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ABBREVIATIONS

AAP—American Academy of Pediatrics
USPSTF—US Preventive Services Task Force
TSB—total serum bilirubin

Opinions expressed in these commentaries are those of the author and not necessarily those of the American Academy of Pediatrics or its Committees.

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In a commentary[1] and update of the 2004 American Academy of Pediatrics (AAP) guideline "Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation"[2] in this issue of *Pediatrics*, Maisels et al recommend that all newborns have a bilirubin measurement before discharge from their birth hospitalization. In contrast, a recommendation statement from the US Preventive Services Task Force (USPSTF),[3] supported by a systematic review,[4]concludes that evidence is insufficient to make that recommendation. As an author of the commentary[1] and the 2004 AAP jaundice guideline[2] who also has been critical of guidelines based on insufficient evidence,[5–11] I have felt particularly torn about this recommendation.

Perhaps partly because I have served as an expert consultant on dozens of heartbreaking kernicterus legal cases,[12] I find the argument in favor of universal bilirubin screening and systematic follow-up persuasive. We know kernicterus is devastating and that, although rare, cases are continuing to occur. Furthermore, anecdotal evidence suggests that many cases could have been prevented by earlier measurement of bilirubin levels, leading to closer follow-up and earlier initiation of appropriate therapy.[13,14] We have not had randomized trials to show that universal screening and systematic follow-up will lead to a reduction in kernicterus, but considerable research in the area of optimizing patient safety suggests that there is room for improvement in the 2004 guidelines. Specifically, we know that in the absence of universal screening, detection and management of clinically significant hyperbilirubinemia during the birth hospitalization relies on several imperfect steps: (1) nurses and doctors need to remember to examine the infant for jaundice; (2) they need to distinguish visually between jaundice that is and is not clinically significant for the infant's age in hours; and (3) they need to combine information from this visual assessment of jaundice and/or a total serum bilirubin (TSB) level with knowledge of the newborn's other risk factors to determine the need for and timing of bilirubin measurements, follow-up visits, and treatments. We also know that nurseries are busy places and that sometimes people may not do things that they should[15] or might do them under suboptimal conditions, such as assessing jaundice in the dim light found in many hospital rooms. Finally, compared with the devastating effects of kernicterus, the costs and risks of screening seem low, particularly with a transcutaneous bilirubinometer, which may actually decrease the number of serum bilirubin measurements obtained.[16]

On the other hand, as a proponent of evidence-based medicine, I recognize the insufficiency of the data to support the recommendation.[3,4] The rationale outlined above would apply whether the incidence of kernicterus were 1 in 10 000 or 1 in 1 million, but surely the potential benefits of screening depend on how much kernicterus there is to

prevent, and this is not known. Even if we knew the incidence of kernicterus, the proportion that might be preventable by screening and systematic follow-up is unclear. Although plaintiffs in malpractice cases commonly assert that infants with bilirubin levels in the 40s at 4 or 5 days must have had proportionately high levels at the time of discharge (even if no or minimal jaundice was noted at that time), there is little evidence to support this assertion. Studies of the predictive value of early bilirubin levels have had much lower levels of hyperbilirubinemia (TSB of 17–20 mg/dL).[3] Because they may have different causes, such as glucose-6-phosphate dehydrogenase deficiency and infection, the very high levels that lead to kernicterus may be less predictable. Moreover, several studies have revealed that in the absence of any jaundice, a TSB level of $\geq$12 mg/dL is extremely unlikely.[17–20] As an experienced generalist who believes he can recognize at least some newborns who definitely are not jaundiced, I sympathize with colleagues who may question the cost-efficacy of measuring bilirubin (particularly if it involves an additional poke or trying to squeeze more blood out of a recalcitrant heel) in a light-skinned 2-day-old who has no hint of jaundice. Requiring a bilirubin measurement for every such infant because some clinicians may forget or be careless feels like keeping the whole class after school for the transgressions of a few.

After doing my best to reconcile these opposing viewpoints, I believe that universal predischarge bilirubin screening is a good idea but that the evidence is not sufficient to recommend it in an AAP guideline. This is consistent with AAP policy. In a 2004 statement, the Steering Committee on Quality Improvement and Management outlined levels of evidence and strengths of AAP guidelines.[21] The policy stated that except in "exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit or harm," if the level of evidence is "expert opinion, case reports, and reasoning from first principles," a course of action should be designated an option rather than a recommendation. Because, as is explicitly acknowledged in the commentary, expert opinion, case reports, and reasoning from first principles are exactly the level of evidence that supports the recommendation for universal bilirubin screening, and because we wanted to make that recommendation, it needed to be published as a commentary rather than a guideline.

Is this AAP policy on evidence and guideline recommendations a good one? I believe it is. Practicing clinicians need and appreciate guidance from experts, but they also recognize the impossibility of following every guideline that an expert committee might recommend for them and need protection from well-meaning but sometimes paternalistic committees with their own agendas.[22] Guideline committees tend to be dominated by academics and subspecialists with special interest, expertise, and even emotional investment in the diseases for which they are producing guidelines.[23] Most of us authors of the hyperbilirubinemia commentary are no exception.[12,24] Although interest and expertise are invaluable, the career focus on a particular disease, with resulting close relationships with funders, patients, advocacy groups, industry, and each other, may lead to a narrow perspective in which heroic efforts at preventing or treating the target disease feel justified, even when a favorable balance of benefits over risks and costs is uncertain.[23] And, although slavishly adhering to evidence standards could lead to failure to recommend beneficial treatments[25,26] even what seem like obvious, common-sense interventions can have unintended adverse consequences.[27,28]

The USPSTF uses a different model for producing guidelines, in which expertise at appraising and synthesizing evidence trumps disease-specific expertise.[29] Recommendations of the USPSTF are typically based on the results of systematic reviews of evidence, often performed by one of the Agency for Healthcare Research and Quality's evidence-based practice centers. Such thorough reviews are not within time, expertise, and budget constraints of most guideline committees. Ironically, however, the recommendation to measure a bilirubin level for every infant before discharge was the subject of just such a review,[4] which concluded that the evidence is insufficient to make a recommendation for or against universal bilirubin screening ("I" rating).[3]

The USPSTF statement comments not only on the lack of evidence that universal bilirubin screening will prevent bilirubin encephalopathy but also on the insufficiency of evidence regarding risks and efficacy of phototherapy.[3] This is important, because an unintended consequence of institution of universal bilirubin screening might be a greater focus on the danger of hyperbilirubinemia, leading to excessive use of phototherapy. There is evidence that this has occurred in the Northern California Kaiser Permanente Medical Care Program, in which increased bilirubin testing was associated with a decrease in bilirubin levels of >25 mg/dL and also an increase in use of phototherapy at levels lower than those recommended in the 2004 AAP guideline.[30] Thus, it is worth stressing that the recommendation for bilirubin screening should not be misinterpreted as suggesting the need for phototherapy at lower bilirubin levels.

The Maisels et al commentary on hyperbilirubinemia published in this is-

sue came about because of a need to clarify the 2004 guideline and because the AAP had been asked for a statement that either recommended universal bilirubin screening or explained why not. I suspect that having the recommendation for universal screening come in the form of a commentary, rather than a guideline, will be disappointing to both advocates and opponents of universal screening. However, I believe it is the right decision. For now, it represents what some bilirubin experts believe is reasonable on the basis of limited evidence. With additional research, we hope to be able to make a stronger recommendation in the future.

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