Editorial

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Healthcare Bundles are Potentially Important in Neonatal Care as Many Disorders are Temporally Clustered

The late fetal and neonatal periods carry a high risk of morbidity and mortality.[1] Each year, we lose nearly 5 million 3rd trimester fetuses and neonates.[2] And as we have mentioned in our previous issues, babies do not talk,[3] or vote,[4] and so, need help.[2] We also need to remind ourselves that since we still do not clearly understand the exact etiology of most neonatal disorders, these need to be viewed as multi-manifestation 'syndromes', not 'diseases'. Hence, to develop treatment strategies that will remain effective despite the clinical variability, we need cohorts from large geographic/climatic regions and with multiple races/ethnicities. A truly multinational group of care-providers drawn from all over the world can also help understand regional differences in clinical approach. The Global South, with its higher fertility rates and limited access to healthcare facilities, definitely needs to be represented.[5–8] These peri-equatorial/tropical regions could also have a greater proportion of cases with underlying/confounding infections, which need to be studied.[9] All these issues need consideration in healthcare planning.[10] The need for access to updated data about healthcare, outcomes, and changing economic status cannot be over-emphasized.[11]

One possible solution for the multidimensional health problems of premature/critically ill infants could be in the application of healthcare "bundles", a concept introduced by the Institute of Health Care Improvement (IHI). These bundles refer to simultaneous application of 3–5 evidence-based or traditionally accepted interventions to prevent/treat specific clinical disorders in all eligible patients.[12–15] The concurrent use of multiple treatment modalities is attractive in premature/critically ill infants as they typically show the highest severity of illness during the early postnatal period and/or at specific corrected gestational/post-conceptional ages.[12,13,16–21] Initial studies have shown an encouraging evidence for this approach.[22] Therefore, the leadership of the Global Newborn Society (GNS) has requested clinician experts from all over the world to develop and then evaluate this approach in various neonatal disorders. A short acronym was chosen to describe this evolving database: LAYA - ***L***ooking ***A***t ***Y***our practices in ***A***pplication.[23]

Our journal, the newborn aims to cover fetal/neonatal problems that begin during pregnancy, at the time of birth, or during the first 1000 days after birth. The movement is growing; since our last issue 3 months back, this journal has now been adopted by 13 more organizations as their official mouthpiece. These include the Association of Pediatricians of Uzbekistan, GNS Cardiology Association of Iraq, Iranian Forum for Infant Nutrition, Nepalese Association for Newborn Health, GNS Forum for Transgenerational Inheritance, PreemieWorld Foundation, GNS Forum for Data Analytics, GNS Forum for Nanomaterials, Neonatology Branch of the Chilean Pediatric Society, Carlo GNS Center for Saving Lives at Birth, Dudeja GNS Center for Infectious Diarrheal Diseases, Anatolian Midwives Association, and the organization, First Breaths of Life. Thus, we now represent a total of 34 groups for their official communications. We will share scientific data, viewpoints, and clinical observations relevant to the care of all ill infants and also focus on important concerns related to Down syndrome, autism, infant nutrition, brain injury, and care of infants in remote areas.

As in our previous issues, we again present 8 important articles here (**Fig. 1**). We bring to you the second in our series of healthcare bundles—this one is focused on Germinal Matrix-Intraventricular Hemorrhages (GM-IVHs).[24–26] GM-IVHs are seen in nearly a 1/3rd of all very-low-birth-weight infants within the first 72 hours after birth, and hence represent an important opportunity for bundled precautionary measures.[24–31] Ben Ayad et al.[32] have carefully evaluated antenatal measures such as the administration of steroids and magnesium sulfate, perinatal measures such as delayed cord clamping and management of thrombocytopenia and/or coagulopathy,

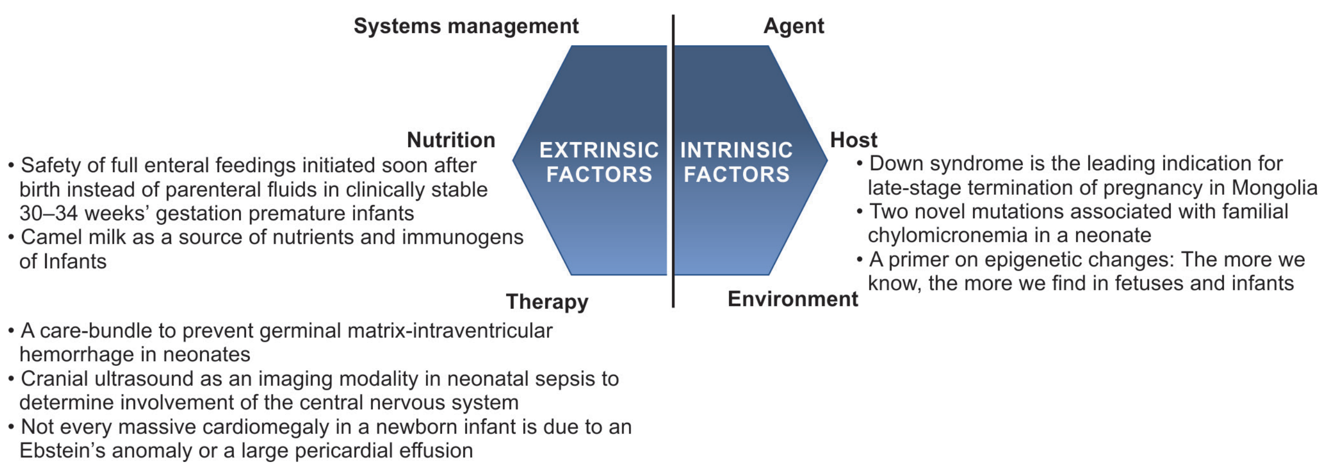

Fig. 1: Areas of focus in the *newborn*, Volume 3, Issue 3. We have expanded the traditional agent-host-environment trinodal disease model to a hexagonal system. The three additional foci represent extrinsic factors that can affect health — those originating in therapy, nutrition, and systems management are shown. This issue covers 3 nodes, namely host factors, treatment/monitoring systems, and nutrition.

and postnatal maintenance of a midline head position, safe transport, efforts to avoid hemodynamic instability, cautious endotracheal suctioning, limit blood withdrawals, and avoid routine flushing of intravascular lines.[32–38] They have proposed a 4-point bundle to prevent GM-IVH in premature infants: (a) appropriate neonatal resuscitation with, if possible, delayed cord clamping; (b) Golden-hour care; (c) gentle care of outborn infants including safe transport and avoiding hemodynamic instability; and (d) cautious management of perinatal thrombocytopenia.[39–45] We will report compliance and the impact on the incidence/severity of GM-IVH in the next 3–5 years.

Badarch et al.[46] examined the medical records of 45,095 women in Ulaanbaatar, Mongolia, to identify the most frequent indications for termination of pregnancy for fetal anomalies (TOPFAs).[47–49] Timely detection of these disorders may help make informed decisions to choose either safe terminations or well-timed fetal procedures for rehabilitation.[50] This information may also be important for appropriate genetic testing to assess the risk of recurrence in later pregnancies. They identified 156 TOPFAs (34.5 per 10,000 pregnancies) in this cohort. These infants with fetal/congenital anomalies were compared with 312 healthy controls to evaluate maternal risk factors. Down syndrome was the most frequent reason (25%) for termination of pregnancy, followed by detection of multiple congenital anomalies (16%), cleft lip/palate (10.9%), and anomalies of the central nervous (9.6%) or musculoskeletal system (9.6%). Maternal age >35 years, higher education, closely spaced successive pregnancies, and previous history of abortion (s) were linked with a higher likelihood of birth defects.

Singh and coworkers[51] have provided an interesting review of epigenetic changes, an emerging area of study focused on heritable information without alterations in the DNA sequence. [1,8,27] The most frequently seen epigenetic changes include DNA methylation, changes in gene expression due to noncoding ribonucleic acids (RNAs), and post-translational modifications of histone proteins.[56] During this period, atypical metabolic reprogramming induced by extrinsic factors such as allergens, viruses, pollutants, diet, or microbiome might also alter cellular metabolism and immune responses.[9] Understanding the variability in epigenetic marks could help understand the pathogenesis of many neonatal disorders, develop new therapeutic approaches, and even explain some of the pleiotropy in syndromic disorders.

Garegrat and her team[52] have reviewed the importance of point-of-care cranial ultrasound (POCUS) in detection of central nervous system (CNS) involvement in neonatal sepsis. POCUS findings can show signs of meningitis, brain abscesses, changes in the spinal cord, and alterations in cerebral blood flow.[53–56] Color doppler may give clues regarding the location of the extra-axial fluid collection(s).[57,58] It can even provide some clues for early identification of fungal and viral infections.[59–66] All this information can aid in appropriate management. The ease of usage, safety, and a short turn-around time makes ultrasound superior to the other imaging techniques in neonatal infections.[60]

Mohammadabadi and Kumar[67] have reviewed the nutritional value of camel milk, which is widely used for feeding infants in arid and semiarid regions. Even though camel milk represents only 0.36% of global milk production, it has several notable characteristics in its composition. It contains 3.4% protein, 4.4% lactose, 3.5% fat, high levels of vitamin C, a favorable ratio of unsaturated to saturated FAs.[68] There are more long-chain FAs, linoleic acid, and unsaturated fatty acids. Camel milk also contains important immune factors such as the VHH (single variable domain on a heavy chain) antibodies/nanobodies, which are much smaller than conventional antibodies and can stimulate immune responses.[69] Camel milk is also hypoallergenic as it does not contain β-lactoglobulin.[70] Finally, its probiotic bacteria and bioactive peptides can reduce cholesterol absorption,[71] further enhancing its health benefits.

Hoyos and Vasquez-Hoyos[72] have reported a quality-improvement effort where they tested the safety and efficacy of enteric feedings beginning within 2 hours after birth in infants born at 30–34 weeks' gestation. They administered oral/nasogastric milk feedings at 70–80 mL/kg/day divided every 3 hours, with 5 mL increments every 12–24 hours until 200 mL/kg/day was achieved. This effort differs from current practice in most centers where such infants are maintained on parenteral fluids for variable periods until hemodynamic stability is confirmed. In this QI effort, early enteral feedings were well tolerated with stable growth and biochemical parameters. The investigators inferred that routine use of parenteral fluids is not necessary in the initial management of these infants.

Jha et al.[73] have described a 12-day-old infant who was presented with respiratory distress, hepatosplenomegaly, and *lipemia retinalis*.[74] The laboratory noted that his sera were unusually viscous and turned opaque milky-white within minutes. There was chylomicronemia with high triglyceride and cholesterol levels. Genetic analysis showed a novel homozygous mutation in the lipoprotein lipase (LPL) gene and a heterozygous missense variation in the sterol regulatory element-binding transcription factor 2 (SREBF2).[75,76] There was rapid improvement with dietary modifications. This case reminds us yet again of a need to be cognizant of non-infectious causes of neonatal respiratory distress. Timely diagnosis and intervention can improve outcomes.

Finally, Barrios et al.[77] have described a term infant with respiratory distress and a massive cardiomegaly noted on a chest radiograph. They considered the usual differential diagnosis of tricuspid valve malformations as in Ebstein's anomaly, large pericardial effusions, fetal cardiomyopathy, and cerebral/hepatic arterio-venous malformations.[78–87] However, magnetic resonance imaging and computed tomography showed a large cyst in the left hemithorax. The heart and major vessels were all normal in size. A left posterolateral thoracotomy was performed to remove the cyst; histopathology showed features of bronchopulmonary foregut malformations.[88,89] We need to consider a wider list of entities in the differential diagnosis of a massively enlarged cardiac silhouette in an infant with respiratory distress.

References

1. World-Health-Organization. Newborn mortality New York City, NY: World-Health-Organization; 2024 [Available from: https://www.who.int/news-room/fact-sheets/detail/newborn-mortality.
2. World-Health-Organization. Every Newborn Action Plan New York City, NY: WHO; 2014 [Available from: https://www.who.int/initiatives/every-newborn-action-plan.

3. World-Health-Organization. Newborn health: WHO-Europe; 2021 [Available from: https://www.who.int/europe/news-room/fact-sheets/item/newborn-health.
4. Bernstein J. Birthright New York City, NY: Caruso, M.; 2011 [Available from: https://newrepublic.com/article/89090/elections-voting-age-limits-democracy.
5. Patrick S, Huggins A. The Term “Global South” Is Surging. It Should Be Retired Washington, D.C.: Carnegie Endowment for International Peace; 2023 [Available from: https://carnegieendowment.org/posts/2023/08/the-term-global-south-is-surging-it-should-be-retired?lang=en.
6. Hogan E, Patrick S. A Closer Look at the Global South Washington D.C.: Carnegie Endowment for International Peace; 2024 [Available from: https://carnegieeurope.eu/research/2024/05/global-south-colonialism-imperialism.
7. Gewin V. Four global-south researchers making cross-border collaborations count. Nature. 2023;624(7991):S2–S6. PMID: 38092923. doi: 10.1038/d41586-023-03902-w.
8. Kim JU, Oleribe O, Njie R, Taylor-Robinson SD. A time for new north-south relationships in global health. Int J Gen Med. 2017;10:401–408. PMID: 29158688. doi: 10.2147/IJGM.S146475.
9. 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. PMID: 34800370. doi: 10.1016/S2352-4642(21)00311-4.
10. Goldstein ND, Palumbo AJ, Bellamy SL, Purtle J, Locke R. State and local government expenditures and infant mortality in the United States. Pediatrics. 2020;146(5). PMID: 33077541. doi: 10.1542/peds.2020-1134.
11. Batko K, Slezak A. The use of big data analytics in healthcare. J Big Data. 2022;9(1):3. PMID: 35013701. doi: 10.1186/s40537-021-00553-4.
12. IHI-Team. What Is a Bundle? Institute for Healthcare Improvement; 2012 [Available from: https://www.ihi.org/insights/what-is-a-bundle.
13. Resar R, Griffin FA, Haraden C, Nolan TW. Using care bundles to improve health care quality. IHI Innovation Series white paper. Cambridge, MA2012 [Available from: https://www.ihi.org/resources/white-papers/using-care-bundles-improve-health-care-quality.
14. Fulbrook P. Developing best practice in critical care nursing: knowledge, evidence and practice. Nurs Crit Care. 2003;8(3):96–102. PMID: 12859079. doi: 10.1046/j.1478-5153.2003.00010.x.
15. Fulbrook P, Mooney S. Care bundles in critical care: a practical approach to evidence-based practice. Nurs Crit Care. 2003;8(6):249–255. PMID: 14725390. doi: 10.1111/j.1362-1017.2003.00039.x.
16. Engle WA. American Academy of Pediatrics Committee on Fetus and Newborn. Age terminology during the perinatal period. Pediatrics. 2004 Nov;114(5):1362–4. PMID: 15520122. doi: 10.1542/peds.2004-1915.
17. Radbone L, Birch J, Upton M. The development and implementation of a care bundle aimed at reducing the incidence of NEC. 2013;14–19. Available from: https://www.infantjournal.co.uk/pdf/inf_049_ime.pdf.
18. Sekhon MK, Grubb PH, Newman M, Yoder BA. Implementation of a probiotic protocol to reduce rates of necrotizing enterocolitis. J Perinatol. 2019;39(9):1315–1322. PMID: 31358866. doi: 10.1038/s41372-019-0443-5.
19. Alshaikh B, Kostecky L, Blachly N, Yee W. Effect of a quality improvement project to use exclusive mother’s own milk on rate of necrotizing enterocolitis in preterm infants. Breastfeed Med. 2015;10(7):355–361. PMID: 26230909. doi: 10.1089/bfm.2015.0042.
20. Maria-Fe Villosis MMTA, Kambiz Rezaie, Karine Barseghyan. A bundle of care that led to sustained low incidence of necrotizing enterocolitis in very low birth weight infants: A 10-year quality improvement project. Pediatrics. 2021;147:759–760. doi: https://doi.org/10.1542/peds.147.3MA8.759b.
21. Mavis SC, Gallup MC, Meyer M, Misgen MM, Schram LA, Herzog DL, et al. A quality improvement initiative to reduce necrotizing enterocolitis in high-risk neonates. J Perinatol. 2023;43(1):97–102. PMID: 35915215. doi: 10.1038/s41372-022-01476-5.
22. Bagga N, Maheshwari A, Jha K, Athalye-Jape G, Jain J, Ben Ayad AE, et al. Development of a clinical care-bundle to prevent necrotizing enterocolitis. Newborn (Clarksville). 2024;3(2):70–82. doi. 10.5005/jp-journals-11002-0094.
23. Bagga N, Maheshwari A, Jha KK, Athalye-Jape G, Jain J, Ben Ayad AE, et al. A clinical care bundle to prevent necrotizing enterocolitis. Newborn (Clarksville, Md). 2024;3(2):70–82. doi: 10.5005/jp-journals-11002-0094.
24. Egesa WI, Odoch S, Odong RJ, Nakalema G, Asiimwe D, Ekuk E, et al. Germinal Matrix-Intraventricular Hemorrhage: A tale of preterm infants. Int J Pediatr. 2021;2021:6622598. PMID: 33815512. doi: 10.1155/2021/6622598.
25. Gilard V, Tebani A, Bekri S, Marret S. Intraventricular hemorrhage in very preterm infants: A comprehensive review. J Clin Med. 2020;31:9(8). PMID: 32751801. doi: 10.3390/jcm9082447.
26. Parodi A, Govaert P, Horsch S, Bravo MC, Ramenghi LA, eur USbg. Cranial ultrasound findings in preterm germinal matrix haemorrhage, sequelae and outcome. Pediatr Res. 2020;87(Suppl 1):13–24. PMID: 32218535. doi: 10.1038/s41390-020-0780-2.
27. Ballabh P. Pathogenesis and prevention of intraventricular hemorrhage. Clin Perinatol. 2014;41(1):47–67. PMID: 24524446. doi: 10.1016/j.clp.2013.09.007.
28. Park YS. Perspectives: Understanding the pathophysiology of intraventricular hemorrhage in preterm infants and considering of the future direction for treatment. J Korean Neurosurg Soc. 2023;66(3):298–307. PMID: 36858804. doi: 10.3340/jkns.2023.0020.
29. Siffel C, Kistler KD, Sarda SP. Global incidence of intraventricular hemorrhage among extremely preterm infants: a systematic literature review. J Perinat Med. 2021;49(9):1017–1026. PMID: 33735943. doi: 10.1515/jpm-2020-0331.
30. Kim KR, Jung SW, Kim DW. Risk factors associated with germinal matrix-intraventricular hemorrhage in preterm neonates. J Korean Neurosurg Soc. 2014;56(4):334–337. PMID: 25371784. doi: 10.3340/jkns.2014.56.4.334.
31. Linder N, Haskin O, Levit O, Klinger G, Prince T, Naor N, et al. Risk factors for intraventricular hemorrhage in very low birth weight premature infants: a retrospective case-control study. Pediatrics. 2003;111(5 Pt 1):e590–e595. PMID: 12728115. doi: 10.1542/peds.111.5.e590.
32. Ben Ayad AE, Athalye-Jape G, Jape K, Huseynova R, Vora N, Varghese NV, et al. A care-bundle to prevent germinal matrix-intraventricular hemorrhage in neonates. Newborn (Clarksville, Md). 2024;3(3):157–179. doi: 10.5005/jp-journals-11002-0107.
33. Wei JC, Catalano R, Profit J, Gould JB, Lee HC. Impact of antenatal steroids on intraventricular hemorrhage in very-low-birth weight infants. J Perinatol. 2016;36(5):352–356. PMID: 27010109. doi: 10.1038/jp.2016.38.

34. Romantsik O, Calevo MG, Bruschettini M. Head midline position for preventing the occurrence or extension of germinal matrix-intraventricular haemorrhage in preterm infants. Cochrane Database Syst Rev. 2020;7(7):CD012362. PMID: 32639053. doi: 10.1002/14651858.CD012362.pub3.
35. Pirlotte S, Beeckman K, Ooms I, Cools F. Non-pharmacological interventions for the prevention of pain during endotracheal suctioning in ventilated neonates. Cochrane Database Syst Rev. 2024;1(1):CD013353. PMID: 38235838. doi: 10.1002/14651858.CD013353.pub2.
36. von Lindern JS, van den Bruele T, Lopriore E, Walther FJ. Thrombocytopenia in neonates and the risk of intraventricular hemorrhage: a retrospective cohort study. BMC Pediatr. 2011;11:16. PMID: 21314921. doi: 10.1186/1471-2431-11-16.
37. Moradi Y, Khateri R, Haghighi L, Dehghani S, Hanis SM, Valipour M, et al. The effect of antenatal magnesium sulfate on intraventricular hemorrhage in premature infants: a systematic review and meta-analysis. Obstet Gynecol Sci. 2020;63(4):395–406. PMID: 32689768. doi: 10.5468/ogs.19210.
38. Morris H, Magers N, Saunders S, Vesoulis Z. Potential risk modifiers for severe intraventricular hemorrhage in very low birthweight infants requiring transport. J Matern Fetal Neonatal Med. 2022;35(15):2988–2991. PMID: 32873087. doi: 10.1080/14767058.2020.1813708.
39. Reuter S, Messier S, Steven D. The neonatal golden hour intervention to improve quality of care of the extremely low birth weight infant. S D Med. 2014;67(10):397–403, 405. PMID: 25423766. doi, https://www.ncbi.nlm.nih.gov/pubmed/25423766.
40. Peleg B, Globus O, Granot M, Leibovitch L, Mazkereth R, Eisen I, et al. "Golden Hour" quality improvement intervention and short-term outcome among preterm infants. J Perinatol. 2019;39(3):387–392. PMID: 30341403. doi: 10.1038/s41372-018-0254-0.
41. Harriman TL, Carter B, Dail RB, Stowell KE, Zukowsky K. Golden hour protocol for preterm infants: A quality improvement project. Adv Neonatal Care. 2018;18(6):462–470. PMID: 30212389. doi: 10.1097/ANC.0000000000000554.
42. Moore CM, O'Reilly D, McCallion N, Curley AE. Changes in inflammatory proteins following platelet transfusion in a neonatal population. Pediatr Res. 2023;94(6):1973–1977. PMID: 37443343. doi: 10.1038/s41390-023-02731-x.
43. Castrodale V, Rinehart S. The golden hour: improving the stabilization of the very low birth-weight infant. Adv Neonatal Care. 2014;14(1):9–14; quiz 15–6. PMID: 24472882. doi: 10.1097/ANC.0b013e31828d0289.
44. Lerner EB, Moscati RM. The golden hour: scientific fact or medical "urban legend"? Acad Emerg Med. 2001;8(7):758–760. PMID: 11435197. doi: 10.1111/j.1553-2712.2001.tb00201.x.
45. Ashmeade TL, Haubner L, Collins S, Miladinovic B, Fugate K. Outcomes of a neonatal golden hour implementation project. Am J Med Qual. 2016;31(1):73–80. PMID: 25194002. doi: 10.1177/1062860614548888.
46. Badarch J, Kumar G, Enkhbayar B, Turbat T, Sereenendorj T, Tumurkhuleg B, et al. Down syndrome is the leading indication for late-stage termination of pregnancy in Mongolia. Newborn (Clarksville, Md). 2024;3(3):180–189. doi: 10.5005/jp-journals-11002-0099.
47. Heaney S, Tomlinson M, Aventin A. Termination of pregnancy for fetal anomaly: a systematic review of the healthcare experiences and needs of parents. BMC Pregnancy Childbirth. 2022;22(1):441. PMID: 35619067. doi: 10.1186/s12884-022-04770-4.
48. Anderson N, Boswell O, Duff G. Prenatal sonography for the detection of fetal anomalies: results of a prospective study and comparison with prior series. AJR Am J Roentgenol. 1995;165(4):943–950. PMID: 7676997. doi: 10.2214/ajr.165.4.7676997.
49. Tsogt B, Seded K, Johnson BR. Strategic assessment t. Applying the WHO strategic approach to strengthening first and second trimester abortion services in Mongolia. Reprod Health Matters. 2008;16(31 Suppl):127–134. PMID: 18772093. doi: 10.1016/S0968-8080(08)31383-4.
50. Melo DG, Sanseverino MTV, Schmalfuss TO, Larrandaburu M. Why are birth defects surveillance programs important? Front Public Health. 2021;9:753342. PMID: 34796160. doi: 10.3389/fpubh.2021.753342.
51. Singh S, Frydrysiak-Brzozowska A, Ben Ayad AE, Khasanova SS, Bordon J, Michie C. A primer on epigenetic changes: The more we know, the more we find in fetuses and infants. Newborn (Clarksville, Md). 2024;3(3):219–232. doi: 10.5005/jp-journals-11002-0104.
52. Garegrat R, Chetan C, Chandrakala BS, Nagpal R, JH, Jethwa N, et al. Cranial ultrasound as an imaging modality in neonatal sepsis to determine involvement of the central nervous system. Newborn (Clarksville, Md). 2024;3(3):206–218. doi: 10.5005/jp-journals-11002-0103.
53. Baruah D, Gogoi N, Gogoi R. Ultrasound evaluation of acute bacterial meningitis and its sequale in infants. Indian J Radiol Imaging. 2006;16(4): 553–558.
54. Raghav B, Goulatia RK, Gupta AK, Misra NK, Singh M. Giant subdural empyema in an infant. sonographic observations. Neuroradiology. 1990;32(2): 154–155. PMID: 1975948. doi: 10.1007/BF00588567.
55. Syrogiannopoulos GA, Nelson JD, McCracken GH, Jr. Subdural collections of fluid in acute bacterial meningitis: a review of 136 cases. Pediatr Infect Dis. 1986;5(3):343–352. PMID: 3725642. doi: 10.1097/00006454-198605000-00014.
56. Chen CY, Huang CC, Chang YC, Chow NH, Chio CC, Zimmerman RA. Subdural empyema in 10 infants: US characteristics and clinical correlates. Radiology. 1998;207(3):609–617. PMID: 9609881. doi: 10.1148/radiology.207.3.9609881.
57. Chen CY, Chou TY, Zimmerman RA, Lee CC, Chen FH, Faro SH. Pericerebral fluid collection: differentiation of enlarged subarachnoid spaces from subdural collections with color Doppler US. Radiology. 1996;201(2):389–392. PMID: 8888229. doi: 10.1148/radiology.201.2.8888229.
58. Seibert JJ, Avva R, Hronas TN, Mocharla R, Vanderzalm T, Cox K, et al. Use of power Doppler in pediatric neurosonography: a pictorial essay. Radiographics. 1998;18(4):879–890. PMID: 9672972. doi: 10.1148/radiographics.18.4.9672972.
59. Littwin B, Pomiecko A, Stepien-Roman M, Sparchez Z, Kosiak W. Bacterial meningitis in neonates and infants—the sonographic picture. J Ultrason. 2018;18(72):63–70. PMID: 29844943. doi: 10.15557/JoU.2018.0010.
60. Gupta N, Grover H, Bansal I, Hooda K, Sapire JM, Anand R, et al. Neonatal cranial sonography: ultrasound findings in neonatal meningitis—a pictorial review. Quant Imaging Med Surg. 2017;7(1):123–131. PMID: 28275563. doi: 10.21037/qims.2017.02.01.
61. Jequier S, Jequier JC. Sonographic nomogram of the leptomeninges (pia-glial plate) and its usefulness for evaluating bacterial meningitis in infants. AJNR Am J Neuroradiol. 1999;20(7):1359–1364. PMID: 10472998. doi, https://www.ncbi.nlm.nih.gov/pubmed/10472998.
62. Patel K, Rathore R, Chaudhuri CR. Cranial ultrasonography in evaluation of meningitis in neonates and infants. Int J Contemp Med Surg Radiol. 2019;4(4):D87–D90. doi: 10.21276/ijcmsr.2019.4.4.21.
63. Han BK, Babcock DS, McAdams L. Bacterial meningitis in infants: sonographic findings. Radiology. 1985;154(3):645–650. PMID: 3881791. doi: 10.1148/radiology.154.3.3881791.

64. Arrumugham R, Katariya S, Singhi P, Singhi S, Suri S, Walia BN. Sonography in pyogenic meningitis. Indian Pediatr. 1994;31(11):1329–1336. PMID: 7896329. doi, https://www.ncbi.nlm.nih.gov/pubmed/7896329.
65. Kapoor R, Saha MM, Gupta NC. Ultrasonic evaluation of complicated meningitis. Indian Pediatr. 1989;26(8):804–808. PMID: 2620982. doi, https://www.ncbi.nlm.nih.gov/pubmed/2620982.
66. Raju VS, Rao MN, Rao VS. Cranial sonography in pyogenic meningitis in neonates and infants. J Trop Pediatr. 1995;41(2):68–73. PMID: 7776399. doi: 10.1093/tropej/41.2.68.
67. Mohammadabadi T, Kumar G. Camel milk as a source of nutrients and immunogens for infants. Newborn (Clarksville, Md). 2024;3(3):195–205. doi: 10.5005/jp-journals-11002-0106.
68. Gorban AM, Izzeldin OM. Fatty acids and lipids of camel milk and colostrum. Int J Food Sci Nutr. 2001;52(3):283–287. PMID: 11400477. doi: 10.1080/713671778.
69. Asaadi Y, Jouneghani FF, Janani S, Rahbarizadeh F. A comprehensive comparison between camelid nanobodies and single chain variable fragments. Biomark Res. 2021;9(1):87. PMID: 34863296. doi: 10.1186/s40364-021-00332-6.
70. Hinz K, O'Connor PM, Huppertz T, Ross RP, Kelly AL. Comparison of the principal proteins in bovine, caprine, buffalo, equine and camel milk. J Dairy Res. 2012;79(2):185–191. PMID: 22365180. doi: 10.1017/S0022029912000015.
71. El-Zahar KM, Hassan MFY, Al-Qaba SF. Protective effect of fermented camel milk containing bifidobacterium longum BB536 on blood lipid profile in hypercholesterolemic rats. J Nutr Metab. 2021;2021:1557945. PMID: 34745660. doi: 10.1155/2021/1557945.
72. Hoyos AB, Vasquez-Hoyos P. Safety of full enteral feedings initiated soon after birth instead of parenteral fluids in clinicallystable 30-34 weeks gestation premature infants. Newborn (Clarksville, Md). 2024;3(3):190–194. doi: 10.5005/jp-journals-11002-0101.
73. Jha VV, Arora G, Arora V. Two novel mutations associated with familial chylomicronemia in a neonate. Newborn (Clarksville, Md). 2024;3(3):238–244. doi: 10.5005/jp-journals-11002-0105.
74. Alsarhani WK, Al Adel FF, Alamri A, Al Malawi RM, AlBloushi AF. Alterations in ocular microcirculation and oxygen metabolism in patients with lipemia retinalis. BMC Ophthalmol. 2022;22(1):295. PMID: 35794613. doi: 10.1186/s12886-022-02515-7.
75. Wang H, Eckel RH. Lipoprotein lipase: from gene to obesity. Am J Physiol Endocrinol Metab. 2009;297(2):E271–288. PMID: 19318514. doi: 10.1152/ajpendo.90920.2008.
76. Bertolio R, Napoletano F, Mano M, Maurer-Stroh S, Fantuz M, Zannini A, et al. Sterol regulatory element binding protein 1 couples mechanical cues and lipid metabolism. Nat Commun. 2019;10(1):1326. PMID: 30902980. doi: 10.1038/s41467-019-09152-7.
77. Barrios N, Velázquez E, Velazquez F, Maidana M, Bordón J. Not every massive cardiomegaly in a newborn infant is due to an Ebstein's anomaly or a large pericardial effusion. Newborn (Clarksville, Md). 2024;3(3):233–237. doi: 10.5005/jp-journals-11002-0100.
78. Eronen M. Outcome of fetuses with heart disease diagnosed in utero. Arch Dis Child Fetal Neonatal Ed. 1997;77(1):F41–146. PMID: 9279182. doi: 10.1136/fn.77.1.f41.
79. Chaoui R, Bollmann R, Goldner B, Heling KS, Tennstedt C. Fetal cardiomegaly: echocardiographic findings and outcome in 19 cases. Fetal Diagn Ther. 1994;9(2):92–104. PMID: 8185846. doi: 10.1159/000263915.
80. Donofrio MT, Moon-Grady AJ, Hornberger LK, Copel JA, Sklansky MS, Abuhamad A, et al. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. Circulation. 2014;129(21):2183–2242. PMID: 24763516. doi: 10.1161/01.cir.0000437597.44550.5d.
81. Hasbini J, Safawi N, Mneimneh S, Rajab M, Berjaoui C, Naous A. Pericardial effusion complicated by umbilical vein catheter in a preterm infant with respiratory distress syndrome: A case report. Radiol Case Rep. 2024;19(2):741–744. PMID: 38074435. doi: 10.1016/j.radcr.2023.11.036.
82. Bonaba J, Marcos JR, Saldun de Rodriguez ML, Soto JA. Cardiomegaly and cardiac insufficiency of early infancy. Am J Dis Children. 1945;73(3):378–379.
83. Reisman M, Hipona FA, Bloor CM, Talner NS. Congenital tricuspid insufficiency—a cause of massive cardiomegaly and heart failure in the neonate. J Pediatr. 1965;66:869–876. PMID: 14279846. doi: 10.1016/s0022-3476(65)80061-0.
84. Kugel MA. Enlargement of the heart in infants and young children. Am Heart J. 1939;17(5):602–615. doi: 10.1016/S0002-8703(39)90039-6.
85. Brenner JI, Berman MA. Massive cardiomegaly in a neonate. Chest. 1975;68(4):573–574. PMID: 126143. doi: 10.1378/chest.68.4.573.
86. Upadhyay S, Law S, Kholwadwala D. A newborn with cardiomegaly. J Emerg Trauma Shock. 2010;3(3):298. PMID: 20930980. doi: 10.4103/0974-2700.66541.
87. Kumar TKS. Ebstein's anomaly in the neonate. Indian J Thorac Cardiovasc Surg. 2021;37(Suppl 1):17–25. PMID: 33603283. doi: 10.1007/s12055-020-00942-z.
88. Heithoff KB, Sane SM, Williams HJ, Jarvis CJ, Carter J, Kane P, et al. Bronchopulmonary foregut malformations. A unifying etiological concept. AJR Am J Roentgenol. 1976;126(1):46–55. PMID: 175683. doi: 10.2214/ajr.126.1.46.
89. Oyachi N, Numano F, Koizumi K, Shinohara T, Matsubara H. Congenital communicating bronchopulmonary foregut malformation including ectopic pancreatic tissue in an infant. Surg Case Rep. 2021;7(1):128. PMID: 34028645. doi: 10.1186/s40792-021-01211-w.

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