Got The D?

Recognizing Glucose-6-Phosphate Dehydrogenase Deficiency (G6PDd) and Improving Outcomes in Newborns

This educational module is provided by the g6pd Deficiency Foundation



Neonatal Severe Hyperbilirubinemia

Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant > or =35 weeks' gestation: an update with clarifications. *Pediatrics*. 2009;124(4):1193-1198. >

Hyperbilirubinemia Management

> American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004;114(1):297–316.

Hyperbilirubinemia Neurotoxicity

> Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant > or =35 weeks' gestation: an update with clarifications. *Pediatrics*. 2009;124(4):1193–1198.

G6PD Deficiency Should Be Considered When...

- ×
- Frank JE. Diagnosis and management of G6PD deficiency. Am Fam Physician. 2005;72(7):1277–1282. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. × Pediatrics. 2004;114(1):297-316.

Epidemiology

- Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. *Lancet*. 2008;371(9606):64–74. Nkhoma ET, Poole C, Vannappagari V, Hall SA, Beutler E. The global prevalence of glucose-6-phosphate dehydrogenase deficiency: a systematic review and meta-analysis. *Blood Cells Mol Dis*. 2009;42(3):267–278. Vidavalur R, Bhutani VK. Economic evaluation of point of care universal newborn screening for glucose-6-phosphate dehydrogenase deficiency in United States. *J Matern Fetal Neonatal Med*. Published online 2021:1–9. Oppenheim A, Jury CL, Rund D, Vulliamy TJ, Luzzatto L. G6PD Mediterranean accounts for the high prevalence of G6PD deficiency in Kurdish Jews. *Hum* ×
- ×
- × Genet. 1993;91(3):293–294. Goo YK, Ji SY, Shin HI, et al. First evaluation of glucose-6-phosphate dehydrogenase (G6PD) deficiency in vivax malaria endemic regions in the Republic of
- × Korea. *PLoS One*. 2014;9(5):e97390. Chinevere TD, Murray CK, Grant E Jr, Johnson GA, Duelm F, Hospenthal DR. Prevalence of glucose-6-phosphate dehydrogenase deficiency in U.S. Army
- \blacktriangleright personnel. Mil Med. 2006;171(9):905-907.

Genetics

> Au W-Y, Lam V, Pang A, et al. Glucose-6-phosphate dehydrogenase deficiency in female octogenarians, nanogenarians, and centenarians. J Gerontol A Biol Sci Med Sci. 2006;61(10):1086-1089.

Biochemistry

Source: (Kaplan M, Hammerman C, Bhutani VK. The preterm infant: A high-risk situation for neonatal hyperbilirubinemia due to glucose-6-phosphate dehydrogenase deficiency. Clin Perinatol. 2016;43(2):325-340.)

WHO Classification

- ➤ Glucose-6-phosphate dehydrogenase deficiency: WHO Working Group. Bull World Health Organ. 1989;67(6):601–611.
- ▶ Frank JE. Diagnosis and management of G6PD deficiency. Am Fam Physician. 2005;72(7):1277–1282.

Neonatal Presentation

- > Johnson L, Bhutani VK, Karp K, Sivieri EM, Shapiro SM. Clinical report from the pilot USA Kernicterus Registry (1992 to 2004). J Perinatol. 2009;29 Suppl 1(S1):S25-S45.
- > Kaplan M, Hammerman C, Vreman HJ, Stevenson Kaplan M, Algur N, Hammerman C. Onset of jaundice in glucose-6-phosphate dehydrogenase-deficient neonates. *Pediatrics*. 2001;108(4):956–959. > Glucose-6-phosphate dehydrogenase deficiency. WHO Working Group. Bull World Health Organ. 1989;67(6):601–611.
- > Updating the WHO G6PD classification of variants and the International Classification of Diseases, 11th revision (ICD-11). Malaria Policy Advisory Committee https://www.who.int/malaria/mpac/mpac-october2010-session7-updatina-G6PD-classification.pdf. Meetina.

Extreme Hyperbilirubinemia Effects, Acute and Chronic

- Newman TB, Maisels MJ. Evaluation and treatment of jaundice in the term newborn: a kinder, gentler approach. *Pediatrics*. 1992;89(5 Pt 1):809–818.
 Wusthoff CJ, Loe IM. Impact of bilirubin-induced neurologic dysfunction on neurodevelopmental outcomes. *Semin Fetal Neonatal Med*. 2015;20(1):52–57.

Kernicterus Spectrum Disorders

> Le Pichon JB, Riordan SM, Watchko J, Shapiro SM. The neurological sequelae of neonatal hyperbilirubinemia: definitions, diagnosis and treatment of the kernicterus spectrum disorders (KSDs). Curr Pediatr Rev. 2017;13(3):199–209.

BIND

- ▶ Koziol LF, Budding DE, Chidekel D. Hyperbilirubinemia: subcortical mechanisms of cognitive and behavioral dysfunction. Pediatr Neurol. 2013;48(1):3–13. oi.nlm.nih.gov/23 ibmed.ncl
- > Wusthoff CJ, Loe IM. Impact of bilirubin-induced neurologic dysfunction on neurodevelopmental outcomes. Semin Fetal Neonatal Med. 2015;20(1):52-57.
- > Bhutani VK, Johnson-Hamerman L. The clinical syndrome of bilirubin-induced neurologic dysfunction. Semin Fetal Neonatal Med. 2015;20(1):6–13.
- > Olds C, Oghalai JS. Audiologic impairment associated with bilirubin-induced neurologic damage. Semin Fetal Neonatal Med. 2015;20(1):42-46.

Adult Outcomes

Hokkanen L, Launes J, Michelsson K. Adult neurobehavioral outcome of hyperbilirubinemia in full term neonates—a 30 year prospective follow-up study. PeerJ. 2014;2:e294. \triangleright

American Academy of Pediatrics, Clinical Practice Guidelines Revised Kemp AR, Newman RB, Slaughter JL et al. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 04 more Weeks of Gestation. American Academy of Pediatrics, Vol. 150, Issue 3. September 2022.

Hidden Risks

MacDonald MG. Hidden risks: early discharge and bilirubin toxicity due to glucose 6-phosphate dehydrogenase deficiency. *Pediatrics*. 1995;96(4 Pt 1):734–738.

Hospital Screening, Current Recommendations

- WHO Working Group. Glucose-6-phosphate dehydrogenase deficiency. *Bull World Health Organ*. 1989;67(6):601–611. Kaplan M, Hammerman C, Bhutani VD. Parental education and the WHO neonatal G-6-PD screening program: a quarter century later. *J Perinatol*. 2015;35(10):779–784. ×

Hospital Screening, US and International

Watchko JF, Kaplan M, Stark AR, Stevenson DK, Bhutani VK. Should we screen newborns for glucose-6-phosphate dehydrogenase deficiency in the United States? J > Perinatol. 2013;33(7):499-504.

Florescent Spot Testing

Cherepnalkovski AP, Marusic E, Piperkova K, et al. Influence of the inherited glucose-t-phosphate dehydrogenase deficiency on the appearance of neonatal hyperbilirubinemia in southern Croatia. Acta Inform Med. 2015;23(5):264–267. >

Spectrophotometric Testing

- Cherepnalkovski AP, Marusic E, Piperkova K, et al. Influence of the inherited glucose-t-phosphate dehydrogenase deficiency on the appearance of neonatal hyperbilirubinemia in southern Croatia. Acta Inform Med. 2015;23(5):264–267.
- Kaplan M, Beutler E, Vreman HJ, et al. Neonatal hyperbilirubinemia in glucose-6-phosphate dehydrogenase-deficient heterozygotes. *Pediatrics*. 1999;104(1):68–74.

Molecular Testing

- Watchko JF, Kaplan M, Stark AR, Stevenson DK, Bhutani VK. Should we screen newborns for glucose-6-phosphate dehydrogenase deficiency in the United States? J Perinatol. 2013;33(7):499-504.
- Nantakomol D, Paul R, Palasuwan A, Day NPJ, White NJ, Imwong M. Evaluation of the phenotypic test and genetic analysis in the detection of glucose-6-phosphate dehydrogenase deficiency. *Malar J.* 2013;12:239.

G6PD/6PGD Assay

- Miao J-K, Chen Q-X, Bao L-M, et al. Determination of optimal cutoff value to accurately identify glucose-6-phosphate dehydrogenase-deficient heterozygous female neonates. Clin Chim Acta. 2013;424:131–135.
- Minucci A, Giardina B, Zuppi C, Capoluongo E. Glucose-6-phosphate dehydrogenase laboratory assay: How, when, and why? *IUBMB Life*. 2009;61(1):27-34.
- ➤ G6PD/6PGD for the diagnosis of G6PD deficiency. Nurex diagnostics website. Accessed August 27, 2021.
- Roper D, Layton M, Rees D, et al. Laboratory diagnosis of G6PD deficiency. A British Society for Haematology Guideline. Br J Haematol. 2020;189(1):24–38.

> Point of Care Device

- <u>https://baebies.com/products/finder/</u>
- > A novel point-of-care device for measuring glucose-6-phosphate dehydrogenase enzyme deficiency https://doi.org/10.1016/j.semperi.2020.151356

Case For Newborn Screening in the US, Slide 1

- Kaplan M, Wong RJ, Stevenson DK. Hemolysis and glucose-6-phosphate dehydrogenase deficiency-related neonatal hyperbilirubinemia. Neonatology. 2018;114(3):223–225.
- Bernardo J, Nock M. Pediatric provider insight into newborn screening for glucose-6-phosphate dehydrogenase deficiency. *Clin Pediatr (Phila)*. 2015;54(6):575–578.

Case for Newborn Screening in the US, Slide 2

- Watchko JF, Kaplan M, Stark AR, Stevenson DK, Bhutani VK. Should we screen newborns for glucose-6-phosphate dehydrogenase deficiency in the United States? J Perinatol. 2013;33(7):499–504.
- Nock ML, Johnson EM, Krugman RR, et al. Implementation and analysis of a pilot in-hospital newborn screening program for glucose-6-phosphate dehydrogenase deficiency in the United States. J Perinatol. 2011;31(2):112–117.
- Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant > or =35 weeks' gestation: an update with clarifications. *Pediatrics*. 2009;124(4):1193-1198.

Case for Newborn Screening in the US, Slide 3

- Kaplan M, Hammerman C. Glucose-6-phosphate dehydrogenase deficiency: a hidden risk for kernicterus. *Semin Perinatol*. 2004;28(5):356–364.
- Joseph R, Ho LY, Gomez JM, Rajdurai VS, Sivasankaran S, Yip YY. Mass newborn screening for glucose-6-phosphate dehydrogenase deficiency in Singapore. Southeast Asian J Trop Med Public Health. 1999;30 Suppl 2:70–71.
- Vidavalur R, Bhutani VK. Economic evaluation of point of care universal newborn screening for glucose-6-Phosphate dehydrogenase deficiency in United States. J Matern Fetal Neonatal Med. Published online 2021:1–9.

Other References

> Up to Date: <u>https://www.uptodate.com/contents/diagnosis-and-management-of-glucose-6-phosphate-dehydrogenase-g6pd-deficiency</u>