INDIAN JOURNAL OF PRACTICAL PEDIATRICS

IJPP

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

Vol.11 No.4	**OCT.-DEC.2009**
Dr. K.Nedunchelian Editor-in-Chief	**Dr. S. Thangavelu** Executive Editor

CONTENTS

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

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

PEDICON 2010. Hyderabad

The 47th Annual Conference of the Indian Academy Of Pediatrics

Venue: Hyderabad International Convention Centre & Hitex Exhibition Centre, Hyderabad

Date: January 7th to January 10th, 2010

We welcome you to Hyderabad for the 47th National Conference of the Indian Academy of Pediatrics. Exuding the atmosphere of 400 years old Deccan splendour, Hyderabad is city of infinite variety. Founded in the 16th century by Quli Qutub Shah, this new city which encircled pre-historic rock structures was laid on the east bank of the river Musi and was named after Hyder Mahal wife of the ruler Quli Qutab Shah. A multitude of influences have shaped the character of the city. Its language and mannerisms still exude it's rich and legendary past. The elegant buildings, marbled temples, minarets and monuments stand testimony to it and have a history and an architectural individuality of their own, which makes Hyderabad a city of enchantment

We, on behalf of the organizing committee invite you to an academic feast and hope you have a pleasant stay in Hyderabad.

ORGANIZING COMMITTEE :

Dr.P.Sudershan Reddy	**Dr.Sanjay Srirampur**	**Dr.U.S.Jagadish Chandra**
Chairman, Organizing Committee	Chief Organizing Secretary	Chairman Reception Committee

REGISTRATION FEES

Category	16/02/09 to 15/05/09	16/05/09 to 31/07/09	01/08/09 to 30/09/09	01/10/09 to 30/11/09
	INR	INR	INR	INR
IAP Member	5,500	6,800	8,200	11,000
Non-IAP Member	6,800	8,200	9,600	12,500
Accompanying Delegate	5,500	6,800	8,200	11,000
*1 P G Student	4,200	5,000	6,000	7,500
*2 Sr.Citizen	4,200	5,600	6,300	7,700
SAARC Delegates	6,800	7,500	9,600	12,500
Foreign Delegates	$600	$650	$720	$850

Note: 1. For PG Student, certificate to be produced from Institute signed by HOD
2. Senior Citizens more than 70 years of age – Registration fees is waivered.
3. For Sr.Citizens , Valid age proof (Driving License / Voters Id/Passport) is required.
4. Registrations close by 30th September.

Duly filled registration forms along with DD to be sent by Registered Post / Courier to the conference secretariat

Dr.Sanjay Srirampur
Chief Organizing Secretary, PEDICON 2010
H.no: 3-4-178, "Guru-Krupa" Lingampally, Hyderabad, AP -500 027
Email id: info@pedicon2010.org
www.pedicon2010.org

PEDICON 2010. Hyderabad

The 47th Annual Conference of the Indian Academy Of Pediatrics

REGISTRATION FORM Receipt No: _____

☐ IAP Member No: _____

Non IAP Member ☐ PG Student ☐ Sr.Citizen ☐ Foreign Delegate /SAARC ☐

Surname: _____ Middle Name _____ First Name _____

Vegetarian ☐ / Nonvegetarian ☐ Accommodation Yes ☐ / No ☐ CME Yes ☐ / No ☐

Accompanying Delegate Name: 1. 2.

3. 4.

Hospital Name / Name of Institute: _____

Designation: _____

Mailing Address: _____

_____

_____ Pin Code: _____

Email _____ *

Mobile: _____* Residence: _____ Office: _____

(*compulsory fields)

IAP Delegate Fee: Rs _____

Non IAP Delegate Fee: Rs _____

Accompanying Person: Rs _____

PG Student: Rs _____

Sr.Citizen: Rs _____

Total: Rs _____

Mode of Payment: by Demand Draft, drawn in favor of Pedicon 2010, payable at Hyderabad

OR Online at www.pedicon2010.org through credit card or cash at Conference Secretariat.

DD NO: _____ Dated: _____

Bank Details: _____ Signature of Delegate

Duly filled registration forms along with DD to be sent by Registered Post / Courier to the conference secretariat

Dr.Sanjay Srirampur
Chief Organizing Secretary, PEDICON 2010
H.no: 3-4-178, "Guru-Krupa" , Lingampally
Hyderabad, AP -500027

Email id: info@pedicon2010.org
www.pedicon2010.org

FROM THE EDITOR'S DESK

This issue is devoted to the topics covered in "IAP-IJPP CME 2009" organized by IJPP on 7th June 2009 at Chennai, which was a great success. It was uniformly felt that the topics from the previous two CMEs were practical and useful. There were requests for scientific material in print or CDs. To fulfill this need, the topics in the CME which did not appear in the journal in the recent past have been brought out as a separate issue.

The topics are selected in such a way that they are of practical importance to the pediatricians and general practioners alike. These topics are from different specialties (eg. Neurology, Pulmonology, etc).Infant mortality rate after the initial decline has come to a halt and is not reducing any further in the recent past. The main reason for this is the neonatal mortality related to perinatal events like hypoxia, asphyxia, infection and gestational age and birth weight related problems. One intervention which can save the babies born with perinatal hypoxia/ asphyxia is "Neonatal Resuscitation Programme (NRP)". In this programme, there are few modifications incorporated recently. The article "What is new in Neonatal Resuscitation?" covers the relevant issues. The care to be given to the neonates after successful resuscitation, should be adequate, other wise the efforts taken to make these babies survive go waste. Broad guidelines on continued care are elaborated in the article "Follow up of high risk new born".

The initial management of any sick child is crucial to tide over the crisis effectively. Article on "Fluid management in shock" attempts to cover various issues on resuscitation with fluid in cases of shock. Other article under critical care is on "Management of cerebral edema". The article on "Malaria-Recent Guidelines" gives clear-cut guidelines on the treatment of malaria in situations of malarial parasite sensitive to chloroquine, resistant to chloroquine, complicated malaria and artesunate combination therapy, etc. Other programme of national importance is "Revised National Tuberculosis Control programme" (RNTCP). The basics of the programme and other practical aspects of the programme are brought out very well in the article. Extensive review on hypertension in children been done in an article and an over view of obesity with its risk for cardiovascular morbidity has been dealt with in another article.

Apart from the articles from the topics covered in the CME, the regular features such as articles under Dermatology series, "Superficial fungal infection - Tinea corporis" and under "Radiologist talks to you" the topic of "Disorders of neuronal proliferation, differentiation and histogenesis" is continued in this issue. Two case studies, one on "Dysgenesis of corpus collosum presenting with intractable convulsions" and the other on "Dermatomyositis presenting as pyrexia of unknown origin" also have been included.

Dr.K.Nedunchelian
Editor-in-Chief

INSTRUCTIONS TO AUTHORS

General

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

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

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

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

Manuscript

1st Page –

Title

Name of the author and affiliation

Institution

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

Word count

No. of figures (colour / black and white)

No. of references

Authors contribution

2nd Page –

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

3rd Page -

Acknowledgement

Points to remember (not more than 5 points)

Text

References

Tables

Figures – should be good quality, 4 copies black & white / colour, (4 x 6 inches – Maxi size) Glossy print. (Each colour image will be charged Rs.1,000/- separately)

Legends

Text

Only generic names should be used

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

References

Recent and relevant references only

Strictly adhere to Vancouver style

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

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

Defective references will entail rejection of article

Tables

Numbered with Roman numerals and typed on separate sheets.

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

Figures and legends

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

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

Article Categories

Review article

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

Case report (covering practical importance)

250 – 600 words, 8 – 10 recent references

Clinical spotters section

100 – 150 words write up

With 1 or 2 images of clinically recognizable condition

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

Letters to the Editor

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

Check List

Covering letter by corresponding author

Declaration (as enclosed) signed by all authors **

Manuscript (4 copies)

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

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

Author's contribution / Authorship Criteria

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

****Declaration by authors**

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

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

Signatures (date)

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

Selection procedures

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

IAP-IJPP CME 2009

FLUID MANAGEMENT IN SHOCK

**** Indira Jayakumar***
***** Sarfaraz Navaz R***

Abstract: *Shock is a common finding in the emergency room and the Pediatric Intensive Care Unit (PICU). The etiology for underperfusion may vary requiring the clinician to make distinctions in the treatment plan. Nevertheless, fluids form the epicenter of the treatment of any shock. In this article, we aim to discuss the nuances of fluid therapy and their indications in different etiologies of shock.*

Keywords: *Shock, Fluids, Colloids, Crystalloids*

The pediatric patient in shock can pose a tremendous challenge. Pediatric practitioners treating acutely ill children are faced with different degrees and causes of shock on a regular basis making shock one of the most common life threatening conditions encountered. Regardless of the cause of shock the airway, breathing and circulation must be immediately evaluated and stabilized. The major physiologic abnormality in most forms of shock is either an absolute or relative intra-vascular hypovolemia. Cumulative evidence from studies of pediatric shock has confirmed the critical importance of early recognition, timely aggressive fluid resuscitation and goal directed therapeutic approach for patient survival. But more importantly, the so called "golden hour" applies not only to initial resuscitation but also to continually maintaining the intravascular volume, while the patient is in the ICU.

* Senior Consultant,
Pediatric Intensive Care Unit,
Mehta Children's Hospital and
Apollo Hospitals, Chennai.

** Asst. Consultant,
Pediatric Intensive Care Unit,
Mehta Children's Hospital, Chennai.

Fluids in shock - How soon?

"As early as possible"

Early recognition and aggressive resuscitation of pediatric septic shock by community physicians can save lives and cause a nine fold increase in survival.[1] Persistent shock was associated with two fold increased odds of mortality. Rivers et al[2] randomly assigned patients who arrived at an emergency department with severe sepsis to receive 6 hours of early goal directed therapy (EGDT) or standard therapy before admission to ICU. In-hospital mortality was 30.5% in the group assigned to EGDT as compared to 46.5% in the group assigned to standard therapy (p=0.009). Deaths due to meningococcal septic shock significantly reduced from 23% in 1992 to 2% in1997 with early intervention.[3]

Fluids in shock - How much?

A landmark paper[4] by Carcillo et al in 1991 demonstrated that rapid fluid resuscitation in excess of 40ml/kg in the first hour following emergency department presentation was associated with improved survival, decreased occurrence of persistent hypovolemia and no increase in the risk of ARDS or cardiogenic

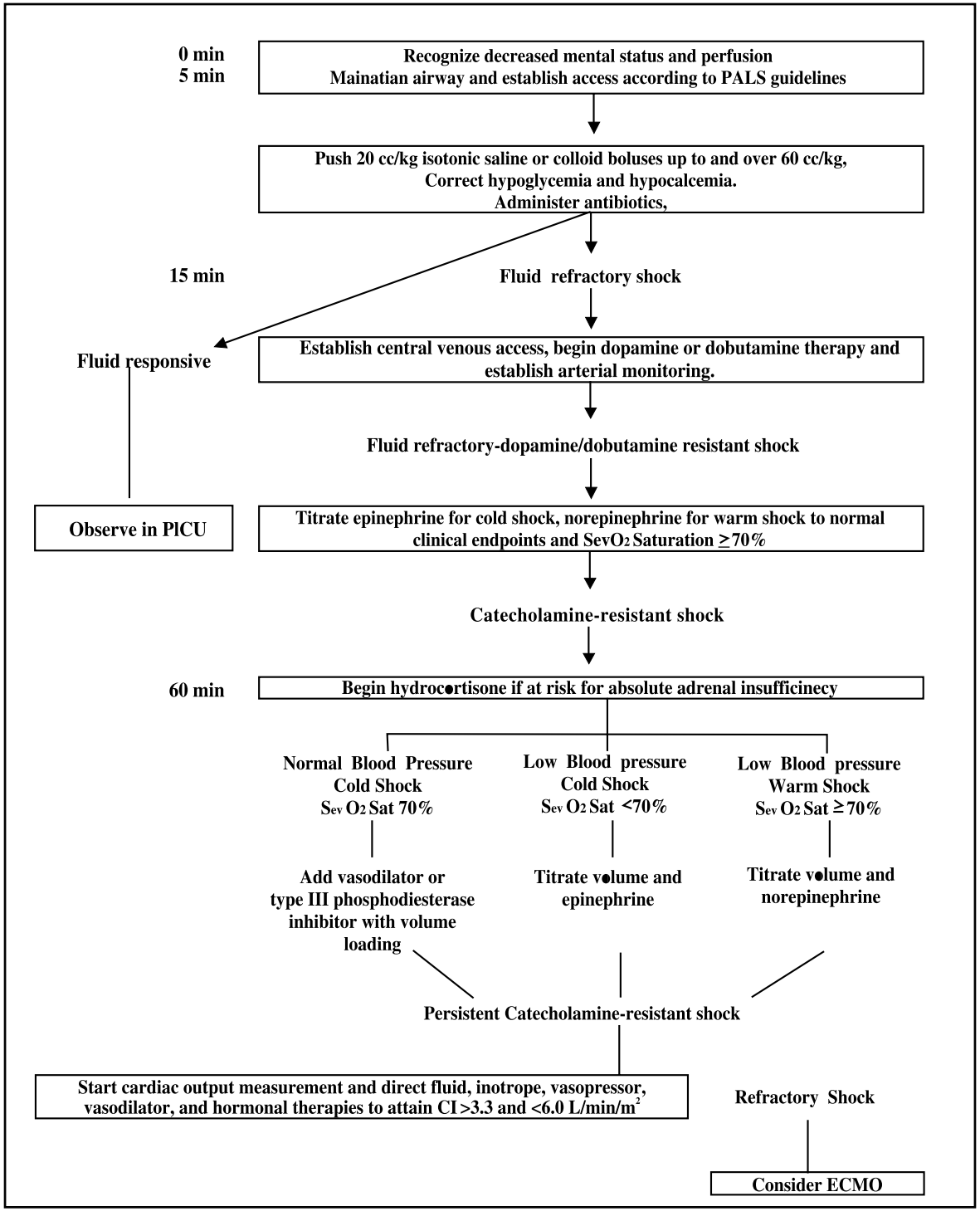


Fig.1. Surviving Sepsis Campaign: International guidelines for pediatric septic shock[5]

pulmonary edema. There was an increased mortality in the group that received <20 ml/kg.

The surviving sepsis guidelines[5] have recommended a protocolized resuscitation of a patient with septic shock (Fig.1). The protocol should be initiated as soon as hypoperfusion is recognized and should not be delayed pending ICU admission. During the first six hours of resuscitation the goals of initial resuscitation of sepsis induced hypoperfusion should include all of the following: Central venous pressure (CVP) 8-12mm Hg, MAP > 55-65 (age dependent), urine output more than 0.5-1 ml/kg/hr, central venous saturation > 70%. The guidelines recommend rapid 20ml/kg fluid boluses over 5 minutes followed by assessment for improved perfusion or fluid overload as evidenced by new onset rales, hypoxemia from pulmonary edema and hepatomegaly. Patients who do not respond rapidly to initial fluid boluses or those with insufficient physiologic reserves should be considered for invasive hemodynamic monitoring. Monitoring filling pressures can help to optimize preload and thus cardiac output. Observation of little change in CVP in response to fluid boluses suggest that the venous capacitance is not over filled and more fluid is indicated. On the other hand, an increase in CVP with reduced mean arterial pressure or increasing heart rate may suggest that too much fluid has been given. Increased fluid requirements may be evident for several days. This is secondary to loss of fluids from the intra vascular compartment when there is profound capillary leak.

Pediatric advanced life support (PALS) guidelines call for an initial intravenous bolus of 20 ml/kg followed by reassessment and rebolus to a total of 60ml/kg in the first hour of resuscitation. Some patients require additional volume of fluids upto 100-200ml/kg. This is not unusual in the first few hours of resuscitation. It is necessary to repeatedly re-evaluate and administer additional 20ml/kg infusions of isotonic fluids in the first hour. The rapidity of fluid resuscitation would depend on the degree of shock. Always attempt to secure two large bore free flowing IV catheters. If vascular access is not achieved then an intraosseous needle may be placed for rapid fluid administration. In severe shock use rapid pull and push technique through syringe rather than IV drip method for bolus administration.

Fluids in shock - Which one?

Since the early 1940s restoration of circulatory blood volume was embraced as pivotal in shock resuscitation. Controversy exists as to which fluids to use for this purpose. Hypotonic fluids (5%dextrose, Isolyte P, 5% Dextrose

Table 1. Properties of crystalloids and colloids

Properties	Crystalloids	Colloids
Distribution	IVS + Interstitium	IVS
Half life	1-2 h	2-6 h
Oncotic pressure	–	Maintained
Cost	Cheaper	Costlier
Side effects	Peripheral edema, Abdominal compartment syndrome	Allergies, coagulation, renal dysfunction

normal saline) distribute equally between all compartments. Isotonic fluids remain in extra cellular compartments (interstitial and intravascular)

Colloids are mainly distributed in the intravascular space (IVS). Even with increased capillary leakage a greater proportion of colloid will remain in IVS compared to crystalloid solutions. On the other hand crystalloids are distributed in the interstitial (75%) and IVS (25%) (Table 1 and Fig.2).

The SAFE study[6] (saline versus albumin for fluid resuscitation in critically ill) documented that there was no difference in outcome with the use of either one of these isotonic fluids. Regardless of the etiology of shock the focus should be on maintaining intravascular volume with isotonic fluids, be it colloids or crystalloids. It makes sense however to use colloids if the patient seems to be requiring a lot of crystalloids.

Studies now recommend isotonic fluids not only for replacement but also for maintenance.

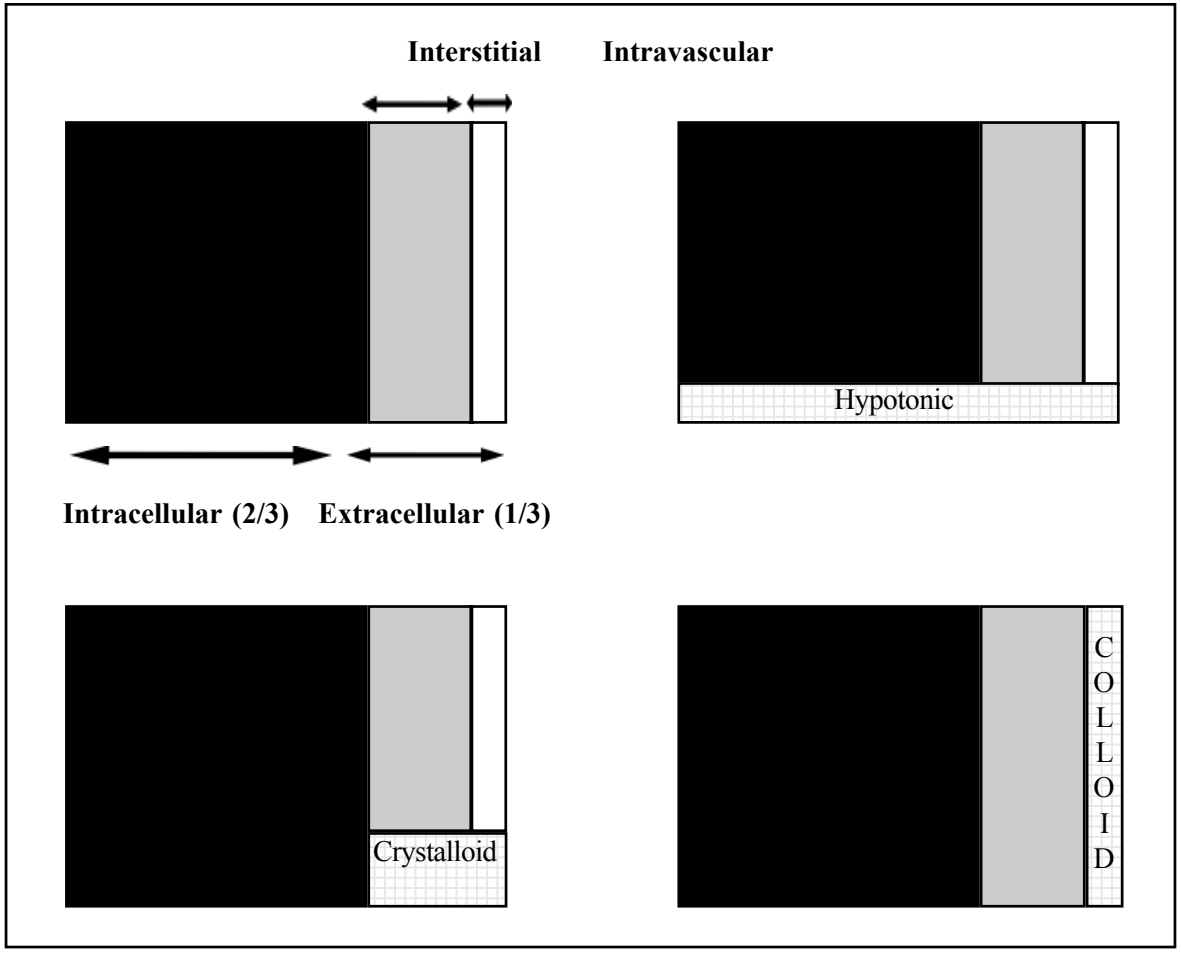


Fig. 2. Fluid compartments in the body are shown. Hypotonic fluids distribute equally in all compartments. Isotonic fluids distribute predominantly in the extracellular compartment. Colloids predominantly stay in the intravascular compartment.

The odds of developing hyponatremia following hypotonic solutions is 17.2 times greater than with isotonic fluids because of high circulating ADH levels.[7] Do not infuse a hypotonic solution if the plasma sodium concentration is less than 138 mmol/L. The concern that isotonic maintenance fluids may cause hypernatremia is misplaced and in fact there is a risk of hyponatremia when isotonic saline is given in large volumes because of ADH causing loss of salt and retention of more water.

The older generation of starches had more side effects owing to the large molecular weight and substitution ratio [6% hetastarch 140/0.5 signifies a molecular weight of 140 (medium molecular weight) and a C2-C6 substitution ratio of 0.5]. Hemaccel has high calcium content accounting for coagulation defects as compared to gelofusine. As it can be seen colloids are suspended in crystalloids and together can cause significant hyperchloremic acidosis (Table 2). This narrow anion gap acidosis can cause delay in renal, intestinal perfusion, confound one's assessment leading to unnecessary therapeutic interventions. Among colloids, Gelofusine has relatively less chloride similar to Ringer Lactate (Table 3). For the above reason "Balanced Solutions" like Ringer Lactate and Plasmalyte are gaining popularity in shock.

Table 2. Comparison of two crystalloids (commonly used)

Properties	Normal saline	Ringer's lactate
Contents (mEq/L)	Na - 154 Cl - 154	Na - 130, K - 4, Ca - 2.7, Cl - 109, Lactate - 28
Side effects	Hyperchloremic acidosis due to high chloride content	Lesser

Table 3. Comparison of two colloids (commonly used):

Properties	Gelatin (Hemaccel, Gelofusine)	Starches (Hetastarch, Voluven, Tetrastarch)
Derived from	Modified bovine collagen	Starch and amylopectin
Half life	1-2 h	2-6 h
Dose limitation	Nil	33 ml/kg
Na and Cl	Hemaccel Na-145, Cl-145, Gelofusine – Na-154, Cl-120	Na - 154 Cl - 154
Side effects	Anaphylactoid	Osmotic nephrosis, pruritus, coagulation defects

Other colloids

Hypertonic saline (3%, 7.5%) is as effective as large volume crystalloid as it has potential benefit of osmotherapy and also maintains intravascular volume in traumatic brain injury and shock due to any cause. In animal models of hemorrhagic and septic shock hypertonic saline resuscitation markedly decreased the inflammatory response.

Dextran prevents microvascular thrombosis and has a role in microvascular surgery. However, it is tainted with undesirable side effects – allergic reactions, coagulopathy.

20% albumin is not a resuscitation fluid. It has a niche role in cirrhosis with

hypoalbuminemia following large volume paracentesis and spontaneous bacterial peritonitis; in both instances to prevent hepatorenal syndrome.

Fluids in malarial shock

Shock in malaria 'algid malaria' carries a high mortality in children and adults. It should be treated initially with oxygen, fluids (with close monitoring of CVP) as it is unclear how aggressive the volume expansion should be in terms of safety and efficacy owing to the risk of pulmonary and cerebral edema in this setting. Intravascular hemolysis, hemorrhage from GIT or ruptured spleen should be excluded. A phase III study[8] in Vietnam of severely acidotic patients with malaria showed a mortality benefit from fluid resuscitation with 4.5% albumin when compared with saline (of 88% children just 2% receiving albumin died compared to 16% receiving cheaper synthetic solutions). In very sick children with malarial shock early use of colloids can reduce mortality by over 50%. The trigger for transfusion in malarial shock is 5 g/dL if there is co-existing respiratory distress, impaired consciousness, or hyperparasitemia. However, many physicians extrapolate the transfusion criteria for critically ill children and transfuse at a trigger of 7 g/dL.

Fluids in dengue

A double blind randomized study[9] comparing three fluids for initial resuscitation of children with DSS concluded that initial resuscitation with Ringer's Lactate (crystalloid) is indicated for moderately severe DSS (DSS III) and Hetastarch (colloids) for severe DSS (DSS IV). WHO has recommended an algorithm for DSS (Fig.3).[10]

The above listed causes of shock warrant aggressive fluid resuscitation. However, in the following situations a slow cautious approach may be more prudent.

Fluid in shock – In traumatic hemorrhagic shock

Traditional practices used aggressive and universal preoperative IV infusions of fluids for patients with trauma and hypotension of hemorrhagic origin. There is now a paradigm shift towards restrictive fluid therapy and targeting low normal blood pressures in treating traumatic hemorrhagic shock though most of these studies have been in the setting of penetrating torso injuries.[11] Aggressive fluid resuscitation before hemostasis has been attained can lead to accentuation of ongoing hemorrhage by dilutional coagulopathy, acidosis, hypothermia (the bloody vicious cycle/ the lethal triad), as well as disruption of the clot if high blood pressures are targeted. The patient should be rushed to the operating room as early as possible to stop the bleed and avoid the vicious cycle of fluid resuscitation and worsening uncontrollable bleed. With associated traumatic brain injury one may resort to early use of vasoconstrictors and hypertonic saline. There are however no clear universal recommendations.

Fluids in cardiogenic shock

Children with hypoperfusion caused due to poor myocardial function are regarded to be in cardiogenic shock. Due to the underperfused state, there is an activation of the renin-angiotensin axis and sodium and water retention is the result. However improving preload can directly increase cardiac output by Frank Starling Law. The decision to optimize preload with isotonic fluids should be based on clinical parameters of perfusion, CVP, Mean Arterial Pressure and maneuvers of preload responsiveness. If fluids are thought to be necessary, then smaller aliquots of colloids and over longer periods (eg: 5 ml/kg over 30-60 min) are preferred especially before drugs for intubation and inodilators. The mainstays of

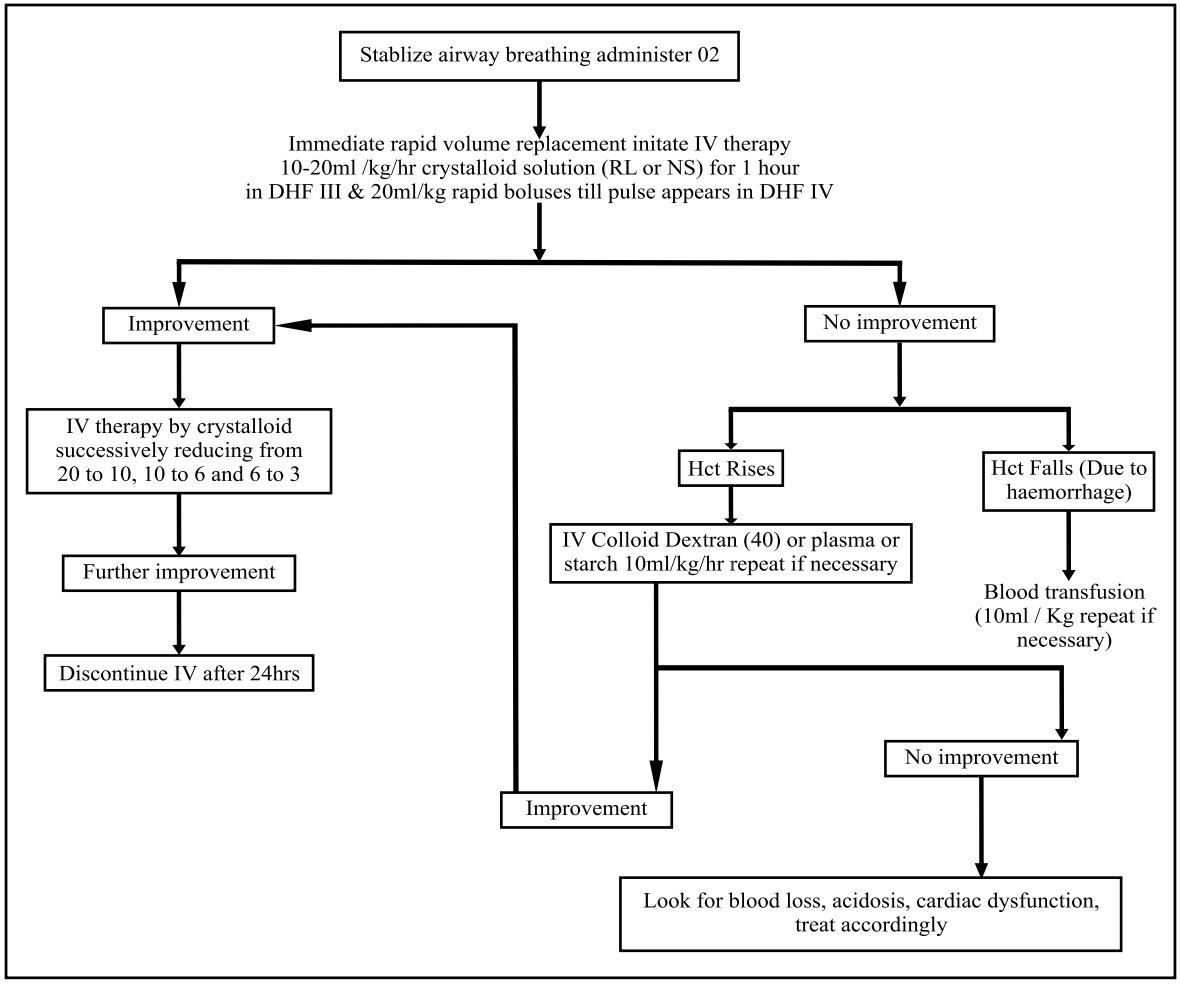


Fig 3. Volume replacement flow chart for patients with DSS grade III & IV

therapy remain dominated by diuretics (introduce after patient is out of shock), vasodilators and inotropes.

Fluids in malnourished child

A severely malnourished child has an altered physiology which is a product of calorie and protein deprivation over relatively long periods. The albumin levels are low and total body sodium is high. They are prone for hypoglycemia. There may be poor myocardial reserve as well. Bearing all these factors in mind, WHO[12] (Table 4) recommends a glucose containing hypotonic fluid for initial resuscitation. The rate of fluid infusion is also slow, and an astute watch should be maintained to assess signs of pulmonary edema. If no improvement is found after the fluid bolus, the child should be assumed to be in septic shock and managed as per protocol. Indian Academy of Pediatrics has devised guidelines for the same.[13]

Table 4. WHO protocol for shock management in a severely malnourished child.[12]

Give this treatment only if the child has signs of shock and is lethargic or has lost consciousness.

- Insert an IV line (and draw blood for emergency laboratory investigations)
- Weigh the child (or estimate the weight) to calculate the volume of fluid to be given
- Give IV fluid 15 ml/kg over 1 hour. Use one of the following solutions (in order of preference), according to availabilty:
  - Ringer's lactate with 5% glucose (dextrose); or
  - half-normal saline with 5% glucose (dextrose); or
  - half-strength Darrow's solution with 5% glucose (dextrose); or, if these are unavailable.
  - Ringer's lactate.

Weight	Volume IV fluid Give over 1 hour (15 ml/kg)	Weight	Volume IV fluid Give over 1 hour (15 ml/kg)
4 kg	60 ml	12 kg	180 ml
6 kg	90 ml	14 kg	210 ml
8 kg	120 ml	16 kg	240 ml
10 kg	150 ml	18 kg	270 ml

- Measure the pulse and breathing rate at the start and every 5-10 minutes.

  If there are signs of improvement (pulse and respiratory rates fall):
  - give repeat IV 15 ml/kg over 1 hour; then
  - switch to oral or nasogastric rehydration with ReSoMal.10 ml/kg/h upto 10 hours;
  - initiate refeeding with starter F-75

  If the child fails to improve after the first 15 ml/kg IV, assume the child has septic shock:
  - give maintenance IV fluid (4 ml/kg/h) while waiting for blood;
  - when blood is available, transfuse fresh whole blood at 10 ml/kg slowly over 3 hours (use packed cells if in cardiac failure); then
  - initiate refeeding with starter F-75
  - start antibiotic treatment

  If the child deteriorates during the IV rehydration (breathing increases by 5 breaths/min or pulse by 15 beats/min), stop the infusion because IV fluid can worsen the child's condition.

Points to Remember

- ***"Early" fluids form the essence of shock management.***
- ***Rate of fluid administration is determined by the suspected etiology of shock.***
- ***Target perfusion and not just pressure. (artificially elevated blood pressure)***
- ***Colloids are generally preferred in severe shock. (eg. Dengue, Malaria)***
- ***Reassess, Reassess and Reassess !!***

References

1. Han YY, Carcillo JA. Early Reversal of Pediatric-Neonatal Septic Shock by Community Physicians is Associated with Improved Outcome. Pediatrics 2003;112:793-799.
2. Rivers E, Nguyen B, Avstad UH, Ressler J, Muzzin A, Knoblich B, et al. Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock. N Engl J Med 2001:345;1368-1377.
3. Booy R, Habibi P, Nadel S, Munter C, Britto J, Morrison A, et al. Reduction in case fatality rate from meningococcal disease associated with improved healthcare delivery. Arch Dis Child 2001;85:386-390.
4. Carcillo JA, Davis AL, Zaritsky A. Role of early fluid resuscitation in Pediatric Septic Shock. JAMA 1991;266:1242-1245.
5. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008;36:296-327.
6. Finfer S, Bellomo R, Boyce N, French J, Myburgh J, Norton R. A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit. The SAFE Study Investigators. N Engl J Med 2004;350:2247-2256.
7. Choong K, Kho ME, Menon K, Bohn D. Hypotonic versus isotonic saline in hospitalised children: a systematic review. Arch Dis Child 2006;91:828-835.
8. Maitland K, Pamba A, English M, Peshu N, Marsh K, Newton C, et al. Randomized Trial of Volume Expansion with Albumin or Saline in Children with Severe Malaria: Preliminary Evidence of Albumin Benefit. Clin Inf Dis 2005;40:538–545.
9. Wills BA, Dung NM, Loan HT, Tam DTH, Thuy TTN, Minh LTT, et al. Comparison of Three Fluid Solutions for Resuscitation in Dengue Shock Syndrome. N Engl J Med 2005;353:877-889.
10. World Health Organization. Treatment of DF and DHF. In:Guidelines for treatment of dengue fever / dengue hemorrhagic fever in small hospitals. SEARO, New Delhi 1999;6-15.
11. Bickell WH, Wall MJ, Pepe PE, Martin RR, Ginger VF, Allen MK, et al. Immediate versus Delayed Fluid Resuscitation for Hypotensive Patients with Penetrating Torso Injuries. N Engl J Med 1994;331:1105-1109.
12. World Health Organization. Triage and emergency conditions. In: Pocket Book of Hospital Care for Children. Guidelines for the management of common illnesses with limited resources. 2005;13.
13. Bhatnagar S, Lodha R, Choudhury P, Sachdev HPS, Shah N, Narayan S, et al. IAP Guidelines 2006 on Hospital Based Management of Severely Malnourished Children (Adapted from the WHO Guidelines) 2007;44:443-461.

NEWS AND NOTES

3rd World Congress of Pediatric Surgery
Hotel Taj Palace and Convention Center, New Delhi
October 21-24, 2010
Post Congress Live Operative Workshop
AIIMS, New Delhi from October 25-26, 2010

Contact: Prof. Devendra K.Gupta
President: 3rd World Congress of Pediatric Surgery
Head, Department of Pediatric Surgery
All India Institute of Medical Sciences, New Delhi-110029.
Tel.: +91-11-26593309, +919810065280 FAX:+91-11-26588663, 26588641
www.pedsurgery.in Email: secretariat@pedsurgery.in, wcps.info@gmail.com ,

IAP-IJPP CME 2009

FOLLOW- UP OF THE HIGH RISK NEONATES

**** Kumutha J***

Abstract: *Medical advancements in neonatology have resulted in improved survival and also increased morbidity among survivors. These infants require follow up to identify growth and neurodevelopmental problems early, to institute appropriate early interventions and to provide continuity of care. Good follow-up screening and early stimulation may lead tobetter quality survival.*

Keywords: *Follow-up, Growth, Neuro-developmental outcome, Early stimulation.*

Advances in obstetric and neonatal care have led to increased survival of high risk neonates. Many of these neonates tend to have higher incidence of growth problems, ongoing medical illnesses and are at-risk for long term morbidities such as developmental delay, visual and hearing problems.[1,2]

Numerous studies have shown that despite substantial improvements in the neonatal mortality, the incidence of chronic morbidities and adverse outcome among survivors have not declined much.[3,4] This mandates the need for a comprehensive follow up care that would ensure systematic monitoring of the general health and neurodevelopmental outcomes

Follow up programs should be an integral extension of every neonatal unit. Specialized care must be made available for problems of growth, development and chronic disease. The monitoring would help early identification and intervention. Because it would be impossible to provide ongoing high risk follow up care for all infants treated in NICU specific criteria have been proposed to identify infants at greatest risk for sequelae.[5]

High risk neonates needing follow-up care

- Babies with birth weight <1800 g and/ or gestation <35 weeks
- Birth depression/ asphyxia/ PPHN
- Intrauterine growth restriction/ Twins with complications
- Neonatal seizures
- Persistent hypoglycemia
- Severe hyperbilirubinemia
- Neonatal meningitis
- Subnormal head circumference & abnormal neurologic examination at discharge
- Major morbidities such as chronic lung disease, intraventricular hemorrhage, and periventricular leucomalacia
- Major congenital malformations
- Infants born to HIV-positive mothers

Parental and the family education on the need for specialised care of high risk infants before discharge ensures adequate follow up. At least 2 responsible caregivers are to be identified and

* Professor of Pediatrics,
Chengalpet Medical College, Chengalpet

trained for care of the infant. They should have demonstrated necessary capabilities to provide all components of care.[6]

The following appropriate elements of primary care are to be completed in the hospital before discharge

- Eyes examination of qualifying infants for retinopathy of prematurity (ROP)
- Hearing evaluation.
- Newborn metabolic screen reviewed
- Appropriate immunizations given based on post natal age
- Baseline neurodevelopmental and neurobehavioural assessment based on corrected age

Chart out an organised program of tracking and surveillance to monitor growth and development (Tables 1 and 2).

At each follow-up visit the infant receives growth monitoring, immunization, checking for ongoing problems, neurodevelopmental assessment. Eye evaluation and Hearing assessment .

Growth monitoring

Growth after discharge is a good measure of physical, neurological and environmental well being. Many factors affect a child's growth. Growth is influenced by gestational age, birth weight, parental stature, chronic illness, and special health needs. Growth approximating

Table 1. The team required for the follow-up program:[7]

S. No	Team member	Role(s)
1	Paediatrician/ Neonatologists	Nodal person of the team To assess growth and screen for developmental delay To manage inter current illness
2	Child psychologist	For formal neurodevelopmental assessment Screening for behavioural problems and their management
3	Paediatric neurologist	Long term management of neurological illness such as seizures
4	Ophthalmologist	Follow up of ROP screening/ treatment Assessment of visual acuity and screening for other problems
5	ENT specialist	Hearing assessment and management of hearing loss if present
6	Dietician	Complementary feeding Management of infants with FTT and those with special needs
7	Medical social worker	Social issues and follow up
8	Physiotherapist	Grading of muscle power Training program for each infant with tone abnormalities Parent education for home exercises
9	Speech/ occupational therapist	Rehabilitation of infants with disability

Table 2. Timing of follow up visits

Cohort	Schedule for follow up
Infant with BW<1800g and /or gestation <35 weeks	• 3-7 days post discharge to check adjustment at home • Every 2 weeks – until weight of 3 kg • At 3, 6, 9, 12, 18 months of corrected age • Then every 6 months until 8 yrs of age
All other conditions	• 2 weeks after discharge • At 6, 10, 14 weeks of post natal age (immunization) • At 3, 6, 9, 12, 18 months of corrected age • Then every 6 months until 8 yrs of age

intrauterine growth is considered by many to be the gold standard for premature infants until term yet controversy exists over the feasibility of replicating growth on an extra uterine basis.

Healthy, LBW, appropriate -for-gestational-age infants generally experience catch up growth during the first 2 years of life, with maximal growth rates between 36 and 40 weeks of gestational age.

Infants who are born SGA or LBW (<1.5 kg) are more likely to experience growth failure than their larger counterparts. Infants with IUGR caused by congenital infections, chromosomal abnormalities and other syndromes may not achieve normal growth.[8,9]

To promote optimal catch up growth of high risk infants, nutrition must be maximised. This is especially important because catch up of head circumference occurs only during the first 6 -12 months after the expected date of delivery.

The evaluation of nutrition includes detailed history of breast feeding, feeding behaviour, adequacy of intake,a physical examination with assessment of oral motor reflexes and observation of a feeding. If an infant is showing poor weight gain on exclusive breast feeding the underlying causes like maternal problems or medical illnesses of the infant if any should be addressed. If all measures fail to give the desired result supplementation may be considered. Complementary feeding is introduced after 6 months of age preferably home prepared semisolid foods which are culturally accepted well.

While monitoring of growth, weight, length and head circumference are useful measurements to help identify nutritional concerns.

Growth charts to use[10]

- Choose respective LBW or VLBW growth chart. Infant Health and Development Program (IHDP)/Wright's growth chart.
- Choose appropriate CDC/WHO growth chart if infant is < 37 weeks but NOT LBW or VLBW. CDC charts allow for comparison of an infant's growth with healthy term infants.
- Use corrected age (40 weeks minus gestational age) until 36 months.

Monitor or track length, head circumference and weight weekly. Plot on growth charts monthly.

When there is a drop in growth, weight will decrease first, then length and a change in head circumference will occur last. For healthy children the most important aspect of growth is that it is regular and consistent. Low weight for length or decline in all growth parameters suggests inadequate nutrition.

Immunization

All infants including VLBW infants should receive their routine paediatric immunizations on the same schedule as term infants based on postnatal age with the exception of hepatitis B vaccine.[11] Medically stable, thriving infants should receive the Hepatitis B vaccine as early as 30 days of age regardless of gestational age or birth weight. If the baby is doing well enough medically to go home before 30 days of age, it can be given at the time of discharge to home.

The American Academy of Paediatrics (AAP) recommends that full doses of DtaP vaccine, IPV, Haemophilus influenza type b (Hib), pneumococcal, varicella, and measles-mumps-rubella (MMR) vaccines be administered at the appropriate chronologic age. Preterm infants, especially those with underlying chronic lung disease would benefit from influenza vaccine.[12]

Medical problems

The management of ongoing illnesses is an integral part of any high risk follow up program. The most common medical conditions found in these infants are asthma, upper and lower respiratory infections, and ear infections. Health problems persist and contribute to frequent hospitalisation, restricted activity, school absence, and poor school performance.

Neurological assessment

A high incidence of neurological abnormalities ranging from 40-80% occurs in high risk infants. A structured age appropriate neuromotor assessment is performed.

Evaluation of muscle tone is an integral part of neurological examination. Assessment of passive muscle tone (Amiel-Tison. Infant Motor Screen) in the first year of life is a useful tool for early detection of motor disability.

Hypertonia or hypotonia is determined by measuring adductor and politeral angles (Table 3).

Active tone, primitive reflexes, postural reflexes assessment and cranial nerve examination should be performed.

Timing of visits for neurological assessment

At 4 months corrected age for documenting problems of inadequate catch up growth and severe neurological abnormality that might require intervention or occupational and physical therapy.

- 8 months corrected age is a good time to identify the presence of cerebral palsy.[13] It is also an excellent time for the first developmental assessment to be performed.
- 18-24 months of age – most transient neurological findings will have resolved and the neurologically abnormal child will be showing some adaptation with improving functional ability.

Table 3. Assessment of tone by adductor and popliteal angles

Age (months)	0-3	4-6	7-9	10-12
Adductor angle	40-80 deg	80-100 deg	110-140 deg	140-160 deg
Popliteal angle	70-110 deg	90-120 deg	110-160 deg	150-170 deg

Red flags

- Brisk reflexes with hypertonia (Scissoring)or hypotonia
- Definitely and consistently elicited asymmetrical signs
- Persistent abnormal posturing or abnormal movements
- Persistent fisting at 3 months of age.
- Hand dominance prior to 18 months.

Tone abnormalities should be taken care of by regular physiotherapy along with orthopaedic evaluation.

Developmental assessment

Assessment of developmental outcomes should be performed using the corrected age. Most developmental experts agree to correct for prematurity at least until two years of age. The four domains usually assessed are a) gross motor, b) fine motor, c) communication and d) personal – social.

Infants who lag behind in any domain should undergo a formal developmental evaluation by a clinical psychologist using tests such as;

- Multi-dimensional Denver Development screening Test (DDST/DENVER II)
- Developmental Assessment of Indian Infant II (DASII II): This scale developed at Baroda University, is based on Bayley Scales of Infant Development.
- Mental developmental index and psychomotor developmental index.
- Trivandrum Development Screening Test for screening babies who are at mild risk for neuro disability.

Poor neurodevelopment outcomes are seen in extreme LBW, Preterms, growth restricted babies birth asphyxia and babies with neonatal morbidities.[14]

Multidisciplinary structured interventions are to be instituted by highly trained interventionists for infants who show developmental delay.

Eye evaluation

ROP is a disorder that interrupts normal vascularisation of the developing retina that potentially leads to blindness. ROP is mainly associated with prematurity. As there are no early clinical signs or symptoms indicate developing ROP, early and regular retinal examination is necessary. it is important that at-risk infants receive carefully timed retinal examinations (Table 4) with indirect ophthalmoscopy by an experienced ophthalmologist.[15]

Who are the infants to be screened: a) infants with BW <1500 g, b) gestational age 32 weeks or less. Selected infants with BW between 1500-2000g or gestational age of >30 weeks with an unstable clinical course who are believed to be at risk.

The onset of serious ROP correlates better with post menstrual age than with postnatal age. The international classification of Retinopathy of Prematurity Revisited should be used to classify and record the retinal findings.

Table 4. Timing of the initial screening

Gestational age	Visit
<27 weeks	Week 6-9
27-28 weeks	Week 5
29-30 weeks	Week 4
31-36/37 weeks	Week 3

Initiation of treatment may be considered for the following retinal findings:

- Zone I ROP: any stage with PLUS disease
- Zone I ROP: stage 3 with no PLUS disease
- Zone II: stage 2 or 3 with plus disease

Treatment (laser photocoagulation) should generally be accomplished when possible within 72 hours of determination of treatable disease to minimise risk of retinal detachment.[16] Follow up examination is usually recommended by the examining ophthalmologist on the basis of retinal findings. All infants with immature fundi or any stage of ROP require close monitoring until the eyes have matured or the ROP has completely resolved. Later follow up to assess for refractive errors, strabismus and amblyopia should be at 1 year of age and at 3 years. Other tests for visual assessments also should be done.

Hearing evaluation

Approximately 1 in1000 newborn infants have significant sensorineural hearing impairment that can have profound effects on speech, language and congnitive development. It is desirable to screen all neonates but mandatory for all babies admitted to NICU/risk factors for hearing impairment.

The average age of diagnosis of hearing impairment in some centres which have implemented universal newborn hearing program is reported be as low as 3months. in contrast the average age of diagnosis of hearing impairment in centres which screen only infants known to have pertinent risk factor is estimated at 24months.[17]

The risk factors associated with hearing loss are

- Any illness requiring admission to NICU for 48 hours or more
- Parental concern regarding speech, language or developmental delay
- Craniofacial anomalies including the pinna and ear canal
- Family history of permanent childhood hearing loss
- Bacterial meningitis, recurrent or persistent otitis media with effusion for at least 3 months
- H/o TORCH infection
- Hyperbilirubinemia requiring exchange transfusion, PPHN associated with mechanical ventilation

Hearing screening tests

The currently acceptable methods for physiologic hearing screening in newborns are auditory brainstem response and evoked otoacoustic emissions (EOAEs). A threshold of > 35 dB has been established as a cut off for an abnormal screen, which prompts further testing.[18]

Evoked otoacoustic emissions (OAE)

Otoacoustic emissions test (OAE)is a non invasive test which tests the auditory pathway up to but not beyond the cochlea .Advantages of OAE are Quick, inexpensive, frequency specific, identifies cochlear and conductive losses. Disadvantages are sensitive to ear canal and middle ear conditions, sensitive to noise and high fail rates in some programs.

Automated auditory brainstem response (AABR)

Automated auditory Brainstem response is a non invasive test which tests the pathway up to the brainstem. AABR identifies cochlear, conductive and neural losses. It is relatively insensible to transient ear canal, middle ear and external noise has a low failure rate than OAE.

Newborn Hearing Screening allows the identification of two groups of babies :

- babies who have passed their hearing screening and therefore need only be investigated further if they are at risk of late onset or progressive hearing loss

- babies who have failed their hearing screen and need to have further testing to establish their hearing status.

Thus behavioural pure tone audiometry remains the standard for hearing evaluation. Prompt audiological assessment must be achieved for all neonates identified by hearing screening and effective intervention must follow for whom the impairment is confirmed.

Current international research indicates that babies whose permanent bilateral hearing impairment is diagnosed before the age of six months and who receive appropriate and consistent early intervention ,have significantly better language levels than those children identified after the age of six months In profound hearing loss, cochlear implants should be considered by 12 months age.

The importance of follow up should be emphasized frequently to the parents and the family.[19] Maximum efforts like telephonic reminder and if possible home visits for patients who do not return for review may improve the follow up and help the goal of achieving the best outcome for these infants. Thus the ultimate aim is a comprehensive care with better care seeking practise from the community.

Points to Remember

- ***Advances in perinatal and neonatal care have improved survival of high risk infants.***
- ***Increased survival does not necessarily mean improved neurodevelopment outcomes.***
- ***ELBW(<1000g) and preterms < 28weeks are the highest risk.***
- ***Neonatal follow –up programs are useful in early identification of growth failure and development delays.***
- ***Early interventions of problems improve the outcome to a great extent.***

References

1. Costello D, Friedman H, Minich N, Siner B, Taylor G, Schuchlter M, Hack M. Improved neurodevelopmental outcomes for extremely low birth weight infants in 2000-2002. Pediatrics 2007;119:37-45.
2. Narayan S, Aggarwal R, Upadhyay A, Deorari AK, Singh M, Paul VK. Surival and morbidity in Extremely Low Birth Weight (ELBW) infants. Indian pediatr 2003;40:130-135.
3. Doyle LW and Victorian Infant Collaborative Study Group. Evaluation of neonatal intensive care for extremely low birth weight infants in Victoria over two decades. Pediatrics 2004; 113:505-509.
4. Piecuch RE, Leonard CH, Cooper BA. Infants with birth weight 1000-1499 grams born in three time periods: Has outcome changed over time? Clin pediatr 1998;37:537-546.
5. Blackman J. Warning signals: Basic criteria for tracking at-risk infants and toddlers. Washington, DC: National center for clinical infants programs, 1986.
6. American Academy of paediatrics. Hospital discharge of the High Risk neonate – Committee on Foetus and Newborn.
7. AIIMS NICU Protocols 2008. Follow- up of High Risk Neonates www.newbornhocc.org
8. Saigal S, Stoskop BL, Streiner DL, Burrows E.; Physical growth and current health status of infants who were of extremely low birth weight and controls at adolescence. Pediatrics 2001;108:407.
9. Hack M, Wissman B, Borawski-Dark E. Catch up growth during childhood among very low

birth weight children.Arch Pediatr Adolesc Med 1996:150:1122.

10. Margaret Broughton, Corinne Eisler, et al, Nutritionists with Vancouver Coastal Health - Growth monitoring in Community settings Birth to 20 years – A reference manual, March, 2005.
11. Ringer SA. Care of the extremely low birth weight infant. In: Manual of neonatal care by John P Cloherty, Eric C Eichenwald and Ann R Stark, 6th edn. Lippcott Williams and Wilkins, New Delhi, 2008; pp78-85.
12. Advisory committee on Immunization practices CACIPJ :2002 Recommedations. Morbidity mortality weekly Rep 2002: 51 CRR02J:1
13. Wilson-Costello D, Elaine Borawski, Harriet Friedman, Raymond Redline, Avroy A. Fanaroff, and Maureen Hack. Perinatal correlates of cerebral palsy and other neurologic impairment among very low birth weight children Pediatrics 1998;102:1.
14. Chaudhari S, Bhalerao M, Chitale A, Pandit A, Nene U. Pune Low Birth Weight Study-A Six Year Follow Up. Indian Pediatr 1999;36:669-676.
15. Policy Statement; Screening examination of premature infants for ROP. Pediatrics 2006;117:572-576
16. Multicentric trial of cryotherapy for retinopathy of prematurity, The natural history ROP: Ocular outcome at 5 1/2 years in premature infants with birth weights less than 1251 gm. Arch Opthalmol 2002;120:595.
17. Arehart K, Itano YC, Thomson V, Gabbard S, Brown SA. State of the states: The status of universal newborn hearing identification and intervention systems in 16 states. Am J Audiol 1998; 7: 101-114.
18. Joint Committee on infants Hearing, Position statement: Principles and guidelines for early hearing detection and intervention programs. Am J Audiol, 2000; 9: 9-29.
19. Tekolste KA, Bennett FC. The high risk infant: Transitions in health, development and family during the first years of life. J Perinatol 1987;868:377.

NEWS AND NOTES

PAED ENDO – 2009

Organised by

Paediatric Endocrine

Division of Institute of Child Health and Hospital for children,

Halls Road, Egmore, Chennai-600 008.

Venue	: Institute of Child Health(ICH) Auditorium
Date & Time	: 28th November 2009, 9AM
Registration	: Free. Prior intimation is a must. Restricted to 100 delegates only.

Contact for Details:

Dr.S.Lakshmi
Organising Secretary
Institue of Child Health & Hospital for Children
Egmore, Chennai-600 008.
Mobile: 9444288811

IAP-IJPP CME 2009

TREATMENT OF MALARIA – RECENT GUIDELINES

** Ravisekar C V*

Abstract : *Malaria is one of the leading cause of morbidity and mortality. In recent years, there is an increase in the incidence of resistance to antimalarial drugs. The recent guidelines on antimalarials for chloroquine (CQ) sensitive malaria, CQ resistance malaria, complicated and severe malaria are discussed in this article.*

Keywords : *Malaria, Management, ACT, Guidelines.*

Malaria is one of the leading causes of morbidity and mortality in developing countries. The mortality currently estimated at over a million people per year has risen in recent years, probably due to increasing resistance to antimalarials.[2] Nearly 248 million cases of malaria are reported annually from South Asia of which 75% cases are contributed by India alone.[2] It is perplexing that the number of falciparum cases is constantly on the rise and in recent years they contribute to nearly 50% of the total cases.

According to the Indian statistics falciparum malaria reistant to chloroquine (CQ) was identified in the north eastern districts along the international border from 2003 onwards. According to National Vector Borne Disease Control Programme, high treatment failure to CQ has been detected in 44 districts of 18 states of India.

* Reader in Pediatrics,
Institute of Child Health and Hospital for Children, Chennai.

In Tamil Nadu, the incidence of P.vivax malaria constitutes more than 90% of total malaria cases. In chennai only 3% of cases are due to falciparum malaria.

The old recommendation of presumptive treatment that any fever in endemic area is to be presumed as malarial fever, a smear to be taken for malarial parasite (MP) and CQ stat dose and 6 hours later dose to be given is no more recommended. If malaria is suspected, always a full course of CQ is to be given. The chances of CQ resistance is more, if only Ist day treatment is given without completing the 2nd and 3rd day course. In areas where CQ sensitive malaria is seen the recommended drug is a full course of CQ (Table 1a).

Artemesimin combination therapy (ACT) is the ideal mode if CQ resistance is suspected. Artemesimin should never be given as mono therapy. The recommendation of ACT is discussed in Table 1b. Artemesinin should always be combined with a single dose of sulfadoxine (25mg/kg) and pyremethamine (1.25 mg/kg) on day one or with mefloquine coformulated tablet. Artemether and lumefantrine also may be given in children. Management of multidrug resistant P.falciparum and failure with artemisinin combination therapy are dealt in Tables 1c and 1d respectively. Untreated severe malaria has a mortality of 100% but with proper treatment it can be reduced to 15 to 20%. Therapeutic concentration of antimalarial can be reached immediately if IV infusion is given. So, in all cases of severe malaria it is preferable to treat with antimalarials as in Table 2 by intravenous infusion initially.

Table 1a. Recommended treatment in chloroquine sensitive malaria[1]

Drug sensitivity	Recommended treatment
P.vivax and chloroquine sensitive P.falciparum	*Chloroquine 10 mg base/ kg stat followed by 5mg/kg at 6,24 and 48 hours or Chloroquine 10mg base/kg stat followed by 10mg/kg at 24 hours and 5mg/kg at 48 hours (total dose 25mg base/kg). §In case of vivax malaria, to prevent relapse, primaquine should be given in a dose of 0.25 mg/kg once daily for 14 days, In case of falciparum malaria, a single dose of primaquine (0.75 mg/kg) is given for gametocytocidal action.

**Chloroquine should not be given on an empty stomach and in high fever. Bring down the temperature first. If vomiting occurs within 45 minutes of a dose of chloroquine, that particular dose is to be repeated after taking care of vomiting by using antiemetic (domperidone/ ondansetron).*

§According to National anti malarial program, a 5 day course of primaquine is advocated because of risk of toxicity and operational feasibility, whereas other authorities advocate 14 days course of primaquine due to lack of evidence to support shorter courses. As primaquine can cause hemolytic anemia in children with G6PD deficiency, they should be preferably screened for the same prior to starting treatment. As infants are relatively G6PD deficient, it is not recommended in this age group and children with 14 days regime should be under close supervision to detect any complication. In cases of borderline G6PD deficiency, once weekly dose of primaquine 0.6 – 0.8 mg/kg is given for 6 weeks.

Table 1b. Recommended treatment in chloroquine resistant P. falciparum[1]

Artesunate 4 mg/kg of body weight once daily for 3 days and a single administration of SP as 25 mg/ kg of sulfadoxine and 1.25 mg/kg of pyrimethamine on day 1 OR artesunate as above and mefloquine 25mg/kg of body weight in two (15 + 10) divided doses on day 2 and day 3.

OR

Co-formulated tablets containing 20 mg of artemether and 120 mg of lumefantrine can be used as a six dose regimen twice a day for 3 days. For 5-14 kg body weight 1 tablet at diagnosis, again after 8 hours and then twice daily on day 2 and day 3. For 15 to 24 kg body weight same schedule with 2 tablets. For 25-35 kg body weight and above 35kg same schedule with 3 and 4 tablets respectively.

(i) Under the previous national drug policy, SP monotherapy in a single dose was used in areas of chloroquine resistance. Countries where SP was introduced following CQ resistance showed its rapid decline in efficacy within few years.

(ii) Currently there are insufficient safety and tolerability data on mefloquine at its recommended dosage of 25 mg/kg body weight in children. Mefloquine shares cross resistance with quinine which is still an effective drug in our country. Health planners of our country do not advocate use of mefloquine.

(iii) Advantage of artemether lumefantrine combination is that lumefantrine is not available as monotherapy and has never been used by itself for the treatment of malaria. Lumefantrine absorption is enhanced by coadministration with fatty food like milk.

Table 1c. Recommended treatment of multidrug resistant P. falciparum (both to chloroquine and sulfadoxine-pyrimethamine)[1]

(1) Quinine, 10mg salt/kg/dose 3 times daily for 7 days.

\+

Tetracycline (above 8 years) 4mg/kg/dose 4 times daily for 7 days

OR

Doxycycline (above 8 years) 3.5mg/kg once a day for 7 days

OR

Clindamycin 20mg/kg/day in 2 divided doses for 7 days.

(2) In case of cinchonism,

Quinine, 10mg salt/kg/dose 3 times daily for 3-5 days

\+

Tetracycline (above 8 years) 4mg/kg/dose 4 times daily for 7 days

OR

Doxycycline (above 8 years) 3.5mg/kg once a day for 7 days

OR

Clindamycin 20mg/kg/day in 2 divided doses for 7 days.

A single dose of primaquine above 1 year age (0.75mg/kg) is given for gametocytocidal action.

(3) Artemether lumefantrine combination as in Table 1b.

(i) Doxycycline is preferred to tetracycline as it can be given once daily and does not accumulate in renal failure.

(ii) One of the drawbacks of quinine therapy is its long course. Unsupervised and ambulatory setting may decrease patient's compliance and many patients might not complete the full course of prescribed therapy.

(iii) Children tolerate quinine better than adults.

Table 1d. Recommended treatment in failure with artemisinin combination therapy (ACT)

Quinine + tetracycline or doxycycline or clindamycin for 7 days as in Table 1c.

(i) Treatment failure within 14 days of receiving an ACT is unusual. It should be confirmed parasitologically by blood slide examination. It is important to determine whether patient has vomited previous treatment or did not complete a full course.

(ii) Failure after 14 days of treatment can be re-treated with first line ACT.

Table 2. Drugs and dosage of antimalarials in complicated and severe malaria[1]

Drug	Dosages
Quinine salt	20mg salt/kg (loading dose) diluted in 10mL of isotonic fluid/kg by infusion over 4 hours. Then 12 hours after the start of loading dose give a maintenance dose of 10mg salt/kg over 2 hours. This maintenance dose should be repeated every 8 hours, calculated from beginning of previous infusion, until the patient can swallow, then quinine tablets, 10mg salt/kg 8 hourly to complete a 7 days course of treatment (including both parenteral and oral).Tetracycline or doxycycline or clindamycin is added to quinine as soon as the patient is able to swallow and should be continued for 7 days. Dosage is as in Table 1c. If controlled IV infusion cannot be administered then quinine salt can be given in the same dosages by IM injection in the anterior thigh (not in buttock). The dose of quinine should be divided between two sites, half the dose in each anterior thigh. If possible IM quinine should be diluted in normal saline to a concentration of 60-100mg salt/ml. (Quinine is usually available as 300mg salt/ml). Tetracycline or doxycline or clindamycin should be added as above.
Artesunate	2.4 mg/kg IV then at 12 and 24 hours, then once a day for total period of 7 days. If the patient is able to swallow, then the daily dose can be given orally. Tetracycline or doxycycline or clindamycin is added to artesunate as soon as the patient can swallow and should be continued for 7 days. Dosage as in Table 1c.
	OR
Artemether	3.2mg/kg (loading dose) IM. Followed by 1.6mg/kg daily for 6 days. If the patient is able to swallow, then the daily dose can be given orally. Tetracycline or doxycycline or clindamycin is added to artemether as soon as the patient can swallow and should be continued for 7 days. Dosage as in Table 1c.

(i) Loading dose of quinine should not be used if the patient has received quinine, quinidine or mefloquine within the preceding 12 hours. Alternatively, loading dose can be administered as 7mg salt/kg by IV infusion pump over 30 minutes, followed immediately by 10mg salt/kg diluted in 10ml isotonic fluid/kg by IV infusion over 4 hours.

(ii) Quinine should not be given by bolus or push injection. Infusion rate should not exceed 5 mg salt/kg/hour.

(iii) If there is no clinical improvement after 48 hours of parenteral therapy, the maintenance dose of quinine should be reduced by one third to one half i.e., 5-7 mg salt/kg.

(iv) Quinine should not be given subcutaneously as this may cause skin necrosis.

(v) Previous maintenance dose of parenteral artesunate of 1.2mg/kg has been modified by WHO to 2.4mg/kg.

(vi) Artesunate, 60mg per ampoule is dissolved in 0.6mL of 5% sodium bicarbonate diluted to 3-5 mL with 5% dextrose and given immediately by IV bolus (push injection).

(vii) Artemether is dispensed in 1 mL ampoule containing 80mg of artemether in peanut oil.

Points to Remember

- ***Chloroquine alone is still used as monotherapy in chloroquine sensitive areas.***
- ***Artemisinin – based combination therapy (ACT) preferred regimen in areas were drug resistance is a problem.***
- ***Artemisinin should never be used as monotherapy.***

References

1. Infectious Disease Chapter, Indian Academy of Paediatrics; management of malaria in children update. Indian Pediatr 2008; 45:731-735.
2. Introduction guidelines for the treatment of malaria general. WHO, 2006; pp1-3.

NEWS AND NOTES

"A GLAD NEWS FROM IAP-VILLUPURAM-PONDICHERRY BRANCH"

A compact disc containing series of lectures(audio&video) delivered over years by legendary teacher Prof.Y.K.Amdekar,Mumbai has been compiled and proudly released by the above branch during 5th East-Coast Pedicon,2009 at Pondicherry. Pediatricians who are interested can get a copy by sending a DD for Rs.150/ (inclusive of postage charges) drawn in favour of 'IAP-VILLUPURAM-PONDY BRANCH' payable at Villupuram.

Mailing address

Dr.R. Palani Raman
Child Health Consultant,
CR WCH Centre,
TINDIVANAM
TAMILNADU
INDIA - 604 001
Mobile - 09345033079

IAP-IJPP CME 2009

APPROACH TO SINGLE - ENHANCING CT LESIONS

** Thilothammal N*

Abstract: *Single enhancing CT lesions are reported more frequently as imaging of brain becomes more frequent. Neurocysticercosis is the most common cause of these lesions. In some patients the lesion may be a tuberculoma. Diagnostic dilemma begins when it is observed in asymptomatic persons and the dilemma in starting cysticidal drug is more when it is single and small. As albendazole therapy is controversial, these patients need to be treated initially with anti epileptic drug (AED) and it may be withdrawn when follow-up CT scan shows resolution of the lesion. Seizures due to calcified lesions should be treated with AED for 2 years. Persistent, symptomatic lesions need to be treated with cysticidal drugs and those lesions of >20 mm should be investigated for tuberculous infection and treated appropriately.*

Key words: *Single enhancing CT lesion, Neurocysticercosis, Tuberculoma, Seizures.*

Single enhancing CT lesions (SECTL) are the commonest radiological abnormality in Indian patients with new on-set seizures. In few cases the lesion may be tuberculoma especially in presence of evidence of tuberculosis else where. However, histopathological studies have proved that neurocysticercosis (NCC) is the most frequent cause for the lesions.[1]

* Retired Professor of Pediatric Neurology, ICH and HC, Chennai.

Incidence

Wadia, et al observed that 26% of patients with partial seizures showed these lesions and the incidence was higher among children as 40% of his patients were below 15 years.[2] Murthy, et al reported single CT lesions in 23.4% of inpatients with all types of epilepsies.[3]

Incidence as high as 72-78% of SECTL has been reported after the first seizure especially in children.[4,5] Poor hygienic conditions of children make them more vulnerable to infections than adults.

It is difficult to estimate community prevalence of SECTL. Neuro imaging was done for patients with partial seizures identified in population based epilepsy surveys. Estimated community prevalence by this method is 4% but other studies mention it to be responsible for half of all partial seizures.[6,7]

Etiology

Single enhancing CT lesions are seen in neurocysticercosis, tuberculoma, metastatic tumours, CNS lymphomas, abscesses, toxoplasmosis, fungal granulomas and rarely with infarction.[8,9]

Clinical picture

Patients with SECTL often present with focal, focal becoming generalized seizures and rarely status epilepticus. Children may present with motor deficits like monoplegia, hemiplegia or ataxia. Large lesions may manifest with features of increased intracranial tension.[10-12]

Neuro-imaging

SECTL is a clinico-radiological entity. Clinical presentation and neuroimaging remain the mainstay of diagnosis in the developing world.

CT scan features

Lesions due to neurocysticercosis appear as irregular hypodense lesion in plain CT scan and contrast study shows smooth, thin walled ring enhancing lesion or disc lesion. The scolex may be seen as contrast enhancing eccentric dot within the cystic lesion (Fig.1).

There is no specific site predilection but, they are seen often at the gray-white matter junction. Ventricular and meningeal lesion may lead to hydrocephalus.

Tuberculous granulomas appear as large (>20mm), irregular thick walled lesions, conglomerating when they are multiple with significant perilesional edema.[13]

Natural course of neurocysticercosis (Table 1)

In patients with new onset seizures these unenhanced cystic lesions (vesicular phase) have never been demonstrated. Second and third stages, which represent dying stages of cysticercus larva, are seen in CT scans of Indian patients with epilepsy. Acute development of inflammation and surrounding cerebral edema is responsible for new –onset seizures in these patients. Because of intense inflammation in and around the parasite in acute stage, patients experience cluster of seizures.

In India 75-85% patients with NCC present with single degenerating (stage 2 and 3) cysticercus, whereas in Latin America and China substantial proportion of infected individuals present with a few viable (stage1) brain cysts. Several studies have showed that 10-20% of symptom free population have one or more intraparenchymal brain calcification. It is

Table 1. Natural course of neurocysticercosis

Stages	Pathology	CT features
I.Vesicular phase	Viable / live larvae inside a translucent liquid filled cyst with thin membrane. No inflammation.	Circumscribed, hypodense, unenhanced, cystic lesion. No surrounding edema.
II. Colloid stage	Host immune mechanism acts on cyst resulting in inflammation. Fluid becomes gelatinous, cyst wall thickens.	Ring enhancing lesion with surrounding edema, scolex may or may not be seen.
III.Granular-Nodular stage	Advanced inflammation due to dying larva. Cyst shrinks; fluid content is replaced by granulomatous tissue.	Disc / coin enhancing lesion with surrounding edema; no scolex.
IV.Calcified stage	Calcification of gliotic scar that replaces the dead parasite.	Calcified lesion.No surrounding edema.

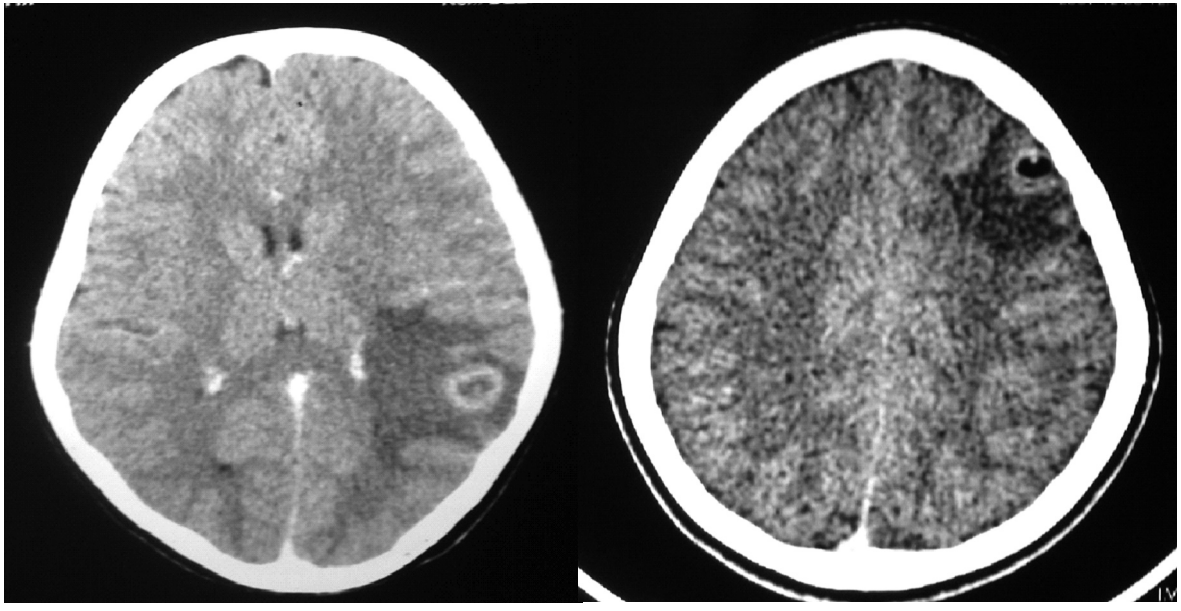


Fig 1. CT Scan : Ring enhancing lesion with scolex

hypothesized that in mild exposures the parasite dies in its early stages by action of the host immune system whereas a small proportion of patients with heavier egg challenge develop multiple viable cysts.

MRI features

MRI is superior to CT scan in revealing smallest lesions and the sensitivity is 95%. Neurocysticercosis is seen as hyperintense lesion with thin hypointense ring and surrounding edema in T2 weighted image. In FLAIR image hyperintense lesion becomes suppressed, i.e., assumes black colour (Fig.2). Contrast study shows ring enhancement with or without scolex. Succinate/ choline peak may be seen in spectroscopy (MRS).

In tuberculoma, T2w image shows hyperintense lesion with hypointense core and surrounding edema. In FLAIR study there is no suppression of lesion and appearance is similar to T2w images. The lesion shows ring enhancement with contrast study and the Magnetic resonance spectroscopy (MRS) shows the characteristic lipid / lactate peaks.[14]

Biopsy of lesion is not recommended but persistent and enhancing lesions must be subjected for biopsy.

Visualisation of scolex as eccentric dot on CT is characteristic of NCC. But this feature may not be sceen always and smaller lesions are often missed by CT scan. Criteria for differentiating NCC from tuberculoma have been described but are not absolute and it may be difficult in smaller lesions to use these criteria. MRI is most sensitive in picking up NCC lesion of smaller size which are not visible in CT scan. Compared to CT scan MRI has better sensitivity to differentiate tuberculoma from NCC though in some instances it is difficult even with MRI. Preliminary experience with proton magnetic resonance spectroscopy shows promise in differentiating tuberculoma from NCC.

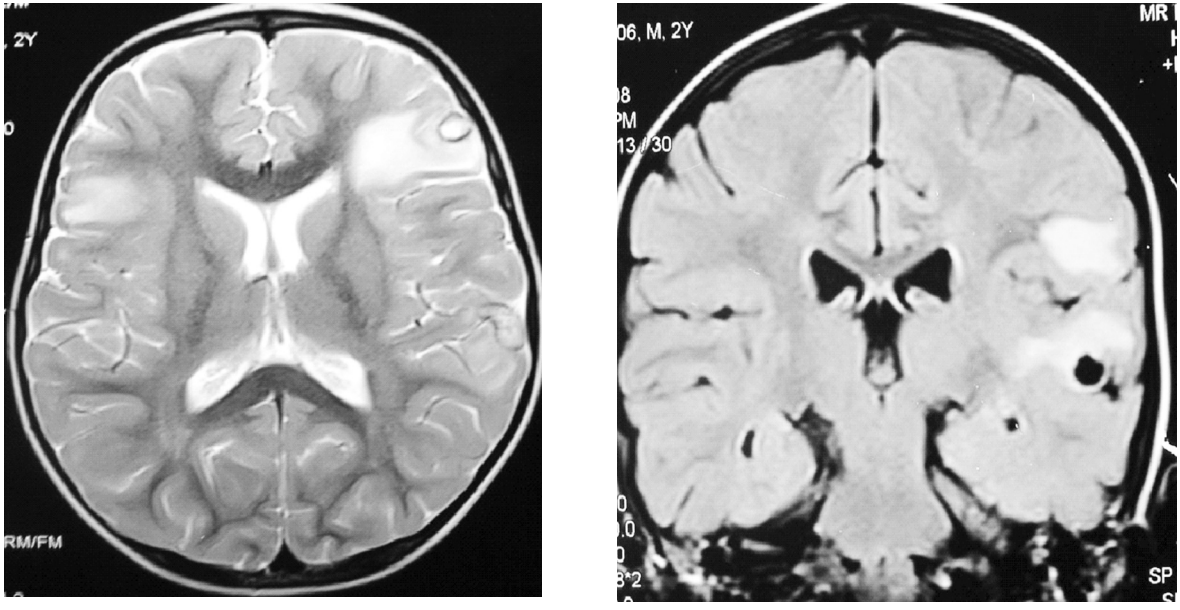


Fig 2. MRI showing ring lesion with perilesional oedema

Immunological tests

Elisa test for cysticercus antibodies in serum and CSF is disappointing as the sensitivity (50%) and specificity (65%) are poor. False positive results due to past infection with T. solium and false negative result due to immune tolerance, inactive disease and localized antibody production in CSF could occur.[15,16]

Enzyme-linked immuno electro-transfer blot (EITB) assays are highly sensitive (98%) and specific (100%) in diagnosing neurocysticercosis. It uses purified glycoprotein antigen from T. solium, but this test is less sensitive with single lesion and calcified lesions.[17]

CSF analysis

When NCC or tuberculoma is restricted to brain parenchyma, CSF is normal. If NCC involves the meninges, there may be mononuclear pleocytosis, elevated protein with normal glucose level. Elevated eosinophil count in CSF has been reported. If tuberculoma co-exists with tuberculous mening0itis then CSF is abnormal with lymphocytic pleocytosis, elevated protein and decreased glucose level.

Criteria for diagnosis of benign SECTL

The clinico radiological picture forms the basis of diagnostic criteria for benign SECTL as proposed by Chandy et al in 1991.[1] All criteria must be satisfied for a diagnosis of benign SECTL.

The clinical criteria are:

1. Seizures (partial or generalized) should be the initial symptom.
2. There should be no features of persistently raised intracranial pressure.
3. There should be no history of a progressive neurological deficit.
4. There should be no evidence of an active systemic disease.

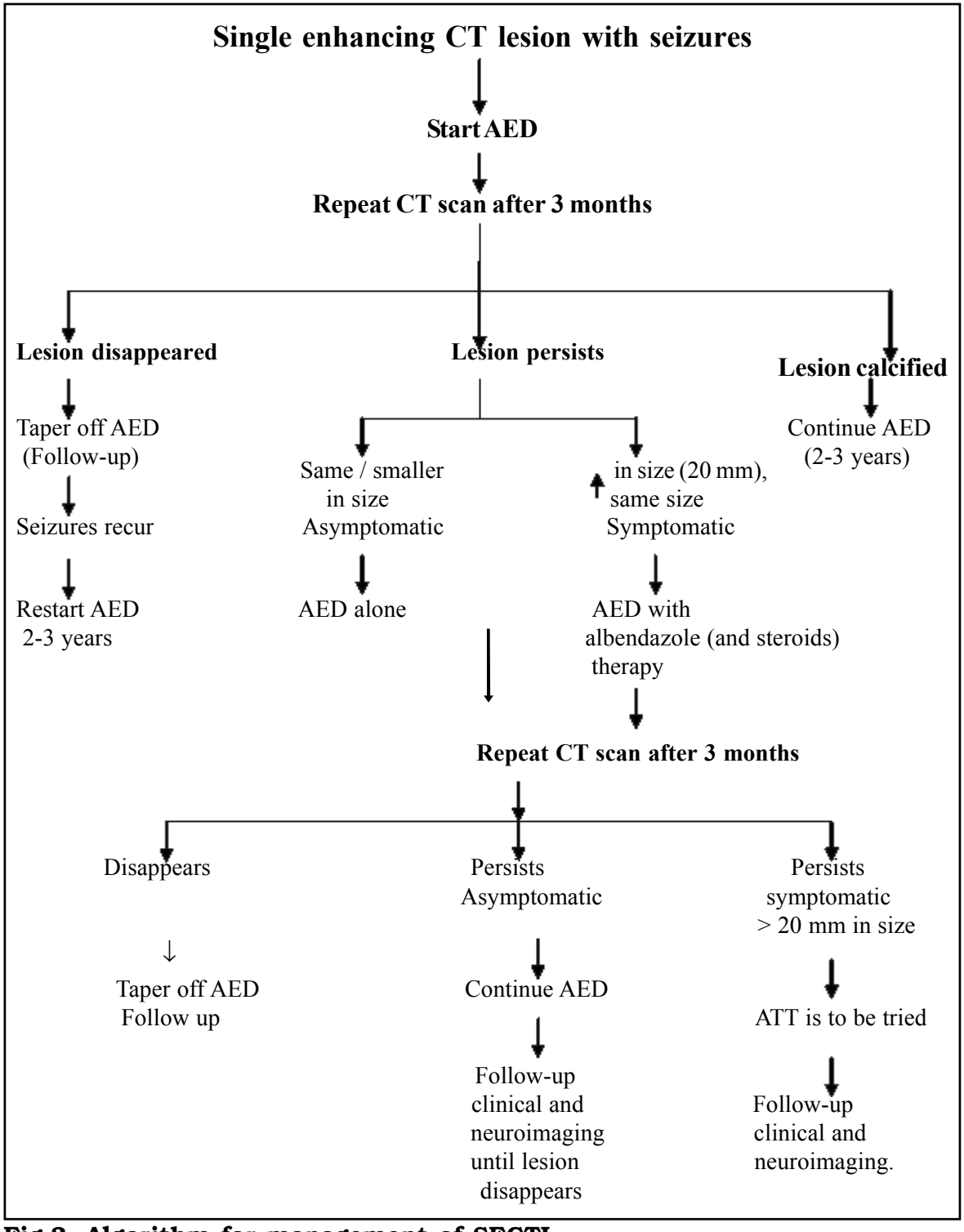


Fig.3. Algorithm for management of SECTL

The radiological criteria are:

1. CT scan should only show a solitary, contrast – enhancing lesion.
2. The lesion should measure less than 20 mm in maximal diameter.
3. Edema may or may not be present, but is not severe enough to produce a shift of the midline structures.

These clinico radiological criteria were found highly sensitive and specific in predicting benign outcome.[1]

Management of SECTL

The controversy in management persists, especially when the treating physicians prefer to err in favour of tuberculosis rather than neurocysticercosis.

Algorithm for management (Fig.3):[18] Patients who do not have raised ICT, progressive neurological deficit, ancillary evidence of tuberculosis or malignancy should be treated with anticonvulsants only as 50-75% of patients show spontaneous regression of lesion on AED's alone. A repeat CT scan is required after 3 months in symptom free patient. Earlier CT scan is recommended if seizures are uncontrollable or new signs and symptoms appear.

Further management depends on CT result : 1) If the lesion is of same size or smaller than base line, edema is less and patient is seizure free, anticonvulsants are continued. 2) If the lesion shows enlargement but still less then 20mm with no shift or ventricular compression, give a course of anti-parasitic drugs along with the anti-convulsants. 3) If the lesion is greater than 20mm with midline shift or gyral compression investigate and treat for tuberculosis.

Cysticidal drugs: Its role in SECTL is controversial. Many studies have shown better resolution, fewer seizure recurrences with albendazole therapy.[19, 20] The advantages of albendazole over praziquantal are that it is orally available as a once daily dose with better penetration into the CSF and its concentration is not affected by steroids.

Albendazole therapy : Albendazole at a dose of 15mg/kg/day in two divided doses for 28 days is preferred. The optimal duration of cysticidal therapy for less common forms such as giant cyst or subarachroaid lesons is not known but should be longer than for parenchymal NCC.[21]

Steriod therapy : Corticosteroid usage has not been standardised and is given empirically for a variable duration of 5-28 days.[20,22] Oral prednisolone is preferred at a dose of 1mg/kg/day for 14 days and is started 2-3 days before starting cysticidal therapy and continued for 7-10 days along with cysticidal drug.[23]

Recommendation for cysticidal drug:[21]

Viable cysts	-	Cysticidal drug and steroid
Enhancing lesion (Single / multiple)	-	AED, cysticidal drugs and steroid
Cysticercotic encephalitis	-	High dose steroid, osmotic diuretics, no cysticidal drug
Calcified lesion	-	No cysticidal drug

Duration of AED: AED may be continued until resolution of SECTL as monitored by CT / MRI and tapered off over next 12 weeks. If seizures are due to calcified parasite then AED is to be continued for 2 years of seizure free period.

Points to Remember

- ***Incidence as high as 72-78% of SECTL have been reported after the first seizures especially in children.***
- ***50% of SECTL resolve spontaneously.***

- ***Initial treatment should include AED alone and it should be tapered off when CT scan shows resolution of lesion.***
- ***Persistent, symptomatic lesions of <20 mm in size in follow-up CT scan should be treated with albendazole.***
- ***Possibility of lesion being a tuberculoma should be considered when it is > 20 mm in size.***
- ***When calcified lesions are seen in patients with seizures, AED therapy is to be continued for 2 years.***

References

1. Chandy MJ, Rajshekhar V, Ghosh S. Single small enhancing CT lesions in Indian patients with epilepsy: clinical, radiological and pathological considerations. J Neurol Neurosurg Psychiatr 1991; 54: 702-705.
2. Wadia RS, Makhale CN, Kelkar AV, Grant KB. Focal epilepsy in India with special reference to lesions showing ring or disc like enhancement on contrast computed tomography. J Neurol Neurosurg Psychiatr 1987;50:1298-1301.
3. Murthy JMK, Subba Reddy YV. Prognosis of epilepsy associated with single CT enhancing lesion: A long term follow-up study. J Neurol Sci 1998;159:151-155.
4. Garg RK, Nag D. Single ring or disc enhancing computed tomographic lesion in Indian children and adolescents after first seizures (letter). Arch Pediatr Adolesc Med 1997;157:632-634.
5. Chopra JS, Sawhney IMS, Suresh N, Prabhakar S, Dhand UK, Suri S. Vanishing CT lesions in epilepsy. J Neurol Sci 1992;107:40-49.
6. Varma A, Gaur KJ. The clinical spectrum of neurocysticercosis in the Uttaranchal region. J Assoc Physi India 2002; 50: 1398-1400.
7. Rajshekhar V, Joshi DD, Doanh NQ, Van Den,Xiaoong Z. Taenia solium cysticercosis in Asia: epidemiology, impact and issues. Acta Trop 2003; 87: 53-60.
8. Rajshekhar V, Chacko G, Haran RP, Chandy MJ, Chandi SM. Clinicoradiological and pathological correlations in patients with solitary cysticercus granuloma and epilepsy focus on presence of the parasite and edema formation. J Neurol Neurosurg Phychiatr 1995;59: 284-286.
9. Kumar N, Narayanaswamy AS, Singh KK. Ring enhancing CT lesion - a diagnostic dilemma. J Assoc Physi India 1995;43:391-393.
10. Sethi PK, Kumar BR, Madan VS, Mohan V. Appearing and disappearing CT scan abnormalities and seizures. J Neurol Neurosurg Phychiatr 1985;48:866-869.
11. Sethi PP, Wadia RS, Kiyatwat DP, et al . Ring or disc enhancing lesions in epilepsy in India. J Trop Med Hyg 1994;97:347-353.
12. Srinivas HV. Disappearing CT lesions – clinical features. J Trop Geograph Neurol 1992;2:88-91.
13. Ahuja GK, Behari M, Goulatia RK, Jaikhani BL. Disappearing CT lesion in epilepsy. Is tuberculosis or Cysticercosis the cause? J Neurol Neurosurg Psychiatr 1989;52: 915-916.
14. Lotz J, Heuulett R, Alkert B, Bowen R. Neurocysticercosis Correlative Patho-morphology and MR imaging. Neuroradiology 1988; 30: 35-41.
15. Schantz PM, Sarti E, Lancarte A. Community based Epidemiologocal Investigations of Cysticercosis due to Tenia Solium: Comparison of serological screening tests and clinical findings in two populations in Mexico. Clin Infect Dis 1994; 18: 879.
16. Pal D, Carpio A, Sander J. Neurocysticercosis and Epilepsy in developing countries. J Neurol Neurosurg Psychiatr 2000; 68: 137-143.
17. Tsang VC, Brand A Boyer A. An Enzyme Linked Immuno Electro Transfer Blot assay by Glycoprotein antigens for diagnosing human Cysticercosis. J Infect Dis 1989; 159: 50-59.
18. Sawheny IMS, Thussu A, Chopra JS. Single small enhancing CT lesions in epilepsy. In Understanding a controversy. Acta Neurol Scandinavia 1991; 44 :204-210.

19. Baranwal AK, Singhi PD, Khandelwal N, Singhi SC. Albendazole therapy in children with focal seizures and single small enhancing computerized tomographic lesions: A randomized, placebo-controlled, double blind trial. Pediatr Infect Dis J 1998; 17: 696-700.

20. Kalra V, Dua T, Kumar V. Efficacy of Albendazole and short-course dexamethasone treatment in children with 1or 2 ring- enhancing lesions of Neurocysticercosis: A randomized controlled trial. J Pediatr 2003; 143: 111-114.

21. Garcia HH, Evans CAW, Nash TE, Takayanagui OM, White AC Jr, Bolero D, et al. Current Consensus Guidelines for Treatment of Neurocysticercosis. Clin Microbiol Rev 2002; 15: 747-756.

22. Singh PD, Jain V, Khandelwal N. Corticosteriod versus Albendazole for treatment of single small enhancing computed tomographic lesions in children with neurocysticercosis. J Child Neurol 2004;19:323.

23. Mall RK, Agarwal A, Garg RK, Kar AM, Shukla R. Short course of prednisolone in Indian patients with solitary granuloma and new onset seizures. Epilepsia 2003;44:1397-1401.

NEWS AND NOTES

FIRST INDIA INTERNATIONAL PEDIATRIC AIDS CONFERENCE (I-IPAC) 2009

Mysore, November 21st and 22nd, 2009

Date(upto)	Delegates(local)	Delegates(International)	Post-graduates
Sept 30th, 2009	2000	70$	1000
Oct 30th, 2009	2500	100$	1500
*Spot registration	3000	150$	2000

* Conference kit not assured

Last date for abstract submission: September 15th, 2009

Scholarship application(full/partial): September 15th, 2009

Late breaker submission: October 1st, 2009

Scholarship consists of

- To and fro travel (as per state wise slabs),
- Accommodation (from 20th to 23rd November)
- Local travel
- Pre and post Conference sightseeing

Registration to the Conference is compulsory for Scholarship applicants. Delegates whose abstracts are accepted for oral presentation, get a waiver of registration.

Conference Secretariat:

Asha Kirana Hospital, #CA-1, Ring Road,
Hebbal Industrial Housing Area,
Mysore-570016, Karnataka.
Ph: 0091-821-4280466 / 0091-821-2497729

IAP-IJPP CME 2009

MANAGEMENT OF CEREBRAL EDEMA

*Abhishek Narayanan
**Bala Ramachandran

Abstract: *Cerebral edema can have multiple causes and is a medical emergency that must be assessed and treated quickly in order to save the child's life and optimize outcome. Treatment consists of general and specific measures. The general measures include attention to the airway, breathing and circulation, positioning, sedation, analgesia, treatment of fever and good supportive care. Specific therapies include hyperventilation, osmotherapy, pharmacotherapy with barbiturates and surgical options. There is only a minimal role for corticosteroids in most instances of cerebral edema.*

Key words: *Cerebral edema, Children, Management*

Cerebral edema or brain edema is an increase in brain water content (normal brain water content is approximately 80%). This cerebral response can be seen secondary to many conditions including traumatic brain injury (TBI), ischemic stroke, intracranial hemorrhage, primary and metastatic tumors, inflammatory diseases (meningitis, ventriculitis, cerebral abscess and encephalitis), and severe toxic– metabolic derangements (hyponatremia and fulminant hepatic encephalopathy).

* Fellow in Pediatric Intensive Care,

** Consultant and Head,

Department of Intensive and Emergency Medicine, Kanchi Kamakoti CHILDS Trust Hospital, Chennai.

Pathophysiology

There are two major types of cerebral edema- cytotoxic and vasogenic. A third variety called interstitial edema (hydrocephalic) is also described. Cytotoxic edema or cellular swelling, results from fluid accumulating within the cells, the commonest cause being cerebral ischemia. This subset affects both gray and white matter and is thought to be resistant to medical treatment. Vasogenic edema results from breakdown of the blood brain barrier (BBB), the common causes being TBI, neoplasms and inflammatory conditions. This variety predominantly affects the white matter and is responsive to medical management. Usually a combination of these subtypes is found with any brain insult.

The consequences of cerebral edema can be well explained by the Monro-Kellie doctrine (the total bulk of three elements inside skull - brain, CSF and blood is at all times constant). As the brain, blood or CSF volumes continue to increase, accommodative mechanisms fail, resulting in significant rise in intracranial pressure (ICP). Greatly raised ICP ultimately leads to a reduction in cerebral blood flow. In these situations, it is the cerebral perfusion pressure (CPP = mean blood pressure – ICP) that maintains the regional and global cerebral blood flow. Furthermore, raised ICP can cause intracranial compartmental shifts leading to herniation syndromes involving vital structures. Early recognition of these syndromes with institution of targeted therapies forms the basis of cerebral resuscitation.

Management

History: Obtain history regarding trauma, vomiting, fever, headache, neck pain, unsteadiness, seizure or other neurological conditions, any visual change, gaze preference, and change in mental status. In infants, look for irritability, poor feeding, lethargy and bulging fontanel.

Assessment: Assess for Cushing response (hypertension, bradycardia and irregular respiration), neck stiffness, photophobia, pupillary response, cranial nerve (III, IV, VI) dysfunction, papilledema, absence of venous pulsations on fundus examination, neurological deficits, extensor plantar reflexes, abnormal posturing, and abnormal mental status examination. Serial bedside monitoring of the Glasgow coma scale (GCS) with findings of new or worsening focal neurological deficits are important.

Urgent Neuroimaging: CT brain is required in all suspected cases. CT may show swelling, midline shift, cisternal compression, sulcal effacement and obliteration of basal cisterns. Normal CT and open fontanel and/or sutures do not rule out raised ICP.

Monitoring of ICP is helpful in patients in whom neurological status is difficult to ascertain serially and to determine an adequate CPP for age. Currently, guidelines for monitoring ICP are present only for TBI and this facility is not widely available in India. Therefore, one has to go by clinical parameters to assess raised ICP. Guidelines for pediatric TBI state that treatment to begin when ICP is > 20 mmHg.

The medical management of cerebral edema (with or without ICP elevation) involves both general measures and specific interventions. General measures include, optimal head and neck positioning for unobstructed intracranial venous outflow, avoidance of systemic hypotension and maintenance of euglycemia and normothermia to mild hypothermia. Specific therapeutic interventions are controlled hyperventilation, administration of corticosteroids or diuretics, osmotherapy and pharmacological cerebral metabolic suppression.

General measures for managing cerebral edema

The primary goal of these measures is to optimize cerebral perfusion, oxygenation, and venous drainage, minimize cerebral metabolic demands and avoid any intervention that may disturb the ionic or osmolar gradient between the brain and the vascular compartment.

The initial management includes stabilization of airway, breathing and circulation with measures directed towards reducing cerebral edema.

Airway

Intubate the child if GCS <8 or with poor upper airway reflexes. Endotracheal intubation should be rapid sequence intubation with analgesia, sedation (avoid ketamine as it causes increase in ICP) and muscle paralysis (avoid succinyl choline as it raises ICP) along with the use of lignocaine. Lignocaine may act directly on brain stem vasomotor centre and blunt ICP response during intubation.

Cervical spine protection with in-line immobilization is required in trauma patients.

Ventilation and oxygenation

Hypoxia and hypercapnia are potent cerebral vasodilators and should be avoided in patients with cerebral edema. Prolonged hypocapnia ($PaCO_2$ < 25 mmHg) causes vasoconstriction leading to ischemia and hence should be avoided. Levels of $PaCO_2$ between 30-35 mmHg should be maintained to support adequate cerebral blood flow and CPP. Oxygen saturation should be

maintained > 96%. To avoid elevations in central venous pressures and impedance of cerebral venous drainage, low PEEP (3-4 cm H_2O) should be applied provided oxygenation is not affected. Use of IV lignocaine 1mg/kg (avoid in liver failure) or fentanyl 1mcg/kg, prior to endo-tracheal suction may blunt the ICP response to this noxious stimulus.

Intravascular volume and cerebral perfusion

Maintenance of adequate CPP using isotonic fluid, in combination with vasopressors if required, is vital in patients with brain injury, irrespective of etiology. Systemic dehydration and the use of hypotonic fluids should be avoided. Daily fluid balance and serum electrolyte monitoring is a must. Systemic arterial and central venous pressure monitoring is required in cases with raised ICP. The recommended goal of a CPP 35-70 mmHg according to age should be targeted (Table 1). The use of antihypertensives to control hypertension may be counterproductive and should be avoided.

Table 1. Recommended goal of CPP according to age

Age	Target CPP[4]
1 month-6 month	> 35 mmHg
6 month-11 month	> 40mmHg
1year-4 years	> 45mmHg
5-9 years	> 50mmHg
10-15 years	> 55mmHg
> 15 years	> 60mmHg

Optimizing head and neck positions

Keeping head up 30 degree and in midline has been observed to promote cerebral venous drainage. The use of restricting devices and garments around the neck (such as devices used to secure endotracheal tubes) has to be avoided as they impair venous outflow.

Sedation, analgesia and neuromuscular blockade

Narcotics, benzodiazepines or small doses of barbiturates are recommended. Non-depolarizing muscular blockade should be used as and when needed. Ketamine and succinyl choline should be avoided.

Seizure management

Seizures should be actively controlled as they raise the cerebral metabolic demand. Use of fosphenytoin (loading dose up to 30mg/kg followed by maintenance doses) is preferred over phenobarbitone as the latter affects sensorium and makes serial clinical assessment difficult. There are not sufficient data supporting the empirical use of anticonvulsants in all forms of brain insult. However, early seizures in TBI can be effectively reduced with the prophylactic use of fosphenytoin or phenytoin for 1-2 weeks. In doubtful cases of sub-clinical or non-convulsive status epilepticus, it is imperative to obtain 24 hour video EEG if available. The control of these subtle seizures will reduce the cerebral metabolic demand.

Management of fever, hyperglycemia, gastric protection

Normothermia is strongly recommended in patients with cerebral edema, irrespective of underlying origin, as fever increases the oxygen demand. The role of mild hypothermia (35-37.0°C) is not clear. Paracetamol is the most common antipyretic used. If required other measures like tepid sponging should be instituted.

Hyperglycemia has been associated with worse clinical outcomes in various forms of brain insult. Hence normoglycemia (sugar levels

between 80-120mg/dl) has to be targeted. Dextrostick/ blood sugar has to be checked every 4 hours.

Any acute brain insult can cause gastric stress ulcers (Curling ulcers). Therefore, either proton pump inhibitors or H_2 antagonists are recommended prophylactically.

Nutritional support

Unless contraindicated, the enteral route of nutrition is preferred. Special attention should be given to the osmotic content of formulations, as increased free water intake may result in a hypo-osmolar state and worsen cerebral edema.

Specific measures for managing cerebral edema

Controlled hyperventilation

Controlled hyperventilation remains one of the most efficacious, short term therapeutic interventions for cerebral edema with raised ICP (bradycardia, hypertension, posturing). A decrease in $PaCO_2$ by 10 mmHg (upto 25mmHg) produces proportional decreases in cerebral blood flow and decrease in blood volume, resulting in rapid and prompt ICP reduction. Overaggressive hyperventilation may actually result in cerebral ischemia. Prolonged hyperventilation has been associated with worse outcomes in patients with TBI – patients should not be routinely hyperventilated. Controlled hyperventilation is used as a rescue or resuscitative measure for a short duration (<5min), until more definitive therapies are instituted and maintained.

Osmotherapy

Osmotherapy remains one of the main therapies to decrease brain water content. It draws out water from the brain by osmotic gradient and decreases blood viscosity, thereby reducing ICP and increasing cerebral blood flow.

Mannitol is an alcohol derivative of the sugar mannose. Its action lasts for 4–6 hours and it is relatively stable in solution. It is a cornerstone for management of intracranial hypertension in pediatric TBI. It acts by two mechanisms – (1) reducing blood viscosity, resulting in increases in cerebral blood flow and CPP and a resultant cerebral vasoconstriction leading to decreased cerebral blood volume, (2) osmotic effect, develops more slowly. Free radical scavenging and inhibition of apoptosis has also been described. Low dosing (0.25- 0.5gm/kg/dose, 3-4 times daily) has been effective with fewer complications. Main side effects include hypotension, acute tubular necrosis and renal failure especially when used with serum osmolarity of more than 320 mOsm. Electrolyte monitoring and daily fluid balance has to be checked. Few data support concomitant use of diuretics.

Hypertonic saline (3%) has been found to be useful in refractory intracranial hypertension in pediatric patients with severe TBI. Animal studies have shown that hypertonic saline modulates CSF production and resorption and increases tissue oxygen delivery. They also seem to modulate inflammatory and neurohumoral responses (arginine-vasopressin and atrial natriuretic peptide) following brain injury. It is given at 1-2ml/kg/hr to target a serum sodium 150-160mEq/L (maintain for 48-72 hours). In the presence of hypertonic saline, high levels of serum osmolarity (360mOsm) are well tolerated. Hypertonic saline can be used in hypotensive states. The side-effect profile is better compared to mannitol and includes extrapontine or central myelinolysis, shrinkage of brain with tearing of bridging vessels leading to subarachnoid hemorrhage, renal failure and rebound intracranial hypertension. Serum sodium should be checked every 4th hourly.

Corticosteroid administration

In cerebral edema, the role of steroids is limited to malignancy, irradiation, surgical manipulation and bacterial meningitis (given before antibiotics to reduce risk of sensorineural hearing loss). Dexamethasone is the preferred agent because it readily crosses blood brain barrier and has low mineralocorticoid action. Corticosteroid use in other forms of cerebral edema is not recommended and has been shown to increase the mortality in TBI.

Pharmacological coma

Barbiturate induced coma has been tried in refractory intracranial hypertension. Barbiturates reduce cerebral metabolic activity, resulting in a coupled reduction in cerebral blood flow (CBF) and cerebral blood volume (CBV). In TBI patients, barbiturates have been shown to reduce ICP but with no improvement in clinical outcome. Thiopentone infusion is given to achieve barbiturate coma - loading dose of 5-10mg/kg over 30 min followed by 5mg/kg every hour for 3 doses, then infusion of 1 mg/kg/hr to achieve burst suppression in EEG. This requires continuous EEG monitoring. Side effects include vasodepressor effects, cardiodepression and immunosuppression. Fluid resuscitation and inotropic support with invasive monitoring is frequently required.

Propofol is an alternative. It reduces cerebral metabolism and has antiseizure action. Hypotension, hypertriglyceridemia and cases of propofol infusion syndrome with prolonged infusions precludes its use.

Surgical measures

Ventricular CSF drainage like ventriculostomy will be helpful and may reduce the need for other therapies. It can be used for both ICP monitoring and draining CSF. Intermittent versus continuous drainage of CSF have not been compared. Prospective randomized trials in pediatric patients are needed.

Lumbar puncture should be avoided to prevent herniation syndromes.

Decompressive craniectomy can be done when all other measures fail.

Treatment of the underlying cause is a must

Points to Remember

- ***Cerebral edema is a medical emergency.***
- ***Urgent evaluation and management are required to prevent mortality and optimize outcome.***
- ***General and specific measures are available for management***
- ***Corticosteroids are effective only in selected patients and are detrimental in head injury.***

Bibliography

1. Tasker RC. "Head and Spinal cord trauma" In: Roger's Textbook of Pediatric Intensive Care. 4th Edn. Lippincott Williams & Wilkins 2008; pp 887-911.
2. Patrick M K, Michael L F, Randell R. "Severe traumatic brain injury in infants and children" In: Pediatric Critical Care (Fuhrman and Zimmerman ed.) 3rd Edn. Mosby Elsevier 2006; pp 1608-1613.
3. Raslan A, Bhardwaj A. Medical management of cerebral edema. Neurosurg Focus 2007;22:E12.
4. Jha SK. Cerebral edema and its management. Medical Journal of Armed Forces India 2003;59:326-331.
5. Johnson HD. Intracranial Hypertension. In: The Harriet Lane Handbook 17th Edn. Mosby Elsevier 2005;pp124-126.
6. Paediatric Intensive Care Guidelines. Royal Children's Hospital, Parkville, Australia. 3rd Edn, 2008.

IAP-IJPP CME 2009

REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME

**** Gowrishankar NC***

Abstract : *Revised National Tuberculosis Control Programme (RNTCP) has revolutionised the treatment of tuberculosis in India. In this system, childhood tuberculosis is classified into 3 categories as in adults, but are divided into four weight bands. Patient wise box (PWB) in RNTCP helps to give the right drugs, in right doses for successful outcome in pediatric tuberculosis.*

Keywords : *RNTCP, Children, Patientwise boxes, Treatment categories.*

Tuberculosis (TB) caused by Mycobacterium tuberculosis, has affected mankind for over 5000 years and continues to be a major cause of morbidity and mortality. Almost one third of the world's population is infected with TB bacilli, which means that they have latent TB. Among them 10% have a life time risk of developing active disease. Poor living conditions, debility and malnutrition predispose population to develop TB disease. HIV infection is the most potent risk factor for a latent TB infection to get converted to active disease. India has the highest TB burden in the world, accounting for one fifth of the global incidence - an estimated 1.9 million cases annually.

* Consultant Pediatrician and Pulmonologist, Chennai

The Government of India started the National Tuberculosis Programme(NTP) in 1962. After three decades of its implementation a joint Government of India and World Health Organization review of the programme revealed several shortcomings.[1] The important findings were that only 30% of the sputum positive cases were diagnosed by this programme and among those diagnosed only 30% completed the treatment. This was mainly due to the over-reliance on X-ray for making a diagnosis of tuberculosis. So, a revised strategy- the Revised National Tuberculosis Control Programme (RNTCP) was planned. The internationally recommended directly observed treatment, short-course (DOTS) was incorporated in the RNTCP. In 1993, RNTCP was started in pilot areas covering a population of 18 million. It was launched as a National Programme in 1997. By March 2006, the entire nation was brought under RNTCP. TB mortality in the country has reduced from an estimated 42/lakh population in 1990 to 28/lakh population in 2006 and the prevalence of TB in the country has reduced from 568/lakh population in 1990 to 299/lakh population by the year 2006 after the implementation of RNTCP as per the WHO 2008 Global TB Report. Treatment success rates have tripled from 25% to 86% and TB death rates have been cut down 7-fold from 29% to 4% in comparison to the pre-RNTCP era.[2]

Goal of RNTCP

The goal of RNTCP is to decrease mortality and morbidity due to TB and reduce transmission of infection until TB ceases to be a major public health problem.

RNTCP aims to control TB by detecting and curing sputum smear-positive patients thereby interrupting the chain of transmission. The objectives of RNTCP are to (a) achieve and maintain a cure rate of at least 85% among new sputum smear positive cases and (b) maintain detection of at least 70% of such cases in the population. RNTCP has shifted the responsibility of cure from the patient to the health system.

Scientific basis of DOTS

DOTS is primarily based on sputum microscopy, domiciliary treatment, short course chemotherapy and directly observed treatment. Sputum smear microscopy provides definitive diagnosis as it is easy to perform, replicable and cost effective.

Domiciliary chemotherapy has been proved to be as effective as sanatoria treatment. The risk of infection among contacts of patients does not increase with domiciliary treatment. The economic burden on society is also lowered by domiciliary treatment.

Several studies in India have shown that six months of chemotherapy gives favourable results when compared with longer terms of treatment.[3,4] Shortcourse chemotherapy (SCC) is therefore more convenient and economical. In addition, the shorter duration makes direct observation more feasible and improves patient adherence to treatment. Intermittent chemotherapy has been found to be as effective as daily chemotherapy. When a colony of M. tuberculosis is exposed to anti-tuberculous drugs TB bacilli stops multiplying for a variable period of time ranging from 2 – 40 days before new growth occurs. This is called the lag phase. RNTCP makes use of this lag phase and anti-tuberculous therapy (ATT) is given intermittently as DOTS. As the quantity of drugs consumed is less, adverse reactions and costs are also lowered. Also intermittent dosing increases the efficacy of treatment by allowing organisms to re-enter the active metabolic phase in which the bactericidal drugs are more effective.

Direct observation of treatment (DOT) wherein an observer watches and assists the patient in swallowing the tablets, ensures that the patient receives the medication. By observing the patients during the entire course of treatment, one ensures that they receive the right drugs, in the right doses, at the right intervals and for the right duration. Intermittent regimens make treatment observation more feasible and convenient for DOT providers and patients.

Identification of tuberculous disease

The most common symptom of pulmonary TB is persistent cough, usually with expectoration in older children. Other symptoms such as weight loss, tiredness, shortness of breath, anorexia and hemoptysis may also be seen.

Diagnosis of pulmonary TB in a young child is difficult as they usually swallow the respiratory secretion after a bout of cough. Also doing gastric lavage or naso pharyngeal swab in out-patient setting is difficult. Hence bacteriological confirmation is not possible in most cases. A diagnosis of TB in children is made by a combination of clinical presentation, sputum examination (wherever possible), chest X-ray, Mantoux test and history of contact with an adult tuberculous patient.

Patients with extra-pulmonary TB (EPTB) who also have cough of any duration, should have 2 sputum samples examined. If the smear result is positive, the patient is classified as pulmonary TB and his/her treatment regimen will be that of a case of smear positive pulmonary TB.

A child with EPTB may have general symptoms like weight loss and fever. Other symptoms depend on the organ affected like swelling of lymph nodes in TB lymphadenitis, pain and swelling of a joint in TB arthritis and alteration in sensorium, convulsions, vomiting, loss

of limb movements in TB meningitis.

Diagnosis of extra-pulmonary TB should be based on: 1. one culture positive specimen from the site of disease or 2. histological evidence of TB, or 3. strong clinical evidence, consistent with active extra-pulmonary TB.

Depending upon the site of the infection, various diagnostic tools may be used. For example, fine needle aspiration cytology (FNAC)/biopsy is used for diagnosing TB lymphadenitis which is the most common variety of EPTB.

For diagnosis of tuberculosis in older children the algorithm as in Fig.1 can be followed.

Grading of sputum / gastric lavage for AFB is shown in Table 1.

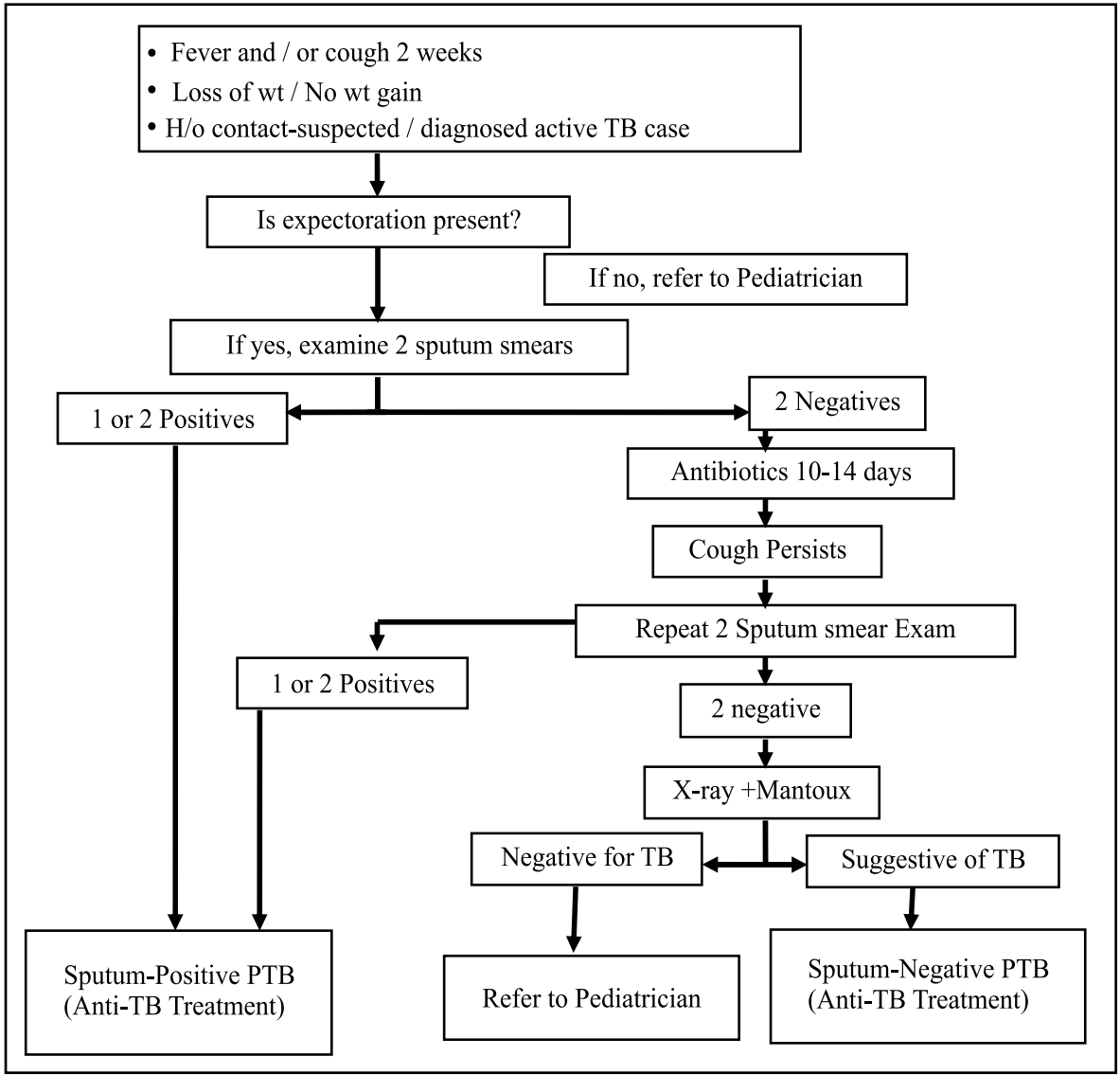


Fig.1. Diagnostic approach to pediatric pulmonary tuberculosis

Table 1. Grading of sputum smear examination[5]

Examination finding	Result as recorded	Grading	No. of fields examined
> 10 AFB / oil immersion field	Positive	3+	20
1–10 AFB / oil immersion field	Positive	2+	50
10–99 AFB/100 oil immersion fields	Positive	1+	100
1–9 AFB /100 oil immersion fields	Positive	Scanty	100

Once a diagnosis of tuberculous disease is made it is classified as pulmonary or extra-pulmonary TB. Pulmonary TB can be either smear positive or smear negative while extra-pulmonary TB can be seriously ill or not seriously ill (Table 2).

Table 2. Classification of extra-pulmonary TB based on severity[5]

Seriously ill	Not seriously ill
• Meningitis • Pericarditis • Peritonitis • Bilateral or extensive pleural effusion • Spinal TB with neurological involvement • Intestinal • Genito-urinary • Co-infection with HIV	• Pleural effusion (Unilateral) • Peripheral joint • Lymph node

All treatment regimens consist of two phases:

Intensive phase (IP) : This aims for a rapid killing of bacilli. This means a shorter duration of infectiousness (< 2 weeks), usually with rapid smear conversion.

Continuation phase (CP) : This eliminates most residual bacilli and reduces failures and relapses. At the start of the CP, there are low numbers of bacilli and less chance of drug resistant mutants. Therefore fewer drugs are needed during this phase.

The five anti-tuberculous drugs used in RNTCP are the following : INH(H), Rifampicin(R), Ethambutol(E), Pyrazinamide(Z) and Streptomycin(S). Tables 3 and 4 show the effectiveness of different drugs against the TB bacilli in various locations and the dosages of individual drugs in intermittent therapy respectively.

Table 3. Target of ATT drugs[5]

Type of TB Bacilli	Effective Drugs
Extra-cellular rapidly multiplying	Rifampicin, Isoniazid, Streptomycin, Ethambutol
Extra-cellular intermittently multiplying/ semi-dormant	Rifampicin
Intra- and extra-cellular acidic environments intermittently multiplying / semi-dormant	Pyrazinamide
Dormant	No drug

Table 4. ATT drug dosage[5]

Drug	Dose (Thrice a week)
INH	10-15 mg/kg
Rifampicin	10 mg/kg
Ethambutol	30 mg/kg
Pyrazinamide	30-35 mg/kg
Streptomycin	15 mg/kg

Children with tuberculous disease are categorized into one of the three categories as shown in Table 5.

Table 5. Disease classification and its treatment in RNTCP

Category	Type of Patient	Conditions
Category I	New sputum smear- positive PTB New sputum smear- negative PTB, seriously ill* New extra-pulmonary TB, seriously ill* $2(HRZE)_3/ 4 (HR)_3$ **	(IAP Group III, IV, V) Consolidation, collapse, bronchiectasis , Lymphadenitis (multiple groups of lymph nodes) Bilateral Pleural effusion Disseminated TB, Miliary TB, Abdominal TB, Ocular TB, Genitourinary TB, Dermal TB, Pericardial TB, Osteoarticular TB, Cavitory TB (Adult type), Endobronchial TB, Tuberculous meningitis, TB Meningoencephalitis, Tuberculoma
Category II	Sputum smear- positive relapse, Sputum smear-positive treatment failure, Sputum smear-positive, treatment after default $2(SHRZE)_3/1(HRZE)_3/5(HRE)_3$	
Category III	New sputum smear- negative, not seriously ill*** New extra-pulmonary TB, not seriously ill*** $2(HRZ)_3/ 4 (HR)_3$	(IAP Group II) Ghon's complex, Pleural effusion (unilateral), Isolated lymphadenitis

* In children, seriously ill sputum smear-negative pulmonary TB includes all forms of sputum smear negative pulmonary TB other than primary complex.

** Prefix indicates the number of months of that section of the treatment and the subscript after the letters indicates the number of doses each week

*** Not seriously ill sputum smear negative PTB includes primary complex.

Not seriously ill extra PTB includes isolated lymphnode TB and unilateral pleural effusion.

Points to note in the above table are

- In TBM - HRZS (instead of HRZE).
- Continuation phase TBM and spinal TB with neurological complications - 6 - 7 months (total treatment 8-9 months).
- Steroids : Prednisolone 1-2 mg/kg/day - TBM and TB pericarditis and tapered over 6-8 weeks.
- In all instances before starting a child on Category II treatment, s/he should be examined by a pediatrician or TB expert, wherever available.

For the ease of administration of drugs certain innovations were made in pediatric RNTCP. The pediatric population is divided into four weight bands for the purpose of easy implementation of RNTCP. They are as follows a) 6 – 10 kg b) 11 – 17 kg c) 18 – 25 kg d) 26 – 30 kg (Table 7). Drugs were made available in patient-wise boxes (PWBs) similar to those supplied for adult patients under RNTCP. This enables optimum dosage for the children as per the respective weight bands without resorting to breaking of the tablets. Pediatric formulations are coded as product code 13 and 14. Tables 6 and 7 give the drug formulations in product codes and drug dosage in different weight bands respectively.

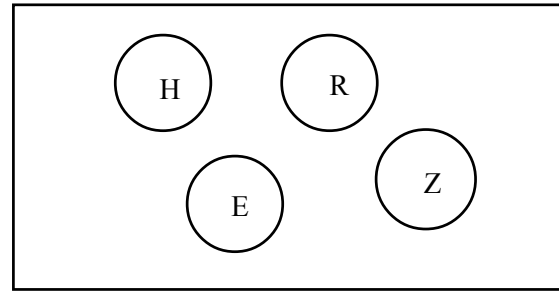
RNTCP box has two pouches a) one having 24 blister packs (one for each day, 3 for each week and so 24 for the two months) for the intensive phase. b)other containing 18 blister packs (one for each week, four for each month and so eighteen for the entire four months) for the continuation phase. None of the tablets are in dispersible form All the tablets for a particular day in the intensive phase will be in a single blister pack while all the drugs for a single week in the continuation phase will be in a single blister pack. Each dose in the intensive phase should be directly observed to ensure adherence and the first dose of each week in the continuation phase is directly observed and the rest is taken at home.

Table 6. Drug formulation and product code

Drugs	Product code 13	Product code 14
INH	75	150
Rifampicin	75	150
Ethambutol	200	400
Pyrazinamide	250	500

The patient has to return the empty blister pack to avail the following week's dose. Figs. 2 and 3 gives a pictoral view of the intensive and the continuation phase blister pack respectively.

Children below 6 kg would be treated as per drugs recommended by pediatricians. Children falling in between the weight bands would be



H- INH : R- RMP : Z- PYZ : E- EMB

Fig. 2. Intensive phase blister pack (for one day)

Table 7. Drug dosage for different weight bands[5]

Drugs	6-10kg	11-17kg	18-25kg	26-30 kg
INH	75	150	225(75+150)	300(150+150)
RMP	75	150	225(75+150)	300(150+150)
EMB	200	400	600(200+400)	800(400+400)
PYZ	250	500	750(250+500)	1000(500+500)
Product code	13	14	13 + 14	14+14

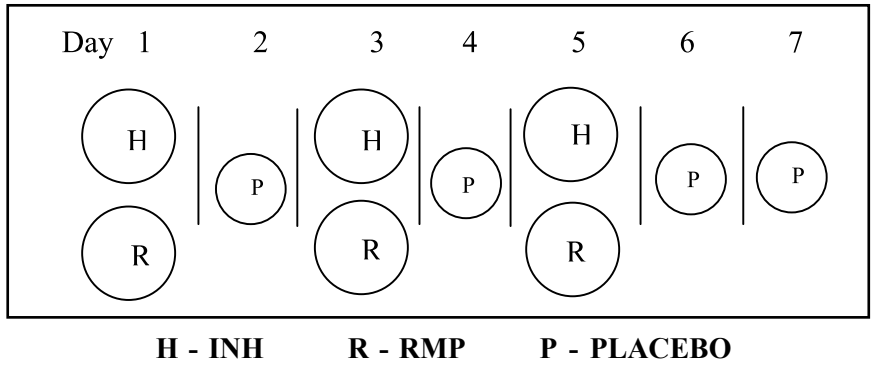


Fig. 3. Continuation phase blister pack (for one week)

treated with the lower weight band boxes - for example if the child's weight is 10.5 kg the child will be put in 6-10 kg weight band and for a child of 17.5 kg it will be in 11-17 kg weight band. The records of the treatment has to be maintained properly so that at any time by going through the records one should be able to make out at what phase of treatment the patient is in. Liver function tests are done as and when needed and not routinely.

In HIV positive children with tuberculosis, ATT should be completed first before starting highly active antiretroviral therapy (HAART) as Rifampicin being an enzyme inducer decreases the effectiveness of certain ART drugs. If child's condition is such that, the child needs HAART also concomittantly, protease inhibitors (PI) should be replaced by Efavirenz till ATT is completed. ATT regimen is the same for both HIV positive and HIV negative children under RNTCP. But care should be taken to monitor general condition and liver function of these children at monthly intervals till ATT is completed.

Latent tuberculous infection (LTBI) as evidenced by a positive mantoux in less than six years of age is treated with INH in a dose of 5 mg/kg daily for a period of six months. INH (100 mg) is supplied separately to be given for children for LTBI in RNTCP.

With the effective participation of each one of the health care provider RNTCP will help to control tuberculosis quickly and effectively and help the nation in a big way.

Points to Remember

- ***Childhood tuberculosis can be easily treated under RNTCP.***
- ***All the drugs are in tablet form though not in dispersible form.***
- ***Patient wise boxes ensure the correct drugs and dosages.***

References

1. Formulation of guidelines for diagnosis and treatment of pediataric TB cases under RNTCP consensus statement. Indian J Tuberc 2004;51:102-105.
2. RNTCP Status Report. TB India 2009;p8
3. Padmini R, Srinivasan S, Nalini P, Mahadevan S. Short course chemotherapy for Tuberculosis in Children. J Trop Pediatr 1993;39:361-364.

4. Campbell IA, Babsow O. Pulmonary Tuberculosis: Diagnosis and treatment. Brit Med J 2006;332:1194-1197.
5. Revised national tuberculosis control programme training module for medical practitioners. Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare, New Delhi 2006.

BOOK REVIEW

Name : Pediknots – Pediatric case Studies

Editor : K.E.Elizabeth

Review : Case scenario based discussion of pediatric problems is the unique specialty of this book. This book will be extremely useful when a reader is confronted with a practical problem like a child with multiple ecchymoses. The reader will get a practical fast food like information to proceed with case management as well as teaching. Author has chosen case scenarios to analyse and discuss common pediatric issues. This type of writing is possible only for those with sound theoretical knowledge and clinical acumen. This book contains 16 topics and in each chapter 6 to 8 issues are discussed. This is a delight for both pediatric postgraduates and practitioners.

A few modifications will definitely add to the quality of the book. Some more details in case scenarios can be given. The reader can be given an opportunity to think and analyse the problem step by step instead of getting the diagnosis straightaway. Sequential questioning and answering in the case development will sustain the interest and reader's enthusiasm to complete the entire study. Theoretical background may be reduced and in its place algorithm for each problem would have been a useful process. Phrasing of the case scenarios is not in a standard book format and appears like ward notes. Though the content does not suffer due to this, it is expected to be corrected in the next edition. Some common and interesting topics like stridor and abdominal pain are not discussed in depth. It is inappropriate to include theoretical topics in community pediatrics in a fast paced book with twists and knots.

At the end of each chapter important tables related to that chapter is provided which is a wise idea. This will save the time for the reader to collect these from various books. This book also contains appendix at the end and nice quotes which are remarkable. Taken as a whole, this will be a valuable book to a practitioner to sort out both common and uncommon issues seen in pediatric practice. A medical teacher can browse this book prior to a teaching session. Of course for a postgraduate, it is a pride possession and a guide to navigate through the ocean of examination.

Publishers: PEEPEE publishers and distributors private Ltd., New Delhi

Price : Rs.350/-

IAP-IJPP CME 2009

ACUTE RHEUMATIC FEVER – UPDATE

* ***Gnanasambandam S***

Abstract : *Acute rheumatic fever continues to be a burden in our country. In the absence of definite laboratory proof, WHO criteria based on the revised Jones criteria is very useful in the diagnosis. Various terminologies of clinical presentation of rheumatic fever are explained. Apart from aspirin, naproxen and methyl prednisolone are also used in selected indications. Primary and secondary prevention are essential in eliminating this illness.*

Keywords : *Rheumatic fever, Streptococcal pharyngitis, Rheumatic heart disease, Jones criteria, Post streptococcal reactive arthritis.*

Acute rheumatic fever (RF) is a nonsuppurative complication due to delayed immune response following Group A β hemolytic streptococcal (GABS) pharyngitis, which is self limiting and involves the joints, skin, brain and the heart. Hence, though considered as a non-communicable disease it results from a communicable disease (streptococcal pharyngitis).[1,2]

Incidence and prevalence

Even though with echocardiograms and other diagnostic aids, it is possible to assess fairly accurately the prevalence of Rheumatic Heart Disease (RHD), the exact prevalence of RF is unclear as symptoms are vague and mild.

Between 1940 and 1983, school surveys estimated the prevalence of RHD to be between 1.8 to 11 per 1000 school children (average 6 per 1000) while from 1989 to 1998, the prevalence was from 1 to 3.9 per 1000. The incidence of acute RF was 0.05 to 1.7 per 1000 in first period and 0.18 to 0.3 per 1000 in the second period.[3]

It is estimated that world wide prevalance of RHD is 15 million while 0.5 million get RF per year. In India, 2 million are affected with RHD and 50,000 get RF each year.

The Jai Vigyan Mission Mode Project (ICMR) on Community Control of RF / RHD in India is being carried out with four main components 1) study the epidemiology of streptococcal sore throat, 2) establish registries for RF and RHD, 3) vaccine development for GABS infection and 4) conducting advanced studies on pathological aspects of RF and RHD.[4]

Prevention

I. Primordial prevention : Measures to prevent the occurrence of GABS sore throat but is not feasible at present.

Role of vaccines: The Jai Vigyan Mission Mode Project at Chandigarh and Vellore has initiated development of such a vaccine.

II. Primary prophylaxis : Treatment of GABS sore throat.

* Assistant Professor,
Department of Cardiology,
Govt. Stanley Medical College, Chennai.

III. Secondary prophylaxis : Prevention of GABS Pharyngitis in patients with previous episodes of RF to prevent of recurrent attacks of rheumatic fever. Secondary prophylaxis should be started only after establishing the diagnosis of acute rheumatic fever and is continued after surgery or intervention for rheumatic valvular disease.

IV. Tertiary prevention : Treatment of cardiac complication of RF by drugs, interventions and surgery for rheumatic valvular disease.

Clinical features of streptococcal infections

Clinical signs and symptoms of group A β hemolytic streptococcal upper respiratory tract infection, by patient age group are shown in Table 1.

Diagnosis of streptococcal pharyngitis: GABS pharyngitis should be diagnosed and differentiated from non streptococcal pharyngitis since the attack rate of RF is 3 per 1000 school children with GABS pharyngitis and may be upto 30 per 1000 during epidemics.

The following features aid in the diagnosis of GABS infection: a) Age younger than 15 years, b) History of fever, c) Tonsillar swelling or exudates, d) Tender anterior cervical lymphadenopathy and e) Absence of cough.

If 4 of the 5 factors are present, the likelihood ratio of streptococcal infection is 4.9 (nearly 50% of cases). If 3 are present the ratio is 2.5 (25%).[5]

Investigations: Throat swab should be cultured and if available, rapid antigen detection test should

Table 1. Group A β hemolytic streptococcal infection at various age groups

Clinical signs and/or symptoms	Infants	School-age children	Adolescents
Anterior cervical lymphadenitis (tender nodes)	++++	++++	++++
Close contact with an infected person	++++	++++	++++
Scarletiniform rash	Unusual	++++	++++
Excoriated nares	++++	Unusual	Unusual
Tonsillar or pharyngeal exudates	Uncommon	++++	++++
Positive throat culture	++++	++++	++++
Fever	++	++	++
Acute onset of symptoms	+	++	++
Abdominal pain	++	++	+
Coryza	++	Unusual	Unusual
Erythema of the pharynx	Not significant	Not significant	Not significant
Hoarseness	Unusual	Unusual	Unusual
Cough	Unusual	Unusual	Unusual

Table 2. Drugs for the treatment of streptococcal pharyngitis and secondary prophylaxis

Drugs	Dose	Sore-throat treatment (duration)	Secondary prophylaxis* (interval)
Benzathine Penicillin G G (deep IM inj)	1.2 million unit (> 27 Kg) after sensitivity test	single dose	21d
	0.6 million unit (<27 Kg) after sensitivity test	single dose	15d
	Contraindication: penicillin allergy		
Penicillin-V (oral)	Children: 250 mg qid	10d	twice a day
	Adult: 500 mg tid	10d	twice a day
	Contraindication: penicillin allergy		
Azithromycin (oral)	12.5 mg/kg/day once daily	5d	Not recommended
Cephalexin (oral)	15-20 mg/kg/dose bid	10d	Not recommended
Erythromycin (oral)	20 mg/kg/dose max 500 mg	Not recommended	twice a day

* Recurrence rate with benzathine penicillin is 1 per 250 patient years compared with 1 per 25 patient years with oral penicillin

Table 3. Diagnosis of acute rheumatic fever[12]

Major criteria	Supportive evidence of preceding streptococcal infection
· Carditis · Polyarthritis	Anti streptolysin O ASO titer: >333 units for children and > 250units for adults.
· Chorea · Subcutaneous nodule · Erythema marginatum	Anti-deoxyribonuclease B (normal values Anti DNase B titer 1:60 unit in preschool, 1:480 units in school children and 1:340 in adults)
Minor criteria	**History of (within previous 45 days)**
· Fever	Streptococcal sore throat
· Polyarthralgia	Scarlet fever
· ↑ESR, ↑CRP, polymorphonuclear leucocytosis	Positive throat culture
· ECG: Prolonged PR interval	Positive rapid streptococcal antigen detection test

be performed. ASO (Antistreptolysin-O), Deoxyribonuclease B (anti-D Nase B) have no use in diagnosing acute GABS pharyngitis or tonsillitis, since it can be interpreted only in retrospect.

Treatment: Drugs for the treatment of streptococcal pharyngitis and secondary prophylaxis are given in Table 2.

Diagnosis of rheumatic fever: 2002–2003 WHO criteria for the diagnosis of rheumatic fever and rheumatic heart disease (based on the revised Jones criteria)[1,6,7] shown in Table 3.

These revised WHO criteria facilitate the diagnosis of : Primary episode of RF, Recurrent attacks of RF in patients without RHD, Recurrent attacks of RF in patients with RHD, Rheumatic chorea, Insidious onset rheumatic carditis and Chronic RHD.

Criteria for diagnosis of rheumatic fever

Primary episode: Two major or one major and two minor criteria plus supportive evidence of previous GABS throat infection.

Recurrence in a patient without established heart disease : Two major or one major and two minor criteria plus supportive evidence of previous streptococcal throat infection.

Recurrence in a patient with established heart disease : Two minor criteria and supportive evidence of previous streptococcal throat infection.

Rheumatic chorea and insidious onset rheumatic carditis : No requirement of other major manifestations or supportive evidence of streptococcal sore throat infection

Chronic valvular lesions of RHD : Patients presenting for the first time as rheumatic heart mitral stenosis or mixed mitral valve disease and/ or aortic valve disease. Do not require any other criteria.

Indicators of recurrence of rheumatic fever in established heart disease are new murmur / change in pre-existing murmur, pericardial rub (and other evidence of pericarditis) unexplained congestive heart failure (CHF), including cardiomegaly.

Terminology

Recurrence: A new episode of rheumatic fever following another GABS infection occurring after 8 weeks following stoppage of treatment.

Rebound: Manifestations of rheumatic fever occurring within 4-6 week of stopping treatment or while tapering drugs.

Relapse: Worsening of rheumatic fever while under treatment and often with carditis.

Sub clinical carditis: When clinical examination is normal but echocardiogram is abnormal. Around 30 percent of patients having chorea present as sub clinical carditis.

Indolent carditis: Patient presents with persistent features of CHF, murmur and cardiomegaly. There are no or very few features of carditis.

Investigations

To establish the diagnosis, relevant tests include throat culture, rapid streptococcal antigen test, ASO, ESR, CRP, complete blood count, platelet count, chest *X*-ray and electrocardiogram (ECG).[8,9]

Echocardiography is not mandatory to establish the diagnosis of rheumatic fever although it has an important role in detection of sub-clinical carditis.[10,11]

Treatment

General measures and symptomatic relief: According to clinical status, treatment for pain relief should be given (codeine or paracetamol till diagnosis is confirmed and aspirin after the diagnosis is confirmed). Hospitalization is needed for moderate to severe carditis, severe arthritis or chorea. Rest is individualized according to

Table 4. Drugs for control of inflammation in acute rheumatic fever[12]

Inflammation	Doses
Arthritis ± mild carditis	
Aspirin *	Regime I starting doses: children 100 mg/kg/day for 2-3 weeks adult 6-8g/day - divide in 4-5 doses Tapering doses: once symptoms resolved, taper to 60-70 mg/kg/day to complete 12 weeks course. For older children 50 mg/kg/day Regime II 50 to 60 mg//kg /day for total 12 weeks
Naproxen(If aspirin intolerance detected)	10-20 mg/kg/day
No response to aspirin in four days	Switch over to steroid. Rule out other conditions like chronic chronic inflammatory/ myelo-proliferative disorders before switching over to steroids.
Moderate to severe carditis	
Steroids*	Regime I Prednisolone: 2mg/kg/day, maximum 80mg/day till ESR normalizes ; usually 2 weeks. Taper over 2-4 weeks, reduce dose by 2.5-5mg every 3rd day. Start aspirin 50-75mg/kg/d simultaneously, to complete total 12 weeks. Regime II Prednisolone same doses × 3-4 weeks. Taper slowly to cover total period of 10-12 weeks
Non responders	
Methyl Prednisolone (Intravenous)	If no response to oral steroid therapy then start IV methyl prednisolone 30mg/kg/day for 3 days

* Consider antacids; Medicines should not be taken on empty stomach.

symptoms. For arthritis, rest for two weeks is adequate. Carditis without congestive heart failure (CHF) needs 4-6 weeks of rest. In cases of CHF, rest must be continued till the CHF is controlled. Appropriate diet is essential for a growing child with cardiac involvement.

Management of inflammatory process (Table 4): Total duration of anti-inflammatory therapy after the diagnosis of acute rheumatic fever is established, must be 12 weeks.

Secondary prophylaxis

Secondary prevention of rheumatic fever is defined as the continuous administration of specific antibiotics to patients with a previous attack of rheumatic fever, or documented RHD. (Table 2.)

Duration of secondary prophylaxis :

- No carditis: 5 years/18years of age, whichever is longer.
- Mild to moderate carditis and healed carditis: 10 years/25 years of age, whichever is longer.
- Severe disease or post intervention patients: Life long. One may opt for secondary prophylaxis up to the age of 40 years.

Post streptococcal reactive arthritis (PSRA)

- Does not fulfill Jones criteria
- Latent period is shorter (1 week)
- Arthritis is additive rather than migratory
- Poor response to salicylates
- Arthiritis persists for a mean period of two months
- Evidence of recent GABS infection is mandatory
- 6% develop mitral heart disease

Duration of Prophylaxis in PRSA

- Low prevalence area - one year
- High prevalence area - 5 years

Points to Remember

- ***GABS pharyngitis is more likely when there is fever, tonsillar exudates, tender lymphnodes and absence of cough.***
- ***In a child with established heart disease, new murmur, changing murmurs and unexplained congestive cardiac failure indicate recurrence.***
- ***Naproxen is indicated if there is intolerance to aspirin.***
- ***IV methyl prednisolone can be used, if there is no response to oral steroid.***

References

1. Rheumatic fever and rheumatic heart disease. Report of WHO study group, Geneva, World Health Organization, 2000 (Technical Report Series, No.923).
2. English PC. Rheumatic fever in America and Britain. A biological, epidemiological and medical history. New Jersey Rutgers University Press, 1999; pp17-52.
3. Padmavathi S. Present status of rheumatic fever and rheumatic heart disease in India. Indian Heart J 2001; 53: 35–37.
4. Falkner F. ed (1980) Prevention in Children of Health Problems in adult life. WHO Geneva.
5. Ebell MH, Smith MA, Barry HC, Ives K, Carey M. The rational clinical examination. Does this patient have streptococcal throat? J Am Med Assoc 2000; 284: 2912 – 2918.
6. Jones TD. Diagnosis of rheumatic fever. J Am Med Assoc 1944; 126: 481-485

7. Special Writing Group of the Committee on Rheumatic Fever, Endocarditis and Kawasaki disease of the council on cardiovascular disease in the young of the American Heart Association. Guidelines for the diagnosis of Rheumatic Fever. Jones criteria 1992 update. J Am Med Assoc 1992; 268: 2069–2073.
8. Carapetis JR, Brown A, Wilson NJ, Edwards KN. On behalf of the Rheumatic Fever Guidelines Writing Group. An Australian guideline for rheumatic fever and rheumatic heart disease: an abridged outline. J Am Med Assoc 2007; 186: 581-586.
9. Nair PM, Philip E, Bahuleyan CG, Thomas M, Shanmugham JS, Saguna Bai NS. The first attack of acute rheumatic fever in childhood: clinical and laboratory profile. Indian Pediatr 1990; 27: 241-246.
10. Narula J, Kaplan EL. Echocardiographic diagnosis of rheumatic fever. Lancet 2001; 358: 2000-2010.
11. Vasan RS, Shrivastava S, Vijayakumar M, Narang R, Lister BC, Narula J. Echocardiographic evaluation of patients with acute rheumatic fever and rheumatic carditis. Circulation 1996; 94: 73-82.
12. Working group on Pediatric Acute Rheumatic fever and cardiology chapter of Indian Academy of Peditrics. Consensus Guidelines on Pediatric Acute Rheumatic Fever and Rheumatic Heat Disease. Indian Pediatr 2008;45:565-573.

NEWS AND NOTES

IAP-IJPP CME 2010

Organised by

Indian Academy of Pediatrics (IAP)

and

Indian Journal of Practical Pediatrics (IJPP)

at Kamarajar Arangam, 492, Anna Salai, Chennai – 600 006.

on Sunday, 13th June 2010

Delegate fee:

Up to 31st May, 2010 Rs.300/- for Post Graduates, Rs.500/- for others.

From 1st June, 2010 Rs.750/-

(by Cash / Cheque / DD drawn in favour of

"IAP-IJPP CME 2010, payable at Chennai)

For further details contact:

Dr.S.Thangavelu

Organizing Secretary, IAP-IJPP CME 2010

1A, Block II, Krsna Apartments,

50, Halls Road, Egmore, Chennai – 600 008.India.

Phone: 044-28190032,42052900, E-mail: ijpp_iap@rediffmail.com

IAP-IJPP CME 2009

WHAT IS NEW IN NEONATAL RESUSCITATION?

*Ratna Kumari TL
** Ramkumar S

Abstract : *The need to evolve a resuscitation programme for neonates with a different emphasis than adult resuscitation was realized in the late seventies when the specialty of neonatology was formally evolving. The basic tenets of airway, breathing, circulation and drugs formed the axis of neonatal resuscitation programme, whereas some details have undergone significant evolution over the years. "Unified guidelines" by International liason committee on resuscitation (ILCOR) in the year 2005 with slight modifications in 2006 have been published giving guiding principles for issues like neonates who were born through meconium stained amniotic fluid (MSAF) and the correct oxygen concentration acceptable to resuscitate a neonate. These details are discussed and also the international guidelines are given verbatim.*

Keywords: *ILCOR (International liason committee on resuscitation), MSAF (Meconium stained amniotic fluid), Oxygen, IPPV, Resuscitation.*

Effective resuscitation of a compromised neonate is the first step in the management of a newly born, which can positively affect the final outcome. To quote Dr.John Kattwinkel, Editor of Textbook of Neonatal Resuscitation, "Birth is beautiful, miraculous and probably the single most dangerous event that most of us will ever encounter in our lifetime".[1] Beautiful in the sense that most of the babies – 90% of them have a smooth transition from intrauterine life to extrauterine existence with no help needed. But indeed 10 % of the babies need some assistance to aid in this transition.

It is from the year 1985, when the formal specialty of neonatology was evolving in the North America and Europe, the principle of neonatal resuscitation was laid down and standardized to train and to teach an appropriate format as a model for "Neonatal Resuscitation Programme". While the basic principles, ie ABCD of the programme remained the same, the science of resuscitation kept changing over the years with evidence based updated inputs coming from various centres of the world.

Before stepping into exploring what is new in neonatal resuscitation, a baseline knowledge about the principles of neonatal resuscitation is essential.

Physiology of transition: Oxygen is an essential factor needed for both in utero and ex-utero existence. In the former, the oxygen is extracted from the mother's blood directly and the lungs do not function as an unit of oxygenation. The lungs are not collapsed contrary to the belief and the alveoli are expanded and filled with fluid. The first vigorous breath accompanying the cry of the newly born effectively pushes this fluid

* Additional Professor of Pediatrics -Neonatology(former)
** Post graduate
Institute of Child Health and Hospital for Children, Chennai

into the interstitium to be subsequently absorbed into the circulation. If the first breath is ineffective, the chain of events that follow prevents effective blood flow to the lungs and hence oxygenation.[2] Lack of oxygen makes the pulmonary blood vessels to remain constricted and it becomes a vicious cycle.

As shown in the flow diagram (Fig.1), basically there are four steps shown as blocks A, B, C, D, which follow an initial assessment block. The time scale is shown on the left as a linear line. Every block has a time scale of 30 seconds and at the end of every block, there is a small evaluation square which evaluates heart rate, respiration and colour.

Based on this, we will now set out to consider in a stepwise manner, what was the earlier stand and what is new and why is it so?

Initial assessment earlier had five questions as given below:

Term gestation

Amniotic fluid – clear/not

Breathing or crying

Good muscle tone

Colour

Currently, colour is not considered as one of the initial assessment pointer since healthy neonate might take >10 min to achieve a preductal saturation of >95% and nearly an hour to have a post-ductal saturation of 95%(level of evidence LOE-5). When a child is breathing vigorously and has a good muscle tone, the colour need not be taken as a pointer as it may be misleading in the initial assessment.

In subsequent evalutions, heart rate, colour and respiration are taken as pointers. Even though the 3 signs are evalutated simultaneously, a seemingly low heart rate is the most important determinant to go to the next block. Note that in neonatal resuscitation, temperature manintenance is of foremost importance and hence airway, breathing, circulation (ABC) is always expressed as temperature, airway, breathing, circulation (TABC).

While using oxygen to resuscitate, to resolve the issue of using 100% oxygen or lesser, the following guidelines are given though current evidence is not that strong.

The guidelines issued by the national neonatal forum (NNF) based on the summary of major changes to the 2005 "American Academy of Pdiatrics (AAP) / American Heart Association (AHA) emergency cardiovascular care guidelines[3] for neonatal resuscitation" is given below.

Use of oxygen during neonatal resuscitation

Current evidence is insufficient to resolve all questions regarding supplemental oxygen use during neonatal resuscitation.

For babies born at term,

- The guidelines recommend use of 100% supplemental oxygen when a baby is cyanotic or when positive-pressure ventilation (PPV) is required during neonatal resuscitation.
- However, research suggests that resuscitation with something less than 100% may be just as successful.
- If resuscitation is started with less than 100% oxygen, supplemental oxygen up to 100% should be administered if there is no appreciable improvement within 90 seconds following birth.
- If supplemental oxygen is unavailable, use room air to deliver positive-pressure ventilation.

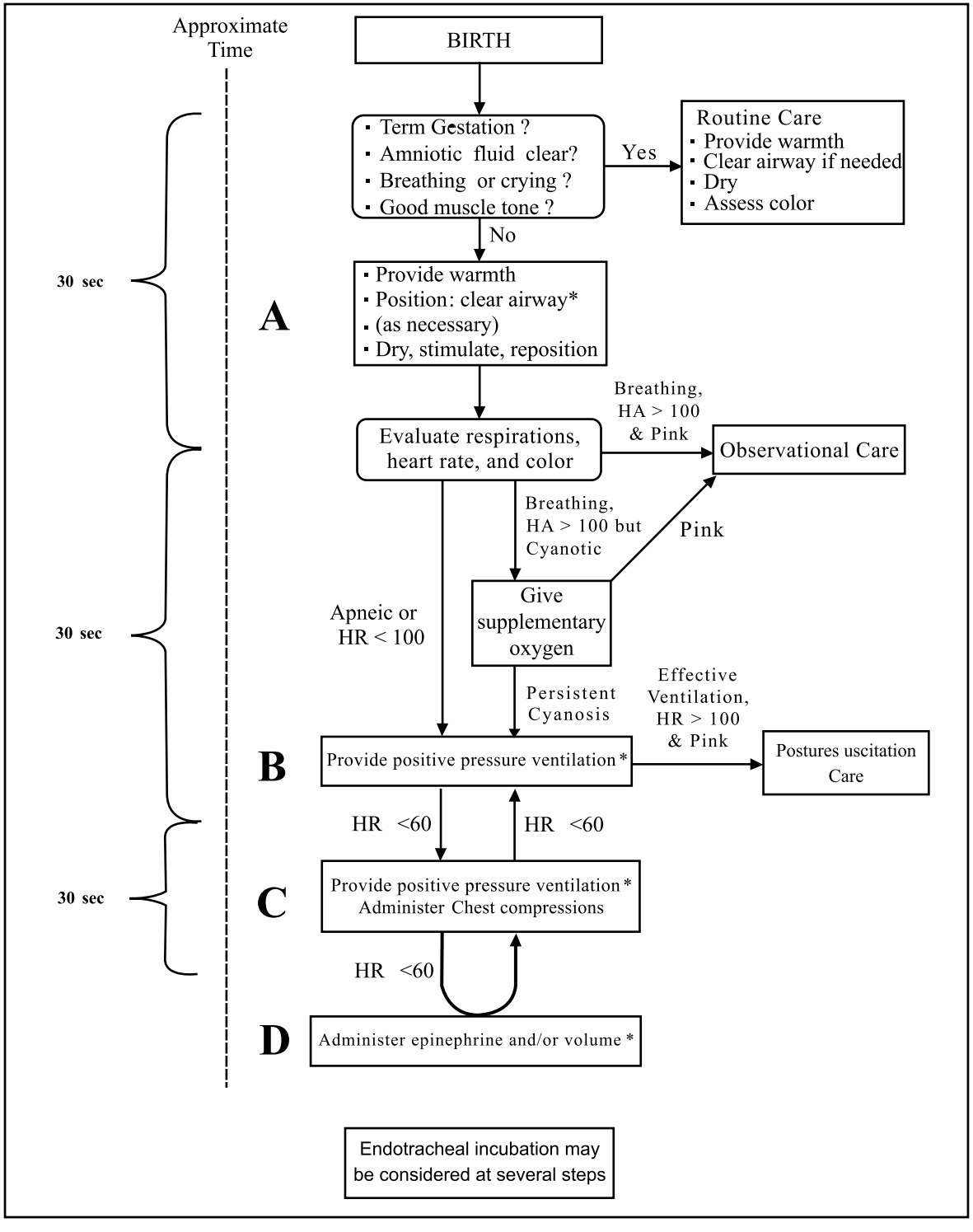


Fig.1. Algorithm of neonatal resuscitation

To reduce excessive tissue oxygenation if a very preterm baby (less than approximately 32 weeks) is being electively delivered at your facility:

- Use an oxygen blender and pulse oximeter during resuscitation.
- Begin PPV with oxygen concentration between room air and 100% oxygen. (No studies justify starting at any particular concentration).
- Adjust oxygen concentration up or down to achieve an oxyhemoglobin concentration that gradually increases toward 90%. Decrease the oxygen concentration as saturation rise over 95%.
- If the heart rate does not respond by increasing rapidly to > 100 beats per minute, correct any ventilation problem and use 100% oxygen.

If your facility does not have an oxygen blender and pulse oximeter in the delivery room, and there is insufficient time to transfer the mother to another facility, the resources and oxygen management described for a term baby are appropriate. There is no convincing evidence that a brief period of 100% oxygen during resuscitation will be detrimental to the preterm infant.

Meconium

It is no longer recommended that all meconium-stained babies routinely receive intrapartum suctioning (i.e., before delivery of shoulder). Other recommendations about post delivery neonatal suctioning remain unchanged.

- Intratracheal suctioning is done for non vigorous babies only (Non vigorous means when HR <100/minute, no respiration and poor muscle tone).

Bag-and-mask ventilation

- Call for assistance when beginning PPV.
- After beginning ventilation at appropriate rate and pressure, ask the assistant to report heart rate and breath sounds as indicators of effective ventilation. Heart rate is assessed first and if not improving, assess chest movement and ask about breath sounds.

Devices for assisting ventilation

Flow-controlled pressure limited mechanical devices (e.g., T-piece resuscitators) are recognized as an acceptable method of administering positive-pressure ventilation during resuscitation of the newly born and in particular the premature infant; however, self-inflating and flow-inflating bag-and-mask equipment and techniques remain the cornerstone of achieving effective ventilation in most resuscitations.

Effectiveness of assisted ventilation

Increasing heart rate is the primary sign of effective ventilation during resuscitation. Other signs are:

- Improving color
- Spontaneous breathing
- Improving muscle tone

Check these signs of improvement after 30 seconds of PPV. This requires the assistance of another person.

Laryngeal mask airway

The laryngeal mask airway has been shown to be an effective alternative for assisting ventilation of some newborns who have failed bag-and mask ventilation or endotracheal intubation.

Use of CO_2 detector

An increasing heart rate and CO_2 detection are the primary methods for confirming ET tube placement.

Epinephrine: If the endotracheal route is used, doses of 0.01 or 0.03 mg/kg will likely be ineffective. Therefore, IV administration of 0.01 to 0.03 mg/kg per dose is the preferred route (Class IIa). While access is being obtained, administration of a higher dose (up to 0.1 mg/kg) through the endotracheal tube may be considered (Class Indeterminate), but the safety and efficacy of this practice have not been evaluated.

Recommended dose

IV: 0.1 to 0.3 ml/kg of 1:10,000 solution. Draw up in 1-mL syringe

ET: 0.3 to 1.0 mL/kg of 1:10,000 solution. Draw up in 3-mL or 5-mL syringe

Naloxone: Naloxone is not recommended during the primary steps of resuscitation

The indications for giving naloxone to the baby require both of the following to be present:

- Continued respiratory depression after positive-pressure ventilation has restored a normal heart rate and color, and
- A history of maternal narcotic administration within the past 4 hours. There are no studies reporting the efficacy of endotracheal naloxone. This route is not recommended.
- Intravenous route preferred.
- Intramuscular route acceptable, but delayed onset of action.

Temperature control

Polyethylene bags may help maintain body temperature during resuscitation of very low birth weight (VLBW) infants.

Therapeutic hypothermia

- Hypothermia may reduce the extent of brain injury following hypoxia-ischemia.
- There is insufficient data to recommend routine use of selective and/or systemic hypothermia after resuscitation of infants with suspected asphyxia. Further clinical trials are needed to determine which infants benefit most and which method of cooling is most effective.

Hyperthermia

- Hyperthermia may worsen the extent of brain injury following hypoxia-ischemia.
- The goal should be to achieve normothermia and to avoid iatrogenic hyperthermia in resuscitated newborns.

Withholding or withdrawing resuscitation

A consistent and coordinated approach to individual cases by the obstetric and neonatal teams and the parents is an important goal. Non-initiation of resuscitation are ethically equivalent, and clinicians should not hesitate to withdraw support when functional survival is highly unlikely. The following guidelines must be interpreted according to current regional outcomes.

- Always resuscitate
- In conditions associated with a high rate of survival and acceptable morbidity, resuscitation is nearly always indicated. This will generally include babies with gestational age > 25 weeks (unless there is evidence of fetal compromise such as intrauterine infection or hypoxia-ischemia) and those with minor congenital malformations.
- In conditions with uncertain prognosis in which survival is borderline, the morbidity rate

is relatively high, and the anticipated burden to the child is high, parental desires concerning initiation of resuscitation should be supported. In the presence of lethal congenital malformation and chromosome anomalies like Patau syndrome, a decision of DNR (do not resuscitate) may be undertaken.

Discontinuing resuscitation efforts

After 10 minutes of continuous and adequate resuscitative efforts, discontinuation of resuscitation may be justified if there are no signs of life (no heart beat and no respiratory effort).

These guidelines are time tested and evidence based and hence form a sound base for building the correct approach for resuscitating the neonate in any scenario be it primary, secondary or tertiary setting.

Points to Remember

- ***Always use 100% oxygen for term babies.***
- ***In preterms use blenders to deliver oxygen.***
- ***Intrapartum suctioning is not required in all MSAF***
- ***Intratracheal suctioning is for non vigorous babies only.***
- ***Prefered route for epinephrine is intravenous only.***
- ***Epinephrine dose has to be higher if intratracheal.***
- ***Nalaxone if given the route is IM or IV only. Never intratracheal.***

References

1. Katt Winkel J. Preface. ln: Text Book of Neonatal Resuscitation, 5th Edn, American Academy of Pediatrics, Jaypee Publication, New Delhi, 2008; P VII-IX .
2. John Kattwinkel, Suzan Nier Meyer, Vinay Natkarni, et al. ILCOR Advisory Statement. Circulation 1999; 99:1927-1938.
3. American Heart Association, American Academy of Pediatrics. Summery of changes to 2005 AAP/AHA. Emergency cardiovascular care guide lines for neonatal resuscitation. www.Americanheart.org / ecc guidelines.

NEWS AND NOTES

IX NEUROPEDICON – 2009 – HUBLI
(National Conference of IAP - Neurology Chapter)
November 28 and 29, 2009
Venue : Karnataka Medical College, Hubli

Contact
Dr.K.M.P.Suresh (Organizing Secretary)
Advanced Neurodiagnostics – Child Neurology Hospital &
Regional Epilepsy Referral Centre.
No. 1 & 2, 2nd Floor, Mallikarjun Avenue, Koppikar Road,
HUBLI – 580020 – Karnataka – INDIA
Contact No: 0836 – 4250428 – 2268596 – 2282428
Mobile : 09448272428
Email: drkmpsuresh@hotmail.com

GENERAL

EVALUATION AND MANAGEMENT OF HYPERTENSION

*Aditi Sinha
**Arvind Bagga

Abstract : *The management of hypertension in children has been influenced by the availability of new consensus recommendations concerning the diagnosis, evaluation, and treatment of hypertension in children. Hypertension in childhood should be confirmed by repeated evaluation, classified for severity, and evaluated for etiology, since pediatric hypertension is usually secondary to renal or renovascular disease. Various methods of measuring blood pressure are compared. Recent information on evidence of safety and efficacy of several new antihypertensive drugs in children has facilitated outpatient management of hypertension. Therapeutic lifestyle changes are the mainstay of therapy for essential hypertension and have an essential role in management of secondary hypertension. Evaluation and periodic monitoring for end organ damage is an integral part of management of children with hypertension. Severe hypertension is a potential medical emergency that needs to be addressed immediately, often with intravenous agents, with the aim of gradually normalizing blood pressure in 48-72 hours followed by a switch to oral treatment.*

Keywords: *Blood pressure, Hypertensive crisis, Kidney disease, Ambulatory monitoring*

* Senior Research Associate,

** Professor of Pediatrics,

Division of Nephrology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi.

The presence of elevated systolic or diastolic blood pressure (systemic hypertension) is increasingly recognized in children and adolescents. The population prevalence of systemic hypertension in childhood and adolescence is estimated as 1-2% in developed countries like the USA;[1] smaller studies from India suggest similar or higher prevalence rates.[2] Secular trends suggest that systemic hypertension is being diagnosed with increasing frequency. This increase is probably attributable to the global epidemic of obesity, change in dietary habits, stressful lifestyle and reduced physical activity.[1]

Monitoring of blood pressure is important because the levels in the higher end of the distribution track into adulthood, resulting in prehypertension, which marks individuals at high risk for progressing to sustained hypertension and consequently, significant cardiovascular morbidity[3]. Children and adolescents with severe hypertension are acutely at increased risk of adverse outcomes, like hypertensive encephalopathy, seizures, cerebrovascular accidents and congestive heart failure.[4,5] Sustained hypertension, even if less severe, contributes to target-organ damage in the long term, especially if associated with other chronic conditions such as chronic kidney disease.[6,7,8] The Indian Society of Pediatric Nephrology has published guidelines on the evaluation and

Table 1. Definition and staging of hypertension in children

Pre-hypertension	SBP or DBP 90th-95th percentile OR >120/80 mm Hg
Hypertension	SBP or DBP >95th percentile
Stage I hypertension	SBP or DBP between 95th percentile and 99th percentile + 5 mm Hg
Stage II hypertension	SBP or DBP > 99th percentile + 5 mm Hg

SBP systolic blood pressure; DBP diastolic blood pressure

management of the condition.[9] Considerable advances have been made in detection, evaluation and management of high blood pressure or hypertension, in children and adolescents. We review the principles of diagnosis, evaluation and management of hypertension in childhood.

Definitions and staging of hypertension

Normative data on blood pressure values, based on gender, age and height percentiles, have been derived from a large multiethnic cohort of children in USA.[10] These values should be used to assess and interpret the diastolic and systolic blood pressures using the guidelines on definition of hypertension proposed in the Fourth US Task Force Report on Hypertension (Table 1). These guidelines are in broad conformity with those proposed for adults by the VII Joint National Commission Report.[11] Based on normative blood pressure, Figs.1 and 2 provide charts for screening and staging of hypertension in boys and girls respectively. If percentiles of systolic and diastolic pressures are different, the higher percentile is used for defining and staging hypertension. Tables providing the 50th, 90th, 95th, and 99th percentiles of blood pressure for age, gender and height percentiles are available at http://www.nhlbi.nih.gov/health/prof/heart/hbp/hbp_ped.htm. In case of infants, normative data from the Second Task Force Report should be used for defining hypertension.[12] Since the severity of hypertension influences its management, it should be staged as given in Table 1.

Patients with pre-hypertension should be followed up every six months with repeated measurements. Patients with stage 1 hypertension should have their blood pressures rechecked at least twice in the next 1-2 weeks or sooner if symptomatic, before the patient is diagnosed to have sustained hypertension. The presence of stage 2 hypertension should be confirmed on a repeat measurement, at the same visit if symptomatic, or within 2-5 days. If the blood pressure is normal, it should be evaluated annually along with routine physical examination.

White coat hypertension

One potential flaw of using office blood pressure measurements alone is the possibility of misidentifying patients as having hypertension when, in fact, their blood pressures are normal, if evaluated in a familiar setting.[13] This phenomenon, known as white coat hypertension, may be seen in 45-60% of children referred for the evaluation of elevated blood pressure.[14] In addition to exaggerated sympathetic response, daily variations in blood pressure, device inaccuracy and measurement inaccuracy may contribute. It does not appear to be associated with the development of hypertensive target-organ damage in children and therefore pharmacological treatment is not required. Since a proportion of the patients may however develop sustained essential hypertension, blood pressure should be monitored over the next 12 months. The magnitude of the white coat effect has been found to rise with the

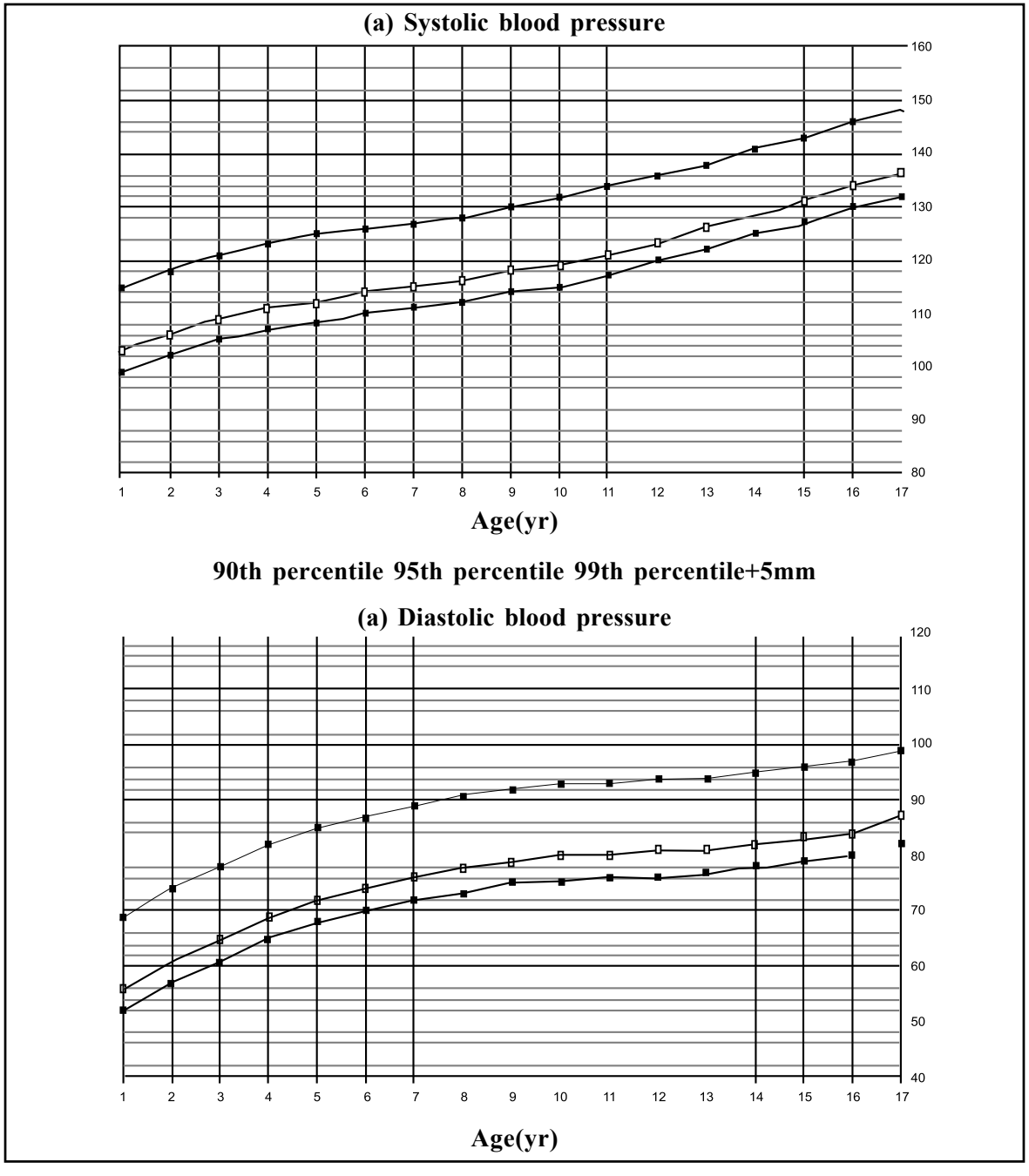


Figure 1: Blood pressure levels for boys at 50th percentile for height. Chart depicting 90th (closed diamonds), 95th (open squares) and 99th + 5 mm (closed triangles) percentile values for (*a*) systolic and (*b*) diastolic blood pressures, representing cut off values for the diagnosis of pre-hypertension, stage I and stage II hypertension respectively in boys (based on the Fourth US Task Force Report on Hypertension). With permission from . Indian Pediatrics 2007; 44: 103-121

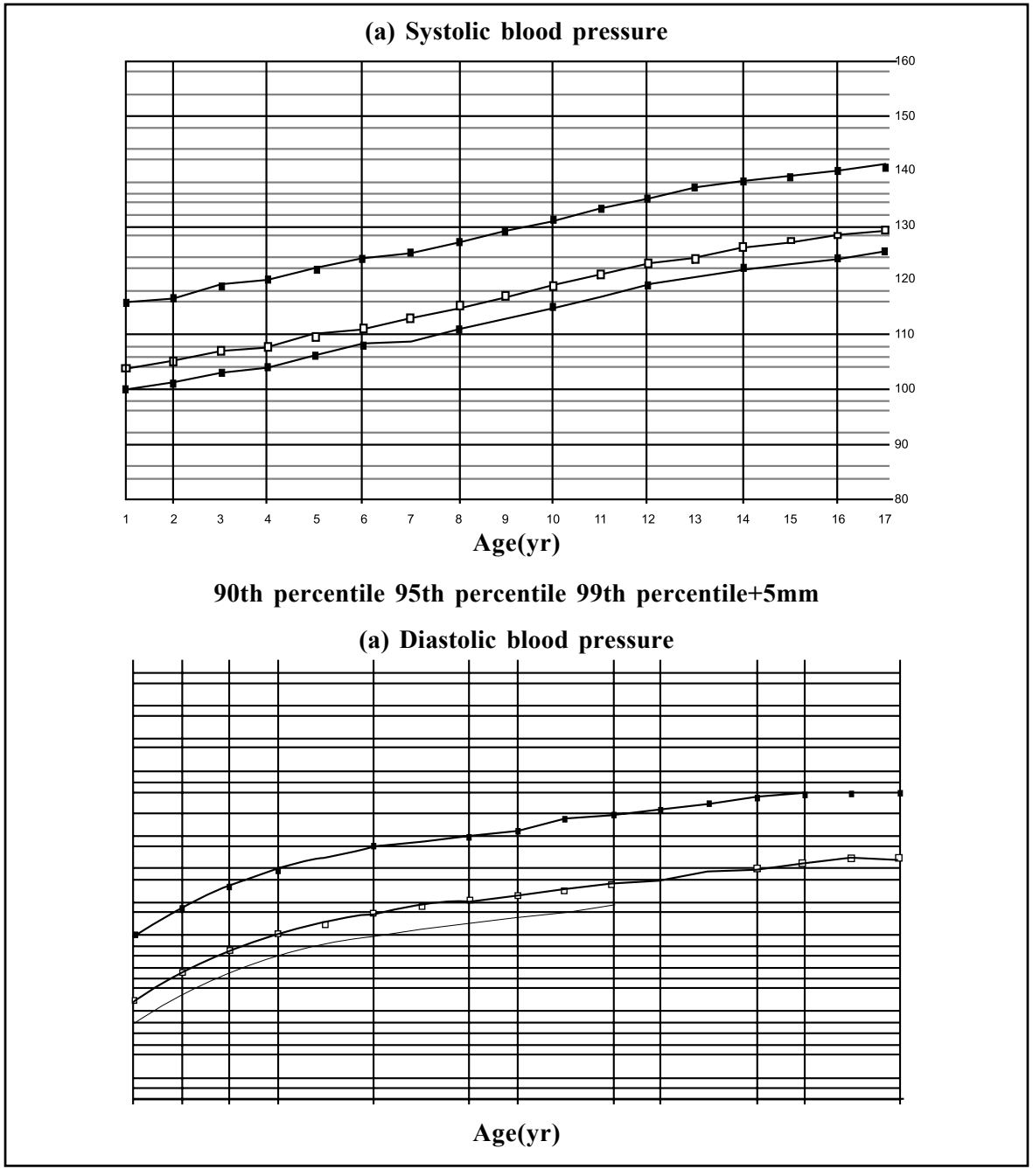


Figure 2: Blood pressure levels for girls at 50th percentile for height. Chart depicting 90th (closed diamonds), 95th (open squares) and 99th + 5 mm (closed triangles) percentile values for (*a*) systolic and (*b*) diastolic blood pressures, representing cut off values for the diagnosis of pre-hypertension, stage I and stage II hypertension respectively in girls (based on the Fourth US Task Force Report on Hypertension). With permission from Indian Pediatrics 2007; 44: 103-121

absolute blood pressure, and is therefore a greater source of error in hypertensive than normotensive children.[15]

Masked hypertension

Masked hypertension is a phenomenon opposite to white coat hypertension and refers to the situation where office blood pressures are normal but the child or adolescent is actually hypertensive. Measurement errors and biological variability may contribute to its occurrence. Masked hypertension is consistently associated with target organ damage and is especially important to identify in children with underlying renal disease in which elevated blood pressures may contribute to progression.[13] In a study in children with chronic renal failure, 'home hypertension' was detected in 17.5% children.[15] Both white coat hypertension and masked hypertension can be detected by ambulatory blood pressure monitoring (ABPM), a technique that is finding greater application in the evaluation of children with elevated blood pressure.[14]

Screening for hypertension

The awareness that essential hypertension has its origin in childhood has resulted in increased emphasis on screening. It is recommended that blood pressure should be measured in all children equal to or above 3 years of age and adolescents, at all medical encounters, as well as in selected children below 3 years of age at risk for hypertension (Table 2).[9,10]

Measurement of blood pressure

It is important that the techniques for measurement of blood pressure are accurate for appropriate diagnosis, staging and follow up. Table 3 shows a comparison of various techniques available. Since the blood pressure norms are based on auscultatory measurement, this remains the preferred method for measurement of blood pressure. It has been suggested that where possible, the choice of blood pressure monitoring (clinic blood pressure *vs.* ABPM) should take into account the pre-test probability of hypertension. Patients with intermediate or high risk of hypertension should be subjected to ABPM for better detection and assessment of hypertension. These include children with obesity, chronic kidney disease (CKD) stages 1 to 3, well controlled diabetes, long term treatment with steroids and autonomic dysfunction (intermediate risk) and those with end stage renal disease, renal allograft recipients, diabetics with micro-albuminuria and end organ damage like left ventricular hypertrophy (high risk).[16]

Table 2. Conditions placing children below 3 years of age at risk of hypertension

History of prematurity, very low birth weight, or other neonatal complication requiring intensive care
Congenital heart disease (repaired or non-repaired)
Recurrent urinary tract infections, hematuria or proteinuria
Known renal disease or urologic malformations
Family history of congenital renal disease
Solid organ transplant
Malignancy or bone marrow transplant
Treatment with drugs known to raise BP
Other systemic illnesses associated with hypertension (*e.g.,* neurofibromatosis, tuberous sclerosis)
Evidence of elevated intracranial pressure

Table 3: An overview of blood pressure monitoring techniques

Technique	Advantages	Drawbacks
Auscultatory (mercury sphygmomanometer)	Most "evidence based" Non-invasive; quick to perform; easily available	White coat effect Observer bias (subject to observer skill) Terminal digit preference (tendency to round off values) Safety hazard with mercury spill
Aneroid manometry	Easily portable; mercury free	Needs frequent calibration
Oscillometric devices	Easy to use Useful in infants, where auscultation is difficult No observer bias	Limited reference data available Values of diastolic blood pressure are derived from mean arterial pressures; may be inaccurate Requires repeated validation Cost & availability
Clinic blood pressure (auscultatory, oscillometric)	Reliable normative data available	Limited number of readings White coat hypertension
Ambulatory blood pressure (ABPM) (auscultatory, oscillometric)	Low cost Detection of white coat, masked hypertension Provides data on diurnal variability (nocturnal dip in blood pressure) Reliable normative data for oscillometric devices[56,57]	Masked hypertension monitoring Considerable cost; need for maintenance of equipment Requires patient cooperation; training of relative May cause anxiety High chances of error with auscultatory devices

SBP systolic blood pressure, DBP diastolic blood pressure,, ABPM ambulatory blood pressure monitoring

All forms of blood pressure measurement in children should be performed after adequate preparation of the patient, including resting quietly for 5 minutes, sitting in an upright position with the back supported and the cubital fossa at the level of the heart. Infants are evaluated in the supine position. Ideally, the child whose blood pressure is to be measured should avoid stimulant drugs or foods, like caffeine, tobacco, theophylline and epinephrine. The right arm is preferred to avoid falsely low readings in patients with coarctation of the aorta and for consistency.[10] At least three measurements are taken on a visit, both for confirming reproducibility of the result, and for decreasing the effect of white coat hypertension. Correct measurement of blood pressure requires the use of a cuff that is appropriate to the size of the child's upper right arm. An appropriate cuff size is a cuff with an inflatable bladder width that is at least 40 percent of the arm circumference at a point midway between the olecranon and the acromion, and bladder length sufficient to cover 80-100% of the arm circumference.[10] Overall, the measurements

are overestimated to a greater degree with a cuff that is too small than they are underestimated by a cuff that is too large and hence a large cuff may be preferred when the appropriate cuff size is not available.[10] However, caution is essential with the use of mercury sphygmomanometer because mercury is a major environmental pollutant and accidental spills must be managed carefully. (For guidelines, refer to US Environment Protection Agency; www.epa.gov).

Blood pressure values on oscillometry, which exceed the 90th percentile, must be confirmed by sphygmomanometry. Only devices that have been validated according to association for the advancement of medical instrumentation (AAMI), British hypertension society (BHS) or European society of hypertension (ESH) standards should be used.

Ambulatory blood pressure monitoring (ABPM) refers to the continuous recordings of blood pressure over 12 or 24-hour; these are believed to reflect true blood pressures accurately, are more reproducible and correlate with target organ damage. Devices are programmed to record blood pressure every 20 to 30 minutes during waking hours and every 30 to 60 minutes during sleep hours. Data are inspected for inconsistencies (outliers), evaluated for reliability (by calibrating against clinic blood pressure records) and assessed in terms of mean blood pressure load (percentage of readings above the ambulatory 95th percentile) and nocturnal dipping (percent day-night difference)[17-19] ABPM is helpful in the evaluation of white-coat hypertension, the risk for hypertensive organ injury, apparent drug resistance and in those showing symptoms of hypotension following antihypertensive medications. ABPM is also useful for evaluating patients for whom more information on blood pressure is needed, such as those with episodic hypertension, chronic kidney disease (CKD), diabetes and autonomic dysfunction.[10,17] A lack of availability of these instruments and normative standards has limited the utility of ABPM for the diagnosis of hypertension in children.[10]

Transient hypertension

Acute or sudden onset hypertension may occur in the course of various conditions, require therapy for brief periods and usually settle with the resolution of the original disease. Examples include acute glomerulonephritis, interstitital nephritis, renal artery or vein thrombosis, hemolytic uremic syndrome, acute urinary tract obstruction, nephrotic syndrome with relapse and acute renal failure of any cause. Non-renal causes include increased intracranial pressure, acute intermittent porphyria, Guillain Barre syndrome, anxiety and hyperthyroidism. Hypertension may be iatrogenic, secondary to fluid or salt overload or medications like corticosteroids, sympathomimetic agents and erythropoietin. Persistence of elevated blood pressures requires detailed evaluation.

Sustained hypertension

Sustained hypertension in children is often secondary to an underlying renal disease (Table 4); renal parenchymal disorders is the underlying cause in 60-70% cases, while an additional 5-10% have hypertension secondary to renovascular disease.[18,19] The likelihood of identifying a cause is inversely related to the age of the child at diagnosis and directly related to the degree of hypertension. Children with CKD are frequently hypertensive and a significant proportion are taking antihypertensive medications.[20,21] In recent years, essential hypertension has become an important health concern. Patients with essential hypertension are usually post pubertal and over-weight, typically show stage 1 hypertension and have no evidence of target organ damage.

The etiology of hypertension varies by age. Thus, while renal artery thrombosis, coarctation

Table 4. Causes of persistent hypertension

Renal parenchymal disease
Glomerulonephritis (GN); (focal segmental glomerulosclerosis, membranoproliferative GN; crescentic GN; lupus GN)
Reflux nephropathy (recurrent pyelonephritis with scarring)
Obstructive uropathy
Polycystic kidney disease; autosomal recessive; autosomal dominant
Renal dysplasia
Post kidney transplant (drug induced, acute rejection, chronic allograft nephropathy)

Renovascular hypertension
Renal artery stenosis (main artery, branch vessel): fibromuscular dysplasia, neurofibromatosis
Renal artery thrombosis
Vasculitis: aortoarteritis (Takayasu disease), Moyamoya syndrome, Kawasaki disease
Trauma to renal artery (surgical, procedural or blunt trauma)

Cardiovascular
Coarctation of aorta (thoracic or abdominal)
Coarctation associated with Turner, Williams Beuren, PHACE* syndromes

Primary (essential) hypertension
Isolated
With metabolic syndrome, syndrome X (obesity, dyslipidemia, type 2 diabetes, hyperandrogenism)

Endocrine
Pituitary: Cushing syndrome, pituitary tumor
Adrenal: congenital adrenal hyperplasia, adrenal adenoma, primary hyperaldosteronism
Thyroid: hyperthyroidism, hypothyroidism
Monogenic disorders: Liddle syndrome, syndrome of apparent mineralocorticoid excess, glucocorticoid remediable aldosteronism

Tumors
Wilms' tumor, pheochromocytoma, neuroblastoma, paraganglioma

Medications/Iatrogenic
Corticosteroids
Substance abuse (ephedra, cocaine, anabolic steroids, amphetamines, phencyclidine)
Herbal supplements (gingko, ginseng, licorice)
Nasal decongestants (phenylephrine, pseudoephedrine, oxymetazoline)
Non steroidal anti inflammatory drugs (naproxen, meloxicam, ibuprofen)
Others: Erythropoietin, calcineurin inhibitors, theophylline, caffeine, anti-depressants

*PHACE posterior fossa malformations, hemangiomas, arterial anomalies, coarctation of aorta, cardiac defects and eye abnormalities

of the aorta, congenital renal diseases and bronchopulmonary dysplasia are the usual causes of hypertension in the neonate, renal parenchymal disease, coarctation of the aorta and renovascular disease are important causes in older infants and children up to 6 years. Renal parenchymal disease followed by renovascular disease are frequent causes of hypertension in older children less than 10 years, and endocrine diseases and essential hypertension are rarely diagnosed; essential hypertension is the most frequent entity when evaluating adolescents with hypertension.[22]

Clinical features and complications

Patients with pre-hypertension and stage 1 hypertension are usually asymptomatic or may have non-specific symptoms.[23] Infants may manifest with irritability, failure to thrive, vomiting, feeding problems, seizures or respiratory distress.[10] Older children may exhibit headache, epistaxis, flush, visual disturbances, vertigo or a decline in school performance.

Hypertensive crisis: Some patients with stage 2 hypertension may present with severe hypertension or hypertensive crisis, which are classified as emergencies or urgencies. Hypertensive emergencies are those situations that require immediate blood pressure reduction to prevent or limit target organ damage. Examples include hypertensive encephalopathy, intracranial hemorrhage, acute left ventricular failure with pulmonary edema, dissecting aortic aneurysm, papilledema and acute renal failure. Children usually present with encephalopathy that manifests as severe headache, vomiting, seizures, ataxia, stupor and visual disturbances. In infants, severe hypertension can present with symptoms of congestive heart failure, such as irritability, respiratory distress, and failure to thrive.

Hypertensive urgencies are those situations in which it is desirable to reduce BP within a few hours, where in end organ damage has not occurred. Examples include upper levels of stage 2 hypertension and severe perioperative hypertension.[24] The occurrence of these complications is related to the rate of rise and duration of hypertension rather than absolute blood pressure values.[25,26] While hypertensive emergencies require reduction of blood pressure within hours, the same may be achieved over 2-3 days in patients with hypertensive urgencies.

Complications of hypertension: Sustained hypertension results in changes in eyes (hypertensive retinopathy), heart (increased left ventricular mass, diastolic dysfunction), kidneys (albuminuria), brain and blood vessels (increased intimal and medial thickness). There is evidence that these changes are common even in patients with long standing stage 1 hypertension.[10,27] Left ventricular hypertrophy (LVH) and increased carotid intima media thickness (IMT), early surrogate markers for cardiomyopathy and atherosclerosis respectively, are common in cross-sectional studies of children with stage 2 to stage 4 CKD.[28,29] While there have been no longitudinal studies of the effect of treatment of hypertension on cardiovascular outcomes in children with CKD, it is likely that appropriate treatment of hypertension would ameliorate, in part, the high risk of cardiovascular disease in children.

Evaluation

Careful history and physical examination should precede costly and invasive investigations, because they may provide important clues to the underlying etiology. History is taken for symptoms related to renal, cardiac or thyroid disorders, dietary habits, abdominal trauma and physical activity. Infants are assessed for history of oligohydraminos and invasive procedures in NICU (e.g., umbilical artery catheterization). Family history is taken for hypertension, diabetes, dyslipidemia, obesity, premature cardiovascular or cerebrovascular disease and renal disorders.

Assessment of the body mass index (BMI) and measurement of blood pressure in all four limbs is necessary.

History suggestive of recurrent urinary infections or stream abnormalities, or the presence of edema and hematuria may suggest renal parenchymal disease. Presence of abdominal/ neck bruit, café au lait spots, neurofibromatosis or neonatal history of umbilical artery cannulation should point to a diagnosis of renovascular hypertension, whereas weak femoral artery pulses suggest coarctation of aorta. Arthritis, arthralgias and rash suggest a connective tissue disease, while a history of weight loss, flushing and sweating is consistent with a neoplasm. Obesity may point towards metabolic syndrome or Cushing's disease; in the latter condition additional abnormalities like moon facies, hirsutism and striae should be looked for. Webbed neck, short stature and widely spaced nipples would suggest Turner syndrome, while elfin facies suggests William syndrome. Acanthosis nigricans is a marker of type 1 diabetes mellitus, while presence of goitre and exophthalmos suggests hyperthyroidism. The presence of palpable kidneys or abdominal mass should suggest severe hydronephrosis, polycystic kidney disease, multicystic dysplastic kidneys, Wilms tumor, neuroblastoma or pheochromocytoma.

Investigations

Since the majority of patients with hypertension have underlying renal or renovascular etiology, screening tests are designed to evaluate for these conditions (Table 5). All patients with hypertension should also be screened for target organ damage. Evaluation of carotid artery intimal thickess and urine 24 hour protein estimation for micro-albuminuria have been recently suggested as additional markers of vascular damage.[10] Such evaluation may be postponed in patients with severe hypertension until they are stable. The presence or new development of end organ damage is an important guide to the choice and intensity of antihypertensive therapy.

Based on clinical features and initial evaluation, a cause for hypertension is suggested in most instances. Confirmation of the diagnosis requires specific investigations tailored to specific needs. For example, an ultrasound suggesting small contracted kidney(s) or hydronephrosis should prompt one to look for vesicoureteric reflux by means of a micturating cystourethrogram or dimercaptosuccinic acid (DMSA) scintigraphy. Presence of nephrotic range proteinuria (3+ or more), significant hematuria (>5 erythrocytes/high power field), with or without derangement in

Table 5. Basic diagnostic work up

Evaluation for cause	Screen for target organ damage
Hemogram	Retinal fundus examination
Blood urea, creatinine, electrolytes	Urine spot protein to creatinine ratio
Fasting lipids, glucose, uric acid	Chest X-ray
Urinalysis, culture	ECG
24-hr urinary protein or spot protein to creatinine ratio	Echocardiography
Chest X-ray	
Renal ultrasonography	

creatinine, suggests a glomerulonephritis and should be investigated appropriately (complement C3, antinuclear antibodies, anti-neutrophilic cytoplasmic antibodies, 24 hour urinary protein and renal biopsy). If metabolic alkalosis or hypokalemia is present, plasma renin activity and serum aldosterone levels, and where available, genetic testing, should be carried out to evaluate for inherited causes of hypertension. When baseline tests are normal, further evaluation includes doppler ultrasound and post diuretic renogram to look for evidence of renal artery stenosis (abnormal results should be confirmed by angiography) and urinary catecholamines to rule out adrenal hyperplasia or adenoma (confirmed with magnetic resonance imaging for adrenals and MIBG scan). The extent of evaluation depends on the patient's age, severity and duration of hypertension, presence of target organ damage and family history. While young children and those with stage 2 hypertension or features of end organ damage are evaluated in detail, an obese adolescent with stage 1 systolic hypertension, family history of hypertension and normal history and physical examination needs no more than the basic evaluation.

Among the causes of secondary hypertension are rare disorders caused by single gene mutations, whose pathophysiology has been recently elucidated. In all cases, hypertension is caused by an upregulation of sodium (Na) reabsorption in the distal nephron, causing an expansion of the extracellular volume.[30]

The known disorders can be grouped as primary disorders of either the distal nephron or the adrenal hormone pathway. In the former, the mutations involve the Na-transport machinery in the distal convoluted tubule (DCT) cell and the principal cell of the collecting duct, e.g., Liddle syndrome (activating mutation of epithelial sodium channel, ENaC), Gordon syndrome (mutations in two regulatory kinases), and syndrome of apparent mineralocorticoid excess or AME (inactivating mutation in the glucocorticoid-metabolizing 11β-hydroxysteroid dehydrogenase type 2 enzyme).

In the latter are disorders with abnormal adrenal steroid production, causing an inappropriate stimulation of the mineralocorticoid receptor (MR) in the distal nephron, e.g., abnormal aldosterone production in glucocorticoid-remediable aldosteronism (GRA) and familial hyperaldosteronism type II (FH II), abnormal cortisol production (in familial glucocorticoid resistance), or other steroid metabolites in congenital adrenal hyperplasia with 11- or 17-hydroxylase deficiency, and GRA. Since this hypertension may be mild and unassociated with classic electrolyte abnormalities, all children with hypertension should be evaluated for these conditions. While plasma renin activity (PRA) is a good screening tool, the differentiation between these conditions is presented in Table 6. While genetic testing is not routinely available, information on testing for clinical purposes can be found at http://www.genetests.org. Useful summary for diagnostic evaluation and management of these causes are shown in Table 6.

Management

It is useful to distinguish essential from secondary hypertension. While the initial management for patients with essential hypertension comprises of therapeutic lifestyle modifications (see below), patients with sustained secondary hypertension require treatment with anti-hypertensive agents.[10] Drug therapy is also indicated in patients with stage 2 hypertension, symptomatic hypertension, persistent hypertension despite non-pharmacologic measures, those with hypertensive target-organ damage and those associated with diabetes type 1 or 2, chronic kidney disease or dyslipidemia.[9]

Table 6. Biochemical characteristics and treatment options for inherited forms of hypertension.

Disorder	Serum K^+	Plasma renin activity (PRA)	Serum aldosterone	Aldosterone: PRA*	Response to glucocorticoid	Response to mineralocorticoid receptor antagonists (eplerenone, spironolactone)	Treatment
Liddle syndrome	N or ↓	↓	↓		None	None	Amiloride, triamterene
Gordon syndrome (pseudohypoaldosteronism type II)	N or ↑	↓	N or ↑	↑	None	None	Triameterene
Apparent mineralocorticoid excess	↓ (N)	↓	↓		None	Yes	Eplerenone spironolactone
Glucocorticoid remediable aldosteronism Familial hyperaldosteronism type I	N or ↓	↓	↑ (N)	↑	Yes	Yes	Glucocorticoids, amiloride, triamterene
Familial hyperaldosteronism type II	N or ↓	↑	↑	↑	None	Yes	Eplerenone spironolactone
Congenital adrenal hyperplasia	N or ↓	↓	↓		None	Yes	Eplerenone spironolactone
Familial glucocorticoid resistance	N or ↓	↓	↓		None	Yes	Eplerenone spironolactone

K potassium, N normal, ↓ decreased, ↑ increased, PRA plasma renin activity, MR-A mineralocorticoid receptor antagonists

* Ratio of aldosterone to PRA is diagnostic if >30, with Aldosterone in ng/dl and PRA in ng/ml/hr

Target blood pressure

In children guidelines recommend lowering blood pressure to below the 95th percentile, unless comorbidity is present, in which case the target is below the 90th percentile.[9,10]

Pre-hypertension

Patients are primarily managed by lifestyle modifications (see below) and re-evaluated 6 months later. The parents of these children are informed and advised regarding careful follow up. Medications are not required unless the patient has comorbid conditions (e.g., chronic kidney disease, diabetes mellitus or dyslipidemia) or evidence of target organ damage.

Essential hypertension

Patients with essential hypertension are initially managed with lifestyle modifications and pharmacological therapy is initiated if indicated (as specified above). Hypertension is a defining characteristic of the metabolic syndrome (MS), characterized by central obesity, insulin resistance and dyslipidemia. Since MS is associated with the development of atherosclerosis in adults, and its components are strongly associated with left ventricular hypertrophy and other target-organ effects of hypertension, the threshold for initiating treatment with antihypertensive medications should probably be lower in children and adolescents with the MS than in non-obese patients with primary hypertension.[31,32] Studies have demonstrated the efficacy of short-term diet and exercise in producing weight loss, reduced blood pressure and improvements in the abnormal laboratory findings in overweight children and adolescents with MS.[33,34] When pharmacotherapy is required, it is important to avoid thiazide diuretics and beta-blockers, especially as a combination, in patients with MS, because the drug combination has a significant diabetogenic potential.[35] While there is no consensus on the appropriate initial therapy, the choices are between CCB and ACEI; β-blockers are a second choice.[35] Screening for dyslipidemia and impaired glucose tolerance should be performed on a regular basis, at least annually or 6 monthly, in patients with MS.

Table 7. Therapeutic lifestyle changes: Summary of recommendations in adults

Weight management	Weight reduction in overweight or obese individuals
Dietary alterations	Prevention of excess or abnormal weight gain Increase in intake of fresh vegetables, fruits, and low-fat dairy[3] Dietary sodium reduction (2.6-3.8 g of salt, or 45-65 mEq or 1-1.5 g sodium in adults)[4] Decrease in portion (meal) size Reduce consumption of sugar-containing beverages, energy dense snacks Regular meals, including a healthy breakfast
Exercise	Regular physical activity for 30–60 minutes every day[5] Restriction of sedentary activity (television watching, video or computer games) to <2 hours a day
Stress reduction	No specific recommendation, likely beneficial
Others	Smoking cessation Interventions to improve sleep quality

Non pharmacological interventions

Also termed as therapeutic lifestyle changes, these are particularly suitable for children with pre-hypertension and stage I hypertension, especially if primary or essential and associated with metabolic syndrome.[10] However, these recommendations hold true also for secondary hypertension and indeed, perhaps, for all children. These include health promoting behaviors such as diet, exercise, weight reduction and stress reduction, summarized in Table 7.

Weight reduction is the primary therapy for obesity-related hypertension. The potential for control of blood pressure in children through weight reduction is supported by studies that suggest that blood pressure levels track from childhood through adolescence and into adulthood in association with weight.[36] Hence, excessive weight gain is likely to be associated with elevated blood pressure over time. Weight loss in overweight adolescents is associated with a decrease in blood pressure,[37] independently and through decreases in dyslipidemia, insulin resistance and sensitivity of blood pressure to salt. Reduction of BMI by 10% is reported to lead to 8-12 mm Hg fall in systemic blood pressure.[10] Prevention of excess or abnormal weight gain limits future increases in blood pressure.

Regular physical activity and decreasing sedentary activity, such as watching television and playing video or electronic games, are important components of pediatric obesity treatment and prevention.[38] Children are likely to comply with the instruction to increase physical activity if aerobic activities are incorporated into their routines, e.g., walking or cycling to school, playing with friends outdoors and swimming, rather than boring exercises as part of their daily routine. Competitive sports and strength training (isometric) exercises (e.g., weight lifting, gymnastics, karate and judo) should be avoided by patients with stage 2 hypertension or target organ damage, until blood pressure is controlled satisfactorily.[10,39]

Dietary modification should be strongly encouraged in children and adolescents who have blood pressure levels in the prehypertensive range as well as in those with hypertension. A 'no added salt diet' is a satisfactory approach to restrict salt intake. Intake of food products high in sodium (processed and canned foods, items prepared in fast food shops including pizzas, pickles and salted potato chips) should be avoided. Though small studies show that increased intake of potassium, magnesium, folic acid, unsaturated fat and fiber and lower dietary intake of total fat are associated with lower blood pressures, no recommendations have be made in this regard.[10]

Secondary hypertension

Patients with sustained secondary hypertension require therapy with antihypertensive agents. Physicians should be aware of the risk of hypertensive emergencies in children with stage 2 hypertension. The treatment plan should incorporate non-pharmacological measures in all patients.

Drug therapy

Though recent clinical trials have expanded the number of drugs that have pediatric dosing information, there is lack of long term data on the benefits or adverse effects of most agents in children. Dosing recommendations for the drugs used are available in standard texts and recommendations.[9,10] Severe, symptomatic hypertension should be treated with intravenous antihypertensive drugs and is discussed subsequently.

When drug therapy is required, it should be initiated with a single drug from any of the following drug classes: ACE inhibitors (ACEI),

angiotensin receptor blockers (ARB), beta (β)-blockers, calcium channel blockers (CCB), and diuretics. Drugs with a longer duration of action (once or twice daily dosing) are preferred for better compliance and less side effects. When required, dose adjustment should be made once in 2-3 days.

Once an initial antihypertensive agent has been chosen, a stepped-care approach should be followed.[39,40] In this approach, one should begin with the recommended initial dose of the desired medication, increase the dose until the desired blood pressure target is reached or the maximum dose is reached, add a second medication with a complementary mechanism of action if blood pressure control is still not achieved and proceed to the highest recommended dose if necessary. If blood pressure is still not controlled, a third antihypertensive drug of a different class may be added and an expert should be consulted. Stepped-care allows for the individualization of therapy according to the needs of the patient and also facilitates detection of adverse effects as drug doses are increased or new agents added. It has been endorsed by the pediatric working group of the NHBPEP as an appropriate approach to the use of antihypertensive drugs in children and adolescents.[10]

Therapy in children is often started with a CCB or ACEI. Among CCBs, chiefly dihydropyridines such as nifedipine, amlodipine, felodipine and isradipine have been used in children. CCBs are preferred in low renin or volume expanded states, and where the hypertension is mediated via the afferent arteriole vasoconstriction (e.g., cyclosporine induced hypertension). A dihydropyridine CCB is not the agent of choice in renal disease because these drugs (unlike their non-dihydropyridine counterparts) may increase proteinuria.[41] Adverse effects of CCBs include headache, flushing, dizziness, tachycardia, fatigue and lower extremity edema. Amlodipine is the most frequently used CCB, and is safe and effective. Nifedipine is available both as immediate release and as a sustained release preparation. The former is useful in emergencies, but the effect is transient and unpredictable; the latter permits once or twice daily dosing, but care should be exercised that it is swallowed whole, and not crushed or chewed.

ACEI include captopril, which is chiefly used in young infants and requires dosing every 6-8 hours, and enalapril which is preferred beyond infancy, because of the ease of administration (1-2 daily doses). Side effects include hyperkalemia and impaired renal functions; infrequently, anemia, neutropenia or dry cough may occur. Hence serum potassium and creatinine should be monitored regularly while on ACEI, and the drug class is avoided in patients with GFR <30 ml/min/1.73 m^2. ACEIs are commonly used in patients with renal disease or diabetes because of their renal protective effect via reduction of proteinuria. They are also the drug of choice in children with left ventricular dysfunction or congestive cardiac failure. ACEI are contraindicated in presence of bilateral renal artery stenosis and should be used cautiously in adolescent girls and women because of the risk of fetopathy (oligohydramnios, hypotension, cardiac defects and renal defects including tubular dysplasia) with use of ACEI in any trimester of pregnancy. Newer ACEI (lisinopril, ramipril, quinapril, fosinopril) require once daily dosing and have fewer side effects; however, quinapril and fosinopril have been rarely associated with liver damage and nasopharyngitis, respectively. ARBs used in children include losartan, valsartan and irbesartan and the indications, contraindications and adverse effects (except cough, not seen with ARBs) are similar to ACEIs. However, experience in pediatric age groups is limited.

Few β-blockers have been studied in children. Adverse effects include postural

hypotension, tachycardia, bronchospasm, fatigue, depression and increased serum triglycerides. β-blockers should be avoided in athletes (decrease exercise output), asthmatics and in those with congestive cardiac failure or diabetes (mask signs of hypoglycemia). Cardioselective β-blockers (atenolol, metoprolol) are effective, relatively safe and need to be given once or twice daily. The dose of atenolol needs to be modified in renal impairment. Propranolol is effective but needs to be given several times a day and has significant adverse effects (decreased concentration, decreased exercise capacity and anorexia). Labetalol, (both α- and β -blocker), is safe and effective where hypertension may be refractory to other medications. Carvedilol is another α- and β -blocker used in adults as an antihypertensive but its application in children has primarily been in congestive heart failure.

Diuretics are used as adjuncts rather than as monotherapy because of their adverse effects, which include fatigue, muscle cramps, nausea, hypokalemia, hyponatremia, metabolic alkalosis and hyperlipidemia. Thiazide diuretics are the diuretics of choice when used as antihypertensives, but are ineffective at GFR <30 ml/minute/1.73m^2. Loop diuretics are more potent, but the efficacy is lower in those with impaired renal function. They are often used in presence of fluid overload and in those with underlying renal disease. Potassium sparing diuretics such as spironolactone are useful in conditions associated with mineralocorticoid excess, or as an adjunct to drugs which increase aldosterone levels, such as vasodilators and CCBs.

Combinations of ACEI and angiotensin receptor blocker have been used for adults, but experience in children is limited. Long term combination of thiazides with β-blockers should be avoided because of their association with impaired glucose tolerance.[35]

Specific recommendations

The choice of medication depends on the cause of hypertension and associated complications. A few illustrative examples are discussed. The hypertension in acute glomerulonephritis is caused by salt and water retention, therefore fluid and sodium restriction is recommended; therapy with loop diuretics may be required if congestive cardiac failure, hypertension and severe edema are present. In the presence of severe hypertension with or without encephalopathy, treatment with intravenous furosemide and a CCB should be initiated; potent intravenous agents are rarely required. In a child with suspected or confirmed renovascular disease, initially a CCB and/or a β-blocker may be used, adding prazosin, labetalol, clonidine, hydralazine and/or minoxidil if hypertension persists. Therapy with ACEI or angiotensin receptor blockers should be avoided in patients with suspected or confirmed bilateral renovascular stenosis, but may be used cautiously in those with unilateral renovascular hypertension. In patients with hyperlipidemia, ACEI or CCB are a good first choice; β-blockers and diuretics should be avoided because they may worsen the dyslipidemia.

It is recommended that blood pressure in children with chronic kidney disease (CKD) should be kept at <90th percentile for age, gender, and height and that ACE inhibitors or ARBs should be used preferentially in children with proteinuric renal disease, because of their known anti-proteinuric and reno-protective effects.[10,42] In patients with CKD stage IV-V (GFR <30 mL/min/1.73 m^2) these drugs should be avoided and either a CCB or β-blocker is used. Other measures to manage hypertension include restriction of salt intake to between 2.6-3.8 g (45-65 mEq or 1-1.5 g sodium) and administration of diuretics to reduce the fluid overload.

While thiazides (hydrochlorothiazide, chlorthalidone) are used commonly, they have poor efficacy in CKD stage IV-V, and in these patients loop diuretics are preferred.[43] Additional medications may be needed, including α-blockers (prazosin, labetalol), centrally acting agents (clonidine) or vasodilators (hydralazine, minoxidil); doses of some agents need modification in renal impairment.

Whether ACE inhibition and level of blood pressure control affect progression of CKD in children is being prospectively evaluated by the Effect of Strict Blood Pressure Control and ACE Inhibition on Progression of CRF in Pediatric Patients (ESCAPE) trial, a multi-center, prospective trial being conducted in Europe using ramipril in children with GFR between 11-80 ml per min per 1.73m.[2,15] Experience with ARB in children with CKD is limited, although available data suggest that losartan is well tolerated and confers sustained antihypertensive and renoprotective effects.[44] Combination therapy with ACE inhibition and ARB may be more beneficial than either class of medication given alone, although previous studies have been limited by the use of submaximal dosing of both the combination ACE inhibitor–ARB and the comparison single drug.[45,46] Recently, the role of aldosterone receptor antagonists in the treatment of hypertensive patients with CKD is being investigated; they have been shown to have beneficial effects on cardiac fibrosis and may also further ameliorate proteinuria in CKD when used in combination with an ACE inhibitor or ARB.[47]

Pheochromocytoma is a rare cause of paroxysmal or sustained blood pressure. The treatment of choice in these patients is labetalol (α- and β blocker) or phentolamine (α-blocking agent). Use of β blocker alone will result in an unopposed α adrenergic activity, which shall worsen the vasoconstriction, resulting in further increase in blood pressure.

Follow up and monitoring

After initiation of drug therapy, follow-up visits are scheduled frequently (every 2–4 weeks) until blood pressure control has been achieved, and then less frequently (every 3 months) thereafter. Home blood pressure monitoring and assessment for medication side effects are reviewed at each follow-up visit. After about 8-12 months of successful blood pressure control, "step down" of therapy may be attempted along with regular (3-monthly) evaluation of blood pressure during follow up. This may be the case in patients with essential hypertension with therapeutic lifestyle changes enabling withdrawal of pharmacotherapy, or where hypertension was secondary to a cause amenable to correction by some intervention, e.g., dilatation of stenotic vessel in renovascular hypertension.

Periodic assessment and laboratory monitoring for adverse effects, as appropriate, should be part of each child's treatment plan. Monitoring for target organ damage should commence as soon as the diagnosis of hypertension is confirmed and continue at regular intervals. One definition of left ventricular hypertrophy (LVH) in adults is left ventricular mass index (LVMI) >51 g/m^2,[7] as calculated by the Devereux formula and then indexed to height (in meters) to the power of 2.7.[48] LVH in adults is associated with a fourfold increase in cardiovascular risk.[49] Although the current recommendations suggest use of this adult cutoff in children, this limit is far above the pediatric 99th percentile for LVM, and any LVH above the 95th percentile for age (about 38 g/m^2)[7] should be considered as significant LVH.[10,50] Children with normal ECHO (LVMI <38 g/m^2)[7] should be monitored annually, those with mild LVH (LVMI 38-51 g/m^2)[7] every 6 months, and those with established LVH (LVMI >51 g/m^2)[7] every 3 months. Hypertensive retinal changes, as assessed by the Keith Wagener Barker

classification, are a marker of hypertensive vascular damage; severe grades predict cardiovascular mortality in adults, in addition to being associated with risk of loss of vision.[51] Annual evaluation is recommended for those with normal evaluation at diagnosis, 6-12 monthly for those with stage I-II retinopathy and 3 monthly for those with stage III-IV retinopathy. There are no available recommendations for the frequency of evaluation of microalbuminuria and blood vessel intima media thickness (by carotid artery ultrasound).

Management of hypertensive crises

Hypertensive crises are usually caused by noncompliance to medications or poorly controlled chronic hypertension. Treatment of a hypertensive crisis should be tailored to each individual based on the extent of end-organ injury and co-morbid conditions.

Hypertensive emergency: Children with stage 2 hypertension may present with acute, life threatening target organ damage. These situations require immediate reduction in blood pressure in order to prevent or limit target organ damage, and constant monitoring and supportive care, necessitating hospitalisation. An emergency is treated with a potent intravenous antihypertensive titrated to produce a controlled reduction in blood pressure, with the aim of decreasing the blood pressure by up to 25% over the first 8 hours of presentation and then gradually to the upper limit of normal (95th percentile) over 24–48 hours.[52,53] Gradual reduction of blood pressure is important because overly rapid control of hypertension may compromise blood flow to important organs causing ischemic damage, especially since autoregulation may be impaired or altered. Therapy with oral antihypertensives should be commenced as soon as patient can take orally, in order to permit intravenous therapy to be withdrawn over the next 24 hours.

Sodium nitroprusside, nitroglycerine, labetalol and nicardipine are the agents usually chosen for intravenous infusion. Sodium nitroprusside is the agent of choice because it is easily available, inexpensive, and has a short half-life and a wide dose range (0.5-8 µg/kg/minute) allowing easy titration. Prolonged therapy (>48 hours) at high doses (>2 ìg/kg/minute) is associated with the risk of cyanide toxicity; this may be prevented with the concomitant use of sodium thiosulfate or hydroxycobalamin. Intravenous sodium nitroglycerine (dose range 1-3 ìg/kg/minute) is a useful alternative, especially in adults with coronary artery disease and children with myocardial dysfunction. Like nitroprusside it has a rapid onset and short duration of action. Adverse effects include headache, tachycardia, methemoglobinemia and tachyphylaxis. With these agents, invasive arterial blood pressure monitoring is desirable. Intravenous labetalol may be used as an infusion (0.25-3 mg/kg/hr) or less optimally, as bolus doses (0.2-1 mg/kg/dose) given every 5-10 minutes. Orthostatic hypotension and abdominal pain are the notable adverse effects. Intravenous nicardipine (1-3ìg/kg/minute) and esmolol (100-500 ìg/kg/minute) are other agents used in management of hypertensive emergencies. While nicardipine has a longer half-life and is both safe and efficacious, it is associated with increased intracranial pressure, and may cause thrombophlebitis if infused through a peripheral line. Fenoldopam (0.2–0.8 mcg/kg/min), a peripheral DA1 receptor agonist, has efficacy and safety similar to nitroprusside in the treatment of hypertensive crisis in adults and has the advantage of maintaining or increasing renal perfusion. However, there is limited experience with use of fenoldopam and esmolol in children.[10]

If continuous infusion of an antihypertensive agent is not immediately available, IV bolus dosing of labetalol, enalaprilat and hydralazine can be used; however, boluses provide less minute

to-minute control of blood pressure compared with continuous infusion therapies. Enalaprilat and hydralazine have inconsistent response that is difficult to titrate. Hydralazine causes reflex tachycardia and salt and water retention.

The use of immediate release nifedipine for hypertensive emergencies has been criticised for its unpredictable effect and association with an increased risk for adverse cardiovascular outcomes in adults. In children, however, nifedipine seems to be effective and well tolerated for decreasing blood pressure, when given at a dose of 0.1-0.25 mg/kg, for hypertensive emergencies.[54]

When a patient presents with hypertensive crisis, one must assess the patient's volume status. Volume status can be depleted (due to decreased oral intake and pressure natriuresis), causing stimulation of the renin–angiotensin system, worsening the hypertension. Volume repletion may lower renin levels, help restore tissue perfusion and prevent a precipitous fall in blood pressure that may occur with antihypertensive therapy.[55] Diuretics should be avoided unless definite evidence of volume overload is present. Conversely, a child may be volume overloaded and need diuretic therapy or dialysis.

Hypertensive urgency: Patients with stage 2 hypertension, no evidence of acute target organ damage and less alarming symptoms (e.g., headache and/or vomiting), but at risk for progression to hypertensive emergencies, are termed as having hypertensive urgencies. Hypertensive urgency can be treated in a non-ICU setting with oral medications over 24 to 48 hours. Oral medications are administered and titrated initially as an inpatient; then the patient can be discharged with close follow-up. During initial therapy, child should be observed closely, since intravenous therapy might be required. Oral medications with relatively short onset of action that can potentially be used for hypertensive urgency are nifedipine (0.25 mg/kg), clonidine (0.05–0.1 mg/dose), labetalol (0.2-1 mg/kg/dose), isradipine (0.05–0.1 mg/kg/dose), captopril (6.25-25 mg), hydralazine (0.2–0.6 mg/kg/dose) and minoxidil (0.1–0.2 mg/kg/dose).

A reflex hypertensive crises can develop in patients who have abruptly stopped taking antihypertensives, particularly clonidine or α blockers. The treatment in these cases is to restart previous medications after the initial reduction of blood pressure with labetolol or sodium nitroprusside. Postoperative hypertension is typically related to catecholamine surge from activation of the sympathetic nervous system. Therefore, the treatment of choice for postoperative hypertensive crisis is with a β blocker or labetolol.

Points to Remember

- ***The management of a patient with hypertension includes careful evaluation to determine the etiology and control of elevated blood pressure with agent(s) considered appropriate based on the underlying cause, ease of administration and adverse effect profile.***
- ***Specific surgical or medical intervention is possible in a few instances.***
- ***Institution of lifestyle changes and monitoring for target organ damage and drug toxicity is necessary on follow up.***
- ***As more medications are approved and validated for use in children, evidence based choices for treatment is likely to become established.***

References

1. Munter P, He J, Cutler JA, Wildman RP, Whelton BK. Trends in blood pressure among children and adolescents. JAMA 2004; 291: 2107-2113.

2. Mohan B, Kumar N, Aslam N, Rangbulla A, Kumbkarni S, Sood NK, et al. Prevalence of sustained hypertension and obesity in urban and rural school going children in Ludhiana. Indian Heart J 2004; 56: 310-314.

3. Lane DA, Gill P. Ethnicity and tracking blood pressure in children. J Human Hypertension 2004; 18: 223-228.

4. Still JL, Cottom D. Severe hypertension in childhood. Arch Dis Child 1967; 42:34–39.

5. Gill DG, Mendes de Costa B, Cameron JS, Joseph MC, Ogg CS, Chantler C. Analysis of 100 children with severe and persistent hypertension. Arch Dis Child 1976; 51: 951–956.

6. Johnstone LM, Jones CL, Grigg LE, Wilkinson JL, Walker RG, Powell HR. Left ventricular abnormalities in children, adolescents and young adults with renal disease. Kidney Int 1996; 50: 998–1006.

7. Mitsnefes MM, Daniels SR, Schwartz SM, Khoury P, Strife CF. Changes in left ventricular mass in children and adolescents during chronic dialysis. Pediatr Nephrol 2001; 16:318–323.

8. Mitsnefes MM, Kimball TR, Witt SA, Glascock BJ, Khoury PR, Daniels SR. Left ventricular mass and systolic performance in pediatric patients with chronic renal failure. Circulation 2003; 107:864–868.

9. Bagga A, Jain R, Vijaykumar M, Kanitkar M, Ali U. Evaluation and Management of Hypertension. Indian Pediatrics 2007; 44:103-121

10. National High Blood Pressure Education Program Working Group. The Fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescents. Pediatrics 2004; 114 (suppl): 555-576.

11. National Heart, Lung and Blood Institute Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. The Seventh Report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure: The JNC 7 report. JAMA 2003; 289: 2560-2572.

12. Report of the Second Task Force on Blood Pressure Control in Children 1987. National Heart, Lung and Blood Institute, Bethesda, Maryland. Pediatrics 1987; 79: 1-25

13. Stabouli S, Kotsis V, Toumanidis S, Papamichael C, Constantopoulos A, Zakopoulos N. White-coat and masked hypertension in children: association with target-organ damage. Pediatr Nephrol 2005; 20: 1151-1155.

14. Stergiou GS, Yiannes NJ, Rarra VC, Alamara CV. Whitecoat hypertension and masked hypertension in children. Blood Press Monit 2005; 10:297–300.

15. Wuhl E, Haldstein C, Mehls o, Schaefer F, ESCAPE trial Group. Home, clinic and ambulatory blood pressure monitoring in children with chronic renal failure. Pediatr Res 2004: 55: 492-97.

16. Hadstein C, Wuhl E. Investigations of hypertension in childhood. In: Geary Df, Schaefer F. Comprehensive pediatric Nephrology 1st ed. Philadelphia: Mosby Elsevier, 2008, p. 645-663.

17. Urbina E, Alpert B,Flynn J, Hayman L, et al. Ambulatory Blood Pressure Monitoring in Children and Adolescents: Recommendations for Standard Assessment. A Scientific Statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young and the Council for High Blood Pressure Research. Hypertension 2008; 52: 433-451.

18. Srivastava RN, Bagga A. Hypertension. In: Srivastava RN, Bagga A. Pediatric Nephrology, 4th edn. New Delhi: Jaypee Brothers, 2005, p. 292-315.

19. Hari P, Bagga A, Srivastava RN. Hypertension in children. Indian Pediatr 2000; 37: 268-274.

20. North American Pediatric Renal Trials and Collaborative Studies 2006 Annual Report. Available at: http://web.emmes.com/study/ ped/ annlrept/annlrept2006.pdf

21. Fivush BA, Jabs K, Neu AM, Sullivan EK, Feld L, Kohaut E, Fine R. Chronic renal insufficiency in children and adolescents: the 1996 annual report of NAPRTCS. North American Pediatric Renal Transplant Cooperative Study. Pediatr Nephrol 1998;12:328–337

22. Lurbe E, Alcon JA, Redon J. Epidemiology and consequences of childhood hypertension. In: Geary DF, Schaefer F. Comprehensive Pediatric Nephrology, 1st edn. Philadelphia: Mosby Elsevier, 2008, p. 637-644.

23. Croix B, Feig DI. Childhood hypertension is not a silent disease. Pediatr Nephrol 2006; 21: 527-532.

24. Blumenfeld JD, Laragh JH. Management of hypertensive crises: the scientific basis for treatment decisions. Am J Hypertens 2001;14:1154–1167

25. Vaughan CJ, Delanty N. Hypertensive emergencies. Lancet 2000; 356: 411-417.

26. Linakis J. The assessment and management of hypertensive emergencies and urgencies in children. Pediatr Emergency Care 2005, 21: 391-396.

27. Flynn JT, Alderman MH. Characteristics of children with primary hypertension seen at a referral center. Pediatr Nephrol 2005; 20: 961-966.

28. Flynn JT. Cardiovascular disease in children with chronic renal failure. Growth Horm IGF Res 2006; 16:S84–S90.

29. Chavers BM, Herzog CA. The spectrum of cardiovascular disease in children with predialysis chronic kidney disease. Adv Chronic Kidney Dis 2004; 11:319–327

30. Vehaskari VM. Heritable forms of hypertension. Pediatr Nephrol published online 24 July 2007; DOI 10.1007/s00467-007-0537-8.

31. Jones KL. The dilemma of the metabolic syndrome in children and adolescents: disease or distraction? Pediatr Diabetes 2006; 7:311–321.

32. Litwin M, Œladowska J, Antoniewicz J,et al. Metabolic abnormalities, insulin resistance and metabolic syndrome in children with primary hypertension. Am J Hypertens 2007; 20:875–882.

33. Monzavi R, Dreimane D, Geffner ME, Braun S, Conrad B, Klier M, Kaufman FR. Improvement in risk factors for metabolic syndrome and insulin resistance in overweight youth who are treated with lifestyle intervention. Pediatrics 2006; 117:e1111–e1118.

34. Chen AK, Roberts CK, Barnard RJ. Effect of a short-term diet and exercise intervention on metabolic syndrome in overweight children. Metabolism 2006; 55: 871–878.

35. Kaplan NM, Opie L.H. Controversies in hypertension. Lancet 2006; 367: 168-176.

36. Lauer RM, Mahoney LT, Clarke WR. Tracking of blood pressure during childhood:The Muscatine Study. Clin Exp Hypertens A 1986; 8: 515–37.

37. Rocchini AP, Katch V, Anderson J, Hinderliter J, Becque D, Martin M, et al. Blood pressure in obese adolescents: Effect of weight loss. Pediatrics 1988; 82: 16–23.

38. Kelley GA, Kelley KS, Tran ZV. The effects of exercise on resting blood pressure in children and adolescents: A meta-analysis of randomized controlled trials. Prev Cardiol 2003; 6:8–16.

39. Lande MB, Flynn JT. Treatment of hypertension in children and adolescents. Pediatr Nephrol published online 24 July 2007; DOI 10.1007/s00467-007-0573-4

40. Flynn JT, Daniels SR. Pharmacologic treatment of hypertension in children and adolescents. J Pediatr 2006; 149:746–754.

41. Gashti CN, Bakris GL. The role of calcium antagonists in chronic kidney disease. Curr Opin Nephrol Hypertens 2004; 13:155–161.

42. Hogg RJ, Furth S, Lemley KV, et al. National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for chronic kidney disease in children and adolescents: Evaluation, classification and stratification. Pediatrics 2003; 111: 1416-1421.

43. Kidney Disease Outcomes Quality Initiative (K/DOQI). Clinical practice guidelines on

hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis 2004; 43:S42–S64.

44. Shatat IF, Flynn JT. Hypertension in children with chronic kidney disease. Adv Chronic Kidney Dis 2005; 12:378–384.

45. Nakao N, Yoshimura A, Morita H, Takada M, Kayano T, Ideura T. Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in non-diabetic renal disease (COOPERATE): a randomized controlled trial. Lancet 2003; 361:117–124.

46. Ellis D, Moritz ML, Vats A, Janosky JE. Antihypertensive and renoprotective efficacy and safety of losartan; a long-term study in children with renal disorders. Am J Hypertens 2004; 17:928–935.

47. Sarafidis PA, Khosla N, Bakris GL. Antihypertensive therapy in the presence of proteinuria. Am J Kidney Dis 2007; 49:12–26.

48. De Simone G, Daniels SR, Devereux RB, et al. Left ventricular mass and body size in normotensive children and adults : assessment of allometric relations and impact of overweight. J Am Coll Cardiol 1992; 20: 1251-60.

49. De Simone G, Devereux RB, Daniels SR, Koren MJ, Meyer RA, Laragh JH. Effect of growth on variability of left ventricular mass: assessment of allometric signals in adults and children and their capacity to predict cardiovascular risk. J Am Coll Cardiol 1995; 25: 1056-62.

50. Matteuci MC, Wuhl E, Picca S, et al. Left ventricular geoometry in children with mild to moderate chronic renal insufficiency. J Am Soc Nephrol 2006; 17:218-226.

51. Svardsudd K, Wedel H, Aurell E, Tibblin G. Hypertensive eye ground changes: prevalence, relation to blood pressure and prognostic importance. the study of men born in 1913.Acta Med Scand 1978; 204: 159-167.

52. Adelman RD, Coppo R, Dillon MJ. The emergency management of severe hypertension. Pediatr Nephrol 2000;14:422–7.

53. Vaughan CJ, Delanty N. Hypertensive emergencies. Lancet 2000;356:411–7.

54. Calvetta A, Martino S, von Vigier RO, Schmidtko J, Fossali E, Bianchetti MG. What goes up must immediately come down! Which indication for short-acting nifedipine in children with arterial hypertension? Pediatr Nephrol 2003; 18: 1-2.

55. Mitsnefes MM. Hypertension in Children and Adolescents. Pediatr Clin N Am 2006; 53: 493–512.

56. Soergel M, Kirschstein M, Busch C, et al. Oscillometric twentyfour- hour ambulatory blood pressure values in healthy children and adolescents: a multicenter trial including 1141 subjects. J Pediatr 1997; 130: 178–184.

57. Wühl E, Witte K, Soergel M, Mehls O, Schaefer F; German Working Group on Pediatric Hypertension. Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. J Hypertens 2002; 20: 1995–2007.

58. He J, Whelton PK, Appel LJ, Charleston J, Klag MJ. Long-term effects of weight loss and dietary sodium reduction on incidence of hypertension. Hypertension 2000; 35: 544–9.

59. Sacks FM, Svetkey LP, Vollmer WM, D, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med 2001; 344: 3–10.

60. Whelton SP, Chin A, Xin X, He J. Effect of aerobic exercise on blood pressure: A meta analysis of randomized, controlled trials. Ann Intern Med 2002; 136: 493–503.

GENERAL

CHILDHOOD OBESITY AND RISK OF CARDIOVASCULAR DISEASE: ROLE OF PEDIATRICIAN

* ***Mangla Sood***

Abstract: *American heart association (AHA) recommends lipid screening in childhood in view of (1) autopsy data which indicate that the atherosclerotic process begins in childhood and that elevated cholesterol levels in childhood are associated with increased risk for cardiovascular disease (CVD) in adulthood; (2) lipid and lipoprotein levels rise rapidly early in life and stabilize by five years of age to levels similar to those of adolescents and (3) the raise in the average weight of children due to the obesity epidemic. If dietary modification is not able to control abnormal lipid profile, pharmacological therapy has to be instituted. Statins are extremely useful in lowering CVD incidence in adults and have excellent safety profiles.*

Keywords: *Lipid screening, Atherosclerosis, Cardiovascular disease, Obesity epidemic.*

Childhood obesity is fast emerging as an epidemic throughout the world with the subsequent increase in risk of type 2 diabetes mellitus, hypertension and cardiovascular disease in older children and adults. Cardiovascular disease (CVD) is the leading cause of death and morbidity in adulthood. The strongest risk factors for adult CVD includes a high concentration of low-density lipoprotein (LDL), a low concentration of high-density lipoprotein (HDL), elevated blood pressure, type 1 or 2 diabetes mellitus, cigarette smoking and obesity. Some of these risk factors may be present at a young age.[1] Research over the last few years has increasingly indicated that the process of atherosclerotic CVD begins early in life and is progressive throughout the life span.[2] There is an important genetic component to the disease process that produces increased susceptibility, but environmental factors, such as diet and physical activity are equally important in determining the course of the disease process. By improving lipid and lipoprotein concentrations during childhood and adolescence, the lifelong risk of CVD can be lowered. The current obesity epidemic among children has increased the need for pediatric health care professionals to be knowledgeable of the risk factors for CVD and to implement the necessary changes in practice to prevent CVD in their patients at later age. They should emphasize the negative effects of excess dietary intake of saturated and trans fats and cholesterol as well as the effect of carbohydrate intake, the obesity epidemic, the metabolic/insulin-resistance syndrome and the decreased level of physical activity and fitness on the risk of adult-onset CVD.

Autopsy studies have demonstrated that the atherosclerotic process begins in childhood.[3] The earliest pathologic finding in atherosclerosis is thought to be the fatty streak. This is characterized by an accumulation of lipid-filled macrophages within the intima of an artery.

* Senior Resident,
Department of Pediatrics,
Indira Gandhi Medical College, Shimla.

The progression of atherosclerosis is characterized by continued accumulation of lipid-filled macrophages and a proliferation of vascular smooth muscle cells. These smooth muscle cells migrate into the arterial intima and form a lesion called a fibrous plaque. This lesion is responsible for adverse clinical outcomes, such as myocardial infarction and ischemic stroke, by either obstructing the arterial lumen or rupture of the plaque with release of thrombogenic substances. Dyslipidemia, high blood pressure and obesity increase these atherosclerotic lesions. Concentration of serum lipids and lipoproteins increases during early childhood and reaches concentrations similar to those seen in young adults by approximately two years of age.[4] The values subsequently decrease during pubertal development and then increase thereafter. This proves that elevated cholesterol concentrations during childhood and adolescence are associated with increased risk of atherosclerosis and CVD in adulthood. Normal cut off of value in children and adolescents is <170mg/dL total cholesterol with LDL <110mg/dL as acceptable, 170-199mg/dL of total cholesterol and 110-129mg/dL of LDL as borderline and >200mg/dL of total cholesterol and >130mg/dL of LDL as elevated.[5]

The optimal screening program recommends screening children with a family history of premature CVD or high blood concentrations of cholesterol to identify children and adolescents with progressive atherosclerosis who are at risk of CVD in adulthood. Screening pediatric patients for whom family history is not known or those who had other risk factors for CVD such as obesity, hypertension and diabetes mellitus is also important. With the prevalence of obesity and high blood pressure increasing, more percentage of children and adolescents would qualify for having their cholesterol concentration determined.[6,7] The American Heart Association has recommended that triglyceride concentrations of >150 mg/dL and HDL concentrations of <35 mg/dL be considered abnormal for children and adolescents.[8]

The metabolic syndrome (hypertension, glucose intolerance, hypertriglyceridemia, decreased HDL, abdominal central obesity) is a clustering of risk factors for CVD and diabetes mellitus that seems to be related to obesity and insulin resistance. The prevalence of the metabolic syndrome has increased in children and adolescents, reflecting the increased prevalence of obesity, prediabetes and type 2 diabetes mellitus. The presence of an increasing number of risk factors (as seen in the metabolic syndrome) is associated with increased risk of fatty streaks and fibrous plaques in the aorta and coronary arteries. The approach to treatment of the metabolic syndrome is focussed on decreasing the BMI percentile of obese children by maintaining weight during growth in height, which is usually accomplished by lifestyle changes in diet and physical activity.

Dietary management

Dietary changes using the population approach are not recommended for children younger than 2 years, because younger children are thought to require a relatively high intake of total fat to support rapid growth and development.[5] For children between 12 months and 2 years of age for whom overweight or obesity is a concern or who have a family history of obesity, dyslipidemia or CVD, the use of reduced-fat milk would be appropriate. Children and adolescents must have a balanced caloric intake with sufficient physical activity to achieve an appropriate weight and consume more fruits, vegetables, fish, whole grains and low-fat dairy products. The intake of fruit juice, sugar-sweetened beverages and foods, and salt should be reduced. Daily recommended calorie intake according to age is 900Kcal for one year age, 1000Kcal for 2-3 year age,

1200 and 1400Kcal for females and males of age group 4-8 years, 1600 and 1800 Kcal for females and males of age group 9-13 years, and 1800 and 2200 Kcal for females and males of 14-18 years of age group. Calorie estimates are based on sedentary lifestyle. Increased physical activity will require additional calories (0–200 kcal/day for moderate physical activity and 200–400 kcal/day if physically very active [1 kcal = 4.2 kJ]). Fat intake should be restricted to 35% of total calorie intake for all age groups, with good helping of fresh fruits and vegetables.[5] The intake of trans fatty acids should be limited to <1% of total calories. The largest source of trans fatty acids is the partially hydrogenated fat used in preparation of both fried and baked products both inside and outside the home.

Initial intervention is focused on changing the diet. However, if this approach does not lower LDL to an acceptable concentration, these children may be candidates for pharmacologic intervention. The recommended diet for the high-risk group restricts saturated fat to 7% of total calories and dietary cholesterol to 200 mg/day. These dietary recommendations are safe and do not interfere with normal growth, development and sexual maturation.[9] For children with a genetic cause of dyslipidemia and LDL concentration of >190 mg/dL, it is unlikely that diet alone will achieve appropriate concentrations of LDL. Nevertheless, it is important to implement dietary changes that are associated with reduction of LDL concentrations, which may allow for use of lower doses of pharmacologic agents when they are started. Dietary changes are still an important part of any long-term intervention. Dietitians help families make the appropriate changes without compromising good nutrition because very low-fat diet without supervision can lead to nutritional insufficiency and failure to thrive. The home environment is very important to help children and adolescents make the best choices and maintain a healthy diet. It is most helpful if everyone in the family is consuming a healthy diet and parents act as a role model for their children.

Dietitians can also help children and their families navigate the food environment outside the house, which has become increasingly important because increasing number of children do more eating outside the home environment. Because of the rapidly changing eating habits of the Indian children and their parents, in schools, homes of friends and restaurants, regulating food intake is becoming increasingly complex. Fast-food restaurants also provide carryout foods to be eaten in the home environment. Making healthful choices in these settings is more difficult because of the myriad external cues for eating, including advertising and the choices of peers.

Some adjuncts to dietary therapy have also been recommended. Increasing the intake of soluble fiber can be helpful in reducing plasma LDL concentration. Fiber is thought to bind with cholesterol in bile acids and remove it from the enterohepatic circulation. An appropriate dose of supplemental fiber is calculated as the child's age plus 5 g/day, up to a dose of 20 g/day at 15 years of age. Plant stanols and sterols lower the absorption of dietary cholesterol and in adults, have been shown to reduce cholesterol concentration by approximately 5% to 10% with minimal adverse effects.[10] Increased physical activity primarily affects HDL and triglyceride concentrations and is useful for improving dyslipidemia in children and adolescents.[11]

Pharmacological intervention

Above 8 years, pharmacological treatment is recommended if:

1. LDL concentration is persistently >190mg/dL despite diet therapy if no other risk factors for CVD are present.

2. LDL concentration is persistently >160 mg/dL despite diet therapy and in the

presence of other risk factors, including obesity, hypertension or cigarette smoking or positive family history of premature CVD

3. LDL concentration is 130 mg/dL in children with diabetes mellitus.[12]

The initial goal is to lower LDL concentration to <160 mg/dL. However, targets as low as 130 mg/dL or even 110 mg/dL may be warranted when there is a strong family history of CVD, especially with other risk factors including obesity, diabetes mellitus, the metabolic syndrome and other higher-risk situations.

In children younger than 8 years pharmacotherapy will be required if they have the dramatic elevation of LDL concentration (>500 mg/dL) as seen with the homozygous form of familial hypercholesterolemia as well as for children and adolescents with diabetes, renal disease, congenital heart disease and collagen vascular diseases.[12]

Drugs useful in management of dyslipidemia in children and adolescents are:

1. Bile Acid–Binding Resins

Bile acid–binding resins work by binding the cholesterol in bile acids in the intestinal lumen, which prevents their reuptake as part of the enterohepatic circulation without having any systemic effects. Average lowering of cholesterol is 10% to 20% below baseline. Gastrointestinal discomfort is the main adverse effect.

2. Niacin

Niacin or nicotinic acid is effective in lowering LDL and triglyceride concentrations while increasing HDL concentration.[13,14] The mechanism of action is by decreasing hepatic production of very low-density lipoprotein (VLDL). Niacin also lower lipoprotein'a'. Because of these effects, niacin is a potentially attractive medication for treatment of dyslipidemia. Adverse effects include flushing, hepatic failure, myopathy, glucose intolerance and hyperuricemia. Because of those adverse effects, niacin can not be recommended for routine use in the treatment of pediatric dyslipidemia.

3. 3-Hydroxy-3-methyl-glutaryl Coenzyme A Reductase Inhibitors (Statins)

Statins inhibit the rate-limiting enzyme 3-hydroxy-3-methyl-glutaryl coenzyme A reductase for endogenous synthesis of cholesterol, which lowers the intracellular cholesterol level and up regulates the LDL receptors, resulting in increased clearance of LDL from the circulation. In general, the statins are well tolerated and result in cholesterol lowering of 20% to 50% below baseline depending on the baseline value and the dose used.[15] Adverse effects of statins are increased hepatic transaminase levels, elevation of creatine kinase and rhabdomyolysis. Due to teratogenic effect they are not recommended for women who are pregnant, seeking to become pregnant or breastfeeding. Patients should be monitored with periodic measurement of liver transaminase, creatine kinase levels and instructed to report symptoms of muscle aches or cramping. US FDA has approved the use of pravastatin for children with familial hypercholesterolemia who are 8 years and older, regardless of pubertal status.

4. Cholesterol absorption inhibitors

The dietary cholesterol-absorption inhibitors represent the newest class of cholesterol-lowering agents. Although they are thought to act mainly on intestinal absorption, unlike resins, these drugs are absorbed, enter the enterohepatic circulation, and may have systemic effects. They are used primarily in combination with statins. Ezetimibe has a good safety profile in adults, either as monotherapy or in combination with a statin, although efficacy and safety data in children are

still lacking. It has been shown to reduce LDL concentrations by 20%. Because the adverse effects are limited to gastrointestinal discomfort and drug comes in a palatable, small tablet form, it can be a potentially important first-line treatment for children in isolated elevation of low-density lipoprotein cholesterol although further studies are required to assess its safety in children.[16]

5. Fibrates

Fabric acid derivatives inhibit the synthesis and increase the clearance of the VLDL apoprotein B, which then leads to a decrease in VLDL production. These medicines also inhibit peripheral lipolysis and decrease hepatic extraction of free fatty acids, which reduces hepatic triglyceride production. These medications should be used cautiously and under the supervision of a pediatric lipid specialist in isolated severe hypertriglyceridemia.[16] The adverse effects of fibrates are similar to those of statins. The risk of myopathy and rhabdomyolysis is markedly increased when fibrates (especially gemfibrozil) are used in combination with statins or in patients with renal insufficiency.

Points to Remember

- ***A healthy diet should be recommended to all children, along with the use of low-fat dairy products for those who have a family history of obesity, dyslipidemia or CVD.***
- ***Overweight or obese children and those with a high triglyceride concentration or low HDL concentration should focus on weight management which includes improvement of diet with nutritional counselling and increased physical activity to produce improved energy balance.***
- ***All children above 2 years of age with a positive family history of dyslipidemia or premature CVD, as well as those for whom family history is not known but with other CVD risk factors, such as overweight (BMI ≥85th percentile, <95th percentile), obesity (BMI ≥95th percentile), hypertension (blood pressure ≥95th percentile), cigarette smoking, or diabetes mellitus should be screened.***
- ***Fasting lipid profile is the recommended approach to screening, with patient retested in 3 or 5 years if values are within the reference range on initial screening.***
- ***Above 8 years with LDL concentration of ≥190 mg/dL (or ≥160 mg/dL with a family history of early heart disease or ≥2 additional risk factors present or ≥130 mg/dL if diabetes mellitus is present), pharmacologic intervention should be considered.***

References

1. Gaut JP, Heinecke JW. Mechanisms for oxidizing low-density lipoprotein. Insights from patterns of oxidation products in the artery wall and from mouse models of atherosclerosis. Trends Cardiovasc Med 2001; 11:103-112.
2. Webber LS, Osganian V, Luepker RV. Cardiovascular risk factors among third grade children in four regions of the United States. The CATCH Study: Child and Adolescent Trial for Cardiovascular Health. Am J Epidemiol 1995; 141:428 –439.
3. McGill HC Jr, McMahan CA, Zieske AW, Malcom GT, Tracy RE, Strong JP. Effect of nonlipid risk factors on atherosclerosis in youth with favorable lipoprotein profile. Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Circulation 2001; 103:1546 –1550.
4. Grossman DC, McCulloch DK. Lipid screening in children and adolescents. Pediatr Ann. 2008; 37:757-762.
5. Lichtenstein AH, Appel LJ, Brands M, et al. Diet and lifestyle recommendations revision 2006:

a scientific statement from the American Heart Association Nutrition.Circulation 2006; 114:82 –96.

6. Cottam R. Obesity and culture. Lancet 2004; 364: 1202-1203.
7. Muntner P, He J, Cutler JA, Wildman RP, Whelton PK. Trends in blood pressure among children and adolescents. JAMA.2004 291:2107 –2113.
8. Kavey RE, Daniels SR, Lauer RM, et al. American Heart Association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. Circulation 2003; 107:1562 –1566.
9. Writing Group for the DISC Collaborative Research Group. Efficacy and safety of lowering dietary intake of fat and cholesterol in children with elevated low-density lipoprotein-cholesterol: the Dietary Intervention Study in Children (DISC). JAMA 1995; 273:1429 –1435.
10. Lichtenstein AH, Deckelbaum RJ. American Heart Association Science Advisory. Stanol/ sterol ester-containing foods and blood cholesterol levels: a statement for healthcare professionals from the Nutrition Committee of the Council on Nutrition, Physical Activity, and Metabolism of the American Heart Association. Circulation 2001; 103:1177 –1179.
11. Strong WB, Malina RM, Blimkie CJ, et al. Evidence-based physical activity for school-age youth. J Pediatr 2005; 146:732 –737.
12. Kavey RE, Allada V, Daniels SR, et al. Cardiovascular risk reduction in high-risk pediatric patients: a scientific statement from the American Heart Association Expert Panel on Population and Prevention Science; Councils on Cardiovascular Disease in the Young, Epidemiology and Prevention, Nutrition, Physical Activity and Metabolism, High Blood Pressure Research, Cardiovascular Nursing, and the Kidney in Heart Disease; and the Interdisciplinary Working Group on Quality of Care and Outcomes Research—endorsed by the American Academy of Pediatrics. Circulation 2006; 114: 2710 –2738.
13. Alsheikh-Ali AA, Karas RH. The safety of niacin in the US Food and Drug Administration adverse event reporting database. Am J Cardiol 2008 ; 101:9B-13B.
14. Colletti RB, Neufeld EJ, Roff NK, McAuliffe TL, Baker AL, Newburger JW. Niacin treatment in hypercholesterolemia in children. Pediatrics 1993; 92:78 –82.
15. Waters DD. What the statin trials have taught us. Am J Cardiol 2006; 98:129 –134.
16. Rodenburg J, Vissers MN, Daniels SR, Wiegman A, Kastelein JJ. Lipid lowering medications. Pediatr Endocrinol Rev 2004; 2:171-180.

NEWS AND NOTES

APLS: PEDIATRIC EMERGENCY MEDICINE COURSE
November 18 and 19, 2009
Venue: Sankardev Kalakhetra, Guwahati

Contact
Dr.Nitin Agarwala
Consultant Pediaric Intensivist
House no.22, bye lane 2, Anil Nagar, Guwahati,
Assam, India-781 007.

Mobile: 9864206868
E-mail: nitindoc2000@yahoo.com
Website : emcon2009guwahati.com

DERMATOLOGY

SUPERFICIAL FUNGAL INFECTION – TINEA CORPORIS

Vijayabhaskar C

Abstract : *Tinea corporis may be mistaken for other common conditions like pityriasis rosea, psoriasis, granuloma annulare, nummular eczema and diaper dermatitis. The typical morphology and distribution of the skin lesion will help in diagnosing the skin conditions and rarely wet mount with KOH is used to diagnose this condition. Smaller lesions are treated with topical antifungal agents but larger lesions or multiple lesions and lesions involving hairy regions should be treated with oral and topical antifungal agents. If treated with appropriate dosage and duration, it is one of the easily curable condition.*

Key words: *Dermatophytes, Tinea corporis, Antifungal agents*

Fungal infections are responsible for significant morbitity of pediatric population. The three major classes of fungii capable of producing cutaneous infections in humans are yeasts, dermatophytes and molds.

Common dermatophytic infections in children are Tinea capitis followed by Tinea corporis. Tinea capitis has already been dealt in the previous issue. "Tinea" - the term denotes dermatophyte infection. It has been in use for more than 1500 years. Romans thought that the "moth-eaten" appearance of scalp affected by dermatophytes resulted due to "tinea moth worm" and that is how the term was coined[1].

* Asst. Professor
Department of Dermatology
Stanley Medical College, Chennai

Tinea corporis

It is a superficial dermatophyte infection with lesions of the glabrous skin.

Age

Affects all age groups but highest incidence is seen in preadolescents.

Etiopathogenesis

Trichophyton, Microsporum and Epidermophyton are the common genera which causes Dermatophytoses. The common species are T.rubrum, T.tonsurans, T.mentagrophytes, M.canis and E.floccosum[2].

In children, the infection is most commonly acquired due to close contact with adults suffering from fungal infection. For example, toddlers carried over the waist by the mother with Tinea corporis in the waist region results in Tinea cruris and Tinea glutealis in the child.

Slight trauma or an abrasion is required for dermatophyte infection to occur in immuno-competent individuals. It inhabits the non living cornified layer of skin, hair and nail due to warm, moist environment conducive to fungal proliferation. Under right circumstances, fungal spores attach to the skin, germinate and penetrates stratum corneum. Fungii releases keratinases to invade deeper into the stratum corneum but does not cross epidermis. This occurs due to nonspecific host defense mechanism that can

include the activation of serum inhibitory factor, complement and polymorphonuclear leucocytes.

Incubation period is 1 to 3 weeks. Invasion occurs in a centrifugal pattern. Due to the infection, the active border has increased epidermal cell proliferation which results in shedding and scaling of the infected skin and new healthy skin is left behind in the centre. Cell mediated immunity plays an important role.

Clinical features

Most of the times this infection is asymptomatic in children.

Annular plaque with itching is characteristic of symptomatic patients. Very rarely burning sensation occurs.

The lesions may be erythematous, annular scaly plaque which enlarges rapidly. In the advancing border, scales, crusts, papules, vesicles and even bullae develop due to the inflammation. It can very rarely present as purpuric macules and is called as corporis purpurica. It involves any part of the body and may be associated with nail or scalp involvement. The following terms are used to denote the various sites of involvement. Tinea capitis – scalp, Tinea cruris – groin, Tinea glutealis – gluteal region, Tinea manuum – hand and Tinea pedis – feet.

Treatment with topical steroids results in a nonclassic presentation termed tinea incognito that may challenge correct diagnosis and lead to deeper hair follicle invasion known as Majocchi granuloma[3].

In immunocompromised children there may be atypical presentation like deep abscesses[4] or a disseminated skin infection.

Differential diagnosis[5]

Pityriasis Rosea – Herald patch of pityriasis rosea could be a close diagnosis of Tinea corporis but crops of multiple erythematous patches with collaratte of scales over the chest, back and limbs are characteristic feature of Pityriasis Rosea.

Psoriasis – Erythematous, scaly plaques involving extensor aspect and scales being silvery in nature differentiates the condition

Granuloma annulare – Characterised by non scaling slightly pink to tan papules organize into annular plaques and the lesions are solitary or multiple commonly over the dorsum of hand and feet.

Nummular eczema – Pruritic, coin shaped circular areas of erythema, scaling which are seen over the torso or extremities. Lesions are circinate rather than annular or ring shaped.

Diaper dermatitis – History of prolonged contact with diaper with well demarcated erythema, scaling and maceration on the surface of contact with diaper.

Investigations

The diagnosis is usually clinical. When in doubt, KOH wet mount will help in diagnosing the condition. Scraping should be done with a blunt scalpel at the border of the lesion to get the highest yield of fungal elements . KOH dissolves the keratin and leaves the fungal element intact revealing septate branching hyphae.

Culture is rarely done when there is clinical suspicion and KOH wet mount is negative.

Treatment

Many cases of tinea corporis resolve spontaneously[6] but due to the contagious nature, the infection has to be treated.

If the lesion is localised, only topical agents need to be used. In case of extensive distribution and involvement of hairy region systemic therapy is initiated.[7]

The commonly used topical agents are

1. Clotrimazole 1% cream
2. Ketoconazole 2% cream
3. Miconazole 2% cream or lotions
4. Oxicanazole 1% cream
5. Terbinafine 1% cream

All these topical agents are to be used twice daily and should be applied atleast 2cm beyond the lesional area for 2 to 4 weeks.

Lesions when in doubt and whenever KOH mount is not available one can empirically start on topical antifungals for 2 weeks and if there is no improvement diagnosis has to be revised. Try to avoid antifungal agents with steroid combinations.

Systemic treatment

This can be combined with topical therapy.

Griseofulvin is one of the old drugs and is still used against extensive tinea corporis. Micronised form at a dosage of 20mg/kg/day orally should be used for a minimum period of 4 to 6 weeks. Ultramicronised forms are used at a dosage of 7.3mg/kg/day.

Fluconazole 3 to 5 mg/kg day twice a week or in adolescents 150mg /day twice a week could be used.

Itraconazole is another drug with a dosage of 100mg/day PO for 2 weeks or 200mg/day PO for 1 week could be used. In children above 2 years 100mg/day PO for 1 week is another alternative.

Ketoconazole 3.3 -6.6 mg/kg PO for 4 weeks in children above 2 years could be used. 200-400mg /day PO for 10 days could be used in adolescent age group. But now a days ketoconazole is not a preferred drug due to its side effects.

All the drugs mentioned above are fungistatic.

The best fungicidal medicine is Terbenafine. In children who are weighing 10-20kgs oral terbinafine could be given 62.5mg/day PO for 2 to 4 weeks. For children weighing 20-40kgs, a dose of 125mg/day is sufficient. Children weighing more than 40kgs, terbinafine 250mg /day is given for 2 to 4 weeks

Follow up

Children have to be followed up after 2 weeks and 4 weeks after starting the treatment to monitor the clinical response. If resistance is seen it has to be dealt with a different antifungal agent.

Prevention

Discourage close contact between infected and non-infected individuals and sharing of fomites. Loose fitting clothes made of cotton to be used to avoid moist environment.

Recurrence

Recurrence occurs mainly due to incomplete treatment.

Immunocompromised status and infection due to resistant organism may lead to recurrence.

Reinfection

Infected hair follicle if not treated along with the body lesions could lead to reinfection

Prognosis

Localised tinea corporis in children has a very good prognosis.

Points to Remember

- ***Tinea corporis refers to dermatophyte infection of the glaborous skin.***
- ***Itchy annular plaque with advancing margin and central clearing is a characteristic feature.***
- ***In case of limited involvement only topical antifungal treatment suffices.***
- ***Extensive involvement of skin, face, hair and nail warrants use of systemic agents along with topical application.***
- ***Important to treat the contact persons.***
- ***Sharing of soaps and towels to be avoided.***

References

1. Friedlander SF, Rende M, Chen BK, Caceres Rios HW. Fungal, Protozoal and Helminthic infections. In:Schachner LA, Hansen RC. (Eds) Paediatric Dermatology. 3rd edn, Mosby, 2003; pp 1093 – 1101.
2. Hay RJ, Moore MK. Mycology. In: Text book of Dermatology, Burns T, Breathrach S, Cox N, Griffiths C, eds, (Vol 2) 7th Edn, Oxford, Black Well Science, 2004; pp 31.25-31.27.
3. Pride HB. Infections and Infestations. Pride HB, Yan AC, Zaenglein AL, (Eds) In:Requisites in Dermatology – Pediatric Dermatology, Saunders Elsevier, 2008; p65.
4. Swart E, Smith FJA. Trichophyton violaceum absecesses. Brit J Dermatol 1979; 101:107 – 183.
5. Verma S, Hefferman MP. Superficial fungal infection: Dermatophytosis, Onychomycosis, Tinea Nigra, Piedra, Fungal Diseases. In:Fitzpatrick's Dermatology in General Medicine, Wolff K, Goldsmith LA, et al, 7th edn. (vol 2), McGraw Hill, 2008; p 1815.
6. Jones HE, Reinhardt JH, Rinaldi MG. Acquired immunity to dermatophytes. Arch Dermatol 109:840 - 848.
7. Smith KJ, Neafie RC, Skelton HG, Barrett TL, Graham JH, Lupton GF. Majocchi's granuloma. J cutan Pathol 1991;18:28 - 35 .

NEWS AND NOTES

RAMACHANDRA INTENSIVE PEDIATRIC POSTGRADUATE EXAM-REVIEW (RIPE) 2009

This course is organized by the Department of pediatrics, SRMC, Porur for everyone who intends to take pediatric post graduate exam DCH/MD/DNB

Highlights

- Case discussions needed for your practical exam by teachers who are potential examiners.
- Separate sessions for viva voce (nutrition/vaccinations/instruments/ X-rays and slides).
- One dedicated OSCE session for DNB examination with attractive cash prize.
- Panel discussion "Career Guidance" explaining the scope of pediatrics and super specialty fellowship programmes in abroad (Australia/UK/USA/Canada) and for successful pediatric general practice.

Dates: 28.11.2009& 29.11.2009 **Venue**: Sri Ramachandra medical college, Porur, Chennai.

Registration fees Before Nov 15st **Rs. 1,500/-** After Nov 15st and spot **Rs. 2000/-**

Payment should be made in favour of "RIPE 2009" payable at Chennai in the form of DD/cheque

For further details contact : **Dr. Julius Scott**, Organizing secretary RIPE 2009
Email: ripe_2009@yahoo.in, Phone: 9488286303/9940578568

RADIOLOGIST TALKS TO YOU

DISORDERS OF NEURONAL PROLIFERATION, DIFFERENTIATION AND HISTOGENESIS (contd...)

* *Vijayalakshmi G*
** *Elavarasu E*
** *Anita A*
*** *Venkatesan MD*

We will see some more disorders under the category of neuronal proliferation, differentiation and histogenesis. One abnormality that often accompanies other CNS abnormalities is agenesis of the corpus callosum. (ACC). The corpus callosum is a large bundle of nerve fibers that connect the two hemispheres across the midline. Its development begins in the 12th week of intrauterine life and is fully formed by the 20th week. ACC can occur as an isolated anomaly or with other congenital abnormalities like migration disorders (heterotopias, lissencephaly, or schizencephaly), Chiari II malformations, cephaloceles, Dandy-Walker malformation, holoprosencephaly and lipomas. ACC is not only accompanied by CNS abnormalities. but also of other systems. Recent medical research classifies ACC under genetic ciliopathy which includes primary ciliary dyskinesia, nephronopthisis, polycystic kidney and liver disease,

ACC can be diagnosed with ultrasound, CT and MRI. There are many features that help in the diagnosis of ACC. In ultrasound, a normal posterior coronal section through the anterior fontanelle will show the choroid plexus in the lateral ventricles as two posteriorly divergent

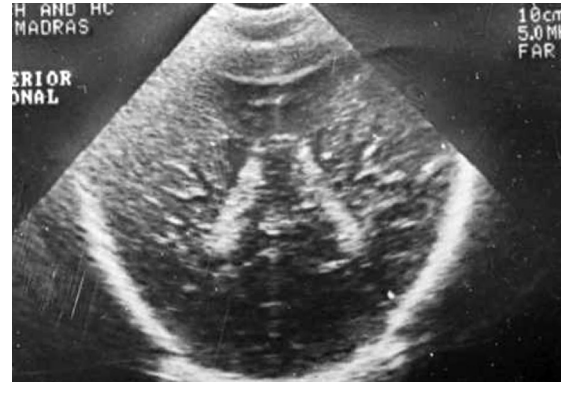


Fig.1 Normal posterioral section

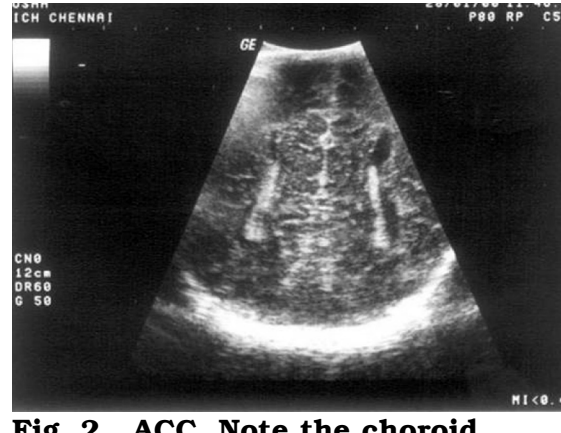


Fig. 2. ACC. Note the choroid plexuses as parallel lines

* Associate Professor
** Asst. Professor
*** Professor
Department of Radiology,
Chengalpet Medical College Hospital,
Chengapet. Tamil Nadu.

white lines(Fig.1) on either side of the midline. In ACC there is no close binding of the two hemispheres with the corpus callosum. The lack of the restraining effect of the corpus callosum causes the choroid plexuses to move apart assuming a parallel configuration (Fig.2). For the same reason, the third ventricle gets pulled up in between the lateral ventricles or there is an interhemispheric arachnoid cyst as in Fig.3 or an interhemispheric lipoma as in Fig.4. Fig.5 is a normal midsagital section. Note the cingulate sulcus as a curved white line above the roof of the lateral ventricle. The other sulci are seen taking off regularly from it. The cingulate gyrus and the sulcus are absent in ACC. Therefore the other sulci seem to be taking off right from the roof of the lateral ventricle (Fig 6).

ACC can be partially or completely absent. It may be true agenesis or may be due to vascular insult or infection. In true agenesis the axons are unable to cross the midline and therefore they run longitudinally along the medial side of the two hemispheres in an anterior-posterior direction. This is evident in MRI and helps in differentiating between true agenesis and agenesis due to other causes like infection and vascular insult where the normally formed corpus callosum is destroyed.

The interhemispherical arachnoid cyst that we mentioned above is not a common location for such cysts. They are more common in the middle cranial fossa around the Sylvian fissure as shown in Fig.7. The temporal lobe (A) is displaced superiorly by the cyst. The picture on the right is a parasaggital view showing the cyst in the temporal fossa. Arachnoid cysts are benign cysts that occur in the cerebrospinal axis in relation to the arachnoid membrane. They do not communicate with the ventricular system. Most cysts are unilateral and smoothly rounded. Arachnoid cysts may indent deeply into the hemisphere or invaginate into major fissures.

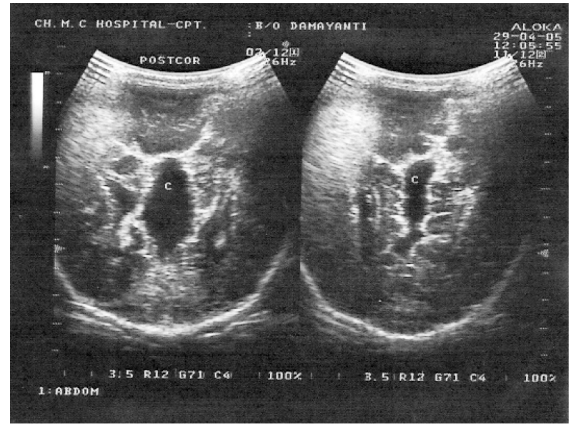


Fig. 3 Interhemispheric cyst

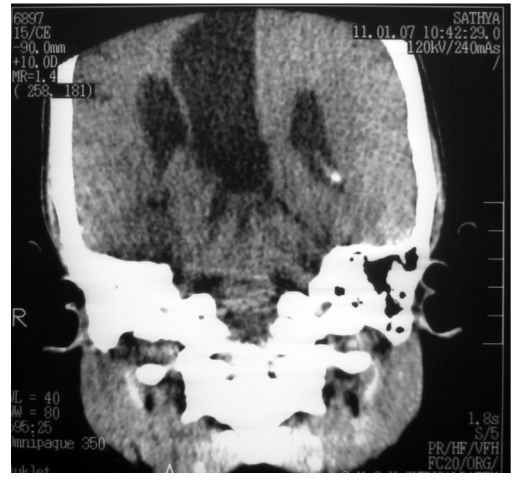


Fig. 4 Interhemispheric lipoma

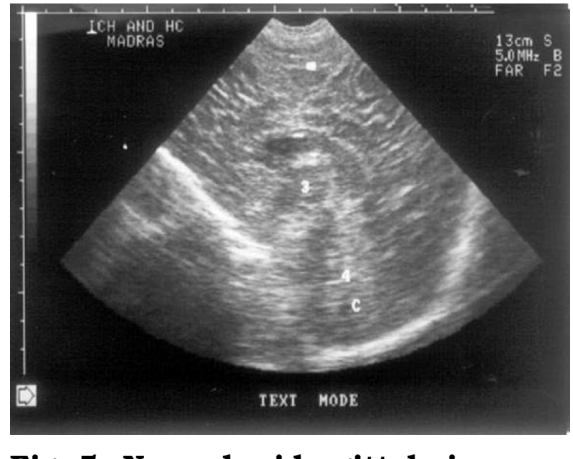


Fig. 5 Normal midsagittal view

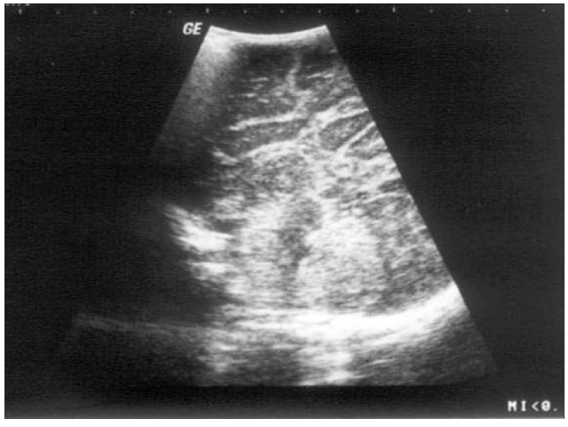


Fig. 6 ACC midsagittal section

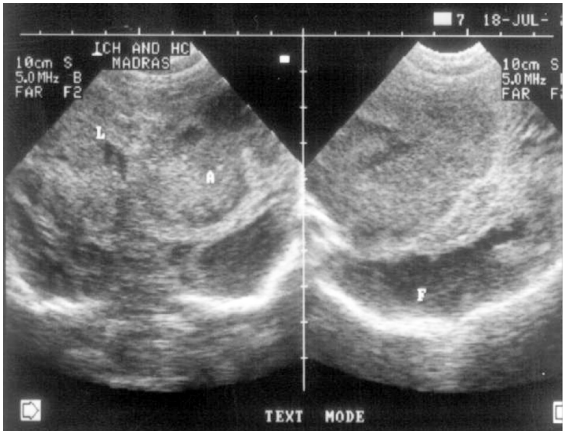


Fig. 7 Temporal arachnoid cyst

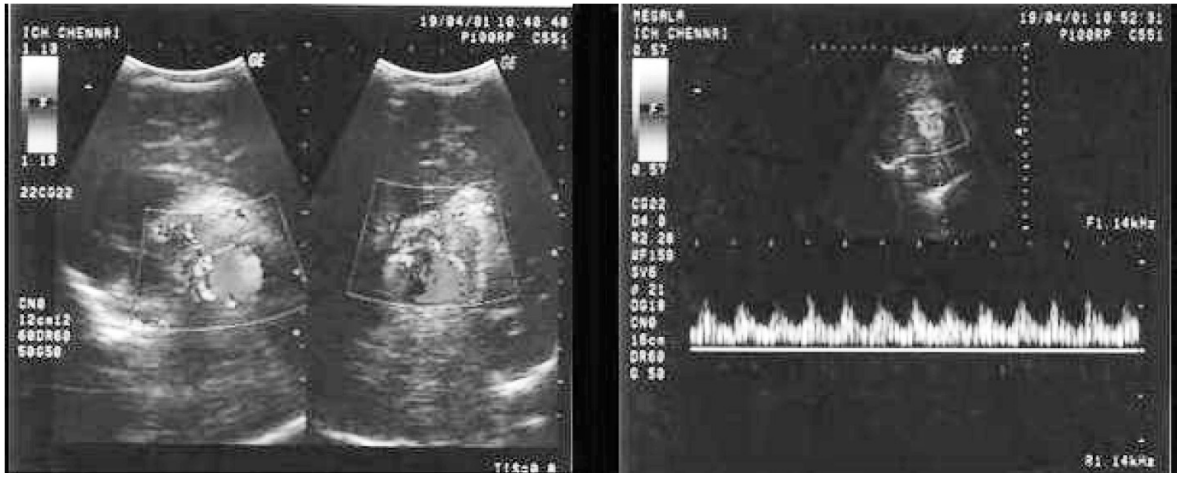


Fig. 8 Vein of Galen aneurysm

Other locations of arachnoid cysts include the suprasellar chiasmatic site , the cerebellopontine angle, the quadrigeminal plate cistern, near the vermis and in the prepontine or interpeduncular cistern..

The vein of Galen aneurysm will also be seen as a central cystic lesion just like a suprasellar arachnoid cyst. But doppler mode will show turbulent flow within(Fig.8). It is a very rare anomaly. The name is a total misnomer. It is not an aneurysm. It is an arterio-venous malformation with arterial inflow from branches of posterior cerebral artery. It is not actually the great cerebral vein or the vein of Galen. It is a persistent median prosencephalic vein that becomes so big that the great cerebral vein does not develop. Ultrasound is an excellent screening investigation, especially when it is required to rule out this condition in a child with CCF that is not responding quickly to treatment.

CASE STUDY

A RARE CAUSE OF SEIZURE- DYSGENESIS OF CORPUS CALLOSUM

*** Rajib Ray***
*** Subhranshu Sekhar Kar***
**** Samarendra Mahapatro***
***** Radha Tripathy***
****** Renuka Mohanty***

Dysgenesis of corpus callosum is a spectrum of callosal anomalies in which there is complete or partial agenesis of corpus callosum.An early failure may lead to complete agenesis, whereas a later one will lead to hypoplasia.[1] It may occur as an isolated condition or in association with other central nervous system and/or systemic malformations.[2,3] As no specific therapy is available,treatment is mainly symptomatic .

Case report

A developmentally normal, fully immunized, 11 year old boy was admitted with one episode of afebrile generalised tonic clonic convulsion lasting for ten minutes followed by hemiparesis involving left side. There was no history of preceding trauma, exanthemata, drug intake or suppurative otitis media. Perinatal history was uneventful. History of contact with open case of tuberculosis was absent.

On examination, the child was conscious; there was upper motor neuron type of left sided hemiparesis. The sensory, autonomic and cerebellar system examination revealed no abnormality. Meningeal signs were absent. No other systemic involvement was noted.

Investigations showed normal blood count with normal cerebro spinal fluid analysis. Computerised tomography scan of brain revealed parallel temporal horns.On magnetic resonance imaging of brain there was partial agenesis of genu and head of corpus callosum and complete agenesis of body and splenium. Electroencephalography is suggestive of seizure disorder. Echocardiography, hematological tests like complete blood counts, High pressure liquid chromatography (HPLC), protein C,S and Antithrombin III estimation, ANA, rheumatoid factor, lupus anticoagulant along with LFT, lactate/ pyruvate levels were done and found normal. Urinary and blood aminoacids/organic acid levels were also within normal range. Karyotyping done to exclude other genetic causes, was also normal.

The child was seizure free and was discharged on antiepileptic therapy.

Discussion

The corpus callosum develops between the 10th and 20th weeks of gestation, from the lamina reuniens.Until the fourth month of gestation, only the most rostral part of the corpus callosum is formed; the caudal portion develops only after the fifth month.[4,5] Disturbance of embryogenesis in the first trimester of gestation leads to failure of the callosal axons to pass across the midline. These arrested axons form the longitudinal oriented bundles of Probst that are located medial

* Asst. Professor,
** Associate Professor,
*** Professor,
**** Prof. and Head,
Hitech Medical College, Bhubaneswar

to the lateral ventricles in patients with agenesis. The defect may be complete or partial, depending on the stage at which callosal development is arrested. In partial agenesis of the corpus callosum, the posterior portion is missing.[6] The incidence ranges from 0.7% to 5.3%.[7,8]

Associated anomalies include central nervous system anomalies(85%)[2] like Dandy walker cyst (11%), Hydrocephalus (30%), Arnold-chiari malformation (7%), Porencephaly and Holoprosencephaly,[2,3] cardiovascular, gastrointestinal as well as genitourinary system anomalies(62%). Though sporadic, incidence is increased in patients with trisomy-8,13 and 18,with chromosome anomalies[2,9,10,11] and with syndromes like Aicardi, Anderman's, Shapiro, Septo-optic dysplasia and Menkes syndrome. An association with maternal rubella and toxoplasmosis has been reported.[12,13] Several familial cases are also reported and males outnumber females. Studies of patients with agenesis of the corpus callosum unrelated to holoprosencephaly show that some have normal intelligence and others are developmentally delayed.[2,14]

Signs and symptoms vary greatly among individuals. Studies of persons with isolated agenesis of the corpus callosum show that some have normal intelligence, while others are developmentally delayed.[14,15] There may be hypotonia, poor motor coordination, delayed gross motor development especially sitting and walking, low pain perception, delayed toilet training, chewing and swallowing difficulties, speech and language delay and social difficulties. Other features are seizure, spasticity, abnormal facial features, hearing impairment and mental retardation.

Antenatal diagnosis is possible from about 20 weeks gestation. Endovaginal ultrasonography findings are a disproportionate enlargement of the occipital horns and an abnormally parallel course of the ventricular walls.

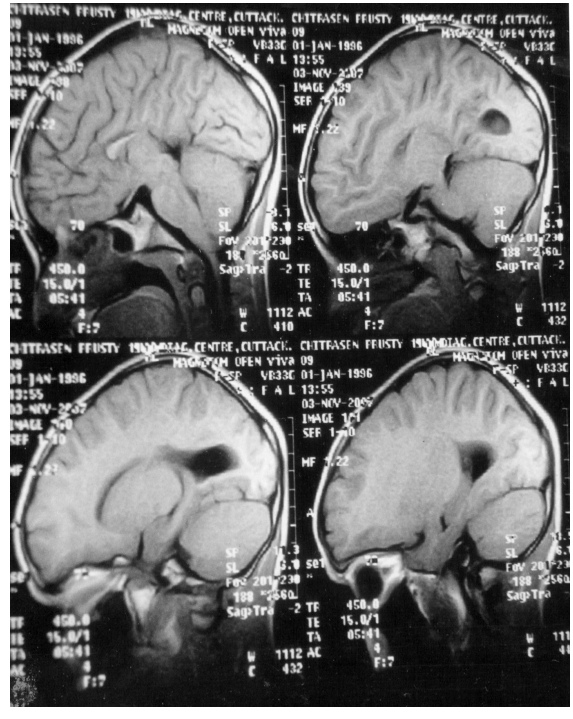


Fig.1. MRI brain : Partial agenesis of genu and head of corpus callosum.

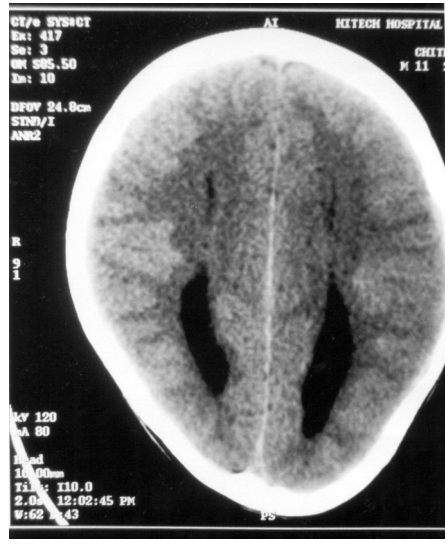


Fig.2. CT brain : Parallel temporal horns.

Findings in coronal sonograms include the following: (1) enlarged atria and occipital horns, (2) parallel and widely separated bodies of lateral ventricles, (3) an enlarged and upwardly displaced third ventricle, (4) absent corpus callosum and septum pellucidum, (5) frontal horns that are sharply angulated laterallly and indented medially by the Probst bundles, (6) medial cerebral gyri and sulci with a radial pattern extending to the roof of the elevated third ventricle and (7) elongation of the interventricular foramen of Monro.

Axial computerised tomography of brain shows parallel imaging modality.[16,17] Sagital T1-weighted images clearly demonstrate the exact extent of callosal dysgenesis. In complete agenesis, the corpus callosum is not visualized, where as in a hypogenetic corpus callosum, the later forming structures are usually absent. Therefore, the corpus callosum may show a posterior genu; a posterior genu and anterior body; a genu and an entire body; or an entire genu, body and splenium with the exception of the rostrum. The third ventricle may be high riding and interposed between the bodies of the lateral ventricles (Fig.1 and 2).

Coronal and axial magnetic resonance imaging sections are best for demonstrating the longitudinal callosal bundles of Probst.

Treatment is symptomatic and antiepileptics are indicated in seizures. As it is a developmental brainproblem, surgery has limited role. But, treatment is available for other physical and medical conditions sometimes associated with callosal disorders, such as hydrocephaly or other midline defects. The individual may benefit from occupational therapy.

Corpus callosum neither degenerates nor regenerates. Mental retardation does not worsen. Although some individuals have normal intelligence and lead a normal life, neuro-physiological testing reveals subtle difference in higher cortical function. The disorder does not cause death. Prognosis is associated with associated malformation.[2,16]

Points to Remember

- ***Dysgenesis of corpus callosum may occur as an isolated condition or in association with other systemic malformations.***
- ***It may present with afebrile seizure and sometimes associated with trisomies, chromosomal anomalies, maternal rubella and toxoplasmosis.***
- ***USG,CT and/or MR scans of brain aid in diagnosis.***
- ***The treatment is mainly symptomatic.***

References

1. Ettlinger G. Agenesis of the corpus callosum. In: Vinken GW, Bruyn PW, eds. Handbook of clinical neurology. Amsterdam: Elsevier/North Holland Biomedical Press 1977;pp30:285-297.
2. Parrish M, Roessmann U, Levinohn M. Agenesis of the corpus callosum. A study of the frequency of associated malformations. Am Neurol 1979;6:349.
3. Harwood-Nash D. Congenital malformation of the brain. Neuroradiol Infants Child 1976;3:1019-1025.
4. Loeser JD, Alvord EC. Clinicopathological correlations in agenesis of the corpus callosum. Neurology 1968;18:745.
5. Loeser JD, Alvord EC. Agenesis of the corpus callosum. Brain 1968;91:533.
6. Warkany J, Lemore RJ, Cohen MM. Agenesis of the corpus callosum, in mental retardation in congenital malformation of the central nervous system. Chicago:Year Book, 1981;pp224-241.
7. Grogono JL. Children with agenesis of the corpus callosum. Dev Med Child Neurol 1968;10:613.

8. Warkany J, Passarge E, Smith LB. Congenital malformation in autosomal trisomy syndromes. Am J Dis Child 1966;112:502.
9. Bertino RE, Nyberg DA, Cyr DR, et al. Prenatal diagnosis of the corpus callosum. J Ultrasound Med 1988;7:251.
10. Comstock C, Culp D, Gonzalez J, et al. Agenesis of the corpus callosum in the fetus: its evolution and significance. J Ultrasound Med 1985;4:613.
11. Amato M, Howald H, Von Muralt G. Fetal ventriculomegaly, agenesis of the corpus callosum, and chromosomal translocation: case report. J Perinatol Med 1986;14:271.
12. Bartoleschi B, Cantore GP. Agenesia del corpo calloso in paziente affeto da toxoplasmosi. Riv Neurol 1962;32:79.
13. Friedman M, Cohen P. Agenesis of corpus callosum as possible sequel to maternal rubella during pregnancy. Am J Dis Child 1947;73:178.
14. Jeret JS, Serur D, Wisniewski KE, et al. Clinico-pathological findings associated with agenesis of the corpus callosum. Brain Dev 1987;9:255-264.
15. Grubben C, deCock P, Borghgraet M, et al. Severe pre- and postnatal growth retardation, developmental delay with hypotonia and marked hypotrophy of the distal extremities, dental anomalies, and eczematous skin.A new autosomal recessive entity.Clin Genet 1992;41:16-21.
16. Byrd SE, Radkowski MA, Flannery A.: The clinical and radiological evaluation of absence of the corpus callosum. Eur J Radiol 1990;10:65-73.
17. Pilu G, Sandri F, Perolo A, et al. Sonography of fetal agenesis of the corpus callosum: a survey of 35 cases. Ultrasound Obstet Gynecol 1993;3:318.

NEWS AND NOTES

5th INTERNATIONAL CONFERENCE ON

CHILDREN'S HEALTH AND THE ENVIRONMENT

Bangalore 1st – 3rd February 2010

Location: National Institute of Advanced Studies
Indian Institute of Science Campus
Bangalore, Karnataka, India

Organized by: International Network on Children's Health Environment and Safety (INCHES) Amsterdam and HP Foundation, Bangalore, India

Theme: Promote Good Health and Prevent Disease Disability from Environment Pollution

Log on to (1) http://www.incheshpfindia.org, (2) http://www.inchesnetwork.net

Contact us: (1) info@incheshpfindia.org (2) dr_paramesh1@yahoo.com
(3) Elizabeth_cherian@yahoo.com

Register Early, Limited Participants

CASE STUDY

DERMATOMYOSITIS PRESENTING AS PYREXIA OF UNKNOWN ORIGIN

*** Jayasree P**
**** Chitra**
***** Sukumaran TU**

Abstract : *7 year old girl presented with fever of 15 days duration. Her physical examination revealed pathognomonic skin lesions of juvenile dermatomyositis (JDM). History and physical examination revealed dysphagia, constipation and proximal muscle weakness. She had elevated muscle enzyme levels and MRI changes were suggestive of JDM. She responded well with steroids.*

Key words: *Juvenile dermatomyositis, Skin lesions, Weakness, MRI.*

Case report

A 7-year-old girl presented with fever of 15 days duration and mild abdominal pain. She was treated for enteric fever elsewhere. The striking feature on physical examination was symmetric shiny erythematous painless papules over ear lobes, proximal interphalangeal joints(Fig.1), elbows, knees and medial malleoli with shallow ulceration in some places. The skin lesions were painless and so were not a complaint at all. Since the skin lesions suggested Gottrons papules, which are pathognomonic of dermatomyositis, other symptoms and signs were sought. This revealed history of severe tiredness and reluctance to walk, difficulty in getting up from squatting position in toilet, dysphagia and constipation. Muscle weakness mistaken for lethargy and dysphagia as anorexia, since both are common accompainments of enteric fever. She had erythematous skin lesions in shawl distribution also. There was heliotrope rash of upper eyelid and lid edema. She had positive Gower's sign and slightly waddling gait. Shoulder girdle muscles were not as weak as hip girdle. Reflexes were preserved and other system examination was normal. Investigations revealed normal Hb and WBC counts. Widal and blood cultures were negative. SGOT was 160(normal up to 40 IU/L), LDH 1335(normal 230-460) CK 283(24-170IU/L). ANA was positive with 25.3 units /mL(more than 10 is positive). ESR was 55 mm at the end of first hour. EMG was normal. Muscle biopsy from gluteus maximus was also normal. But MRI of hip and shoulder girdle muscles showed features suggestive of myositis in adductors of hip, iliopsoas and gluteus maximus(Fig.2).

Since she had significant weakness with swallowing difficulty, methyl prednisolone 30mg/kg/day was administered for three days followed by oral prednisolone 1mg/kg /day. She improved with the treatment and was discharged after a week. On follow up two weeks later she had better muscle power with negative Gower's sign.

Discussion

Dermatomyositis is one of a group of muscle

* Assistant Professor,
** Resident,
*** Professor,
Department of pediatrics, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala.

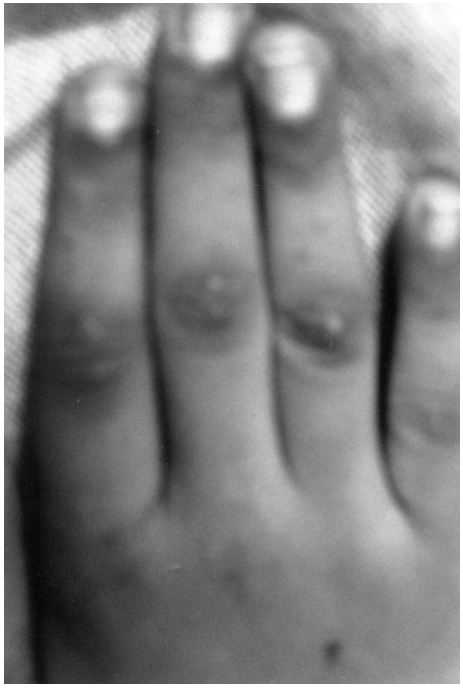


Fig.1. Papules over proximal interphalangeal joints.

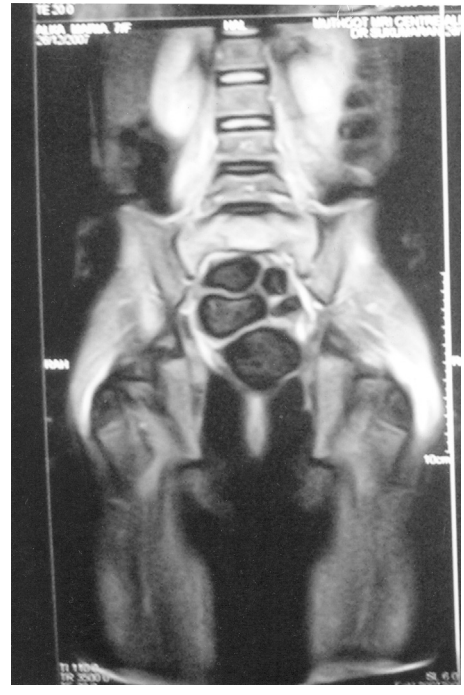


Fig.2. MRI hip showing increased signal intensity of hip girdle muscles suggestive of myositis

diseases known as inflammatory myopathies, which are characterized by chronic muscle inflammation, accompanied by muscle weakness. The cardinal symptom of dermatomyositis is skin rash that precedes or accompanies progressive muscle weakness.[1] Sometimes rash may occur without obvious muscle involvement. Calcinosis can occur about 1-3 years after disease begins.

Criteria for diagnosis of dermatomyositis were put forward by Bohan and Peter.[2] There are five criteria.

1. Symmetric weakness of proximal musculature. 2. Characteristic cutaneous changes consisting of heliotrope discoloration of eyelids with periorbital oedema and an erythematous scaly rash over the dorsal aspects of the metacarpophalangeal and proximal interphalangeal joints (Gottrons papules). 3. Elevation in serum levels of one or more of skeletal muscle enzymes. CK, AST, LDH and aldolase. 4. EMG demonstration of characteristic myopathy and denervation. 5. Muscle biopsy documenting histologic evidence of necrosis and inflammation.

A diagnosis can be made if there is pathognomonic rash and any 2 of the other criteria. MRI clearly demonstrates the extent and focal nature of muscle abnormalities. T2 weighted images correlate with disease activity[3,4] and can be used for monitoring disease activity.[5]

Our patient had typical skin changes with elevated enzymes and characteristic proximal muscle weakness. EMG and muscle biopsy were negative. But negative muscle biopsy does not exclude the diagnosis because this can occur if the specimen taken is inadequate or taken from

muscle tissue, which is relatively spared. Muscle involvement is often spotty and a generous specimen should be obtained for examination.[6] Value of EMG in identifying continuing inflammatory activity of muscle during course of JDM has not been adequately documented.[7,8,9]

MRI findings are not included in the criteria but have been found to be very useful in association with other findings. It also helps in localizing areas of affected muscle for biopsy. In our patient MRI findings were typical of myositis and involved mainly hip girdle muscles.

Points to Remember

- ***Dermatomyositis can present as PUO.***
- ***Thorough physical examination is invaluable in diagnosis.***
- ***MRI is a valuable tool to detect muscle involvement as EMG and muscle biopsy need not be always positive.***
- ***Introduction of steroids has revolutionized treatment of JDM.***

References

1. National Insitute of Neurological Diseases and Stroke. Inflammatory myoathies facts sheets revised. National Institute of Health, US Department of Health and Human Services, Bethesda, Marryland 2007. Publication No.07-5321.
2. Bohan and Peter JB. Polymyosits and dermatomyositis. New Engl J Med 1975;292: 344-403.
3. Hernandez RJ, Keim DR, Sullivan DB, et al: Magnetic resonance imaging appearance of muscles in childhood dermatomyositis. J Pediatr 1990;177:546-550.
4. Keim DR, Hernandez RJ, Sullivan DB: Serial MRI in juvenile dermatomyositis. Arthritis Rheum 1991;34:1580-1584.
5. Cassidy JT, Petty RE. Juvenile dermatomyositis, Textbook of Pediatric Rheumatology 4th edn, Philadelphia, WB Saunders 2001;p489.
6. Cassidy JT, Petty RE: Juvenile dermatomyositis, Textbook of Pediatric Rheumatology 4th edn, Philadelphia, WB Saunders 2001;p488.
7. Smyth DP: Quantitative electromyography in babies and young children with primary muscle disease and neurogenic lesions. J Neurol Sci 1982;56: 199-207.
8. Haridasan G, Sanghvi SH, Jindal GD, et al: Quantitative electromyography using automatic analysis. A comparative study with a fixed fraction of a subject's maximum effort and two levels of thresholds for analysis. J Neurol Sci 1979;42: 53-64.
9. Partanen J,Lang H: EMG dynamics in polymyositis. A quantitative single motor unit potential study. J Neurol Sci 1982;57: 221-234.

NEWS AND NOTES

5th CONFERENCE ON IRON DEFICIENCY
Organised by
Dr.J.C.Patel Medical Research Foundation
at Shanti Sarovar, Hyderabad
on 5 – 7 February, 2010

- Only first 150 out-station delegates would be registered and would be provided free accommodation.
- Local delegates not requiring accommodation will have unrestricted registration.
- Last date for submission of abstracts for free papers is 15/11/09. All accepted abstracts would receive cash awards based on merits. For details visit www.ghrc-bk.org

AUTHOR INDEX

SUBJECT INDEX

"The Second National Assembly on Pediatric Emergency Medicine"

Venue: NIMHANS, Bangalore, Date: April 2nd, 3rd and 4th 2010

The preconference workshop

- Will be held on 2nd April 2009.
- The workshop and the conference aimed at providing details on various aspects of pediatric emergencies.
- Focus will be on issues such as disasters, abuse, transport, triage, and various procedures.

The conference

- will focus on providing protocolised management of conditions such as trauma, sepsis, asthma and seizures.
- Aim will be to reduce hospitalizations and improve outcome.
- This conference has a unique feature of having public participation as an initiative to improve child safety.

Kindly register early as we will have only limited registrations.

Cheque or DD payable to "National Assembly on Pediatric Emergency Medicine"

Registration Fees

Category of delegates	Before January 31st	After February 1st (If vacancy exists)
Conference Regular Delegates	Rs.2500	Rs.3500
Post Graduates	Rs.1500/-	
Workshop Fee	Rs.1000/-	

Address for correspondence:

Dr Gnanam

Manipal Hospital, Pediatric Emergency,

No.98, Rustam Bagh, Airport Road,

Bangalore- 560017

Email- ped.er2010@gmail.com

Phone -91-9379146252

Website-napem.org.in

TRYPEDICON 2010

35th ANNUAL STATE CONFERENCE OF IAP-TNSC

Host : *I. A. P.* Trichy Chapter - Tamil Nadu State

Venue : Hotel Sangam, Trichy. Date : August 13th to 15th 2010

Dr. Sunil Srinivasan	Dr. Pannerselvam	Dr. Suresh Chelliah
Organising Chairman.	Organising Secretary	Treasurer

Registration Fees

Dates	I.A.P (Rs.)	NON I.A.P (Rs.)	P.G (Rs.)	Accompanying Person (Rs)
17.08.09 - 31.12.09	2500	3000	2000	2250
01.01.10 - 30.04.10	3000	3500	2500	2750
01.05.10 - 31.07.10	3500	4000	3000	3250
01.08.10 - 15.08.10	4500	5000	4000	4250

1.Mode of Payment : Cash in Person / Cheque / D.D 2. Senior citizens above 70yrs (as on 15.08.2010) Free(Age proof required) 3. Children below 5yrs (as on 15.08.2010) Free 4.Letter from H.O.D for P.G'S required 5. Delegate Kit Cannot be guaranteed for those registering after 01.08.2010 6. Add Rs 50/- extra for outstation cheques. 7.Detailed Registration form and Accomodation and travel details will follow in first announcement brochure and will also be available in conference website Shortly.

CONTEST FOR CONFERENCE THEME AND LOGO

LAST DATE 31.12.2009. SEPARATE PRIZES WILL BE GIVEN

REGISTRATION FORM

1.TITLE : i) PROF ii) DR iii) MR iv) MRS 2. Name 3. Age 4. sex. 5. I.A.P. Membership No 6. Position 7. Designation 8. Department 9. Non I.A.P Member 10. PG- Student 11. Senior citizen 12. Mailling Address 13. City 14. State 15. PINCode 16. Telephone No: 17. Mobile No. 18. E-mail 19. Fax No 20. Food 21. Registration Fees Amount 22. Names of Accompanying persons. 23.Accomodation

Mode of Payment

Cash ☐ Cheque ☐ DD ☐

in favour of **"TRYPEDICON 2010" PAYABLE at TRICHY.**

Date.....Bank..... Branch .....

Signature

Suggestions are welcome to improve the Performance of the conference

Conference Secretariat

Dr.S.PannerSelvam Organising Secretary - TRYPEDICON 2010 74/C3 Mullai Salai, Annamalai Nagar, Trichy - 620 018. Cell: 94436 - 50515 E.mail: dr.pannerselvam@gmail.com

INDIAN JOURNAL OF PRACTICAL PEDIATRICS

SUBSCRIPTION TARIFF

IJPP

JOURNAL OFFICE
1A, Block II, Krsna Apartments,
50, Halls Road, Egmore,
Chennai 600 008, Tamilnadu, India.
Phone: +91-44-28190032, 42052900.
Email: ijpp_iap@rediffmail.com

Official Journal of the Indian Academy of Pediatrics
A quarterly medical journal committed to practical pediatric problems and management update

Enter Subscription for [ONE] year / [TEN] years

For office use

Ref. No.

Cash / DD for Rs.

DD No.

Receipt No. & Date

Name .....

Address .....

.....

City .....State .....

Pin ..... Phone (R) ..... (O).....

Mobile ..... Email .....

Designation ..... Qualification.....

I am enclosing a DD No. …….. dated …… drawn on ……..…….....

favoring **Indian Journal of Practical Pediatrics** for Rs……

Signature

Subscription rate

Individual	Annual	Rs.400/-
	Ten Years	Rs.4000/-
Institution	Annual	Rs.500/-
	Ten Years	Rs.5000/-
Foreign	Annual	US $ 60/-

Send your subscription, only by crossed demand draft, drawn in favour of **INDIAN JOURNAL OF PRACTICAL PEDIATRICS**, payable at **Chennai** and mail to **Dr. K. NENDUNCHELIAN,** Editor-in-Chief, 1A, Block II, Krsna Apartments, 50, Halls Road, Egmore, Chennai 600 008, Tamilnadu, India.