Screening for Sickle Cell Disease in Newborns: U.S. Preventive Services Task Force Recommendation Statement

- The U.S. Preventive Services Task Force (USPSTF) makes recommendations about preventive care services for patients without recognized signs or symptoms of the target condition.
- Recommendations are based on a systematic review of the evidence of the benefits and harms and an assessment of the net benefit of the service.
- The USPSTF recognizes that clinical or policy decisions involve more considerations than this body of evidence alone. Clinicians and policy-makers should understand the evidence but individualize decision-making to the specific patient or situation.

Summary of Recommendations and Evidence

The U. S. Preventive Services Task Force (USPSTF) recommends screening for sickle cell disease in newborns. (This is an **A recommendation.**)

Rationale

Importance: Sickle cell anemia (hemoglobin SS) affects 1 in 375 African American newborns born in the United States and smaller proportions of children in other ethnic groups. Without prompt diagnosis and the initiation of prophylactic antibiotics and pneumococcal conjugate vaccination by 2 months of age, children with sickle cell anemia are vulnerable to life-threatening pneumococcal infections.[1]

Detection: In the United States, most state-based screening programs utilize thin-layer isoelectric focusing (IEF) or high performance liquid chromatography (HPLC) techniques performed on capillary blood collected from a heel stick and absorbed onto filter paper. The sensitivity and specificity of each of these tests approaches 100%.[2]

Benefits of detection and early intervention: There is good evidence that early detection of sickle cell anemia followed by prophylactic oral penicillin substantially reduces the risk of serious infections during the first few years of life. Additional benefits result from pneumococcal conjugate vaccination and parental education about early warning signs of infection. Finally, detection of sickle cell disease permits counseling for family members about disease management and future reproductive decisions.

Harms of detection and early treatment: Incidental detection of sickle cell carrier status and hemoglobin disorders of questionable clinical significance has the potential to cause psychosocial harms, which may include exposure of non-paternity, stigma and discrimination, negative impact on self-esteem, and anxiety about future health.

The USPSTF concludes that there is high certainty that the net benefit of screening for sickle cell disease in newborns is substantial.

Clinical Considerations

Patient population under consideration: This recommendation applies to all newborns.

Screening tests: Screening for sickle cell disease in newborns is mandated in all 50 states and the District of Columbia. Most states use either thin-layer isoelectric focusing (IEF) or high performance liquid chromatography (HPLC) as the initial screening test. Both methods have extremely high sensitivity and specificity for sickle cell anemia. Specimens must be drawn prior to any blood transfusion due to the potential for a false negative result as a result of the transfusion. Extremely premature infants may have false positive results when adult hemoglobin is undetectable.[3]

Timing of screening: All newborns should undergo testing regardless of birth setting. In general, birth attendants should make arrangements for samples to be obtained, and the first physician to see the child at an office visit should verify screening results. Confirmatory testing should occur no later than 2 months of age.

Treatment: Children with sickle cell anemia should begin prophylactic penicillin by 2 months of age and receive pneumococcal immunizations at recommended intervals.

Other Considerations

Research Needs/Gaps: Screening tests will identify approximately 50 sickle cell carriers for every infant diagnosed with sickle cell disease. Research is needed to determine the psychosocial effects of communicating newborn carrier status information, and to identify the types of counseling practices most likely to benefit families and minimize harmful effects. Research is also needed on alternative methods of screening capable of identifying only clinically significant hemoglobinopathies.

Discussion

In 1996, the USPSTF reviewed the evidence for screening for sickle cell disease in newborns and recommended screening.[1] In 2007, the USPSTF performed a brief literature review and determined the benefits of screening continue to be well established. This update included a search for new and substantial evidence on the benefits and harms of screening.[4] The USPSTF found no new substantial evidence on the benefits and harms of screening for sickle cell disease in newborns, and therefore reaffirms its recommendation that all newborns be screened for sickle cell disease. The 1996 recommendation statement and supporting materials, and the 2007 summary of the updated literature search, can be found at www.preventiveservices.ahrq.gov.

Recommendations of Others

The American Academy of Family Physicians,[5] the American Academy of Pediatrics,[6] and the American College of Medical Genetics[7] strongly recommend universal newborn screening for sickle cell disease.

References

1. U.S. Preventive Services Task Force. Screening for Hemoglobinopathies. In: Guide to Clinical Preventive Services, 2nd edition. Alexandria, VA: International Medical Publishing; 1996:485-94.
2. Lorey F, Cunningham G, Shafer F, Lubin B, Vichinsky E. Universal screening for hemoglobinopathies using high-performance liquid chromatography: clinical results of 2.2 million screens. Eur J Hum Genet 1994;2(4):262-71.
3. National Institutes of Health. The Management of Sickle Cell Disease, 4th Ed. revised June 2002. NIH National Heart, Lung and Blood Institute. NIH Publication No. 02-2117. http://www.nhlbi.nih.gov/health/prof/blood/sickle/sc_mngt.pdf. Accessed August 2, 2007.
4. Lin K, Barton M. Screening for Hemoglobinopathies in Newborns: A reaffirmation update for the US Preventive Services Task Force. Evidence Synthesis #52. Rockville, MD: Agency for Healthcare Research and Quality. AHRQ Pub No. 07-05104-EF-1. Available at http://www.ahrq.gov/clinic/serfiles.htm#sicklecell.
5. American Academy of Family Physicians. Summary of Recommendations for Clinical Preventive Services. Revision 6.3, March 2007, p. 8: Hemoglobinopathies. Available at http://www.aafp.org/online/en/home/clinical/exam.html. Accessed August 2, 2007.
6. Kaye CI, Accurso F, La Franchi S, et al. Newborn screening fact sheets. Pediatrics 2006;118(3):e934-63.
7. American College of Medical Genetics. Newborn screening: toward a uniform screening panel and system. Genetics in Medicine 2006;8(5, Suppl):1S-11S.

Members of the U.S. Preventive Services Task Force

Corresponding Author: Ned Calonge, MD, MPH, Chair, U.S. Preventive Services Task Force, c/o Program Director, USPSTF, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, e-mail: uspstf@ahrq.gov.

Members of the U.S. Preventive Services Task Force* are Ned Calonge, MD, MPH, Chair, USPSTF (Chief Medical Officer and State Epidemiologist, Colorado Department of Public Health and Environment, Denver, CO); Diana B. Petitti, MD, MPH , Vice-chair, USPSTF (Adjunct Professor, Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Sierra Madre, CA);Thomas G. DeWitt, MD (Carl Weihl Professor of Pediatrics and Director of the Division of General and Community Pediatrics, Department of Pediatrics, Children's Hospital Medical Center, Cincinnati, OH); Allen J. Dietrich, MD (Associate Director for Population Sciences, Dartmouth Medical School, Hanover, NH); Leon Gordis, MD, MPH, DrPH (Professor, Epidemiology Department, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD); Kimberly D. Gregory, MD, MPH (Director, Women's Health Services Research and Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Cedars-Sinai Medical Center, Los Angeles, CA); Russell Harris, MD, MPH (Professor of Medicine, Sheps Center for Health Services Research, University of North Carolina School of Medicine, Chapel Hill, NC); George Isham, MD, MS, (Medical Director and Chief Health Officer, HealthPartners, Minneapolis, MN); Michael L. LeFevre, MD, MSPH (Professor, Department of Family and Community Medicine, University of Missouri School of Medicine, Columbia, MO); Rosanne M. Leipzig, MD, PhD (Professor, Department of Geriatrics and Adult Development, Medicine, and Health Policy; Vice Chair for Education; Mount Sinai School of Medicine, New York, NY): Carol Loveland-Cherry, PhD, RN (Executive Associate Dean, Office of Academic Affairs, University of Michigan School of Nursing, Ann Arbor, MI); Lucy N. Marion, PhD, RN (Dean and Professor, School of Nursing, Medical College of Georgia, Augusta, GA); Virginia A. Moyer, MD, MPH (Professor, Department of Pediatrics, University of Texas Health Science Center, Houston, TX); Judith K. Ockene, PhD (Professor of Medicine and Chief of Division of Preventive and Behavioral Medicine, University of Massachusetts Medical School, Worcester, MA); George F. Sawaya, MD (Associate Professor, Department of Obstetrics, Gynecology, and Reproductive Sciences and Department of Epidemiology and Biostatistics, University of California, San Francisco, CA); and Barbara P. Yawn, MD, MSc (Director of Research, Olmstead Research Center, Rochester, MN).

*Members of the Task Force at the time this recommendation was finalized. For a list of current Task Force members, go to www.ahrq.gov/clinic/uspstfab.htm.

AHRQ Publication No. 07-05104-EF-2
September 2007

TABLE 1

What the USPSTF Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.	Offer/provide this service only if there are other considerations in support of the offering/providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality or conflicting, and the balance of benefits and harms cannot be determined.	Read “Clinical Considerations” section of USPSTF Recommendation Statement. If offered, patients should understand the uncertainty about the balance of benefits and harms.

TABLE 2

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The U.S. Preventive Services Task Force defines certainty as **"**likelihood that the USPSTF assessment of the net benefit of a preventive service is correct**".** The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: - the number, size, or quality of individual studies; - inconsistency of findings across individual studies; - limited generalizability of findings to routine primary care practice; or - lack of coherence in the chain of evidence.

	As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: - the limited number or size of studies; - important flaws in study design or methods; - inconsistency of findings across individual studies - gaps in the chain of evidence; - findings not generalizable to routine primary care practice; or - a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.