Screening for Phenylketonuria (PKU): U.S. Preventive Services Task Force Reaffirmation Recommendation Statement

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Summary of Recommendation & Evidence

The United States Preventive Services Task Force (USPSTF) recommends screening for phenylketonuria (PKU) in newborns. (This is a grade "A" recommendation.)

Rationale

Importance
PKU is an inborn error of phenylalanine metabolism that occurs in from 1 per 13,500 to 1 per 19,000 newborns in the United States. In the absence of treatment during infancy, most persons with this disorder will develop severe mental retardation.(1, 2)

Detection
Two approaches, fluorometry and tandem mass spectrometry, are in common use. The sensitivity and specificity of fluorometry are 100% and 51%, respectively, and of tandem mass spectrometry, 100% and 98%, respectively.(3)

Benefits of Detection and Early Intervention
There is good evidence that detection by neonatal screening and early treatment of PKU substantially improve neurodevelopmental outcomes for affected persons.

Harms of Detection and Early Treatment
False-positive tests could generate considerable parental anxiety.

USPSTF Assessment
The USPSTF concludes that there is high certainty that the net benefit is substantial for screening for PKU in newborns.

Clinical Considerations

Patient Population
This recommendation applies to newborns.

Screening Tests
Screening for PKU is mandated in all 50 states, though methods of screening vary. There are three principal methods used for PKU screening in the United States: the Guthrie Bacterial Inhibition Assay (BIA), automated fluorometric assay, and tandem mass spectrometry. Screening tests are most accurate if performed after 24 hours of life but before the infant is 7 days old.

Treatment
It is essential that phenylalanine restrictions be instituted shortly after birth to prevent the neurodevelopmental effects of PKU.

Timing of Screening
Infants who are tested within the first 24 hours after birth should receive a repeat screening test by 2 weeks of age. Premature infants and those with illnesses should be tested at or near 7 days of age, but in all cases before newborn nursery discharge.

Discussion

In 1996 the USPSTF reviewed the evidence for screening for PKU in newborns and found that the benefits substantially outweighed the harms of screening. The benefits of screening for PKU continue to be well established. This update focused on 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 PKU and therefore, reaffirms that clinicians should screen for PKU in newborns. The 1996 recommendation statement, the 1996 evidence report, and the summary of the updated literature search can be found at www.preventiveservices.ahrq.gov.

Recommendations of Others

According to the American Academy of Pediatrics, PKU screening should occur in newborns older than 24 hours and younger than 7 days. Infants screened before 24 hours of life should be re-screened by 2 weeks of age to detect possible missed cases. All infants should be screened at the time of nursery discharge or transfer regardless of age. Sick infants and premature infants should be screened by 7 days of age, regardless of feeding history or antibiotic treatment.(5) The American Academy of Family Physicians strongly recommends that physicians screen neonates for phenylketonuria.(6) The American College of Medical Genetics recommends that PKU screening be mandated as part of state newborn screening programs.(7)

References

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U.S. Preventive Services Task Force

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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.