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Editorial

GAPPD: Ending Preventable Child Deaths From Pneumonia And Diarrhoea By 2025

Currently, pneumonia and diarrhoea are the leading killers of children under the age of five, together accounting for 29% of all child deaths globally. Children are dying from these preventable diseases because of ineffective interventions across all communities.

The Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD) by WHO /UNICEF recognizes that prevention and control of pneumonia and diarrhoea cannot be adequately dealt with separately but only through integrated programmes. Working together, we can end preventable deaths of young children around the world from two of the leading child killers, pneumonia and diarrhoea. Current interventions need to be implemented - such as exclusive breastfeeding and good nutrition, hand washing, safe drinking water, zinc and oral rehydration solution, amoxicillin, vitamin A and vaccination - particularly for those most vulnerable and poorest.

Despite substantial progress, MDG4 can only be achieved through an intensified, integrated and sustained effort to reduce pneumonia and diarrhoea deaths. Three main indicators have been used to monitor child health under MDG 4: the under 5 mortality rate (U5MR), infant mortality rate (IMR), and the proportion of one year-old children immunized against measles. "Infant mortality rate (IMR), a measure of child survival, is considered to be one of the strongest indicators of a country's wellbeing, as it reflects social, economic and environmental conditions in which children (and others in society) live, including their health care." (Alderman & Behrman, 2004: vii) The millennium development goal 4 has only one target: "t**o reduce the under-five mortality rate by two-thirds in the period between 1990 and 2015".** Accordingly, a decrease in worldwide rate of mortality in children under-five by over 50 percent, reducing from 90 to 43 deaths per 1,000 live births between 1990 and 2015 has been achieved.

As it has now become the norm, at the end of the every 15 years, the global community under the cloak of the United Nations, comes together and formulates another 'to-do list' that should span over the next one and a half decades. So this time also on September 2015 the international community converged and approved a global agenda consisting of a series of 17 goals to be achieved before 2030.

The agenda, dubbed as **Sustainable Development Goals (SDGs)** takes over from the almost expired **Millennium Development Goals (MDGs)** that were drafted at the turn of the century. The goal of the newly released *Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea **(GAPPD)*** is to reduce deaths from pneumonia to fewer than 3 children per 1000 live births, and from diarrhea to less than 1 in 1000 by 2025.

Dr Santanu Bhakta
Editor in Chief

From the President's desk

Every year the EZAP holds the midterm CME and Executive Board meeting which provides a formal mechanism whereby Executive Body members of the academy provide input regarding academy policies and activities along with half a day of scientific seminar. It is a forum in which members can identify and advocate for policies and practices that they consider to be important for Children and Pediatricians.

The proceedings of the Executive Board meeting is extremely vibrant and dynamic and truly gives all members an opportunity to affect change and create meaningful policies for children and the profession.

I hope that you enjoy reading this edition of PEDI INFO newsletter and please share it with a colleague, patients or friend. We welcome all suggestions for articles in the next issue. It is an avenue of communication and for those who share the passion of caring for children and improving our care for children.

We are proud to bring the edition of PEDI INFO for all our esteemed members. Dr. S. Bhakta has put together another excellent edition which highlights important upcoming events and interesting articles of interest and qualitative research. As always in EZAP, we encourage members to become actively involved in the work and to suggest new ideas and projects that will advance pediatric innovation. Thank you all for your passion and dedication to EZAP and to children.
Long live IAP,
Long live EZAP

Dr.Debasish Das
President,EZAP 2016

Instructions for all State Branches :

Criteria for Selection of Awards

Criteria for IAP Pioneer Awards, Purbanchal:

Mandatory	(1)	Age not exceeding 55 years (Except the Organizing Secretary of EZ PEDICON who is an automatic)
Mandatory	(2)	IAP Membership No. (Central IAP)
Mandatory	(3)	Must be a member for at least 10 years of a State Branch of East Zone Academy of Pediatrics
Mandatory	(4)	Must have attended (Excluding own State) at least 3 East Zone PEDICON.
Mandatory	(5)	Application must be forwarded by State Branch IAP.
Mandatory	(6)	Any of the following criteria is mandatory
	(a)	Have involvement in IAP activities of the State (President, Vice President, Secretary, Treasurer, Jt. Secretary, Organizing Secretary of the State PEDICON, Editor at least for one term or Executive Board Member at least for 2 term)
	(b)	Have involvement in IAP East Zone activities (Office Bearer for at least one term and/ or Executive or Scientific Committee (any one member of IAP East Zone Coordination Committee at least for 2 terms)
	(c)	10 Published papers in medical journals.

Criteria for Shishu Vishesagya Shiromani Award, Purbanchal:

Mandatory (1) Age above 58 years and the gap from the Pioneer Award must be a minimum of 3 years.

Mandatory (2) Central IAP Membership for at least 15 years (IAP Membership Number)

Mandatory (3) Must be a member of IAP State Branch for 15 years.

Mandatory (4) Must have attended one IAP East Zone Conference outside their own State.

Mandatory (5) Any of the following Criteria is mandatory.

(a) Teaching experience of 20 years/Practicing Pediatricians for at least 25 years.

(b) Published 2 papers in Medical Journals of National, International, State level.

(c) Did outstanding research activities.

Other Rules

(1) If the person applied directly to the Secretary East Zone Academy of Pediatrics, who will send back the application to the Secretary of respective State Chapter and ask for his kind opinion, so that the grievance of State member comes in the eyes of the IAP State Secretary. But it is mandatory for the State Secretary to consider his name. State IAP Secretary should discuss the matter in his Executive Board and should send a comment to IAP East Zone Secretary.

(2) The number of Awards per state will be restricted according to the following:

a) Purbanchal Shishu Vishesagya Shiromani Award

One- if the membership strength is upto 500

Two-n if the membership strength crosses 500 marks

b) IAP Purbanchal Pioneer Award

One- if the membership strength is upto 500

Two-n if the membership strength crosses 500 marks

(3) The decision of East Zone Award Committee is Final. They are the main selective authority. They have the right to cancel any application even recommended by the State Branch. In that case the committee is bound to give the reason why they are not selecting the candidate.

(a) The Secretary of East Zone Academy of Pediatrics will circulate the form and notice of Awards to the Secretary of respective State by March 31st of each year.

(b) The Secretary of the State should circulate the form in their newsletter, Bulletin of Journals or should sent form to individual member. Application must be processed through the State Branch.

The Secretary of the State IAP should inform that the filled up form must come back by 31st March and he should call an Executive Board meeting and finalised the names and inform the East Zone Academy of Pediatrics latest by June 30th of that year.

(c) The Secretary of East Zone Academy of Pediatrics will be chairperson of the Award Committee.

The other members of Award Committee will comprise of

(i) President Elect

(ii) Imm. Past President

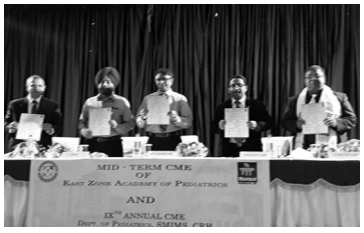
(iii) 2 Vice Presidents

Award paper session of post graduates in East Zone PEDICON:

1. This should be mandatory program in the IAP East Zone Annual Conference.
2. The organising secretary must invite award papers from post graduates in each brochure.
3. Postgraduates students of the subject Pediatric medicine, Pediatrics surgery, Social and Preventive Medicine can participate in this program. Postgraduates Students of other specialities of medicine can also participate if the topic of the paper is related to Child Health, Neonatology and Adolescence.
4. There must be minimum 3 prizes (i) the first prize will be given by IAP West Bengal Branch minimum prize money will be Rs 2000/-, a certificate and a memento are also be given either by the organiser or by the respective State Branch who is giving the prize money. (ii) The second Prize will be given in memory of Prof. B.N. Dasgupta and will be donated by IAP Jharkhand Branch or Dr. Manoranjan Sahay. The prize money will be Rs 1,500/-. A certificate and a memento are also to be given either by the organiser or by the respective State Branch who is giving the prize money. (iii) The third prize will be given by Dr. Ksh. Chourjit Singh, Imphal, Manipur, the prize money will be Rs 1,000/-. A certificate and a memento are also to be given either by the organiser or by the respective State Branch who is giving the prize money.

East Zone Mid Term CME 28 May 2016, Gangtok, Sikkim







Review Article

MRI of The Brain at Term Equivalent Age in Extremely Premature Neonates – To Scan or Not To Scan?

Tej Narayan, Nistha Kishore, Daizy NG, Rupa Mukherjee, S Dutta
SMIMS and CRH, Gangtok, Sikkim

Abstract
In the last decade, the role of magnetic resonance imaging (MRI) in neonatal care for prematurely born infants has rapidly expanded and evolved. Recent investigations addressed many of the practical issues pertaining to image acquisition and interpretation, enabling high-quality MR images to be obtained without sedating medications in preterm infants at any institution. Expanded application has demonstrated MRI providing superior ability to assess cerebral development and identify and define cerebral injury in comparison to other imaging modalities. Term equivalent MRI results have been shown to correlate with neurodevelopmental outcomes, providing improved predictive ability over other neuroimaging, clinical, or physical examination measures. Regular utilization of MRI in this population is fundamental to gaining the knowledge and expertise necessary for rational, accurate application .Ongoing experiences will continue to shape the nature and type of information available to clinicians and families using MRI, further refining its role as a routine element of neonatal care.

Introduction

In recent decades, survival rates for very preterm infants (born less than 30 weeks gestation) have improved dramatically due to advances in perinatal and neonatal care. In contrast to this improvement in mortality, long-term neurodevelopmental outcomes have not improved and remain problematic, with significant associated costs to individuals, families, and society[1-5] . In recent years, significant investigation has been undertaken correlating varied demographic, perinatal, medical, and physical examination finding with long -term neurodevelopmental outcomes in attempt to identify the infants at greatest risk.

Despite these efforts, clinicians and researchers continue to possess limited ability to definitily predict and meaningfully improve neurodevelopmental outcomes[6], with only significant abnormalities on cranial ultrasound (US) strongly predictive of poor neurodevelopmental outcome[7,8]. Application of magnetic resonance imaging (MRI) in this population has provided an improved ability to assess cerebral development, providing clinicians with a novel mechanism for identifying at-risk infants.

In recent years, MRI scanners have become increasingly available. Currently, the majority of high-level care facilities containing Neonatal Intensive Care Units (NICUs) also possess MRI scanners suitable for studying neonates. Increased utilization of these scanners has demonstrated that image acquisition is typically well tolerated by even the youngest and smallest patients. Additionally, scans can be performed successfully without the use of sedating medications, eliminating the risk associated with this procedure. Increased application in this group has permitted improvements in pulse sequences used to acquire images and enabled development of infant-specific head coils, improving the quality of the images obtained. Further, growing experience has provided neuro radiologists with necessary knowledge and tools for image interpretation, as population-specific

norms for sequences such as diffusion weighted imaging (DWI) and magnetic resonance spectroscopy (MRS) have been established[9-12]. As a result, most institutions now possess the ability to obtain high-quality MRI scans on prematurely-born infants at term equivalent (TE) age.

In the last 15 years, the role of MRI in neonatal care has been increasingly investigated by clinicians and researchers. As practical issues pertaining to image acquisition and interpretation have been more clearly determined, investigators have transitioned to defining the role of MRI in the clinical domain. Recent inquiries have demonstrated the potency of MRI as a diagnostic tool used to assess brain development and injury in this population[13-16].

Subsequent investigations have demonstrated MRI findings obtained on a routine clinical scan can also provide invaluable information regarding neurodevelopmental outcomes that can be utilized for dictating individualized care plans, counselling families, and ultimately improving outcomes in this high-risk group. As a result of these inquiries, a growing body of evidence supports routine use of MRI as a component of NICU clinical care for prematurely-born infants.

Practical Considerations Pertinent to MRI Acquisition in Preterm Infants

(a) Several practical issues must be considered when performing MRI scans in prematurely born Infant.

The time required to prepare each infant for the scan is approximately 30–60 minutes, and can be readily coordinated with individualized care and feeding plans for each infant by the NICU staff. Establishment of imaging protocols at several institutions has demonstrated a ready ability to obtain high-quality images in non-sedated infants, eliminating the risk and cost associated with this procedure. The equipment required to perform these studies is relatively limited, inexpensive, and commercially available, consisting of items such as ear protection, head stabilizing devices, and MRI-compatible cardiopulmonary monitoring equipment. Isolettes that can be taken into the MR suite can also be obtained, though these are not typically required for scanning TE prematurely-born infants.

(b) Guidelines published by Mathur have now been successfully utilized to safely obtain MRI scans without sedation on greater than 1000 gm prematurely born infants[17].

These practices are readily transferrable between institutions. The procedures detailed by Mathur were successfully implemented to perform non-sedated MRI scans in preterm infants at TE at another nearby institution[18]. This group was able to complete non-sedated MRI studies at a 94% success rate, with satisfactory image quality realized in more than 97% of attempts. Further, complication rates and time away from the NICU for scan acquisition were both significantly reduced when sedation was not used. Other institutions have also published results obtained from successfully scanning infants without sedation[19,20]. Most recently, Neubauer demonstrated the feasibility of performing MRI scans in non-sedated infants at an "inexperienced center"[21].

(c) Assessment of Cerebral Development and Injury Using MRI in Preterm Infants

When performed successfully, MRI provides non-invasive, high-resolution images of the entirety of cerebral anatomy obtainable in less than an hour. These images are superior in quality and more inclusive than those available using other commonly available imaging modalities, including US and computerized tomography (CT). Additionally, MRI does not present the same long-term risks to the developing brain associated with radiation exposure found with CT scans. Further, these scans can be performed serially throughout early development making longitudinal assessment feasible.

In recent years, MRI has been increasingly applied to characterize the patterns and timing of these, changes in prematurely-born infants in a manner previously available only through neuropathological investigations This work has produced detailed descriptions of normative folding patterns for infants, enabling quantification of these configurations.

Accurate assessment of cortical folding on TE studies provides an important marker for structural brain growth and maturation during this critical developmental period.

MRI also enables non-invasive assessment and characterization of myelination, another critical component of normative cerebral development. In typically developing brains, myelination involving the posterior limb of the internal capsule (PLIC) is first apparent on

MRI scans at around 36 to 38 weeks gestation, before expanding to incorporate other regions in a stereotyped pattern throughout early development[15,16]. It is often most readily identifiable on T1-weighted scans, but can also be identified on T2-weighted images (Figure 3). Evaluation of its presence and symmetry on TE MRI scans also provides insight into ongoing cerebral development. MRI is currently the only clinically available imaging modality that enables accurate assessment of these important developmental benchmarks. In addition to information on cerebral development, MRI also enables comprehensive assessment of brain injury, providing detailed information regarding injury type, location, extent, and timing. Recent application has served to re-establish normative values regarding frequency and severity for specific injury types in this population. In a large, multicenter trial, Kidokoro recently found that 33% of infants demonstrate cerebral injury on TE MRI scan, including 12% of infants with periventricular leukomalacia, 19% of infants with intraventricular hemorrhage, and 10% of infants with cerebellar hemorrhage.

(d) Correlation of MRI Findings with Neuro-developmental Outcome using TE Scans

Over the course of the last decade, multiple studies have demonstrated the utility of MRI scans as a tool for neurodevelopmental outcome prediction in prematurely-born infants. The predominance of these investigations correlated results from a TE MRI scan with neurodevelopmental outcomes in the first several years of life, though some groups have investigated more long-term outcomes. Importantly, these inquiries have demonstrated that MRI outperforms other neuroimaging, clinical, or physical examination measures for outcome prediction in this high-risk group. MRI's predictive ability has most commonly been contrasted with US, which has been demonstrated to have high specificity but low sensitivity[7,22,23]. In recent years, improvements in image quality, growing experience with image interpretation and development and institution of new tools for image assessment, have continued to widen this gap, increasing the predictive potency of these scans.

Early application of MRI as an outcome prediction tool correlated qualitative assessments of scan results with neurodevelopmental outcomes. In one of the earliest investigations of this type, Valkama correlated results from a TE scan with 18 month outcomes, demonstrating 100% sensitivity (improved from 67% with US for the same cohort) and 79% specificity for subsequent motor impairment or diagnosis of cerebral palsy , based upon qualitive assessmentof MRIscans[24].

Conclusion

Recent practices have demonstrated that high-quality MRI scans can be safely and routinely performed in prematurely-born infants at TE without sedating medications at any institution.

Over the last decade, the role of MRI in NICUs has rapidly expanded. Growing experience applying the technique to study this population has provided invaluable lessons for clinicians, most prominently that MRI is highly effective with routine implementation. The knowledge gained through regular use of MRI translates to enhanced skill necessary for appropriate acquisition and interpretation of the imaging studies by a multidisciplinary group of health care providers. Ultimately, this information can be translated to identify high-risk infants, allowing implementation of interventions designed to improve neurodevelopmental outcomes via development of targeted, cost-effective health care plans initiated during the NICU course and continued following discharge. In the coming years, ongoing experiences will continue to shape the nature and type of clinical information available to clinicians and families from a single MR scanning session, further solidifying its role as a routine and necessary component of NICU care .

Key Points

1. High-quality magnetic resonance imaging (MRI) studies can be performed without sedating medications in term equivalent prematurely-born infants at any institution.
2. Term equivalent MRI scans provide invaluable information regarding brain injury and development. Results can also be utilized as an effective tool for neurodevelopmental outcome prediction.
3. Term equivalent MRI scans should be considered a routine component of NICU care for prematurely-born infants. Regular utilization is fundamental to gaining the knowledge and expertise necessary for rational, accurate application.*Smyser et al.*

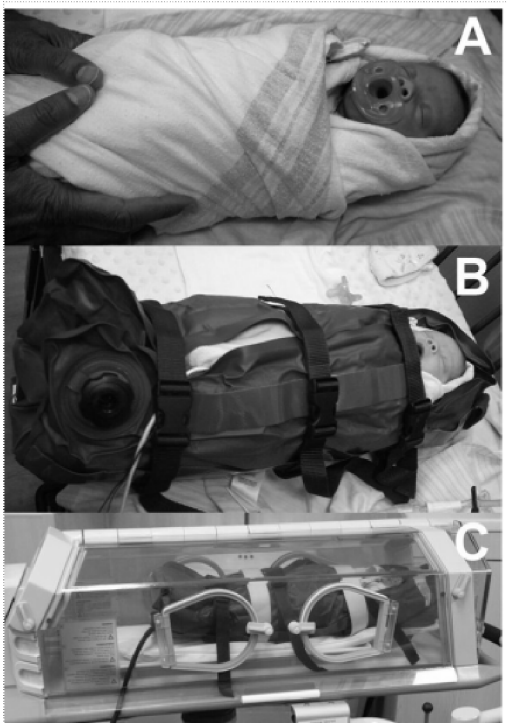


Figure 1. Procedures for preparing infant for non-sedated MRI scan

Procedures for preparing infants prior to placement in the MRI scanner includes A) snuggly wrapping the infant prior to placement in the vacuum bag; B) securing the infant in the stabilizing vacuum bag; C) placing the stabilized infant in the MR-compatible isolette for movement into the scanner.

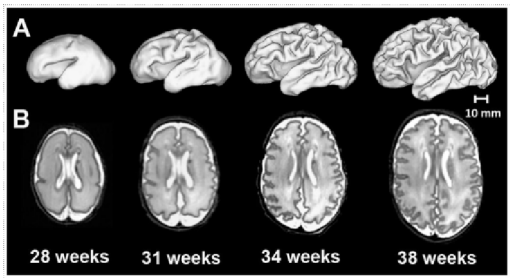


Figure 2. Development of cortical folding in the premature human brain

Representative A) 3-dimensional surfaces and B) axial T2-weighted images illustrating regionally-specific cortical folding occurring in the premature brain secondary to sulcation and gyration throughout early development. Provided are images obtained from a single preterm infant from MRI scans performed at 28, 31, 34, and 38 weeks post-mentrual age. Note the marked increase in brain size and folding complexity between each set of images.

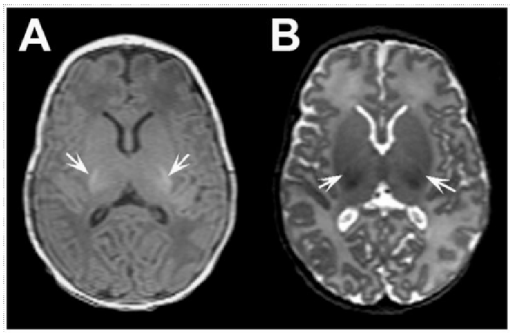


Figure 3. Myelination of the posterior limb of the internal capsule

Representative axial A) T1- and B) T2-weighted MR images from a very preterm infant at term equivalent age demonstrating myelination evident in the the posterior limb of the internal capsule bilaterally. Note myelinated white matter appears hyperintense on T1- weighted images and hypointense on T2-weighted images (arrows).

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Announcement

Review Article

Atopic March – From Skin to The Airways

Rashna Dass Hazarika
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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 know in depth about this concept for understanding the natural history of these allergic conditions as well as for appropriate management. The risk of developing 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]. In 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 rhinitis 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 influence of eczema on the development of asthma from childhood to adult life and found that childhood eczema was significantly 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 processed by the Langerhans cells and then they migrate to draining lymph nodes and interact 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. Similarly one must treat the asthmatics aggressively with inhaled bronchodilators and inhaled steroids wherever the situation demands.

Treatment of Atopic March:

This essentially covers the treatment of three different organs i.e., the skin, nose and the chest. In most patients there would be an overlap of symptoms and would require medications targeting more than one organ system involvement.

A. Management of Atopic Dermatitis – Effective treatment of eczema is a key factor in the prevention of future AR or asthma. Therefore the skin should be managed aggressively. However one has to explain to the parents and the children that there is no permanent cure of AD. The aggresive management is necessary to prevent worsening, reduce and eliminate itching, reduce emotional stress, prevent infections and thickening of the affected skin. Scientific evidence has graded the therapies which can be used in AD. As per the recommendations of the American Family Physician (table 1), the main stay of therapy remains the use of emollients or moisturizers. Liberal use of such methods as wet dressings and creams, lotions, emollients and oils is advised. The main idea is to keep the skin fully hydrated. Oils may be applied before a bath. Normal or lukewarm water should be used for bathing as hot water baths tend to wash off the natural oil layer on the body. After bath and before drying an emollient must be applied all over the body on wet skin followed by pat drying of the skin. Liberal use of moisturizers should be done at least twice a day or more especially in the dry winter season. Lotions are used over large body areas and areas with hairs. Creams

can be used for more dry areas. Topical steroids remain the first line of therapy with AD flare ups. Various formulations are available but one has to choose the appropriate steroid as systemic absorption varies in different areas of the body. For example the rate of absorption is about 7% from the face, 30% from the eyelids and genitalia, 1% from the forearms and palm and 0.05% from the soles. So one has to choose wisely as prolonged use of a potent steroid on the face, genitalia or eyelids may cause significant systemic side effects. The dictum generally followed for topical steroid use is to use less potent steroids such as hydrocortisone or desonide for the eyelids and genitalia, high potent steroids like betamethasone in the soles and the rest of the areas one can use moderately potent steroids such as mometasone or fluticasone. On the face the steroid preparation is to be used mixed in equal proportion with a moisturizer cream and applied twice a day for about 5 to 7 days. Once the lesions improve the steroid preparation is stopped and only the moisturizer cream is continued as a preventive medication. The appropriate dose of steroid is about 5 gms per application on a specified area and it is equivalent to one fingertip of the medication. Steroid ointments are used when one desires more effect whereas a cream is preferred for large areas and humid climate. Lotions are used in hairy areas. Regular antihistamines is generally not recommended in AD. The only anti-histamine that is sometimes used and recommended s hydroxyzine in those patients who have a sleep disturbance due to itching as this helps to break the pruritis cycle. A 5 day course is usually sufficient to alleviate the symptoms. Antibiotics are only useful if there is an associated infection or there is a flare up which has not responded to the usual treatment. Staphylococcus aureus and Streptococci are the most common bacterial infections associated with AD and usually respond well to topical antibiotics. Topical calcineurin inhibitors like tacrolimus and pimecrolimus are used as a second line therapy and act by blocking T cell activation in the skin. Both have been found to be safe in infants and children and act as a steroid sparing agent. Other measures for skin care include use of mild soaps or soap free cleansers with a pH near to that of the skin (pH 5.5) and avoidance of irritants such as woollen clothing in winters and tight garments.

Table 1: American Family Physician recommendations of treatment for AD with rating of grade of evidence.

Therapy	Grading
Emollients are the mainstay of maintenance therapy for atopic dermatitis (Moisturize)	B
Topical corticosteroids should be first-line treatments for patients with atopic dermatitis flare-ups	A
Sedating antihistamines are indicated for the treatment of atopic dermatitis when patients have sleep disturbances and concomitant allergic conditions	A
Antibiotics should be reserved for the treatment of acutely infected lesions associated with atopic dermatitis	A
Topical calcineurin inhibitors should be second-line treatments for atopic dermatitis flare-ups and maintenance	A

B. Treatment of Allergic Rhinitis – The nose is said to be the accessible part of the lung. AR treatment has two components - environmental control and medications. Environmental control consists of reducing the outdoor pollutant exposure, avoidance of passive smoking, use of cleaner fuels for cooking, improved ventilation of houses, avoidance of overcrowding, sun drying of all beddings and upholstery, control of cockroaches in the house and eating more traditional foods (avoidance of artificial preservatives and colours). As in asthma a step ladder treatment approach is used for AR. Nasal decongestant can be used but only for a short duration as it leads to rebound inflammation on stoppage. Oral second generation non-sedating anti-histamines like

fexofenadine and levocetrizine are preferred esp. in adolescents and school going children. Of these two levocetrizine is the preferred drug if it does not cause any sedation. There are ample studies to demonstrate that levocetrizine use in AR prevents the progression of the disease to asthma and the effect of a course of levocetrizine is seen to last for more than 18 months even after stoppage of the drug. Intranasal antihistamines such as azelastine (0.15%) nasal spray (> 5 years of age) or 0.6% olopatadine nasal spray (> 6 years of age) can be used in those in those children with severe nasal itching and runny nose. The most efficacious medication is intranasal steroid sprays. The effect starts in 6-8 hours and peaks in 2 weeks. Intranasal steroid sprays improves the quality of life significantly by relieving the nasal blockade and reducing the nasal secretions. These can be used on a long term basis without the fear of atrophy or systemic side effects. The choice of intranasal steroids depends on the receptor affinity and systemic bioavailability of the drug and based on these factors both mometasone and fluticasone are found to have minimal systemic bioavailability and highest receptor affinity and hence the preferred choices. Intranasal cromones are of not much use. The second drug which can be added on for treatment of AR is montelukast. It is particularly effective when the AR is associated with co-morbid conditions such as asthma and urticaria. The minimum recommended duration is for 3 months. Saline nasal spray (iso or hypertonic) are useful for regular cleaning of the nose. This should be particularly used before using the steroid nasal spray as it helps to remove the mucus layer and facilitates for better penetration of the steroids in the nasal mucosae. Immunotherapy has a definite role and in the current understanding of things, they are used only in the difficult or recalcitrant cases of AR. Here also the preferred route of administration is sublingual and not subcutaneous. There is no role of cough syrups containing a bronchodilator and antihistamine in a case of AR or asthma.

C. Treatment of asthma – The treatment depends on the severity of the illness. Inhaled bronchodilators and steroids form the cornerstone of therapy. All cases from mild persistent to severe persistent illness warrant a course of inhaled steroids. Inhaled bronchodilators use is need based. In addition to inhaled medications, one has to actively look for the presence of AR or AD and treat these conditions aggressively. Home based peak flow meter monitoring is a good way to asses control.

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.

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Approach to Lower GI Bleed in Children

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Lower GI bleed (LGIB) in children is as common as upper GI bleed (UGIB) when compared with adults where the later is more common. The spectrum of LGIB varies from minor bleeds caused by anal fissures to life threatening massive bleeds caused by vascular malformations. The morbidity and mortality associated with LGIB still remains as high as in case of UGIB and hence equal importance needs to be given to lower GI bleed like upper GI bleeds. Children with LGIB mainly present to pediatric emergency room(ER) which creates panic among the parents or caretakers irrespective of severity. In 1990, a study from Boston hospital ER documented 0.3% of all presentation to pediatric emergencies as LGIB. Apt skillful and timely intervention is usually life saving in such cases.

Definitions

Lower GI bleed is defined as any bleeding that happens from below the ligament of Treitz which is the junction between foregut and midgut.So the location can be from jejunum, ileum, colon and anorectal region.

Acute lower GI bleed: Active bleeding occurring less than 72 hours which may be accompanied by shock, pallor, altered sensorium or requiring blood transfusions[1].

Severe bleeding: Bleeding that continues for more than 24 hours, requiring two or more packed cells, or a decrease in hematocrit of 20 % or more.

Recurrent bleeding: Happens after 24 hours of stability defined as further need for transfusion, further drop of hematocrit by 20 % or readmission of LGIB within one week of discharge.

Hematochezia:

Two schools of thought are there. It can be either a bleeding that is fresh and originating from rectum or left colon, or a maroon color stools from proximal colon or small intestine. Although usually of colonic origin, rarely it can be seen in massive upper GI bleed which is associated with or without rapid intestinal transit.

Melena:

Black tarry sticky stools which is a product of acid hematin and is usually seen in upper GI bleed.It can be seen in bleeding from proximal colon and small bowel (duodenum, jejunum and ileum) lesions.

Occult GI bleed:

No visible blood in stool and patient presents with pallor and features of chronic iron deficiency.Stool occult blood will be positive.

Obscure GI bleed:

Inspite of extensive investigations, the location or etiology of bleed cannot be localized in the intestines.

The fresh bleeding per rectum can be small or massive. The blood is usually fresh and bright red and is due to bleeding from left colon and rectum.

Epidemiology

All age groups are affected by LGIB with varying etiology and severity. In a large nationwide survey, majority patients belonged to mid and late adolescent age or toddler age groups (78%). Taking in to account of all the causes of LGIB, the commonest causes includes anal fissures, polyps, infections and vascular malformations. LGIB in children is known to recur in 10 to 20% cases. Inspite of advances in early diagnosis and treatment modalities, still the mortality ranges from 0.5% to 5%[2]. Occurrence of LGIB as a part of the spectrum of generalized bleeding or coagulation disorders should also not be forgotten.

Clinical course

Even though the LGIB is less severe than UGIB, pediatric patients can deteriorate faster. The most important parameters indicating severity includes hemodynamic instability after one hour of stabilization, gross blood on rectal examination and hematocrit less than 35%. The clinical features depends on the underlying etiological factor responsible for bleeding. History taking is very important. Important points to take focused history to give clue to the diagnosis of underlying conditions are given in table1. The focused examination is given in table 2. There are many masqueraders of LGIB which if not detected can create unnecessary panic, investigations or interventions. Fresh bleed like symptoms can occur after intake of beet roots, fresh fruits, meat fibers, flavored gelatin, bismuth, red licorice, and antibiotics like Rifampicin and Ampicillin whereas black stools can be due to ingestion of iron, black grapes or blackberry. Only reassurance is needed in such cases.

Etiologies

Various etiologies of LGIB in children are given in table 3 and further classification of commonly encountered causes as per age groups and severity has been given in table 4. Brief account of common causes of bleed are discussed.

Anal fissure

One of the commonest causes of painful LGIB in children[3], fissure can be nightmare for both the child and the parent. The child has a long history of severe constipation with prolonged toilet sitting time and fear to pass stools. Sometimes, it is noted by the parents. Management is adequate treatment of constipation, lignocaine jelly for topical application and sitz bath for 2 weeks.

Solitary Rectal Ulcer Syndrome (SRUS)

SRUS is another cause for painful LGIB in children. There is often history of mucus in stools, tenesmus,

Table 1 : Focused history giving clue to the diagnosis

Constipation	Fissure, SRUS, Stercoral ulcer
Mass per rectum / anorectal area	Polyps, varices , rectal prolapse, fistula
Fever, pain abdomen, mucus/blood with stools	Colitis Infections: Dysentery/tuberculosis/amebiasis Inflammatory: Ulcerative colitis, Crohn's colitis, radiation colitis
Red currant jelly stools	Intussusception
Jaundice, stigma of cirrhosis	Rectal varices/hemorrhoids
Drug intake	NSAIDs induced bleed
Generalised bleed	Coagulopathy or thrombocytopenia
Pain abdomen , joint pains, rashes	Vasculitis (including HSP)
Skin lesions	Vascular malformations
Allergy and atopy	CMPA or Eosinophilic colitis
Family history	Polyposis coli, colon cancer, liver diseases, bleeding disorders

Table 2: Focused examination of the patient

HEENT area	
Icterus	Chronic liver disease (portal hypertension)
Telangiectaisa	Osler Rendu Weber syndrome
Oral Pigmentation	Peutz Jegher Syndrome
Petechiae	Bleeding disorders
Osteoma	Gardner syndrome
Trauma	
Abdomen	
Tenderness	Colitis
Lump	Volvulous , duplication cysts, Intussusception, tumors
Hepatosplenomegaly, dilated veins	Cirrhosis portal hypertension
Congenital heart disease	Vascular malformations(eg Heyde's syndrome)
Dysmorphism	Syndromic : Turner, Noonan, Klippel trenauny
Skin	
Hemangioma	GI hemangiomas
Telangiectaisa	Osler Rendu Weber syndrome
Erythema nodosum, pyoderma gangrenosum, clubbing	Crohn's disease/Ulcerative colitis
Acral pigmentation	Peutz Jegher's syndrome, Cronkite Canada syndrome
Lipoma, osteoma	Gardner's syndrome
Hemihypertrophy	Macrocephaly with capillary malformation Phakomatosis pigmentii vascularis type 2

Table 3 : Etiology of LGIB

Infections	
Bacterial	Salmonella, Shigella, Campylobacter, Yersinia, C.Difficile, Aeromonas, Enterohemorrhagic E.Coli, tuberculosis
Parasitic	Entamoeba, Necator americanus, Strongyloides, Ascaris lumbricoids
Viral	Adenovirus, CMV, HIV, Rotavirus
Fungal	Candida sp.
Inflammatory	IBD, lymphonodular hyperplasia, , eosinophilic gastrointestinal disorders, vasculitis, graft versus host disease, radiation enteritis, anastomotic ulcers, primary immune deficiency related eg: chronic granulomatous disease necrotizing enterocolitis
Polyps	Juvenile polyps or Familial (eg:Peutz Jegher's, FAP)
Neoplastic	Leiomyoma, Kaposi Sarcoma, lymphoma, carcinoid, adenocarcinoma
Trauma	Anal fissure, foreign body, sexual abuse
Congenital & Vascular	Meckel's diverticulum, duplication cysts, volvulous, arteriovenous malformations, Hirschsprung enterocolitis, hemorrhoids, telangiectasia, rectal varices
Miscellaneous	Massive upper GI bleeding, NSAID induced ulcers, intussusception, SRUS, coagulopathy, thrombocytopenia, hemolytic uremic syndrome

Table 4: Age and severity wise classification:

Severity	Infant	Child	Adolescent
Mild	Anal fissure Dietary protein allergy (CMPA) Vitamin K deficiency Lymphoid nodular Hyperplasia Perianal excoriation Rectal prolapse Intussusception	Anal fissure Infectious colitis Polyp: Juvenile or syndromic IBD SRUS Intussusception	Infectious colitis Anal fissure Hemorrhoids SRUS Koch's Amebiasis Eosinophilic Strongyloides Radiation colitis
Moderate/Severe	Necrotizing enterocolitis Hirschsprung enterocolitis Malrotation with volvulus Duplication cyst Vascular malformation Meckel's diverticulum	Meckel's diverticulum Henoch-Schonlein purpura Hemolytic uremic syndrome Duplication cyst Vascular malformation Intussusception Typhlitis/neutropenic colitis Dieulafoy lesion	NSAID enteropathy IBD Vascular malformation Meckel's Diverticulum

perianal pain and prolonged straining and toilet sitting time. The genesis is secondary to ischemia caused by a asynchrony between the contraction of pelvic floor and external anal sphincter[4]. The typical location is in the anterior rectal wall 5 to 10 cm from the anal verge. Endoscopic findings can vary from normal to mucosal nodularity, hyperemia, and pallor to frank ulcerations. Multiple biopsies are often required for making the diagnosis. Histology is the gold standard for diagnosis and shows intercrypt smooth muscle proliferation and fibro muscular obliteration. Cognitive behavioral therapy, mesalamine, steroids, laxatives, sucralfate enema, endoscopic steroid injection or argon laser photocoagulation are various modalities of treatment depending on the severity[4].

Colitis

Infectious causes include Campylobacter, Shigella, Salmonella (including Enteric fever), *E coli*, *C. difficile*, Yersiniosis which commonly presents with constitutional symptoms and responds promptly to antibiotic therapy. Amebic colitis is a very common condition in the tropics but uncommon in children. Tuberculous ulcers are usually transverse as they follow the path of colonic lymphatics. They bleed less as the ulcer base has obliterative endarteritis. Among the viruses CMV causes notorious bleeds in immunocompromised children and is an important cause for exacerbation of IBD. The ulcers are either diffuse or large > 1cm, discrete and oval. Histopathological examination shows typical Warthin Finkeldy giant cells with inclusions. Other rare infectious causes include Histoplasma, Atypical mycobacteria, Aeromonas, and Strongyloides.

Inflammatory bowel disease (IBD)

Both Crohn's disease (CD) and ulcerative colitis(UC) are known to present with LGIB and in cases of earlier onset IBD defined as onset in age < 6 years, both have an overlapping feature. Pain abdomen is a dominant feature of CD seen in more than 60 % cases. Colonoscopy shows geographic ulcers, cobblestoning, skip lesions, rectal sparing in CD[5] whereas a diffuse

colitis in form of friability and bleeding is more seen with UC[6]. Immunosuppressants including steroids or biologicals are main front in therapy .Mimickers of IBD in children include Chronic granulomatous disorder(CGD), Bechets disease and many of the primary immune deficiencies including autoimmune enteropathy(IPEX syndrome), Autoimmune lymphoproliferative syndrome type 2 etc. which may present with colitis.

Vasculitis

Vasculitis may present with LGIB in children. Henoch Schonlein Purpura(HSP) is known to cause bleed secondary to intusucception or apart from that. Abdominal pain, joint pains and purpura of dependant areas, orchitis are the usual accompaniments. Other vasculites known to cause LGIB includes poly arteritis nodosa(PAN), Churg Strauss syndrome and SLE. Kawasaki syndrome is an unfortunately under diagnosed clinical condition which can rarely manifest with LGIB. Kawasaki syndrome has been associated with most protean GI manifestations including perforations, intestinal obstruction, neonatal hepatitis etc. IVIg is life saving if diagnosed accurately and treated on time.

Stercoral ulcer

Is an unfortunate manifestation in a child with constipation. It is due to pressure necrosis of the less vascular rectosigmoid area and chronic fecal impaction. This causes ischemia, pain abdomen and hematochizia. Endoscopic hemostasis needs to be done on majority of the cases[7].

Drug induced

NSAIDs are notorious to cause UGIB as well as LGIB.It acts by inhibiting the prostaglandin synthesis and inducing microcirculatory changes. Chemotherapeuic agents can causes LGIB by causing mucositis. Methotrexte is the prototype example.

Cow's milk protein allergy (CMPA)

One of the commonest causes of mild LGIB in infants and children less than 3 years of age. The type 4 hypersensitivity is responsible for the colitis part and manifests as bleeding per rectum anytime under 6 months of age. Stopping of milk and milk products rapidly brings clinical response. At times, stoppage of intake of milk and milk products by the mother is needed in 10% cases. Rectal biopsy is diagnostic which shows eosinophil > 6/ hpf or eosinophilic abscesses. Rare cases of CMPA associated with thrombocytopenia are described in literature.

Eosinophilic colitis

The mucosal type of eosinophilic colitis presents with LGIB and there can be involvement of esophagus, stomach and small bowel. Etiology is not well understood but food allergy and atopy are seen in atleast 1/3 of the cases.

Nodular lymphoid hyperplasia

Occurs commonly secondary to viral infections or food allergies . This condition commonly causes a mild LGIB. It is associated with IgA deficiency and Common variable immunodeficiency.

Meckel's diverticulum

It is a common cause of moderate to massive painless LGIB in infants and young children < 2 years of age. It causes bleeding due to ulceration of ectopic gastric mucosa[8].It can undergo torsion and can be a lead point for intussusceptions. Diverticulitis is also a known complication.Techninium-99 pertechnate scan detects the ectopic gastric mucosa in the anomaly and is useful for diagnosis. Treatment is surgical resection.

Intussusception

Common cause of pain and LGIB in children usually less than 3 years. There can be red currant jelly stools due to the sloughing of necrosed tip of intusucceptum.A pathological lead point is common in older children in the form of lymphoid hyperplasia, polyps or tumors. Abdominal examination shows an empty RIF known as sign de dance. Ultrasound shows a target sign or a pseudokidney sign. Air or barium reduction and surgery

in selective cases are different modes of therapy. Recurrences are common.

Vascular malformations

Hemagiomas, telangiectasia, arteriovenous fistulas and angiodysplasias are different vascular malformations seen in the colon. Syndromes associated with these include Turner, Noonan, Klippel Trenauny Weber, Osler Rendu Weber, Blue rubber bleb nevus, macrocephaly with capillary malformation syndrome. They classicaly present with recurrent episodes of significant LGIB. Endoscopy is diagnostic and intervention in the same sitting is often needed.

Polyps

Common cause of LGIB in children. Commonest are juvenile polyps which are hamartomatous and commonest location is the rectosigmoid region (90%). Bleeding usually occurs from the mucosal erosion but can be severe in case of auto amputation as it originates from the stalk which has a vascular pedicle attached to the mucosa. Endoscopic polypectomy is curative. Recurrences are known in 5% cases. Polyposis associated syndromes include Juvenile polyposis syndrome, Puetz Jegher's syndrome, Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, Familial adenomatous polyposis syndrome[9]. Some of these conditions have a malignant potential. A polyp can be a lead point for intussusception also.

MISC of LGIB include duplication cyst (communicating type), hemolytic uremic syndrome, hemorrhoids, rectal varices, radiation colitis, graft versus host disease, Hirschsprung disease associated enterocolitis, Dieulafoy lesion of small bowel or rectum, streptococcal proctitis, malignancies like lymphomas and Kaposi sarcoma, child abuse, coagulation disorders, bleeding disorders like Von Willebrand's disease or idiopathic thrombocytopenic purpura, Munchausen syndrome by proxy, anastomotic ulcers and massive UGIB. In newborns always consider vitamin K deficiency, necrotizing enterocolitis and thrombocytopenia as upfront causes of LGIB.

Investigations and approach to a child with LGIB

Hemoglobin with PCV for severity of the bleed, stigma of iron deficiency anemia as in chronic blood loss with indices and peripheral blood film, thrombocytopenia as a cause of bleed, leukocytosis in infection, inflammation and acute blood loss, coagulation parameters, eosinophilia and raised Ig E in eosinophilic disorders, stool for occult blood in occult GI bleed, calprotectin in infection and inflammation, and stool culture for infectious colitis. HIV should be done in clinically suspected cases and before elective intervention along with other viral markers.

An approach to a child with significant LGIB is given in Algorithm 1.

Endoscopy:

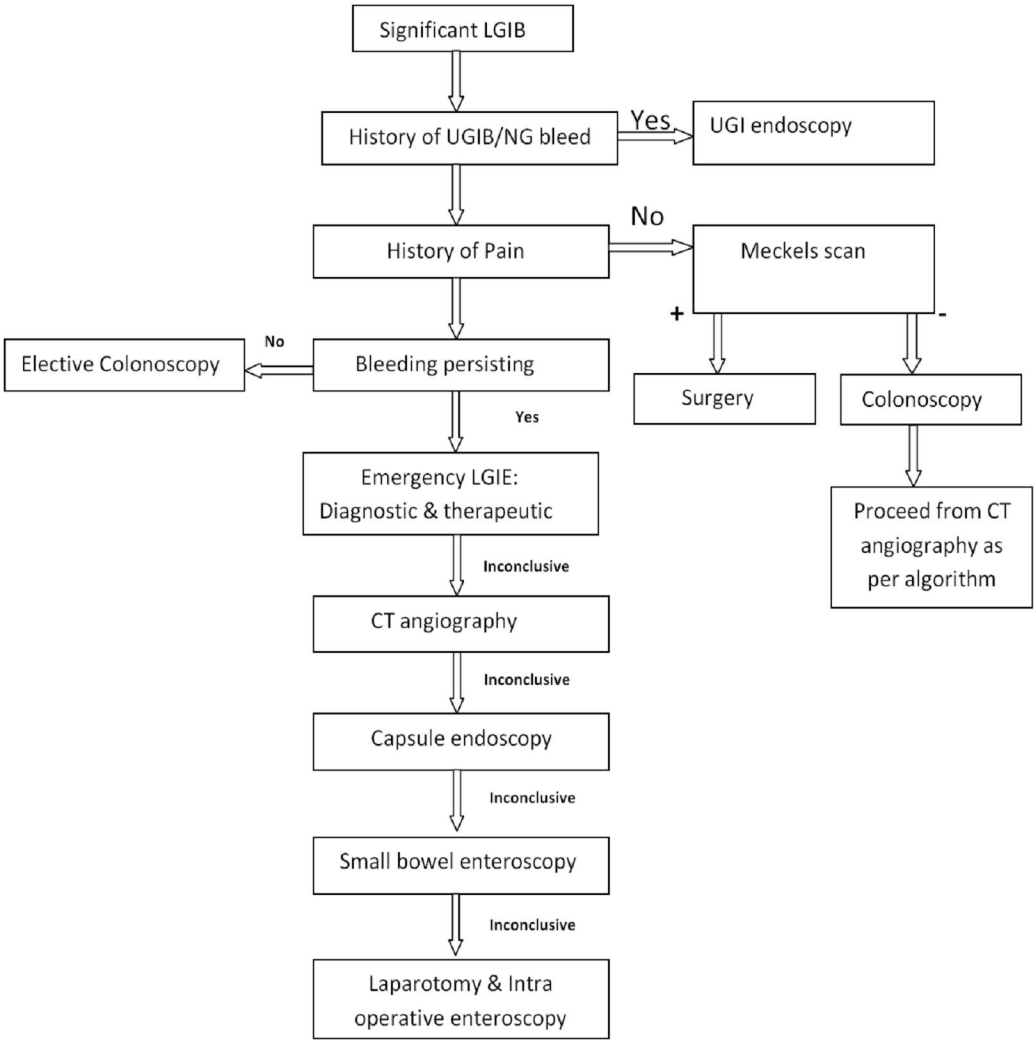
Endoscopy is the corner stone investigation in the diagnosis of GI bleed of which the two modalities being upper GI endoscopy and colonoscopy. The UGIE scopy should be considered first if there is moderate to massive LGIB, or any blood in aspirate by nasogastric tube. Sigmoidoscopy has a very important role for diagnosing a source in left colon but total colonoscopy with ileoscopy is always superior. If both UGIE and colonoscopy are found to be normal, the bleeding may be originating from the small bowel. Many conditions have typical endoscopic picture like SRUS, polyps, Crohns disease, tuberculosis, ulcerative colitis etc which can be biopsied and meticulous investigations can be provided further as per the necessity. Endoscopy has therapeutic value in conditions like polyps and vascular malformations.

Tc99 based RBC scan

Uses Tc 99 labelled RBC s to localize the bleed and serial scintigraphy is used to collect focal collection radiolabelled material. It can detect a bleed as slow as 0.04ml/min. It is useful only if an early scan is positive for RBC extravasations i.e from 30 min to 4 hours in which accuracy rate can be even upto 78%. But false positive localization is seen if transit of luminal blood is fast.

99 Technetium pertechnate scan

Useful to detect ectopic gastric mucosa in Meckels



Algorithm 1 : Approach to significant LGIB in a child

diverticulum and communicating duplication cysts.It will detect the ectopic gastric mucosa in 60 % cases but can be false negative in upto 40% cases[10].It can be used as the first modality before endoscopy in infants or toddlers presenting with a significant painless LGIB with especially maroon colored stools for the diagnosis of an ectopic gastric mucosa in a Meckel's divertivculum or a duplication cyst.

Plain X-ray abdomen

Pneumatosis intestinalis of necrotising enterocolitis and volvulous can be detected in a new born. Other conditions like fecolith, free air under diaphragm, features of subacute intestinal obstruction, mesenteric ischemia(thumb printing) and calcified lymph nodes (in Kochs) may be seen.

Ultrasound abdomen

It's a useful modality for detecting conditions like Intussusception which shows a classical target sign (also called bulls eye or coiled spring sign) or a pseudokidney sign. It can also detect duplication cysts in the lower GI tract which may bleed secondary to luminal communication.USG can also show inflammatory bowel pathology, strictures, vascular malformations in liver, spleen and other intra abdominal viscera.

CT and MR angiography

These have superseded conventional angiography as an important tool in the diagnosis of LGIB.CT angiography can be done in an emergency basis without sedating the child and also gives a faster result. The sensitivity of CT angiography is around 90 % and specificity is 99-100% making it a brilliant diagnosing modality[11].But the utility in an obscure GI bleed is only 50 %.MRA has advantage because it doesn't use radiation but requires sedation of the child and is time consuming. So it is not useful as an emergency procedure. MRA is useful more in bleed associated with inflammatory pathologies like IBD, polyposis and tumors[12].

Conventional angiography

This detects bleeding if the rate is more than 0.5ml/min. Various studies report a result varying from 12 to 70 %.Complications are seen in about 1 to 3 % cases including femoral artery thrombosis, hematoma formation, bowel ischemia and acute kidney injury. It may not detect the specific lesion causing the bleed. The major advantage is embolisation can be performed to control some of the actively bleeding lesions.

Contrast Enema

Air, hydrostatic or barium is used as contrast in cases of suspected Intussusception in which this can be both diagnostic and therapeutic. Least complication is seen with air as barium can cause radiation exposure and perforation with peritonitis and hence adhesions. Hydrostatic enema can cause dyselectrolytemia. Any of the above agents are strictly contraindicated in cases of suspected perforation.

Wireless Capsule Endoscopy (WCE):

Has revolutionized medical science in the diagnosis of LGIB especially the occult GI bleed (OGIB). The device is a camera pill that that transmits the images of the whole intestine over a period of over 8 hours which is recorded by a device worn externally and can be retrieved in to a computer with the help of a specialized program. The most common indication for WCE in young children is OGIB which can be secondary to ulcers, duplication cysts, polyps, vascular malformations, or even a Meckel's diverticulum[13]. The sensitivity to detect OGIB is upto 60 %. It should not be the first line in investigating a child with chronic inflammatory pathology like Crohns, Koch's or Chronic granulomatous disease as there is a high chance of hold up at stricture site. It is never an alternative to endoscopy and the biggest disadvantage is the cost factor in developing countries.

Small bowel enteroscopy

Is used when the above mentioned modalities fail. Different techniques used are push enteroscopy, balloon enteroscopy (single or double balloon) or a spiral enteroscopy. The best approach could be a combined transoral and a transanal approach.The diagnostic yield is around 80% in cases of OGIB and when combined with a WCE, this can reach upto 95%.Inconclusive cases may require an xploratory laparotomy with 'running the bowel' to detect mass lesions and subsequent enteroscopy on table to detect the pathology. In such cases a diagnostic yield can reach upto even 95%.

Management

Parents of children irrespective of the severity of LGIB presents in intense panic and anxiety as a mere sight of blood in stool is regarded as an alarming symptom. Majority of cases of LGIB in contrast to UGIB can be managed on OPD basis and counseling of parents is of utmost importance. In case of a moderate to severe bleed,

the child should be inserted with two wide bore cannulas one for sampling to look for electrolytes, BUN, blood gas analysis, hemoglobin, platelet and coagulation parameters. Immediate crystalloid solution should be started at 20ml/kg rapid run upto a maximum of 60ml/kg and packed cell transfusion initiated through the other cannula.In case of air hunger, child should be started on oxygen support and supportive management of congestive heart failure should be instituted. Any thrombocytopenia or coagulopathy is to be corrected with platelet or fresh frozen plasma transfusions. A thorough history is elicited and the approach is as per the Algorithm 1.

Endoscopic management

Hemodynamic stability should be assured before endoscopy is attempted. Ideal colonoscopy can be done by preparing bowel with polyethylene glycol per orally or through nasogastric tube on an emergency basis. Informed written consent is to be taken before the procedure. The caliber of the endoscope is standardized as per the weight of the child. Different modalities used to achieve hemostasis include Injection therapy using sclerosants, ethanol, epinephrine and tissue adhesives. Thermal modalities used include heater probe, multipolar probe and argon plasma coagulation. They act by tissue edema, coagulation and blood vessel contraction. Hemoclips arrests bleeding by mechanical tamponade and are particularly useful in post polypectomy bleeds and for a spurting vessel from a ulcer base[14]. Hemospray is a novel therapeutic approach to arrest an active bleeding vessel. This act by concentrating clotting factors at the site of bleed[15]. It is yet to be validated in children in LGIB. Another modality is Over-the-scope clip designed in Tubingen Germany. Device utility is yet to be validated in children. In adults it is used in case of a large vessel bleed due to its greater surface area and also due to the more compression force executed[16].

Other diagnosed causes of LGIB are treated as per the standard methods. Meckel's diverticulum, duplication cysts and intussusceptions (which are not reducible) are managed surgically, infectious causes are treated with antibiotics, inflammatory causes by immunosupressants, vascular malformations by beta blockers, interferon alpha, vincristine, thalidomide or bevacizumab.

Conclusion

Etiology of LGIB can be secondary to an extremely benign cause like constipation to a life threatening cause from a major vessel malformation. Minor bleeds can be managed conservatively. Massive LGIB can be at times a nightmare for the treating physician. A thorough history, focused examination, and rapid but accurate intervention can be life saving. The emergence of recent modalities like capsule endoscopy, double balloon enteroscopy and various new treatment methods have revolutionized the approach to LGIB.

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An Approach to Cough in Children

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Cough is perhaps the most frequent presenting symptom in the pediatric age group. It can appear harmless but may represent serious underlying diseases; on the other hand, it may be an ignorable clinical problem but very disturbing for the child & the family. It is important to remember that cough is an essential response that may occur several times during the day in a healthy child. For all practical purpose it is assumed that cough in young children is almost always dry in nature[1,2].

Cough is an important protective reflex, its purpose being expulsion of respiratory secretions or foreign particles from the air passages. This reflex is controlled by a centre in medulla. Irritation of pharynx, larynx, trachea, bronchi & pleura transmit afferent impulses through vagus & glossopharyngeal nerves. The efferent pathways are in the nerve supply to larynx & respiratory muscles. A few cough receptors are also present in pericardium, esophagus, diaphragm, stomach & external ear. Cough occurs through the stimulation of a complex reflex arc except in the psychogenic cause.

The knowledge of the normal physiology of cough is essential in the evaluation of the cough in a child[1].

Clinical types of cough

Our respiratory tract can be broadly divided into 2 parts. The upper airways include nose, pharynx and larynx. And the lower airways include trachea, bronchi and the bronchioles. In majority of the cases, the origin of cough may be in the pharynx, larynx, trachea or bronchioles. The type of cough itself can aid in distinguishing the sites of origin & even the possible etiology. The characteristics of the cough on the basis of the sites of origin can be described as given below.

1. Pharyngeal cough:

Cough of pharyngeal origin is a dry cough which increases in lying down position due to posterior nasal drip. It is associated with irritation of the posterior pharyngeal wall. It should be noted that viral cough is always harassing in nature. Viral infection is associated with viral prodrome like running nose, sneezing, dryness in throat & watering from the eyes etc. Bacterial infection is associated with toxicity & there will be absence of the viral prodrome[2].

2. Laryngeal cough:

Cough of laryngeal origin is also a dry cough which is associated with hoarseness of voice. Sometimes there is symptom of pain in the larynx while coughing[2].

3. Tracheal cough:

Tracheal cough is also dry in nature. In most of the times the child will have retro-sternal pain during coughing[2].

4. Bronchial cough:

Bronchial cough is always spasmodic in nature. It comes in bouts, is more at night or in the early hours of the day. It is associated with vomiting & will have dramatic response to bronchodilators. Cough increases for 2-3 days following use of bronchodilators. This is due to the relief of bronchospasm[2].

How do we evaluate cough?

A systematic approach to the diagnosis and treatment of

these children consists of assessing whether the symptoms are the manifestation of a minor problem or a life-threatening process; determining the most likely underlying pathogenic mechanism; selecting the simplest effective therapy for the underlying process, which often is only symptomatic therapy; and carefully evaluating the effect of therapy. Causes of cough in children are different from those in adults. It is very much important to collect enough information pertaining to the causes of cough. We should target a few things such as[3,4] ;

1. Take a detailed & careful history
2. Give stress on pertinent points
3. Perform a careful physical examination.

Clinical history – The properly taken history of cough will give a lot of clues to the likely causes of cough. The following questions are to be stressed while taking the clinical history (2,3):

1. What is the age of the child?
2. What is the duration of cough?
3. What is the nature of the cough?
4. Is there any diurnal variation?
5. Circumstances around the onset of cough?
6. Is there any noisy breathing?
7. Associated symptoms, if any?

What is the age of the child?

Cough from birth or early infancy is noted in congenital anomalies such as TOF, tracheomalacia, laryngeal cleft etc. Cough may start from early infancy in situations like lower airway malformations, aspiration in GERD, suppurative changes in cystic fibrosis etc.In school age children, the common causes of cough are airway allergy, asthma, posterior nasal drip, viral infections, psychogenic. On the other hand sudden onset cough in a healthy infant or child may suggest FB aspiration[2,3].

What is the duration of cough?

Cough is categorized as 'acute' when it is present for less than 3 weeks and 'chronic' beyond that[1]. Acute cough, generally suggests a disease of shorter duration, while chronic cough points towards a long standing problem.

However acute cough can also represent long standing lung disease. Likewise viral cough can persist for several weeks following an acute viral upper respiratory tract (URT) infection. Table 1 shows a partial list of few conditions that cause cough in children[1,2].

Table 1:

Acute cough	Chronic cough
Viral URT Infection	Asthma
Bronchiolitis	Adenoiditis
Pneumonia	Pulmonary TB
Aspiration	Aspiration Upper GI anomalies
Congestive Cardiac Failure	Inhaled Foreign Body
Acute Laryngo-tracheobronchitis (LTB)	Sinusitis
Bronchial activity/Asthma	GERD

What is the nature of the cough?

Cough is loosely categorized as dry (non-productive) or wet (productive) cough. Naturally the dry type is more common in young children & often does not point towards any specific cause. Children less than 6 years of age are usually unable to expectorate. Wet cough may be expected in pneumonia & suppurative lung diseases. Post-tussive vomiting, often regarded as a hallmark of pertussis, is non-specific and can occur with any forceful cough, specially in young children[1].

Is there any diurnal variation?

The Timing of the cough can be a helpful feature. Table 2 shows the timing of cough with the possible etiology of cough[3].

Table 2:

Timing of cough	Causes
Worse at night	Post nasal drip, asthma
Worse in the evening	Exposure to pollutants
Early morning	Asthma
After having food, or as soon as child lies down	GERD
Soon after play or exercise	Asthma
Loud & bizarre cough, absent during sleep	Psychogenic

Circumstances around the onset:

These are also helpful to find out the possible causes of

cough. Cough starting with a viral type infection which then lingers may be a post viral cough. Please refer to Table 3 for some other examples[2].

Table 3:

Circumstances	Causes
Presence of viral prodrome	Post viral cough
Contact with an adult with viral infection	Bronchiolitis
Associated with feeding	Aspiration in to lung
Associated with vomiting	GERD
Family history of allergic tendency	Reactive airway disease

Is there any noisy breathing?

This is important because additional sounds can point towards airway pathology, and it is possible to differentiate between intrathoracic and extra thoracic airway problems. Table 4 shows the relationship clearly[1].

Table 4:

Type of noise	Airway level of obstruction
Stridor: Low pitched sound,better heard during inspiration (may be biphasic also)	Upper airway/ extra thoracic
Wheeze : High pitched sound, better heard during expiration (may be biphasic also)	Lower airway/ intra thoracic

Associated symptoms if any?

Associated symptoms are also essential to find out the cause of cough. Table 5 shows few examples of clinical importance[1].

Table 5:

Associated symptoms	Causes
Rhinitis,atopy,wheeze	Asthma
Fever,cold,diarrhoea,rashes	Viral infection
Reccurent pneumonia,sinusitis, otitis media	Immune deficiency
Malabsorption with FTT	Cystic fibrosis

How do we treat the cough in children?

The mild cough can be treated with simple cough remedies like ginger with honey or tulsi with honey, steam inhalation, good hydration & elevated head end while sleeping. Hydration helps to liquefy bronchial secretions and relief of the irritation and thereby relief of cough. The soothing agents increase salivation which exerts protective effect, reduce afferent impulses from the irritated mucosa (reduce receptor activation)[2].

Bronchodilators: A bronchodilator (Salbutamol /ß2 agonist) alleviates cough associated with bronchospasm. It is not of much benefit in other forms of cough. Bronchodilators are indicated in the following situations[2]:

(a) Children with bronchial cough

(b) Children with previous history of recurrent cough

(c) Children with history of atopy ,personal or family

(d) Children with previous history of treatment AND relief of cough with bronchodilator.

Cough suppressants:

In most situations, the simple home remedies are the best treatment. But in presence of severe & distressing cough a pure cough suppressant may be administered. The drugs like Dextromethorphan is safe in children with minimal or no side effects (3, 6).

The anti-tussive therapy is indicated for

(a) posterior nasal drip,

(b) allergic dry cough,

(c) whopping cough,

(d) habit cough and

(e) disturbing cough (which affects the feed & sleep of the child).

Cough & cold preparations ?

Now a days the market is flooded with the combinations of cough suppressants, expectorants, sympathomimetics, antihistamines, and/or analgesics. They are not scientifically approved and have no or little evidence to support their efficacy. With many combinations, dose of each individual drug may be inadequate or inappropriate and large number of ingredients may expose the child to unnecessary adverse effects. Anti-histaminics present in the combinations dry up mucosal secretion, lead to more irritation of respiratory tracts and aggravate cough. They cause drowsiness which is dangerous in presence of bronchospasm. They are known to cause acute urinary

retention (anticholinergic action)[2,3,5].

Expectorants and Mucolytics:

There is no place for expectorants and mucolytics in the treatment of cough in children. A child below 6 years age is unable to expectorate. Cough expectorants will cause accumulation of secretions, increase irritation of the mucosa & thereby increase the cough. Clinical evidence of efficacy is lacking and many consider expectorants to be of no value other than a placebo (2, 3, 5). Mucolytics will dislodge the mucus plugs in the bronchioles, block the bronchioles & increase the respiratory distress. Many mucolytics are being used but these have not demonstrated consistent improvement in lung function[2].

Specific treatment:

Usual treatment is to address the underlying disorder. We have to consider therapy for asthma, allergic rhinitis or GERD if suggestive findings exist. For all non specific chronic cough, reassurance and periodic reevaluation for identification of signs & symptoms is advisable (3).

Conclusions :

1. Cough is an important defence mechanism of respiratory system.
2. Further workup is dependent on associated symptoms.
3. Determination of the cause of a cough is essential for the purpose of treatment.
4. Use single active ingredient and avoid irrational combination of pharmacological agents.
5. There is No role of cough & cold preparations in the treatment of cough in children.
6. Advise to prevent children from pollutants and allergens.

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An Appeal

Shubho Vijaya and Happy Diwali to you all.

This is fourth time, I am getting the opportunity to communicate with you through this official journal of East Zone Academy of Pediatrics, "Pedi- Info". On the eve of this 23rd East Zone PEDICON 2016, I would like to welcome you all in the writing panel of this journal.

Needless to say that, in spite of repeated request, there is a very poor response in contributing the articles for the journals. It becomes increasingly difficult for me to bring out this journal without your active cooperation. My request to all of you to please send articles for the regular publication of journal otherwise its future may be in jeopardy.

An Approach

Approach to Liver Abscess in Children

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Children with liver abscesses constitute more than 79 per 100,000 pediatric admissions (<12 yrs age) in tertiary care centres in India[1]. In larger series from developing nations(Brazil) it is documented in frequency of approximately 1 out of 140 admissions[2]. However in developed countries it is rare with an incidence of 25 per 100,000 admissions in USA[3] to 11 out of 100,00,00 admissions in Denmark[4]. It is a cause of significant morbidity and mortality. For unknown reasons male children akin to male adults are affected by liver abscesses more than female children[2,5].

Predisposing causes

Children have unique set of predisposing causes for liver abscess.

Parasitic infestations:

Almost all parasitic infestations including ascariasis, schistosomiasis, *Trichuris trichura, Necator americans, Ancylostoma duddenalis* have been reported as association. Significant increased parasitic infestation has been demonstrated in children with pyogenic lier abscess when compared with controls of similar background[6]. Staphylococcus bacterimia in presence of parasitic infestation predisposes to liver abscess formation[7]. Salmonella infection has also been associated with parasitosis. The pathogenic mechanism has been thought to be stimulation of T2 immunity in patients with worm infestations. This is hypothesized to suppress the T1 effector limb thereby compromising phagocyte handling of bacteria and also fungi. Liver granulomas around parasites, their larvae and eggs are believed to trap bacteria in the grannulomatous reaction around them serving as nidus[8,9]. Biliary ascariasis associated with cholangitis and liver abscesses is quite common in Kashmir valley of India[10].

Genetic disorder :

(1) Chronic Grannulomatous Disease (CGD) is a rare inherited primary immunodeficiency disorder where phagocytes cannot destroy catalase-positive bacteria and fungi. Defect in phagocytic cells' respiratory bursts lead to life threatening infections including liver abscesses. Fever is the most common presenting symptom. These abscesses are often recurrent, multiple and difficult to treat. Commonest micro-organism is staphylococus though gram negative rods, nocardia and fungal infections are also reported. Surgical resection is more rewarding than percutaneous drainage[11].

(2) Papillon-Leferve syndrome is a rare autosomal recessive disease comprising palmoplantar keratoderma and periodontitis. Pyogenic liver abscess is an increasingly recognized complication[12].

(3) CI complement deficiencies has been associated with liver abscess in children.

(4) Hyper Immunoglobulin E (Job syndrome) is associated with recurrent abscesses involving

several organs including liver.

Skin infection:

Skin infections are common in children. These when associated with bacteremia may include infection in liver. Significant co-relations have been documented between pyogenic liver abscesses and skin infections in some large series of children with liver abscesses[2,8].

Protein calorie malnutrition:

There is likelihood of corelation with liver abscesses and malnutrition in children. Liver abscesses in children are rare in developed countries whereas they are common in developing countries.

Abdominal infections and liver abscesses:

At the beginning of this century portal route of entry of infections constituted a large proportion of patients with liver abscesses. However this has declined, with increasing ease of diagnosing such infections and treating them. However case reports[13] and series[14] are still published, emphasizing their importance. Previous portal vein catheterization also can predispose to portal pyaemia and liver abscesses. Choledochal cysts can predispose to recurrent cholangitis and liver abscesses in children[14]. Similarly congenital hepatic fibrosis can predispose to cholangitis and liver abscesses.

Post trauma:

Trauma predisposes to liver abscesses both by direct injury to liver or by providing habitat for proliferation of organisms elsewhere. Child abuse can sometimes be the cause of sepsis and liver abscesses[15]. Unusual organisms like clostridia can flourish and this needs to be kept in mind[16].

Microbiology of liver abscesses

Most of the liver abscesses in children are pyogenic in nature with amoebic liver abscesses constituting 21-30% of cases[17,18,19] or more (50%)[20]. However in an appropriate epidemiological setting one may see cases of amoebic liver abscesses presenting as neonatal sepsis[21]. Among cases of pyogenic liver abscesses, Staphylococcus is the leading cause in most series[1-3,5,7,11,17,19]. Anaerobes constitute an important proportion of upto 30% of organisms[3,4,22] and include microaerophilic streptococci. Gram negative rods like *E. coli*[5,20] and klebsiella[23] are common isolates as are other enterobacter species[4].

Unusual micro-organisms :

Fungal hepatic microabscesses either alone or in association with spleenic microabscesses may occur in children with acute leukemia[24]. Tubercular liver abscesses are rare but are known to occur[18,25].

Typhoid fever can have associated hepatic abscesses[26] and in an appropriate setting, cat scratch disease, brucella, meliodosis, can all be suspected as cause of hepatic and spleenic abscesses usually associated with a systemic dissemination of infection.

Location and number of liver abscesses:

Irrespective of any etiology most of liver abscesses(approx 2/3rd) occur in the right lobe of liver and majority(approx 2/3rd) are solitary[1,5]. Left lobe abscesses should be treated with caution as they are frequently associated with complications like rupture into peritoneum and pericardium and cause pericardial effusions[27] each of which may be life threatening. Left sided liver abscesses require drainage far more often (85% cases) when compared to right sided lesions, even when aetiology is amoebic[28]. Multiple liver abscesses constitute 20- 25 % of all cases[1,29]. Majority ie 2/3rd of multiple pyogenic liver abscesses are confined to right side of liver[19]. With multiple liver abscesses mortality may be almost twice that in solitary cases[29].

Clinical presentation signs and symptoms

Irrespective of pyogenic or amoebic etiology,fever often with chills, abdominal pain specially in right upper quadrant and tender hepatomegaly are common presenting signs and symptoms[1,20,23]. Nausea and vomiting, anorexia, unexplained anemia, and cough with breathing difficulty[30] or simply fever are other common complaints. Whereas fever is the most common symptom in children, afebrile presentations of liver abscesses specially of amoebic aetiology are well known in series of mixed age groups[31]. In one series of amebic liver abscesses, majority i.e. 58% of patients had subacute presentation with right upper quadrant dullache, weight loss, fatigue, anemia and low to moderate grade fever[27]. On the other hand

liver abscesses may present as fulminant sepsis[21] or acute abdomen[32]. Clinical presentations do not distinguish amoebic from a bacterial etiology unless there is an obvious precipitating source for eg. abdominal infections. It is uncommon to get a positive history of colitic diarrhea from patients of amebic liver abscesses.

Investigation

Anemia, leucocytosis and raised sedimentation rates are usual findings on hemogram. Altered liver enzymes specially alkaline phosphatase point to liver as an involved organ. Majority of children has a prolonged prothrombin time[20]. The blood cultures are positive in 50% of patients Cryptogenic abscesses are often monomicrobial with staph aureus as the lead single agent in children without underlying liver or intestinal tract disease. Multiple microabscesses are most commonly secondary to bacteremia, condidemia, or cat scratch disease.

Recovery of *E.histolytica* from the stool is pathogenic and highly suggestive of amebic abscess but must be distinguished from *Entamoeba dispar*, which looks similar but is nonpathogenic; antiamebic antibodies help to identify *E.histolytica*.

Enzyme-linked immunoabsorbent assay testing for *E.histolytica* (galactose/N-acetyl-D-galactosamine) lectin in serum is usually positive in amebiasis.

Chest X-rays might show elevation of the right hemi – diaphragm with decreased mobility or a right pleural effusion. Ultrasound or CT confirm diagnosis. Solitary liver abscess (70% of cases) in the right lobe of liver (75% of cases) are more common then multiple abscesses or solitary left lobe abscess.

Treatment

Medical therapy:

At presentation, it is important to resuscitate a sick septic patient with I.V. fluids and other supportive measures. Appropriate analgesics may be essential but NSAIDs should be avoided if intervention is planned. A combination of anti-staphylococcal drug like cloxacillin, an anti-anerobic and anti-amebic drug like metronidazole and an aminoglycoside or cephalosporin for gram negative bacilli is a good initial choice. Therapeutic drainage is not mandatory in all cases of pyogenic liver abscesses[1]. However experiences with most series suggest that 80-90% pyogenic liver abscesses require some form of drainage[20,29]. Medical antibiotic cover is additionally required for a period of 3-4 weeks.

95% of amebic abscesses do well on medical therapy alone[33,34] and require therapy with nitroimidazoles for a total duration of ten days only. Metronidazole is the drug of choice. Oral dose is 30-50mg/kg/d, and i.v. dose is 7.5 mg/Kg/dose 6th hourly.

Role of aspiration:

Aspiration is safe, is helpful in diagnosis of abscess and provides material for microbiological assessment. Abscess aspiration (sometimes repeated) in combination with antibiotics has been successfully tried worldwide. In pyogenic liver abscesses, aspiration along with antibiotics help[4,20] and reasonable results can be achieved. This strategy has been reported to be helpful in amoebic liver abscesses too[35] but in a randomized trial conducted by us, we did not find any added benefit of aspiration in uncomplicated amoebic abscesses[33] Aspiration must be attempted in solitary,unilocular lesions and on carefully selected patients but if sepsis persists, prompt drainage is required.

Role of percutaneous drainage:

Percutaneous drainage has now come to a centrestage in management of liver abscesses that require more than just a medical management. Safety and efficacy of percutaneous abscess drainage in selected patients is now well established. Even multiloculated liver abscesses can be managed with aggressive percutaneous techniques that include disruption of loculations and placement of large bore sump catheters. Percutaneous drainage is indicated when

(a) Volume of abscess is large and there is risk of spontaneous rupture(specially left lobe abscesses). (b) When actual rupture has occurred, then along with abscess cavity drainage of extraneous collection. (c) When there is lack of response to medical therapy with clinical signs of persistent sepsis or enlarging abscesses, or persistent symptoms. (d) When there is evidence of liver failure.

Absence of a secure route is the only contraindication.

Good results have been reported in series on children[3,4,23]. Failure is mostly due to technical causes like (a) Inappropriate approach into a non- dependant portion of cavity. (b) Failure to recognize and respond to septation. and (c) Premature withdrawal of drains[36]. Catheters should be withdrawn once there is negligible(<10 ml) pus drain per day and when patient is apyrexic. Complications are bacteremia, and bleed externally or into the peritoneum or GIT (haemobilia), and sometimes Nematodeiatrogenic superinfection.

Role of surgery:

Presently surgical drainage is usually reserved for patients (a) who have failed percutaneous drainage, (b) those who require management for an underlying abdominal problem, (c) selected patients with multiple macroscopic abscesses, (d) those on steroids and (e) patients with ascites.

Transperitoneal approach is the usual method used. This is because the entire liver can be exposed, best Novdrainage site can be determined, multiple abscesses identified with an intraoperative USG, and entire abdomen explored for the primary source of infection. Good results with a low mortality has been reported in literature.[19]

Complications

List of possible complications are long. However pleuro-pulmonary complications are the commonest[37]. It may be in form of pleural effusion, empyema, pneumonitis, and hepatopleural or hepato-bronchial fistula. Other complications may be in form of ascites, Budd-chiari syndrome, intraperitoneal rupture of abscess and peritonitis, intrapericardial rupture, pericardial efusion, septic shock, hemobilia and jaundice. Rare complication like perforations into a hollow viscus like colon, stomach and duodenum and cerebral amoebiasis are also reported.

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Case Report

Posterior Reversible Encephalopathy Syndrome in a Child Following Drowning

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Abstract:

Posterior reversible encephalopathy syndrome(PRES) is a recently described condition characterized by acute, transient and mostly reversible alteration of consciousness ,seizures, headache and visual disorders associated with abnormal neuroimaging findings in the cortex. The literature describes hypertension and immunosuppressive therapy as frequent associations. We hereby report PRES in a child following drowning ,an hitherto unreported association.

Key words: *PRES; accidental strangulation, Reversible Posterior Leukoencephalopathy Syndrome(RPLS)*

Introduction:

Posterior Reversible Encephalopathy syndrome (PRES) (also called reversible posterior leukoencephalopathy syndrome) is a recently described mostly transient and reversible neurological disorder clinically characterized by seizures, blindness, altered consciousness associated with radiological abnormalities especially in the posterior white matter . Hypertension has been implicated as the most common cause[1,2]. But ,PRES associated with transient cerebral anoxia following drowning in a previously normal child has not been reported in literature.

Case Report:

A 3 year old male child presented with deep unconsciousness following accidental drowning. The child had drowned while playing with other children by the side of a village pond near his house. He was rescued by his family members and was brought to the ER of our hospital after about an hour of the episode. The baby was healthy before this incident without any history suggestive of perinatal hypoxia and was achieving developmental milestones within the expected time limits.

On initial examination, he was deeply comatose. Glasgow coma scale (GCS) was assessed as E1V1M1 with bilaterally dilated pupils which were sluggishly responding to light. His heart rate was 102/min, respiratory rate was 20/min and blood pressure was 78/50 mm/Hg on admission. Rectal temperature was 96^0F. Following immediate resuscitative measures in the emergency room, he was transferred to PICU where he was intubated and ventilated along with other supportive measures like intravenous fluids, antibiotics etc and mannitol for raised intracranial tension. Complete blood count, electrolyte levels, renal and liver function tests sent on D1 of admission and also on subsequent days were within normal limits. He responded to supportive measures, condition gradually stabilized and could be weaned off ventilator on D8. But, after regaining consciousness, it was revealed that the child had

developed complete loss of vision. The blood pressure and urine output had remained normal throughout the course of illness.MRI scan of brain on 9th day of admission revealed hyperintense signals in both parietoccipital regions with mild diffusion restriction in T2 flair images . (Fig I).

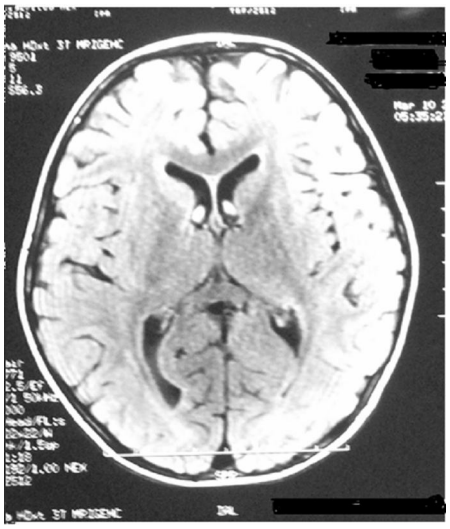

Fig I. Hyperintense signals in both parieto-occipital regions with mild diffusion restriction in T2 flair images (Arrows)

He was discharged on day 15 with advice for follow up. His neurological examination was normal at discharge apart from blindness. Gradually, his vision regained on follow up and he could see clearly at about 4 months after the incident. Repeat MRI scan after 6 months showed complete disappearance of the hyperintensities(Fig2). At one year of follow up , he was thriving well without any neurological sequelae.

Discussion:

Posterior Reversible leukoencephalopathy syndrome (PRES) (also termed reversible posterior leukoencephalopathy syndrome)is a recently described neurological disorder clinically characterized by headache, seizures, blindness, unconsciousness associated with radiological features of oedema involving

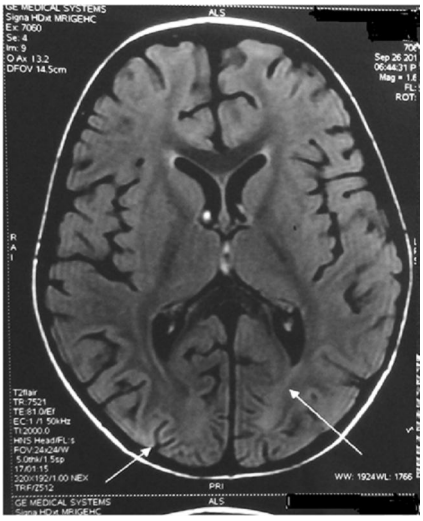

Fig 2. Complete disappearance of the hyperintensities after 6 months.

the white matter in the posterior regions of the brain [1,2]. It was first reported by Hinchey et al in 1996 after an observational study on 15 patients[1]. Since then ,a few case reports and some case series have been published in literarture describing this condition[3,4,5,6,7].

The most frequently implicated causes suggested in published literature till now are hypertension, renal failure, fluid retention, and some immunosuppressive drugs. It has also been reported in the clinical setting of hypocholesterolemia, hypomagnesaemia, hypercalcaemia, aluminum overload, high-dose methylprednisolone therapy, uremic encephalopathy, pheochromocytoma, systemic lupus erythematosus, Henoch-Schönlein purpura, acute hepatic failure, thrombotic thrombocytopenic purpura, and human immunodeficiency virus infection[5,6,7].

Many non-hypertensive causes are coming up as etiological associations of PRES especially in children. The reason for more non –hypertensive causes in childhood may be of absence of arteriosclerosis and good plasticity of vessel walls in children making the vessel walls less vulnerable to sudden changes in blood

pressure . To the best of our knowledge PRES associated with hypoxic injury due drowning has hitherto never been reported. This report adds to the list of non-hypertensive causes of PRES.

The exact pathophysiology is not yet known. It has been hypothesized that the clinical features might be due to sudden disruption of the autoregulatory mechanisms of the central nervous system vasculature, leading to vasoconstriction followed by vasodilatation.It may result in endothelial dysfunction and breakdown of the blood-brain barrier. Sudden elevation of blood pressure could be one of the factors leading to this disruption. The predilection for involvement of posterior circulation territories may be due to the relatively less sympathetic innervations of the vertebrobasilar circulation[7].

Management of PRES is mainly symptomatic and supportive and correction of causative factors without delay[1,2,4]. It is important for us to be aware of this condition to be able to differentiate it from other more common neurological conditions like CNS infection and metabolic defects which present with similar clinical picture of headache, seizures and altered consciousness. But, typical MRI with complete reversibility of both clinical and imaging picture are important pointers to the diagnosis.Typical lesions, that predominate in the posterior white matter, are hyperintense on T2-weighted images; and usually hypointense or isointense on diffusion-weighted images, with an increase of the apparent diffusion coefficient, indicative of vasogenic edema[4].

Although PRES is a serious life-threatening condition, it is, almost always ,completely reversible if appropriately recognized and managed in the acute stage. More awareness and follow up studies should give us more clue regarding the exact etiopathogenesis especially in children.

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Clue to the answer of quiz:

On further prodding, the mother admitted of giving a katori full of boiled vegetables which included one carrot each to the siblings daily since 6 months of age.

Answer of quiz on Page No.44

Newer Antibiotics

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In their 2008 report on the pipeline of new antimicrobial agents, the IDSA concluded that the number of new agents in the pipeline is disappointing and there were no agents solely for the purposes of countering Gram-negatives or the emerging carbapenemases. It is unlikely that there will be any major advance in ability to treat antibiotic-resistant infections.

Between 1983 and 1987 the Federal Drug Administration (FDA), America's drug regulator, approved 16 new antibiotics. Over the next four years, that fell to 14, and kept falling. Between 2008 and 2012 only two new antibiotics were approved, one every other year. Resistance to antibiotics is high among bacteria that cause serious infections in humans. Resistance is increasing among certain Gram-negative bacteria. Very few antibacterial agents with new mechanisms of action are under development to meet the challenge and there is a particular lack of new agents for multidrug-resistant Gram-negative bacteria. There is a significant decrease in the involvement of top pharmaceutical companies in the area of anti-microbial drug development.

The emergence of antibiotic resistance, combined with the lack of innovation in the development of new antibiotic molecules has increased greatly the challenge of treating and eradicating certain infecting pathogens. According to a recent study, the approval of new antibiotics in the US has fallen in recent decades by 60%; from 30 during the decade 1983 to 1992, to 12 over the period 1998 and 2009.

In India Drug Controller General of India approves only a few new antibiotics. A variable degree of acceptance is offered to the new antibiotics as sometimes they are either similar to some drugs already in use or they occupy an important but narrow treatment niche. MRSA (Methicillin Resistant Staph.aureus) which were once acquired only in Health care settings are now widespread in communities across the nation. Even Vancomycin resistant Enterococci(VRE) are being increasingly found in tertiary care centre.

List of Newer Antibiotics:-

Daptomycin

Linezolid

Ranbelozid

Eperezolid

Ertapenem

Doripenem

Quinopristin-dalfopristin

Tigecycline

Gemifloxacin

Telithromycin

Oritavancin

Dalbavancin

Telavancin

Iclaprim

Cefditoren

Ceftobiprole

Ceftaroline

Daptomycin

Class

Cyclic lipopeptide

Initially discovered in 1980s but clinical developed put to near halt by toxicity concerns.It has been finally approved by US FDA in 2003.

Mechanism of action:

Rapidly bactericidal by lysing the membranes of Gram-positive bacteria.

Indications

Primarily active only against Gram–positive bacteria

Complicated skin & skin structure infections by:-

- Staph aureus (including MRSA)
- Strepococcus pyogenes
- Strptococcus agalactiae
- Streptococcus dysgalactiae
- Enterococcus foecalis
- Staph aureus blood stream infections
- VRE

Potential problems-

- Raised CPK
- Pseudomembranous colitis

Dosage

4 mg/kg over a 30 minute period by IV infusion in NS q 24h

Ranbezolid (RBX 7644)

It has been tested on pneumococcal & staphylococcal strains.

This compound has showed a very good activity against both gram positive and gram-negative anaerobes.

Eperezolid

It is active against multi drug resistant gram-positive organisms

Ertapenem

Class-Cabapenem.

It was first approved by US FDA for clinical use in 2001

Mechanism of action

It acts by inhibiting peptidoglycan synthesis. They are primarily bactericidal

Indications

- Complicated Intra-abdominal infections
- Complicated Skin & skin structure infections
- CAP
- Complicated UTI
- Active Pelvic infection

Potential problems

- Renal toxicity
- Pseudumembranous colitis

Dosage

1 gm either given once daily for 7 days by IM inj or upto 14 days by IV injections

Newer Carbapenems

Doripenem

It is bactericidal against most of the gram-positive & gram-negative aerobic infections causing HAP. It is not that active against MRSA & VRE. Doripenem appears to be more active than Meropenem against Psudomonas aeruginosa.

It was approved by the US FDA in 2007 for the treatment of complicated Intra-abdominal infections and UTI, HAP & VAP.

Quinopristin- dalfopristin (Synercid)

IV injection: powder for reconstitution, 10 mL contains 150 mg quinupristin, 350 mg dalfopristin.

Class:One of the Streptogramins,this molecule is a 30:70 combination of a type B and a type A streptogramin.It is a water soluble injectable preparation approved by FDA in 1999.

Mechanism of action:

The 2 components act synergistically on late & early bacterial protein synthesis and though individually bacteriostatic combination of them is bactericidal.

Indications

- VRE(E.foecium) infections
- Complicated Skin & skin-structure infections caused by MSSA or Strep. pyogenes
- Endocarditis caused by E. foecium resistant to Penicillin, Vancomycin & aminoglycoside

Potential problems

- Phlebitis
- Myalgia & Arthralgia
- Drug interactions

Dosage

7.5 mg/kg IV every 8 hrs

Tigecycline

Class:Glycylcycline derived after modification at nine position of Minocycline

Mechanism of action

Bacteriostatic & act by binding to the bacterial 30s ribosomal subunit

Indications

- Complicated skin & skin-structure infections
- Complicated intra-abdominal infections
- Community acquired Pneumonia (CAP)

Potential problems

- Nausea & Vomiting
- Permanent teeth discoloration

Gemifloxacin

Class:Fluoroquinolone approved in 2003 by US FDA

Indications

- Acute Bacterial exacerbation of Chronic Bronchitis
- CAP due to MDRSP, HIB, M.catarrhalis, Mycoplasma pneumonia, Chlamydia pneumonia

Potential problems

- Diarrhoea, Nausea & Rash
- Prolongation of QT interval

Dosage

- AECB-320 mg/d for 5 days
- CAP-320 mg/d for 7 days

Telithromycin

Class:Semisynthetic derivative of Macrolide approved by US FDA in 2004

Mechanism of action

Binds to domain V & domain II of 23S rRNA more tightly than erythromycin

Indications

- CAP due to MDRSP
- AECB
- Acute Bacterial Sinusitis

Potential problems

- Nausea, Diarrhoea, Headache & Dizziness
- Prongation of QTc interval
- Drug interactions

Dosage

- 800 mg/d for 5 to 10 days

Glycopeptides & derivatives

Oritavancin

Bactericidal against MRSA & VRE

Potential problems

- Alteration in lysosome activity leading to mixed lipid storage disorder
- Injection site reactions
- Raised liver enzymes

Dalbavancin

A lipoglycopeptide bactericidal for all resistant Pneumococci and MSSA & MRSA

Indications

- Skin & skin-structure infections
- Catheter related bacteremia

Telavancin

An investigational lipoglycopeptide, inhibits cell wall synthesis by binding to peptidoglycan precursors.

Indications

- Skin & skin-structure infections
- Nosocomial Pneumonia

Potential problems

- Taste disturbances
- Nausea, Headache & Insomnia

Iclaprim

A synthetic diaminopyrimicine,inhibits Dihydro folate reductase similar to trimethoprim and prevents synthesis of bacterial DNA & RNA

Indications

- HAP due to gram-positive pathogens
- Active against Atypical pathogens like C. pneumonia & Legoinella pneumophilia
- Complicated skin & skin-structure infections

Oral preparation underway to enable switch therapy

Newer Cephalosporins

Cefditoren

Newer third generation cephalosporin available for oral administration.

Approved by US FDA in 2001

Indications

- CAP
- AECB
- Uncomplicated SSSI

Ceftobiprole

An investigational fifth generation cephalosporin with a broad spectrum of activity against both gram-positive and gram-negative organisms

Inhibits cell wall synthesis by binding to Penicillin binding proteins

Has completed phase III trials for treatment of cSSSI, CAP and HAP including VAP

Ceftaroline

Another broad spectrum cephalosporin with greater activity against MRSA, MSSA, VISA, S. pneumonia including penicillin-intermediate and –resistant strains.

Has completed phase III trials for CAP, cSSI

Loracarbef

(Lorabid).

Capsule: 200 mg.

Suspension: 100 mg/5 mL, 200 mg/5 mL

Class:Carbacephem very closely related to cefaclor (2nd generation cephalosporin) active against S. aureus, Streptococcus, H. influenzae, M. catarrhalis, E. coli, Klebsiella,and Proteus.

Dosage

Children: 30 mg/kg/24 hr divided q 12 hr PO (max dose: 2 g).

Adults: 200-400 mg q 12 hr PO (max dose: 800 mg/24

hr).Cautions: ß-Lactam safety profile (rash, eosinophilia). Renally eliminated.

Drug interaction: Probenecid.

Mezlocillin sodium

Class:Extended-spectrum penicillin active against E. coli, Enterobacter, Serratia and Bacteroides; limited antipseudomonal activity.

Dosage

Neonates: Postnatal age =7 days: 150 mg/kg/24 hr divided q 12 hr IV; >7 days: 225 mg/kg divided q 8 hr IV.

Children: 200-300 mg/kg/24 hr divided q 4-6 hr IV; cystic fibrosis 300-450 mg/kg/24 hr IV.

Adults: 2-4 g/dose q 4-6 hr IV (max dose: 12 g/24 hr).Cautions: ß-Lactam safety profile (rash, eosinophilia); painful given intramuscularly; each gram contains 1.8 mEq sodium. Interferes with platelet aggregation with high doses; increase of enzymes noted in liver function test results. Renally eliminated. Inactivated by ß-lactamase enzyme.

Drug interaction: Probenecid

Nafcillin sodium

Nafcil, Unipen.

Injection.

Capsule: 250 mg.

Tablet: 500 mg.

Class

Penicillinase-resistant penicillin active against S. aureus and other gram-positive cocci, except Enterococcus and coagulase-negative staphylococci.

Dosage

Neonates: Postnatal age =7 days 1,200-2,000 g: 50 mg/kg/24 hr divided q 12 hr IV or IM; >2,000 g: 75 mg/kg/24 hr divided q 8 hr IV or IM; postnatal age >7 days 1,200-2,000 g: 75 mg/kg/q 8 hr; >2,000 g: 100 mg/kg divided q 6-8 hr IV (meningitis: 200 mg/kg/24 hr divided q 6 hr IV).

Children: 100-200 mg/kg/24 hr divided q 4-6 hr IV.

Adults: 4-12 g/24 hr divided q 4-6 hr IV (max dose: 12 g/24 hr).Cautions: ß-Lactam safety profile (rash, eosinophilia), phlebitis; painful given intramuscularly; oral absorption highly variable and erratic (not recommended).

Adverse effect: Neutropenia.

Ticarcillin-clavulanate

Timentin

Injection

Class:Extended-spectrum penicillin (ticarcillin) combined with a ß-lactamase inhibitor (clavulanate) active against S. aureus, H. influenzae, Enterobacter, E. coli, Serratia, P. aeruginosa, Acinetobacter, and Bacteroides.

Dosage

Children: 280-400 mg/kg/24 hr q 4-8 hr IV or IM.

Adults: 3.1 g q 4-8 hr IV or IM (max dose: 18-24 g/24 hr).Cautions: ß-Lactam safety profile (rash, eosinophilia); painful given intramuscularly; each gram contains 5-6 mEq sodium. Interferes with platelet aggregation; increase of enzymes in liver function tests. Renally eliminated.

Drug interaction: Probenecid.

Answer of quiz:

Diagnosis : carotenemia
The mother was advised against giving carrot to the babies.
The yellow discolouration subsided and the skin colour gradually returned to normal after about 4 months (Fig1b).
Carotenemia is benign condition, important to avoid confusion with jaundice and unnecessary diagnostic studies.
The absence of yellow pigment in the sclera is a clue to distinguish carotenemia from jaundice.