breast Feeding.*

Friends, I profusely thank with respectful gratitude to those who have encouraged, helped, supported & worked with me through out the year.

Wish you all a Merry Christmas & very Happy & Prosperous New Year, 2014.

Yours Sincerely,

Dr. Pankaj Jain, Secretary
IAP Meghalaya State Branch

Editorial

Dear members of IAP Meghalaya

It gives me immense pleasure to bring out the 2013 issue of our Journal on the occasion of our Annual conference.

This year the Journal contains a wide potpourri of varied topics both current and of sustained interest. The authors of the articles also are from varied backgrounds which will add to the interest.

Vitamin D has been a hot topic for some years now and there is an extensive review of literature regarding the topic. There is also an article on atopy which is one of the perennial problems with which we struggle. There are articles on current relevant topics ranging from Neonatology to vaccinology and intensive care which will definitely enlighten us on many aspects.

I hope that we all will benefit from the knowledge that is being disseminated through this journal.

Wishing you all Merry Christmas and a very happy New Year in advance.

Long live IAP Meghalaya

Thanking you

Yours sincerely

Sourabh Gohain Duwarah

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Exclusive Breast Feeding & Vitamin D Deficiency
- a review of literature

Dr. Pankaj Jain, MD Paediatrics
Consultant Woodland & Supercare Hospital

Introduction

Globally as many as 1.45 million lives are lost due to suboptimal breast-feeding in developing countries. WHO analysis of childhood deaths has listed suboptimal breast-feeding as one of the most powerful sharedriskfactorsandestimatedthat1.3milliondeaths can be prevented in 42 high mortality countries by increasing the level of breast-feeding amongst infants. 1RicketsattributabletovitaminDdeficiency is known to be a condition that is preventable with adequate nutritional intake of vitamin D. Despite this knowledge, cases of rickets in infants attributable to inadequate vitamin D in take and decreased exposure to sunlight continue to be reported particularly with exclusively breast fed infants and infants with darker skin pigmentation[2-6].

Prevalence and risk factors for deficiency

The prevalence of hypo vitamin os is D in exclusively breast fed infants has been reported to be 82,52 and 20 percent from UAE[2], Pakistan[3] and China[4] respectively but there is a paucity of data from India regarding the same. The vitamin D stores of the new born depend entirely on the vitamin D stores of the mother. Hence, if the mother is vitamin D-deficient, the infant will be deficient because of decreased maternalfoetaltransferofvitaminD[5]. Therearereports suggesting that the bone mass oft he newborn is related to the vitamin D status of the mother[6].Impaired foetal bone ossification in association with maternal vitamin D deficiency has been reported[7].The risk factors associated with low maternal 25-OHD include low educational level, insufficient intake of vitamin D in dietanddressinghabits[8]. Inaddition,airpollutionmay decrease the ultraviolet light exposure and thereby vitamin D production by the skin. In a study from India, enrolling 9-24 month old infants with the same socio- economic conditions and with no vitamin D supplementation, the group living in the region with intensiveairpollutionhadlowerserum25-OHDlevels than those living in the region with noairpollution[9]. It has been observed that women who dressed themselves in black covering their hands and face had lower 25-OHD levels[8,10]. In a study from Pakistan[11], high prevalence of vitamin D deficiency in breast-fed infants and nursing mothers were observed in 55 percentofinfantsand45percentofnursing mothers. Preterm infants [20-30% of very low birth weight (<1500 g) and 60-75 per cent of extremely low birth weight babies(<1000g)]areatriskofdeveloping osteopaenia of prematurity due to poor intestinal absorption of calcium and impaired conversion of vitamin D into its active metabolites and their serum vitamin D levels are usually low orb order line [12].Inaseriesofcasesofhypo calcaemiainearlyinfancy reported from Turkey, majority was due to vitamin D deficiency in exclusively breast-fed infants[13]. Symptomatic hypocalcaemia in young infants due to vitamin D deficiency has been reported in two studies from UK[14], [15].Acaseseriesof13excl usivelybreast-fed infants presenting with hypocalcaemic seizures with proven vitamin D deficiency has been reported from India[16].

Finally, the lack of adequate training of physicians in a rickets- free era coupled with the lack of adequate recommendations for vitamin D supplementation by professional organizations may also contribute to the development of rickets in exclusively breast-fed babies[17].

Breast-feeding and vitamin D deficiency

It has been estimated that breast milk from a vitamin D replete mother contains between 20 and 60 IU/l of vitaminD[18] and hence adequate intake of vitamin D cannot be met with human milk as the sole source of vitamin D in a breast-feeding infant[18,19].In a study by Rothberget al20,lactating mothers were administered daily supplements of 500 and 1000 IU of vitamin D from delivery and in spite of this, 25-OHD levels of their infants measured at six weeks were not altered. In contrast, daily supplements of 400 IU of vitamin D to infa ntssignificantlyincreasedthe25-OHDlevelsatsix weeks. A study from Finland had concluded that when themothersweresupplementedwith2000IUofvitamin D, their infants had 25-OHD levels similar to those receiving daily supplements of 400 IU of vitamin D indicating that it ism ore efficient to supplement infants ratherthantheirmothers[21].

Diagnosis

The diagnosis of rickets isba se don its characteristic clinical and biochemical findings. VitaminD deficiency results in hypocalcaemia, hypophosphataemia, elevated alkaline phosphatase levels and secondary hyperparathyroidism. Tsang[22] had reported that a low phosphate level combined with a low 25- hydroxy vitamin D concentration and radiologic evidence of rickets confirms the diagnosis of vitamin D deficiency rickets. Based on serum 25-OHD concentrations[23],vitaminDdeficiencyisclassifiedas:

Mild vitamin D deficiency: Serum25-OHD concentration of 25-50 nmol/l. Serum levels over 50 nmol/l prevent secondary hyperparathyroidism and elevatedalkalinephosphataselevels.

Moderate vitamin D deficiency: Serum 25-OHD concentration of 12.5-25 nmol/l. The incidence of hypocalcaemia and rickets increases with moderate deficiency.

Severe vitamin D deficiency: Serum 25-OHD concentration less than 12.5 nmol/l. Vitamin D concentrationslessthan12.5nmol/lareseeninover70 per cent of children with rickets and over 90 percent of children with hypocalcaemia.

However, the cut-off for hypovitaminosis D in neonates is still being debated. Zeghoudetalfound neonatal 25-OHD concentrations <30 nmol/l (12 ng/ ml) be associated with elevated parathyroid hormone (PTH) and hence proposed that concentration as the cut- off for diagnosing hypovitaminosis D in the newborn[24]. Concentrations of calcitriolmaybelow, normalorhigh at the time of diagnosis and hence is of no value in makingthediagnosis.

Prevention

The American Academy of Pediatrics (AAP) has issued updated guidelines (2013) for vitamin D intake in infants, children, and teens to prevent rickets and vitamin D deficiency. Specific recommendations to ensure that healthy infants, children, and adolescents meet the required vitamin D intake of at least 400 IU per day are as follows:

1. Beginning in the first few days of life, breast-fed and partially breast-fed infants should be supplemented with 400 IU per day of vitamin D, and this should be continued unless the infant is weaned to at least 1 L per day or 1 quart per day of vitamin D–fortified formula or whole milk. Vitamin D levels in breast milk range from less than 25 to 78 IU/L, putting exclusively breast-fed infants at greater risk for vitamin D deficiency.
2. A vitamin D supplement of 400 IU per day is indicated for all non–breast-fed infants and for older children who are consuming less than 1000 mL per day of vitamin D–fortified formula or milk. The daily intake of each child may include other dietary sources of vitamin D, such as fortified foods.
3. A vitamin D supplement of 400 IU per day is indicated for adolescents who do not ingest 400 IU of vitamin D per day from vitamin D–fortified milk (100 IU per 8-oz serving) and vitamin D–fortified foods (such as fortified cereals and egg yolks).
4. Serum concentrations of 25-hydroxyvitamin D in infants and children should be at least 50 nmol/L (20 ng/mL), based on the available evidence.
5. Despite ingesting 400 IU per day, children at increased risk for vitamin D deficiency, such as those with chronic fat malabsorption and those chronically treated with antiepileptic drugs, may continue to be vitamin D deficient. Children with dark skin pigmentation require 5 to 10 times longer to generate vitamin D_3 from sunlight exposure. Children in these groups may require higher doses of vitamin D supplementation to achieve normal vitamin D status, which should be evaluated with laboratory tests for concentrations of serum 25-hydroxyvitamin D and parathyroid hormone and measures of bone mineral status. When a vitamin D supplement is prescribed, 25-hydroxyvitamin D levels should be monitored every 3 months, and parathyroid hormone and bone mineral status should be monitored every 6 months, until levels normalize.
6. Pediatricians and other health care professionals should ensure that vitamin D supplements are readily available to all children in their community, especially to those who are at greatest risk. Pregnant and lactating women who are vitamin D deficient may expose their offspring to a higher risk for vitamin D deficiency after birth and during lactation, and their vitamin D status should therefore be monitored. Although insufficient vitamin D intake in pregnant women adversely affects fetal skeletal development, tooth enamel formation, and general fetal growth, universal recommendations for high-dose vitamin D supplementation during pregnancy are not currently available.

Sunlight and vitamin D

One of the potential sources of vitamin D synthesis is in the skin from the UV-B fraction of sunlight. Our traditional practice of oil massage and sunbath to the baby helps in the synthesis of vitamin D in the skin. Two hours is the required minimum weekly period of exposure to sunlight for infants if only the face is exposed, or 30 min if the upper and lower extremities are exposed[22].

Dietary supplement

Oily fish such as salmon, mackerel and sardines, cod liver oil and liver and organ meats are rich natural sources that are not commonly consumed by children. Fortified foods are being recognized as an important source of vitamin D. Fortification of milk has been found to be safe, effective and acceptable method. However, in a setting like

India, where the per capita milk consumption is very low, consideration for other methods of fortification such as fortification of oil, cereal powders and even salt needs consideration.

References

1. LauerJA, BetranAP, BarrosAJ, deonisM. Deaths and years of life lost due to suboptimal breast feeding among children in the developing world: a global ecological risk assessment. PublicHealthNutr2006; 9:673-85.
2. DawoduA, AgarwalM, HossainM, KochiyilJ, ZayedR. HypovitaminosisD and vitamin D deficiency in exclusively breast - feeding infants and their mothers in summer: a justification for vitaminD supplementation of breast-feeding infants. JPediatr2003;142:169-73.
3. AtiqM, SuriaA, NizamiSQ. VitaminD status of breastfed Pakistani infants. ActaPaediatr1998;87:737-40.
4. Ho ML, Yen HC, Tsang RC, Specker BL, Chen XC, Nichols BL. Randomized study of sunshine exposure and serum 25- OHDinbreastfedinfantsinBeijing,China.JPediatr1985;107:928-31.
5. SalleBL, DelvinEE, LapillonneA, BishopNJ, GlorieuxFH. Perinatalmetabolism of vitaminD. AmJClinNutr2000;71(Suppl):1317S-24S.
6. KrishnamachariKA, IyengarL. Effect of maternal malnutrition on the bone density of neonates. AmJClinNutr1975;28:482-6.
7. AnastCS, CarpenterTO, KeyLL. Metabolic boned is orders inchildren. In: AvioliLV, KraneSM, editors. Metabolicbone disease and clinically related disorders. Philadelphia: Saunders;1990.p.850-84.
8. PehlivanI, HatunS, AydoganM, BabaogluK, GokalpAS. Maternal vitamin D deficiency and vitamin D supplementation inhealthyinfants.TurkJPediatr2003; 45:315-20.
9. SpeckerBL, Ho ML, OestreichA. Prospective study of vitamin D supplementation and rickets in China.JPediatr1992;120:733-9.
10. AlagölF, ShihadehY, BoztepeH, AzizlerliH, SandalcýO. Sunlight exposure and vitamin D deficiency in Turkish women.JEndocrinolInvest2000;23:173-7.
11. AtiqM, SuriaA. Maternal vitamin-D deficiency in Pakistan. ActaObstetGynecolScand1998;77:970-3.

12. SinghM. Metbolic disorders. In. SinghM, editor. Care of the new born. NewDelhi: SagarPublications;2004,p.353-75.

13. HatunS, OzkanB, OrbakZ, DonerayH, CizmeciogluF, ToprakD, etal. VitaminD deficiency in early infancy.JNutr2005;135:279-82.

14. LadhaniS, SrinivasanL, BuchananC, AllgroveJ. Presentation of vitaminD deficiency. ArchDisChild2004;89;781-4.

15. PalBR. Rickets resurgence in the United Kingdom: improving antenatalmanagementinAsians.JPediatr2001;139:337-8.

16. BalasubramanianS, ShivbalanSo, SaravanakumarP. Hypocalcemia due to vitaminD deficiency in exclusively breastfed infants.IndianPediatr2006;43:247-51.

17. CaraFJ.VitaminDdeficiencyricketsinbreastfedinfants.Availablefrom:http://www.medscape.com/viewarticle/420205,accessedonMay15,2007.

18. HollisBW,RoosBA,DraperHH.VitaminDandits metabolitesinhumanandbovinemilk. JNutr1981;111:1240-8.

19. Reeve LE, Chesney RW, DeLuca HF. Vitamin D of human milk :identificationof biologically active forms. Am J ClinNutr1982;36:122-6

20. Rothberg AD, PettiforJM, Desmond FC. Maternal infant vitaminDrelationshipsduringbreast-feeding.JPediatr1982;101:500-3.

21. Ala-Houhala M. 25-Hydroxyvitamin D levels during breast-feedingwithorwithoutmaternalorinfantilesupplementation ofvitaminD.JPediatrGastroenterolNutr1985;4:220-6.

22. SpeckerBL,ValanisB,HertzbergV,EdwardsN,TsangRC.Sunshine exposure and serum 25-hydroxyvitamin D concentrations inexclusivelybreast-fedinfants. JPediatr1985;107:372-6.

23. Tsang R. Endocrinology update for pediatricians. Vitamin D- deficiency rickets. Presented at the Annual Meeting of the AmericanAcademyofPediatrics;October29,2000;Chicago, Illinois.

24. ZeghoudF, VervelC, GuillozoH, Walrant-DebrayO, BoutignonH,GarabedianM. SubclinicalvitaminDdeficiency inneonates:definitionandresponsetovitaminDsupplements. AmJClinNutr1997;65:771-8.

Atopic March – From skin to the airways

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Introduction:

Diseases such as atopic dermatitis (AD) or eczema, allergic rhinitis (AR) and asthma are allergic in nature. The incidence of these diseases is on the rise and approaching about 20% in developed nations [1]. They tend to occur in families because of a strong genetic propensity and such patients demonstrate high levels of IgE antibodies specific to certain allergens. The natural history of appearance of these conditions during a certain age period is characterised by a sequence of clinical events which is now described as the atopic or allergic march. It is important to understand this concept for understanding the natural history of these allergic conditions as well as for appropriate management. The risk of develop¬ing these atopic diseases is however complex and it may not be a simple progression in a temporal pattern as de¬scribed in the atopic march because both genetic and environmental factors strongly influence the development of these diseases.

What is atopy?

Atopy is described as the inherited harmful immunological response to a harmless substance. In scientific terms it is described as personal and/or family propensity to produce IgE antibodies and sensitization in response to environmental triggers[2]. Underlying atopy is now considered to be critical in linking AD, AR and asthma[3].

Atopic dermatitis (AD) - the first step in the atopic march:

AD is one of the most common and important skin problems of childhood. The International Study of Asthma and Allergies in Childhood (ISAAC, phase-1 study) reported the prevalence of AD in 56 countries to be around 3-20.5% [4]. During the same study about 37,000 children were surveyed in 14 different centers in India and the prevalence of AD ranged from 2.4% to 6% except for Kottayam in Kerala where the prevalence was >6% [4]. The ISAAC phase 3 study when compared with the phase 1 study in India showed that the prevalence of AD is increasing in children from 6-7 and 13-14 years of age though the rates are much lower than the global prevalence rates[4]. From various Indian studies, the mean age of disease onset was 4.2 to 4.5 months for infantile AD, 4 to 4.1 years for childhood AD [5,6]. Males are generally seen to be more affected than females [4]. AD is an inflammatory cutaneous disease characterized by erythema, pruritis altered barrier function and immune dysfunction resulting in IgE sensitization. A dysfunction of antimicrobial peptides such as defensins, psoriasins, cathelicidins occurs and this results in an increased susceptibility to infections by Staphylococcus aureus which in turn causes AD exacerbations[7]. The epidermis of the skin has multiple components such as claudin, desmoglein, filaggrin, ceramide and protease inhibitors (SPINK). These prevent water loss and also function as a barrier to allergens and bacteria. Deficient / absent SPINK gene and decreased filaggrin causes increased transepidermal water loss, increased levels of specific IgE reponses to dust mite and cat and are associated with an increased incidence of AD, AR and asthma in later life due to the

early sensitization to allergens especially the aeroallergens [8, 9] . Studies have demonstrated that 30-50% of the children with AD develop asthma at an older age and two-thirds of them develop AR [10, 11]. The risk factors which have been suggested to facilitate the progression of AD to AR and asthma are atopy in parents, presence of cats in the house, the development of eczema prior to 4 years of age and other factors such as smoke exposure [7]. Approximate 70% of patients with severe AD develop asthma compared with 20-30% of patients with mild AD and approximately 8% in the general population. Only children with the mildest AD did not develop either asth¬ma or allergic rhinitis[12].

Progression to the end point – Allergic rhinitis & Asthma:

Epidemiologic studies have consistently shown a strong association between rhinitis and asthma[1]. Both the diseases share anatomical, physiological, immunopathological, and therapeu¬tical factors[13]. AR is an inflammatory condition af¬fecting the nasal mucosal membranes. In sensitized individuals, allergens such as pollens, molds, and animal dander provoke this allergic response. Clinically these patients will complain of perpetual nose block, sneezing especially in the morning or on exposure to an allergen like dust and frequent itching of the nose. Allergic rhinitis is however often trivialized and many clinicians tend to be unaware of the fact that it has a significant impact on quality of life, affects the normal activities of children such as studies and physical activities, and it is associated with multiple co¬morbidities, including asthma. Cardinal features of asthma in¬clude airway inflammation and airway hyperreactivity to aller¬gens associated with structural remodeling. Studies on the prevalence of asthma in patients with rhinitis varies consider¬ably, but has been reported to be as high as 80% [13]. Many pa¬tients with AR have lower airway hyperreactivity or bronchial hyperresponsiveness. AR as an important risk factor for developing asthma has been supported by several studies [1]. In a study by Leynaert et al. approximately 75% of subjects with asthma reported rhinitis; patients with rhinitis had increased risk for asthma and lower airway reactivity compared with patients without rhinitis; and the risk for asthma increased from 2.0% in subjects without rhi¬nitis to 18.8% in subjects with AR either when ex¬posed to pollen or to animal dander [14]. So these studies support the fact that allergic rhinitis may precede the development of asthma. This coupled with the previous studies that patients with AD are prone to develop AR and asthma, it becomes obvious that the three conditions of AD, AR and asthma are a continuum of the same disease process with manifestations occurring at different ages of the child and many a times the skin manifestations become passive by the time the AR and asthma develop. The Tasmanian Longitudinal Health Study investigated the in¬fluence of eczema on the development of asthma from child¬hood to adult life and found that childhood eczema was signifi¬cantly associated with new-onset asthma in three separate life stages: pre-adolescence (hazard ratio 1.70; 95% confidence in¬terval [CI] 1.05–2.75), adolescence (2.14; 1.33–3.46), and adult life (1.63; 1.28–2.09) as well as over the life-span from the ages of 8 to 44 years (1.73; 1.42–2.12).23 This study strongly suggests that the atopic march progresses well past childhood. It is still unclear why some of the infants with AD outgrow the disease with increasing age, whereas others will “march” to develop other atopic conditions such as allergic rhinitis and/or asthma in later stages of life [15].

Food allergy and AD:
AD and food allergy commonly co-exist, par¬ticularly in those with early onset, severe and persistent atopic eczema. Food allergy is a known provoking cause of AD and the prevalence of IgE-mediated food allergy among children with AD is about 35% of affected children[16]. Whether children with IgE-mediated food allergy are at increased risk of developing subsequent other allergic manifestations (asthma and AR) is unclear as there may be a number of other factors that may influence the development of subsequent AR and asthma.

Current concepts on the potential mechanisms underlying the atopic march:
Previous explanations of the underlying mechanisms had focussed more on the "hygiene hypothesis" and the "Th1-Th2 paradigm" i.e. less exposure to infectious agents resulted in more allergic responses and Th-2 type of immune responses. However the current concepts are increasingly focussing on the disruption of the epithelial barrier of the skin as a trigger for the development of an allergic response and AD. Once the skin epithelial barrier is disrupted, allergens are captured and pro¬cessed by the Langerhans cells and then they migrate to draining lymph nodes and inter¬act with naïve T cells to promote Th2 immunity eventually leading to sys¬temic allergies such as AR and asthma[17].

Therapeutic implications of understanding the atopic march:
It is important to understand the concept of the atopic march because early therapeutic interventions can halt to a significant extent the progression of the disease and also aide in improving the quality of life of the patients and even in a certain group of patients a prolonged remission. If one can identify the infants with AD at increased risk for AR and asthma, an early critical window of opportunity can be accessed for an appropriate intervention for life. So AD needs to be treated aggressively at an early stage. The treatment must aim to keep the skin integrity intact, maintain the hydration of the skin as well as prevent superadded infections especially with Staphylococcus aureus. Liberal use of neutral pH moisturizers, occasionally topical steroids and tacrolimus ointments should be done to treat AD. Avoidance of allergans such as animal dander, dust and smoke is a must. At the current levels of understanding of the atopic march it is not recommended to stop any particular type of food unless the child has a clear temporal relation of an allergic reaction to a particular kind of food. Similarly while treating for asthma one must actively seek any history suggestive of allergic rhinitis and treat it. Failure to the treat a co-existing AR is often the most important cause of an unresponsive or partially responsive asthmatic. AR is usually treated by a combination of oral long acting anti-allergic medications such as cetrizine, levocetrizine, fexofenadine or loratidine, oral montelukast and in very severe cases intranasal steroids. Most of the patients would require a 2- 3 month trail of the AR medications to achieve a good clinical response. Regular clinical assessments must be done to judge the response and gradually try to reduce the number of drugs and come to a stage where the patient will require minimal drugs such as montelukast will help to keep the patient asymptomatic. Similarly one must treat the asthmatics aggressively with inhaled bronchodilators and inhaled steroids wherever the situation demands.

New therapies to prevent the atopic march:

Other suggested therapies which have been seen to modify the allergic response and thus prevent the atopic march are probiotics and Vitamin D. Probiotics are cultures of beneficial bacteria that positively affect the host by enhancing the microbial balance and restore normal intestinal permeability and gut microecology. They also improve the immunological barrier function of the intestine and reduce the generation of proinflammatory cytokines characteristic of allergic inflammation. Vitamin D is said to promote immunological tolerance, suppress pro-allergy immune response, maintain epithelial barrier and also produce antimicrobial peptides such as defensins and cathelicidin 18. Exclusive breast feeding is another important factor that helps in prevention of early sensitization to allergens and thus prevents the development of the atopic march.

Conclusion:

There is now increasing evidence that support the concept of the atopic march. Infants who develop AD should be followed up closely for the development of AR and asthma. Similarly patients with asthma must be actively looked for the presence of AR and treated for AR to halt the atopic march and improve outcomes in these patients. Treating one inadequately or failing to treat an associated condition will result in treatment failures and poor outcomes and poor quality of life.

References:

1. Zheng T, Yu J, OM Hee and Zhu Z. The atopic march: Progression from atopic dermatitis to allergic rhinitis and asthma. Allergy Asthma Immunol Res 2011; 3 (2); 67-73.
2. Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. J Allergy Clin Immunol 2004; 113:832-6.
3. Spergel JM. Atopic march: link to upper airways. Curr Opin Allergy Clin Immunol 2005;5:17-21.
4. Bearley R, Keil V, Mutius EV, Pearce N. World wide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema ISAAC. Lancet. 1998;351:1225–32.
5. Dhar S, Kanwar AJ. Epidemiology and clinical pattern of atopic dermatitis in North Indian pediatric population. Pediatr Dermatol.1998;15:347–51.
6. Sarkar R, Kanwar AJ. Clinico-epidemiological profile and factors affecting severity of atopic dermatitis in north Indian children. Indian J Dermatol. 2004;49:117–22.
7. Hogan MB, Peele K, Wilson NW. Skin barrier function and its importance at the start of the atopic march. J Allergy 2012. doi: 10.1155/2012/901940.
8. Y. Ohshima, A. Yamada,M. Hiraoka et al., "Early sensitization to house dust mite is a major risk factor for subsequent development of bronchial asthma in Japanese infants with atopic dermatitis: results of a 4-year follow-up study," Annals of Allergy, Asthma and Immunology, vol. 89, no. 3, pp. 265–270, 2002.

9. R. van den Oord and A. Sheikh, "Filaggrin gene defects and risk of developing allergic sensitisation and allergic disorders: systematic review and meta-analysis," BMJ, 2009; vol. 339, 2433.

10. J. M. Spergel and A. S. Paller, "Atopic dermatitis and the atopic march," Journal of Allergy and Clinical Immunology, vol. 112, no. 6, pp. S118–S127, 2003.

11. J. M. Spergel, "Epidemiology of atopic dermatitis and atopic March in children," Immunology and Allergy Clinics of North America. 2010, 30 (3),269–280.

12. Gustafsson D, Sjöberg O, Foucard T. Development of allergies and asthma in infants and young children with atopic dermatitis--a prospective follow-up to 7 years of age. Allergy 2000;55:240-5.

13. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 2008; 63 Suppl 86:8-160.

14. Leynaert B, Neukirch C, Kony S, Guénégou A, Bousquet J, Aubier M, Neukirch F. Association between asthma and rhinitis according to atopic sensitization in a population-based study. J Allergy Clin Im¬munol 2004;113:86-93.

15. Burgess JA, Dharmage SC, Byrnes GB, Matheson MC, Gurrin LC, Wharton CL, Johns DP, Abramson MJ, Hopper JL, Walters EH. Childhood eczema and asthma incidence and persistence: a co¬hort study from childhood to middle age. J Allergy Clin Immunol 2008;122:280-5.

16. Eigenmann PA, Sicherer SH, Borkowski TA, Cohen BA, Sampson HA. Prevalence of IgE-mediated food allergy among children with atopic dermatitis. Pediatrics 1998;101:E8.

17. McGrath JA, Uitto J. The filaggrin story: novel insights into skin-barrier function and disease. Trends Mol Med 2008;14:20-7.

18. Vassallo MF, Camargo CA Jr. Potential mechanisms for the hypothesizel link between sunshine, vitamin D, and food allergy in children. J Allergy Clin Immunol 2010; 126: 217-222.

Newer Vaccine delivery systems

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Use of new vaccine delivery systems has revolutionized immunization practises and will continue to do more so in the future. The last century has witnessed rapid advances in molecular biology, immunology, virology, bacteriology and biochemistry. This has led not only to the discovery of new vaccines but also allowed us different approaches towards vaccination for diseases. The next century promises to give us new vaccines which are better than the ones of the last generation, safer technologies of administration and solutions to surmount problems associated with non compliance etc.

Techniques have focussed on -

a) The presentation of antigens to the immune system as well as modulation of the immune system itself.

b) Assist in the discovery and characterization of new antigens (genomics)

c) Structure determination and genome mining (bioinformatics)

d) Modes of administration (patches, microneedles, nasal route)

e) Analysis of the immune responses in humans (immunochips, flow cytometry)

Let us look at some of these vaccine delivery systems –

1) **Conjugation:** Bacterial polysaccharide conjugate vaccines are defined as delivery systems composed of bacterial capsular polysaccharide or lipopolysachharide antigens, which are coupled to protein carrier molecules. Isolated polysachharide antigens are poorly immunogenic in infants because they generate a T cell independant response. Conjugation with a T cell dependant protein carrier elicits a good immunological response and memory. Carrier proteins for conjugation are derived from a number of bacteria such as Corynebacterium diphtheria, Clostridium tetani, Vibrio cholera, Pseudomonas aeruginosa. This has resulted in conjugate Hib, PCV and Meningococcal conjugate vaccines

2) **Recombinant proteins:** For pathogens grown with difficulty in the laboratory such as Hepatitis B or C, Mycobacterium leprae, Helicobacter pylori, Plasmodium falciparum, the solution for producing vaccines seems to be through the production of recombinant proteins through genetic engineering. The genes expressing the antigens are inserted into a plasmid, which is then introduced into a host cell (by transfection) such as a bacterium like E. Coli, yeast like S. cerevisie, or mammalian culture cell lines (vero cells). The host cells express the recombinant molecule, which has retained its antigenic and immunogenic properties. Recombinant proteins can be produced in large quantities, are easy to purify and are stable. The current Hepatitis B vaccine was developed according to this model.

3) **Synthetic peptides :** The principle is to develop a synthetic peptide, containing well defined antigen, in order to induce an effective and specific response. Encouraging results in the field of cancer are present. Advantages of synthetic peptide vaccines are use without risk of integration within the host genome, induction of a well defined, mono functional immune response and a reproducible, large scale extremely pure production. Disadvantages are low immunogenicity. Mono specificity of the immune response may allow mutating organisms to escape the immune response. Degradation by serum peptidases may reduce availability.

4) **Viral vectors:** A viral vector is a virus carrying the genes of pathogenic antigens that have been inserted into its own genome. Advantages of vaccines based on viral vectors include their ability to target specific cells or tissues and their high efficacy to induce both humoral and cellular immune responses. Often only a single injection is sufficient. Disadvantages are related to the pathogenicity of the viral vector itself. Canarypox virus is being tried as a vector for a HIV vaccine. Several HIV genes are inserted into canary pox and inoculation into humans induces small quantities of antibodies, but a strong cytotoxix T cell response.

5) **DNA vaccines:** DNA vaccines contain the gene or genes for an antigenic portion of a virus, such as the core protein or the envelope protein. Host cells take up the foreign DNA, and express the viral gene and manufacture the corresponding viral protein inside the cell. A DNA vaccine against influenza exists and there is potential for such vaccines for HIV, Hep B, rabies, Herpes simplex, Papilloma virus, Mycobacterium tuberculosis etc. Advantages of DNA vaccines are tremendous. They are easier to produce than "classical vaccines". They are stable, heat resistant, easy to store, easy to transport, easy to distribute and inexpensive. Efficacy of these vaccines is still under study and there is a theoretical risk of integration into genome of host cells thereby inducing malignant transformation of the cell.

6) **Recombinant viral or bacterial vectors:** this approach utilises recombinant DNA technology to create new viral or bacterial vectors to introduce genes coding for immunogenic peptides of various pathogens into the host. A number of recombinant vaccinia virus constructs have been created to produce vaccines for potential protection against HIV and rabies.

7) **Novel adjuvants:** Adjuvants are substances that are added to vaccines to enhance their immune response by increasing the production of antibodies (augment, modify or prolong the immune response). "Adjuvare"(Latin) meaning "to help".

   a. **Liposomes:** are generated from phospholipids and other polar amphiphiles, which under certain physical conditions form closed concentric bilayer membranes when in the presence of excess water. Liposomes can augment both humoral and cellmediated immunity to a wide variety of antigens including bacterial

polysaccharide and influenza subunit vaccine. A liposome based Hepatitis A is approved for clinical use. Research is underway for developing trivalent influenza, diphtheria and tetanus toxoid vaccines. Disadvantages include special storage and handling, variable purity, expensive and poor adjuvant activity.

b. **Virosomes:** Are tiny spherical vesicles, which contain viral proteins embedded in their membranes. These proteins enable the virosome membranes to fuse with cells of the immune system and thus deliver their contents, in this case, vaccine specific antigens directly to their targets. Once they have delivered their contents, the virosomes are completely degraded. Advantages are that they mimic the natural process of antigen presentation; stimulate both arms of the immune system; have target specific delivery; are completely biodegradable; can be administered by injection or nasally.

c. **Immune stimulating complexes (ISCOMs):** A vaccine formulation which combines a multimeric presentation of antigen with built in adjuvant. The ISCOM borne antigen induces an enhanced cell mediated immunity.

d. **Microspheres:** Encapsulation of antigens with particles to protect degradation in the stomach following oral administration. The microparticles which act as adjuvants are made of polyactide coglycolide (PLGA) and other similar compounds.

e. **CpG motifs in vaccination:** Bacterial DNA has abundance of unmethylated CpG dinucleotides compared to mammalian DNA. These CpG oligonucleotides are potent agents that could be used as an adjuvant to aid humoral as well as cellular immune responses.

f. **Cholera toxin and E.coli lymphotoxin:** Are highly immunogenic and when co administered with with antigen by mucosal route, induce strong systemic and mucosal Th_2 type cytokine response to antigen. Advantages are that they circumvent need for prolonged administration of antigen and for large doses of antigen. They are extremely effective mucosal adjuvants and can be given orally. Problem is they are highly toxicogenic.

Mucosal immunisation

Live oral vaccines have in use for quite some time but non living oral vaccines would be degraded during passage through the gut. Intranasal route would be a better alternative for mucosal immunisation because of absence of acidity and degrading enzymes. Nasal live attenuated influenza vaccine has been found to replicate in the cold nasal mucosa but not in the lungs.

Vaccines can be administered by aerosols e.g live attenuated influenza vaccine is delivered by aerosols be a device which produces large droplets which do not go beyond the nasal cavity. Similarly small aerosol measles vaccine has been used that penetrates upto lungs.

Edible vaccine

Edible vaccines are prepared by introducing selected genes into plants and inducing transgenic plant to express encoded protein by a process called molecular farming. Foods

under study include bananas, potatoes, tomatoes, rice, wheat, lettuce, soya bean, corn etc. Edible vaccines are in the pipeline for Norwalk virus, ETEC, V. cholerae, hepatitis B, H.pylori &Rabies. The advantages of plant based oral vaccines include multiple vaccinations per plant (in theory), stimulation of mucosal immunity, more efficacy against pathogens that invade mucosal surfaces, safe, painless administration, low cost, ability to be produced in developing countries and being attractive to children. The disadvantage is that large amounts of edible vegetables have to be consumed to elicit an immune response.

Needle free vaccination systems

Jet injectors deliver liquid vaccine through a nozzle via high pressure that penetrates skin. The site of injection may be intramuscular, subcutaneous or intradermal depending on the mechanical properties of the fluid system. The vaccines are dispersed more widely into the tissue due to high pressure. This particular technique is desirable because of safety to vaccinee, esp children, health care provider and community.

Microneedle immunization

Microneedles are used to penetrate the epidermis and access Langerhans cells. There is ease of administration and minimal pain. It can induce both systemic and mucosal immune response.

Bioject B2000

This device is used for intramuscular and subcutaneous injection. It is a gas powered (CO_2 ampoule) which can inject drugs or vaccines filled from a normal vial.

Many of the above technologies are still in the laboratory but they do hold tremendous promise for allowing mass production of vaccines which are better, safer and more immunogenic than the existing vaccines. Vaccines which are on the verge of being mass produced after clinical trials include ones for malaria, dengue, HIV, a new TB vaccine and vaccine for Alzheimer's disease.

Suggested reading:

1. Parthasarathy A, Duraisamy R. Newer vaccine delivery systems: Newer technologies for vaccine delivery. Immunization in clinical practise. Editors: Navin Thacker, Nitin K Shah; Jaypee brothers; 264-270
2. Anil Kr Dutta, Tapan Kr Ghosh. Newrer vaccine delivery system. Controversies answered: A monograph on vaccinology. Editors: Tapan Kr Ghosh, Ritabrata Kundu, Nupur Ganguly, Monjori Mitra, Jaydeep Choudhury, Kheya Ghosh Uttam. An IAP Infectious Diseases Chapter Publication; 120-124
3. Yewale Vijay N, Choudhury Jaydeep, Agarwal Rohit. Newer technologies and vaccine delivery systems: Vaccines at doorstep and in pipeline. Editor: Tapan Kr Ghosh. An IAP Infectious Disease Chapter Publication, 149-169
4. Vashistha Vipin M, Kalra Ajay, Kumar Arun, Sharma Sangeeta; Vaccines in the pipeline; FAQs on vaccines and Immunization practices; Jaypee, 317-342

Paediatric Burns

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Children, particularly when unattended are most likely to sustain burn injuries at home, especially in the kitchen and bathroom. Commonly seen burns in children are due to hot liquids (water, tea, beverages). Children's skin is much thinner than that of the adults and therefore more susceptible to deep burns.

Burns are classified into First degree, Second degree and Third degree burns according to the depth of burn.

First degree burns, also called Epidermal burns involves only the epidermis, is red, painful and heals quickly (5-7 days) with minimal wound care and symptomatic treatment.

Second degree burns, also called Partial Thickness burns is further divided into superficial and deep dermal burns depending on the depth of the burnt dermis. Superficial dermal burns involves only the superficial part of the dermis and is characterised by blisters, pain, pink blister base, normal capillary refill and spontaneous healing within 2 weeks. Deep dermal burns involves the deeper part of the dermis and is characterised by loss of capillary refill, reduced sensation, botchy red blister base and may take 3-4 weeks to heal or may require skin grafting.

Third degree burns, also known as Full-thickness burns involves the epidermis and full dermis and is characterised by white / yellow / gray / waxy / charred / dry appearance, thrombosed veins, no capillary refill and no sensation.

Flame burns occurring in a closed space may also cause acute Inhalational Injury characterised by hypoxia, upper airway obstruction (oropharyngeal edema) and lower airway injury (Pulmonary edema/ tracheobronchitis) due to inhalation of Carbon monoxide, smoke and products of combustion of noxious gases. Inhalation injury is the most important factor contributing to burn morbidity and mortality(30-40%) and should be suspected if there is history of burns in closed space, facial burns and the child presents with carbonaceous sputum, stridor and wheezing.

Criteria for hospital admission

1. Partial thickness burns greater than 10% TBSA (Total Body Surface Area).
2. Full thickness burns greater than 2% TBSA.
3. Inhalation injury.
4. Burns of face, hands, perineum or feet.
5. All electric burns.
6. Suspected child abuse or neglect.
7. Age less than 3 years.
8. Pre-existing medical problems.

Assessment of extent of burns:

No treatment of burns can be complete without the accurate assessment of the extent of the burnt area as it is the most important factor in planning fluid therapy and surgical intervention.

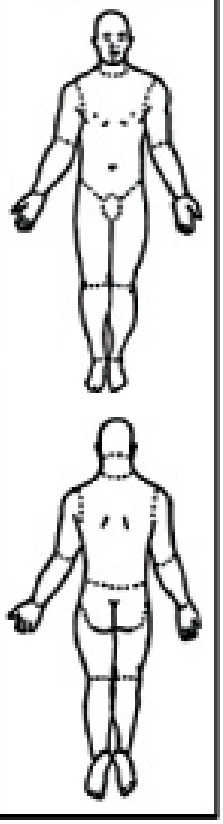
The "Wallace Rule of Nine" cannot be used for burn size estimation because in children, the size of the head is larger as compared to the lower limbs. As the age advances, the proportion keeps changing till 12 years of age. Therefore, modified Lund-Browder chart gives a more accurate estimate of burn size in children.

For burns less than 10% TBSA, the child's own handprint represents 1% of his/her TBSA.

Modified Lund-Browder Chart

Area	Birth to 1 year	1 to 4 years	5 to 9 years	10 to 14 years	15 years	Adult	2nd*	3rd*	TBSA
Head	19	17	13	11	9	7			
Neck	2	2	2	2	2	2			
Anterior trunk	13	13	13	13	13	13			
Posterior trunk	13	13	13	13	13	13			
Right buttock	2.5	2.5	2.5	2.5	2.5	2.5			
Left buttock	2.5	2.5	2.5	2.5	2.5	2.5			
Genitalia	1	1	1	1	1	1			
Right upper arm	4	4	4	4	4	4			
Left upper arm	4	4	4	4	4	4			
Right lower arm	3	3	3	3	3	3			
Left lower arm	3	3	3	3	3	3			
Right hand	2.5	2.5	2.5	2.5	2.5	2.5			
Left hand	2.5	2.5	2.5	2.5	2.5	2.5			
Right thigh	5.5	6.5	8	8.5	9	9.5			
Left thigh	5.5	6.5	8	8.5	9	9.5			
Right leg	5	5	5.5	6	6.5	7			
Left leg	5	5	5.5	6	6.5	7			
Right foot	3.5	3.5	3.5	3.5	3.5	3.5			
Left foot	3.5	3.5	3.5	3.5	3.5	3.5			
						Total:			

Burn diagram



*—Second-degree burns are now more often designated as superficial partial-thickness or deep partial-thickness burns, and third-degree burns are designated as full-thickness burns.

Management of paediatric burns

History should be directed at finding the time of burn, mode of burn, who saw it, what was done immediately, length of cooling and to rule out child abuse.

Primary survey

Airway: if hoarse voice, stridor, cough, carbonaceous sputum…early intubation.
Breathing: rule out carbon monoxide poisoning…give 100% Oxygen.
Circulation: if shock is present, look for alternative cause.

Acute treatment of burns

1. Record vital signs, temperature and bodyweight.
2. Remove child's clothing and any constricting jewellery.
3. Secure IV line, start Ringer Lactate.
4. Estimate burn size/depth.
5. Calculate IV fluid requirement.
6. Insert Foley's catheter.
7. If burns greater than 20% TBSA, insert a nasogastric tube.
8. Tetanus immunization.
9. Cool the burn with tap water or normal saline for 20 minutes. (No ice/ice water).
10. Analgesia- opiates/morphine/fentanyl.
11. Occlusive dressing.
12. Fasciotomies/Escharotomies if compartment syndrome of extremities exists.
13. ECG monitoring if high voltage electric injury, ventricular arrhythmia, cardiac arrest
14. Osmotic diuresis (Mannitol),urine alkalinisation if myoglobinuria present
15. In chemical burns, wound irrigation with water for 20-30 mts(1 hr for alkali)
16. Alkali burn to eye: continuous irrigation for 8 hours.
17. Avoid use of steroids.
18. Inhalation injury: early intubation, ventilator support with PEEP, pulmonary toilet, antibiotic therapy to cover Staphylococcus aureus and Gram negative organisms.

Complete secondary survey to rule out concomitant injuries

Calculation of fluid requirement (Parkland formula)

First 24 hours: **Ringer Lactate = 4ml / kg/ % TBSA burn**

50% during 1st 8 hours from time of burn, 25% during 2nd 8 hours, 25% during 3rd 8 hours.

Second 24 hours: **DNS (with 20mEq KCl/L) = (35+%TBSA) x TBSA / hr**

Colloid (FFP or 5% Human Albumin) may be started if response is not satisfactory.

Fluid resuscitation is considered adequate if **urine output of 1-2 ml/kg/hr** is achieved; serum electrolytes, albumin, glucose, urea, creatinine, hematocrit and ABG remain within normal limits.

Initial Wound care is done by cleaning the burn wound with bland soap water (savlon), removing all dirt, devitalised tissue and loose skin. Blisters are debrided unless smaller than 1-2 cms. Shave the burns of scalp. After cleaning, apply a topical antibacterial agent and a bulky dressing. Commonly used agents are Silver Sulfadiazine, Silver Nitrate, Bacitracin and Mafenide. Silver Sulfadiazine 1% has a broad antimicrobial activity against gram-negative, gram-positive bacteria and yeast with moderate eschar penetration. It is contraindicated in premature and new borns, G6PD deficiency and patients sensitive to

sulfa drugs. Silver Nitrate 0.5% has broad-spectum bacteriostatic activity with poor eschar penetration, and may cause hyponatremia/ hypochloremia. Bacitracin has predominant activity against gram-positive bacteria and is useful for superficial burns and for facial burns. Mafenide has excellent activity against Pseudomonas aeruginosa and excellent eschar penetration.

Subsequent wound care is done by dressing the burn wound once or twice a day, and sending regular wound cultures. Burn wounds usually are colonized by gram positive bacteria in the first one week after burns, thereafter the spectrum changes over to gram negative or the bacterial strains predominant in the hospital. Antibiotics are added as per the culture reports or guided by the prevalent hospital strains. Wounds may be subjected to early Tangential excision or may be taken up for skin grafting once they are graftable. Joints of the extremities should be splinted and mobilised by a physiotherapist to prevent joint contractures. Pillows should be avoided and cervical collar used round the clock to prevent neck contractures.

Nutritional support is crucial in the care of burned child as burn is a catabolic state, and every effort should be made to institute early oral/enteral feeds. The estimated calorie requirement for a child is: 35Kcal/Kg body weight + 60 Kcal/ % TBSA burn. Protein requirement is increased 2-4 times normal. It is important to supplement vitamin A, B, C, K, Folate, zinc, chromium, magnesium, calcium and phosphorus. Parenteral nutrition should be reserved for patients whose calorie and protein requirements cannot be met by oral and enteral routes.

Late complications like hypertrophic scarring and contractures have an increased incidence after deeper burns and commonly occur over joints, eyelids, neck, lips and axilla. These can be prevented by proper positioning, splinting, range of motion exercises, coconut oil massages , silicone sheets and custom-made pressure (>25mmHg) garments. Any surgical correction of contractures should wait until the scar matures (6-12 months).

References:

1. Sherrell J. Aston, Robert W. Beasly, Charles H.M. Thorne (ed.) Grabb and Smith's Plastic Surgery(5th ed.).Philadelphia: Lippincott-Raven, 1997.
2. Robert E. Condon, Lloyd M. Nyhus (ed.) Manual of Surgical Therapeutics (9th ed.). Boston:Little,Brown,1996

"Competency Based Curriculum On Safer Intravenous Infusions - Need For Research"

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INTRODUCTION

The history of intravenous (IV) therapy dates back to the Middle ages. The first experiments with IV injections were carried out in the 1600s using quills and bladders of animals as instruments.1During the cholera epidemic of 1831-1832, Dr. Thomas Latta pioneered the use of IV saline infusion.[2] In the 20th century, 2 world wars established a role for IV therapy as routine medical practice.[3,5]

Intravenous (IV) therapy has seen a major revolution in the last 50 years as a result of very strong technological development in the health industry.[5] Thus, the placement of a peripheral intravenous (PIV) catheter became one of the most common invasive procedures in current clinical practice.[6] It is estimated that a PIV catheter is placed in 80% of all patients admitted to hospitals.[7]

It is commonly accepted that the administration of intravenous therapy by peripheral route is the safest and provides the best cost-benefit ratio when compared with the central lines, usually used when the patient's hemo-dynamic status is severely compromised or when peripheral access no longer exists.[8]

A number of complications including phlebitis, thrombophlebitis, infiltration, extravasation, and infections are associated with IV therapy.

Studies have determined that, depending on the definition, medical-surgical patients overall develop infusion-related phlebitis at rates ranging from 2.5% to 70%.[9,10] Karadag and Gorgulu[11] with 36.8%, Maki and Ringer[12] with 41.8%. In India, incidence of phlebitis was 56.5% and 29.8% which occurred in the same setting.[13,14] However, CDC and INS recommendations revealed that the accepted phlebitis rate is 5% or less.

Despite the range of phlebitis rates associated bacteremia remain very low at < 0.2%.[15,16],it may lead to very serious life threatening complications. Haley et al[17] estimated that a primary bacteremia adds 7.4 days to the average hospital stay.

Palefski SS reported that Incidence of infiltration 7.5% and 13.9% among the VAD inserted by infusion nurses and generalist nurses respectively.[18] In India, Incidence of infiltration was found to be 31.5% which quiet higher than any published reports. [13] The incidence of infiltration and extravasation is hard to determine because of limited reporting.[19] Extravasation injury from cancer chemotherapy is reported to be 11% in children and 22% in adults.[20] The incidence of peripheral vein extravasation has been reported to range from 0.1% to 6.5%[21].

Infiltration - the inadvertent leakage of a nonvesicant solution into surrounding tissue-and extravasation-the inadvertent leakage of a vesicant solution into surrounding tissue[22] are both known risks of intravenous (IV) therapy.[19] While the injury is usually minor and resolves

spontaneously,[23] some cases result in serious complications, including full-thickness skin loss and muscle and tendon necrosis requiring reconstructive surgery or even amputation, leading to longer hospital stays, increased morbidity,[24] and increased costs.[25,26]

Infiltration and extravasation can be caused by mechanical, physiologic, or pharmacologic factors. Mechanical factors, occurring either during initial catheter insertion or while the catheter is in place,[19,27] and physiologic factors relating to preexisting or emerging vein problems,[30,31] can be contributing factors.[28,32]

Factors contributing to the risk for infiltration and extravasation are mechanical factors (small size and poor condition of veins[27], larger catheter size relative to vein size[19], choice of site (eg. Areas of joint flexion, dominant hand)[19], unstable catheter[19], poor securing of implanted port access needle[28], patient activity[19], multiple venipuncture sites (eg, a second puncture above the first) [19], use of an infusion pump or power injector during the infiltration or extravasation event[19], catheter port separation or catheter fracture[29]), physiologic factors (clot formation above the cannulation site[19], thrombus or fibrin sheath at the catheter tip[27], lymphedema[27]), and pharmacologic factors (pH, osmolarity, vasoconstrictive potential, cytotoxicity). According to the Infusion Nursing Standards of Practice, an extravasation injury should be considered a sentinel event and should be documented.[22]

Apart from the sepsis and pain from the infiltration and phlebitis related to peripheral intravenous cannulae, they also cause increased morbidity and mortality rates, increased length of hospitalization, increased staff workload and increased financial burden on the patients.

However, Management of infiltration and extravasation lacks evidence-based standardization, and many institutions do not have adequate policies and procedures in place. While such injuries may be minimized or prevented through adherence to standards of practice and evidence-based treatment, further study is needed to address unresolved questions and controversies surrounding extravasation management and ways to broaden clinicians' awareness of the treatment options.[33]

The wide variation in incidence rates of phlebitis may be attributed to measurement error, observational biases, limited samples, using wide variety of tools, retrospective and lack of control. In fact, published reports may be underestimating the true incidences of phlebitis, infilteration, and extravasation in clinical set up. Clinical audit revealed that research nurses by observation identified more cases of phlebitis and infiltration than recorded in charts.[34]

Poor practices in documentation add difficulty in estimating true incidence of phlebitis, infiltration and extravasation in actual clinical situation. The clinical audit found that just over half of the catheters & IV sets had no date labeled in the dressing, serious flaws regarding the catheter's insertion site protection, stabilization methods and the use of unsterile material.[35] Underestimating of the incidences of phlebitis, infiltration and extravasation poses greater threat as magnitude of the problem goes unnoticed.

Because of errors associated with IV administration can result in fatal or life-threatening outcomes, administration of IV fluids and medications can be high-risk, with adverse outcomes potentially leading to malpractice claims.[36]

Given the many complications that can arise from peripheral intravenous cannulation, and IV therapy, ensuring that nurses performing the procedure are competent is paramount.[37]

NEED FOR THE STUDY AND RELATED LITEARTURE

Nurses are at the forefront in providing IV therapy; their knowledge and skill can minimize infusion-related complications and affect patient safety, satisfaction, health care costs, and length of hospital stay.[4]

The rapidly advancing technologies relating to devices, modalities of access, and types of infusates require that a nurse maintain a highly developed knowledge base to administer infusion therapy competently.[18]

Although, length of catheter in situ, catheter over joints, infusion of antibiotics, solution of high osmality & low pH increase the risk of phlebitis. The role of factors such as age, sex, size & type of catheter, skin preparation and dressing material in the development of phlebitis remain controversial. The published studies reported varying results.

Saini R repoted that Around 85% of the cannulae inserted by the staff nurses developed infiltration and phlebitis as compared to 15% of cannulae inserted by the nursing student, the relationship was found statistically significant (p=0.532).This study revealed inappropriate aseptic technique during insertion and handling of cannulae, placement of cannulae of forearm, involvement of the elbow joint, presence of soiled securement device, placement of cannula more than 2 days, use of IV infusion sets for more than 24 hours.[13]

A questionnaire survey revealed that knowledge of risk factors of infusion phlebitis is incomplete even among experienced nurses in Swedish and the study suggested that change of habits and knowledge of new risk factors could reduce the risk of infusion phlebitis.[38] It has been shown that the skills of the staff, who insert and maintain the PIVs, are of importance for the incidence of phlebitis.[39],40Obviously, the educational level on risk factors of infusion phlebitis was not up to date. It has been shown that manual skill of the staff and good routines decrease the risk of phlebitis.[39,40]

The skill of the infusion nurse in placing the VAD resulted in a lower leakage rate, a lower infiltration rate, a lower phlebitis rate, and longer device dwell time.[18] The resultant increase in quality of care and decrease in patient morbidity correspond to decreased healthcare costs.[41, 42]

Proper documentation, surveillance, and expert skills in early identification of these complications would assist in proper reporting of cases and subsequent treatment. Ahlgvist M reported that only 46.2 % records contain the data regarding insertion site, hand side and lumen size of PVC, extent of PVC documentation in medical records was very low and suggested that education of nurses on proper PVC documentation should be given priority.[43]

Peripheral infusion devices placed by infusion nurses exhibited significantly lower rate of leakage (6.4% Vs 15.3%), phlebitis and infiltration(7.5% Vs 13.9%) than generalist nurses. VAD inserted by infusion nurses were in the vein for significantly longer periods (2.2 days Vs 2 days) than those of generalist nurses. Perhaps the most plausible explanation for the observed difference in complication rates between infusion nurses and generalist nurses was a difference in skill level, although skill was not directly assessed. If higher skill

level is to hold as the most plausible explanation for the infusion nurse group's reduced complication rates, then specific skills and practices must be enumerable.[18]

All nursing staff and physicians need to be educated about the guidelines for the management of peripheral catheters. In addition, proof of IV competency should be required for nurses' entrance into and continuation in clinical practice. Therefore, the development of a competency-based evaluation tool is needed to assist in providing a comprehensive infusion therapy program, similar to the Infusion Nurses Society Competency Validation Program in the United States. [44]

In India, Nurses practice related to intravenous therapy largely depend up on personal experience, knowledge gained during basic nursing program, and day to day practice. They are seldom exposed to any form Continuing Education Program. Intravenous cannulaton skills are primarily acquired by an apprentice system and the manner by which intravenous cannulations are subsequently placed, may be governed by the habits formed early in training. Current practices are not supported by evidenced based guidelines. Saini reported that Hand washing was not practiced in any case of peripheral intravenous cannula insertion and subsequently while handling the peripheral intravenous cannula. These findings revealed that lack of motivation and casual attitude among Nurses. Further, no proper documentation system is in place which makes it impossible to estimate incidences and related factors of phlebitis, infiltration and extravasation. To date, No specific curriculum or course is available to update the knowledge and practice of the nurses regarding infusion or intravenous curriculum in India.

Although, IV teams seem to be effective[11] in reducing IV related complications, implementation of such team approach in Indian set up won't be cost effective and feasible, considering direct and indirect costs associated with training, dedicated manpower etc. The best alternative will be training the existing nurses in the field of infusion nursing.

COMPETENCY BASED CURRICULUM

The Joint Commission for Accreditation of health care Organizations requires that clinical competence be assessed for all nursing staff and holds institutional leaders accountable for ensuring that competency of all staff is assessed, maintained, demonstrated, and continually improved (JCAHO, 1999).[45]

The competency based curricular framework incorporates evidence based, theory guided critical thinking and core practice. The familiar traditional behavioral objectives are replaced with "outcome competencies" in each course and module. Real world focus, learner centered, competency based and flexible are the principles of Competency Based Curriculum Design. The assessment of competent practice in the service sector has received considerable attention the past 25 years, the implementation of competency assessment models in nursing education has moved at a much slower pace.[46]

CONCLUSION:

Although there were numerous studies on topic, most of the factors related to complications of IV therapy were not addressed adequately leaving uncertainty among the practitioners. Further, Studies investigating the association of Nurses' competence and complications

related IV therapy were very limited. Hence, most of the risk factors (catheter specific & procedure specific) associated with complications of IV therapy largely depend up on the person knowledge, skill and competence who perform or maintain the cannulation, Unfortunately, to date, no study investigated this burning issue.

Extensive review of literature lead to important questions regarding IV therapy that remains unanswered, inconclusive and controversial.

1. What is the incidence of phlebitis, infiltration and extravasation in Indian Setup?
2. What are the factors predisposing phlebitis, infiltration and extravasation in Indian setup?
3. Are personnel responsible for the initiation and maintenance of IV therapy knowledgeable and competent and do they use this knowledge and competency when tending IV therapy?
4. Do competency based educational programs affect the practice, patient outcome and institutional outcome over a period of time?

Hence, well designed research studies are needed at Indian set-up to address this burning issue. Intravenous therapy related research studies should be given top priority by all funding organizations and professional associations .

BIBLIOGRAPHY

1. Feldmann H. History of Injections. Pictures from the History of Otorhinolaryngology Highlighted by Exhibits of the German History of Medicine Museum in Ingolstadt. Laryngorhinootologie. 2000; 79(4): 239-246.
2. Lewins R. Injection of Saline Solutions in Extraordinary Quantities Into the Veins in Cases of Malignant Cholera. Lancet. 1832; 2: 243-244.
3. Milliam D. The History of Intravenous Therapy. J Intraven Nurs. 1996; 19(1): 5-14.
4. Dychter SS.et al, Intravenous Therapy-A Review of Complications and Economic Considerations of Peripheral access. Journal of Infusion Nursing 2012 35(2)84-91.
5. Panadero A, Lohom G, Taj J, Mackay N, Shorten G. A Dedicated Intravenous Cannula for Postoperative Use Effect on Incidence and Severity of Phlebitis. Anaesthesia. 2002;57:921-925.
6. Weinstein S, ed. Plumer's Principles and Practice of Intravenous Therapy. Philadelphia, PA: Lippincott Williams & Wilkins; 2007.
7. Zingg W, Pitter D. Peripheral Venous Catheters: an Under-Evaluated Problem. Int J Antimicrob Agents. 2009;34:38-42.
8. Giacomo MD. A Stepped Approach to Vascular Access Device Selection. Br. J Nurs. 2010; 19:22-24. .
9. Martinez JA, Piazuelo M, Almela M, et al. Evaluation of Add-on Devices for the Prevention of Phlebitis and Other Complications Associated with the Use of Peripheral Catheters in Hospitalized Adults : A Randomized Controlled Study. J Hosp Infect. 2009; 73: 135-142.
10. Karadag A Gorgulu S. Effect of Two Different Short Peripheral Catheter Materials on Phlebitis Development. J Intraven Nurs. 2000; 23(4): 158-166.

11. Maki D, Ringer M. Risk Factors for Infusion-Related Phlebitis with Small Peripheral Venous Catheters. Ann Intern Med. 1991; 114: 845-854.
12. Uslusoy E, Mete S. Predisposing Factors to Phlebitis in Patients with Peripheral Intravenous Catheters : A Descriptive Study. Am Acad Nurse Pract. 2008; 20: 172-180.
13. Saini R, Agnihotri M. Epidemiology of Infiltration and Phlebitis. Nursing and Midwifery Research Journal. 2011,7(1)22-33.
14. Kaur P,Thakur.R. Assessment of risk factors of phlebitis amongst intravenous cannulated patients. Nursing and Midwifery Research Journal. 2011,7(3)107-114.
15. Gallant P, Schultz AA. Evaluation of A Visual Phlebitis Scale for Determining Appropriate Discontinuation of Peripheral Intravenous Catheters. J Infus Nurs. 2006; 29(6): 338-345.
16. Infusion Nurses Society. Infusion Nursing Standards of Practice. J Infus Nurs. 2011; 34(1s).
17. Haley RW, Schaberg DR, Von Allmen SD, McGowan JE Jr. Estimating the Extra Charges and Prolongation of Hospitalization Due to Nosocomial Infections : A Comparison of Methods. J Infect Dis. 1980; 141: 248-257.
18. Paleski SS, Stoddard GJ.The infusion Nirse and Patient Complication Rates of Peripheral -Short Catheters-A Prospective Evaluation.Journal of Intravenous Nursing.2001.24(2).113-123.
19. Hadaway L. Infiltration and extravasation. AJN.2007.107(8).64-72.
20. Kassner E. Evaluation and treatment of chemotherapy extravasation injuries. J Pediatr Oncol Nurs 2000;17(3):135-48.
21. Sorrel DC. Developing extravasation protocols and monitoring outcomes. Journal of Intravenous Nursing.1998.21(4):232-239.
22. Infusion Therapy Society. Infusion Nursing Standards of Practice. J Infus Nurs. 2006; 29(1)(suppl): s1-s92.
23. Bellin MF, Jakobsen JA, Tomassin I et al. Contrast Medium Extravasation Injury : Guidelines for Prevention and Management. Eur Radiol. 2002; 12(11): 2807-2812.
24. Upton J, Mulliken JB, Murray JE. Major Intravenous Extravasation Injuries. Am J Surg. 1979; 137(4): 497-506.
25. Diehl-Svrjeek BC, Dawson B, Duncan LL. Infusion Nursing : Aspects of Practice Liability. J Infus Nurs. 2007; 30(5): 274-279.
26. Liau DW. Injuries and Liability Related to Peripheral Catheters : A Closed Claims Analysis. Newsl Am Soc Anesthesiol. 2006; 70(6).
27. Goolsby TV, Lombardo FA, Extraavasation of Chemotherapeutic Agents : Prevention and Treatment. Semin Oncol. 2006; 33(1): 139-143.
28. Schulmeister L, Camp-Sorrell D. Chemotherapy Extravasation from Implanted Ports. Oncol Nurs Forum. 2000; 27(3): 531-538.
29. Sauerland C, Engelking C, Wickham R, Corbi D. Vesicant Extravasation, I : Mechanisms, Pathogenesis, and Nursing Care to Reduce Risk. Oncol Nurs Forum. 2006; 33(6): 1134-1141.

30. Rudolph R, Larson DL. Etiology and Treatment of Chemotherapeutic Agent Extravasation Injuries : A Review. J Clin Oncol. 1987; 5(7): 1116-1126.
31. Ignoffo RJ, Friedman MA. Therapy of Local Toxicities Caused by Extravasation of Cancer Chemotherapeutic Drugs. Cancer Treat Rev. 1980; 7(1): 17-27.
32. Haynes S. Infusion Phlebitis and Extravasation. Prof Nurse. 1989; 5(3): 160-161.
33. Doeliman D,Hadaway L. Infiltration and Extravasation. .Journal of Infusion Nursing.2009.32(4).203-211
34. Groll D. Davis B. Evaluation of the psychometric Properties of the phlebitis and Infiltration Scales for the assessment of Complications of Peripheral Vascular Access Devices. Journal of Infusion Nursing.2010.33(6).385-390.
35. de Rego Fertado LC.m. Maintenance of Peripheral Venous Access and Its Impact on the Development of Phlebitis: A Survey of 186 Catheters in a General Surgery Department in Portugal. Journal of Infusion Nursing.2011.34(6).382-390.
36. Diehl-Scrjcek BC, Dawson B, Duncan LL. Infusion Nursing : Aspects of Practice Liability. J Infus Nurs. 2007; 30(5): 274-279
37. Ung L, Cook S, Edwards.B Peripheral Intravenous Cannulations in Nursing-Performance Predictors. Journal of Infusion Nursing.2002.25(3).189-195.
38. Lanbeck P,Odenholt I. Perception of Risk Factors for Infusion Phlebitis Among Swedish Nurses.Aquestionnaire Survey. Journal of Infusion Nursing.2004.27(1).25-30.
39. Tomford JW, Hershey CO, Mc Laren CE, Porter DK, Cohen DI. Intravenous Therapy Team and Peripheral Venous Catheter Associated Complications. Arch Interm. Med. 1984; 144: 1191-1194.
40. Lundgren A, Wahren LK. Effect of Education on Evidence-Based Care and Handling of Peripheral Intravenous Lines. J Clin Nurs. 1998; 8(5): 577-585.
41. Miller JM, Goetz AM, Squier C, Muder RR. Reduction in Nosocomial Intravenous Device-Related Bacteremias After Institution of an Intravenous Therapy Team. J Intraven Nurs. 1996; 19: 103-106.
42. Meier PA, Fredrickson M, Catney M, Nettleman MD. Impact of a Dedicated Intravenous Therapy Team on Nosocomial Bloodstream Infection Rates. Am J Infect Control. 1998; 26: 388-392.
43. Ahlqvist, M., Berglund, B., Wirén, M., Klang, B. and Johansson, E. (2009), Accuracy in documentation – a study of peripheral venous catheters. Journal of Clinical Nursing, 18: 1945–1952. doi: 10.1111/j.1365-2702.2008.02778.x)
44. Lopez V, Molassiotis A. An Intervention Study to Evaluate Nursing Management of Peripheral Intra Vascular Devices. J Infus Nurs. 2004; 27(5): 322-325.
45. Joint Commission on Accreditation of health care Organizations.(1999).Comprehensive Accreditation Manual for hospitals:The official handbook.Oak Park:Authour.
46. Redman RW. Competency Assessment: Methods for Development and Implementation in Nursing Education.The online Journal of Issues in Nursing.1999.4(2).

Thalidomide in Tubercular meningitis- how effective is it

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Tuberculosis of the central nervous system (CNS) is the most serious complication in children and is fatal without prompt and appropriate treatment. Tubercular meningitis complicates about 0.3 % of untreated tubercular infections in children. It usually arises from the formation of a metastatic caseous lesion in the cerebral cortex or meninges that develops during the lymphohematogenous dissemination of the primary infection. This initial lesion increases in size and discharges small numbers of tubercle bacilli into the subarachnoid space. The resulting gelatinous exudate infiltrates the corticomeningeal blood vessels, producing inflammation, obstruction, and subsequent infarction of cerebral cortex. The brain stem is the site of greatest involvement. The exudate also interferes with the normal flow of cerebrospinal fluid (CSF) in and out of the ventricular system at the level of the basilar cisterns, leading to a communicating hydrocephalus. The combination of vasculitis, infarction, cerebral edema, and hydrocephalus results in severe brain damage[1].

Tubercular meningitis has been classified into stages 1,2 and 3 and the prognosis is worse as the disease progresses. In addition to the innate virulence of the organism, the host immune response to the bacilli also plays a major role in the pathogenesis of the disease.

Tubercule bacilli have the capacity to invade and multiply within macrophages. Within the CNS, microglialcells are the resident macrophages, and they are the principal target in the CNS. The cytokine tumor necrosis factor alpha (TNF) is critical in the neuropathogenesis of M. Tuberculosis.Although TNF-α plays a definitive role in granuloma formationand containment of mycobacterial infections, localCNS production of TNF-α in experimental bacterial meningitisleads to altered blood-brain barrier (BBB) permeability andcerebrospinal fluid (CSF) leukocytosis and hasbeen implicated in fostering the progression of TBM in amurine model [2].

The treatment of tubercular meningitis is dependent on standard anti tubercular medications as well as medications against the inflammatory changes. Improvement of status does not improve only after anti tubercular medications despite reductions in bacillary load. It has been observed that after initiation of therapy, patients often progress to severe neurologic signs and death. This may be due to antibiotic killing of mycobacteria and release of cell wall products which further increase the inflammation in the CNS, resulting in damage of the vessels accompanied by infarcts, brain edema, and necrosis[3]. For this reason, standard anti-TB therapy usually includes Glucocorticoids as adjunctive anti-inflammatory medication. Glucocorticoidsdiminish transcription of proinflammatory cytokines and chemokines, diminish adhesion molecules expression, diminish cell recruitment, activation and proliferation, decrease CSF matrix metalloproteinase 9 concentrations[4], diminish local inflammation, reduce swelling and congestion of the meninges and ICP, CNS edema and CSF outflow resistance, diminish synthesis of lipolytic and proteolytic enzymes, promote blood brain barrier repair[5]. However, the use of corticosteroids has been associated with

its own share of complications. Concerns have remained that their use might worsen outcome in CNS-TB because of failure of immune response against the organism. Some have also suggested that the reduced inflammation achieved by corticosteroid treatment, could reduce the ability of drugs to seep into the subarachnoid space[3].

In these circumstances some have reported usage of the anti-inflammatory medication Thalidomide in CNS tuberculosis. This article will try to review some of the literature on the use of Thalidomide in CNS tuberculosis.

TNF-α plays an important role in the development of protective responses against tuberculosis. it induces a cascade of cellular responses in monocytes,macrophages,polymo rphonuclear cells and other cells.It plays a role in formation and maintenance of granuloma which helps to seal off the bacilli. It also helps in activation of the macrophages. Besides these it has also been implicated in the development of cachexia in tubercular infected patients[6].

The immunomodulatory effects of thalidomide were first recognized when it was incidentally shown to heal the inflammatory skin lesions of erythema nodosumleprosum in patients with leprosy on being used as an analgesic. This was probably due to the reduction in TNF-α circulating levels, mediated by thalidomide[7].

In the CNS, TNF-α triggers the release of other cytokines, influences transport of compounds into the brain by ‘‘opening’’ the blood-brain barrier, correlates with increased levels of inter- leukin (IL)-6 and protein, as well as low glucose levels. In addition, TNF-α and IL-1b levels are associated with prolonged fever, seizures, spasticity, and death. Moreover, TNF-α affects vascular endothelium by inducing procoagulant activity, formation of thrombi, and production of nitric oxide synthase, thus causing endarteritis. Occlusions of large or small vessels are the most common reason for cranial nerve palsies, hemiparesis, and paralysis[8].

The first experiments involving Thalidomide was carried out during 1997-98. Experimentsperformed on rabbit model of acute mycobacterial CNS infection showed that inoculation oflive Mycobacterium bovis Ravenel (MbR) intracisternally induced leukocytosis, high proteinlevels, and release of TNF-α into the CSF within 1 day. Histologically,there was severe meningitis with thickening of leptomeninges, vasculitis and encephalitis and mortality was 75%by day 8.In animals treated with anti-TB antibiotics only,inflammation and lesions of brain persisteddespite a decrease in mycobacteria; 50%of the rabbits died. When thalidomide treatmentwas combined with antibiotics, a marked reductionin TNF-α levels, leukocytosis and brainpathology was verified. With this treatment,100% of the infected rabbits survived, suggestinga role of TNF-α in the pathogenesis of TBM andthe potential clinical use for thalidomide in thissetting[9,10]

The same authors also examined whether combining antituberculous drugs with a new thalidomide analog, immunomodulatory drug 3 (IMiD3), would be effective in reducing morbidity and mortality in an experimental rabbit model of TBM. Intracisternal inoculation of Mycobacterium bovis Ravenel in rabbits induced progressive subacute meningitis characterized by high cerebrospinal fluid (CSF) leukocytosis, protein influx, release of tumor necrosis factor (TNF), substantial meningeal inflammation, and mortality by day

28. Treatment with antituberculous drugs or with antituberculous drugs plus thalidomide improved the clinical course of disease somewhat and increased survival to about 50%. In contrast, treatment with antituberculous drugs in combination with IMiD3 limited pathological neurologic changes and resulted in marked improvement (73%) in survival. IMiD3 treatment was also associated with reduced leukocytosis in the CSF and significantly lower levels of TNF in CSF and plasma. Histologically, the meningeal inflammation in animals treated with antituberculous drugs plus IMiD3 was considerably attenuated compared to that of the other treatment groups. These results suggest a potential role for IMiD3 in the management of TBM in patients[11].

Subsequently,a clinical study to determine the safety and tolerability of thalidomide as adjunct therapy in children with tuberculous meningitis was carried out. Children with stage 2 tuberculous meningitis received oral thalidomide for 28 days in a dose-escalating study, in addition to standard four-drug antituberculosis therapy, corticosteroids, and specific treatment of complications such as raised intracranial pressure. Clinical and laboratory evaluations were carried out. Fifteen patients (median age, 34 months) were enrolled. Thalidomide was administered via nasogastric tube in a dosage of 6 mg/kg/day, 12 mg/kg/day, or 24 mg/kg/day. The only adverse events possibly related to the study drug were transient skin rashes in two patients. Levels of tumor necrosis factor-alpha in the cerebrospinal fluid decreased markedly during thalidomide therapy. Clinical outcome and neurologic imaging showed greater improvement than that experienced with historical controls. Thalidomide appeared safe and well tolerated in children with stage 2 tuberculous meningitis[12].

The same authors did a double-blind randomized controlledtrial which enrolled 47 children with stage 2 or 3 TBM, using thalidomide (24mg/kg/day orally), as adjunctive therapy to anti-TB drugs and steroids, vs placebo,which was publishedin 2004. The study was terminated early because all adverse events (worse motor functionat 1 month and two deaths) occurred in the thalidomide treatment arm. These results do notsupport the use of adjunctive high-dose thalidomidetherapy in the treatment of TBM[13].

In 2003 Roberts Mt et al presented two cases of TBM in adults complicated by focal neurological deficitswhich showed disease progression on steroids. In case 1 an MRI demonstrated multiple ring-enhancinglesions compressing the optic chiasm,leading to bitemporal hemianopsia. After introductionof thalidomide the patient showedprogressive improvement, demonstrated by bothMRI imaging and the resolution of hemianopsia.In case 2, two months into anti-TB treatmentwith steroids, the patient developed fluctuatingright sided paralysis with the MRI demonstratinga large ring-enhancing mass encasing the left internalcarotid and middle cerebral arteries.Thalidomide was introduced as an immunomodulatoryadjunct and subsequently the patient made a complete neurological recovery[14].

Schoeman et al described three children withgiant TB abscess, and a fourth with chronicbasal arachnoiditis with progressive loss of vision.Three of the four patients had relentlessneurologic deterioration, and all showed diseaseprogression on neuroimaging despite full medicaland appropriate surgical treatment. Markedclinical and neuroradiologic improvement occurredafter thalidomide was added to the anti-TB treatment regimen of

these four patients. So,the Authors suggested that adjunctive thalidomidemight have some role in the management of intractable intracranial TB, but it needs further investigations [15].

They also described a 7-year-old child, on maintenance chemotherapy for acute lymphoblastic leukemia who developed TBM complicated by progressive basal meningeal inflammation and abscess formation, in spite of adequate TB treatment and adjunctive corticosteroid therapy. The child became blind as a result of involvement of the optic chiasm. After 2 months of adjunctive thalidomide therapy, the child regained vision and cranial MRI showed marked reduction of the inflammatory changes previously demonstrated. This case suggests a role for thalidomide in the treatment of blindness due to involvement of the optic chiasm in progressive basal TBM[16].

The main adverse effect of thalidomide has been the development of a peripheral sensory neuropathy leading to some loss of fine touch in the fingers, improved by discontinuing thalido- mide. Patients treated with thalidomide and low dose corticosteroids do not experience relapsing inflammation, in contrast to patients treated with prednisolone as the sole immunosuppressant[3].

Use of thalidomide as a standard therapy for tuberculosis is not yet conclusive because of varied reports. However, it has been shown to be an effective adjuvant for TB patients complicated with severe inflammatory reaction or wasting conditions.

The British infection society guidelines recommend that all patients with TBM receive adjunctive corticosteroids regardless of disease severity at presentation. According to theses guidelines thalidomide should not be used for the routine treatment of TBM , but may be helpful in patients with tuberculomas that are not responding to anti-tuberculosis drugs and high dose corticosteroids [17].

Therefore, thalidomide should not be used for the routine treatment of TBM, but it may be helpful as a “salvage therapy” in patients with tuberculomas not-responding or poor-responding to anti-TB drugs and high dose corticosteroids. However, there is need of a well designed study to answer the questions that are yet unanswered regarding its use in CNS tuberculosis.

1. Mycobacterial infections. Jeffrey R. Starke, F. Munoz. Nelsons textbook of Pediatrics.19thed.

2. Central Nervous System Tuberculosis:Pathogenesis and Clinical Aspects.Clin. Microbiol. Rev. 2008, 21(2):243. DOI: Molitor and Phillip K. Peterson,R. Bryan Rock, Michael Olin, Cristina A. Baker, Thomas W.

3. Management of central nervous system tuberculosis in children: light and shade.D.Buonsenso,D.Serranti,P.Valentini. European Review for Medical and Pharmacological Sciences. 2010; 14: 845-853.

4. Dexamethasone, cerebrospinal fluid matrix metalloproteinase concentrations and clinical outcomes in tuberculous meningitis.Green JA, Tran CT, Farrar JJ, Nguyen MT, Nguyen PH, et al. PLoSONE 2009; 4: e7277

5. COYLE PK. Glucocorticoids in Central Nervous System bacterial infection. Arch Neurol 1999; 56:796-801

6. Thalidomide as an Anti-TNF-a Inhibitor: Implications for Clinical Use.JEFFREY D. KLAUSNER, VICTORIA H. FREEDMAN, AND GILLA KAPLAN.Clinical Immunology and immunopathology . Vol. 81, No. 3, December, pp. 219–223, 1996.Article No. 0181.

7. The influence of thalidomide on the clinical and immunological manifestation of erythema nodosumleprosum AMPAIO EP, KAPLAN G, MIRANDA A, NERY JA, MIGUEL CP, VIANA SM, SARNO EN. J Infect Dis 1993; 168: 408-414

8. SENOVA L, BERGTOLD A, FREEDMAN VH, YOUNG RA, KAPLAN G. Tumor necrosis factor a is a determinant of pathogenesis and disease progression in mycobacterial infection in the central nervous system. ProcNatlAcadSci 1999; 96: 5657-5662

9. Effect of cytokine modulation by thalidomide on the granulomatous response in murine tuberculosis.Moreira AL, Tsenova-Berkova L, Wang J, Laochumroonvorapong P, Freeman S , Freedman VH, Kaplan G.Tuber Lung Dis. 1997;78(1):47-55.

10. A combination of thalidomide plus antibiotics protects rabbits from mycobacterial meningitis-associated death.Tsenova L, Sokol K, Freedman VH, Kaplan G.Infect Dis. 1998 Jun; 177(6):1563-72.

11. Use of IMiD3, a thalidomide analog, as an adjunct to therapy for experimental tuberculous meningitis.Tsenova L, Mangaliso B, Muller G, Chen Y, Freedman VH, Stirling D, Kaplan G.Antimicrob Agents Chemother 2002 Jul;46(7):2313.

12. Adjunctive thalidomide therapy of childhood tuberculous meningitis: possible anti-inflammatory role. Schoeman JF, Springer P, Ravenscroft A, Donald PR, Bekker LG, van Rensburg AJ, Hanekom WA, Haslett PA, Kaplan G.J Child Neurol. 2000 Aug;15(8):497-503

13. Adjunctive thalidomide therapy for childhood tuberculous meningitis: results of a randomized study.Schoeman JF, Springer P, van Rensburg AJ, Swanevelder S, Hanekom WA, Haslett PA, Kaplan G.J Child Neurol. 2004 Apr;19(4):250-7.

14. The use of thalidomide in the treatment of intracranial tuberculomas in adults: two case reports.Roberts MT, Mendelson M, Meyer P, Carmichael A, Lever AM.J Infect. 2003 Oct;47(3):251-5

15. Intractable intracranial tuberculous infection responsive to thalidomide: report of four cases. Schoeman JF, Fieggen G, Seller N, Mendelson M, Hartzenberg B.J Child Neurol. 2006 Apr;21(4): 301-8.

16. Recovery of vision after adjuvant thalidomide in a child with tuberculous meningitis and acute lym- phoblasticleukemia.STEFAN DC, ANDRONIKOU S, FREEMAN N, SCHOEMAN J.. J Child Neurol 2009; 24: 166-169.

17. British Infection Society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. Guy Thwaites,Martin Fisher ,Cheryl Hemingway,Geoff Scott, Tom Solomon, John Innes. Journal of Infection (2009) 59,167e187.

Management of Head injury in infant, Children and adolescent

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Introduction

Traumatic brain injury in children is prevalent universally with potentially poor out comes. Domestic accidents, motor vehicle accidents, recreational injuries and sports mishaps are the common causes; however child abuse must be kept in mind in children especially in toddlers. The reported mortality in developed countries in hospital setting is 9-35%. The incidence in developing countries is poorly documented,however mortalityis higher in developing counties.

Primary brain injury is the direct result of physical trauma. It may result in uncomplicated concussion with quick recovery and no residual deficit or in serious hemorrhage, contusion or hematomas. Whereas these all are visible on a CT scan, diffuse axonal injury can be a severe condition where the initial CT scan may look deceptively benign.Secondary brain injury may occur after the primary event due to potentially preventable causes like hypoxia, hypoperfusion, hypercarbia, heamatoma etc.

Management

Management of Head injury and controlling of ICP is started right from the site of accident. Immediate stabilization of the ABC with cervical spine immobilizationshould be done followed by detailed evaluation.

Mode of injury

Time of injury

Neurological condition of the child

Seizures may occur immediately or soon after the injury.

Loss of consciousness of>5 minutes warrants imaging and evaluation. Recovery from early LOC with a secondary lapse may be indicative of extra-dural hematoma.

Vomiting after even trivial head injury is not uncommon in children, but observation for this is usually advisable.

Neurological deficit may be transient after an impact seizure. If the child presents with coma deficit cannot be assessed, a previous observation by parents or doctor is noted and need to be followed.

The AVPU can provide valuable information

A - Alert

V - Responds to Verbal commands

P - Responds to pain

U - Unresponsive

Glasgow Coma Scale (GCS): The GCS is used to assess the depth of coma after head injury in adults and children above 5years of age. In those below 5 years modified GCS should be used (Table 1)

Table 1: Modified Glasgow Coma scale in Pediatrics

Eye opening		Score
Spontaneous		4
To Verbal stimuli		3
To Pain		2
None		1
Verbal Response		
Nonverbal children	Best verbal response	Score
Smiles oriented to sound follows objects interacts	Criented and converses	5
Consolable when crying and interacts inappropriately	Disoriented and converses	4
Inconsistently consolable and moans; makes vocal sounds	Inappropriate words	3
Inconsolable irritable and restless; cries	Incomprehensible sounds	2
None	None	1
Motor response		
Obeys commands		6
Localizes pain		5
Flexion withdrawal		4
Abnormal flexion (decorticate rigidity)		3
Extension (decerebrate rigidity)		2
None		1

Classification of head injury Using GCS

- 13-15 Mild
- 9-12 Moderate
- 3-8 Severe

Clinical criteria for discharge from ER after 2 hours of observation

- No Loss of Consciousness
- No Vomiting
- No amnesia
- Normal mental status
- No focal neurological deficit
- No neurological deterioration
- No post traumatic seizure including impact seizure
- No Ottorhea or Rhinorhea or bleeding
- No shock or other organ involvement that would preclude discharge
- No anticoagulant, anti-inflammatory drug or bleeding diathesis

- No suspicion of child abuse no matter how trivial the injury
- Radiological criteria for minor head injury
- No intracranial abnormality related to the head injury on CT scan

Skull fracture are acceptable except

- Those that cross the middle meningeal artery
- Those that cross the dural sinuses
- Those that are depressed more than the thickness of the adjacent skull.

In children fulfilling the above criteria for minor head injury, delayed deterioration is extremely uncommon and can be safely discharged. All other patients should be admitted. Pain, Fever, retention of urine should be treated immediately. Constrictive cervical collar or large bore internal jugular catheter should be avoided. Supine position with the head end elevatedto 30* is preferred for adequate venous drainage. All unnecessary touch, rough handling, moving, noise should be controlled or kept to minimum. Severe hyperglycaemia >180mg/dl and hypoglycaemia should be avoided.

Tracheal intubation is indicated for children with GCS ≤8. Children with multi-trauma, inhalation injury, airway/facial injury and shock with inaccessible head injury should be intubated, especially if at risk for increased ICP from pain and agitation. The cervical spine must be protected. Orotracheal intubation is preferred as it is quicker, requiring less manipulation of the neck, avoids aggravating any anterior basilar skull fracture or introducing infection into the anterior cranial vault.

All patients should be presumed to be full stomach. The jaw thrust manoeuvreis used during bag mask ventilation and head tilt & chin lift manoeuvre should be avoided. Common medications used during intubation include thiopenetone and lidocaine. Etomidate is useful but adrenal suppression cannot be ignored. It can be emphasized that even comatose patients must have good sedation and muscle relaxant during intubation to avoid sudden rise in ICP.

Hypotension is common and blood loss should never be attributed to the head injury alone. A diligent search should be made for the source of bleeding. Only in children < 2 years can scalp and head trauma cause hypotension. Rapid and aggressive treatment is needed to prevent secondary damage from hypoxic-ischemic injury. A low BP at the time of presentation is associated with poor prognosis. Hypotension of neurogenic origin is rare and indicates severe brain stem or cervical spine injury. Hypertension as part of Cushing's triad- hypertension, bradycardia and hypoventilation are more common. This indicates raised ICP. The hypertension may mask the hypovolumia and the BP measurement alone should not be accepted as a sign of normovolumia. Normal saline is the best choice for initial resuscitation.

There is no role for skull X-ray in head injury. Normal ultrasound cranium in an infant may give false sense of security as it will miss details. CT scan is very helpful and threshold should be low for ordering a CT in patients with

- Any focal deficit
- Any History of LOC > 5mins
- GCS persistent< 13

- Unable to examine the patient because of sedation, paralysis or intubation for other reasons
- Pupillary inequality
- CSF leak
- Depressed skull fracture
- Vomiting> 3times

It is not necessary to repeat a scan after 24-48hrs if there is no clinical deterioration or change in the GCS.

A quick cross table lateral X-ray can help to visualize at least the top 3 vertebrae. Cervical spine should also be scanned during the CT head to avoid repeated radiation exposure.

Other associated injury to be ruled out and should be treated simultaneously if required.

The following conditions warrants early surgical intervention

- Acute extra-axial hematomas of 1cm or more in thickness
- Subdural or epidural hematomas of more than 5mm in thickness with midline shift
- Hematomas >5mm with midline shift in patients with moderate brain injury with effacement of the basal cisterns
- Depressed skull fractures

CSF rhinorhea and otorhea need conservative approach avoiding packing of ears and nose. Almost all cases resolve spontaneously over 7-10days. CSF leaks less likely to heal are: developing after days or weeks, post-surgical repair or accidental trauma, massive leaks immediately after surgery, gunshot injury and with normal CSF pressure. Antibiotic prophylaxis remains controversial

Intracranial pressure (ICP): The intracranial vault is a closed compartment- although with some potential for expansion in the infant, follows the Monroe-Kellie Doctrine hypothesis. Brief increases in ICP for <5 min are not associated with significant damage. Sustain increases of >20 mmHg that do not return to base line in 5 minute probably require attention. Most of the evidences in adults and children set the acceptable high ICP level at 20mmHg. In a study by Esparza, an ICP > 40 mmHg was associated with a 100% mortality and those between20-40mmHg had a 28% mortality, and with 0-20mmHg had 7% mortality or disability. The current recommendation is to keep the ICP < 20 mmHg

Cerebral Perfusion pressure (CPP): This is the critical determinant of cerebral blood flow and brain perfusion. It is defined as the difference between mean arterial pressure and the ICP. Studies showing outcomes at various CPP levels confirm that a higher CPP level usually above 60mmHg is associated with worse outcome. However, there does not seem to be difference of outcome in 40-60mmHg. 2012 guidelines recommended CPPof 40 mmHg as the threshold for infants & younger children and 50mmhg for older children.

Monitoring devices:Intra-ventricular catheters, Intra-parenchymal pressure transducer, subdural bolt can be used as invasive devices and transcranial doppler can be used as non invasive device. Advance monitoring like jugular venous oxygenation and brain tissue oxygenation are technologies measuring the adequacy of oxygen delivery to the brain directly.Regional oxygenation can be measured with Near Infrared Sceptroscopy (NIRS).

Steroids have no benefit in head injury as the oedema is cytotoxic in nature.

Hypocapnia reduces the cerebral blood flowby vasoconstriction and hence reduces ICP. However, it will also reduce cerebral blood flow (CBF) to the point of reducing CPP and cause ischemia. Hyperventilation for a brief period of <10minutes may be employed in the setting of a sudden rise in ICP or impending herniation preferably under ICP and CPP monitoring. The goal of therapy is to maintain eucapnia with PaCO2 of 32-35mmHg.

Mannitol 0.25- 1gm/Kg is still the most commonly used agent by reducing the blood viscosity reduces the cerebral vasoconstriction, improves the cerebral blood flow and prevents stasis. This action is immediate and last about 75minutes. Take 15 minutes to 6 hours for osmotic reduction of brain water in an intact blood brain barrier. It may also deposit in injured brain cells after prolonged use for >48hours, resulting in rebound oedema.

3 -7% saline has been successfully used in the treatment of traumatic brain injury. The hyperosmolar state induced is more sustained and the reduction in ICP tends to be more sustained with fewer peaks requiring intermittent measures. The exact dosage is still unclear and bolus doses from 6.5ml-10ml/Kg have been advocated followed by an infusion of 0.1 -2.5ml/kg/hr. Serum Sodium levels upto 160 mmol/L have been reported with no side effects. Serum osmolarity rather than sodium level should be monitored for effect, with a target osmolarity of 340-370. Gradual tapering of about 10% every 6hour is required if continuous infusion is used for more than 48-72hrs.

Barbiturates are used for reducing the metabolic activity of the brain, thereby its oxygen consumption. Short acting barbiturates like thiopentone in a loading dose of 4mg/kg followed by 2-4mg/kg/hr as an infusion is most commonly used. Significant side effect includes hypotension in 54% requiring fluids and vassopressors, anergy, pneumonia, sepsis and hyponatremia.

Moderate hypothermia with a core temperature of 32-34* C may be useful but did not improve outcome in children.

A seizure does worsen ICP and the severe head injury patient has a high incidence of early symptomatic seizure, prophylactic medication like Fosphenytoin, Valproate or Leveracetum should be administered. Seizures may occur even in minor trauma. Immediate seizure may occur on impact or within the first 24 hrs. Most appears within the first 3 hrs, are short lived, generalized and without any CT scan abnormality. They do not predict future epilepsy, require no treatment and bear a good prognosis. If the seizure is complex, prolonged, or localized; further observation and treatment is warranted.

Decompressive craniectomy may be required for severe head injury and medically refractory intracranial hypertension in conditions like

1. Diffuse cerebral swelling on cranial CT imaging
2. Sustain ICP>40 mmHg before surgery
3. GCS 3 at some point of subsequent to injury
4. Secondary clinical deterioration
5. Evolving cerebral herniation syndrome

Delayed lethargy, behavioural changes may be seen after head injury in a child with normal CT scan and normal neurological examination known as Postconcussive syndrome. Vomiting, migraine and cortical blindness can occur. Recovery is the rule with good prognosis.

Further reading:

1. Kochanek PK, Carney N, Adelson PD, Ashwal S, Bell MJ, Bratton S et al. Guidelines for the acute medical management of severe traumatic brain injury in infants, children and adolescents- Second edition. Ped Cit Care Med 2012;13(suppl-1)

2. Adelson PD, Bratton S, Carney N et al. Guidelines for the acute medical management of severe traumatic brain injury in infants, children and adolescents.Ped Cit Care Med 2003;4(3suppl):S1-75

3. Hutchinson JS, Ward RE, Lacroix J, Hebert PC, Barnes MA, Bohn DJ et al. Hypothermia therapy after traumatic brain injury in children. N Eng J Med. 2008;358:2447-2456

4. McHugh GS, Engel DC, Butcher I, Steyer EW, Lu J, Mushkudiani N et al. Prognostic value of secondary insults in traumatic brain injury: results from the IMPACT study. J Neurotrauma. 2007;24(2):287-293

5. Coles JP, Minhas PS, Fryer TD, et al. Effect of Hyperventilation on cerebral blood flow in traumatic head injury: clinical relevance and monitoring correlates. Crit Care Med. 2002; 30: 1950-1959.

6. Muizelaar JP, Marmarou A, Ward JD. Adverse effect of Prolong hyperventilation in patients with severe head injury: a randomised control trial. J Neurosurg 1991;75:731-739

7. Wakai A, Roberts IG, Schierhout G. Mannitol for acute traumatic brain injury. Cochrane Database of Systematic Reveiws 2007, Issue 1. Art.No.: CD001049

8. Muizelaar JP, Wei EP, Kontos HA. Mannitol causes compensatory vasoconstriction and vasodilatation in response to blood viscosity changes. J Neurosurg. 1983; 59:828

9. Ichai C, Armando G, Orban JC, Berthier F, Rami L, Samat-Long C et al. Sodium lactate versus mannitol in the treatment of intracranial hypertensive episodes in severe traumatic brain –injured patients. Intensive care Med. 2009;35(3): 471-479

10. Jagannathan J, Okonnkwo DO, Dumant AS, Ahmed H, Bahari A, Prevedello DM et al. Outcome following decompressive craniectomy in children with severe traumatic brain injury: a 10 year single-center experience with long term follow up. J neurosurgerg 2007;106(4 suppl): 268-275

Parenteral nutrition in NICU

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Introduction

Adequately supplying the nutritional needs of preterm infantsremains a significant clinical challenge, especially for very low birth weight (VLBW) and extremely low birth weight (ELBW) infants Although ratesof survival of these infants have improved, growth failure isnearly universal, and multiple recent studies have documentedthe poor growth and nutritional deficits in this populationof infants. At the time of birth, only about 18% of ELBW infantsare less than the 10th percentile for weight and length, butat 36 weeks corrected gestational age this value reaches almost 100%. In these infants, full enteral feedings are generally delayed because of the severity of medical problems associated with prematurity In addition, early enteral feeds are also delayed because of concerns that aggressive feeding may lead to complications such as feeding intolerance or necrotizing enterocolitis. As a result, the nutritional requirements of VLBW infants are rarely met by enteral feeds in the first two weeks after birth 1.The impact of early malnutrition can have long-lastingnegative effects on central nervous system development and growth. Parenteral nutrition (PN) can meet the goal of providing nutrition in this time[2,3].

PN for the premature infant includes the following:

- Adequate calories for energy expenditure and growth
- Carbohydrates to prevent hypoglycemia and, in combination with lipids, provide the caloric intake to meet the energy needs of the infant
- Adequate protein intake including essential amino acids to achieve positive nitrogen balance required for growth
- Fatty acids to prevent essential fatty acid deficiency and maximize overall non-protein energy intake
- Essential nutrients including minerals (ie, calcium magnesium, and phosphorus), electrolytes, vitamins, and trace elements (eg, copper, zinc, and selenium) are needed for growth.

The recommended nutrient needs for medically stable and growing premature infants receiving either parenteral or enteral nutrition is shown in Table 1.

Carbohydrate

Glucose is transported across the placenta via facilitated diffusionand is the principal energy substrate for the fetus. The primarystorage form of glucose is glycogen, which is only producedduring the third trimester. Glucose is the chief energy sourcefor the neonatal brain and is of paramount importance for preterminfants who, in addition to having limited glycogen stores,also have especially metabolically active organs. Endogenousglucose

production varies with age and was estimated to be 8mg/kg per minute in term newborns and 6 mg/kg per minute inpreterm infants [4]. These production rates provide anappropriate starting point for glucose infusion rates in PNfor term and preterm infants. The upper rate of glucose administrationis dictated by the maximal glucose oxidative capacity for energyproduction and glycogen deposition. When glucose is given inexcess, it is converted into lipid via lipogenesis. This conversionis inefficient, increases energy expenditure, and may have additionalclinical consequences via increased carbon dioxide productionand exacerbation of lung disease[5].The maximum glucoseoxidation capacity is 12 mg/kg per minute in term newborns andpreterm infants receiving long-term PN and generally shouldnot exceed this concentration.

Proteins

The delivery of adequate intakes of both protein and energy, and an optimal mixture of essential/nonessential amino acids is required to achieve a positive nitrogen balance, which results in protein accruement and growth6. With no amino acid intake, VLBW infants lose the equivalent of 0.5 to 1 g/kg per day of protein due to protein catabolism in the first days after birth. The impact can be seen in the following example. A 26-week gestation 1,000-g birthweight infant begins withbody protein stores of approximately 88 g. Without any proteinintake, the infant loses approximately 1.5% of total body proteinper day. At the same time, the fetus in utero accumulates approximately2 g/d of body protein. To achieve this rate of accretion, theplacenta supplies substantially more than 2 g/kg per day ofamino acids to the developing fetus. After only 3 days withoutprotein intake, body protein stores are reduced by 5% from birthand are 10% less than a fetus of comparable age. It is obviousthat significant body protein deficits can and most often doaccumulate rapidly in ELBW infants in early postnatal life,particularly if the initiation of intravenous amino acids isdelayed for even a few days after birth.(Figure 1).

Traditionally aminoacids were started as 1 g/kg/d on D1 of life and then increased sequentially to 3-3.5 g/kg/d in increments of 0.5g/kg/d to 1g/kg/d. However, the preference for a stepwise procedure is solely empirical, based on fluid limitations, worries about intolerance, and fear of hyperglycemia in case of mixed glucose/amino acid solutions. Since even few days of delay can result in negative nitrogen balance and significant protein deficits that can have long term implications in term of growth, many investigators have tried supplementing aminoacids at high dose starting from D1 of life. Trials show that doing this leads to conversion to neutral or positive nitrogen balance suggestive of anabolism, increase albumin synthesis, increased glutathione synthesis[4,7,8]. Negative side effects observed with early high dose amino acid infusion — such as increased mean peak serum indirect bilirubin, lower base excess, lower concentrations of bicarbonate, and increased plasma urea nitrogen — were without clinical implications.In these studies aminoacids (AA) were given on day one of life to maximum of 2.5g/kg/d.

Although the short-term metabolic safety of early amino acid administration is well established, less information is available assessing longer-term outcomes. Beneficial long-term effects on neurodevelopment have been difficult to prove, since nutrition is only one of the many variables determining neurodevelopment

Aminoacid supplementation should be started on day one of life. Starting at 2.5 gm/kg/d is safe in both short term and long term. Initial studies show that starting aminoacid at 3.6

g/kg/d along with lipids at 2 g/kg/d can be considered safe and beneficial for short term outcomes but long term outcomes need to be seen before making it a standard of care.

Lipids

Intravenous lipid administration provides essential fatty acids (ie, linoleic and linolenic acids) that cannot be synthesized by humans and is an important non-protein source of energy. Small amounts of essential fatty acids (approximately 4 percent of caloric intake or 0.5 g/kg per day) are required to prevent essential fatty acid deficiency. Without supplementation, clinical manifestations of fatty acid deficiency (such as dermatitis, thrombocytopenia, and increased likelihood of infection and failure to thrive) become apparent by the end of the first week after birth.

Intravenous fat emulsion (IL) formulations used in premature infants contain varying combinations of soybean, safflower, or fish oils, with glycerin and egg yolk phospholipids added as emulsifiers. When given as early as PN, intravenous lipid prevents essential fatty acid deficiency, provides needed energy for tissue healing and growth, and balances the distribution of non-protein calories[9].

Practical tips for lipid infusion:

- Use of 20% lipid emulsion is preferable to a 10% solution to decrease the risk of hypertriglyceridemia, hypercholesterolemia, and hyperphospholipidemia.
- Initiate lipids at starting dose of 0.5 or 1.0 g/kg per day
- Plasma triglycerides are monitored after each increase in dose, and concentrations are maintained at less than 200 mg/dL (2.26 mmol/L)
- If the infant has severe hyperbilirubinemia or severe respiratory disease without evidence of PVR, provide lipids at 0.5 to 1.0 g/kg per day, maintaining a serum triglyceride value of no greater than 200 mg/dL (2.26 mmol/L)
- Maximum lipid dosage is usually 3 g/kg per day
- The lipid infusion hourly rate correlates best with plasma lipid concentrations. Hourly infusion should not exceed 0.12 g/kg per hour.

Minerals

- Sodium, Potassium and Chloride are essential minerals for survival. In VLBW infants, sodium intake should be restricted during first phase of fluid balance to reduce risk of bronchopulmonary dysplasia[10]. Till 6 – 10% of weight loss has occurred sodium should not be added to PN. Potassium should not be added till diuresis sets in. Sodium and potassium are added to PN usually from day 3 onwards, depending on serum levels.
- In premature infants, inadequate intakes of calcium and phosphorus result in bone undermineralization. The optimal ratio of Ca to P in PN is generally between 1:1.3 and 1:1.7 by weight and nearly a 1:1 molar ratio. Presently IV phosphorus preparation is not available in India. Isolated Calcium supplementation can lead to hypercalcemia and hypercalciuria, and without phosphorus is not utilized for bone accretion

Vitamins:

Parenteral vitamins are usually applied as a mixture of different vitamins. Vitamins should be added to lipid emulsion to increase stability and reduce peroxide formation[12]. Vitamin

induced peroxide load can be reduced by shielding of tubing from light exposure[13]. Except vitamin K, all vitamins should be supplemented daily. Adult MVI is the only preparation available in our country. It contains benzoic acid as stabilizer which is not recommended for neonates and should be used with caution. The dose of adult MVI is 0.5 ml/kg (comparing parenteral vitamin supplement doses as suggested by ESPGHAN with constitution of adult MVI) [14]. It is added on day 1.

Trace elements

In utero accretion of trace elements primarily takes place in the final trimester of pregnancy. As a result, premature infants are at risk for deficiency of these nutrients because of their low body stores and increased requirements for growth.

The only trace elements recommended from the first day PN are zinc and selenium. The other trace elements are not needed until after two weeks of age. Iron, another trace element, is not needed in the first few weeks after birth and is not routinely added to PN. In India the preparation of trace elements is available in form of Celecel 4,5.
Preparations of parenteral nutrition along with manufacturer are listed in table 2.

Summary and recommendations: The contents of early PN (on the day of birth or soon thereafter) include the following:

- Glucose starting at 4 mg/kg per minute (5 g/kg day) and slowly increasing to 12 mg/kg/min over several days.
- Amino acids at 2 – 2.5g/kg per day with increasing increments as tolerated to 4 g/kg per day.
- Lipids at 1 g/kg per day with increasing increments as tolerated to 3 g/kg per day. (See 'Lipids' above.)
- Electrolytes are not initially included in early PN but added as needed based upon laboratory evaluation.
- Other nutrients — Calcium (60 to 80 mg/kg per day) (Not ideal without IV phosphorus) and multivitamins.

Conclusion:

In the first weeks after birth before adequate enteral nutrition can be established, parenteral nutrition should be initiated to meet the nutritional needs of preterm and lessen growth failure in very low birth weight premature infants. Neonates started on PN should be monitored to avoid excesses or deficiencies of any given nutrient and to monitor for PN-associated complications, such as cholestasis and metabolic bone disease.

References:

1. Berry MA, Conrod H, Usher RH. Growth of very premature infants fed intravenous hyperalimentation and calcium-supplemented formula. Pediatrics 1997; 100:647.
2. Embleton NE, Pang N, Cooke RJ. Postnatal malnutrition and growth retardation: an inevitable consequence of current recommendations in preterm infants? Pediatrics 2001; 107:270.

3. Stephens BE, Walden RV, Gargus RA, et al. First-week protein and energy intakes are associated with 18-month developmental outcomes in extremely low birth weight infants. Pediatrics 2009; 123:1337.
4. Kalhan SC, Kilic I. Carbohydrate as nutrient in the infant and child: range of acceptable intake. Eur J ClinNutr. 1999;53:S94–S100
5. Nose O, Tipton JR, Ament ME. Effect of the energy source on changes in energy expenditure, respiratory quotient, and nitrogen balance during total parenteral nutrition in children. Pediatr Res. 1987;21:538–541
6. Zlotkin SH, Bryan MH, Anderson GH. Intravenous nitrogen and energy intakes required to duplicate in utero nitrogen accretion in prematurely born human infants. J Pediatr 1981; 99:115.
7. Salas-Salvadó J, Molina J, Figueras J, et al. Effect of the quality of infused energy on substrate utilization in the newborn receiving total parenteral nutrition. Pediatr Res 1993; 33:112.
8. Bhatia J. Fluid and electrolyte management in the very low birth weight neonate. J Perinatol. 2006;26(suppl 1):S19–S21
9. Gutcher GR, Farrell PM. Intravenous infusion of lipid for the prevention of essential fatty acid deficiency in premature infants. Am J ClinNutr 1991; 54:1024.
10. Hartnoll G, Betremieux P, Modi N. Randomized controlled trial of postnatal sodium supplementation on body composition in 25 to 30 week gestational age infants. Arch Dis Child Fetal Neonatal Ed 2000;82:F24-F28
11. Fitzgerald KA, MacKay MW. Calcium and phosphate solubility in neonatal parenteral nutrient solutions containing TrophAmine. Am J Hosp Pharm 1986; 43:88.
12. Silvers KM, Darlow BA, Winterbourn CC. Lipid peroxide and hydrogen peroxide formation in parenteral nutrition solutions containing multivitamins. J Parenter Enteral Nutr. 2001;25:14-17
13. Bassiouny MR, Almarsafawy H, Abdel-Hady H, Nasef N, Hammad TA, Aly H. A randomized controlled trial on parenteral nutrition, oxidative stress, and chronic lung diseases in preterm infants. J PediatrGastroenterolNutr 2009;48:363-369.
14. Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R for the Parenteral Nutrition Guidelines Working Group. 8. Vitamins. J PediatrGastroenterolNutr 2005; 41:S47–S53.

Table 1. Composition of fluid, energy and nutritional intake for stable growing preterm infants

Components, units	Units/kg/day	
	Parenteral	Enteral
Water, ml	120-160	135-200
Energy, kcl	90-100	110-135
Protein, g	3.0-3.8	3.5-4.5
Fat, g	3-4	5.3-7.2
Carbohydrates, g	9.7-15	

Figure 1.

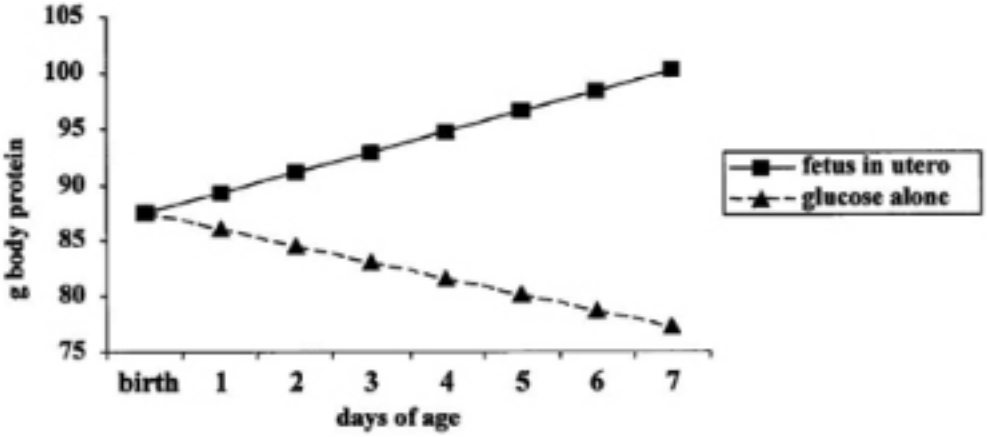

Table 2: Market preparations available in India

Constituent	Preparation	Manufacturer	Availability
Dextrose	5%, 10%, 25%, 50%		25, 100, 500
Aminoacids	Aminoven Infant 6%, 10%	Fresinuskabi India pvt.limited	100 ml
	Primene	Baxter health care	100 ml
Lipids	Intralipid 10% PLR	Fresinuskabi India pvt.limited	100
	Intralipid 20% PLR	Fresinuskabi India pvt.limited	100
	Omegavan	Fresinuskabi India pvt.limited	100
	Clinoleic 20%	Baxter health care	500
Trace elements	Celecel 4	Claris healthsciences	1,3,5
	Celecel 5	Claris healthsciences	1,3,5

Pediatric Pain Management

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Pain is an unpleasant sensory and emotional experience, associated with actual or potential tissue damage, or described in terms of such damage. The structural components necessary to perceive pain are already present at about 25 weeks gestation, whereas the endogenous descending inhibitory pathways are not fully developed until mid-infancy [1]. Both neonates and infants are able to mount a graded hormonal stress response to surgical interventions and adequate intra- and postoperative analgesia will not only modify the stress response but has also been shown to reduce morbidity and mortality [2, 3].

Routes of Analgesic Administration in Children

- Oral
- Intramuscular: Painful administration and wide fluctuations in absorption from muscle
- Intravenous
- Transmucosal
- Subcutaneous continuous infusions
- Transdermal
- Regional analgesia

Pain Assessment in Infants and Children

There are many well established self-report pain scales developed for young children which includes the Poker Chip Scale, Wong-Baker Faces Scale, the Faces Pain Scale-Revised (FPS-R) and the Oucher Scale[4-8]. The Poker Chip Scale asks children to quantify their pain in "pieces of hurt," with more poker chips representing more pain; body outlines allow young children to point to the location of their pain. The Poker Chip Tool appears to have the most utility as a simple clinical assessment tool to identify the presence or absence of pain and general estimates of pain intensity in young children [4]. The Oucher Scale is well accepted in children over 6 years of age. It is available in different ethnic versions and permits children to rate their pain intensity by matching it to photographs of other children's faces depicting increasing levels of pain. Another famous pain rating scale in children is the FLACC (Face, Legs, Activity, Cry, Consolability) Behavioral Pain Assessment scale [9]. (Table 1)

	Score		
Categories	**0**	**1**	**2**
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up

Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry, (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching hugging or being talked to, distractible	Difficulty to console or comfort

Table 1. FLACC (Face, Legs, Activity, Cry, Consolability) Behavioral Pain Assessment [9]

The commonly used drugs – their dosages and route of administration in the pediatric population is outlined in Table 2.

Drug	Route	Dose	Comments
Paracetamol	Suspension- 120mg/5ml 250mg/5ml Tablets- 500mg Soluble tablets- 500mg Suppositories- 60, 120, 250, 500mg	20mg/kg 6 hourly PO/PR LOADING of up to 40mg/kg PR or 30mg/kg PO	Given orally, it is rapidly absorbed from the small bowel with almost 100% bioavailability and has a similar onset time to IV preparation. Rectally uptake is slower and more variable; doses of 20mg/kg are often not therapeutic and take 2-4 hrs to reach therapeutic concentrations. Therefore PR 40mg/kg followed by 20mg/kg doses are recommended.
Intravenous Paracetamol	Only to be prescribed if oral route not available 50mls- 500mg 100mls- 1g	<10kg- 7.5mg/kg 6 hourly >10kg- 15mg/kg 6 hourly >50kg- 1g max 6 hourly	IV dose will result in higher plasma & effect site concentrations.
Ibuprofen	Suspension- 100mg/5ml Tablets- 200, 400mg	<6months- 5mg/kg 8 hourly PO >6 months- 10mg/kg 8 hourly PO Maximum daily dose 30mg/kg or 1.2g	In orthopaedic procedures benefits outweigh the risks of reduced bone healing in most cases. Avoid if non-union or scoliosis surgery.

Diclofenac Sodium	Enteric coated 25, 50mg Slow release 75, 100mg Suspension- 50mg/5ml Suppositories- 12.5, 25, 50, 100mg	Not recommended in children <6 months 300 micrograms- 1mg /kg 8 hourly PO/PR Maximum daily dose 3mg/kg or 150mg	Diclofenac: Oral and rectal dose are equivalent. Peak plasma concentrations from oral dose at 1 hour
Morphine	Oral morph- 10mg/5ml Tablets- 10, 20mg Injection- 10mg/ml	Orally <12 months- 50 micrograms/kg 4 hourly >12 months- 100-300 micrograms/kg 4 hourly Intravenous- <6 months 100 micrograms/kg 6 hourly >6 months 100 micrograms/kg 4 hourly	With few exceptions, opioids should be administered to children either via the oral or intravenous route. Intramuscular injections should be avoided unless absolutely necessary.
Anti-emetic Ondansetron	Intravenous Oral	0.1mg/kg 8 hourly <4 years- 2mg 8 hourly >4 years- 4mg 8 hourly	Can cause severe constipation. May be ineffective in opioid induced nausea and vomiting.

TABLE 2: Commonly used drugs in the pediatric population

Pediatric analgesia can also be achieved with:

1. Continuous opioid infusions: Patient controlled analgesia (PCA) is widely used for postoperative pain relief in both children and adults. With appropriate preoperative teaching and encouragement, children as young as 6 to 7 years of age can independently use the PCA pump to provide good postoperative pain relief [10]. In Paediatrics morphine PCA provides superior analgesia to the intramuscular route or to continuous infusion of morphine, with comparable outcome to epidural morphine. For toddlers and children, commonly recommended initial morphine infusion rates are roughly 0.025 mg/kg/hr[11]. Due to the pharmacokinetic and pharmacodynamic factors described above, initial infusion rates in newborns are much lower and range from 0.005 to 0.01 mg/kg/hr. PCA may be administered either alone or in conjunction with a low-dose continuous infusion.

2. Regional anaesthesia produces excellent postoperative analgesia and attenuation of the stress response in infants and children[12, 13]. Epidural anaesthesia (including caudal epidural analgesia) can decrease the need for postoperative ventilation. Suggested maximum dosages of bupivacaine, levobupivacaine, and ropivacaine in neonates and children are given in table 3. The same dose is recommended for each drug.

Table 3

Paediatric caudal adjuncts has been used to prolong the duration of analgesia without

Single bolus injection	Maximum dosage
Neonates	2mg/kg
Children	2.5mg/kg
Continuous postoperative infusion	Maximum infusion rate
Neonates	0.2 mg/kg/hour
Children	0.4 mg/kg/hour

increasing side-effects such as motor blockade. The commonest were ketamine, clonidine, fentanyl and diamorphine. Preservative-free S(+)-ketamine is more potent and may reduce neuro-psychiatric effects[14]. The routine use of opioids as additives for postoperative analgesia has recently been critically challenged [15]. Although there is a risk of respiratory depression, less dramatic side-effects such as itching, nausea and vomiting, urinary retention, and decrease gastrointestinal motility are more troublesome [16].

3. Eutectic Mixture of Local Anesthetics (EMLA) Eutectic mixtures of local anesthetics such as lidocaine/prilocaine and lidocaine/tetracaine are effective in reducing pain from dermatologic procedures, venipuncture, etc. However, this dosage form requires 30 to 60 minutes to become fully effective after application.

4. Iontophoresis: Iontophoresis of lidocaine employs an electrical field to drive local anesthetics in their charged ionic form across the stratum corneum[17]. It can provide deeper levels of analgesia with a much shorter onset time (10 to 25 minutes). Though there is a mild tingling sensation during drug delivery, this is generally well tolerated.

5. Liposomal lidocaine: Lidocaine can be dispersed in liposomes to facilitate transcutaneous delivery. This formulation (ELA-max) is available as an over-the-counter medicine and can be massaged into the skin without occlusion, providing skin anesthesia within 30 minutes. Its analgesic effects may be equivalent to EMLA, even with this shorter application time [18].

6. Vapocoolant spray: Vapocoolant sprays provide inexpensive, rapid and effective analgesia for short duration procedures, such as venipuncture and immunization[19]. The vapocoolant can both be sprayed directly onto the skin or onto a cotton ball and then applied to the injection site for 15 seconds.

7. Oral sucrose solution can be used prior to minor painful procedures in babies under 3 months; it can relieve pain in neonates during minor procedures such as venepuncture, cannulation, intramuscular injections, subcutaneous injection, lumbar puncture etc. However, it should not be given in necrotising enterocolitis, suspected hyperglycaemia,

ventilated or paralysed babies. The dose is administered onto the baby□s tongue approximately 2 minutes prior to the procedure. After administration the baby should be given a dummy or comforter to suck on as this can potentiate the analgesic effect of sucrose. The effect may last for approximately 10 minutes.The usual dose is:

Preterm neonates: 0.5ml of 24% sucrose solution

Term neonates (up to 3 months): 1ml of 24% sucrose solution

Conclusion:

Children of all ages deserve compassionate and effective pain treatment. The safety of analgesic therapy has improved with the development of new drugs and fuller understanding of their pharmacokinetics and dynamics in neonates, infants and children, and in disease states. Concerted efforts should be undertaken to reduce or eliminate pain whenever possible for routine medical procedures in children. Where complex analgesia is needed, management by a multidisciplinary acute pain team with paediatric expertise is the most effective approach.

References

1. Wolf A. Development of pain and stress responses. In: Proceedings of the 4th European Congress of Paediatric Anaesthesia, Paris, 1997
2. Aynsley-Green A. Pain and stress in infancy and childhood— where to now? Paediatr Anaesth 1996; 6: 167–72
3. Aynsley-Green A, Ward-Platt MP, Lloyd-Thomas AR. Stress and pain in infancy and childhood. Bailliere's Clin Paediatr 1995; 3: 449–631
4. Cohen LL, Lemanel K, Blount RL et al. Evidence-based assessment of pediatric pain. J Ped Psychol. 2008;33(9):939-955.
5. Wong DL, Hockenberry-Eaton M, Wilson D, Winkelstein M, Schwartz P. Essentials of Pediatric Nursing. 5th ed. St. Louis: Mosby; 2001:1301.
6. Beyer JE, Denyes MJ, Villarruel AM. The creation, validation, and continuing development of the Oucher: a measure of pain intensity in children. J Pediatr Nurs. 1992;7:335-346.
7. Hester NO, Foster R, Kristensen K. Measurement of pain in children: generalizability and validity of the Pain Ladder and the Poker Chip Tool. In: Tyler DC, Krane EJ, eds. Pediatric Pain. Vol 15. Advances in Pain Research and Therapy. New York: Raven Press Ltd.; 1990:70-84.
8. Hicks CL, von Baeyer CL, Spafford P, van Korlaar I, Goodenough B. The Faces Pain Scale – revised: Toward a common metric in pediatric pain measurement. Pain. 2001;93:173-183.
9. Merkle SI, Shayevitz JR, Voepel-Lewis T, Malviya S. The FLACC: A behavioral scale for scoring postoperative pain in young children. Pediatr Nurs. 1997;23:293-297.
10. Berde CB, Lehn BM, Yee JD, Sethna NF, Russo D. Patient-controlled analgesia in

children and adolescents: a randomized, prospective comparison with intramuscular administration of morphine for postoperative analgesia. J Pediatr. 1991;118:460-466.

11. Esmail Z, Montgomery C, Courtrn C, Hamilton D, Kestle J. Efficacy and complications of morphine infusions in postoperative paediatric patients. Paediatr Anaesth. 1999;9:321-327.
12. Wolf AR, Doyle E, Thomas E. Modifying infant stress responses to major surgery: spinal vs extradural vs opioid analgesia. Paediatr Anaesth 1998; 8: 305–11
13. Wolf AR, Eyres RL, Laussen PC, et al. Effect of extradural analgesia on stress responses to abdominal surgery in infants. Br J Anaesth 1993; 70: 654–60
14. Koinig H, Marhofer P. S(+)-ketamine in paediatric anaesthesia. Paediatr Anaesth 2003; 13: 185–7
15. Lonnqvist PA, Ivani G, Moriarty T. Use of caudal-epidural opioids in children: still state of the art or the beginning of the end? Paediatr Anaesth 2002; 12: 747–9
16. Lloyd-Thomas AR, Howard RF. A pain service for children. Paediatr Anaesth 1994; 4: 3–15
17. Irsfeld S, Klement W, Lipfert P. Dermal anaesthesia: comparison of EMLA cream with iontophoretic local anaesthesia. Br J Anaesth. 1993;71:375-378.
18. Eichenfield LF, Funk A, Fallon-Friedlander S, Cunningham BB. A clinical study to evaluate the efficacy of ELA-Max (4% liposomal lidocaine) as compared with eutectic mixture of local anesthetics cream for pain reduction of venipuncture in children. Pediatrics. 2002;109:1093-1099.
19. Reis EC Jacobson RM Tarbell S Weniger BG Taking the sting out of shots: control of vaccination-associated pain and adverse reactions. Pediatr Ann. 1998;27:375-386.

Japanese Encephalitis

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Japanese encephalitis(previously known as Japanese B encephalitis) is a disease caused by the mosquito-borne Japanese encephalitis virus. The Japanese encephalitis virus is a virus from the family Flaviviridae.Domestic pigs and wild birds are the reservoirs of the virus;transmission to humans may occur. Amongst the most important vectors of this disease are the mosquitoes Culex tritaeniorhynchus and Culex vishnui

Epidemiology

Countries which have had major epidemics in the past, but which have controlled the disease primarily by vaccination, include China, Korea, Japan, Taiwan and Thailand. Other countries that still have periodic epidemics include Vietnam, Cambodia, Myanmar, India, Nepal, and Malaysia. Japanese encephalitis has been reported on the Torres Strait Islands and two fatal cases were reported in mainland northern Australia in 1998. The spread of the virus in Australia is of particular concern to Australian health officials due to the unplanned introduction of Culex gelidus, a potential vector of the virus, from Asia. However, the current presence on mainland Australia is minimal.

Human, cattle and horses are dead-end hosts and disease manifests as fatal encephalitis. Swine acts as amplifying host and has very important role in epidemiology of the disease. Infection in swine is asymptomatic, except in pregnant cows, when abortion and fetal abnormalities are common sequelae. The most important vector is Culex tritaeniorhynchus, which feeds on cattle in preference to humans, it has been proposed that moving swine away from human habitation can divert the mosquito away from humans and swine. The natural host of the Japanese encephalitis virus is bird, not human, and many believe the virus will therefore never be completely eliminated.In November 2011, Japanese encephalitis virus was reported in the Republic of Korea.

Recently whole genome microarray research of neuron in JE virus infection has shown that neurons play an important role in their own defense against Japanese encephalitis viral infection. Although this challenges the long-held belief that neurons are immunologically quiescent, an improved understanding of the proinflammatory effects responsible for immune-mediated control of viral infection and neuronal injury during JEV infection is an essential step for developing strategies for limiting the severity of CNS disease.

CLINICAL FEATURES

Incubation period – 5 to 15 days

Only 1 in 300 to 1 in 1000 infections develop into encephalitis, rest asymptomatic
Course of the Disease is characterized by;

Prodromal Stage: High grade fever with or without rigors, headache(frontal or generalised),malaise, nausea and vomiting. Adolescents complain of retrobulbar pain, photophobia, pain in the legs, neck, back and respiratory symptoms, while infant may present with irritability and lethargy.

Encephalitic stage: Marked CNS symptoms from 3rd to 5th day, which manifest with altered sensorium, convulsion, neck stiffness, muscle rigidity, mask like face and abnormal movements.

Features of raised ICP are frequently present. Focal neurological signs may be stationary, progressive or fluctuating. Seizure is a prominent feature of encephalitis. JE characterized by rapidly changing CNS signs e.g. hyperreflexia followed by hyporeflexia or changing plantar response.

Some children may appear to be mildly affected initially only to lapse into coma and die suddenly. In others high fever, violent convulsions interspersed with bizarre movement, hallucinations alternating with brief periods of clarity followed by complete recovery.

Death usually occurs at first week.

Late stage: About 1/3rd recover neurological function. Residual neurological impairment includes speech defects, aphasia, paresis and intellectual deficit. Localized paresis is more common and upper limb is commonly involved.

Atypical presentation of JE: Presents with only brief period of altered sensorium and may diagnosed as atypical febrile seizures. Some present with a short duration of altered behaviour and few present with acute flaccid paralysis like illness as initial presentation.

Laboratory investigations

1. Blood:

- Complete blood count
- Renal Function test
- Liver function tests
- Blood glucose
- Blood gas, Ammonia,lactate
- Blood culture / Serology test

2. Lumbar puncture and CSF analysis: This is the most important investigation in such cases, unless there are contraindications. Contraindications of LP are elevated ICP owing to a suspected mass lesions of the brain or spinal cord, symptoms and signs of pending cerebral herniation, crictical illness and platelet count less than 20,000/mm.

CSF pressure, glucose, protein, cell count and differentiation, gram staining, LDH, LDA and culture and sensitivity. If history and physical examination indicate, a portion of CSF should be sent for viral(PCR or antibody)studies(HSV1 and 2, enterovirus).

Condition	Pressure (mm H2O)	Leukocytes/ mm3	Protein (mg/dl)	Glucose
Viral meningitis or Meningoencephalitis	Normal or Slightly ¤	PMN early; rarely >1000; mononuclear cells predominate during most of cousrse	50-200	Generally normal; may be ¤ to <40 mg/dl in various viral diseases, particularly mumps(15-20%)

3.Radiological evaluation

CT scan, MRI,

Condition	CT scan/ MRI Findings
JE	Involvement of thalamus, basal ganglia, mid brain, pons and medulla. MRI shows extensive hyper intense lesions of the thalamus, cerebrum, and cerebellum. MRI is more sensitive than CT in detection of these lesions.

4. Immunological tests

JE i.Detection of JE virus, antigen or genome in tissues, blood or other body fluid by immunoflurescence or by PCR.

ii. JE virus specific IgM in CSF and blood by IgM capture Elisa.

iii. Four fold or greater rise in JE virus specific antibody in paired sera through IgM/IgG by Elisa.

Treatment

There is no specific treatment for Japanese encephalitis and treatment is supportive; with assistance given for feeding, breathing or seizure control as required. Raised intracranial pressure may be managed with mannitol..There is no transmission from person to person and therefore patients do not need to be isolated.

PREVENTION AND CONTROL

Vector Control

a) Reduction of breeding source for larvae

b) Reduction in man mosquito contact

c) Control of adult mosquitoes.

Prevention

JE VACCINATION

Three types of vaccine are used worldwide

1. Inactivated mouse brain vaccine (India-Nakayama Strain)
2. Inactivated hamster kidney cell vaccine
3. Live attenuated hamster kidney vaccine

VACCINE	AGE	DOSE	ROUTE	SCHEDULE	BOOSTER
JE vaccine, inactivated	≥17 years	0.5 mL	IM	0, 28 days	≥1 year after primary series
	3 years through 16 years	0.5 mL	IM	0, 28 days	Data not yet available
	2 months through 2 years	0.25ml	IM	0, 28 days	Data not yet available

Psychiatric Approach To The Management Of Hysteria In Children

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Introduction: The term Hysteria (recent nomenclature-Dissociative/Conversion Disorder) refers to a condition in which patients present with loss of function or altered function or dysfunction with no organic basis and with positive psychological basis. This is a common condition seen in the emergency or outdoor department. Studies have shown ranging from 20-30% in our country as compared to 1-2% in western countries.

Clinical presentation:
Fits or pseudo-seizures
Fainting spells (or attacks of unresponsiveness)
Abnormal movements (shaking of limbs, tremulousness, hyperventilation, hiccups)
Motor weakness, aphonia, amnesia and possession attacks
Most of the above clinical presentations especially in an emergency clinic are very frightening for parents, teachers or relatives. Many duty doctors miss the dissociative attacks and many are shifted to ICU with oxygen and detail monitoring which further makes the family stressed.

Clinical Evaluation and Diagnosis-
Detailed history taking is the key to formulate the management plan for the index patient. Special attention needs to be given for the following-

1. Parent interview: eyewitness account of the 'attack', family's perception and explanatory model for the problem, level of stress and distress in family, response of the family members to symptoms, health of family members, past consultations and advice, child's temperament and presence of any other behavioral or emotional symptoms.
2. Child interview: exploration of stressors faced by the child (in school, home, with peers, etc.) and their association with the symptoms. Also circumstances of the first experience of the symptoms/attack, tension/ anxiety preceding the symptoms, any recent worries or life events.
3. Other sources of history: school reports, notes or past consultations
4. Direct observation: induction of symptoms by suggestion, effect on symptoms when child is distracted.
5. Physical examination: detailed general, neurological and other systemic examination
6. Investigations: relevant physical investigations, Psychometric evaluations as needed.

In an emergency setting it may not be possible to elicit or unearth all the underlying psychological factors. However repeated and sensitive interviewing will most often help to get the detailed history. Brief interview must be taken to establish predisposing, precipitating and maintaining factors of the episode.

Differential Diagnosis:

Any organic condition must be ruled out prior to considering a Functional illness or Dissociative disorder. Commonly encountered conditions include- seizure disorders, movement disorders, syncope attacks, panic attacks, SSPE, GB syndrome, Porphyrias, drug and alcohol use disorders

Treatment:

Multimodal treatment packages approach recognizes the presence of multiple factors that initiate and maintains symptoms. Accordingly a set of procedures are followed to deal with problems. Indian setup- NIMHANS MODEL (National Institute of Mental Health and Neuro Sciences, Bangalore) has been evolved and followed, which comprises of the following components-

1. Family crisis resolution: the aim here is the alleviation of family distress and enhancing the family's competence in dealing with the crisis/situation. This step is the most crucial in the emergency setup towards helping the family and resolving immediate stress. A typical explanation provided to the family members would be- 'Illness that your child has developed is neither very serious nor life threatening. Many young children having such psychological factors are playing a role in causing this problem. If you become anxious or too worried about the child's symptoms, then it could get communicated to the child and further lead to escalation of the symptoms. Conversely, if you are confident and reassure the child to relax, s/he will recover faster.
2. Normalization: this step is done to counter the sick role and illness behavior. Techniques like daily activity schedules, reduction of secondary gains, use of behavior modification techniques, all help to bring the child/adolescent back to a functional level. Family members are involved, in order to facilitate this process.
3. Individual therapy: this step involves intensive and gentle exploration to uncover stressors and conflicts that the child is facing. During the sessions aspects related to psychological, interpersonal and social experience are explored. Behavioral and cognitive strategies are used to enhance the child's coping skills. This helps the child to actively counter the symptoms.
4. Family therapy: Intra-family dysfunction and psychopathology in family members are not uncommon. They may range from child rearing practices, Faulty parenting, parental discord, alcohol abuse in the family members, etc. In other words 'child's problems are the symptom of family pathology'. Having explored the family dynamics more focused family therapy may be prescribed.
5. Others: in all interactions from various sources, the issues that are uncovered are then addressed through further work with the child, family, significant others, school, etc.

6. Related issues: in the acute variety most often symptoms remit or subside with initial intervention as described earlier. However treatment becomes challenging, if the child presents with repeated and chronic symptoms. As an adjunctive measure, procedures like Thiopental interview, hypnosis, or graded physiotherapy may be used.
7. Need for admission: Individual case which require admission, may have issues related to diagnostic clarifications, severe symptoms, high level of family distress. Also repeated episodes which are resistant to routine OPD treatment.
8. Use of medication: appropriate medication on case basis may be considered. If co-morbid depression or anxiety is significant, some family members may ask for medication despite reassurance. In such situations use of placebo may be considered.

Conclusion: Causation of any psychiatric illness is understood in the background of Bio-Psycho-Social Model. This is more evident in the aetio-patho-genesis and management of Dissociative Disorder. Timely and effective management of Dissociative Disorders in the initial stage is very important. Many of these children may in long term go on to develop depression, anxiety spectrum disorders, adjustment at their personal/social-occupational areas.

Pituitary Stalk Interruption Syndrome: A Case Report

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Key words: pituitary stalk interruption, hypoglycaemia, growth hormone.
Contributors: NMD was involved in analysis of findings, planning work up of the patient, drafting the paper and will act as guarantor for the paper. PPB and MPB were involved in finalization of draft and primary care of the patient. PA was involved in radiological work up of the patient.
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Abstract:
Pituitary stalk interruption syndrome (PSIS) is characterized by an absent pituitary stalk on MRI, hypoplasia of the anterior pituitary gland, and ectopic posterior pituitary. We hereby report a healthy term neonate presented with hypoglycaemia, dysmorphic facies, microphallus, cryptorchidism and prolonged conjugated hyperbilirubinemia and later on diagnosed as a case of PSIS by MRI with multiple anterior pituitary hormone deficiency.

Introduction:
Pituitary stalk interruption syndrome (PSIS) is characterized by an absent pituitary stalk on MRI, hypoplasia of the anterior pituitary gland, and ectopic posterior pituitary [1]. Exact prevalence of PSIS is uncertain. Cases are mostly reported from western hemisphere and except some scattered cases there is no large study of clinical features of PSIS in Asian people. We herein report a neonate with PSIS and to the best of our knowledge and belief this is the first case report of PSIS from this remote part of North-East India.

Case Report:
A healthy term male baby was delivered outside in a private hospital by caesarean section due to transverse lie with complete uterine septum. Baby had an uneventful perinatal period. Baby developed cyanosis along with hypoglycaemia at 4 hours of birth for which baby was admitted in neonatal intensive care unit (NICU). There was no maternal history of gestational diabetes mellitus. Baby developed recurrent episodes of hypoglycaemia on breast feeding. Intravenous fluid (IVF) was started and glucose infusion rate (GIR) had to increase up to 10 mg/kg/min to maintain euglycemia. But in view of persistent

hypoglycaemia, lethargy and neonatal jaundice baby was referred on day 4 to our NICU. On examination baby had dysmorphic facies characterised by upward slanting of eyeball with low set ears and depressed nasal bridge. There were microphallous along with bilateral cryptorchidism. Baby was lethargic and hypotonic with weak cry. Baby was hemodynamically stable and systemic examination does not reveal any positive findings. Baby had icterus upto palm and sole.

Baby was admitted for evaluation and started with glucose infusion along with expressed breast milk. GIR had to be increased upto 10 mg/kg/min to maintain euglycemia. Necessary investigations were sent for evaluating cause of hypoglycaemia. Sepsis screen, blood culture, hemogram and urine culture were normal. Urine for reducing substance and ketone bodies were absent. Serum ammonia and lactate levels were normal and metabolic screening revealed normal study. Blood gas was normal. Growth hormone (0.01 ng/mL) and cortisol (0.44 µg/dL) level were low at the time of hypoglycaemia. Serum insulin level was normal (2.14 mU/L) which was sent at critically low blood sugar level. There was prolonged neonatal conjugated hyperbilirubinemia. Thyroid function test, electrolytes and kidney function test were normal. Ultrasound whole abdomen was normal. MRI Brain report revealed ectopic posterior pituitary gland in relation to the tuber cinerium and median eminence. The pituitary stalk is absent. The anterior lobe of the pituitary appears small. Thus the overall clinico-radiological and biochemical profile confirmed the diagnosis of PSIS.

Discussion:

PSIS was first reported by Fujisawa et al. in 1987 and was characterised by an absent pituitary stalk on MRI, hypoplasia of the anterior pituitary gland (adenohypophysis), and ectopic posterior pituitary leading to a series of clinical findings[1]. Thus patient with PSIS have various degrees of anterior pituitary hormone deficiency with normal posterior pituitary function [2].

Exact prevalence of PSIS is uncertain. El Chehadeh et al claimed an incidence of approximately 0.5/1000,000 births[3]. Prevalence was more in male. The pathogenesis of PSIS is unclear. The traumatic and perinatal hypothesis states that breech delivery and dystocia leads to obvious deformation of head, which may result in injury and breaking of pituitary stalk [4]. As per literature, 70-80 % of the dystocia due to breech delivery may lead to injury of pituitary [5]. However this hypothesis failed to explain the fact that significant percentage of patients with this abnormality delivered normally. In our case mother had complete uterine septum with transverse lie which was not seen in any previous case report and that may be a contributing factor of PSIS. Another explanation suggest some possible gene defects of patients leading to dysplasia of hypothalamus and pituitary [6].

The common modes of presentation include neonatal hypoglycaemia; prolonged neonatal jaundice, micropenis, cryptorchidism and short stature [7]. Infrequently,the radiological entity of PSIS may be associated with other midline craniofacial anomalies like Chiari malformations, septo optic dysplasia, and single central incisor or absent left internal carotid [7, 8]. But our case had dysmorphic facies characterised by upward slanting of eyeball with low set ears and depressed nasal bridge. Karyotyping revealed normal study. Diagnosis of gonadotropin deficiency was made on clinical grounds because of presence of microphallus and cryptorchidism. Length was normal and Guo Q et al also reported that

heights of 25 % PSIS patients were within the normal range [9].Hypoglycaemia in our case was caused by GH and cortisol deficiency;the latter is known to impair gluconeogenesis[10].

Conclusion:

PSIS is although a rare cause of neonatal hyperglycemias but it should be suspected in certain cases with some peculiar physical findings along with laboratory evidence of isolated growth hormone or multiple anterior pituitary hormone deficiency. More reporting of such cases will results in exact prevalence of this rare condition in Asian countries.

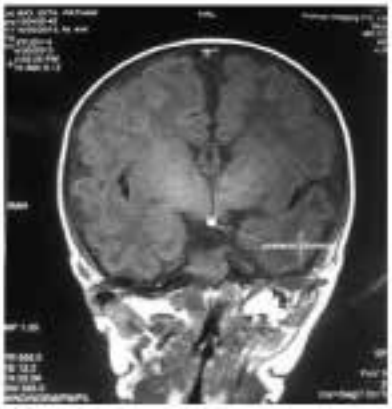

Fig: 1

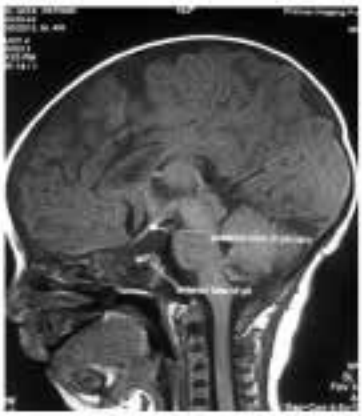

Fig: 2

Fig 1: Coronal slice: The ectopic posterior pituitary hyper intense signal is at the median eminence (arrow).

Fig 2: Sagital slice: Ectopic posterior pituitary gland in relation to the tuber cinerium and median eminence. The pituitary stalk is absent and the anterior lobe of the pituitary appears small (hypoplasia)

References:

1. Fujisawa I, Kikuchi K, Nishimura K, Togashi K, Itoh K, et al. (1987) Transection of the pituitary stalk: development of an ectopic posterior lobe assessed with MR imaging. Radiology165: 487–489.
2. Vijayanand P, Mahadevan S, So Shivbalan, Reddy N, Ramdoss N (2007) Pituitary stalk interruption syndrome (PSIS). Indian J Pediatr 74: 874–875.
3. El Chehadeh-Djebbar S, Callier P, Masurel-Paulet A, Bensignor C, Me´jean N,et al. (2011) 17q21.31 microdeletion in a patient with pituitary stalk interruption syndrome. Eur J Med Genet 54: 369–373.
4. Gacs G1984 Perinatal factors in the etiology of hypopituitarism. Helv Paediatr Acta 42:137–144.
5. Craft WH,Underwood LE,Van Wyk JJ (1980) High incidence of perinatal insult in children with idiopathic hypopituitarism. J Pediatr 96: 397–402.
6. Hamilton J, Blaser S, and Daneman D (1998) MR imaging in idiopathic growth hormone deficiency. AJNR Am J Neuroradiol 19: 1609–1615.
7. Pinto G, Netchine I, Sobrier M. L., Brunelle F, Souberbielle J. C and Brauner R (1997): Pituitary Stalk Interruption Syndrome: A clinical-biological-genetic assessment of its Pathogenesis. J Clin Endocrinol Metab 82: 3450-3454.

8. Patkar D, Patankar T, Krishnan A, Prasad S, Shah H, Limdi J. MR Imaging in children with ectopic pituitary gland and anterior hy[popituitarism. J Postgad Med 1999; 45: 81-83.
9. Guo Q, Yang Y, Mu Y, Lu J, Pan C, et al. (2013) Pituitary Stalk Interruption Syndrome in Chinese People: Clinical Characteristic Analysis of 55 Cases. PLoS ONE 8(1): e53579. doi:10.1371/journal.pone.0053579
10. Blethen SL 1996 Hypopituitarism. In: Lifshitz F, ed. Pediatric endocrinology. New York: Marcel Dekker, Inc; 19–23

Acquired Ptosis due to Ocular Cysticercosis : A Case Report

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INTRODUCTION

Cysticercosis is the most common parasitic disease of the nervous system. The disease occurs when humans become the intermediate host in the life cycle of Taenia solium by ingesting its eggs from contaminated food[1,2] . The most common sites of involvement of cysticercosis are soft tissue, eye and central nervous system. Unusual location of the cysts may result in uncommon manifestations mimicking a host of neurological disorders . Ocular cysticercosis can involve both the intraocular structures and extra ocular muscles. Extra ocular muscle cysticercosis is rare[3,4] . We are reporting the unusual manifestation of ptosis (LPS palsy) due to cysticercosis. The patient was successfully treated with systemic steroids and albendazole.

CASE DETAILS

A 8yr old, male child origin from Upper Assam district, Assam presented to pediatric medicine OPD of Assam Medical college with drooping of left eyelid from one month. The drooping of eyelid was not associated with pain and swelling. There was no history of fever, headache, and vomiting. There was no history of any weakness of limbs, deviation of mouth or slurring of speech and any trauma to eye and skull. There is no diurnal variation of the degree of ptosis and was not associated with weakness of any part of the body. To exclude congenital ptosis childhood photographs were asked for, which revealed ptosis of recent onset (figure 1).

On examination patient was conscious and oriented with stable vitals. Rest of general examination was normal. On Nervous system examination higher functions were normal. Ptosis of left eye was present (figure 2), with MRD1(Margin reflex distance) -1mm,MRD2-6mm and LPS excursion-4mm with intact bells phenomenon , with rest of the movements normal in both eye(figure1- 5). There was no conjunctival, redness, proptosis, or exophthalmos. Bilateral pupils were normal in size reacting to light and accommodation was normal. Fundus examination was normal. Other cranial nerves were intact and no neurodeficit was present. No signs of raised intracranial tension were noticed. A provisional diagnosis of acquired ptosis due to mechanical factor was made and evaluated.

FIGURE 1

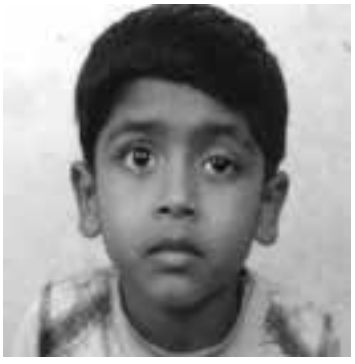

FIGURE 2
Ptosis of left eye

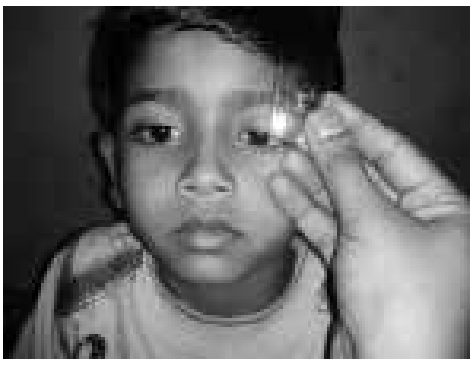

FIGURE 3
Margin reflex distance 1

FIGURE 4

LPS excursion

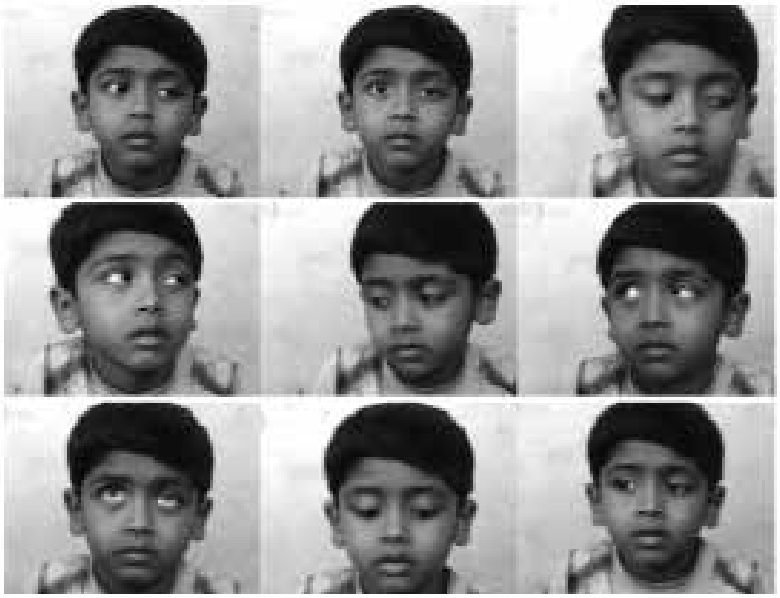

FIGURE 5

Normal extra ocular movements.

EVALUATIONS:

Routine investigations were normal. The orbital sonogram revealed a cystic lesion in the superior rectus muscle with an echogenic intramural nodule(fig-6) . So he was planned for an MRI scan of orbit and brain The magnetic resonance imaging of the orbit showed an intra-conal retro-orbital mass involving the LPS muscle of the left eye suggestive of ocular cysticercosis(fig-7). MRI brain revealed a ring enhancing lesion suggestive of neurocysticercosis in the right cerebellar hemisphere. The enzyme-linked immunosorbent assay for serum antibodies IgG against the cysticercosis was positive(-2.22 IU/ml). The ptosis improved with oral albendazole and oral steroids as per protocol . patient is put on oral carbamazapine 10mg/kg for a period of one year and albendazlole to continue for 28days. Child will undergo MRI after 6 months of therapy for complete recovery from infestation

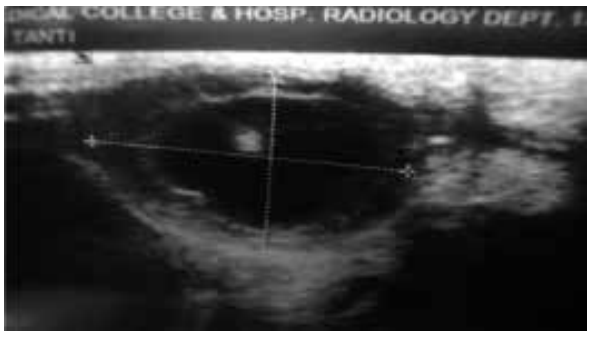

FIGURE 6

The orbital sonogram revealed a cystic lesion in the LPS muscle with an echogenic intramural nodule.

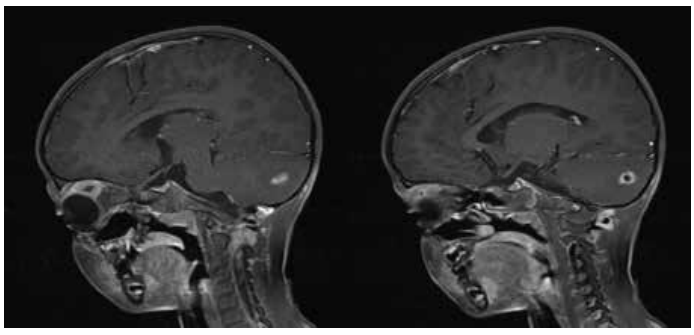

FIGURE 7

MRI shows parenchymal neurocysticercosis in colloidal vesicular stage involving right cerebellar hemisphere with orbital myocysticercosis invoving left superior rectus muscle near its insertion site inciting moderate inflammation.


Patient after 6 week MRD 1 (3mm)

DISCUSSION:

Cysticercosis is caused by haematogenous spread and encystment of the larval form of the swine tapeworm Taenia solium, in various body tissues. It is the most common parasitic disease of the central nervous system and also affects the eye, skeletal muscle, and subcutaneous tissue.

Soemmering et al. reported the first case of ocular cysticercosis in 18305 . Ocular manifestations may be devastating as the cysticercus enlarges. In the eye cysticerci may be situated intraocular or extra ocular. In India most common site of localization is orbit, whereas posterior segment involvement is more common in western people6. Cysticercosis can occur in vitreous body and sub retinal area but some may be found in the anterior chamber and subconjunctival parts . The most damaging location is intravitreal and subretinal location which leads to blindness in 3 to 5 years unless the parasite is removed.

It has been pointed out by Malik et al that the left eye is more commonly involved. Kundra et al has reported a unilateral ptosis due to cysticercosis in a 11 year old girl. Therefore, extraocular muscle cysticercosis should be considered in patients who present with restricted ocular motility and inflammatory signs or an acquired mechanical Ptosis7. The association of brain tissue cysticercosis is very rare with eye cysticercosis .

The treatment of ocular cysticercosis is conflicting. Where the intraocular cyst responds best by surgery, surgical removal of extraocular cysticercosis is fraught with complications. R Sihota et al evaluated the efficacy of oral albendazole in extraocular cysticercosis in the randomized clinical trial and reported a marked clinical respond in the patients . In our case patient was treated with systemic steroids and cysticidal therapy and the response was dramatic.

CONCLUSION:

In conclusion, a high index of suspicion for LPS myocysticercosis is needed for patients from endemic regions with acquired ptosis. Similar to cysticercosis of other extraocular muscles, orbital imaging is important in making this diagnosis. The resolution of ptosis appears favourable with medical therapy.

REFERENCES

1. Daniel Albert, Frederick Jakobiec, Nancy Robinson Principles & Practice of Ophthalmology, W.B. Saunders Co, copyright 1994; 462,1711 1751, 2308, 2319, 3073.
2. SJ Ryan. Ocular Cysticercosis Retina. 2nd ed. vol. 2. St. Louis (USA): C V Mosby and Co; 1994.
3. Malik SRK, Gupta AK, Chowdhary S. Ocular Cysticercosis. Am J Ophthalmol 1986; 66:1168–71.
4. Kundra R, Kundra SN. Uniocular ptosis due to cysticercosis of extra ocular muscle. Indian J Pediatr 2004; 71:181-2.
5. Kaliaperumal S, Rao VA, Parija SC. Cysticercosis of the eye in South India - a case series. Indian J Med Microbiol 2005; 23:227-30.
6. Sekhar GC, Lemke BN. Orbital cysticercosis. Ophthalmology 1997; 104:1599-604.
9. Pushker N, Bajaj MS, Betharia SM. Orbital and adnexal cysticercosis. Clin Experiment Ophthalmol 2002; 30:322-33.

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