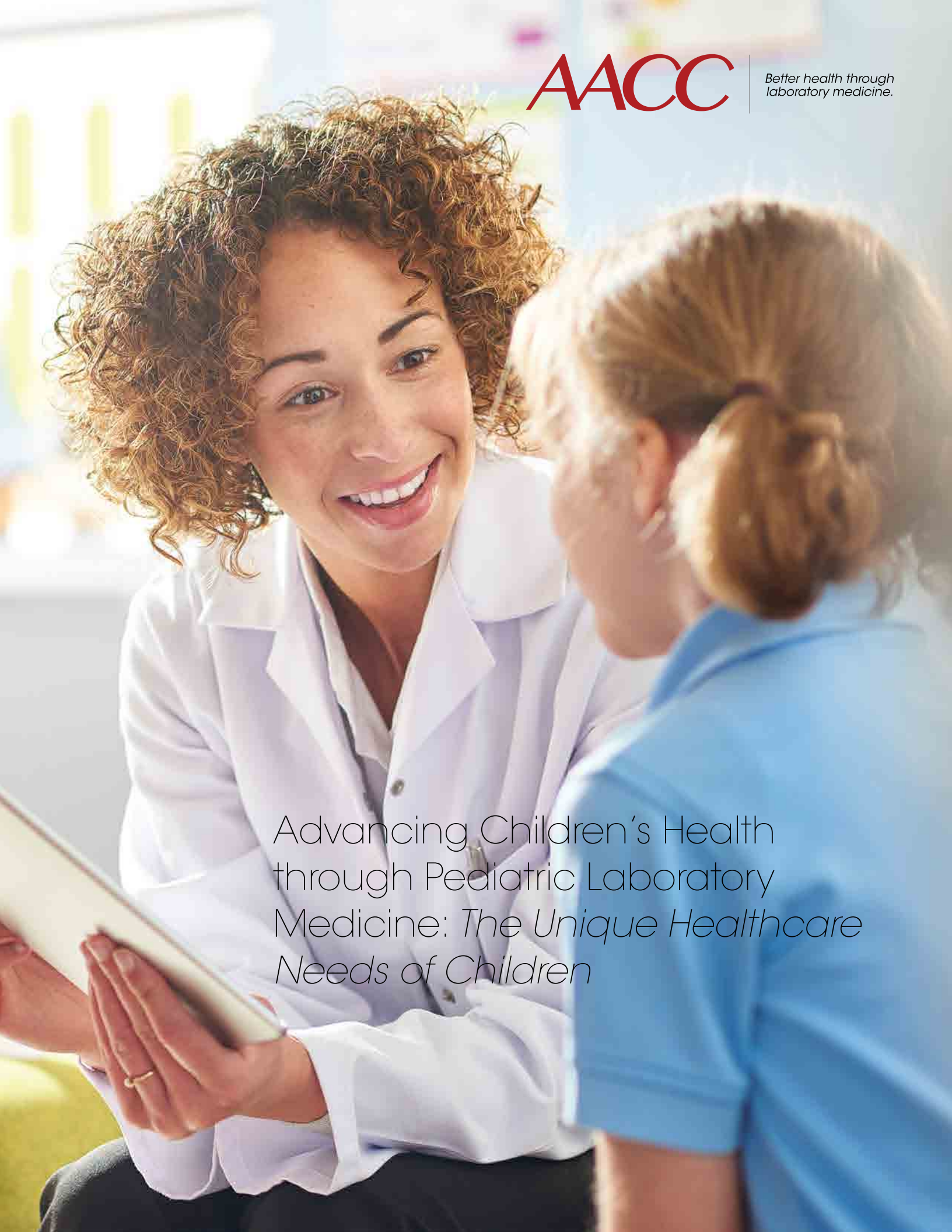
AACC

Better health through laboratory medicine.



Advancing Children's Health through Pediatric Laboratory Medicine: *The Unique Healthcare Needs of Children*

Advancing Children's Health through Pediatric Laboratory Medicine: *The Unique Healthcare Needs of Children*

AACC

Better health through laboratory medicine.

The Unique Healthcare Needs of Children

Pediatric laboratory medicine is integral to the healthcare of infants, children, and adolescents [1]. About 30 percent (97.1 million) of the U.S. population is under the age of 18 [2]. Annually, youths account for more than two million hospitalizations and about 25 million outpatient visits, in addition to annual well-patient visits. Approximately three billion pediatric laboratory tests are performed in more than 250,000 Clinical Laboratory Improvement Amendment (CLIA)-certified laboratories in the U.S. [1, 3, 4, 5, 6].

As essential members of the healthcare team, pediatric laboratory professionals ensure high quality and timely test results that can have different implications depending on the child's developmental stage, gender, ethnicity, and age. Lab professionals can help physicians interpret and better understand lab results. With this information, pediatricians, family practice and other related physicians assess health, diagnose disease, and plan and monitor treatment for the patients under their care.

Pediatric laboratory professionals continually assess and adapt to today's complex, changing healthcare environment and offer their vital professional expertise to clinicians. Young patients and their families receive accurate diagnoses and treatment every day for common and rare childhood illnesses partly thanks to the resources provided by pediatric laboratory medicine experts.

Clinical Laboratory Improvement Amendments

In 1988, Congress passed and President Ronald Reagan signed into law the Clinical Laboratory Improvement Amendments. This statute, for the first time, placed all laboratory testing under a single set of standards administered by the Centers for Medicare and Medicaid Services. The regulations mandate that laboratories comply with personnel, quality control, quality assessment, and proficiency testing requirements and participate in biennial inspections to ensure they are providing reliable testing.

About Pediatric Laboratory Professionals

Pediatric laboratory medicine teams produce essential, objective test results for healthcare providers. They work in a variety of public and private settings, including hospitals, academic institutions, physicians' offices, and independent facilities. The laboratories might or might not serve solely pediatric patients; however, pediatric laboratory specialists emphasize pediatric healthcare regardless of the overall setting in which they work.

In U.S. hospitals, most newborn blood draws are performed by phlebotomists, who have at least one year of specialized practical experience in addition to a high school diploma or equivalent. Phlebotomists use specialized techniques to draw small-volume blood samples from pediatric patients with minimal pain or discomfort. Clinical laboratory scientists run laboratory tests on standard equipment following protocols and procedures for small-volume samples that ensure reliable results. These well-trained professionals typically have two- and/or four-year degrees in a relevant scientific discipline with hands-on professional pediatric training and preferential certification. With at least a bachelor's degree, specialist certification, and years of experience, pediatric laboratory managers or supervisors are responsible for daily laboratory operations, including quality control and other regulatory compliance activities.

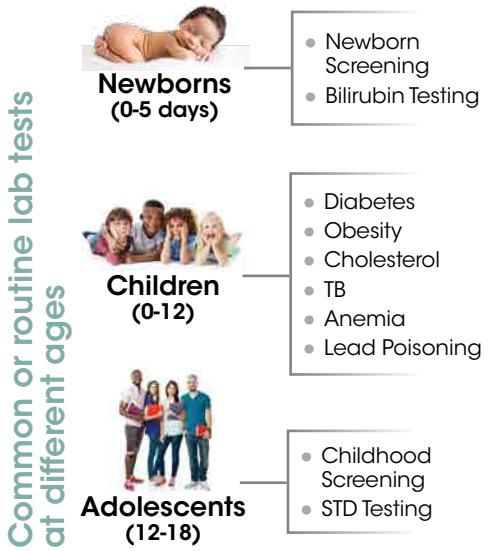
Pediatric laboratory directors oversee clinical and operational aspects of the laboratory. These individuals are Board-certified pathologists with medical degrees (**MD or MD/PhD**) in pathology, pediatric pathology or a related specialty, or Board-certified clinical chemists and other PhD-level scientists in related fields. They ensure the laboratory meets all quality standards and regulatory requirements while meeting clinical needs. This includes validating the accuracy and precision of FDA-approved tests and addressing gaps in commercially available test offerings with laboratory developed tests. They also ensure completion of quality assurance testing on laboratory equipment. Regularly, they evaluate the process of clinical testing, from when the test is ordered and the sample collected, to when the result reaches the physician. Laboratory directors use the findings of these assessments to improve laboratory procedures. They also work with clinical partners to make test utilization and results interpretation efficient and effective.

With their advanced degrees and scientific expertise, laboratory directors often conduct research, working to translate scientific discoveries into clinical care. Additionally, they generate and contribute laboratory data to clinical practice guidelines and evidence-based medicine and work with physicians to integrate and maximize the usefulness of informatics [1]. At academic institutions, laboratory directors are faculty members, responsible for educating students and doctors in training. Pediatric laboratory directors undertake these activities with an emphasis on children's health.

Together, laboratory professionals play an integral role in providing high quality patient care.

Pediatric Lab Tests

Laboratory tests and screens are integral components to pediatric healthcare in all stages of childhood. In the U.S., pediatric laboratory screening begins within 48 hours of birth for more than four million infants per year. Pediatricians and family practice physicians rely on laboratory screens and tests to ensure the health and well-being of their patients from birth through adolescence [7, 8, 9, 10].



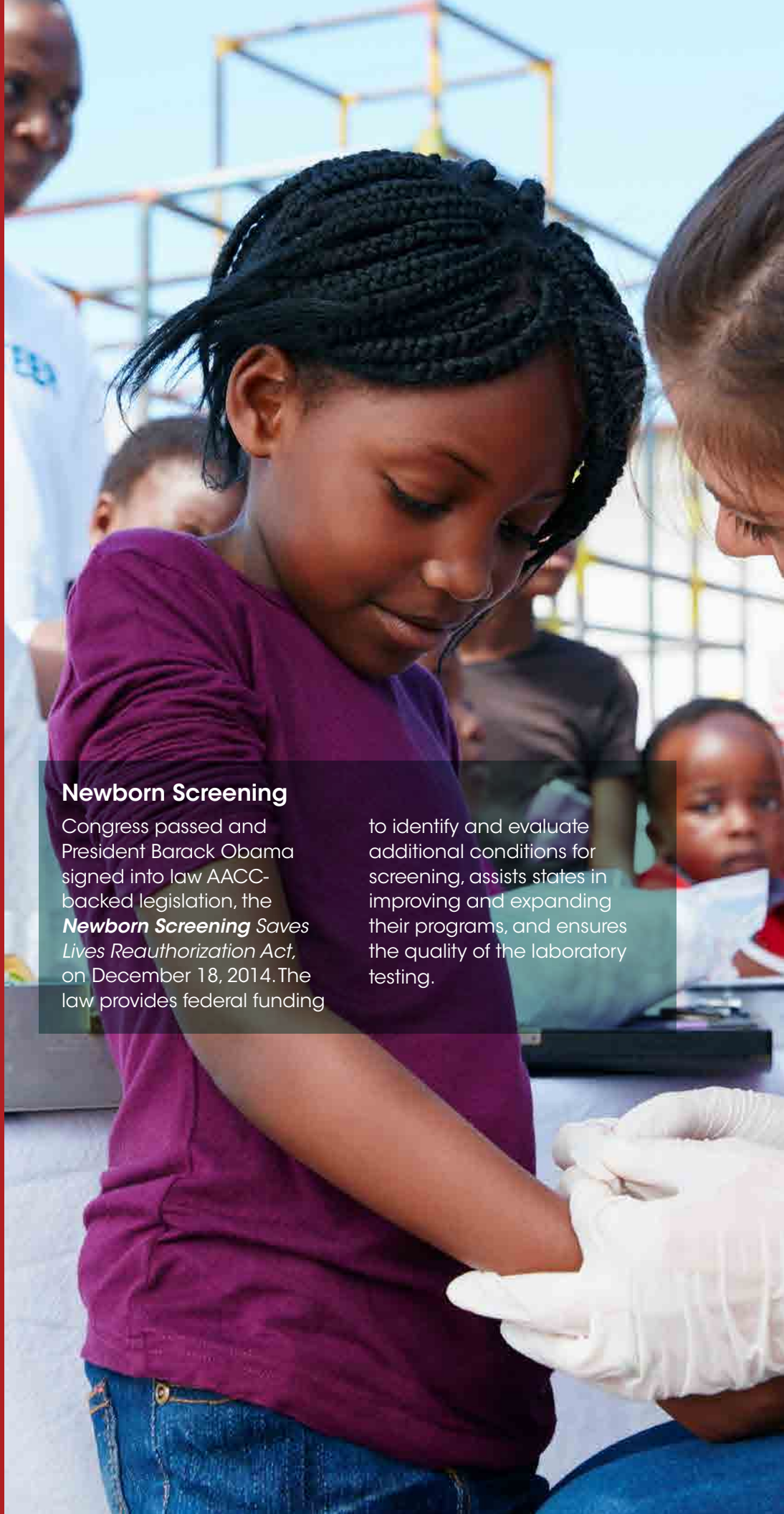
In addition to standard screens, a bilirubin test might be ordered on infants who appear jaundiced. Bilirubin is a by-product of the normal breakdown of red blood cells and its build up in the blood results in the characteristic yellow skin and eye discoloration of jaundice. Most two- to four-day-old newborns have mild jaundice, but as the liver matures this naturally dissolves within one to two weeks [11, 12]. If untreated, very high bilirubin levels can cause brain and central nervous system damage that can result in seizures and permanent hearing loss, and the blood test is required to determine whether bilirubin levels are sufficiently high to warrant treatment.

During annual wellness visits, pediatricians may request children (0 to 12 years old) be screened for diabetes, obesity, high cholesterol, tuberculosis, iron deficiency anemia and lead poisoning, depending on determined risk. According to the CDC, about 250,000 children between one and five years old have blood lead concentrations above recommended levels [13]. Additionally, the rate of obesity has more than doubled in children and quadrupled in adolescents in the U.S. during the past 30 years, increasing the number at risk for cardiovascular disease and diabetes [14].

With physician discretion and risk assessment, teenagers (13 to 18 years old) may be screened for some of the same conditions as younger patients at annual visits. The CDC also recommends testing for certain sexually transmitted diseases, like HIV. In 2014, an estimated 9,731 youths in the U.S. aged 13 to 24 were diagnosed with HIV [15, 16].

Spotlight on Pediatric Laboratory Medicine

In support of children and their families, pediatric laboratory professionals work with pediatricians, and provide their unique expertise to help improve health outcomes. Impactful examples of key areas pediatric laboratory professionals contribute include:



Newborn Screening

Congress passed and President Barack Obama signed into law AACC-backed legislation, the ***Newborn Screening*** *Saves Lives Reauthorization Act,* on December 18, 2014. The law provides federal funding to identify and evaluate additional conditions for screening, assists states in improving and expanding their programs, and ensures the quality of the laboratory testing.

Public Health and Prevention

Spotlight on Pediatric Laboratory Medicine

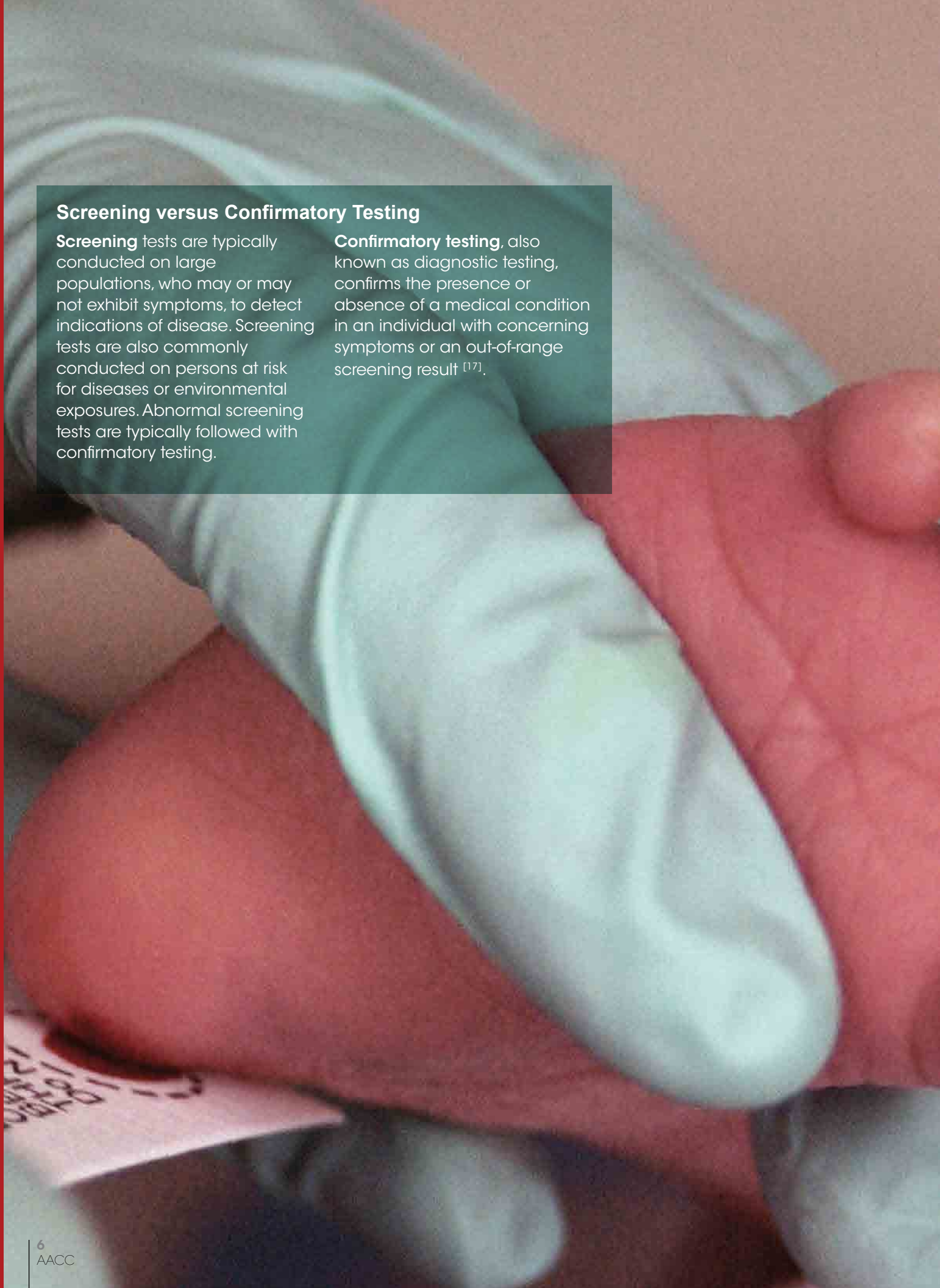
Clinical laboratory testing is integral to public health programs, which focus on identifying diseases, either within an individual or within a population, to prevent them from causing harm to the individual or spreading to others. These programs may employ targeted testing or universal screening approaches. Children may be tested because they meet specific criteria for being at risk for a disease or condition. Alternatively, all children, despite risk, may be screened for a specific disease or condition. In either case, lab tests can detect diseases or conditions before signs and symptoms occur, allowing for treatment before permanent damage is done. This is especially important in pediatrics, as catching problems early in a developing child prevents long-term complications, like cognitive or physical impairment.

Screening children for lead exposure is an example of how the judicious use of lab tests has vastly improved public health. Lead is a poison that is found in the environment as a result of the historical use of leaded paints and gasoline, and aging plumbing. Exposure to lead can cause irreversible cognitive damage. Children are more susceptible to lead toxicity than adults because they have not fully developed the metabolic system to eliminate lead from their bodies efficiently. Young children are also more likely to be exposed to lead because they play and crawl on the floor and have tendencies to ingest non-food objects, like paint chips. The impact of lead poisoning to the brain and overall development may not be apparent until long after the exposure occurs. However, clinical laboratory testing can detect lead in a child's blood, so treatment can be initiated to remove lead from the child, and action can be taken to eliminate the source of the lead from the child's environment.

> "Lab tests can detect diseases or conditions before signs and symptoms occur, allowing for treatment before permanent damage is done."

Pediatric laboratory medicine professionals have developed the capability to detect very low levels of lead in a child's blood. This technological advance was critical because detrimental health effects can begin with low levels of exposure, and very high lead concentrations are difficult to remove from an individual. As a result of the expertise and diligence of laboratory professionals, low-level lead testing is now widely available in hospitals, physician's offices, and mobile health centers.

Although lead poisoning is one example, **newborn screening** and cholesterol screening are other commonly encountered examples where lab tests are prominent components of public health and prevention programs for children.



Screening versus Confirmatory Testing

Screening tests are typically conducted on large populations, who may or may not exhibit symptoms, to detect indications of disease. Screening tests are also commonly conducted on persons at risk for diseases or environmental exposures. Abnormal screening tests are typically followed with confirmatory testing.

Confirmatory testing, also known as diagnostic testing, confirms the presence or absence of a medical condition in an individual with concerning symptoms or an out-of-range screening result [17].

Newborn Screening

Spotlight on Pediatric Laboratory Medicine

Newborn screening (NBS) is a premier public health program that identifies newborns who may appear healthy immediately after birth but may have a severe-but-treatable congenital or inherited genetic disorder. Fortunately for more than 12,000 affected children and their families in the U.S. each year, early laboratory testing and disease classification through initial newborn **screening** leads to faster life-altering interventions [8, 18].

As of today, nearly 98% of all infants born in the U.S. are screened, through state-run NBS programs, for most or all of the 34 disorders recommended by the federal Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) [19, 20]. If the screening identifies an abnormal result, professional NBS coordinators will contact the healthcare provider to convey the laboratory results. As necessary, the physician will then make an appropriate medical referral for additional **confirmatory diagnostic testing** to be performed by pediatric laboratory specialists [19].

Phenylketonuria (PKU) is a treatable genetic disorder screened in all U.S. states to enable preventative treatment. The condition is characterized by the inability of the body to breakdown phenylalanine, an amino acid found in protein-based foods. If untreated, PKU can lead to irreversible brain damage, resulting in mental disability, seizures, and other adverse outcomes. Early diagnosis of PKU enables patients to lead healthy, able lives with an adjusted diet. Pediatric laboratory professionals developed the PKU screen in response to the then-emerging scientific knowledge of how PKU develops and the ongoing clinical need for the test.

Another disease that is screened by many U.S. state newborn screening programs is cystic fibrosis (CF), which causes severe damage to the lungs and the digestive system. CF is caused by defects in a protein that controls the movement of salt in and out of cells. Patients with this disease are prone to lung infections and intestinal problems due to thick mucus in the airways and the pancreas. Babies with a positive screen for cystic fibrosis are referred to specialized pediatric testing centers for confirmatory testing. Then, laboratory professionals may confirm the diagnosis by measuring chloride in a patient's sweat, and if affected, the child is started on life-long treatment [21].

NBS programs also aim to identify many inborn errors of metabolism in which the infant's body cannot make essential chemicals needed for proper body functioning. This leads to accumulation of toxic substances related to the breakdown of food into nutrients (metabolites) that may cause seizures, loss of muscle tone, failure to thrive, coma and even death. Early and accurate laboratory diagnosis is the key to managing and treating these children.

Childhood Illnesses

Spotlight on Pediatric Laboratory Medicine

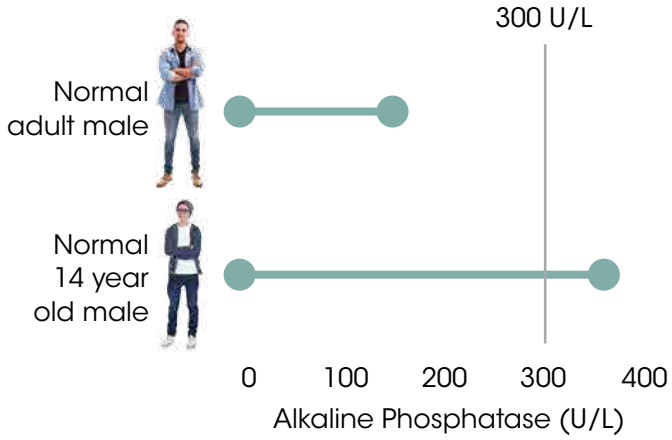
Children's diseases are often unique and different from adult disorders. Specialized laboratory tests are required to accurately diagnose, treat, and manage these diseases. Many childhood illnesses are caused by infectious agents. Although vaccinations have tremendously decreased the incidence of a number of previously common infectious diseases, infections still remain the leading cause of childhood illnesses.

Common childhood infections include respiratory syncytial virus (RSV) infection which may cause airway inflammation and pneumonia, and streptococcus bacterial (strep) infection that is a leading cause of sore throat. Since children, particularly newborns, do not have fully developed immune systems, prompt diagnosis is needed to treat these patients. To diagnose these and other infections, laboratory professionals generally use rapid screening tests that provide quick preliminary diagnosis for early patient management. Definitive tests are used to confirm the results of screening tests. For example, a rapid strep test can provide results within a few minutes from a patient throat swab. If the test is positive, the physician prescribes antibiotics and treatment can begin immediately, minimizing disease duration and the risk of the patient spreading the infection to others. If the screen is negative, the laboratory will perform a culture from the throat swab sample to confirm the negative preliminary results. If the throat culture turns out to be positive, the laboratory professional contacts the ordering physician so the patient can be prescribed antibiotics at that time [22].

> "Children are not small adults."

Another example of a childhood disease is Type 1 diabetes. In this disease, a child's body cannot make a hormone called insulin. This hormone is needed to process the sugar glucose, which is a primary source of the body's energy. Patients with Type 1 diabetes have increased glucose in the blood and urine resulting in increased thirst and urination. Since the body cannot appropriately utilize glucose, the pediatric patient experiences extreme hunger and increased food intake. If untreated, Type 1 diabetes can lead to serious complications, such as heart, kidney and eye disease. Laboratory professionals play an important role in the diagnosis and treatment of diabetes. They develop sensitive and precise laboratory and point-of-care glucose tests. They invest time and resources into the development of reference intervals and they collectively collaborate on standardization and harmonization initiatives. They do all this in addition to daily quality assurance and management efforts to ensure accurate test results.

Normal Alkaline Phosphatase Intervals



Pediatric Reference Intervals

AACC supports the creation of a national repository to collect and store pediatric samples from healthy children that can be used by medical device manufacturers and clinical laboratories to develop more-precise age, ethnicity, development and gender specific reference intervals [23].

Pediatric Reference Intervals

Spotlight on Pediatric Laboratory Medicine

To interpret laboratory results, clinicians rely on reference intervals developed by laboratory medicine professionals. Reference intervals, sometimes called the "normal" range, are the set of values for any given lab test that would be expected in a healthy person. If a patient's test result falls outside a reference interval, it can provide a clue to the clinican regarding potential disease in the patient. Without precise reference intervals that accurately reflect the healthy range, physicians may misdiagnose a condition, which could result in patient harm and increased healthcare costs [23].

Pediatric laboratory professionals have long recognized that reference intervals in children differ not only from those for adults, but also amongst themselves, as the intervals will vary at different developmental stages. Alkaline phosphatase, an enzyme found at high levels in both the bone and liver, provides a classic example of how reference intervals in healthy children and adults dramatically differ. In adults, elevated levels of alkaline phosphatase typically indicate liver or bone disease. In children going through puberty, it is normal to have high levels of alkaline phosphatase in the blood, due to bone growth. During growth spurts, levels may reach particularly high levels. A standard reference interval for alkaline phosphatase in a healthy adult male is 53-128 U/L[1]. However, an appropriate reference interval for alkaline phosphatase in a healthy 14 year old boy is 54-369 U/L[1]. Therefore, a result of 300 U/L could trigger a misdiagnosis in a 14 year old boy if the physician relies on the reference interval for a healthy adult male [24].

> "The establishment of robust pediatric reference intervals is critical to ensure accurate diagnosis and treatment of children."

Pediatric laboratory professionals strive to provide clinicians with precise reference intervals to assess the children under their care. The most robust reference intervals are those established using blood samples from healthy children. Unfortunately, the development of more precise pediatric reference intervals is hindered by the limited access to blood samples from healthy children. The establishment of robust pediatric reference intervals is critical to ensure accurate diagnosis and treatment of children [23].

"I find inspiration in the college graduation of a former 2-day-old patient, who was diagnosed and subsequently treated for a genetic disorder."

2016 AACC President
Patricia M. Jones, PhD

Future Directions

Pediatric laboratory medicine is a vital, dynamic, evolving field. Laboratory professionals continually work to develop new and better tests to more quickly identify and diagnose medical conditions and diseases affecting children. Through their dedication, skills and expertise, they have become an integral part of the team that cares for children and saves their lives.

Many children are born with metabolic disorders that can be treated if the disease is identified early enough. Not very long ago, many of these children died or suffered from life-long debilitating conditions because there was no way to diagnose them. Thanks to the collaboration of the laboratory and medical communities, screening tests and treatment plans were developed, and now virtually all newborns are screened for more than 30 diseases/conditions ensuring earlier life-saving treatments. This number is likely to grow as laboratory professionals, medical researchers, and clinicians partner to advance children's health.

Pediatric laboratory medicine is a vital, dynamic, evolving field.

Today, several point-of-care molecular tests exist for the detection of infectious agents. These tests are faster and more precise than their predecessors and allow pediatricians to personalize their patients' care. Laboratory experts continue to develop new and unique molecular tests to promote even more efficient and effective treatment of common childhood infections and diseases.

Advances in pediatric laboratory medicine enable physicians to better assess the risks and benefits to their patients of various care options and choose a plan of action to optimize outcomes [25, 26]. As laboratory medicine continues to advance and increase in promise and complexity, the collaborative development of clinical practice guidelines will be critical to ensure diagnostic advances are appropriately applied. Guidelines provide clinicians with vital information and direction for diagnosing and treating their patients, and laboratory tests are often critical components of decision-making. When laboratory professionals inform the recommended testing paradigms, they enhance the effectiveness of clinical guidelines in improving patient care and reducing overall healthcare costs.

Pediatric laboratory professionals are increasingly at the center of the rapidly changing healthcare delivery system. Clinicians need timely, accurate test data to make faster, more effective patient care decisions. The most vulnerable population is children, many of whom are unable to adequately describe their ailments. Laboratory professionals are the voice of their patients, providing clinicians with the information they need. Pediatric laboratory professionals go to work each day knowing they are helping countless infants, children, and adolescents lead healthier lives.

References

1. Pysher, Theodore J., MD; Bach, Philip R., PhD; Geaghan, Sharon M., MD; Hamilton, Marilyn S., MD, PhD; Laposata, Michael, MD, PhD; Lockitch, Gillian, MBChB, MD, FRCPC . . . Woods, Gail, MD. (2006). "Teaching Pediatric Laboratory Medicine to Pathology Residents" Arch Pathol Lab Med—Vol 130. Pages 1031 – 1038.
2. United States Census Bureau. (2016). "U.S. and World Population Clock." 2 June 2016. http://www.census.gov/popclock/
3. The Lewin Group. (2008). Laboratory Medicine: A National Status Report 2008.[http://wwwn.cdc.gov/futurelabmedicine/pdfs/2007 status report laboratory_medicine_-_a_national_status_report_from_the_lewin_group_updated_2008-9.pdf]
4. Porter, Sheri. (2014). AAFP. COLA White Paper Urges New Focus on Office Lab Protocols. [http://www.aafp.org/news/practice-professional-issues/20141117colapaper.html].
5. Price, Christopher & St John, Andrew. (2014). Clinica Chimica Acta. Anatomy of a value proposition for laboratory medicine. 436, 104–111. doi:10.1016/j.cca.2014.05.017 or [http://www.sciencedirect.com/science/article/pii/S000898811400237X]
6. The Lewin Group. (2009). The Value of Laboratory Screening and Diagnostic Tests for Prevention and Health Care Improvement. [http://www.chi.org/uploadedFiles/Industry_at_a_glance/Lewin Report on Dx Tests (2009).pdf]
7. NIH. Eunice Kennedy Shriver National Institute of Child Health and Human Development. (2013). How many infants are screened in the United States? 14 March 2016. [https://www.nichd.nih.gov/health/topics/newborn/conditioninfo/Pages/infants-screened.aspx]
8. Hopkins, Patrick V. (2013). "The Current State of Newborn Screening (NBS)." 2013 APHL Annual Meeting and 7th Government Environmental Laboratory Conference. Presentation. 17 June 2016. [http://www.aphl.org/conferences/proceedings/Documents/2013/2013-APHL-Annual-Meeting/34Hopkins.pdf#search=12000 babies]
9. The Nemours Foundation. (2016). KidsHealth. "A Directory of Medical Tests" 17 June 2016. http://kidshealth.org/en/parents/labtest2.html#
10. CDC. (2014). "Newborn Screening Laboratory Bulletin." 25 May 2016. [http://www.cdc.gov/nbslabbulletin/bulletin.html]
11. Lab Tests Online. (2015). "Jaundice." 15 April 2016. [https://labtestsonline.org/understanding/conditions/jaundice/]
12. The Nemours Foundation. (2016). KidsHealth. "Jaundice in Healthy Newborns." 25 May 2016. [http://kidshealth.org/en/parents/jaundice.html]
13. Lab Tests Online. (2013). Screening Tests for Children (Ages 2 to 12). 2 June 2015. [https://labtestsonline.org/understanding/wellness/b-children-1/]
14. CDC. Adolescent and School Health. (2015). Childhood Obesity Facts. 2 June 2015. [http://www.cdc.gov/healthyyouth/obesity/facts.htm].
15. Lab Tests Online (2013). Screening Tests for Teens (Ages 13-18). 2 June 2015. [https://labtestsonline.org/understanding/wellness/c-teen-1/]
16. CDC. HIV/AIDS. (2016). "HIV Among Youth." 17 June 2016. http://www.cdc.gov/hiv/group/age/youth/
17. Health Knowledge. (2008). "Differences between screening and -diagnostic tests, case finding." 17 June 2016. [http://www.healthknowledge.org.uk/public-health-textbook/disease-causation-diagnostic/2c-diagnosis-screening/screening-diagnostic-case-finding]
18. AACC. (2014). "Newborn Screening and Improving Childrens Health Position Statement." 25 May 2016. [https://www.aacc.org/health-and-science-policy/advocacy/position-statements/2014/newborn-screening-and-improving-childrens-health]
19. AACC. (2008). "Expanded Newborn Screening." The National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines. 2 June 2016. [https://www.aacc.org/science-and-practice/practice-guidelines/expanded-newborn-screening]
20. U.S. Department of Health and Human Services. Advisory Committee on Heritable Disorders in Newborns and Children. (2016). "Recommended Uniform Screening Panel Core Conditions". 9 May 2016. http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendedpanel/uniformscreeningpanel.pdf
21. Lab Tests Online. (2015). "Cystic Fibrosis." 10 May 2016. https://labtestsonline.org/understanding/conditions/cystic-fibrosis/
22. Lab Tests Online. (2013). "RSV Testing." 5 May 2016. https://labtestsonline.org/understanding/analytes/rsv/tab/test
23. AACC. (2016). "Pediatric Lab Results: The Need for 'Normal'". 5 July 2016. https://www.aacc.org/health-and-science-policy/advocacy/position-statements/2016/pediatric-lab-resultsthe-need-for-normal
24. Burtis, C., Ashwood, E., Bruns, D. (2012). "Tietz Textbook of Clinical Chemistry and Molecular Diagnostics." 5th ed. St. Louis, Missouri: Elsevier.
25. AACC. (2015). "Advancing Personalized/Precision Medicine." 28 June 2016. https://www.aacc.org/health-and-science-policy/advocacy/position-statements/2015/advancing-personalized-precision-medicine
26. Managed Care. (2011). "The History and Future of Personalized Medicine." 28 June 2016. http://www.managedcaremag.com/archives/2011/8/history-and-future-personalized-medicine

Click headings to return to section.

Better health through laboratory medicine.

900 Seventh Street, NW, Suite 400
Washington, DC 20001

Phone: +1.202.857.0717 or
800.892.1400

www.aacc.org

© 2016 American Association for Clinical Chemistry