podcasts available has also significantly increased from a modest 1 or at most 2 per issue to about 5. Podcasts are ideal to catch up on the latest from Clinical Chemistry while driving or commuting, as well as to gain some unpublished insights from the author.

We hope that you have enjoyed this audio feature, and if you have not yet listened, we invite you to sample those that might interest; look for the distinctive red earbud icon in the Table of Contents. The Clinical Chemistry podcasts are available to all, with no subscription or fee required. It is the journal’s intent to continue this feature, as well as to further explore video and other capabilities of electronic media.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

References

Newborn Screening by Whole-Genome Sequencing: Ready for Prime Time?

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In a recent article in in Science Translational Medicine, Knoppers et al. bring to light issues surrounding a potential shift in newborn screening (NBS) programs from biochemical assays to sequencing (1). As the cost of whole-genome sequencing (WGS) falls, genetic testing of all newborns is increasingly a fiscal option. This proposition is exciting, terrifying, or both, depending on your perspective. The initial and current tenant of NBS programs is to benefit the “best interests of the child.” Testing has been intentionally limited to detection of severe health conditions for which early treatment improves morbidity or mortality. Because NBS is currently well accepted by society as being fully for the well-being of the child and the family, testing is completed with no explicit consent from parents. If this testing is expanded to WGS, however, studies show that some parents may choose to opt out (2).

The amount of information generated by shifting to WGS for all newborns would be an exponential increase. Single-gene and multigene disorders could be added to the current diseases tested. Gene testing could also increase the accuracy of current testing and could add pharmacogenetic information, both of which have the potential to improve patient care. Families could seek preventive or therapeutic interventions for their child at an early age and improve the child’s medical or developmental outcome. Identification of some diseases could facilitate diagnosis and treatment of previously undiagnosed family members or inform parents of their carrier status to assist in family planning decisions. The potential for population and research studies to discover new disease associations would be virtually limitless. In addition, the emotional stress and significant cost of

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Nonstandard abbreviations: NBS, newborn screening; WGS, whole-genome sequencing; ACMG, American College of Medical Genetics and Genomics.
a family’s “diagnostic odyssey” for a sick child could be dramatically shortened (1).

Not all knowledge, however, is necessarily beneficial, and even beneficial information is not always desirable. This was recently exemplified by the American College of Medical Genetics and Genomics’ (ACMG) retraction of their requirement for laboratories to report incidental findings from 56 “medically actionable” genes regardless of patient preferences. This policy change also demonstrates the “moving target” nature of ethical issues surrounding genetic testing expansion. There will be genetic information with unclear clinical significance, which places a burden on families and the healthcare system. Even deleterious genetic changes may have no immediate consequence. The ACMG and the American Academy of Pediatrics have recently reinforced their recommendation that discovery of late-onset conditions be deferred until adulthood, when the patient is psychologically able to consent to obtaining this information. Furthermore, the data generated at NBS, whether stored as interpreted variants or raw sequencing files, will undoubtedly be incomplete or inaccurate when the child reaches adulthood. Storage of this information until the newborn reaches consenting age could also place an overwhelming burden on healthcare systems—not to mention the responsibility for disclosing information at the proper time with an updated interpretation.

The most concerning potential outcome is launching the largest expansion to date of NBS without properly preparing physicians and parents. Mandating testing for many additional diseases by a new technology will be understandably daunting to parents if they are not educated before the birth of their child. This can be expected to result in decreased compliance unless parents and physicians are fully informed about the potential benefits and risks of NBS by WGS. Primary care physicians often feel overwhelmed by current rare disorders discovered by NBS, and significantly expanding NBS will place even more burden on these physicians. Despite the numerous obstacles, implementation of NBS by WGS is likely inevitable. If we begin the educational process now, we just might be able to prepare physicians and parents before the floodgates of genetic information open.

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References

A New Series from JAMA: Diagnostic Test Interpretation

The Journal of the American Medical Association (JAMA) has started a new educational series of interest to Clinical Chemistry readers, particularly AACC’s Society for Young Clinical Laboratorians (SYCL) members. The May 21, 2014, issue of JAMA included the first article in the Diagnostic Test Interpretation series (1). The series uses real patient examples of common, yet difficult or confusing, clinical situations to discuss the added value of a specific test. Each article includes the patient’s test results with reference ranges, and readers are asked to select the best interpretation of the result in the given scenario. A brief summary of the test characteristics, including known limitations and the evidence base for its diagnostic utility, follows. Alternative diagnostic strategies and cost information are also provided. The goal is to aid readers in building their diagnostic test interpretation and utilization skills.

Reference