



INDIAN JOURNAL OF PRACTICAL PEDIATRICS



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

Vol.27 No.2 (APR.- JUN.) 2025

Dr.T.L.Ratnakumari
Editor-in-Chief

Dr.G.Durai Arasan
Executive Editor

CONTENTS

IAP – IJPP CME - 2024

Rational use of antibiotics in neonatal intensive care units 105

Giridhar Sethuraman, Monisha Rameshbabu

Post asphyxial management in level I and II neonatal intensive care units 112

Prakash V, Elayarani Elavarasan

Scarlet fever 122

Balasubramanian S, Vignesh N

Pediatric septic shock – Revisiting key updates 131

Lakshmi Prashanth

Timing of interventions in common congenital heart defects 139

Saileela Rajan

Very early onset inflammatory bowel disease in children 148

Malathi Sathiyasekaran, Ganesh R

Rational anti-seizure medication treatment 158

Lakshminarayanan Kannan

DRUG PROFILE

Plasma-derived therapeutic proteins in pediatrics – part II 165

Jeeson C Unni, Aarthi Ramesh

GENERAL ARTICLE - A CAPSULE

Challenges in interpreting laboratory test results 176

Janani Sankar

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

RADIOLOGY**Radiology - Imaging in gastrointestinal disorders****177**

Vijayalakshmi G, Kasi Visalakshi KP

CASE REPORT**Rowell syndrome with basal ganglia calcification in a child with neuropsychiatric systemic lupus erythematosus****182**

Ananda Kesavan TM, Deepa Anirudhan, Deepthi R

LEARNING TOGETHER**OSCE - Gastroenterology****186**

Thangavelu S, Annamalai Vijayaraghavan

CLIPPINGS**111,130,138,147,157,175,181,185,190****FOR YOUR KIND ATTENTION**

- * The views expressed by the authors do not necessarily reflect those of the sponsor or publisher. Although every care has been taken to ensure technical accuracy, no responsibility is accepted for errors or omissions.
- * The claims of the manufacturers and efficacy of the products advertised in the journal are the responsibility of the advertiser. The journal does not own any responsibility for the guarantee of the products advertised.
- * Part or whole of the material published in this issue may be reproduced with the note "Acknowledgement" to "Indian Journal of Practical Pediatrics" without prior permission.
- * The write up should be in accordance with the recommendations of Central IAP particularly with issues involving National Programmes like Immunization, Public Health Programs and Nutrition.

EDITORIAL BOARD

Published by Dr. T.L.Ratnakumari, Editor-in-Chief, IJPP, on behalf of Indian Academy of Pediatrics, from 1A, Block II, Krsna Apartments, 50, Thamizh Salai (Halls Road), Egmore, Chennai - 600 008. Tamil Nadu, India and Printed by Mr. D.Ramanathan, at Alamu Printing Works, 9, Iyyah Street, Royapettah, Chennai - 600 014.

IAP - IJPP CME - 2024

RATIONAL USE OF ANTIBIOTICS IN NEONATAL INTENSIVE CARE UNITS

***Giridhar Sethuraman**
****Monisha Rameshbabu**

Abstract: Antibiotics are among the most frequently prescribed medications in neonatal intensive care units, often serving as lifesaving interventions in the context of suspected or confirmed sepsis. However, their overuse contributes to serious adverse outcomes such as antimicrobial resistance, disruption of the neonatal microbiome, increased incidence of necrotizing enterocolitis, invasive fungal infections and even mortality. Neonates pose unique challenges for antibiotic therapy due to diagnostic uncertainty, immature organ function affecting pharmacokinetics, and variability in clinical practice. This article outlines a rational framework for antibiotic use in neonates-emphasizing the selection of the right patient, appropriate antibiotic, route, dosage and treatment duration. It discusses the nuances of empirical therapy, the role of biomarkers and organism-specific considerations. The article further highlights antimicrobial stewardship strategies tailored to specific institutions, including prescription audits, formulary restrictions, selective susceptibility reporting, and de-escalation protocols. Adopting these measures is essential for optimizing therapeutic outcomes, minimizing harm and curbing the growing threat of antimicrobial resistance in neonatal care.

Keywords: Antimicrobial stewardship, Infant, Newborn.

Points to Remember

- *Antibiotics are among the most frequently prescribed medications in neonatal intensive care units, often serving as lifesaving interventions.*
- *Rational frame work for antibiotic use in neonates is challenging and one size fits all is a myth.*
- *Antibiotic stewardship strategies are always tailored to every NICU and they have to be adhered to strictly.*
- *Use of unit specific antimicrobial policies are the most useful one and it differs from region to region.*
- *Use of computerized physician order entry (CPOE) systems will help and aid clinical decision making.*

References

1. Laxminarayan R, Bhutta ZA. Antimicrobial resistance-a threat to neonate survival. *Lancet Glob Health*. 2016 Oct; 4(10):e676-7. doi: 10.1016/S2214-109X(16)30221-2. PMID: 27633421.
2. Polin RA, Papile LA, Baley JE, Benitz W, Carlo WA, Cummings J, et al. Management of Neonates with Suspected or Proven Early-Onset Bacterial Sepsis. *Pediatrics*. 2012;129:1006-1015. doi: 10.1542/peds.2012-0541.
3. Puopolo KM, Draper D, Wi S, Newman TB, Zupancic J, Lieberman E, Smith M, Escobar GJ. Estimating the probability of neonatal early-onset infection on the basis of maternal risk factors. *Pediatrics*. 2011 Nov;128(5):e1155-63. doi: 10.1542/peds.2010-3464. Epub 2011 Oct 24. PMID: 22025590; PMCID: PMC3208962.
4. Kaiser Permanente Research : Neonatal early onset sepsis calculator - Probability of Neonatal Early-Onset Sepsis Based on Maternal Risk Factors and the Infant's Clinical Presentation. Available at: <https://neonatalsepsiscalculator.kaiserpermanente.org/InfectionProbabilityCalculator.aspx>) Accessed on : 21st July 2025.

* Professor

email: giridharsethu@gmail.com

** Assistant Professor,

Department of Neonatology,

Chettinad Hospital and Research Institute, Chennai.

5. National Neonatology Forum. Clinical Practice Guidelines: Diagnosis and Management of Neonatal Sepsis. 2021
6. Chiesa C, Natale F, Pascone R, Osborn JF, Pacifico L, Bonci E. C reactive protein and procalcitonin: reference intervals for preterm and term newborns during the early neonatal period. *Clin Chim Acta*. 2011 May 12; 412(11-12):1053-9. doi: 10.1016/j.cca.2011.02.020. Epub 2011 Feb 19. PMID: 21338596.
7. Boscarino G, Romano R, Iotti C, Tegoni F, Perrone S, Esposito S. An Overview of Antibiotic Therapy for Early- and Late-Onset Neonatal Sepsis: Current Strategies and Future Prospects. *Antibiotics (Basel)*. 2024 Mar 10; 13(3):250. doi: 10.3390/antibiotics13030250. PMID: 38534685; PMCID: PMC10967557.
8. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis*. 2016 May 15; 62(10):e51-77. doi: 10.1093/cid/ciw118. Epub 2016 Apr 13. PMID: 27080992; PMCID: PMC5006285.
9. Antimicrobial resistance and antimicrobial stewardship: appropriate and judicious use of antimicrobial agents. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Elk Grove Village, IL: American Academy of Pediatrics; 2018. p. 906-10.
10. Pollack LA, Srinivasan A. Core elements of hospital antibiotic stewardship programs from the Centers for Disease Control and Prevention. *Clin Infect Dis*. 2014 Oct 15; 59 Suppl 3(Suppl 3):S97-100. doi: 10.1093/cid/ciu542. PMID: 25261548; PMCID: PMC6521960.
11. Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: a WHO practical toolkit. *JAC Antimicrob Resist*. 2019 Nov 12;1(3):dlz072. doi: 10.1093/jacamr/dlz072. PMID: 34222945; PMCID: PMC8210188
12. Chandy SJ, Michael JS, Veeraraghavan B, Abraham OC, Bachhav SS, Kshirsagar NA. ICMR programme on Antibiotic Stewardship, Prevention of Infection & Control (ASPIC). *Indian J Med Res*. 2014 Feb; 139(2): 226-30. PMID: 24718396; PMCID: PMC4001333
13. National Neonatology Forum. Clinical Practice Guidelines: Antimicrobial Stewardship in neonates. 2021.
14. Echols RM, Kowalsky SF. The use of an antibiotic order form for antibiotic utilization review: influence on physicians' prescribing patterns. *J Infect Dis*. 1984 Dec;150(6):803-7. doi: 10.1093/infdis/150.6.803. PMID: 6501926.

IAP - IJPP CME - 2024**POST ASPHYXIAL MANAGEMENT IN LEVEL I AND II NEONATAL INTENSIVE CARE UNITS*****Prakash V******Elayarani Elavarasan**

Abstract: Perinatal asphyxia remains a major challenge in developing countries, contributing significantly to neonatal morbidity and mortality. Level I and level II neonatal care units often serve as the first point of contact for affected newborns. It is essential that these units are equipped appropriately with gadgets and personnel to promptly recognize the signs of hypoxic ischemic encephalopathy, stabilize affected neonates and facilitate timely referral to higher centers when necessary. This article focuses on the clinical presentation of neonatal encephalopathy, interventions available and the immediate management protocols for hypoxic-ischemic injury.

Keywords: Perinatal asphyxia, Therapeutic hypothermia, Neonatal seizures.

Points to Remember

- Cord arterial blood gas or any blood gas should be undertaken within one hour of birth in cases of suspected perinatal asphyxia to enable early identification of babies with hypoxic ischemic encephalopathy.
- Neonatal units providing only Level I or II care should avoid using uncontrolled or unmonitored cooling methods, as therapeutic hypothermia requires specialized equipment and trained personnel available in tertiary centers.
- Early referral within 4 hours of birth to a tertiary care centre with facilities for therapeutic hypothermia is advised if baby has moderate or severe asphyxia, ensuring initiation of cooling therapy within the critical 6-hour window.
- In neonates with mild encephalopathy or with suspected perinatal asphyxia, periodic assessment using modified Sarnat and Sarnat staging should be done to monitor progression to moderate encephalopathy.

References

1. World Health Organization. Perinatal mortality: A listing of available information. Geneva: World Health Organization; 1996.
2. National Neonatal Perinatal database NNPD 2002-2023. Indian council of Medical Research, New Delhi. 2005
3. Perin J, Mulick A, Yeung D, Villavicencio F, Lopez G, Strong KL, et al. Global, regional, and national causes of under-5 mortality in 2000-19: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet Child Adolesc Health*. 2022; 6(2):106-115.
4. Krishnan V, Kumar V, Variance GFT, Carlo WA, Bhutta ZA, Sizonenko S, et al. Newborn Brain Society Guidelines and Publications Committee. Need for more evidence in the prevention and management of perinatal asphyxia and neonatal encephalopathy in low and middle-income countries: A call for action. *Semin Fetal Neonatal Med*. 2021; 26(5):101271.

* Head and Clinical Lead,
Department of Neonatology and Pediatrics

** Associate Consultant,
Pediatrics,
Prashanth Superspeciality Hospital, Kolathur.
email: dr_praky76@yahoo.com

5. Ellis M, Manandhar N, Shrestha PS, Shrestha L, Manandhar DS, Costello AM. Outcome at 1 year of neonatal encephalopathy in Kathmandu, Nepal. *Dev Med Child Neurol*. 1999; 41(10):689-95.
6. Armour EA, Curcio AM, Fryer RH. Neonatal Hypoxic Ischemic Encephalopathy: An Updated Preclinical and Clinical Review. *OBM Neurobiol*. 2020; 4(3):1-5.
7. Thayyil S, Oliveira V, Lally PJ, Swamy R, Bassett P, Chandrasekaran M, et al. HELIX Trial group. Hypothermia for encephalopathy in low and middle-income countries (HELIX): study protocol for a randomised controlled trial. *Trials*. 2017; 18(1):432.
8. Schendel D. Executive summary: neonatal encephalopathy and neurologic outcome, Report of the American College of Obstetricians and Gynecologists' task force on neonatal encephalopathy. *ObstetGynecol*. 2014; 123(4):896-901.
9. Davidson JO, Dean JM, Fraser M, Wassink G, Andelius TC, Dhillon SK, et al. Perinatal brain injury: mechanisms and therapeutic approaches. *Front Biosci (Landmark Ed)*. 2018; 23(12):2204-26.
10. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, Donovan EF, et al. National Institute of Child Health and Human Development Neonatal Research Network. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Engl J Med*. 2005; 353(15):1574-84.
11. Laptook A, Tyson J, Shankaran S, McDonald S, Ehrenkranz R, Fanaroff A, et al. National Institute of Child Health and Human Development Neonatal Research Network. Elevated temperature after hypoxic-ischemic encephalopathy: risk factor for adverse outcomes. *Pediatrics*. 2008; 122(3):491-9.
12. Welsford M, Nishiyama C, Shortt C, Isayama T, Dawson JA, Weiner G, et al. International Liaison Committee on Resuscitation Neonatal Life Support Task Force. Room air for Initiating term newborn Resuscitation: A Systematic Review with Meta-analysis. *Pediatrics*. 2019; 143(1):e20181825.
13. Chiruvolu A, Wiswell TE. Appropriate Management of the Nonvigorous Meconium-Stained Newborn Meconium. *Neoreviews*. 2022; 23(4):e250-e261.
14. Malin GL, Morris RK, Khan KS. Strength of association between umbilical cord pH and perinatal and longterm outcomes: systematic review and meta-analysis. *BMJ*. 2010; 340:c1471.
15. Singh Y, Katheria AC, Vora F. Advances in Diagnosis and Management of Hemodynamic Instability in Neonatal Shock. *Front Pediatr*. 2018; 6:2. doi: 10.3389/fped.2018.00002. PMID: 29404312; PMCID: PMC5780410.
16. Tanigasalam V, Plakkal N, Vishnu Bhat B, Chinnakali P. Does fluid restriction improve outcomes in infants with hypoxic ischemic encephalopathy? A pilot randomized controlled trial. *J Perinatol*. 2018; 38(11):1512-17.
17. Pressler RM, Abend NS, Auvin S, Boylan G, Brigo F, Cilio MR et al. Treatment of seizures in the neonate: Guidelines and consensus-based recommendations-Special report from the ILAE Task Force on Neonatal Seizures. *Epilepsia*. 2023; 64(10):2550-70.
18. Young L, Berg M, Soll R. Prophylactic barbiturate use for the prevention of morbidity and mortality following perinatal asphyxia. *Cochrane Database Syst Rev*. 2016; 2016(5):CD001240.
19. Glass HC, Wood TR, Comstock BA, Numis AL, Bonifacio SL, Cornet MC, et al. Predictors of Death or Severe Impairment in Neonates With Hypoxic-Ischemic Encephalopathy. *JAMA Netw Open*. 2024; 7(12):e2449188.

IAP - IJPP CME - 2024**SCARLET FEVER**

***Balasubramanian S**
****Vignesh N**

Abstract: *Scarlet fever is an acute infectious disease caused by toxigenic strains of Streptococcus pyogenes (Group A Streptococcus) characterized by fever, pharyngitis, a sandpaper-like rash and “strawberry tongue.” Historically associated with high morbidity and mortality, scarlet fever is now effectively managed with antibiotics, notably penicillin V or amoxicillin. Recent outbreaks with atypical seasonality and increased mortality highlight the need for continued awareness and surveillance. Diagnosis is primarily clinical, supported by laboratory tests such as rapid antigen detection and throat culture. Management includes prompt antibiotic therapy to reduce transmission and prevent complications, which may be suppurative or immune-mediated. Prevention focuses on early treatment, respiratory hygiene and outbreak control in community settings.*

Keywords: *Scarlet fever, Streptococcus pyogenes, Pharyngitis, Rash, Antibiotic therapy, Rapid antigen detection test.*

Points to Remember

- *Scarlet fever presents with fever, sore throat, a characteristic scarlatiniform rash, and strawberry tongue.*
- *Diagnosis is clinical but can be supported by rapid antigen detection tests and throat cultures.*
- *Molecular PCR assays offer high sensitivity but are not universally available.*
- *Oral penicillin V is the first-line therapy; amoxicillin is preferred in regions where penicillin V is not readily available.*
- *Alternatives exist for penicillin-allergic patients but resistance to macrolides should also be kept in mind.*
- *Complications can be suppurative (e.g., otitis media, abscesses) or nonsuppurative/immune-mediated (e.g., acute rheumatic fever, post-streptococcal glomerulonephritis).*
- *Prompt treatment is the key.*

References

1. Erwin H. Ackerknecht. In 'A short history of Medicine' Chapter 9, page 99. revised edition: 1982 JHU press; Baltimore Maryland. accessed on 5.8.2025. ISBN 0801827264, 9780801827266
2. <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON429>.
3. Meghan B, Erin Y, Jennifer Z, Kayla B, Christopher J Gregory, Samuel R Dominguez et al- MMWR. 'Notes from the Field': Increase in Pediatric invasive Group A Streptococcus infections - Colorado and Minnesota; US Department of Health .../Centers for Disease Control and Prevention MMWR/March 10, 2023 / Vol. 72 / No.10
4. Göte H, Raahave D. Surgical scarlet fever. Ann Chir Gynaecol. 1989; 78(2):153-154.

* Senior Consultant Pediatrician

** Junior Resident - DNB Stream,
Kanchi Kamakoti CHILDS Trust Hospital, Chennai.

5. Metzgar D, Zampolli A. The M protein of group A *Streptococcus* is a key virulence factor and a clinically relevant strain identification marker. *Virulence*. 2011; 2(5):402-412. doi:10.4161/viru.2.5.16342
6. Braun MA, Gerlach D, Hartwig UF, Ozegowski JH, Romagné F, Carrel S, Köhler W, Fleischer B. Stimulation of human T cells by streptococcal “superantigen” erythrogenic toxins (scarlet fever toxins). *J Immunol*. 1993 Mar 15; 150(6):2457-66. PMID: 8450222.
7. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al; Infectious Diseases Society of America. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012 Nov 15;55(10): e 86-102. doi: 10.1093/cid/cis629. Epub 2012 Sep 9. Erratum in: *Clin Infect Dis*. 2014 May; 58(10):1496. Dosage error in article text. PMID: 22965026; PMCID: PMC7108032
8. Chiesa C, Pacifico L, Nanni F, Orefici G. Recurrent attacks of scarlet fever. *Arch Pediatr Adolesc Med*. 1994 Jun;148(6):656-60. doi: 10.1001/archpedi.1994.02170060110024. PMID: 8193698.
9. Balasubramanian S, Amperayani S, Dhanalakshmi K, Senthilnathan S, Chandramohan V. Rapid antigen diagnostic testing for the diagnosis of group A beta-haemolytic streptococci pharyngitis. *Natl Med J India*. 2018 Jan-Feb; 31(1):8-10. doi: 10.4103/0970-258X.243433. PMID: 30348914.
10. Thompson TZ, McMullen AR. Group A *Streptococcus* Testing in Pediatrics: the Move to Point-of-Care Molecular Testing. *J Clin Microbiol*. 2020 May 26; 58(6):e01494-19. doi: 10.1128/JCM.01494-19. PMID: 32161094; PMCID: PMC7269410.
11. Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link K. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making*. 1981;1(3):239-46. doi: 10.1177/0272989X8100100304. PMID: 6763125.
12. McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. *CMAJ*. 1998 Jan 13; 158(1):75-83. PMID: 9475915; PMCID: PMC1228750.
13. Le Marechal F, Martinot A, Duhamel A, Pruvost I, Dubos F. Streptococcal pharyngitis in children: a meta-analysis of clinical decision rules and their clinical variables. *BMJ Open*. 2013 Mar 9; 3(3):e001482. doi: 10.1136/bmjopen-2012-001482. PMID: 23474784; PMCID: PMC3612811.
14. National Heart Foundation NZ. Group A Streptococcal sore throat management guideline: 2019 update: <https://assets.heartfoundation.org.nz/documents/shop/hearthealthcare/non-stock-resources/gas-sore-throat-rheumaticfever-guideline.pdf?1615455698>.
15. Best JM. Rubella. *Semin Fetal Neonatal Med*. 2007 Jun; 12(3):182-92. doi: 10.1016/j.siny.2007.01.017. Epub 2007 Mar 2. PMID: 17337363.
16. Ben Z. Katz and William J. Muller, 2023 *Herpes Viridae: (208) Epstein-Barr Viruses (M...)* Ed. Long SS, in *Principles and practice of pediatric infectious diseases 6th edn.* Elsevier-Philadelphia. ISBN-13:978-0-323-75608-2.
17. Barros Pinto MP. Staphylococcal toxic shock syndrome. *J Hematop*. 2023 Sep; 16(3):189-190. doi: 10.1007/s12308-023-00547-6. Epub 2023 May 11. PMID: 38175396.
18. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al; Infectious Diseases Society of America. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012 Nov 15;55(10): e86-102. doi:10.1093/cid/cis629.
19. Curtin-Wirt C, Casey JR, Murray PC, Cleary CT, Hoeger WJ, Marsocci SM, et al: Efficacy of penicillin vs. amoxicillin in children with group A beta hemolytic streptococcal tonsillopharyngitis. *Clin Pediatr (Phila)*. 2003 Apr; 42(3):219-25. doi: 10.1177/000992280304200305. PMID: 12739920.
20. Pichichero ME. A review of evidence supporting the American Academy of Pediatrics recommendation for prescribing cephalosporin antibiotics for penicillin-allergic patients. *Pediatrics*. 2005 Apr; 115(4):1048-57. doi: 10.1542/peds.2004-1276. PMID: 15805383.
21. Tanz RR, Shulman ST. Chronic pharyngeal carriage of group A streptococci. *Pediatr Infect Dis J*. 2007 Feb;26(2):175-6. doi: 10.1097/01.inf.0000255328.19808.be. PMID: 17259882.
22. Richter SS, Heilmann KP, Beekmann SE, Miller NJ, Miller AL, Rice CL, Doern CD, Reid SD, Doern GV. Macrolide-resistant *Streptococcus pyogenes* in the United States, 2002-2003. *Clin Infect Dis*. 2005 Sep 1;41(5):599-608. doi: 10.1086/432473. PMID: 16080080.
23. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, Martin JM, Van Beneden C. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012 Nov 15;55(10):1279-82. doi: 10.1093/cid/cis847. Erratum in: *Clin Infect Dis*. 2014 May;58(10):1496. Dosage error in article text. PMID: 23091044.

24. Shaikh N, Leonard E, Martin JM. Prevalence of streptococcal pharyngitis and streptococcal carriage in children: a meta-analysis. *Pediatrics*. 2010 Sep;126(3):e557-64. doi: 10.1542/peds.2009-2648. Epub 2010 Aug 9. PMID: 20696723.
25. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, Martin JM, Van Beneden C. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012 Nov 15;55(10):1279-82. doi: 10.1093/cid/cis847. Erratum in: *Clin Infect Dis*. 2014 May; 58(10):1496. Dosage error in article text. PMID: 23091044.
26. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, Martin JM, Van Beneden C; Infectious Diseases Society of America. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012 Nov 15; 55(10):e86-102. doi: 10.1093/cid/cis629. Epub 2012 Sep 9. Erratum in: *Clin Infect Dis*. 2014 May;58(10):1496. Dosage error in article text. PMID: 22965026; PMCID: PMC7108032.
27. Kaplan EL, Top FH Jr, Dudding BA, Wannamaker LW. Diagnosis of streptococcal pharyngitis: differentiation of active infection from the carrier state in the symptomatic child. *J Infect Dis*. 1971 May; 123(5):490-501. doi: 10.1093/infdis/123.5.490. PMID: 5115179.
28. <https://www.cdc.gov/group-a-strep/hcp/clinical-guidance/scarlet-fever.html> / March 2024 , accessed 05.08.2025.
29. Gewitz MH, Baltimore RS, Tani LY, Sable CA, Shulman ST, Carapetis J, et al, American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015 May 19; 131 (20): 1806-18. doi: 10.1161/CIR.0000000000000205. Epub 2015 Apr 23. Erratum in: *Circulation*. 2020 Jul 28;142(4):e65. doi: 10.1161/CIR.0000000000000889. PMID: 25908771.
30. Francisca A, Mark J. Abzug, Anna M. Acosta, Edward P. Acosta, Paula E. Agger, Ibne Karim Ali, et al- Collaborators Group A streptococcal infection ed David W. Kimberlin; in *Red Book: Report of committee on infectious diseases* 32nd Ed., 2021 Itasca, AAP.
31. Dale JB, Penfound TA, Chiang EY, Walton WJ. New 30-valent M protein-based vaccine evokes cross-opsonic antibodies against non-vaccine serotypes of group A streptococci. *Vaccine*. 2011 Oct 26;29(46):8175-8. doi: 10.1016/j.vaccine.2011.09.005. Epub 2011 Sep 13. PMID: 21920403; PMCID: PMC3195966.
32. Rivera-Hernandez T, Carnathan DG, Jones S, Cork AJ, Davies MR, Moyle PM et al. An Experimental Group A Streptococcus Vaccine That Reduces Pharyngitis and Tonsillitis in a Nonhuman Primate Model. *mBio*. 2019 Apr 30;10(2):e00693-19. doi: 10.1128/mBio.00693-19. Erratum in: *mBio*. 2020 Dec 1;11(6):e02995-20. doi: 10.1128/mBio.02995-20. PMID: 31040243; PMCID: PMC6495378.
33. Vekemans J, Gouvea-Reis F, Kim JH, Excler JL, Smeesters PR, O'Brien KL et al. The Path to Group A Streptococcus Vaccines: World Health Organization Research and Development Technology Roadmap and Preferred Product Characteristics. *Clin Infect Dis*. 2019 Aug 16;69(5):877-883. doi: 10.1093/cid/ciy1143. PMID: 30624673; PMCID: PMC6695511.
34. Iyer V, Sagar V, Toor D, Lyngdoh V, Nongrum G, Kapoor M, Chakraborti A. Group A Streptococcus Infections: Their Mechanisms, Epidemiology, and Current Scope of Vaccines. *Cureus*. 2022 Dec 30; 14(12):e33146. doi: 10.7759/cureus.33146. PMID: 36721580; PMCID: PMC9884514.

IAP - IJPP CME - 2024**PEDIATRIC SEPTIC SHOCK -
REVISITING KEY UPDATES*****Lakshmi Prashanth**

Abstract: *Septic shock, a subset of sepsis is characterized by profound circulatory and metabolic abnormalities. The pathophysiology involves complex interactions between the host immune response and pathogens, leading to endothelial dysfunction, vasoplegia, relative hypovolemia and myocardial depression. Management strategies include fluid resuscitation, vasopressor support and early antibiotic therapy. Recent years have seen significant updates in the definition, recognition and management of pediatric septic shock. Current emphasis is on early recognition, fluid-sparing resuscitation strategies, early institution of norepinephrine and individualized care (rather than a “one-glove-fits-all” approach). The Phoenix sepsis score, a novel score that identifies life threatening organ dysfunction, is a promising tool for risk stratification.*

Keywords: *Septic shock, Vasoplegia, Myocardial dysfunction, Fluid resuscitation, Vasoactives, Nor-epinephrine, Phoenix sepsis score.*

Points to Remember

- *Septic shock in children is a complex syndrome involving relative hypovolemia, vasoplegia and myocardial dysfunction.*
- *Early recognition using clinical markers and age-specific vital signs is essential.*
- *The three pillars of hemodynamic support are fluids, vasopressors and inotropes.*
- *Management has shifted from aggressive fluid resuscitation to restrictive, individualized fluid therapy combined with early vasoactive support, primarily norepinephrine.*
- *Resuscitation endpoints include adequate cardiac output, MAP/DBP for organ perfusion and avoidance of congestion.*
- *The Phoenix Sepsis Score offers a practical tool for risk stratification.*

References

1. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of pediatric and neonatal sepsis: a systematic review. *Lancet Respir Med.* 2018 Mar; 6(3):223-230.
2. Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, Inwald DP, et al. Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. *Pediatr Crit Care Med.* 2020 Feb; 21(2):e52-e106.
3. Schlapbach LJ, Watson RS, Sorce LR, Argent AC, Menon K, Hall MW, et al. Society of Critical Care Medicine Pediatric Sepsis Definition Task Force. International Consensus Criteria for Pediatric Sepsis and Septic Shock. *JAMA.* 2024 Feb 27; 331(8):665-674.
4. Ranjit S, Natraj R. Hemodynamic Management Strategies in Pediatric Septic Shock: Ten Concepts for

* Senior Consultant Pediatrician,
Kauvery Hospital and PICU In Charge,
St Isabels Hospital,
Chennai.
email: laks.med@gmail.com

- the Bedside Practitioner. *Indian Pediatr.* 2024 Mar 15; 61(3):265-275.
5. Ranjit S, Kissoon N, Argent A, Inwald D, Ventura AMC, Jaborinsky R, et al. Haemodynamic support for pediatric septic shock: a global perspective. *Lancet Child Adolesc Health.* 2023 Aug; 7(8):588-598.
 6. Ranjit S, Aram G, Kissoon N, Ali MK, Natraj R, Shresti S, et al. Multimodal monitoring for hemodynamic categorization and management of pediatric septic shock: a pilot observational study. *Pediatr Crit Care Med.* 2014 Jan; 15(1):e17-26.
 7. Sanfilippo F, La Rosa V, Grasso C, Santonocito C, Minardi C, Oliveri F, et al. Echocardiographic Parameters and Mortality in Pediatric Sepsis: A Systematic Review and Meta-Analysis. *Pediatr Crit Care Med.* 2021 Mar 1; 22(3):251-261.
 8. Byrne L, Obonyo NG, Diab SD, Dunster KR, Passmore MR, Boon AC, et al. Unintended Consequences: Fluid Resuscitation Worsens Shock in an Ovine Model of Endotoxemia. *Am J Respir Crit Care Med.* 2018 Oct 15; 198(8):1043-1054.
 9. Hippensteel JA, Uchimido R, Tyler PD, Burke RC, Han X, Zhang F, et al. Intravenous fluid resuscitation is associated with septic endothelial glycocalyx degradation. *Crit Care.* 2019 Jul 23; 23(1):259.
 10. Perner A, Cecconi M, Cronhjort M, Darmon M, Jakob SM, Pettilä V, et al. Expert statement for the management of hypovolemia in sepsis. *Intensive Care Med.* 2018 Jun; 44(6):791-798.
 11. Duff JP, Topjian AA, Berg MD, Chan M, Haskell SE, Joyner BL Jr, et al. 2019 American Heart Association Focused Update on Pediatric Advanced Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2019 Dec 10; 140(24):e904-e914.
 12. Scott HF, Brou L, Deakyne SJ, Fairclough DL, Kempe A, Bajaj L. Lactate Clearance and Normalization and Prolonged Organ Dysfunction in Pediatric Sepsis. *J Pediatr.* 2016 Mar; 170:149-55.e1-4.
 13. Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO, et al. FEAST Trial Group. Mortality after fluid bolus in African children with severe infection. *N Engl J Med.* 2011 Jun 30; 364(26):2483-95.
 14. Sankar J, Das RR, Banothu KK. Fluid resuscitation in children with severe infection and septic shock: a systematic review and meta-analysis. *Eur J Pediatr.* 2024 Sep; 183(9):3925-3932.
 15. Ranjit S, Natraj R, Kandath SK, Kissoon N, Ramakrishnan B, Marik PE. Early norepinephrine decreases fluid and ventilatory requirements in pediatric vasodilatory septic shock. *Indian J Crit Care Med.* 2016 Oct; 20(10):561-569.
 16. Owen VS, Rosgen BK, Cherak SJ, Ferland A, Stelfox HT, Fiest KM, et al. Adverse events associated with administration of vasopressor medications through a peripheral intravenous catheter: a systematic review and meta-analysis. *Crit Care.* 2021 Apr 16; 25(1):146.
 17. Paul R, Melendez E, Wathen B, Larsen G, Chapman L, Wheeler DS, et al. A Quality Improvement Collaborative for Pediatric Sepsis: Lessons Learned. *Pediatr Qual Saf.* 2017 Dec 29; 3(1):e 051.

IAP - IJPP CME - 2024

TIMING OF INTERVENTIONS IN COMMON CONGENITAL HEART DEFECTS*** Saileela Rajan**

Abstract: Congenital heart defects are the most common amongst birth anomalies. Timely intervention can prevent complications and reduce the mortality associated with these defects. This article discusses the timing of intervention for common congenital heart defects and is largely based on the Indian guidelines proposed by the working group on the management of congenital heart diseases.

Keywords: Congenital heart defects, Timing of intervention, Surgery, Device closure.

Points to Remember

- *Early diagnosis and timely intervention improve survival and quality of life in children with congenital heart defects.*
- *Weight of the child is not a criterion to plan the timing of intervention.*
- *Spontaneous closure is not seen in large left to right shunts.*
- *There is no role for pharmacological closure (ibuprofen/indomethacin) in term neonates with PDA.*

References

1. Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. J Pediatr. 2008; 153(6):807-13.doi: 10.1016/j.jpeds.2008.05.059.
2. Hoffman JI. The global burden of congenital heart disease. Cardiovasc J Afr. 2013; 24:141-5.doi: 10.5830/CVJA-2013-028.
3. Saxena A, Relan J, Agarwal R, Awasthy N, Azad S, Chakrabarty M et al. Indian guidelines for indications and timing of intervention for common congenital heart diseases: Revised and updated consensus statement of the Working group on management of congenital heart diseases. Ann Pediatr Cardiol. 2019; 12(3):254-286. doi: 10.4103/apc.APC_32_19.
4. Ritu Sachdeva Chapter: Atrial Septal Defects; in Moss and Adams' Heart Disease in Infants, Children and Adolescents.....Allen HD, Shaddy RE, Penny DJ, Feltes TF, Cetta F. ..9th ed Wolters Kluwer, 2016. pp 739-756.©
5. Cohen MS, Lopez L. Ventricular Septal Defects. In: Allen HD, Shaddy RE, Penny DJ, Feltes TF, Cetta F. Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult. 9th ed. Philadelphia: Wolters Kluwer; 2016; pp 784-798.

* Consultant Pediatric Cardiologist,
MIOT Centre for Children's Cardiac Care,
MIOT Hospital,
Chennai.
email: drsaileelarajan@gmail.com

6. Keith JD, Rose V, Collins G, Kidd BS. Ventricular septal defect. Incidence, morbidity, and mortality in various age groups. *Br Heart J* 1971; 33Suppl:817. doi: 10.1136/hrt.33.suppl.81.
7. Corone P, Doyon F, Gaudeau S, Guerin F, Vernant P, Ducam H, et al. Natural history of ventricular septal defect. A study involving 790 cases. *Circulation* 1977;55:908-15. doi: 10.1161/01.cir.55.6.908.
8. Fyler DC. Endocardial cushion defect: report of the New England Regional Infant Cardiac Program. *J Pediatr* 1980; 65:441-444.
9. Beekman RH. Coarctation of the aorta. In: Allen HD, Shaddy RE, Penny DJ, Feltes TF, Cetta F. Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult. 9th ed. Philadelphia: Wolters Kluwer; 2016. p 1107.
10. Bertranou EG, Blackstone EH, Hazelrig JB, Turner ME, Kirklin JW. Life expectancy without surgery in tetralogy of Fallot. *Am J Cardiol*. 1978; 42(3):458-66. doi: 10.1016/0002-9149(78)90941-4.

IAP - IJPP CME - 2024

VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE IN CHILDREN

*** Malathi Sathiyasekaran**
**** Ganesh R**

Abstract: *Very early onset inflammatory bowel disease, defined as inflammatory bowel disease with onset before 6 years of age, represents a distinct and increasingly recognized subset of pediatric inflammatory bowel disease. While sharing some phenotypic similarities with later-onset disease, very early onset inflammatory bowel disease often presents with unique challenges in diagnosis, pathogenesis, and management. This review aims to provide an overview of the current understanding of very early onset inflammatory bowel disease, highlighting its clinical characteristics, underlying myriad genetic etiologies, diagnostic approaches and therapeutic strategies.*

Keywords: *Very early onset inflammatory bowel disease, Children, Genetics, Biologicals.*

Points to Remember

- *Very early onset inflammatory disease (VEO-IBD) occurs in children younger than 6 years old.*
- *The causes of VEO-IBD can be varied and may involve a combination of genetics, the immune system and environmental factors. In some cases, there may be an underlying monogenic etiology or primary immune deficiency. Genetic testing is important for diagnosis.*
- *Early detection is crucial to ensure children receive timely treatment to manage inflammation, promote healthy growth and development and prevent complications.*
- *Children with IBD may experience extra-intestinal manifestations such as joint pain, eye inflammation, skin problems and mouth ulcers. In VEO-IBD, monitoring for growth failure and delayed puberty is particularly important.*
- *Psychological support is an important aspect of care, as children with VEO-IBD and their families may face challenges in coping with a chronic illness, managing medications and navigating school and social activities.*

PS : *All standard abbreviations of gene related locations and receptors are left as such for the users to refer to text books.*

References

1. Huang JG, Aw MM. Pediatric Inflammatory Bowel Disease in Asia: Epidemiology and natural history. *Pediatr Neonatol.* 2020 Jun; 61(3):263-271.
2. Kelsen JR, Sullivan KE, Rabizadeh S, Singh N, Snapper S, Elkadri A, et al. North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Position Paper on the Evaluation and Management for

* Senior Consultant,
Pediatric Gastroenterologist

** Senior Consultant and Head,
Department of Pediatrics,
Rainbow Children's Hospital,
Chennai.
email : mal.bwcs@gmail.com

- Patients With Very Early-onset Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr.* 2020 Mar; 70(3):389-403.
3. Ouahed J, Spencer E, Kotlarz D, Shouval DS, Kowalik M, Peng K, et al. Very Early Onset Inflammatory Bowel Disease: A Clinical Approach With a Focus on the Role of Genetics and Underlying Immune Deficiencies. *Inflamm Bowel Dis.* 2020 May 12; 26(6): 820-842.
 4. Kuenzig ME, Fung SG, Marderfeld L, Mak JWY, Kaplan GG, Ng SC, et al. Insight Scope Pediatric IBD Epidemiology Group; Benchimol EI. Twenty-first Century Trends in the Global Epidemiology of Pediatric-Onset Inflammatory Bowel Disease: Systematic Review. *Gastroenterology.* 2022 Apr; 162(4):1147-1159.e4.
 5. Uhlig HH, Schwerd T, Koletzko S, Shah N, Kammermeier J, Elkadri A, et al. COLORS in IBD Study Group and NEOPICS. The diagnostic approach to monogenic very early onset inflammatory bowel disease. *Gastroenterology.* 2014 Nov; 147(5):990-1007.e3.
 6. Srivastava A, Sathiyasekharan M, Jagadisan B, Bolia R, Peethambaran M, Mammayil G, et al. Pediatric inflammatory bowel disease in India: a prospective multicentre study. *Eur J Gastroenterol Hepatol.* 2020 Oct; 32(10):1305-1311.
 7. Poddar U, Aggarwal A, Jayalakshmi K, Sarma MS, Srivastava A, Rawat A, et al. Higher Prevalence of Monogenic Cause Among Very Early Onset Inflammatory Bowel Disease in Children: Experience From a Tertiary Care Center From Northern India. *Inflamm Bowel Dis.* 2023 Oct 3; 29(10):1572-1578.
 8. Huang JG, Wong YKY, Chew KS, Tanpowpong P, Calixto Mercado KS, Reodica A, et al. Epidemiological characteristics of Asian children with inflammatory bowel disease at diagnosis: Insights from an Asian-Pacific multi-centre registry network. *World J Gastroenterol.* 2022 May 7; 28(17):1830-1844.
 9. Hall CHT, de Zoeten EF. Understanding very early onset inflammatory bowel disease (VEOIBD) in relation to inborn errors of immunity. *Immunol Rev.* 2024 Mar; 322(1):329-338.
 10. Crowley E, Muise A. Inflammatory Bowel Disease: What Very Early Onset Disease Teaches Us. *Gastroenterol Clin North Am.* 2018 Dec; 47(4):755-772.
 11. Li QQ, Zhang HH, Dai SX. New Insights and Advances in Pathogenesis and Treatment of Very Early Onset Inflammatory Bowel Disease. *Front Pediatr.* 2022 Mar 1;10:714054.
 12. Nambu R, Muise AM. Advanced Understanding of Monogenic Inflammatory Bowel Disease. *Front Pediatr.* 2021 Jan 22; 8:618918.
 13. Blaydon DC, Biancheri P, Di WL, Plagnol V, Cabral RM, Brooke MA, et al. Inflammatory skin and bowel disease linked to ADAM17 deletion. *N Engl J Med.* 2011 Oct 20; 365(16):1502-8.
 14. Fiskerstrand T, Arshad N, Haukanes BI, Tronstad RR, Pham KD, Johansson S, et al. Familial diarrhea syndrome caused by an activating GUCY2C mutation. *N Engl J Med.* 2012 Apr 26; 366(17):1586-95.
 15. Marks DJ, Miyagi K, Rahman FZ, Novelli M, Bloom SL, Segal AW. Inflammatory bowel disease in CGD reproduces the clinicopathological features of Crohn's disease. *Am J Gastroenterol.* 2009 Jan;104(1): 117-24.
 16. Zhu L, Shi T, Zhong C, Wang Y, Chang M, Liu X. IL-10 and IL-10 Receptor Mutations in Very Early Onset Inflammatory Bowel Disease. *Gastroenterology Res.* 2017 Apr; 10(2):65-69.
 17. Ganesh R, Sathiyasekeran M, Srinivas S, Narayanan RK. Clinical Spectrum of Monogenic Infantile-Onset Inflammatory Bowel Disease. *Indian J Pediatr.* 2022 May; 89(5):497-502.
 18. Pedersen J, LaCasse EC, Seidelin JB, Coskun M, Nielsen OH. Inhibitors of apoptosis (IAPs) regulate intestinal immunity and inflammatory bowel disease (IBD) inflammation. *Trends Mol Med.* 2014 Nov; 20(11):652-65.
 19. Nameirakpam J, Rikhi R, Rawat SS, Sharma J, Suri D. Genetics on early onset inflammatory bowel disease: An update. *Genes Dis.* 2019 Oct 15; 7(1):93-106.
 20. Zheng HB, de la Morena MT, Suskind DL. The Growing Need to Understand Very Early Onset Inflammatory Bowel Disease. *Front Immunol.* 2021 May 26;12: 675186.

IAP - IJPP CME - 2024**RATIONAL ANTI-SEIZURE MEDICATION TREATMENT*****Lakshminarayanan Kannan**

Abstract: *Pediatricians and neurologists often face challenges when managing children with epilepsy, including issues such as delayed initiation of treatment, medication non-adherence, social stigma, drug resistance and adverse effects related to treatment. Additionally, behavioral and cognitive co-morbidities are common in children with epilepsy. Understanding different types of epilepsy, and selecting appropriate medications tailored to each type is crucial for effective management. A systematic approach that includes understanding the unique characteristics of each patient's epilepsy, maintaining open communication, ensuring close follow-up, and timely referral to specialist care can help address these challenges effectively.*

Keywords: *Drug-resistant epilepsy, Childhood epilepsy, Antiseizure medication, Polytherapy.*

Points to Remember

- *A “one-size-fits-all” approach is ineffective in treating epilepsy; treatment should be individualized.*
- *Treatment should focus on the patient's clinical condition, not just EEG or MRI reports.*
- *Accurately identifying the seizure and epilepsy type is essential for selecting the appropriate first-line anti-seizure medication.*
- *Polytherapy is considered only when monotherapy options have been fully exhausted.*
- *A systematic approach to treatment yields better outcomes in epilepsy management.*

References

1. Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med.* 2000; 342:314-319.
2. Chen Z, Brodie MJ, Liew D, Kwan P. Treatment Outcomes in Patients With Newly Diagnosed Epilepsy Treated With Established and New Antiepileptic Drugs: A 30-Year Longitudinal Cohort Study. *JAMA Neurol.* 2018; 75:279-286.
3. Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Hauser WA, Mathern G, et al. Definition of drug resistant epilepsy: Consensus proposal by the International League Against Epilepsy (ILAE) and International Bureau for Epilepsy (IBE). *Epilepsia.* 2010; 51:1069-1077.
4. Symonds JD, Elliott KS, Shetty J, Armstrong M, Brunklaus A, Cutcutache I, et al. Early childhood epilepsies: epidemiology, classification, aetiology and socio-economic determinants. *Brain.* 2021; 144:2879-2891.
5. Piero Perucca, Melanie Bahlo, Samuel F Berkovic. *Annurev - genom* 2017; 40: 129-146 PMID: 32339036. doi: 10.1146/annurev-genom-120219-074937.

* Senior Consultant Pediatric Neurologist and Epileptologist,
Gleneagles Hospitals, Chennai.
email: drklnaiims@gmail.com

6. Chung WK, Wensel T, Dubeau F, et al. Genetic and structural contributions to the development of drug-resistant epilepsy in children: A retrospective study. *Epilepsia*. 2011; 52:1447-1456.
7. Srikumar G, Bhatia M, Jain S, Maheshwari M. Usefulness of short term video-EEG monitoring in children with frequent intractable episodes. *Neurol India*. 2000; 48: 29-32.
8. Montenegro MA, Sproule D, Mandel A, Cappell J, Chiriboga CA, Jacob S, et al. The frequency of non-epileptic spells in children: Results of video-EEG monitoring in a tertiary care center. *Seizure*. 2008; 17:583-587.
9. Riquet A, Lamblin M-D, Bastos M, Bulteau C, Derambure P, Valleet L, et al. Usefulness of video-EEG monitoring in children. *Seizure*. 2011; 20:18-22.
10. Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. *Epilepsia*. 2017; 58(4):522-530.
11. Specchio N, Wirrell EC, Scheffer IE, Nabbout R, Riney K, Samia P, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: Position paper by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022; 63:1398-1442.
12. Matricardi S, Scorrano G, Prezioso G, Burchiani B, Di Cara G, Striano P, et al. The latest advances in the pharmacological management of focal epilepsies in children: a narrative review. *Expert Rev Neurother*. 2024; 24:371-381.
13. Patsalos PN. Drug interactions with the newer antiepileptic drugs (AEDs)-part 1: pharmacokinetic and pharmacodynamic interactions between AEDs. *Clin Pharmacokinet*. 2013; 52:927-66.
14. Gambardella A, Labate A, Mumoli L, Lopes-Cendes I, Cendes F. Role of Pharmacogenomics in Antiepileptic Drug Therapy: Current Status and Future Perspectives. *Curr Pharm Des*. 2017; 23:5760-5765.
15. Guerrini R, Zaccara G, la Marca G, Rosati A. Safety and tolerability of antiepileptic drug treatment in children with epilepsy. *Drug Saf*. 2012 Jul 1;35(7):519-33.
16. Kumar S, Sarangi SC, Tripathi M, Gupta YK. Evaluation of adverse drug reaction profile of antiepileptic drugs in persons with epilepsy: A cross-sectional study. *Epilepsy Behav*. 2020 ; 105:106947.
17. Striano P, Minassian BA. From Genetic Testing to Precision Medicine in Epilepsy. *Neurotherapeutics*. 2020; 17:609-615.
18. Talwar A, Estes E, Aparasu R, Reddy DS. Clinical efficacy and safety of cannabidiol for pediatric refractory epilepsy indications: A systematic review and meta-analysis. *Exp Neurol*. 2023; 359:114238.
19. Wirrell EC, Lagae L, Scheffer IE, Cross JH, Specchio N, Strzelczyk A. Practical considerations for the use of fenfluramine to manage patients with Dravet syndrome or Lennox-Gastaut syndrome in clinical practice. *Epilepsia Open*. 2024; 9:1643-1657.
20. Sourbron J, Klinkenberg S, van Kuijk SMJ, Lagae L, Lambrechts D, Braakmanet HMM, et al. Ketogenic diet for the treatment of pediatric epilepsy: review and meta-analysis. *Childs Nerv Syst*. 2020; 36:1099-1109.
21. Ali I, Houck K. Neuromodulation in Pediatric Epilepsy. *Neurol Clin*. 2021; 39:797-810.
22. Li H, Ji S, Dong B, Chen L. Seizure control after epilepsy surgery in early childhood: A systematic review and meta-analysis. *Epilepsy Behav*. 2021; 125:108369.

DRUG PROFILE**PLASMA-DERIVED THERAPEUTIC PROTEINS IN PEDIATRICS - PART II**

*** Jeeson C Unni**
**** Aarthi Ramesh**

Abstract: *Part II of the deliberations on PDTP therapies will deal with issues related to the less commonly used products including thrombin for local hemostasis, Von Willebrand factor for treatment of Von Willebrand disease and antithrombin for acquired antithrombin deficiency associated with major cardiac surgery, also, alpha-1 antitrypsin for alpha-1 antitrypsin deficiency, C1 esterase inhibitor concentrate for hereditary angioedema or C1 esterase deficiency and fibrinogen concentrate for the management of congenital fibrinogen deficiency.*

Keywords: *Thrombin, Von Willebrand factor, Antithrombin, Alpha-1 antitrypsin, C1 esterase inhibitor concentrate, Fibrinogen concentrate.*

Points to remember

- *Plasma-derived therapies, including those for rare diseases, are being used in clinical practice and pediatricians need to be updated.*
- *With advances in Recombinant DNA technology, plasma-derived products remain vital and play a significant role in improving patient outcomes.*
- *Emphasis must be made to ensure that these therapies are available, despite challenges in supply.*
- *Continuous research and development is required to explore new fractionation processes and improve quality control measures.*
- *To enhance effectiveness of PDTPs.*
- *Population suffering from rare coagulation disorders with PDTP / rare orphan diseases, have treatment options however limited in supply.*

References

1. Brister SJ, Ofosu FA, Buchanan MR. Thrombin: its key role in thrombogenesis: implications for its inhibition clinically. Boca Raton, FL: CRC Press; 1994
2. Ham SW, Lew WK, Weaver FA. Thrombin use in surgery: an evidence-based review of its clinical use. J Blood Med. 2010; 1:135-42. doi: 10.2147/JBM.S6622. Epub 2010 Jul 22. Retraction in: J Blood Med. 2022 Mar 21;13:165-166. doi: 10.2147/JBM.S366691. PMID: 22282693; PMCID: PMC3262329.
3. Lawson JH. The clinical use and immunologic impact of thrombin in surgery. Semin Thromb Hemost. 2006 Apr; 32(Suppl 1):98-110. doi: 10.1055/s-2006-939559.
4. Patterson C, Stouffer GA, Madamanchi N, Runge MS. New tricks for old dogs: nonthrombotic effects of thrombin in vessel wall biology. Circ Res. 2001; 88(10): 987-997. doi: 10.1161/hh1001.091447

* Editor-in-Chief,
IAP Drug Formulary,
Senior Lead consultant

** Specialist,
Department of Pediatrics and Neonatology,
Aster Med City,
Kochi.
email: jeeson1955@gmail.com

5. Dahlback B. Blood coagulation. *Lancet*. 2000; 355 (9215):1627-1632. doi: 10.1016/S0140-6736(00)02225-X
6. Flaherty MJ, Henderson R, Wener MH. Iatrogenic immunization with bovine thrombin: a mechanism for prolonged thrombin times after surgery. *Ann Intern Med*. 1989;111(8):631-634. doi: 10.7326/0003-4819-111-8-631.
7. Zehnder JL, Leung LL. Development of antibodies to thrombin and factor V with recurrent bleeding in a patient exposed to topical bovine thrombin. *Blood*. 1990; 76(10): 2011-2016
8. Lawson JH, Pennell BJ, Olson JD, Mann KG. Isolation and characterization of an acquired antithrombin antibody. *Blood*. 1990; 76(11):2249-2257
9. Rapaport SI, Zivelin A, Minow RA, Hunter CS, Donnelly K. Clinical significance of antibodies to bovine and human thrombin and factor V after surgical use of bovine thrombin. *Am J Clin Pathol*. 1992; 97(1):84-91. doi: 10.1093/ajcp/97.1.84.
10. US Food and Drug Administration FDA Approves Human Thrombin for Topical Use in Surgery FDA News. Aug 28, 2007. Available at <https://www.fda.gov/media/71754/download>. Accessed on 17/5/25
11. Doria C, Fischer CP, Wood CG, et al. Phase 3, randomized, double-blind study of plasma-derived human thrombin versus bovine thrombin in achieving hemostasis in patients undergoing surgery. *Curr Med Res Opin*. 2008; 24(3):785-794. doi: 10.1185/030079908X273426
12. FDA-RECOTHROM Product Approval Information. Available at: <http://www.fda.gov/Biologics/BloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/ucm089451.htm>. Available at <https://www.fda.gov/media/75321/download>. Accessed on 17/5/25.
13. US Food and Drug Administration FDA News. Jan 17, 2008. Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116838.htm>. Available at: https://www.upi.com/Science_News/2008/01/17/FDA-OKs-novel-surgical-clotting-solution/90481200600937/ Accessed on 17/5/25
14. Chapman WC, Lockstadt H, Singla N, Kafie FE, Lawson JH. Phase 2, randomized, double-blind, placebo-controlled, multicenter clinical evaluation of recombinant human thrombin in multiple surgical indications. *J Thromb Haemost*. 2006; 4(9):2083-2085. doi: 10.1111/j.1538-7836.2006.02067.x.
15. Zhu H, Hoppensteadt D, Adiguzal C, Jeske W, Messmore H, Fareed J. Cross Reactivity of Human Recombinant thrombin (Recothrombin) to Antibovine Thrombin Antibodies. Clinical Implications. *FASEB J*. 2009 Apr 1; 23:569, 511. 1 MeetingAbstracts.
16. Singla NK, Ballard JL, Moneta G, Randleman CD, Jr, Renkens KL, Alexander WA. A phase 3b, open-label, single-group immunogenicity and safety study of topical recombinant thrombin in surgical hemostasis. *J Am Coll Surg*. 2009; 209(1):68-74. doi: 10.1016/j.jamcollsurg.2009.03.016.
17. King Pharmaceuticals Inc Prescribing information: Thrombin-JMI, 2007.
18. Sabel M, Stummer W. The use of local agents: Surgicel and Surgifoam. *Eur Spine J*. 2004; 13(Suppl 1):S97-S101. doi: 10.1007/s00586-004-0735-z.
19. Schwartz M, Madariaga J, Hirose R, et al. Comparison of a new fibrin sealant with standard topical hemostatic agents. *Arch Surg*. 2004; 139(11):1148-1154. doi: 10.1001/archsurg.139.11.1148
20. Glickman M, Gheissari A, Money S, Martin J, Ballard JL. A polymeric sealant inhibits anastomotic suture hole bleeding more rapidly than gelfoam/thrombin: results of a randomized controlled trial. *Arch Surg*. 2002; 137(3):326-331. doi: 10.1001/archsurg.137.3.326. discussion 332
21. Taylor LM, Jr, Mueller-Velten G, Koslow A, Hunter G, Naslund T, Kline R. Prospective randomized multicenter trial of fibrin sealant versus thrombin-soaked gelatin sponge for suture- or needle-hole bleeding from polytetrafluoroethylene femoral artery grafts. *J Vasc Surg*. 2003; 38(4):766-771. doi: 10.1016/s0741-5214(03)00474-9.
22. Casari C, Berrou E, Lebreton M, et al. von Willebrand factor mutation promotes thrombocytopenia by inhibiting integrin α IIb β 3. *J Clin Invest*. 2013; 123(12):5071-5081. doi: 10.1172/JCI69458.
23. Castaman G, Goodeve A, Eikenboom J. Principles of care for diagnosis and treatment of von Willebrand disease. *Haematologica*. 2013; 98(5):667-674. doi: 10.3324/haematol.2012.077263
24. Rodeghiero F, Castaman G, Tosetto A. How I treat von Willebrand disease. *Blood*. 2009; 114(6):1158-1165. doi: 10.1182/blood-2009-01-153296
25. Castaman G, Lethagen S, Federici AB, et al. Response to desmopressin is influenced by the genotype and the phenotype in type 1 von Willebrand disease (VWD): results from the European study MCMDM-1 VWD. *Blood*. 2008; 111:3531-3539. doi: 10.1182/blood-2007-08-109231
26. Mannucci PM, Chediak J, Hanna W, Byrnes J, Marlies L, Ewenstein BM, Alphanate Study Group Treatment of von Willebrand disease with high-purity factor VIII/von Willebrand factor concentrate: a prospective, multicenter study. *Blood*. 2002; 99:450-456. doi: 10.1182/blood.v99.2.450

27. Mannucci PM, Kempton C, Millar C, et al. Pharmacokinetics and safety of a novel recombinant human von Willebrand factor manufactured with a plasma-free method: a prospective clinical trial. *Blood*. 2013;122(5):648-657. doi: 10.1182/blood-2013-01-479527
28. Gill JC, Castaman G, Windyga J, et al. Hemostatic efficacy, safety, and pharmacokinetics of a recombinant von Willebrand factor in severe von Willebrand disease. *Blood*. 2015; 126(17):2038-2046. doi: 10.1182/blood-2015-02-629873.
29. Natalie Smith, Beth Boulden Warren, Julie Smith, Linda Jacobson, Jennifer Armstrong, Jihye Kim, Jorge Di Paola, Marilyn Manco-Johnson, Antithrombin deficiency: A pediatric disorder, *Thrombosis Research*, Volume 202, 2021, Pages 45-51, ISSN 0049-3848
30. ATryn for Injections: U.S Package Insert. Framingham, MA: GTC Biotherapeutics, Inc.; 2010. Nov.
31. U.S. Food and Drug Administration. Cumulative List of Orphan Products Designations and Approvals. [Accessed May 22,2013];1999.
32. U.S. Food and Drug Administration. Approval Letter-ATryn. [Accessed May 22, 2013]; 2009 Feb 6; Available at: <http://www.fda.gov/Biologics Blood Vaccines/Blood Blood Products/ApprovedProducts/Licensed Products BLAs/Fractionated Plasma Products/ucm134046.htm>.
33. Bassler D, Millar D, Schmidt B. Antithrombin for respiratory distress syndrome in preterm infants. *Cochrane Database Syst Rev*. 2006 Oct 18; 2006(4): CD005383. doi: 10.1002/14651858.CD005383.pub2. PMID: 17054254; PMCID: PMC8885308.
34. Chapman KR, Burdon JG, Piitulainen E, Sandhaus RA, Seersholm N, Stocks JM, Stoel BC, Huang L, Yao Z, Edelman JM, et al.; RAPID Trial Study Group. Intravenous augmentation treatment and lung density in severe α 1 antitrypsin deficiency (RAPID): a randomised, double-blind, placebo-controlled trial. *Lancet* 2015; 386:360-368.
35. Hubbard RC, McElvaney NG, Sellers SE, Healy JT, Czerski DB, Crystal RG. Recombinant DNA-produced alpha 1-antitrypsin administered by aerosol augments lower respiratory tract antineutrophil elastase defenses in individuals with alpha 1-antitrypsin deficiency. *J Clin Invest* 1989; 84:1349-1354.
36. Hubbard RC, Brantly ML, Sellers SE, Mitchell ME, Crystal RG. Anti-neutrophil-elastase defenses of the lower respiratory tract in alpha 1-antitrypsin deficiency directly augmented with an aerosol of alpha 1-antitrypsin. *Ann Intern Med* 1989; 111:206-212.
37. Strauss P, Stolk J, McElvaney G, Piitulainen E, Seersholm N, Chapman KR, Hopkinson N, MacNee W, Runold M, Vogelmeier C, et al. Phase II/III, double-blind, randomized, placebo-controlled, international study evaluating the safety and efficacy of inhaled, human, α 1-antitrypsin (AAT) in α 1-antitrypsin deficient patients (AATD: update in alpha one deficiency [abstract]. *Am J Respir Crit Care Med* 2014;D38
38. Lykavieris P, et al. Liver disease associated with ZZ alpha1-antitrypsin deficiency and ursodeoxycholic acid therapy in children. *Journal of Pediatric Gastroenterology and Nutrition*. 2008; 47(5):623-9. doi: 10.1097/MPG.0b013e31817b6dfb
39. Feldman A, Sokol RJ. Alpha-1-Antitrypsin Deficiency: An Important Cause of Pediatric Liver Disease. *Lung Health Prof Mag*. 2013; 4(2):8-11. PMID: 27019872; PMCID: PMC4805363.
40. Ivanov I, Matafonov A, Sun MF, Mohammed BM, Cheng Q, Dickeson SK, Kundu S, Verhamme IM, Gruber A, McCrae K, Gailani D. A mechanism for hereditary angioedema with normal C1 inhibitor: an inhibitory regulatory role for the factor XII heavy chain. *Blood*. 2019 Mar 07; 133(10):1152-1163
41. Zanichelli A, Bova M, Coerezza A, Petraroli A, Triggiani M, Cicardi M. Icatibant treatment for acquired C1-inhibitor deficiency: a real-world observational study. *Allergy*. 2012 Aug;67(8):1074-7. doi: 10.1111/j.1398-9995.2012.02853.x.
42. Barmettler S, Li Y, Banerji A. New and evolving therapies for hereditary angioedema. *Allergy Asthma Proc*. 2019 Jan 01; 40(1):7-13
43. C1 Esterase inhibitor deficiency. Royal children's hospital Melbourne, clinical practice guidelines. Available at https://www.rch.org.au/clinicalguide/guideline_index/c1_esterase_inhibitor_deficiency/. Accessed on 17/5/25.
44. icatibant acetate, 30mg, solution for injection in pre-filled syringe (Firazyr®). Scottish Medicines Consortium, NHS Scotland. Available at https://scottishmedicines.org.uk/media/1808/icatibant_firazyr_resubmission_final_february_2012_amended_060312_for_website.pdf. Accessed on 17/5/25.
45. Palla R, Peyvandi F, Shapiro AD. Rare bleeding disorders: diagnosis and treatment. *Blood*. 2015;125(13): 2052-2061. doi: 10.1182/blood-2014-08-532820.
46. Paraboschi EM, Duga S, Asselta R. Fibrinogen as a pleiotropic protein causing human diseases: The mutational burden of A α , B β and γ chains. *Int J Mol Sci*. 2017;18(12):2711. doi: 10.3390/ijms18122711
47. Tziomalos K, Vakalopoulou S, Perifanis V, Garipidou V. Treatment of congenital fibrinogen deficiency: overview and recent findings. *Vasc Health Risk Manag*. 2009; 5: 843-848. doi: 10.2147/vhrm.s5305
48. Bolton-Maggs PHB, Perry DJ, Chalmers EA, Parapia LA, Wilde JT, Williams MD, Collins PW, Kitchen S, Dolan G, Mumford AD. The rare coagulation disorders-Review with guidelines for management from the United Kingdom Haemophilia Centre Doctors'

- Organisation. *Haemophilia*. 2004; 10:593-628. doi: 10.1111/j.1365-2516.2004.00944.x
49. Szanto T, Lassila R, Lemponen M, Lehtinen E, Neerman-Arbez M, Casini A. Whole Blood Thromboelastometry by ROTEM and Thrombin Generation by Genesia According to the Genotype and Clinical Phenotype in Congenital Fibrinogen Disorders. *Int. J. Mol. Sci.* 2021;22:2286. doi: 10.3390/ijms22052286
50. Vakalopoulou S, Rizopoulou D, Zafiriadou E, Perifanis V, Tziomalos K, Lefkou E, Hill M, Dolan G, Garipidou V. Management of acute bleeding in a patient with congenital afibrinogenaemia. *Haemophilia*. 2006;12: 676-678. doi: 10.1111/j.1365-2516.2006. 01340.x
51. Casini A, Undas A, Palla R, Thachil J, De Moerloose P, Subcommittee on Factor XIII and Fibrinogen Diagnosis and classification of congenital fibrinogen disorders: Communication from the SSC of the ISTH. *J. Thromb. Haemost.* 2018; 16:1887-1890. doi: 10.1111/jth.14216.
52. Nascimento B, Goodnough LT, Levy JH. Cryoprecipitate therapy. *Br. J. Anaesth.* 2014;113:922-934. doi: 10.1093/bja/aeu158.
53. Simurda T, Asselta R, Zolkova J, Brunclikova M, Dobrotova M, Kolkova Z, Loderer D, Skornova I, Hudecek J, Lasabova Z, Stasko J, Kubisz P. Congenital Afibrinogenemia and Hypofibrinogenemia: Laboratory and Genetic Testing in Rare Bleeding Disorders with Life-Threatening Clinical Manifestations and Challenging Management. *Diagnostics (Basel)*. 2021 Nov 19; 11(11):2140. doi: 10.3390/diagnostics11.112140. PMID: 34829490; PMCID: PMC8622093.

CASE REPORT**ROWELL SYNDROME WITH
BASAL GANGLIA CALCIFICATION IN
A CHILD WITH NEUROPSYCHIATRIC
SYSTEMIC LUPUS ERYTHEMATOSUS*****Ananda Kesavan TM******Deepa Anirudhan******Deepthi R**

Abstract: *In patients diagnosed with systemic lupus erythematosus, any acute neurological symptom, even subtle, warrants thorough evaluation for neuropsychiatric systemic lupus erythematosus. Immunosuppressive therapy can be life-saving in cases of lupus with severe systemic symptoms. Features such as early age of onset/presentation, history of consanguinity in parents, negative anti-ds DNA antibody status and predominant neurological manifestations should prompt suspicion of complement deficiency-associated systemic lupus erythematosus.*

Here, we report a complex case of an eight-year-old girl presenting with cutaneous manifestations consistent with Rowell syndrome, progressive neuropsychiatric involvement refractory to initial therapy, and imaging findings of basal ganglia calcifications, highlighting the diagnostic and therapeutic challenges encountered. This case underscores the importance of early aggressive immunosuppression and consideration of complement deficiency in pediatric lupus with prominent neurological symptoms.

Keywords: *Systemic Lupus erythematosus, Erythema multiforme, Basal ganglia calcification.*

References

1. Levy DM, Kamphuis S. Systemic Lupus Erythematosus in Children and Adolescents. *Pediatr Clin North Am.* 2012; 59(2):345-364. doi: 10.1016/j.pcl.2012.03.007.
2. Ota Y, Srinivasan A, Capizzano AA, Bapuraj JR, Kim J, Kurokawa R, et al. Central Nervous System Systemic Lupus Erythematosus: Pathophysiologic, Clinical and Imaging Features. *Radiographics.* 2022; 42(1):212-232. doi: 10.1148/rg. 210045.
3. Solanki LAL, Dhingra M, Thami GP. Rowell syndrome. *Indian Pediatr* 2012; 49:854-855. <https://doi.org/10.1007/s13312-012-0183-5>.
4. Jiang WEI, Mei S, Deng Q, Lei C, Pang A. A Case of Cerebral Large-Vessel Vasculitis Concomitant Fahr Syndrome in Systemic Lupus Erythematosus. *Neurologist.* 2024; 29(1):17-21. doi: 10.1097/NRL.0000000000000520.
5. Sharma M, Goel S, Band IS, Rawat A. Complement deficiency in systemic immune disease. *Indian J Pract Pediatr.* 2021; 23(2):147-154.

* Professor

** Assistant Professor,
Department of Pediatrics,
Government Medical College, Thrissur.
email: deethu217@gmail.com

Cite as: Ananda Kesavan TM, Deepa Anirudhan, Deepthi R, Rowell syndrome with basal ganglia calcification in a child with neuropsychiatric systemic lupus erythematosus, *Indian J Pract Pediatr.* 2025; 27(2):182-185.