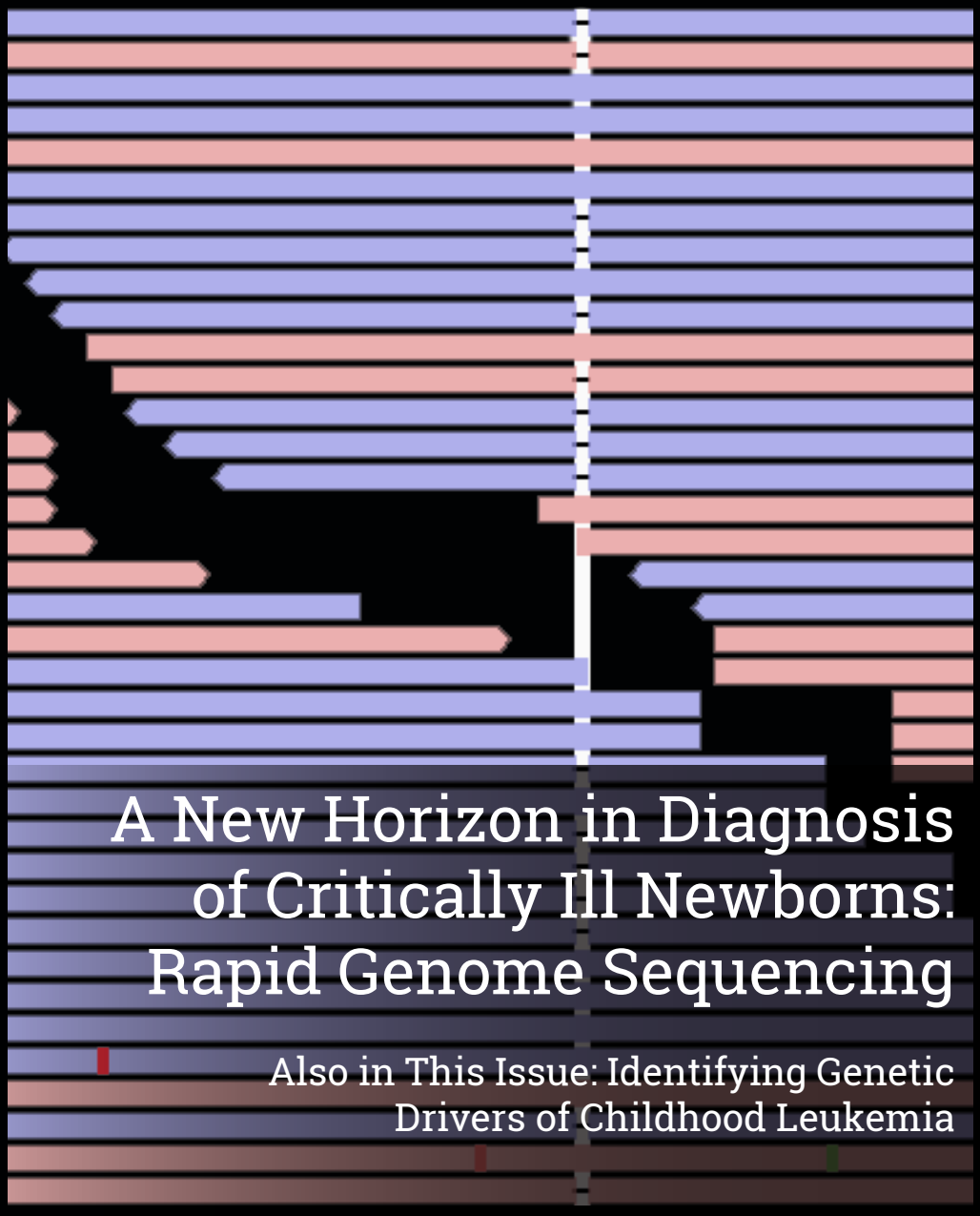
MAGNIFY

the art & science of diagnostic medicine

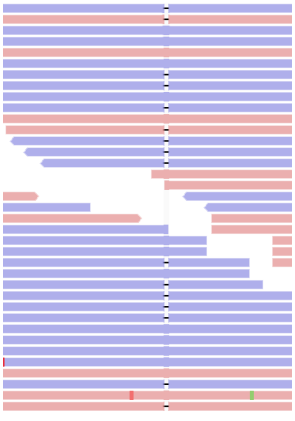


A New Horizon in Diagnosis of Critically Ill Newborns: Rapid Genome Sequencing

Also in This Issue: Identifying Genetic Drivers of Childhood Leukemia

ARUP LABORATORIES

WINTER 2026



About the

Cover

A deidentified example of data generated from massively parallel sequencing that indicate a sequence variant. Data are analyzed to identify pathogenic variants.

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Contents

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A Message From the CEO

At ARUP Laboratories, we understand that the clinical needs of children are unique, often urgent, and deeply personal. Not one among us can bear to see a child suffer.

Through the years, ARUP has remained committed to combining a robust menu of pediatric tests with an investment in research, education, and consultation that helps pediatric care teams make the most informed decisions for each child.

We're proud to lead the clinical laboratory industry in the validation of pediatric-specific reference intervals for test results interpretation and in advancing diagnostic innovation in specialty areas such as biochemical genetics, cytogenetics, autoimmune disease testing, rapid whole genome sequencing, newborn drug screening, pediatric oncology testing, and more.

In this edition of Magnify, we share our approach to pediatric testing, with a special focus on:

- The promise of rapid whole genome sequencing for critically ill newborns, including what we've learned from collaborative efforts that deliver answers in days and inform timely care
- The work of our Hematopathology and Cytogenetics teams for the Children's Oncology Group to detect genetic drivers in pediatric leukemia and clarify findings that guide targeted therapy
- Laboratory stewardship in children's hospitals and how the right guardrails help ensure the right test at the right time, guided by evidence and empathy for young patients and their families

Spend some time with this edition, and I believe you'll emerge with a clear sense of why our teams—and the hospital partners we serve—are unwavering in our efforts on behalf of children. It's work worth celebrating.

Andy Theurer, CEO

ARUP Supports Clinicians With Broad Menu, Expert Guidance in Pediatric Laboratory Medicine

Few things elicit a more immediate response than seeing a child suffering, hearing a whimper of pain or fear.

We immediately want to know what's wrong, and often, the child is not yet capable of communicating why or how they're hurting.

Clinicians rely on laboratory tests to provide answers, but testing can be complicated when the patient is a child. "Children are not just small adults. They have unique clinical needs," said ARUP Laboratories Chief Medical Officer Jonathan Genzen, MD, PhD, MBA, who is also ARUP's senior director of governmental affairs. "Clinicians know that it's vital that the lab tests they order are appropriate for children, and [that they] are provided with appropriate ways to interpret results."

More than 10% of tests performed at ARUP are for patients younger than 18 years, and half of ARUP's hundreds of hospital and health system clients nationwide are medical centers with specialty pediatric care needs or children's hospitals. In ARUP, they find a reference lab with a broad test menu and a comprehensive, caring approach to pediatric testing.

ARUP has led the clinical laboratory industry in validating pediatric-specific reference intervals for test results interpretation and in advancing innovation in biochemical genetic testing, cytogenetics, autoimmune disease testing, rapid whole genome sequencing, newborn drug testing, and pediatric cancer testing, to name just a few areas of specialization.

ARUP also supports clinicians and laboratory leaders with expert consultations and education that differentiate it from other providers of pediatric testing. “We do have expertise that is recognized beyond ARUP, definitely,” said Joely Straseski, PhD, MS, MLS(ASCP), DABCC, FADLM, head of clinical operations for Clinical Chemistry, Toxicology, and Biochemical Genetics.

A Focus on Pediatric Reference Intervals

Straseski, who is also a medical director of Endocrinology and codirector of the Automated Core Laboratory at ARUP, has been a leader of ARUP’s renowned Children’s Health Improvement through Laboratory Diagnostics (CHILDx™) program, which over time has established reliable pediatric reference intervals for numerous assays important in pediatric care.

Reference intervals specific to children at different ages are necessary to accurately interpret test results because children’s biochemistry changes rapidly as they grow and develop, she said. Appropriate reference intervals therefore must account for continuous physiologic changes.

Validating intervals that reflect the gradual nature of development is challenging because it’s difficult to collect enough samples from healthy children across the development spectrum to properly validate reference intervals for different age ranges. CHILDx succeeded because thousands of specimens were collected either during screening before elective surgeries or via community recruitment from healthy children 6 months to 17 years old, with a goal to have from 120 to 240 samples for each year of life from both boys and girls. ARUP built a well-characterized repository of specimens from healthy pediatric patients that enabled a concerted effort to establish intervals for many commonly used tests, resulting in dozens of scholarly publications. Pediatric reference intervals are included on relevant tests in ARUP’s Laboratory Test Directory.

Due to the volume of testing it performs as one of the nation’s four largest reference labs, ARUP also is able in some instances to establish pediatric reference intervals using statistical modeling. Kelly Doyle, PhD, DABCC, FADLM, medical director of Special Chemistry, Endocrinology, and Mass Spectrometry at ARUP, recently did so for a test for

From collecting specimens to accurately interpreting results, pediatric testing requires an approach that considers the unique clinical needs of children.

glucose-6-phosphate dehydrogenase (G6PD) deficiency, a condition that inhibits the body from protecting red blood cells against oxidative stress.

G6PD deficiency is one of the most common genetic deficiencies and can lead to hemolytic anemia, Doyle said. In newborns, it can lead to even more severe consequences, such as bilirubin neurotoxicity, which occurs when bilirubin—a byproduct of damaged red blood cells—builds up in the brain.

Because ARUP has performed tens of thousands of tests in pediatric patients, it's possible to use modeling techniques to look at the distribution of test results in the different age brackets and determine reference intervals for different age ranges that indicate G6PD deficiency.

"These reference intervals are only possible when you have sufficient data," he said. "You couldn't launch a new test and use this type of approach. You have to have a repository of data already to evaluate."

Advocating for Test Harmonization

As ARUP continues to add to the base of knowledge about pediatric reference intervals, the company also is engaged in advocacy for national policy initiatives that aim to create a comprehensive, ethnically and geographically diverse repository of pediatric reference interval data, Genzen said.

ARUP was among 42 clinical laboratories, pediatric hospitals, and medical societies and associations that signed a February 10, 2025, letter coordinated by the Association for Diagnostics & Laboratory Medicine (ADLM), appealing to the U.S. House and Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, to provide the CDC with $10 million in funding to advance a pediatric reference interval repository initiative.

Without a nationwide effort, gaps will continue to exist for many tests, particularly for certain populations for which data are especially hard to collect, such as premature infants, said Dennis Dietzen, PhD, division chief of Pathology and Laboratory Medicine at Phoenix Children's Hospital and chairman of the ADLM Policy and External Affairs Core Committee.

He also cited a challenge with "harmonization" of reference intervals for kids. Discord in reference intervals comes not

[CHILDx]

What is CHILDx™?
The Children's Health Improvement through Laboratory Diagnostics (CHILDx™) program launched in 1999 as the largest pediatric reference interval study of its kind. Marzia Pasquali, PhD, FACMG, ARUP medical director of Biochemical Genetics, chaired the first board of directors, which was established with representation from 15 institutions.

Why was it created?
The goal of CHILDx has been to establish pediatric reference intervals for a variety of analytes to address a critical need. Before the program began, intervals were often based on small sample sizes, leading to unreliable or nonrepresentative test results.

What did it do?
Starting in 2002, blood specimens were collected from thousands of healthy children from 6 months to 17 years old with an eye toward characterizing specimens that were meticulously categorized by factors such as age and Tanner stages (five stages that describe the physical changes of puberty in boys and girls).

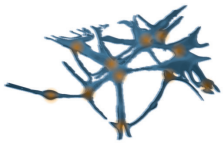
This large repository of specimens set the program apart by providing unparalleled access to well-characterized samples that enabled more precise and meaningful laboratory diagnostics for children.

The researchers have created pediatric reference intervals for dozens of analytes and produced dozens of academic papers and abstracts. In addition to Pasquali, they included current and former ARUP experts Ed Ashwood, MD, Mark Astill, MS, Cheryl Coffin, MD, Harry Hill, MD, Nicola Longo, MD, PhD, Wayne Meikle, MD, Sherrie Perkins, MD, PhD, Theodore Pysher, MD, William Roberts, MD, PhD, Joely Straseski, PhD, and many others.

What is CHILDx's legacy?
CHILDx has made a lasting impact by setting new standards for pediatric laboratory diagnostics and demonstrating the importance of large, well-curated specimen repositories. Its legacy continues to serve ARUP's clients and to influence the field, especially as new approaches to reference intervals and renewed advocacy efforts seek to build on its foundation.

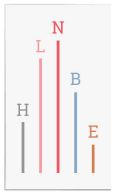
Pediatric Testing at ARUP

ARUP offers pediatric testing across all specialties. Notable examples include:



Autoimmune disease: Tests aid in the diagnosis of diseases that occur when the immune system mistakenly attacks healthy cells and tissues. Examples of available tests include panels for autoimmune pediatric central nervous system (CNS) disorders, which cover the autoantibodies associated with autoimmune neurologic disease in patients younger than 18 years.

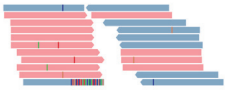
Biochemical genetics: Tests aid in the diagnosis and monitoring of metabolic disorders, which can lead to conditions such as intellectual disability and organ failure if left untreated. Tests available include amino acid quantitation, organic acid analysis, and acylcarnitine profile assessment.



Newborn drug testing: Comprehensive drug detection panels test for a range of substances, including opioids, stimulants, and sedatives. ARUP analyzes specimens by mass spectrometry up front, eliminating the need for reflex testing in most cases.

Pediatric cancer: Tests aid in the diagnosis of a variety of cancers, including hematologic malignancies such as leukemia and lymphoma and solid tumors such as neuroblastoma and nephroblastoma, among others. ARUP offers numerous biochemical, phenotyping, molecular, and immunohistochemical analyses, as well as Children's Oncology Group-certified testing such as minimal residual disease (MRD) monitoring by flow cytometry and a full cytogenetics suite that includes chromosome analysis, fluorescence in situ hybridization (FISH) analysis, and genomic microarray.

Prenatal and constitutional cytogenetics: Tests aid in the diagnosis of heritable genetic abnormalities. ARUP's Cytogenetics Laboratory offers testing for constitutional cases, including chromosome analysis, FISH analysis, and genomic microarray. fluorescence in situ hybridization (FISH) analysis, and genomic microarray.



Rapid whole genome sequencing: The test helps determine the genetic cause of symptoms when a genetic condition is suspected in patients in acute clinical settings, particularly critically ill newborns. ARUP's assay includes copy number variants, mitochondrial sequence variants, and *SMN1* deletions for spinal muscular atrophy.

Visit ARUP's Laboratory Test Directory for more information: ltd.aruplab.com.

only from the use of biased analytic systems but from differing interpretations of the data that characterize the biochemistry of childhood development. "This lack of standardization limits the generalizability and utility of the intervals," Dietzen said. "Efforts to harmonize assays across institutions have been ongoing, but significant inconsistencies remain, making it difficult to establish universally accepted pediatric reference intervals."

He said advocacy efforts have succeeded in raising awareness and garnering moral support from organizations and Congress. "It's really hard for a congressman to say, 'I don't care about children's health.' That would be at their own electoral peril," Dietzen said.

Nonetheless, financial investment is still lacking, he said.

Joely Straseski, PhD, MS, MLS(ASCP), DABCC, FADLM, Head of Clinical Operations for Clinical Chemistry, Toxicology, and Biochemical Genetics at ARUP

Laboratory-Developed Tests Essential in Pediatric Care

Dietzen and Genzen also noted another challenge for pediatric testing. Many tests common in pediatric care are laboratory-developed tests (LDTs), primarily because commercial, FDA-cleared or approved tests often do not exist for the unique clinical needs of children.

Reliance in pediatrics on LDTs meets an important need, but it also contributes to the harmonization issue because tests, and pediatric reference intervals validated for those tests, vary across institutions and geographic regions, Dietzen said.

Genzen added that regulatory uncertainty around LDTs remains a concern. While a federal court ruling in March 2025 ended the most recent attempt by the FDA to regulate LDTs as medical devices, which potentially would have forced labs to discontinue some tests, congressional action that could result in further regulation of LDTs is still anticipated at some point.

Clinical laboratories are already highly regulated under the Centers for Medicare & Medicaid Services Clinical Laboratory Improvement Amendments (CLIA). Genzen has been a leader in advocating on behalf of clinical laboratories for common sense updates to the existing regulatory framework that are reasonable and predictable so that ARUP and other labs can continue to meet the needs of pediatric patients.

Kelly Doyle, PhD, DABCC, FADLM, Medical Director of Special Chemistry, Endocrinology, and Mass Spectrometry at ARUP

Diagnoses That Save Lives

ARUP is proud of the important role it plays in the practice of pediatric medicine and celebrates when a test leads to lifesaving treatment, as it did in the case of Woody Tribe, who was the first Utah infant to be diagnosed with guanidinoacetate methyltransferase (GAMT) deficiency. Detection of the rare inherited condition resulted from the disorder being added to a state's newborn screening panel through the efforts of Marzia Pasquali, PhD, FACMG, ARUP medical director of Biochemical Genetics, and Nicola Longo, MD, PhD, a pediatrician who was then chief of the

Dennis Dietzen, PhD, Division Chief of Pathology and Laboratory Medicine at Phoenix Children's Hospital and Chairman of the ADLM Policy and External Affairs Core Committee

Jonathan Genzen, MD, PhD, MBA, Chief Medical Officer and Senior Director of Governmental Affairs at ARUP

Medical Genetics division at University of Utah Health.

The stories of Beckett Lippincott, who was diagnosed with juvenile dermatomyositis, and Cal Taylor, who was diagnosed with nemaline rod myopathy, are other important examples. Read more about these and other patient stories at aruplab.com/patient-stories.

Genzen said ARUP's test development pipeline is robust and will continue to evolve to meet emerging needs. "If you think about just the spectrum of our extensive test menu and the testing options available, a lot of it really is designed to help serve pediatric patients."

"Children's health is a topic that everything can filter through: harmonization, LDTs, and access to testing are key examples," he said. "Issues that are important throughout laboratory medicine apply especially in children's health."

Lisa Carricaburu, lisa.carricaburu@aruplab.com

Learn More About Pediatric Testing at ARUP

Medical Experts
Medical Experts/Pediatric Specialty or Subspecialty

Online Resource
ARUP Testing Specialties: Pediatrics

Online Resource
ARUP Consult® offers numerous disease topics and testing algorithms specific to pediatric care.

Webinar
ARUP Uses Statistical Modeling To Establish Reference Intervals for Pediatric Patients

Research
Pediatric Reference Intervals Research

Podcast
An Interview With Dr. Kelly Doyle: Detecting G6PD Deficiency in Children

Identifying Genetic Drivers of Childhood Leukemia:

ARUP's Cytogenetics Team Leverages Expertise To Provide Answers for Patients in Children's Oncology Group Trials

ARUP has a dedicated team of cytogenetic technologists who evaluate genetic abnormalities for pediatric patients with cancer (left to right): Monica Theriot, MLS(ASCP)^{CM}CG^{CM}, Melissa Johnson, CG(ASCP)^{CM}, Elzbieta Drozd-Borysiuk, MS, George Bonnet, CG(ASCP)^{CM}, and Cleve Bigman, BS (ACS).

For children who are diagnosed with acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML), understanding the driver of disease can drastically affect their outcomes.

As a laboratory certified by the Children's Oncology Group (COG), an organization dedicated to childhood cancer research, ARUP's Cytogenetics Laboratory performs testing to determine the genetic abnormalities that drive cancer in the pediatric population. Through exhaustive effort, they apply their expertise and experience to contribute to improving outcomes for pediatric patients with cancer. ARUP processes a large percentage of COG cytogenetic testing for ALL and AML in the United States, averaging between 150 and 200 cases each year.

"In pediatric oncology, especially in cancer of the blood and bone marrow, knowing what the abnormality is cytogenetically allows providers to specifically treat what is driving the disease," said Monica Theriot, MLS(ASCP)^{CM}CG^{CM}, the lab supervisor for the Cytogenetics Laboratory at ARUP.

AML and ALL are classified into different subtypes based on genetic abnormalities that drive disease, and treatment strategies vary accordingly.

The ARUP Cytogenetics Laboratory began joining in cytogenetic studies for COG clinical trial cases more than two decades ago. Through the dedicated efforts of medical directors and lab technologists, significant improvements have enhanced the lab's performance when it comes to COG cases.

Bo Hong, MD, FACMG, medical director of Cytogenetics and Genomic Microarray at ARUP, oversees cytogenetic testing performed for Children's Oncology Group (COG) cases at ARUP.

Monica Theriot, MLS(ASCP)^{CM}CG^{CM}, leads the team of cytogenetic technologists who decipher the complex genetic abnormalities that drive childhood cancers for children enrolled in Children's Oncology Group (COG) trials.

"Our work for cases in COG trials largely focused on improving the abnormality detection rate for pediatric B-ALL," said Bo Hong, MD, FACMG, medical director of Cytogenetics and Genomic Microarray. "B-ALL is a predominant pediatric neoplasm, with 75% of cases occurring in children younger than six years old. Cytogenetic findings are crucial for diagnosis, treatment planning, and prognosis assessment. We carefully process and review each COG case, submitting the cytogenetic data to the COG committee for central review to ensure proper patient enrollment in COG trials."

To be certified to perform testing for COG cases, participating laboratories are required to demonstrate an abnormality detection rate of at least 55%—a standard that ARUP far exceeds year after year.

Identifying cytogenetic abnormalities for these pediatric cancer cases is particularly challenging.

For example, in a standard case within the adult population, an abnormality can often be found within the first 20 cells that are analyzed. For COG cases, technologists often analyze hundreds of cells to detect just two abnormal cells, a finding that is required to establish clonality, said Theriot. As clonal diseases, ALL and AML derive from a mutated cell that propagates, giving rise to a cancerous cell population.

Pediatric cases pose additional challenges. Obtaining a sufficient bone marrow sample from a pediatric patient is difficult, and the quality of the metaphase cells in pediatric malignancies creates challenges in comparison to other types of malignancies that the team examines.

"The work we do can be grueling. Sometimes you spend hours and hours trying to find the answer, the abnormal clone, and still do not find it. You pour a lot of heart into the work, and at the end of the day, still have to sign it out as normal," said Theriot. "Then there are those days where you do find that clone and know that you're able to provide answers that are going to make a difference."

Some cases require multiple tests to accurately define the abnormality. For example, hypodiploidy, which is a loss of chromosomes, can appear as the opposite—hyperdiploidy, a gain in chromosomes.

"We can look at the karyotype and figure out that the gains are masking hypodiploidy," Theriot said. "A cell line can essentially double and look like a hyperdiploid gain of chromosomes, when it is actually the doubling of a hypodiploid clone."

While hyperdiploidy is associated with good prognosis, hypodiploidy is often associated with poor prognosis. Distinguishing the difference is critical for determining appropriate treatment.

"At the ARUP Cytogenetics Lab, we offer comprehensive testing, including karyotyping, fluorescence in situ hybridization (FISH), and genomic microarray for COG cases to enhance diagnostic yield.

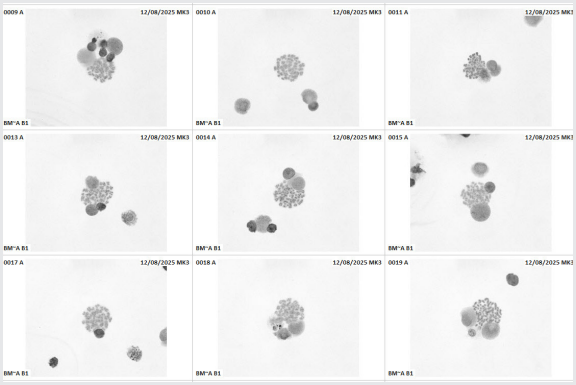
Certain high-risk abnormalities, like masked hypodiploidy and intrachromosomal amplification of chromosome 21 (iAMP21), can be missed or misinterpreted by karyotyping and FISH due to the suboptimal mitotic index and chromosome morphology as well as technical limits, impacting treatment and outcome. Therefore, we integrate genomic microarray, a crucial tool for diagnosing these specific abnormalities and cases with uninformative results from karyotyping and FISH," Hong said.

ARUP has a dedicated team of experienced cytogenetic technologists who work on COG cases.

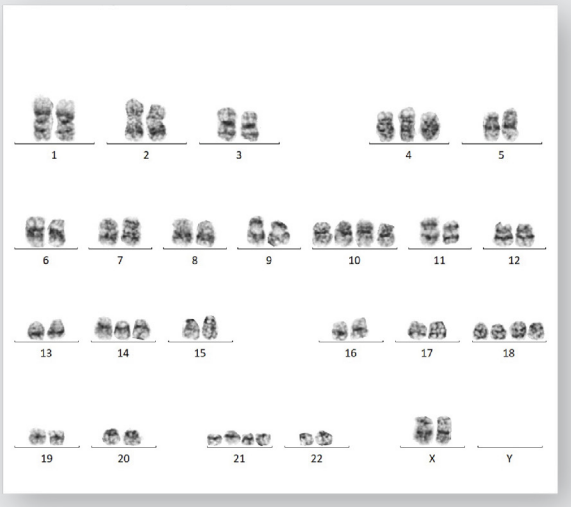
"Our team knows what they are looking for—how to dig into these cases and keep pushing until they find the answer," Theriot said.

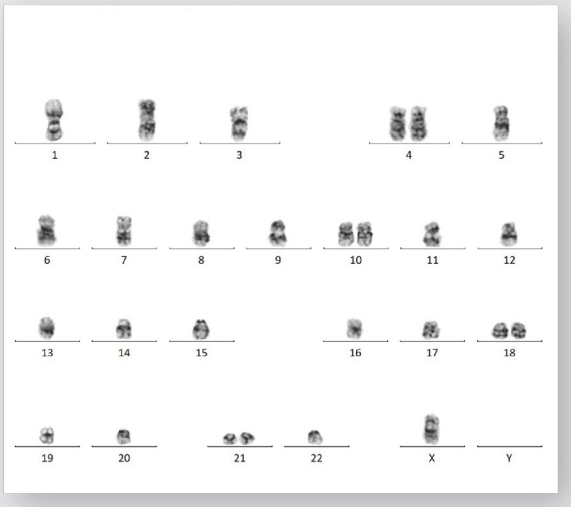
As a result of the efforts of the many who have contributed to better understanding and treatment of childhood cancers, survival rates have drastically improved.

For some childhood cancers, the increase in survival rates has been so dramatic that clinical studies are shifting to focus on minimizing the adverse effects of therapy.



An example of a gallery image that cytotechnologists examine to identify chromosomal abnormalities in cases of pediatric cancer. For Children's Oncology Group (COG) cases, technologists often analyze hundreds of cells to detect just two abnormal cells.





Hypodiploidy (≤43 chromosomes in B-cell acute lymphoblastic leukemia [B-ALL]) is a poor prognostic indicator in B-ALL. However, a hypodiploid clone may double and result in pseudohyperdiploidy, a finding that can be misclassified as true hyperdiploidy, which is associated with a favorable prognosis. In this case, what initially appeared to be hyperdiploidy (depicted by the karyotype on the left) was determined to be hypodiploidy after further evaluation (depicted by the karyotype on the right). Distinguishing the difference is essential for treatment selection.

Rodney Miles, MD, PhD, medical director of Hematopathology at ARUP, has been involved with the Children's Oncology Group (COG) since early in his career and is now a member of the COG committee for non-Hodgkin lymphoma (NHL).

> ***"I've come full circle, from starting as a young investigator myself to having a role in engaging new young investigators. It's important that we prepare the next generation to continue the work of COG."***
>
> **Rodney Miles, MD, PhD**

"One of the challenges is that the therapy they use to achieve these good outcomes is severe, and the patients can have lifelong adverse effects, such as decrease in cardiac function, cognitive decline, emotional and mental health challenges, or damage to other organs," said Rodney Miles, MD, PhD, medical director of Hematopathology at ARUP.

Now, studies are focused on determining whether the same outcome can be achieved with less intensive therapy.

Miles has been involved with COG since early in his career as a young investigator, and he is now a member of the COG committee for non-Hodgkin lymphoma (NHL).

In 2011, Miles contributed to an international study[1] to determine whether adding rituximab to the standard chemotherapy regimen improved event-free survival in children and adolescents with advanced-stage B-cell NHL. The study found that rituximab prolonged event-free survival, which was 93.9% at 3 years.[2]

Miles, along with retired ARUP CEO Sherrie Perkins, MD, PhD, reviewed all of the U.S., Australian, and Canadian cases to confirm the diagnosis.

"This trial redefined the standard of care for mature B-cell NHL in children," Miles said. "In fact, they had to stop the trial early."

The new therapy demonstrated enough success that it became necessary to administer that therapy to all of the study participants rather than continue the trial.

Miles also serves as the COG vice chairman for faculty development, taking an active role in helping young investigators build their careers and become involved in COG.

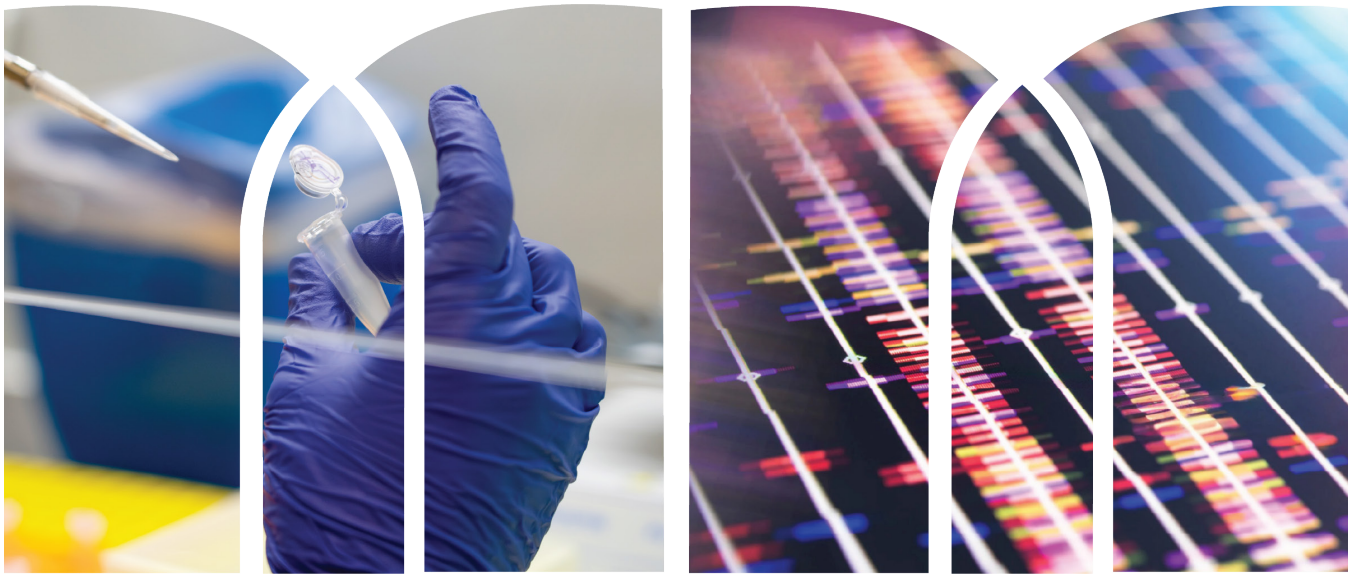
"I've come full circle, from starting as a young investigator myself to having a role in engaging new young investigators," Miles said. "It's important that we prepare the next generation to continue the work of COG."

In addition to cytogenetic testing, ARUP also performs COG-accredited testing to detect minimal residual disease in both blood and bone marrow in lymphoblastic leukemia cases, as well as markers to evaluate residual disease after CD19-targeted therapy.

"Every study keeps increasing the odds for these patients. To know that we are directly contributing and making a difference is so fulfilling," said Theriot.

Kellie Carrigan, kellie.carrigan@aruplab.com

1. Clinicaltrials.gov. Intergroup randomized trial for children or adolescents with B-cell non Hodgkin lymphoma or B-acute leukemia: rituximab evaluation in high-risk patients. Updated Jun 2017; accessed Jan 2026.
2. Minard-Colin V, Aupérin A, Pillon M, et al. Rituximab for high-risk, mature B-cell non-Hodgkin's lymphoma in children. *N Engl J Med.* 2020;382(23):2207-2219.



Diagnosing Critically Ill Newborns: The Evolution of Testing and the Promise of Rapid Whole Genome Sequencing

The prenatal ultrasound revealed enlarged echogenic, or unusually bright, kidneys, polydactyly, and club feet that curved inward. The development of the fetus at 32 weeks of gestation already indicated the presence of a genetic disorder. By the day after birth, the infant was enrolled in a research study to rapidly diagnose newborns with genetic disorders. By day six, the parents and their new baby had received an answer: Bardet-Biedl syndrome.

Rapid whole genome sequencing (rWGS), a test that analyzes the entire genome for pathogenic variants in just a few days, made it possible for this family to receive a diagnosis in less than a week.

"With a traditional testing modality, it may have taken years for someone to realize the clinical picture matched Bardet-Biedl syndrome," said Hunter Best, PhD, FACMG, head of the Molecular Division at ARUP and medical director of Molecular Genetics and Genomics. "The patient would probably have been to literally dozens of doctor visits without receiving a diagnosis."

Bardet-Biedl syndrome is a rare genetic disorder characterized by excessive childhood weight, poor eyesight, kidney dysfunction, extra fingers or toes, and impairments in thinking, learning, and speaking. The symptoms of Bardet-Biedl syndrome develop slowly over time, making timely diagnosis difficult.

"The symptomology that is the hallmark of Bardet-Biedl syndrome was not present in the infant," Best said. "This means that rWGS is providing a diagnosis before the full clinical picture has evolved."

By identifying genetic disorders within a few days of birth, rWGS better informs management strategies and enables specialist intervention. In some cases, timely diagnosis may even prevent permanent harm or mortality.

"It may sound like a small thing to refer these patients to a specialist, but early specialist intervention makes a huge impact in the outcome of these patients," Best said.

This patient was one of 65 newborns who were enrolled in the Utah NeoSeq Project, a collaborative research effort to evaluate the clinical value of rWGS for critically ill infants being treated in the neonatal intensive care unit (NICU) at the University of Utah Hospital. ARUP Laboratories performed testing and data analysis for each of the patients enrolled in NeoSeq, which launched in February 2020 and concluded in May 2023.

Of the 65 infants enrolled during that period, rWGS identified causative variants in 40% of the patients and strong candidates in an additional 11% of the patients. To compare the rWGS results with those of traditional testing modalities, standard-of-care testing was also ordered. In the infant with Bardet-Biedl syndrome, standard tests didn't yield results until two weeks after the results of rWGS testing were in.

"When we say rapid, we mean rapid," Best said. "It's not rapid with a disclaimer; it's rapid. We have spent years optimizing our workflow to guarantee our published turnaround times." rWGS yields results in just three to seven days.

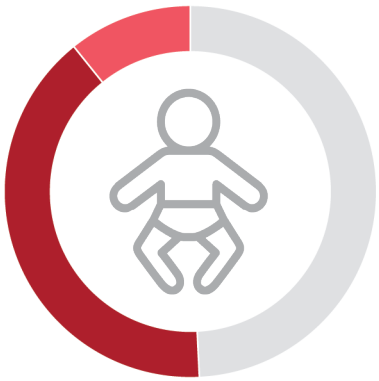
For critically ill infants in the NICU, rapid diagnosis is essential to initiate treatment in time or facilitate management strategies.

Best has led the development of whole genome sequencing at ARUP, in collaboration with ARUP's Genetics and Genomics teams. The whole genome sequencing assays now include copy number variants (CNVs), mitochondrial sequence variants, and *SMN1* deletions to identify spinal muscular atrophy.

ARUP's teams have extensive experience performing and interpreting genomic sequencing. They were early adopters of the test method used to sequence genomes, known as massively parallel or next generation sequencing, and participants in early research initiatives such as the Utah NeoSeq Project.

"There are many different types of large copy number variant-type abnormalities that we can detect with the improved assays," said Patti Krautscheid, MS, LCGC, genetic counselor and supervisor of Genetic Counseling Services at ARUP. "Adding CNV detection makes the tests a one-stop shop for great first-line diagnostic tests."

Utah NeoSeq Project



Newborn patients enrolled:

65

Cases with causative variants detected:

40%

Cases with strong candidate variants detected:

11%

The Utah NeoSeq Project, a collaborative research effort that included several departments at the University of Utah and ARUP Laboratories, investigated the clinical utility of rapid whole genome sequencing (rWGS) for diagnosing critically ill newborns in the neonatal intensive care unit.

Clinical evidence in support of genomic sequencing as a first-tier testing strategy is mounting. In July 2025, the American Academy of Pediatrics (AAP) published updated recommendations for the evaluation of children with global developmental delay (GDD)/intellectual disability (ID). The recommendations include using exome or genome sequencing as an initial, or first-tier, test for diagnosing GDD/ID. This follows recommendations that were already established by the American College of Medical Genetics and Genomics (ACMG) and the National Society of Genetic Counselors (NSGC).

As a result of these guideline recommendations, several major insurance companies and state Medicaid programs have expanded coverage for rWGS, especially for critically ill newborns who are being treated in the NICU. As of September 2025, 17 state Medicaid programs cover rWGS for critically ill children younger than 1 year, and an additional four states have introduced coverage policies that have not yet been enacted.

By sequencing the entire genome, rather than testing for variants in a targeted gene, a broader range of genetic disorders can be identified.

"Whole genome sequencing provides more data on coding and noncoding regions, increasing the diagnostic yield," Best said. "This test should be considered as a first-line diagnostic test when an inherited disorder is suspected but the patient phenotype does not suggest any single disorder."

Genomic sequencing produces an incredible amount of data. ARUP has built a custom analysis tool, NGS.web, to help filter the data, but relies on the expertise of the team's medical directors and clinical variant scientists to interpret it.

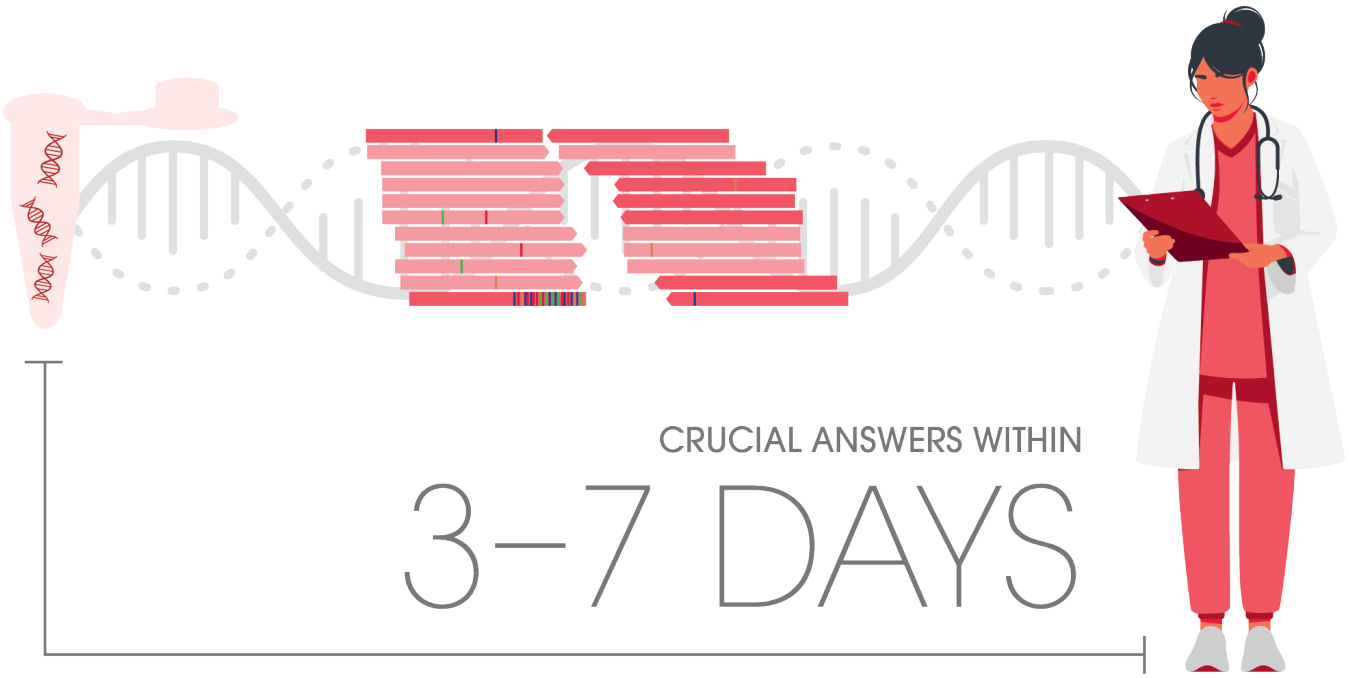
"This testing is very complex, and it's not directed at one single marker," Best said. "We use limited artificial intelligence (AI) tools to filter the data, but we manually interpret variants 100% of the time, using the significant years of experience that our teams have. It's not possible to replace that experience."

Although ARUP's genomic sequencing assays are currently only used to evaluate symptomatic patients with suspected inherited disorders, several studies and organizations are investigating the utility of rWGS as a general newborn screening tool.

While genomic sequencing is not yet as rapid as other newborn screening methods, it is an incredibly informative tool that has significant implications for diagnosing critically ill newborns.

"As genome sequencing becomes cheaper, it starts to become more feasible to utilize this technology to help drive healthcare decisions, even in healthy populations," Best said. "Genomics can be harnessed to start directing personalized care."

Kellie Carrigan, kellie.carrigan@aruplab.com



Building a Robust Newborn Screening Program

When Marzia Pasquali, PhD, FACMG, joined ARUP Laboratories in 2001, the state of Utah only included five conditions in its newborn screening program.

Pasquali, medical director of Biochemical Genetics at ARUP, initiated a pilot project in collaboration with the Utah Department of Health and Human Services (DHHS) and the University of Utah Metabolic Clinic. Its goal: to expand the newborn screening program and adopt a more efficient testing technology, known as tandem mass spectrometry.

The project aimed to combine the strengths of each organization to build a robust program that not only identified affected patients but ensured appropriate follow-up care.

"ARUP and the Biochemical Genetics lab know how to run the mass spectrometer and interpret the results, while the DHHS has an amazing follow-up program, and the clinic does a marvelous job in taking care of the patients. I thought, let's put our heads together and build a program," Pasquali said.

Tandem mass spectrometry, the new technology Pasquali proposed, has the capacity to simultaneously measure many analytes with a high degree of specificity and sensitivity. Additionally, it requires only a small sample size, which is ideal when drawing blood from a newborn baby. Tandem mass spectrometry can detect markers for up to 70 conditions simultaneously and can return results within a few hours.

"Turnaround time is a very important consideration in newborn screening," said Pasquali. "For some conditions that are critical, symptoms can develop within 48 to 72 hours. To prevent a complication, the morbidity associated with a disease, or even mortality, you need to be very fast."

Several other important considerations affect which diseases are included in a newborn screening panel, such as whether a marker of the disease can be identified in asymptomatic patients and whether the disease has a treatment, said Pasquali.

ARUP validated the screening by tandem mass spectrometry, and the expanded and improved newborn screening program launched on January 1, 2006. ARUP performed the testing until 2019, by which time the DHHS had the capability to run tandem mass spectrometry.

Since that time, Pasquali has continued to advocate for newborn screening and has worked to expand the number of diseases in the screening panels. Her efforts have included groundbreaking work on guanidinoacetate methyltransferase (GAMT) deficiency, and she worked closely with Heidi Wallis, the mother of two children diagnosed with the deficiency, to improve screening for the condition.

GAMT deficiency leads to a lack of creatine in the brain, a condition that can be treated with a creatine supplement. Without diagnosis and treatment, the deficiency results in lifelong damage, including intellectual disability, limited speech development, recurrent seizures, and autistic-like behavior.

In 2015, Utah became the first state to begin screening for GAMT deficiency in all newborn infants. A few years later, in 2021, Woodward Tribe became the first infant diagnosed with GAMT deficiency through Utah's newborn screening program. As a result of his early diagnosis, Woodward, or Woody, as he is called, was able to receive timely treatment that significantly improved his outcome. (Find the Wallis family story and Woody's story at aruplab.com/patient-stories.)

Through Pasquali's efforts and those of her collaborators, Utah has expanded the number of diseases in its newborn screening program from five to 35.

While rapid whole genome sequencing (rWGS) has demonstrated the potential to diagnose newborns being treated in the neonatal intensive care unit (NICU) who appear to have a genetic disorder, Pasquali believes that traditional newborn screening will continue to meet an important need in screening the entire newborn population for critical metabolic disorders.

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Marzia Pasquali, PhD, FACMG, medical director of Biochemical Genetics at ARUP, has been a driving force in the adoption of tandem mass spectrometry for newborn screening and the expansion of Utah's newborn screening program.

Through Pasquali's efforts and those of her collaborators, Utah has expanded the number of diseases in its newborn screening program from five to 35.

Already under pressure from declining reimbursements, children's hospitals are expected to lose billions of dollars due to recent Medicaid cuts. Laboratory stewardship can help hospitals continue to do what's best for pediatric patients while achieving cost savings.

For Children's Hospitals, Laboratory Stewardship Creates Pathways to Better Patient Care

When children's hospital laboratorians receive a specimen for testing, they are acutely aware that "there's a child tied to that sample, and it took an invasive procedure to get it," said Tony Smith, BSHCM, MLT(ASCP)^{CM}, CLSSBB, a senior healthcare consultant with ARUP Healthcare Advisory Services.

"It's not just a tube of blood. It's a baby's tube of blood," he said.

The weight of that responsibility is one reason children's hospitals were early pioneers in laboratory stewardship, according to Smith. Clinicians and laboratorians alike want to ensure that pediatric patients receive the right testing at the right time to avoid unnecessary testing and the harm that can result.

Now, financial pressures are driving a renewed push for laboratory stewardship in pediatric settings. A mean of 47.2% of children's hospital discharges are paid for by Medicaid, according to RAND, a nonprofit, nonpartisan research group. However, Medicaid reimbursement rates are not keeping up with hospital costs. An American Hospital Association survey found that Medicaid reimbursements only cover 83% of hospital costs.

These financial challenges are expected to worsen for children's hospitals in the wake of H.R.1, legislation that reduces federal Medicaid spending by about $900 billion over a decade. The Children's Hospital Association reported that, collectively, children's hospitals will lose billions of dollars of revenue once the legislation is fully implemented.

Laboratory stewardship is not just about cost savings—it's mostly about doing what's best for the patient. "Knowing that reimbursement was already tight and is getting tighter in the face of recent policy changes, we want to make sure that every test that's ordered for a child is backed by evidence and empathy—and stewardship is how you honor both of those things," Smith said.

Unique Patients, Unique Challenges

When it comes to laboratory stewardship, children's hospitals face some unique challenges compared with adult healthcare facilities. For example, many pediatric illnesses are rare and require esoteric testing not performed by in-house laboratories, which leads to the use of numerous specialty reference laboratories. Before Boston Children's Hospital began its stewardship efforts, it had relationships with more than 250 reference laboratories, said Mark Kellogg, PhD, associate director of Chemistry and director of the Quality and Regulatory Program at Boston Children's.

Another challenge is that pediatric hospitals have fewer clinical pathways—models that outline recommended diagnostic approaches for patients with specific symptoms or conditions. Clinicians in adult settings follow clinical pathways for chest pain, suspected stroke, and sepsis, among many other conditions.

"These sorts of pathways don't exist as much in a pediatric hospital because there are not a lot of common presentations to build these pathways around," said Dennis Dietzen, PhD, division chief of Pathology and Laboratory Medicine at Phoenix Children's Hospital. "You're making it up as you go, so laying a blanket of stewardship on that is really hard."

Laboratory stewardship efforts first began to take shape in the 1990s. One example is ARUP's Analyzing Test Ordering Patterns™ (ATOP®) program, which launched in the '90s to help laboratories identify opportunities for improvement.

In the mid-2000s, innovations in genetic testing caused laboratory budgets to balloon, and children's hospitals started to focus on laboratory stewardship more intently.

"If anyone knows the importance of lab stewardship, it's pediatric institutions," said Smith, who was instrumental in the development of Children's Hospital Colorado's stewardship program beginning in the mid-2000s.

Smith and other clinical laboratory leaders who are seasoned in building and improving laboratory stewardship programs within pediatric settings offer the following advice.

Build a Committee That Carries Authority

It's important to ensure that the hospital stewardship committee wields real power and is not just an advisory committee, said Dietzen, who served at St. Louis Children's Hospital for 23 years before joining Phoenix Children's. Dietzen helped St. Louis Children's launch its stewardship program about 15 years ago and is now spearheading Phoenix Children's first stewardship committee.

"I've spent the past several months figuring out where in the hospital hierarchy this committee needs to live so that it has proper authority to enforce the protocols it deems necessary," he said. "You need an administrative champion, someone within the hierarchy of the hospital who will support what you're doing no matter what."

At Children's Colorado, the stewardship program was tied to hospitalwide quality improvement initiatives, which helped to "put some weight behind it at the executive level," Smith said. "We had to reach all the way up to the C-suite."

Get Clinicians Involved

Sandy Richman, MBA, C(ASCP), vice president, ARUP Healthcare Advisory Services, said it's important to a stewardship effort to "get the right people in the room so that it's not lab driven—it's more lab supported. But it has the involvement of clinicians who can help make those clinical decisions and also be a voice for the committee and take information back to their colleagues."

Clinician participation helps secure organizational support from other clinicians. At Boston Children's, the stewardship committee membership must transition every two years. "In the years when we couldn't get clinical volunteers and it became lab heavy, that's when we saw the biggest pushback," Kellogg said.

Gather Data

Successful stewardship interventions depend on quality data sources. "You have to have data dashboards and analytics, and that's something that we can help our clients with," Smith said. "It's really the backbone of stewardship."

Data are essential for helping stakeholders "understand why the process you want to implement is in the best interest of the patients and the physicians who are taking care of those patients," Dietzen said. "Data from multiple institutions, from peer-reviewed studies, and your own internal data are absolutely essential to convince people."

Unfortunately, internal data can be difficult to access. When Boston Children's began to focus on stewardship, it had two staff members who were primarily dedicated to retrieving data. "That's all they did because it was so intense," Kellogg said. "We're now down to one data analyst, and maybe 30% of her job is pulling data for the stewardship group. But it took her years to develop the databases."

Build a Test Formulary

Developing a test formulary is one way to manage test options and reduce misutilization. "Oftentimes, test formulary creation can be met with resistance because providers feel that the lab is telling them which tests they can order and which they can't," Richman said. "A better way to position that is, 'We're making it easier for you to order the **correct** test.' So, rather than giving them multiple options, remove some of those tests that are commonly misordered, and direct them to the tests they should be ordering."

Dietzen noted that a test formulary makes it possible to create a tiered permission system. "Within that formulary, have tests that everybody can order, and then another tier of tests that can be ordered by specialists only, and then another tier of tests where it takes an act of Congress to order that test. You have to have those guardrails in place," he said.

Establish Approval Pathways

Some tests may require, if not an act of Congress, at least some form of oversight and approval. Boston Children's created a subcommittee that reviewed all requests for genetic tests. Over time, the committee established guidelines and a pathway that clinicians could follow to order genetic tests without previous approval. "Now, only a handful of requests don't meet the criteria and need to go to the committee for review," Kellogg said.

Some hospitals require approval when clinicians want to order testing from a new specialty reference laboratory or when the test cost meets a certain threshold. Part of that approval process may include helping the patient's family understand the expected expense for them and gaining their acknowledgement and consent before moving forward.

Narrow the Pool of Reference Labs

"Children's hospitals serve a unique population and provide a lot of specialized care. Most pediatric hospitals use more than 50 reference labs, so there's a financial opportunity in consolidating those labs," Richman said.

If the same test is being ordered from multiple reference labs, hospitals can remove duplicate testing from the formulary to ensure clinicians are ordering the most cost-effective option. Consolidating labs also makes it easier to negotiate volume-based discounts and monitor quality metrics.

When Children's Colorado began to focus on stewardship, it ordered from a pool of 155 reference labs. At Boston Children's, clinicians were ordering from more than 250 different reference labs. Over time, both of those hospitals were able to reduce the number of reference labs to about 50.

To achieve this reduction, Boston Children's assembled a test selection committee to identify which tests should be on its formulary and to choose the appropriate reference laboratories to perform sendout testing. "It was the first time we ever did true RFIs [requests for information] to identify the right lab partners. We developed a robust program for gathering data about labs, evaluating tests, and making

recommendations to the lab director and medical staff," Kellogg said.

Take Advantage of Information Technology Solutions

"Fully utilizing IT [information technology] infrastructure is a great way to help improve efficiencies and guide appropriate utilization," Smith said. "At Children's Colorado, we worked with Epic and our analysts in the lab to develop utilization management workflows that placed ordering guardrails around tests that were under stewardship management."

These guardrails can range from mild notifications to test-access restrictions. "You can hide the orders. You can make it so that a certain subset of clinicians can't even see that order. That's a little drastic," Dietzen said. "The gentlest action is a suggestion: 'This might not be the best test. Have you considered X test?' Make them provide information about the patient and check the appropriate boxes. Finally, the most stringent control is making it so they cannot order the test without approval."

Keep the Focus on Patients

For laboratorians working in pediatric settings, it's impossible to forget that each test is linked to a child and that clinicians and anxious parents are waiting for answers. "Disconnecting from that emotion is hard," Smith said. "Whether it's an adult or a pediatric patient, it doesn't change the need to do what's right for the patient. Stewardship creates pathways to better diagnostic care for patients."

Heather Stewart, heather.stewart@aruplab.com

Laboratory stewardship is not just about cost savings—it's mostly about doing what's best for the patient.

Tony Smith Brings a Patient-Focused, Analytic Approach to Clinical Laboratory Consulting Projects

Tony Smith, BSHCM, MLT(ASCP)^{CM}, CLSSBB, senior healthcare consultant with ARUP Healthcare Advisory Services, draws on his real-world laboratory experience to help labs strengthen stewardship efforts, improve workflows, and implement analytics tools.

Tony Smith, BSHCM, MLT(ASCP)^{CM}, CLSSBB, was in college and working toward medical school when his mother became seriously ill. He chose to step away from college to help his family and found his plans for the future becoming less certain. Then, one of his friends who was studying medical laboratory science (MLS) suggested that Smith consider a two-year medical laboratory technician program at the technical college.

"I knew I needed to keep going to school. But I knew it wasn't going to be the medical school path that I had wanted," Smith said. "When my friend was telling me about the MLS program and lab science, I thought, well, that sounds like it's aligned more with my strengths and interests, especially compared with the bureaucracy that often comes with clinical practice today."

Now a senior healthcare consultant with ARUP Healthcare Advisory Services, Smith has forged a career that's enabled him to improve the lives of patients while helping clinical laboratories operate to their fullest potential.

Smith worked as a specimen processor and a phlebotomist while in college, and that experience sparked a passion for working in pediatrics. "I was really good with kids," he said. "I could get along with them and make them feel comfortable—and then stick a needle in their arm and still get them to smile and walk away happy."

As a phlebotomist, he got to see how various parts of the hospital functioned, from the emergency department to postsurgical care to the pediatric department. "Being involved in that level of the organization expanded my bandwidth as far as experience, because many laboratorians have only ever worked in a lab setting," Smith said.

After earning his associate degree as a medical laboratory technician, Smith worked in transfusion medicine for Mayo Clinic Laboratories, where he gained further clinical experience and greater exposure to the reference laboratory setting. Then, seeking a somewhat warmer climate, he left Minnesota for Denver, Colorado, and joined Children's Hospital Colorado in 2005. Smith started in

a technical role at Children's Colorado, but his analytic approach and attention to detail soon propelled him into operational roles, starting with the creation of the laboratory's client services department.

"I helped manage a lot of preanalytic processes for specimen processing, sendouts, and the client services team. We were focused on improving processes, creating a structure to better utilize purchased services and resources with our reference laboratories," he said.

This work ultimately led to the development of the laboratory stewardship program at Children's Colorado. Smith started by working with the organization's medical director to review and approve orders for certain high-cost tests. "I had implemented stewardship before I knew it to be stewardship," he said. "We were a pediatric academic institution using 155 reference labs. Providers had no guardrails. If it existed in a catalog, someone was ordering it."

At first, Smith tackled stewardship without an official role or title and without a stewardship committee to guide the work. "We were just hobbling along and trying to keep up with things," he said. After a couple of years, he helped spearhead the development of a formal stewardship committee. He worked collaboratively across departments to build a committee structure, identify projects, and implement a test review model.

Thanks to Smith's leadership, in 2013, Children's Colorado became a founding member of Patient-centered Laboratory Utilization Guidance Services (PLUGS), a collaborative that now includes roughly 200 member organizations.

"Lab stewardship and test utilization have been a big focus of this stage of my career," said Smith, who joined ARUP Healthcare Advisory Services in 2021. Now, he draws on his real-world experience in a clinical laboratory to help other labs as they work to strengthen stewardship efforts, improve processes and workflows, and implement analytics tools.

Smith said this lived experience is a unique advantage of working with ARUP's consultants. "We relate to our clients because we've walked the same paths. We've been through accreditation cycles. We've been through operational improvement cycles. We've been through leadership transitions. That shared background gives us practical, grounded experience."

The 16 years Smith spent at a pediatric hospital remain foundational to how he approaches his work as a consultant. "Children are the most fragile population of patients, and this magnifies the importance of providing a high standard of care," he said. "I feel blessed that as part of ARUP, I get to be a voice for children and help improve services for pediatric patients."

Heather Stewart, heather.stewart@aruplab.com

"Children are the most fragile population of patients, and this magnifies the importance of providing a high standard of care. I feel blessed that as part of ARUP, I get to be a voice for children and help improve services for pediatric patients."

Tony Smith, BSHCM, MLT(ASCP)^{CM}, CLSSBB
Senior Healthcare Consultant

Bella Church Pieces Puzzles Together for ARUP Healthcare Advisory Services Clients

Senior Healthcare Consultant Bella Church, MS, C(ASCP)CM, has been solving complex puzzles in the lab for 20 years. Now part of ARUP Healthcare Advisory Services, she's snapping pieces into place for clients industrywide.

In 2006, ARUP Senior Healthcare Consultant Bella Church, MS, C(ASCP)CM, was dreaming of her future as a clinician after receiving her master's degree in exercise physiology from the University of Utah. First, however, she needed an interim job to keep the lights on while she planned her next steps. Luckily, a family member already employed at ARUP was able to help her land one—a technologist trainee position in what was then known as the Trace Elements and Calculi Laboratory.

It meant taking a side step from her plans, but every day at the bench, she found herself enthralled by the puzzle-like nature of clinical testing. In every specimen, she saw patterns to be determined and a specific riddle to be solved. Computers hadn't yet become ubiquitous and powerful enough to assist with large amounts of laboratory work. While the testing itself involved puzzle solving, processes weren't particularly efficient.

"Everything was manual then. Everything," Church said. "You had to take very detailed notes and write a lot of physical descriptions by hand. We were entering information into old MS-DOS programs. The IT department didn't really have resources for a bench-level interface, and there were no templates for this kind of work."

Church said she felt there must be a more efficient way to report on specimens. She opened a Microsoft Excel file, and using Visual Basic commands she'd learned, she created a rudimentary automation interface to streamline data entry. Instead of typing paragraphs of information, she devised a numeric code to allow technicians to enter everything with a few keystrokes.

"For instance, if you were dealing with a kidney stone, you would have to write out that it was orange, and it was a certain size, among other things," Church said. "I was by no means a programmer—and it was very, very basic—but I defined some commands where you could use a 10-key number pad instead. You could, say, hit '8' for orange, and mark the size as '1,' as well as a few other variables. Then, it output to an Excel sheet and we put that into Pathnet Classic."

Her supervisors took the creation seriously. It led to cleaner reports—no spelling errors, no missing spaces, and better formatting so that reports could be more easily read by clients. Critically, though, it instantly made work more efficient for technicians and reduced turnaround times. For Church, it was one of the earliest steps into the oncoming wave of automation that would crest over the next couple of decades. She said the lab used her Excel program for "seven

or eight years" before ARUP's IT team created what was essentially a standalone version of her system.

Church never turned back to her plans to become a clinician. Instead, in 2026, she's celebrating her 20th year at ARUP. The puzzles, she said, and her desire to solve them, simply never waned. She realized medical laboratory science, which she called the "quiet backbone of healthcare," was the place where she could have the greatest effect on patient outcomes. One test improvement could affect thousands of patients at once.

By 2009, she had been promoted to technical specialist and was extending her expertise to mass spectrometry testing while also becoming more involved in space planning and test validation. She led the charge in moving the Trace Elements clean room when ARUP relocated it to a new facility some years later. In 2012, she moved into a lead position in the Clinical Toxicology 1 Laboratory, where she could delve more deeply into mass spectrometry work. It was the perfect fit for her methodical mind. By 2016, Church was the technical supervisor of ARUP's Clinical Toxicology 2 Laboratory.

"There are no out-of-the-box tests in mass spectrometry," she said. "Everything in mass spec is lab developed. Looking at chromatograms is like looking at a logic puzzle. There are all these pieces that must be there for you to report patient results, and that's motivating and fun for me."

One test ARUP did not perform in-house during this period was a whole blood test for phosphatidylethanol (PEth), a biomarker associated with alcohol consumption. Once Research and Development (R&D) validated an in-house test, it was up to Church to implement it—and taking a new test live on a new instrument platform is a bit of a high-wire act. The stakes were high. They rose even higher as the test finally went live for clients in early 2020, just as COVID-19 began sowing chaos.

"We knew as soon as we flipped the switch—it wouldn't be a slow ramp-up," Church said.

Before the launch, ARUP was receiving 1,000 to 2,000 specimens per month for the whole blood PEth test that were passing through to referral partners. Church said she knew those numbers would grow as clients found the test easier to access, so she wanted to make sure her lab could handle even larger volumes.

"It was the right move, because by the end of that year, we were processing up to 6,000 specimens per month," Church said.

Most of the PEth test procedures Church helped establish are still in use today, with a handful of upgrades to handle even larger volumes. ARUP now performs more than 10 times the number of tests that were being referred at the point that ARUP's test went live. Some of those upgrades happened as Church's lab moved into a new facility, which she helped to design.

In 2021, Church joined ARUP Healthcare Advisory Services and now leverages the experience she gained during her years at the bench to develop efficient strategies for ARUP's clients, whether for individual diagnostic tests or for enterprisewide process optimization. She still finds major puzzles to crack, both in the lab and across the industry. She notes that clients ask about new opportunities for automation, something she understands intimately because of her work in mass spectrometry.

"Anyone who has experienced pipetting into a 96-well plate knows that can be a hard task," Church said. "There are so many little mistakes that could be made, and in working with mass spectrometry, we worked with so many things manually. Automation ideas came naturally out of that."

Church said medical laboratory science's constant learning environment remains rewarding, and she has had the opportunity to improve outcomes for far more patients in the lab than she might have as a clinician.

"I was lucky to have many years solving a variety of interesting problems in my lab work, and now I get to apply that experience to our clients," she said. "Each one has a unique challenge that requires unique solutions. I'm glad I get to play a role here."

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Hunter Best, PhD, FACMG, head of the Molecular Division at ARUP and medical director of Molecular Genetics and Genomics, has led the development of whole genome sequencing (WGS) at ARUP, along with his colleagues in the Sequencing and Clinical Analytics Division.

New Variant Classes Added to ARUP's Whole Genome Sequencing Assays Expand Diagnostic Capabilities

Whole Genome Sequencing Transforms Diagnosis and Creates Possibilities for Preventive Care

The Human Genome Project, which was completed in 2003, sequenced the 3 billion base pairs of the human genome over the course of 13 years at a cost of $3 billion, or roughly $1 per base pair. Two decades later, whole genome sequencing (WGS) assays can now sequence an entire human genome in less than a day.

Advances in genomic sequencing technology—increased speed and accessibility and reduced cost—have transformed our ability to identify and understand genetic drivers of disease. WGS facilitates rapid diagnosis, guides timely interventions, and may even offer untapped potential in preventive medicine.

"The field of genomics is really exploding, and that means there is a significant increase in the number of patients that we will be able to diagnose and help with this technology," said Hunter Best, PhD, FACMG, head of the Molecular Division at ARUP and medical director of Molecular Genetics and Genomics.

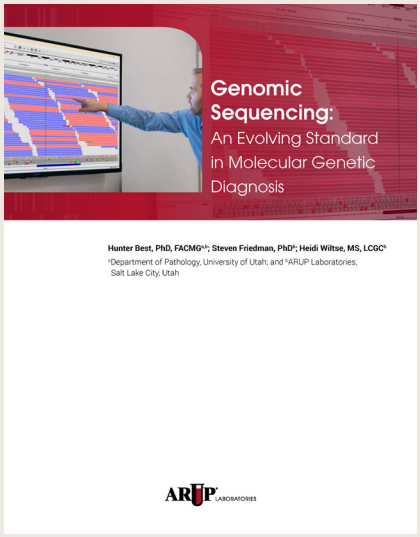
Targeted gene panels and assays that sequence the protein-coding regions of the genome, known as whole exome sequencing (WES) assays, have been in clinical use for some time. The exome contains 180,000 exons across 22,300 protein-coding regions, but only comprises 1.5–2% of the entire genome. By comparison, WGS sequences the entire genome, both the coding and noncoding regions, providing a more holistic view of the genetic factors that may cause disease, particularly if a genetic disorder is suspected but the patient's presentation doesn't suggest a specific condition.

"As a comprehensive assay, WGS turns up positive variants that otherwise might not have been considered, even by a very experienced genetics provider, due to an atypical presentation," said Jessica Ponce Hidalgo, PhD, MS, LCGC, genetic counselor lead in Cytogenetics.

In November 2025, ARUP Laboratories added new variant classes to its WGS assays, including copy number variants (CNVs), mitochondrial sequence variants, and *SMN1* deletions associated with spinal muscular atrophy.

These additional variant classes have expanded the capabilities of the tests, making it possible to detect more pathogenic variants that may otherwise have been missed.

"There are many different types of large copy number variant-type abnormalities that we can detect with the improved assays," said Patti Krautscheid, MS, LCGC, supervisor of Genetic Counseling Services at ARUP. "Adding CNV detection makes the tests a one-stop shop for great first-line diagnostic tests."



In a new white paper, "Genomic Sequencing: An Evolving Standard in Molecular Genetic Diagnosis," Hunter Best, PhD, FACMG, Steven Friedman, PhD, and Heidi Wiltse, MS, LCGC, provide an overview of the clinical findings that support the use of WGS, as well as emerging applications. Download it here:

Patti Krautscheid, MS, LCGC, supervisor (left), and Jessica Ponce Hidalgo, PhD, MS, LCGC (right), genetic counselor lead, steer ARUP's Genetic Counseling Services team, which offers guidance on genetic test ordering and results interpretation for providers.

$5.8M–$7.8M SAVED
due to avoided inpatient days[1]

$16K–$28K SAVED
by the payer system per patient[1]

289 DAYS → 13 DAYS
average time to diagnosis decreased when WES/WGS was used as first-tier testing[2]

DIAGNOSTIC YIELD
for WGS up to[3] **44–54%**

Clinical studies have demonstrated that using WGS, especially as a first-line test, can significantly increase the likelihood of diagnosis and improve patient outcomes.

A 2016 study[4] that involved 3,040 cases found that the overall diagnostic yield of WES was 28.8%, whereas a later study[5] cited a yield of 34% for WES. More recent studies have found that the added yield of WGS over WES is 10–20%, Best said.

Not only is WGS more likely to provide a clear diagnosis for patients, but studies have also shown that it can drastically reduce the time it takes to arrive at a diagnosis.

A study to evaluate[2] diagnostic yield and time to precise genetic diagnosis found that 42.3% of pediatric inpatients received a precise genetic diagnosis, and the average time to diagnosis decreased from 289 days to just 13 days, when rapid WES/rapid WGS was used as first-tier testing.

"Without WGS, these patients may go down a whole saga to receive a diagnosis," Hidalgo said. "It would require multiple tests, multiple blood draws to arrive at a diagnosis. Not only is that not great stewardship, but it increases the stress on patients and the cost of care."

The strong evidence in support of WGS as a diagnostic tool has led several organizations to develop guidelines that recommend WGS as a first-line test. Most recently, the American Academy of Pediatrics (AAP) published guidelines

in July 2025[6] that recommend WES/WGS as first-line tests for global developmental delay and intellectual disability because of superior diagnostic yield and cost-effectiveness. These guidelines follow similar, previous recommendations from the American College of Medical Genetics and Genomics (ACMG).[4] The National Society of Genetic Counselors (NSGC) recommends WGS for unexplained epilepsy in individuals of all ages.

The Forefront of Analysis and Interpretation

WGS generates an astonishing amount of data. Each genome sequenced produces approximately 3 million variants. The sheer volume of data creates a monumental task for the individuals who analyze the data for clinically relevant information.

"ARUP is at the forefront of interpretation and analysis," said Steven Friedman, PhD, ARUP Sequencing and Clinical Analytics director. "Our team of clinical variant scientists is immersed in genetic variant interpretation all day, every day."

ARUP's team of highly experienced and qualified clinical variant analysts, clinical variant scientists, and medical directors personally reviews and interprets each case to ensure the information reported is accurate and clinically relevant.

"We provide the highest quality result out there. We manually review the data 100% of the time. There really is no substitute for the years of experience that our team has," Best said.

ARUP has been performing genetic testing for more than 25 years and was an early adopter of massively parallel sequencing, also known as next generation sequencing.

ARUP's scientists and medical directors are experts in variant interpretation who regularly contribute to the body of genetics research and knowledge as well as classification determinations. Several members of the team volunteer on the expert panels for ClinGen, a collaborative effort funded by the National Institutes of Health (NIH) to standardize variant classifications. ARUP also contributes to ClinVar, a public database of genetic variants and their clinical relevance. ARUP's team members leverage their expertise to ensure the most clinically relevant and actionable information is reported.

"Our analysis is very thorough," said Hidalgo. "We have multiple eyes and various teams reviewing the interpretation and the reports. We provide a lot of detail that other laboratories may not give."

NGS.web software

- One-stop shop for genetics case review
- Incorporates data analysis, genetic databases, and reporting tools
- Developed in-house

Clinical variant analysts

- Assess quality metrics and triage cases

Clinical variant scientists

- Experts with advanced degrees
- Perform variant interpretation
- 50+ years of combined experience in variant interpretation

Medical directors

- Review and confirm variant interpretations
- Provide consultation on test selection and results interpretation
- 60+ years of combined experience in genomic testing and variant interpretation

Genetic counselors

- Provide consultations on test selection and results interpretation

To facilitate data analysis, ARUP has developed a cutting-edge user interface, known as NGS.web, which incorporates data analysis, data from genetics databases, and reporting tools.

"While we do use tools to aid in filtering data, at the end of the day, our team members perform the interpretation," Best said. "There's a lot of nuance in the interpretation of genetic variants, which can be lost when relying solely on AI [artificial intelligence] approaches."

ARUP teams also align their interpretation with clinical findings to ensure the information provided matches the clinical presentation and is thus the most actionable information.

"The analysis is phenotype driven," Krautscheid said. "The more robust clinical information providers can supply, the better we can analyze and report those pathogenic variants."

WGS: An Avenue to Preventive Medicine?

Currently, WGS is used to diagnose patients who present with symptoms that suggest a genetic disorder, but genomic data can also provide information on a patient's risk for developing conditions later in life, such as hereditary cancer and many other conditions. The genome contains a wealth of information that can be mined to inform those future risks and even prevent complications from developing.

"Many of the health issues that people deal with through their life have a genetic link," Best said.

For example, individuals may have a genetic predisposition for blood clots that could develop into deep vein thrombosis and become life-threatening. By taking inexpensive medication, patients could avoid a dangerous condition and the associated costs of hospitalization.

"If genomic sequencing is targeted and focused on actionable genetic data, it can do a lot to improve patient outcomes," Best said. "Genomic sequencing is an incredibly powerful tool in the right clinical scenario. There's so much information that could be harnessed to support preventive care."

Kellie Carrigan, kellie.carrigan@aruplab.com

Steven Friedman, PhD, ARUP Sequencing and Clinical Analytics director, and his team members have recently updated ARUP's whole genome sequencing (WGS) assays to include copy number variants (CNVs), mitochondrial sequence variants, and *SMN1* deletions, increasing the diagnostic capabilities of the tests.

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Many Places, One Purpose: A Former ARUP Fellow's Voyage Through Laboratory Medicine

Kayode Balogun, PhD, DABCC, FIBMS, FADLM, is now the director of Clinical Chemistry and Immunology Laboratories at Montefiore Medical Center.

From a teaching hospital in Nigeria to the academic corridors of the United Kingdom, Canada, and then the United States, Kayode Balogun, PhD, DABCC, FIBMS, FADLM, has built a career defined by curiosity, compassion, and a drive to improve patient care—especially for the most vulnerable.

A Journey Across Continents and Disciplines

Balogun's interest in pathology began with a clinical lab internship at the Lagos University Teaching Hospital in Nigeria. This early experience working in a resource-limited environment left a lasting impression. "The interaction between clinical laboratorians and providers was mind blowing," he said. "Even with limited resources, their passion for patient care was remarkable."

After earning his bachelor's degree in biochemistry, he went on to complete a master's degree in biomedical science in London, where he undertook advanced academic and practical training in laboratory medicine. Balogun said he has been "glued to the field ever since."

Next came a doctorate in biochemistry in Newfoundland, Canada, which led to postdoctoral research at the University Health Network in Toronto, where Balogun investigated the effects of HIV treatment in pregnancy. This work identified novel biomarkers for adverse pregnancy outcomes and contributed to changes in clinical guidelines—an early sign of the impact Balogun would have on the field.

ARUP: A Transformative Fellowship

Drawn to ARUP Laboratories for its reputation and advanced technology, Balogun earned a spot as a clinical chemistry fellow. He found the fellowship experience both rigorous and inspiring. "ARUP is unique," he said. "The exposure to faculty with both generalist and focused expertise, the diversity of cases, and the camaraderie among fellows and mentors—it's an experience that stays with you throughout your career."

Collaborations and friendships formed at ARUP continue to shape Balogun's career, with ongoing research partnerships and mentorship ties that have endured well beyond the fellowship years.

Championing Pediatric Reference Intervals

During his time at ARUP, Balogun worked with Tatiana Yuzyuk, PhD, ABMGG, ARUP medical director of Newborn Screening and Biochemical Genetics, to establish distinct reference intervals for children and adults for red blood cell fatty acid profiles.

A central theme in Balogun's work is infant health. "Children are not small adults," he emphasized.

Establishing accurate reference ranges for test results for children is challenging but essential, especially for special populations. "Understanding the chemistry and needs of these children allows us to provide the right care and interventions."

Impact and Recognition

Now serving as director of Clinical Chemistry and Immunology Laboratories at Montefiore Medical Center in the Bronx, New York, Balogun oversees the reporting of millions of tests annually and strives to mentor the next generation of laboratorians. His current research on HIV-exposed, uninfected children in the Bronx has revealed important public health insights, highlighting the need for ongoing vigilance and support for this growing population.

Balogun's contributions have been recognized with honors such as the "40 Under Forty" award from the American Society for Clinical Pathology (ASCP) and inclusion on The Pathologist magazine's 2025 Power List, a testament to a career marked by excellence.

Advice for Future Fellows

Having made his home in New York, Balogun finds balance in a vibrant city that offers both professional fulfillment and opportunities for relaxation. "There's always something for you in New York—great work, great community, and time to recharge. That's what you need for success."

For those considering a fellowship, he offers this advice: "Enjoy the experience and learn as much as you can. Build relationships with mentors. They become lifelong connections. And while the training is broad, find a specific area of focus that you're passionate about. That's how you make your mark."

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ARUP is seeking news from former fellows and residents to feature!

Fill out this form to share your news or nominate a colleague, and a representative from ARUP will follow up with you by email.

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