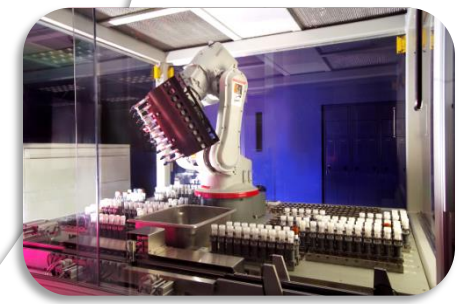


Laboratory Testing for Pediatric Patients: Concerns, Challenges and Solutions

Joely Straseski PhD, MT(ASCP), DABCC, FACB

Assistant Professor, University of Utah

Medical Director, ARUP Laboratories

Endocrinology and Core Laboratories

ARUP LABORATORIES | NATIONAL REFERENCE LABORATORY

Outline

ARUP: Background, Resources, Research and Development

Pediatric Reference Intervals: Challenges and Concerns

CHILDx Initiative

Current Improvements and Future Developments

Conclusions and Questions

Outline

ARUP: Background, Resources, Research and Development

Pediatric Reference Intervals: Challenges and Concerns

CHILDx Initiative

Current Improvements and Future Developments

Conclusions and Questions

ARUP: More Than a Lab

30 Years of service ARUP LABORATORIES

- Formed in 1984
- Privately held
- Nonprofit enterprise of the University of Utah and its Department of Pathology

UNIVERSITY OF UTAH SCHOOL OF MEDICINE

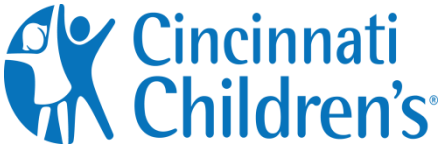
Department of Pathology

70 medical directors and consultants (board certified; MD and/or PhD)

ARUP: More Than a Lab

- Has one of the broadest test menus in the industry
  - > 3,000 tests and test combinations
- Performs 99 percent of all testing on-site
- Operates 24 hours per day, seven day a week
- Processes more than 30,000-35,000 specimens of blood, body fluid, and tissue biopsies per day

ARUP: Pediatric Hospitals Are Well Served



ARUP is the most automated laboratory in North America

Bottom line: Consistent handling of specimens, patient safety

Hawker et al., Clin Chem (2014) 60:463

ARUP Institute for Clinical and Experimental Pathology®

- Research arm of ARUP Laboratories
- Founded in 1996
- More than 50 technical sections, 50 medical directors, and 75 scientists
- Unique combination of investigator-initiated and goal-oriented research effectively brings new tests to market and improves existing assays, ultimately improving patient care

MAJOR FOCUS AREAS:
Creating new lab tests
Improving current lab tests
Evaluating lab tests (including testing site protocols)
Basic and clinical research

ARUP Institute for Clinical and Experimental Pathology®

of peer-reviewed research publications in leading journals published by ARUP research scientists (since 2000)

1600

in-house tests developed by the institute

600

improved and validated

200

developed by institute scientists

400

Pediatric Testing

Why do so many children's hospitals in the United States use ARUP as their reference laboratory?

R&D

- Approximately 10 percent of ARUP R&D budget is used for test development related to pediatrics

Extensive menu

- Accommodates more than 99 percent of pediatric testing requests
- Majority performed at ARUP
  - Allows children's hospitals to be more operationally efficient

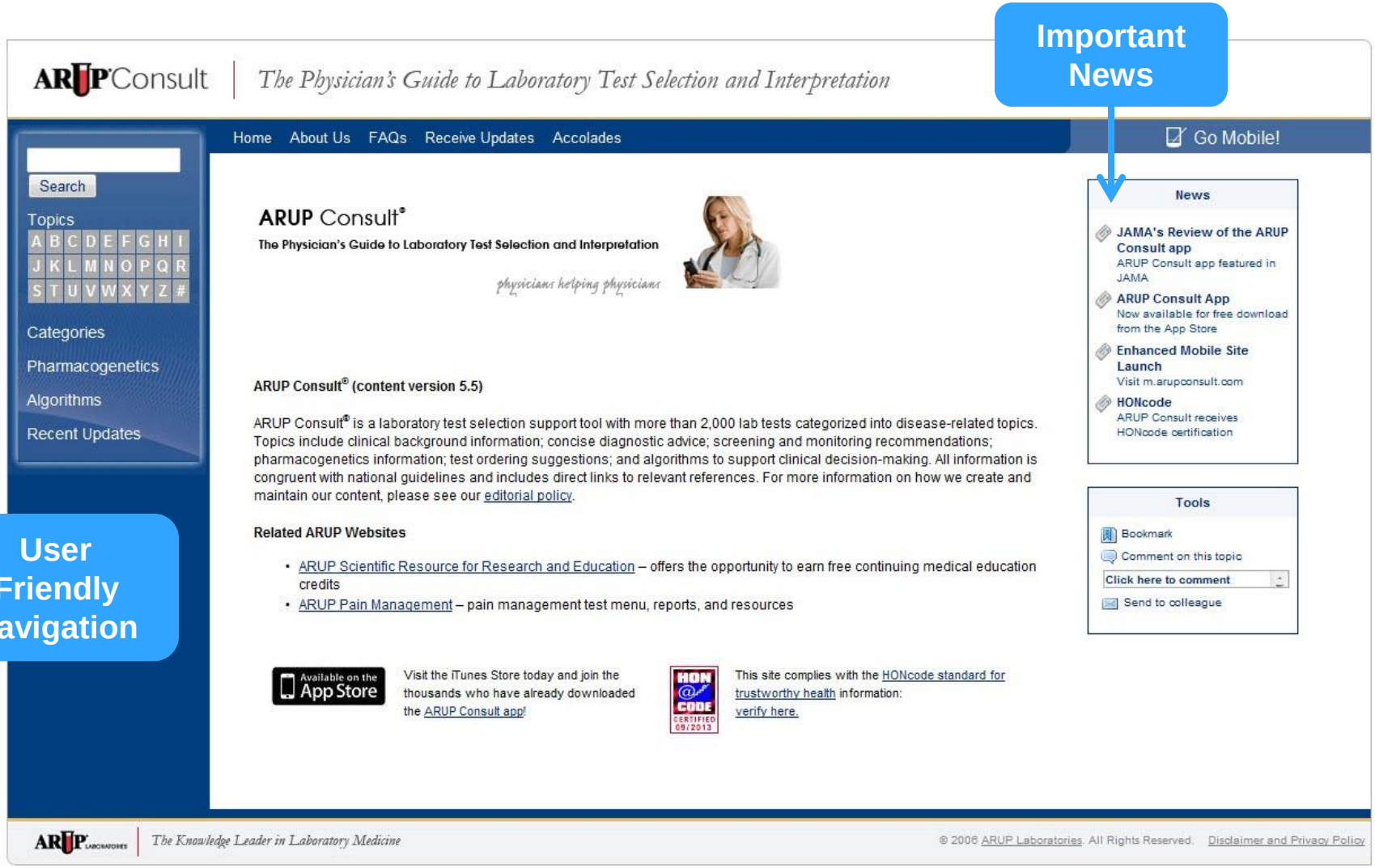
Test Interpretation

- Pediatric Pathology Consultation Services
  - Academic affiliation with University of Utah's Division of Pediatric Pathology
- ARUP Consult
  - Physician's Guide to Laboratory Test Selection and Interpretation

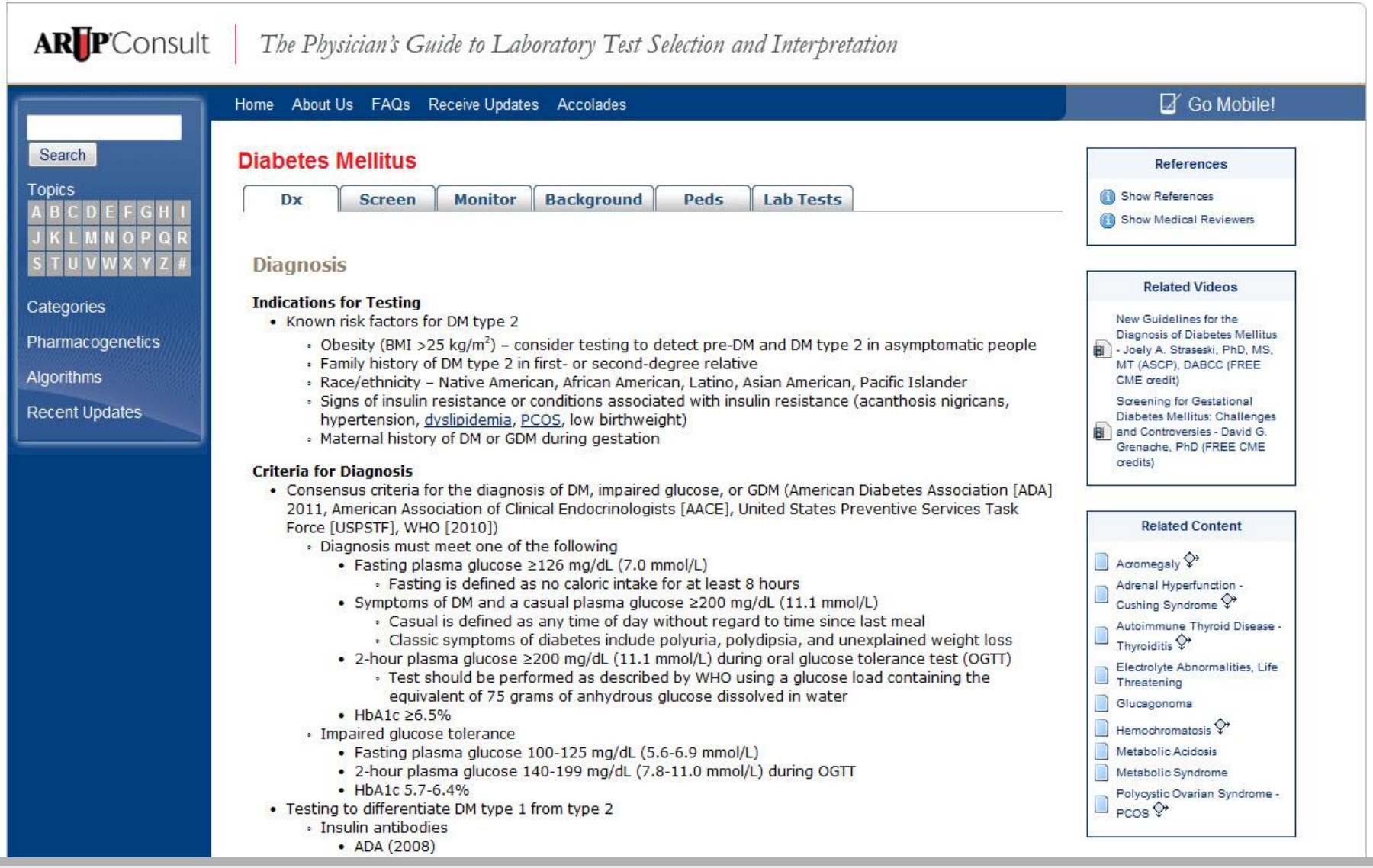
Pediatric Testing – Specialty Services

- Biochemical genetics
- Electron microscopy
- Fetal autopsy
- Kidney and liver
- Molar pregnancy
- Muscle and nerve
- Pediatric pathology (including tumors)
- Perinatal pathology
- Placental pathology

ARUP Consult®



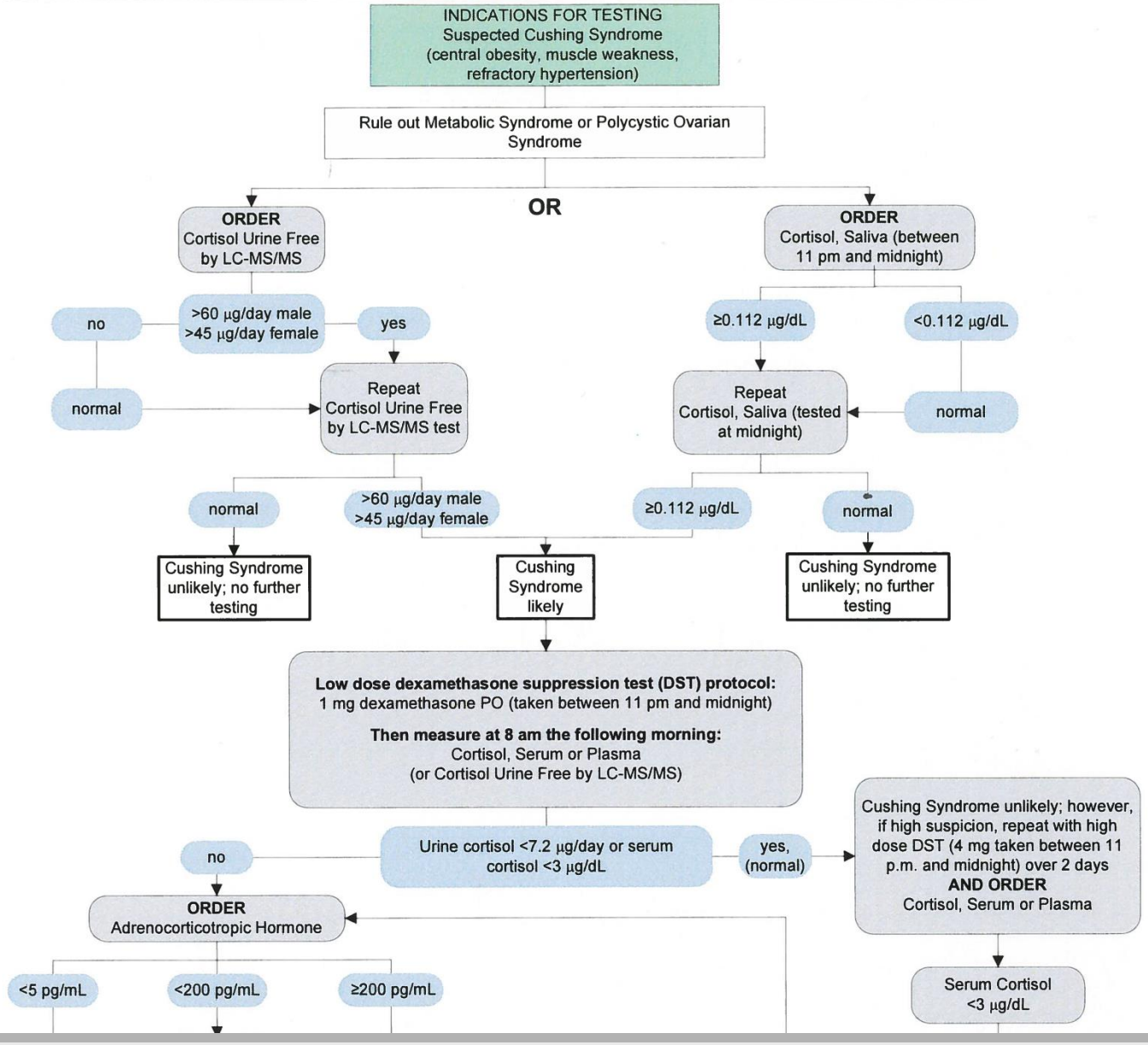
ARUP Consult®



Adrenal Hyperfunction (Cushing Syndrome) Testing

ARUP Consult

Click here for topics associated with this algorithm



Outline

ARUP: Background, Resources, Research and Development

Pediatric Reference Intervals: Challenges and Concerns

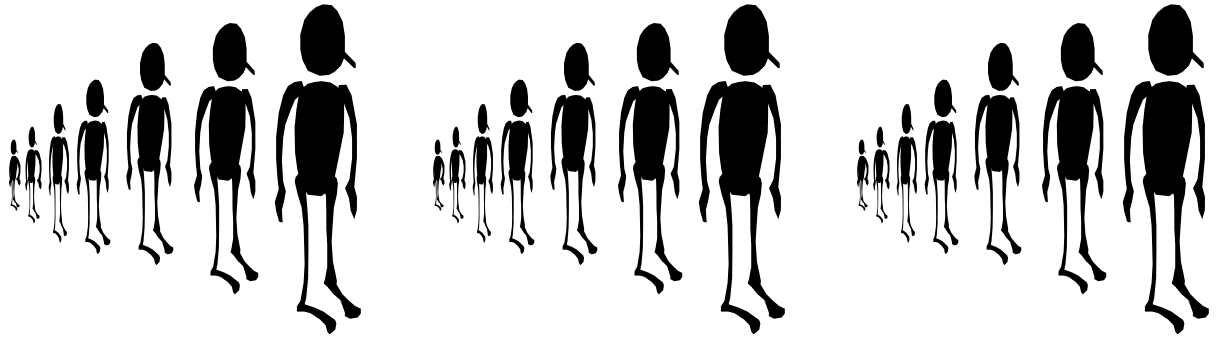
CHILDx Initiative

Current Improvements and Future Developments

Conclusions and Questions

How are reference intervals determined?

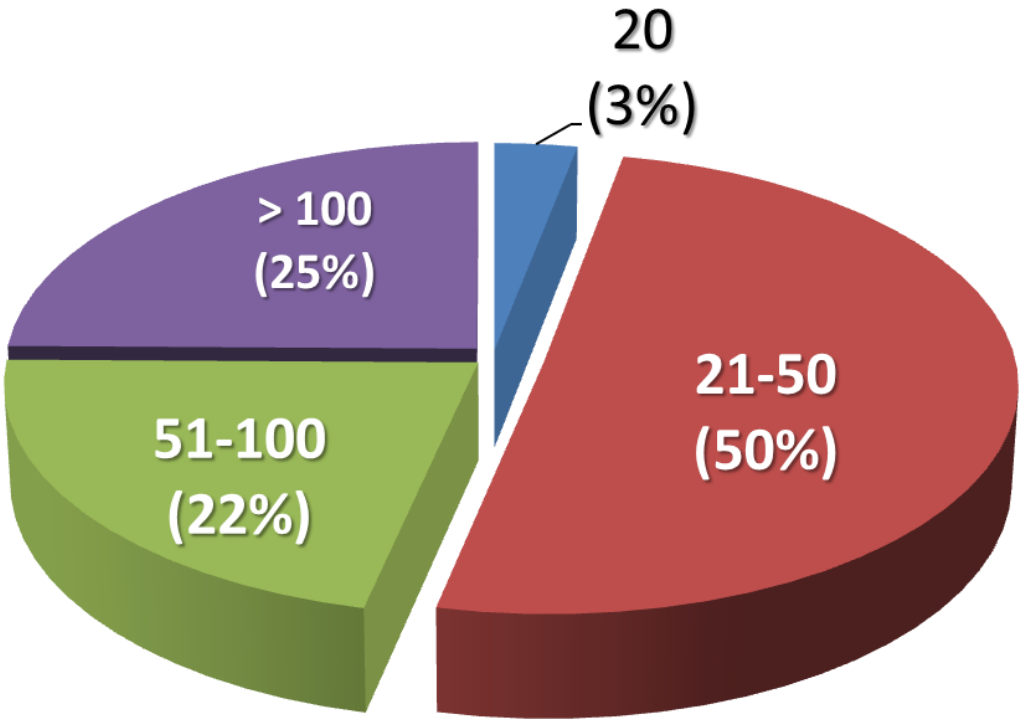
1. Identify a reference population
2. Measure analyte
3. Determine the most common results
4. Establish lower and upper limits of “healthy”



Reference Intervals (RIs): Standard Approaches

- Verify
  - 20 samples per partition
- Establish
  - 120 samples per partition

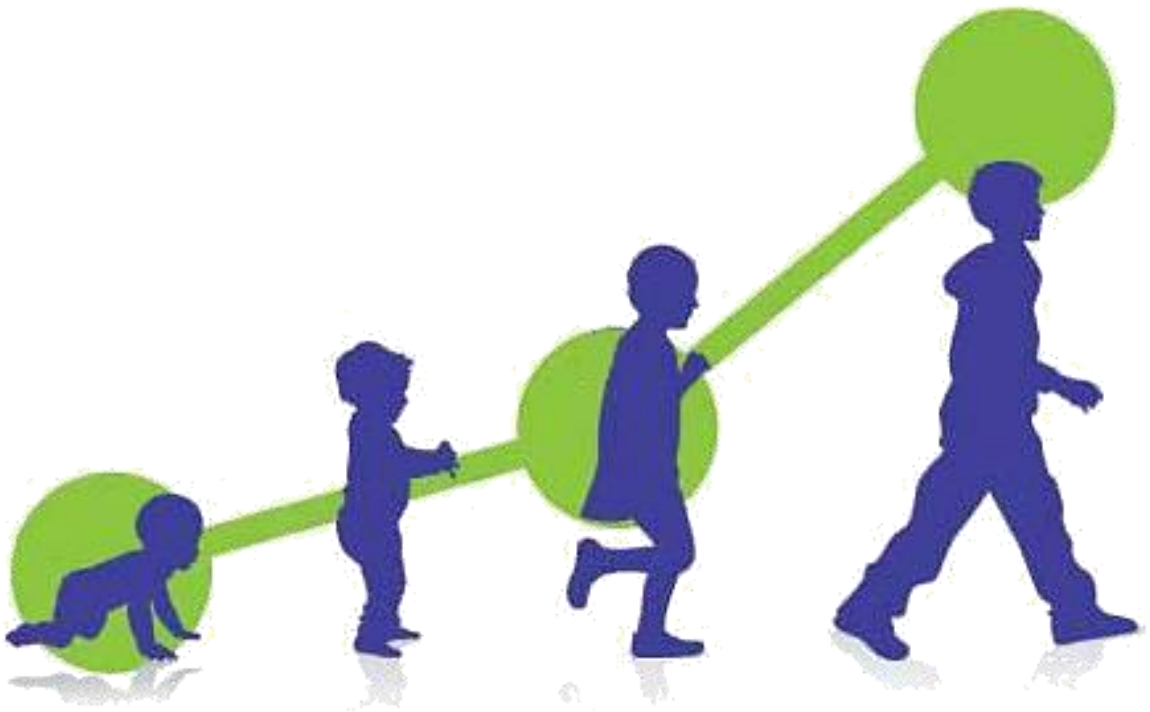
Establishing RIs: Number of Healthy Adults Studied



Potassium
N = 129 labs

From: Friedberg et al., Arch Pathol Lab Med (2007) 131:348

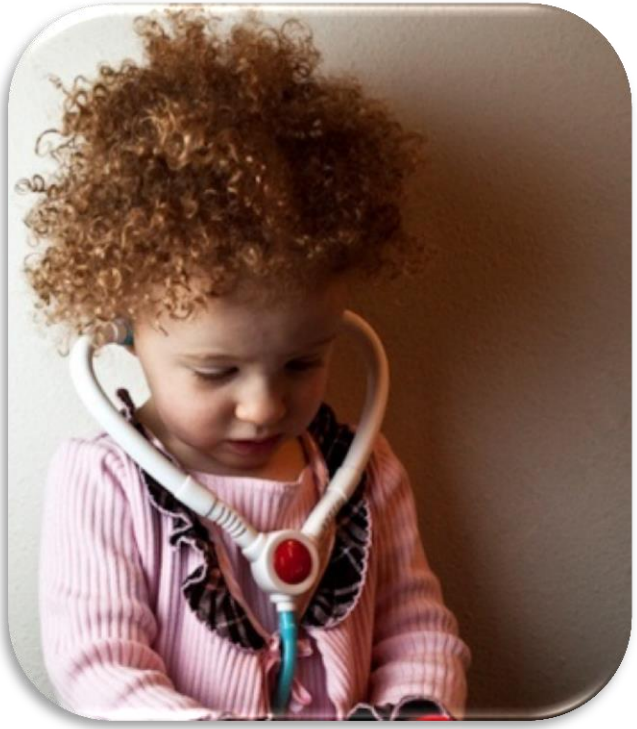
Lab Values Throughout Childhood: Moving Targets



TSH

Creatinine

Establishing Pediatric RIs: Inherent Challenges



- Healthy volunteers
  - Define “healthy”
  - Consent
  - Research Ethics Board
- Dynamic testing
- Tanner staging
  - Subjective
- Sampling limitations
- Numerous partitions
  - Appropriate, relevant

Establishing Pediatric RIs: Statistical Approaches

Clinical Biochemistry 47 (2014) 166–172

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Validity of establishing pediatric reference intervals based on hospital patient data: A comparison of the modified Hoffmann approach to CALIPER reference intervals obtained in healthy children

Julie L.V. Shaw [a,b,1], Ashley Cohen [a], Danijela Konforte [a,b,2], Tina Binesh-Marvasti [b], David A. Colantonio [a,b], Khosrow Adeli [a,b,*]

[a] Clinical Biochemistry Division, Department of Pediatric Laboratory Medicine, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada
[b] Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada

Establishing Pediatric RIs: Statistical Approaches

Findings:

- Reference intervals based on hospitalized populations are commonly wider than those based on healthy populations
- Ideally, >50% of data from healthy individuals (Soldin et al., Clin Biochem 2008;41:937)
- RI validation per CLSI guidelines may not be appropriate in pediatric populations
- *Hoffmann statistical approach is limited in pediatrics, particularly when data originates from tertiary care center*

Establishing Pediatric RIs: Statistical Approaches

Clinical Biochemistry 43 (2010) 933–934

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Letter to the Editor

Limitations of the Hoffman approach to determine pediatric reference intervals for two steroids

William L. Roberts*
Alan L. Rockwood
Department of Pathology, University of Utah, Salt Lake City, UT, USA
*Corresponding author. ARUP Laboratories, 500 Chipeta Way, Salt Lake City, UT 84108, USA.
E-mail address: william.roberts@aruplab.com (W.L. Roberts).

Ashley M. Bunker
Mark M. Kushnir
ARUP Laboratories, Salt Lake City, UT, USA

A. Wayne Meikle
Department of Pathology, University of Utah, Salt Lake City, UT, USA
Department of Internal Medicine, University of Utah, Salt Lake City, UT, USA

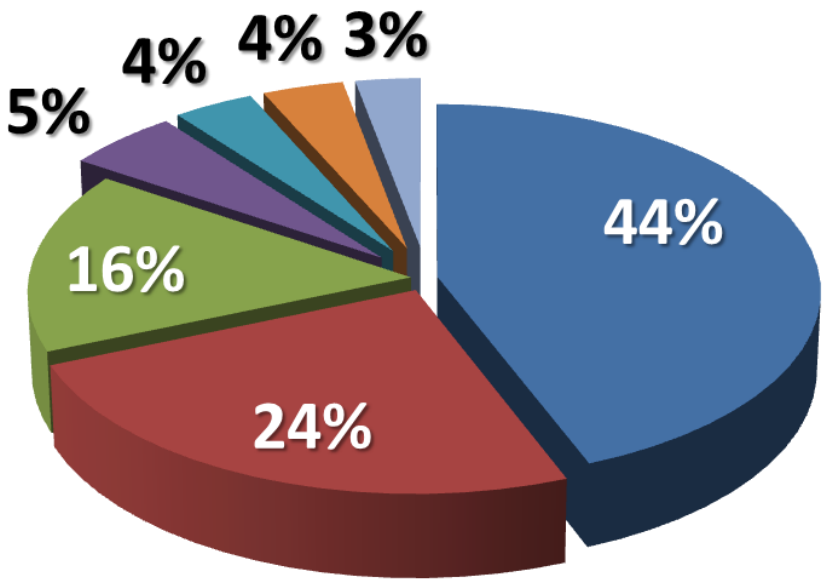
16 July 2009

Evaluating Existing Pediatric RIs: Critical Questions

- Reference population?
  - Small sample number
  - Data mining or indirect-sampling
  - Sick vs. healthy
  - Test bias
  - Tanner staging
- Method?
  - Method specific
  - Outdated methods

- Historical literature?
- Rampant adoption without validation
  - Lab to lab to lab…
  - Method specific
  - Are RIs even valid anymore?

Pediatric RIs: Sources



TSH
N = 134 labs

- Pkg Insert
- Literature, Textbooks
- Internal Study
- Other Labs (Internal Validation)
- Medical Staff Recommendation
- Other
- Other Labs (No Internal Validation)

From: Friedberg et al., Arch Pathol Lab Med (2007) 131:348

Practical Concerns in Pediatric Testing

Sample volumes:

- Adequate volume for dilution
- Adequate volume for repeat testing
- Multiplex testing when possible
- Avoid sample splitting

Outline

ARUP: Background, Resources, Research and Development

Pediatric Reference Intervals: Challenges and Concerns

CHILDx Initiative

Current Improvements and Future Developments

Conclusions and Questions

CHILDx
AN ARUP INITIATIVE

Children's Health Improvement Through Laboratory Diagnostics

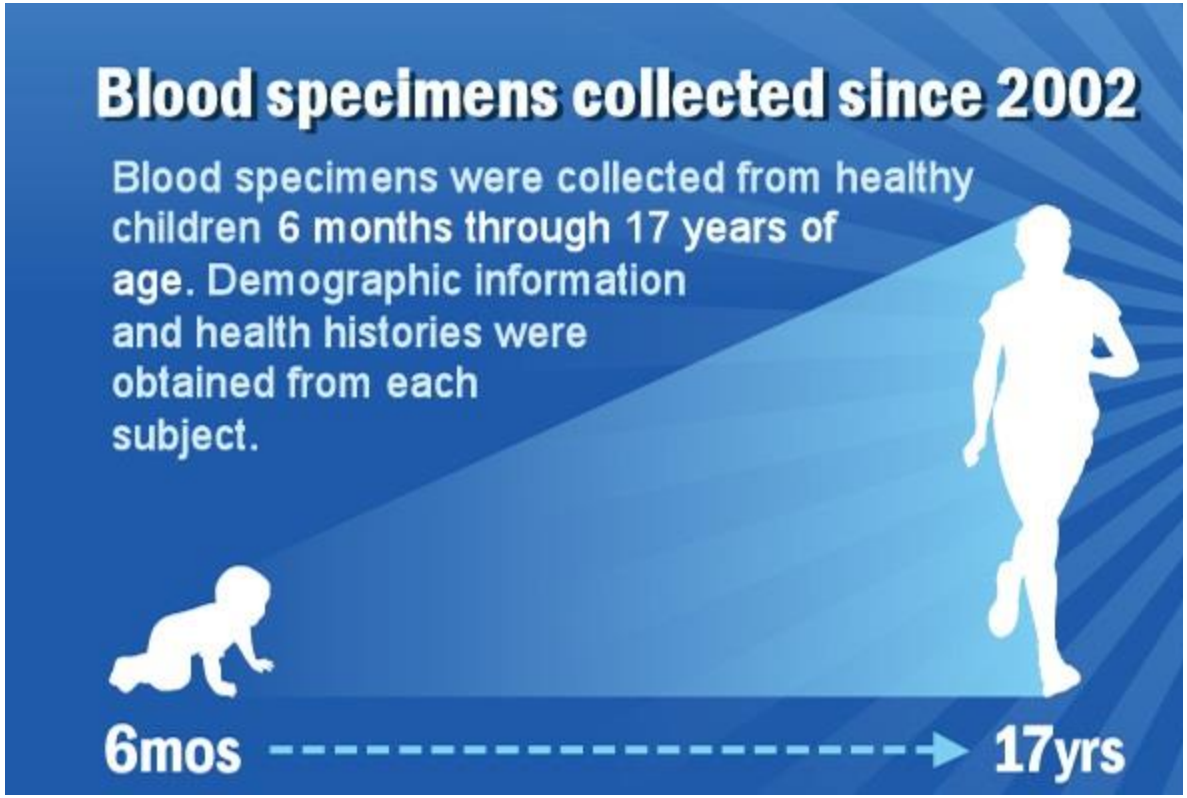
- Formed in 1999
- Address:
  - Poor number of analytes
  - Poor sample size
- Board of Directors established, 15 institutions
- Largest U.S. study of its kind

National Advisory Board:

- Marzia Pasquali, PhD: Chair
- Edward Ashwood, MD
- Mark Astill, MS
- Phillip Bach, PhD
- Carlo Brugnara, MD
- Gregory Buffone, PhD
- Cheryl Coffin, MD
- Sharon Geaghan, MD
- Marilyn Hamilton, MD, PhD
- Harry Hill, MD
- Patricia Jones, PhD
- Michael Laposata, MD, PHD
- Nicola Longo, MD, PhD
- Naomi Luban, MD
- Wayne Meikle, MD
- Mary Murray, MD
- Jeanne Panlener, MS, MT(ASCP)
- Sherrie Perkins, MD, PhD
- Deborah Perry, MD
- Maria Proytcheva, MD
- Theodore Pysher, MD
- William Roberts, MD, PhD
- Joe Rutledge, MD
- Suresh Shelat, MD, PhD
- Paul Steele, MD
- Darrel Yamane, MBA

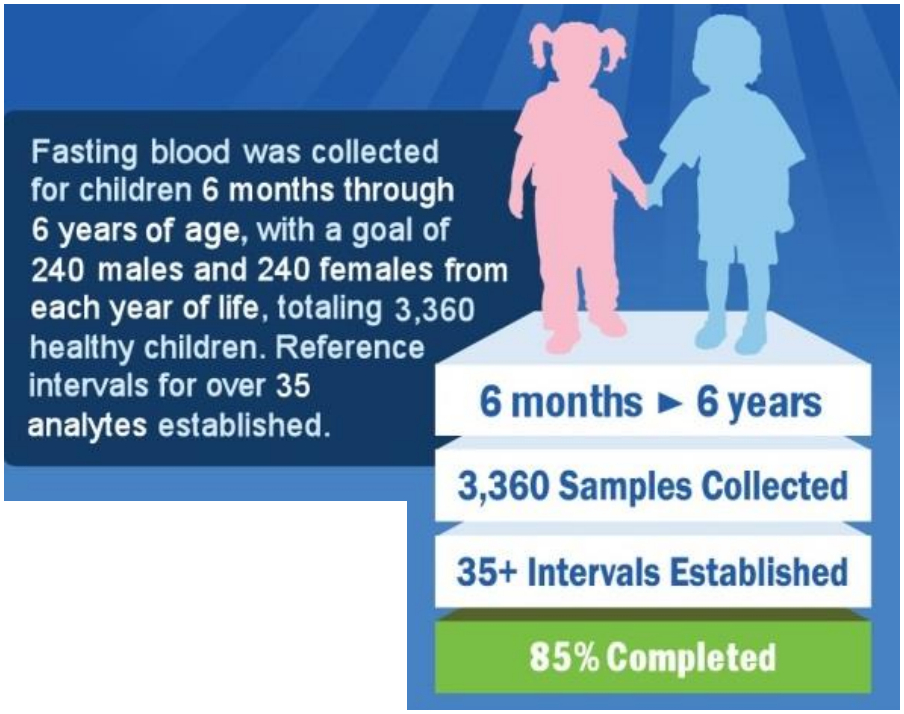
Goal: Establish reference intervals for pediatric patients, for a wide variety of analytes

ARUP Pediatric Reference Interval Study:



6 mos through 6 yrs 7 yrs through 17 yrs

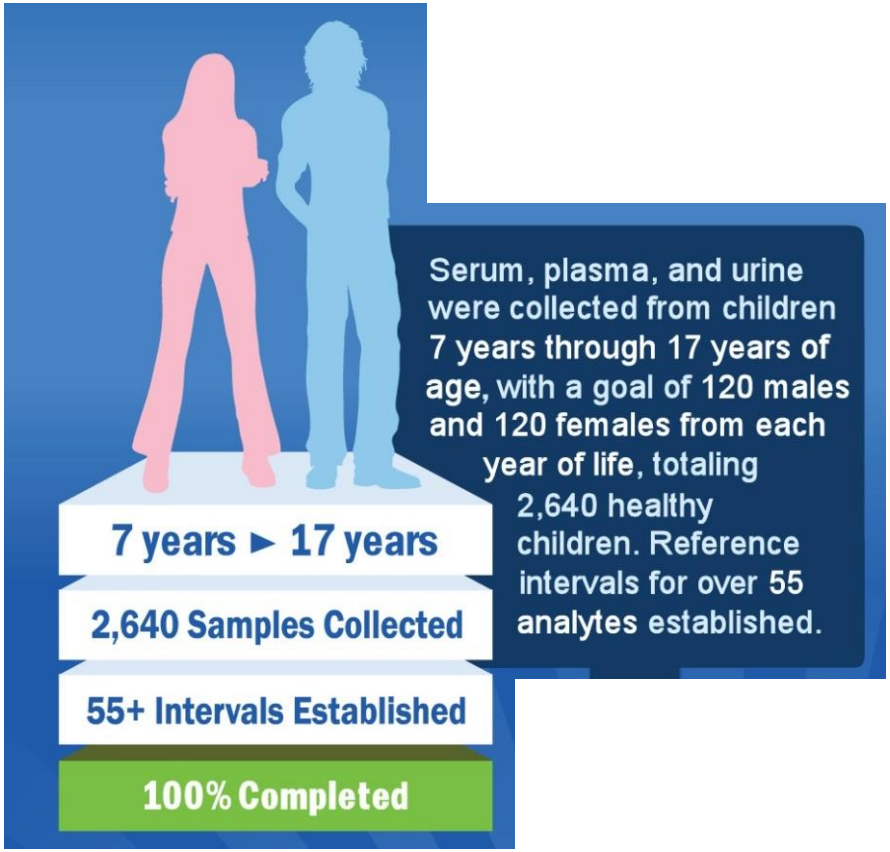
6 Months Through 6 Years:



- Started 2006, collection ongoing
- Goal = 3,360 children
  - 240 boys each year of life
  - 240 girls each year of life

- Screened prior to elective surgeries
- Fasting
- No prescription medications
- Blood (serum) collected through IV, after induction of anesthesia
- Height and weight (BMI)
- Chart review, no exam

7 Years Through 17 Years:



- Started 2002; completed Spring, 2011
- Goal = 2,640 children
  - 120 boys each year of life
  - 120 girls each year of life
- Recruited via community advertisement
- No prescription medications
  - Allergy, BCP, acne, antidepressants
- Serum, citrated plasma, and urine collected
- Physical exam, including Tanner stage and BMI
  - Performed by single individual

Expanded Collection: Fasting Samples

- Started 2011; collection ongoing
- Serum collection, fasting individuals
- Ages 7 through 17 years
- Goal = 880 children
  - 40 boys each year of life
  - 40 girls each year of life
- Collections > 30% completed

Example: RI by Age & Gender

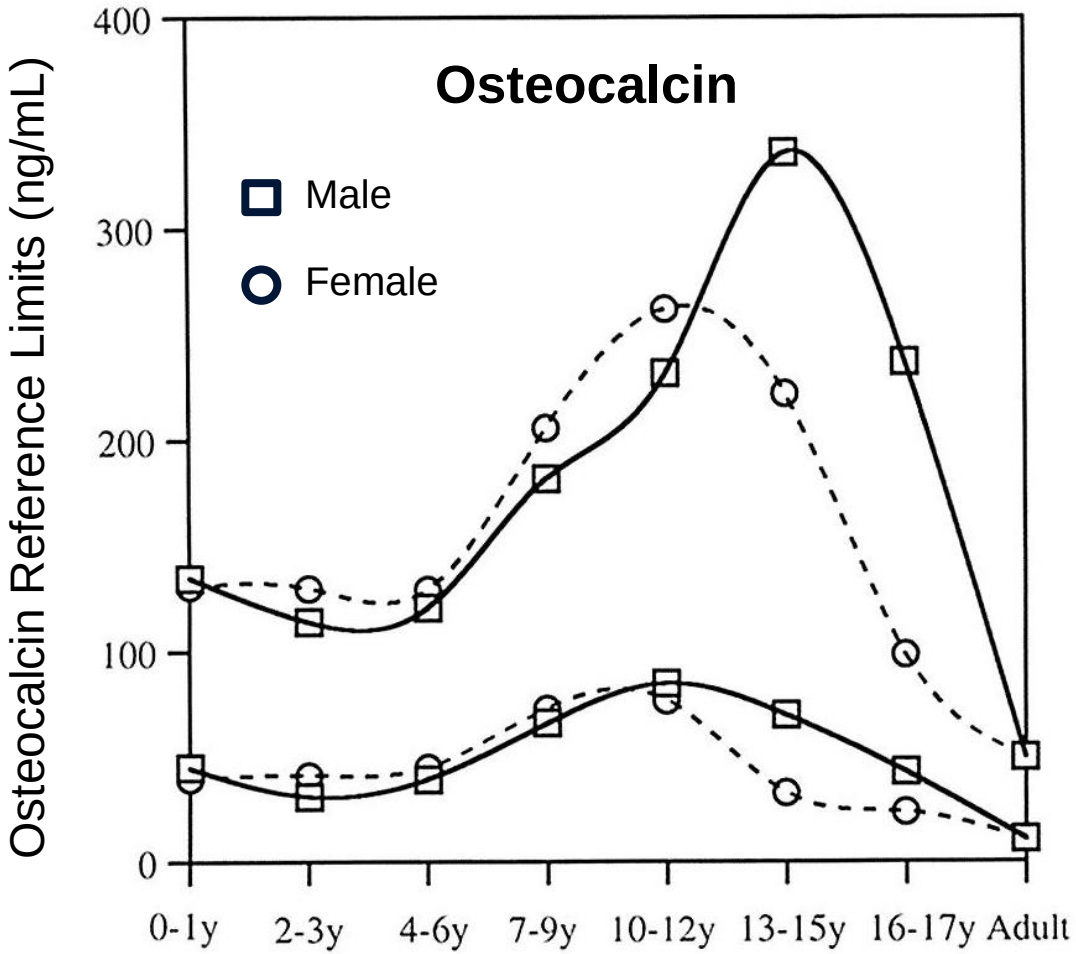


Table 1. Serum androgen reference intervals for males according to TS and age.

	N	Androstenedione, ng/L	DHEA, ng/L	Testosterone, ng/L
TS				
1	278	35–320	110–2370	16–150
2	131	79–480	370–3660	33–3030
3	140	140–870	750–5240	100–8510
4 and 5	204	270–1070	1216–67030	1620–8470
Age				
6–24 months	123	25–150 (<140)[a]	<2500 (<2170)	<370 (<280)
2–3 years	125	<110 (<100)	<630 (<430)	<150 (<130)
4–5 years	125	23–170 (<150)	<950 (<880)	<190 (<180)
6–7 years	125	10–290 (20–240)	60–1930 (80–1780)	<130 (10–130)
7–9 years	206	30–300	100–2080	17–81
10–11 years	140	70–390	320–3080	23–1650
12–13 years	143	100–640	570–4100	30–6190
14–15 years	141	180–940	930–6040	310–7330
16–17 years	136	300–1130	1170–6520	1580–8260
18–40 years	70	330–1340	1330–7780	2070–6970
40–67 years	61	230–890	630–4700	1320–6930

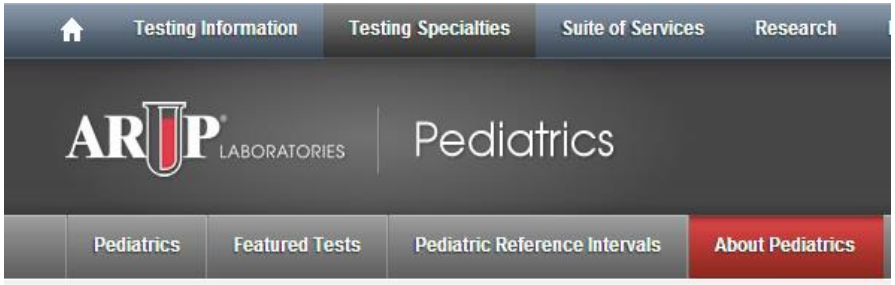
[a] Values in parentheses correspond to the central 90% of the distribution.

Table 2. Serum androgen reference intervals for females according to TS, menstrual status, and age.

	N	Androstenedione, ng/L	DHEA, ng/L	Testosterone, ng/L
TS				
1	296	45–510	140–2760	19–170
2	120	150–1370	830–4870	45–400
3	135	370–2240	1080–7560	100–630
4 and 5	205	350–2050	1240–7880	110–620
Menstrual status				
Before menarche	413	48–1080	160–4050	19–350
After menarche, ≤18 years	323	330–2130	1110–7700	100–630
Premenopausal, >18 years	104	260–2140	1120–7430	90–550
Postmenopausal	86	130–820	600–5730	47–320
Age				
6–24 months	92	<150 (<130)[a]	<1990 (<780)	<90 (<90)
2–3 years	126	<160 (<130)	<850 (<680)	<200 (<140)
4–5 years	127	20–210 (<180)	<1030 (70–770)	<300 (10–200)
6–7 years	131	20–280 (40–300)	<1790 (120–1520)	<70 (10–60)
7–9 years	206	40–420	140–2350	10–110
10–11 years	148	90–1230	430–3780	29–320
12–13 years	142	240–1730	890–6210	60–500
14–15 years	143	390–2000	1220–7010	60–520
16–17 years	138	350–2120	1420–9000	90–580
18–40 years	74	NA[b]	1330–7780	NA[b]
>40 years	116	NA[b]	630–4700	NA[b]

[a] Values in parentheses correspond to central 90% of the distribution.
[b] NA, not applicable because menstrual-status dependent.

Kushnir MM et al. Clin Chem. 2010 Jul;56(7):1138-47



- **37 analytes**
- **53 articles and abstracts**

Published Articles and Abstracts

Aldolase

Jacobsen JR, Bunker AM, Roberts WL. Age– and gender–specific pediatric reference intervals are necessary for serum aldolase and uric acid. *Am J Clin Path* 2007;128:505 (presented at the ACLPS annual meeting in San Diego).

Bunker AM, Roberts WL. Reference intervals for seven chemistry analytes for children 6 months through 6 years old. *Am J Clin Path* 2009;132:457–8 (presented at the ACLPS annual meeting in Los Angeles).

Clifford SM, Bunker AM, Jacobsen JR, Roberts WL. Age– and gender–specific pediatric reference intervals for aldolase, amylase, ceruloplasmin, creatine kinase, pancreatic amylase, prealbumin, and uric acid. *Clin Chim Acta* 2011;412:788–90.

Alpha-Fetoprotein (AFP)

La'ulu SL, Rasmussen KJ, Roberts WL. **Pediatric reference intervals for serum alpha–fetoprotein**. *Clinica Chimica Acta* 2011;412(17–18):1695–6.

Amylase

Jacobsen JR, Bunker AM, Roberts WL. Age– and gender–specific pediatric reference intervals are necessary for serum aldolase and uric acid. *Am J Clin Path* 2007;128:505 (presented at the ACLPS annual meeting in San Diego).

Bunker AM, Roberts WL. Reference intervals for seven chemistry analytes for children 6 months through 6 years old. *Am J Clin Path* 2009;132:457–8 (presented at the ACLPS annual meeting in Los Angeles).

Clifford SM, Bunker AM, Jacobsen JR, Roberts WL. Age– and gender–specific pediatric reference intervals for aldolase, amylase, ceruloplasmin, creatine kinase, pancreatic amylase, prealbumin, and uric acid. *Clin Chim Acta* 2011;412:788–90.

Androstenedione

Kushnir MM, Blamires T, Rockwood AL, Roberts WL, Yue B, Erdogan E, Bunker AM, Meikle AW. LC–MS/MS assay for androstenedione, dehydroepiandrosterone, and testosterone with pediatric and adult reference intervals. *Clin Chem* 2010;56:1138–47.

...

CHILDx:

Recent Publications & Manuscripts

Letter to the Editor

Pediatric reference intervals for four serum bone markers using two automated immunoassays

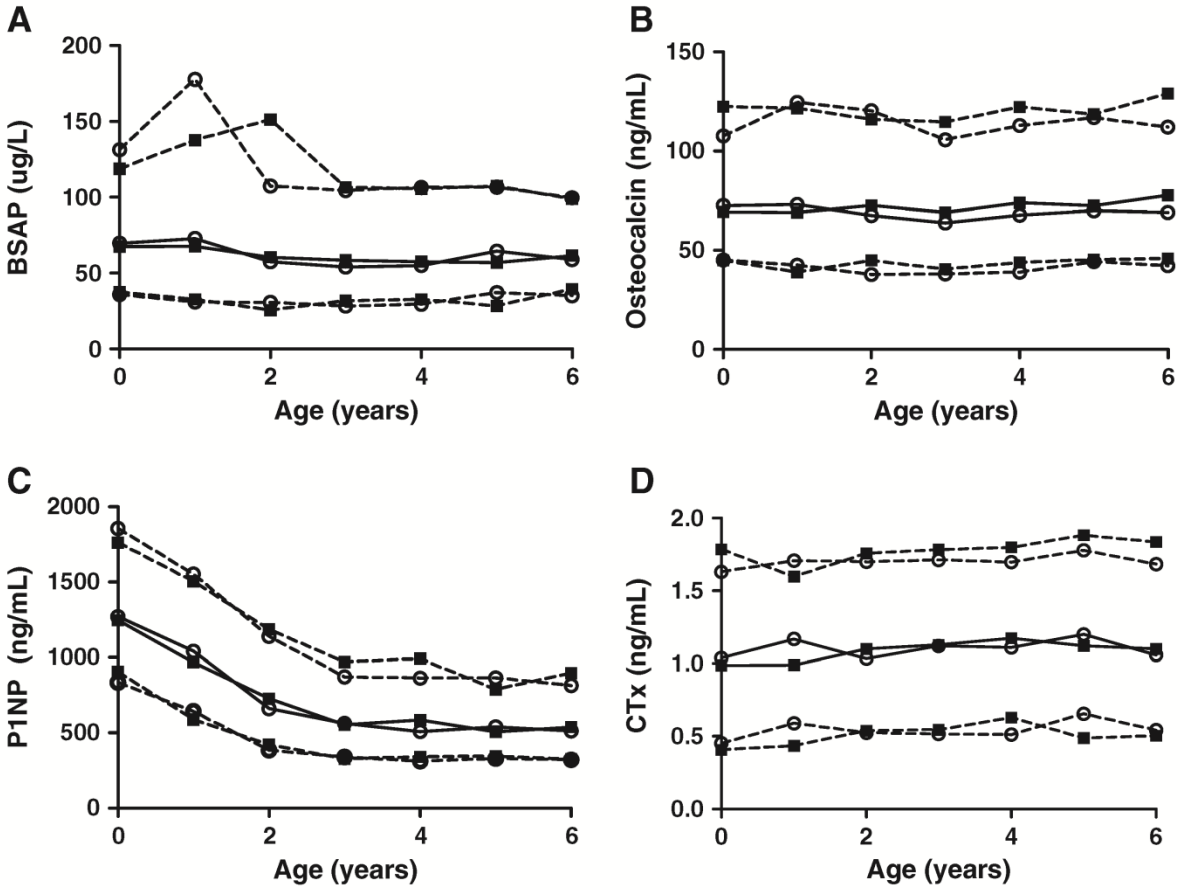
Clinica Chimica Acta 415 (2013) 169–172

Sara P. Wyness
William L. Roberts
Joely A. Straseski*
ARUP Institute for Clinical and Experimental Pathology, Salt Lake City, UT, United States
Department of Pathology, University of Utah Health Sciences Center, Salt Lake City, UT, United States

CHILDx:

Recent Publications & Manuscripts

- Beckman Dxl
- Roche Modular E170



Clinica Chimica Acta 415 (2013) 169-172

CHILDx:

Recent Publications & Manuscripts

Thyroglobulin Reference Intervals for the Access 2 Immunoassay:

Gender	Age Range (years)	N	Lower Reference Limit (ug/L)	90% CI*	Upper Reference Limit (ug/L)	90 % CI*
M&F	0.5 - 3	279	7.4	6.2 - 8.6	48.7	44.0 - 62.1
M&F	4 - 7	284	4.1	2.5 - 5.5	40.5	34.0 - 43.6
M&F	8 - 17	698	0.8	0.3 - 1.3	29.4	27.2 - 33.8

*CI = confidence interval

Manuscript Accepted, Clinica Chimica Acta 2014

CHILDx:

Recent Publications & Manuscripts

FT4 Reference Intervals Using ED-MS/MS:

Gender	Age Range (years)	N	Lower Limit (pmol/L)	95% CI* (Lower Limit)	Upper Limit (pmol/L)	95% CI* (Upper Limit)
M&F	0-6	840	18.0	16.7 – 18.0	34.7	33.0 – 37.3
M&F	7-17	1373	14.2	14.2 – 14.2	25.7	25.7 – 27.0

*CI = confidence interval

CHILDx:

Recent Publications & Manuscripts

FT3 Reference Intervals Using ED-MS/MS:

Gender	Age Range (years)	N	Lower Limit (pmol/L)	95% CI* (Lower Limit)	Upper Limit (pmol/L)	95% CI* (Upper Limit)
F	0-6	401	5.8	5.4 – 6.3	13.1	12.1 – 13.4
F	7-12	378	5.5	5.4 – 5.8	10.0	9.8 – 10.1
F	13-17	305	4.5	4.3 – 4.8	8.6	8.6 – 9.1
M	0-6	438	5.7	5.4 – 6.3	11.8	11.5 – 12.1
M	7-12	381	5.7	5.2 – 6.0	9.8	9.7 – 10.1
M	13-17	310	5.2	5.1 – 5.5	9.4	9.1 – 9.8

*CI = confidence interval

Outline

ARUP: Background, Resources, Research and Development

Pediatric Reference Intervals: Challenges and Concerns

CHILDx Initiative

Current Improvements and Future Developments

Conclusions and Questions

New Resource:
ARUP Pediatrics Website

www.aruplab.com/pediatrics

www.aruplab.com/pediatrics

Testing Information | Testing Specialties | Suite of Services | Research | Education | About ARUP | ARUP Connect

ARUP LABORATORIES | Pediatrics

Laboratory Test Directory | Search Site

Browse A–Z | Search the LTD.

Pediatrics | Featured Tests | Pediatric Reference Intervals | About Pediatrics | About ARUP | Additional Resources

Find a test.
Search our online database for a pediatric test.

Reference intervals.
Read more about ARUP's Pediatric Reference Interval Study.

ARUP Genetics.
Visit our Genetics website for all genetic tests related to pediatrics testing.

Find an expert.
Visit our Pediatric Experts page to contact one of our specialists pertaining to a test.

Welcome to ARUP Pediatrics

Why do so many children's hospitals in the United States use ARUP as their reference laboratory?

Commitment to Pediatric Patient Care

Our commitment to children's health prompted ARUP to initiate the **Children's Health Improvement through Laboratory Diagnostics (CHILDx) study** more than a decade ago. The study established laboratory reference intervals for a variety of analytes for pediatric patients. Thus far, we have completed 92 percent of the 6,000 specimens needed to reach our goal and commitment to this special group of patients.

ARUP Laboratories provides quality care for pediatric patients and offers one of the most extensive reference laboratory test

Send us your feedback!
Please provide any suggestions on how to improve our new website.

What's New

- **Congenital CMV screening**
  Utah-mandated CMV testing
- **Newborn screening**
  (formerly "PKU test")
- **Umbilical cord and meconium testing**
  Neonatal drug testing

Educational Opportunities

www.aruplab.com/pediatrics

Testing Information | Testing Specialties | Suite of Services | Research | Education | About ARUP | ARUP Connect

ARUP LABORATORIES | Pediatrics

Laboratory Test Directory | Search Site

Browse A–Z | Search the LTD.

Pediatrics | Featured Tests | Pediatric Reference Intervals | About Pediatrics | About ARUP | Additional Resources

ARUP Pediatrics Test Menu

ARUP offers a test menu that accommodates more than 99 percent of pediatric testing requests for the diagnosis and management of conditions that affect the healthy growth and development of the pediatric patient. With a large percentage of testing performed at ARUP, children's hospitals can be more operationally efficient with their referral testing.

Search our Full Laboratory Test Directory

Search our entire Laboratory Test Directory for all available pediatrics testing:

Search LTD

Featured Tests | Experts

Search:

Test #	Test Name	Additional Information
0081335	1,5 Anhydroglucitol (Glycomark)	
0092331	11-Deoxycortisol Quantitative by LC-MS/MS, Serum or Plasm	
0092333	17-Hydroxypregnenolone Quantitative by LC-MS/MS, Serum or Plasma	

Featured Pediatric Tests

- Allergens
- Cardiovascular
- Developmental Delay Evaluation
- Drugs, Toxins, and Trace Elements
- Endocrine Disorders
- Gastrointestinal Disease
- Hematology
  - Inherited Hematological/ Hemostasis Disorders
  - Leukemia, Lymphoma, and Oncology
- Immunologic and Autoimmune Disorders
- Infectious Disease Testing
  - Bacteriology/Virology
  - Molecular
  - Parasitology
  - Serology
- Inherited Metabolic Disorders
- Maternal/Fetal
- Molecular Testing for Inherited

www.aruplab.com/pediatrics

Testing Information | Testing Specialties | Suite of Services | Research | Education | About ARUP | ARUP Connect

ARUP LABORATORIES | Pediatrics

Laboratory Test Directory | Search Site

Browse A–Z | Search the LTD.

Pediatric Reference Intervals

ARUP is committed to establishing pediatric reference intervals. Jointly sponsored by ARUP Laboratories and the University of Utah Department of Pathology, the **Children's Health Improvement through Laboratory Diagnostics (CHILDx)** program was formed in 1999 and included a National Advisory Committee.

CHILDx focused on the unique challenges of pediatric laboratory medicine. Working in partnership with pediatric healthcare professionals across the country, the program aspired to improve the healthcare of children through service, education, and research in pediatric laboratory testing.

To validate a method for use in the diagnosis of clinical disorders, the hormones or chemical substances must be measured in large normal populations of various ages and both genders. In 2002, the pediatric reference interval study was initiated at ARUP for the purpose of determining pediatric reference intervals for a number of clinical laboratory assays. Demographic and health histories were obtained on each subject, with specimens collected at ARUP and Primary Children's Medical Center in Salt Lake City, Utah.

Children 6 months through 6 years:

- Fasting serum collected
- Collection goal: 240 males and 240 females from each year of life (85 percent complete)
- 35 reference intervals established toward the 66 proposed

Children 7 years through 17 years:

- Full physical exam

Send us your feedback!
Please provide any suggestions on how to improve our new website.

ARUP Client Services

ARUP Client services is available 24 hours per day.

(800) 522-2787
clientservices@aruplab.com

Supporting Literature

- Pediatric Testing Services
- Genetics Services
- Molecular Testing Services
- Umbilical Cord Testing

www.aruplab.com/pediatrics

Testing Information | Testing Specialties | Suite of Services | Research | Education | About ARUP | ARUP Connect

ARUP LABORATORIES | Pediatrics

Laboratory Test Directory | Search Site

Browse A–Z | Search the LTD.

Pediatrics | Featured Tests | Pediatric Reference Intervals | About Pediatrics | About ARUP | Additional Resources

ARUP Pediatrics Experts

Consultations for anatomic and clinical pathology for pediatrics are provided by ARUP's medical directors and clinical consultants. These staff members hold faculty appointments in the Department of Pathology at the University of Utah School of Medicine and are board-certified in their areas of specialty. They conduct research and remain current on diagnostic and therapeutic issues through their involvement in academics and clinical practice.

Peter E. Jensen, MD

Chair, Department of Pathology and ARUP Board

Jerry W. Hussong, MD, MS

Vice President
Chief Medical Officer and Director of Laboratories

Division of Pediatric Pathology

Theodore J. Pysher, MD

Chief, Pediatric Pathology and Electron Microscopy

Amy Lowichik, MD, PhD

Staff Pathologist, Pediatric Pathology

Jessica Comstock, MD

Pediatric Pathologist

Mouied Alashari, MD

Pediatric Pathologist

Send us your feedback!
Please provide any suggestions on how to improve our new website.

Ordering Information

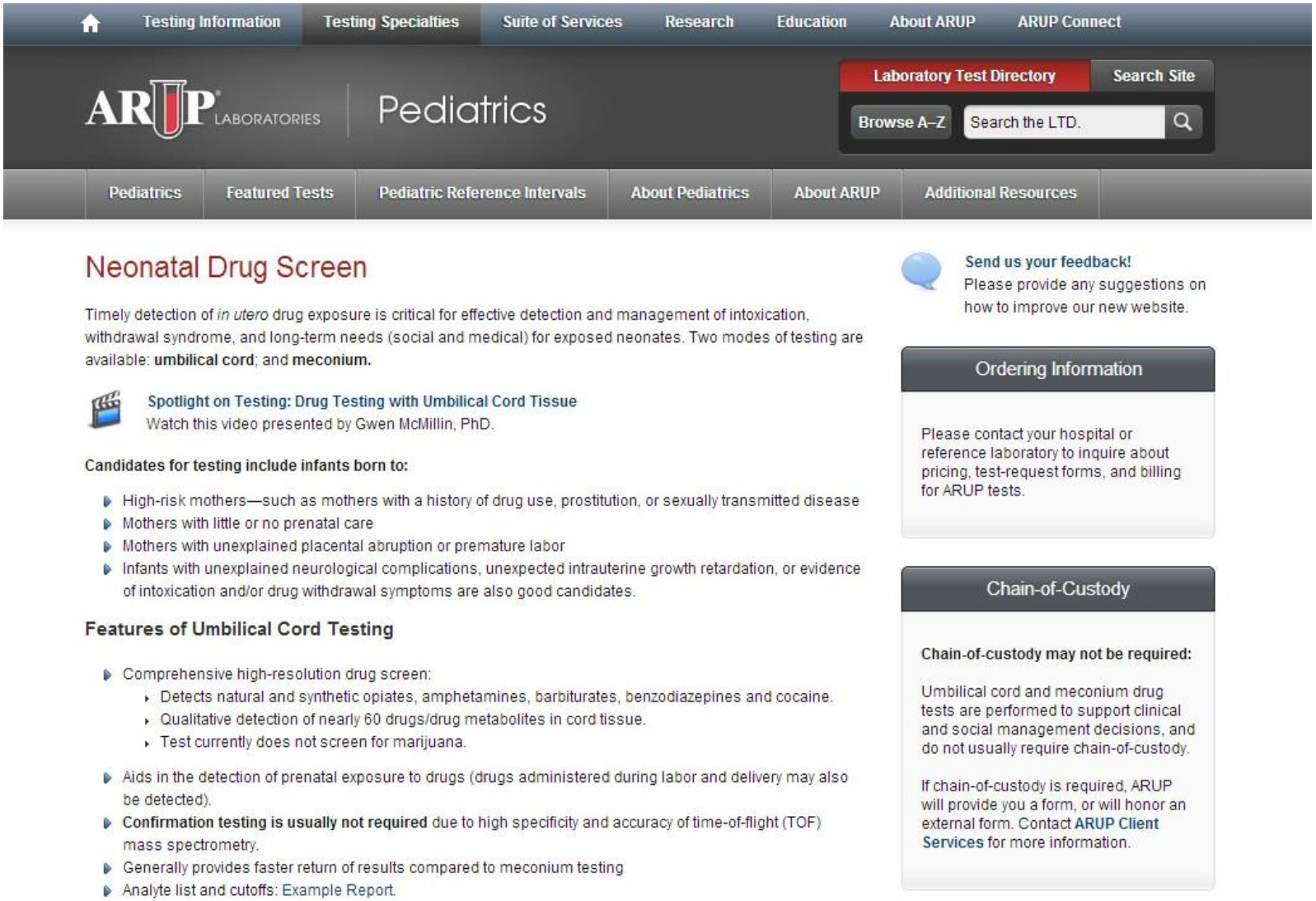
Please contact your hospital or reference laboratory to inquire about pricing, test-request forms, and billing for ARUP tests.

ARUP Client Services

ARUP Client services is available 24 hours per day.

(800) 522-2787
clientservices@aruplab.com

www.aruplab.com/pediatrics



Reference Intervals and Reporting:

IGF-1 (Insulin-Like Growth Factor 1) Pubertal Ranges by Tanner Stage:

FEMALE PUBERTAL RANGES BY TANNER STAGE

AGE	TANNER STAGE I	TANNER STAGE II	TANNER STAGE III	TANNER STAGE IV & V
3 years	26–162 ng/mL	–	–	–
4 years	32–179 ng/mL	–	–	–
5 years				
6 years				
7 years				
8 years				
9 years				
10 years				
11 years				
12 years				
13 years				
14 years				
15 years				
16 years				
17 years				
18 years				

MALE PUBERTAL RANGES BY TANNER STAGE

AGE	TANNER STAGE I	TANNER STAGE II & III	TANNER STAGE IV & V
3 years	20–141 ng/mL	–	–
4 years	25–157 ng/mL	–	–
5 years	30–174 ng/mL	–	–
6 years	37–192 ng/mL	–	–
7 years	44–211 ng/mL	–	–
8 years	52–231 ng/mL	39–264 ng/mL	–
9 years	61–252 ng/mL	52–304 ng/mL	–
10 years	71–275 ng/mL	67–347 ng/mL	–
11 years	82–299 ng/mL	86–393 ng/mL	277–673 ng/mL
12 years	93–324 ng/mL	106–443 ng/mL	265–652 ng/mL
13 years	106–350 ng/mL	130–497 ng/mL	241–612 ng/mL
14 years	120–377 ng/mL	156–554 ng/mL	220–574 ng/mL
15 years	127–391 ng/mL	185–616 ng/mL	199–537 ng/mL
16 years	–	201–648 ng/mL	180–501 ng/mL
17 years	–	–	161–467 ng/mL
18 years	–	–	144–434 ng/mL

Endocrine-Related Analytes With RIs by Tanner Stage: *Examples*

- Follicle Stimulating Hormone
- Luteinizing Hormone
- Free Testosterone
- Bioavailable Testosterone
- Total Testosterone
- Sex Hormone Binding Globulin
- Androstenedione
- 17-Hydroxyprogesterone
- 17-Hydroxypregnenolone
- Fractionated Estrogens
- Pregnenolone
- Dehydroepiandrosterone
- Dehydroepiandrosterone Sulfate
- 11-Deoxycortisol
- IGF-1
- IGFBP-3

Endocrine-Related Panels: *Examples*

- Congenital Adrenal Hyperplasia Panel, 11-beta Hydroxylase Deficiency
- Congenital Adrenal Hyperplasia Panel, 21-Hydroxylase Deficiency
- Congenital Adrenal Hyperplasia Treatment Panel
- Adrenal Steroid Quantitative Panel
- Virilization Panel 1
- Virilization Panel 2
- Hirsutism Evaluation Panel

ARUP LABORATORIES | 500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: (801) 583-2787 | toll free: (800) 522-2787
JERRY W. HUSSONG, MD | Laboratory Director
www.aruplab.com

Enhanced Report

Hepatitis C Virus RNA Quantitative, Real-Time PCR

ARUP Accession number:
Patient:
Date of birth:
Age:
Gender:

Collection date:
Received in lab:
Completion date:

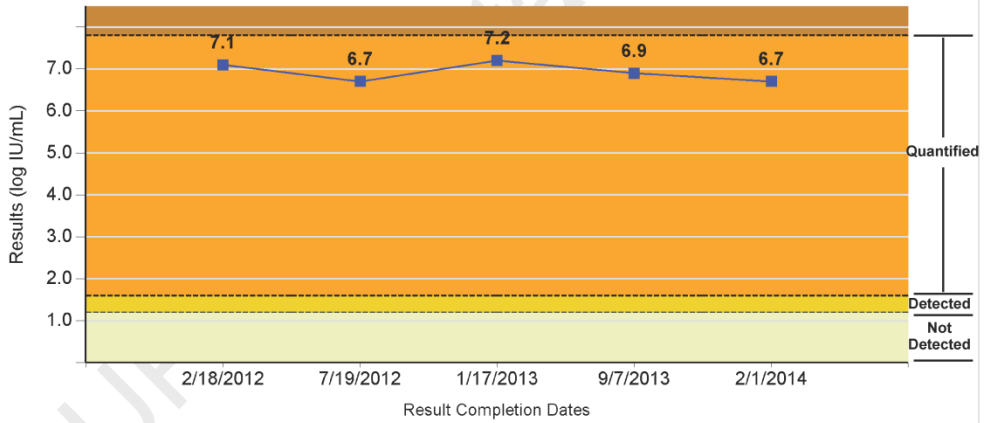
ARUP Test Code: 0098268

Physician:
Client ID:
Client:

Patient History *

Patient Name	Accession	Result (log IU/mL)	Collected	Completed
		7.1	2/16/2012 3:30:00 PM	2/18/2012 9:05:45 AM
		6.7	7/17/2012 9:00:00 AM	7/19/2012 7:20:17 AM
		7.2	1/16/2013 1:00:00 PM	1/17/2013 6:46:20 PM
		6.9	9/5/2013 1:40:00 PM	9/7/2013 7:54:03 PM
		6.7	1/30/2014 1:44:00 PM	2/1/2014 5:32:56 PM

Hepatitis C RNA Viral Load Results



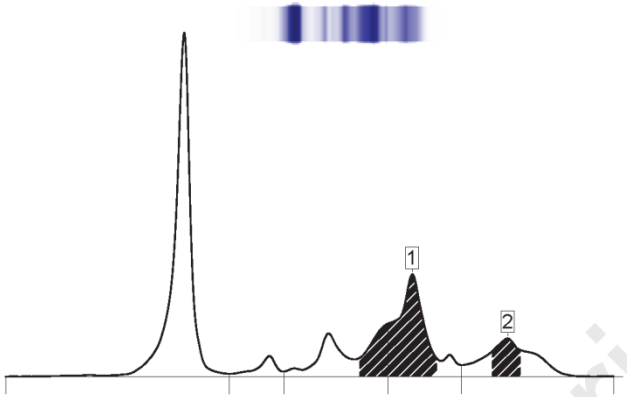
- Detected – Quantified or above linear range.
- Detected – Not Quantified (< 1.6 log IU/mL; virus cannot be accurately quantified below this level).
- Not Detected – Below limit of detection (< 1.2 log IU/mL).

*Consecutive test results are displayed on this chart; however, this result set may be incomplete due to variations in the demographic information submitted for prior tests. If the information shown on this chart appears incomplete, please consult this patient's prior charts.

ARUP LABORATORIES

500 Chipeta Way Salt Lake City, UT 84108
801-583-2787
CapillarysA S/N: 1230
Date : 3/11/2014

Name:
Accession # :
Date of birth:
Age:
Patient ID #:
Sample date:
Sample #:



Total Protein: 8.5 g/dL T.P. Ref. Range: 6.0 - 8.3 g/dL

Fractions	Rel %	g/dL		Ref. %	Ref. g/dL
Albumin	43.3	3.68	-	55.1 - 65.7	3.75 - 5.01
Alpha 1	3.2	0.27		3.1 - 5.6	0.19 - 0.46
Alpha 2	16.7	1.42	+	8.0 - 12.7	0.48 - 1.05
Beta	22.5	1.91	+	8.5 - 12.8	0.48 - 1.10
Gamma	14.3	1.22		10.3 - 18.2	0.62 - 1.51

Peaks	%	g/dl
1	27.2	2.31
2	6.5	0.55

Operator Initials: LT

Interpretation:

M-spike in the alpha-2/beta region. The monoclonal protein peak accounts for 2.31 g/dL of the total protein in the alpha-2 and beta regions. This quantitation may include transferrin components. M-spike in the gamma region. The monoclonal protein peak accounts for 0.55 g/dL of the total 1.22 g/dL of protein in the gamma region. Suggest IFE to identify the monoclonal protein(s). Immunofixation electrophoresis (IFE) is a more sensitive technique for the identification of small M-proteins.

ARUP LABORATORIES | 500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: (801) 583-2787 | toll free: (800) 522-2787
JERRY W. HUSSONG, MD | Laboratory Director
www.aruplab.com

Enha

Chromosome Analysis, Amniotic Fluid

ARUP Accession number:	Collection date:	Physician:
Patient:	Received in lab:	Client ID:
Date of birth:	Completion date:	Client:
Age:		
Gender:	ARUP Test Code: 2002293	

Interpretation

Specimen received

Specimen type: Amniotic Fluid
Reason for referral: Abnormal U/S:Oligohydramnios,
Selective Intrauterine Growth Restriction of Mono/Di Twins
Test performed: Chromosome Analysis

Laboratory analysis

Number of cells counted: 15
Number of colonies counted: 15
Number of cells analyzed: 15
Number of cells karyotyped: 15
ISCN Band level: 400
Banding Method: G-Banding

Chromosome results: 46,XX

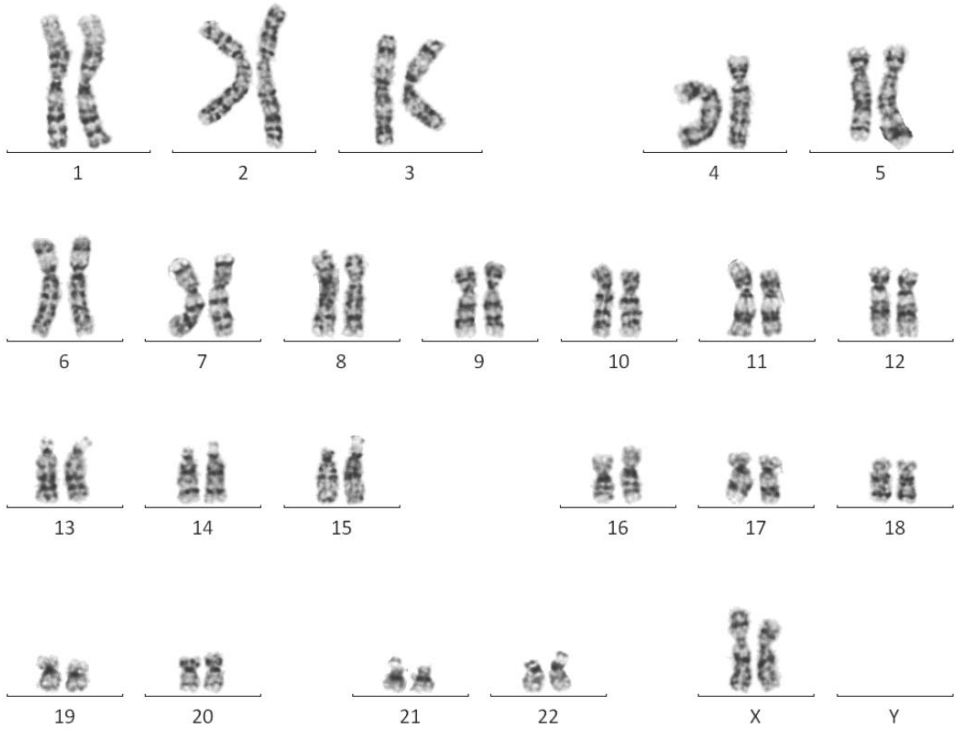
Diagnostic Impression:
Metaphase cells analyzed from multiple cultures of amniocytes revealed a normal female chromosome complement. The standard cytogenetic methodology used in this analysis may not detect small rearrangements or low level mosaicism, and cannot detect submicroscopic deletions or duplications that are detectable by microarray analysis.

NOTE: FISH was performed on this sample and reported under patient ID#(14-023-109730). FISH results were NORMAL.

This result has been reviewed and approved by Jia Xu, M.D., FACMG
Electronic Signature

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C

Slide ID: 0011



ARUP LABORATORIES | 500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: (801) 583-2787 | toll free: (800) 522-2787
JERRY W. HUSSONG, MD | Laboratory Director
www.aruplab.com

Enhanced Report

Calculi (Stone) Analysis with Photo

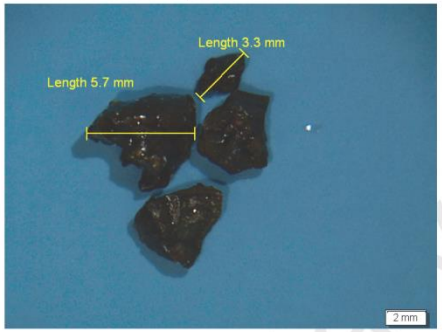
ARUP Accession number:
Patient:
Date of birth:
Age:
Gender:

Collection date:
Received in lab:
Completion date:

ARUP Test Code: 2005231

Physician:
Client ID:
Client:

Patient's calculi specimens submitted for testing



Component	Unit	Test Result
Calculi Mass	mg	188
Calculi Number		4
Calculi Size	mm	Various
Calculi Description		Specimen consists of four, various sized, dark brown, irregular calculi fragments.
Calculi Composition		Calculi composed primarily of calcium oxalate monohydrate.

Interpretive Information

Calculi are the products of physiological processes that yield crystalline compounds in a matrix of biological compounds and blood. Matrix components are not reported. The clinically significant crystalline components identified in calculi specimens are reported. Gross description may not be consistent with the composition determined by FTIR analysis.

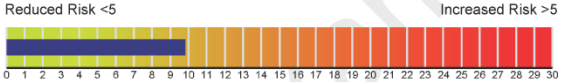
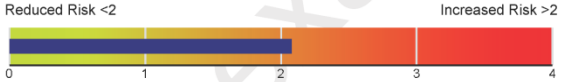
For additional information please refer to Nephrolithiasis Kidney (Stone) topic at www.arupconsult.com

ARUP LABORATORIES | 500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: (801) 583-2787 | toll free: (800) 522-2787
JERRY W. HUSSONG, MD | Laboratory Director
www.aruplab.com

Enhanced Report

Supersaturation Profile, Urine

ARUP Accession number:	Collection date:	Physician:
Patient:	Received in lab:	Client ID:
Date of birth:	Completion date:	Client:
Age:		
Gender:	ARUP Test Code: 2008771	

Calculus	Calculated Risk	Relative Supersaturation
Calcium Oxalate	9.83	
Calcium Phosphate	2.08	
Uric Acid	1.88	

Calculated risk is derived by a computer program that models the thermodynamics of calculi formation using measured urine components.

Component Results

Analyte	Result	Units	Reference Interval	Effect
Total Volume	800	mL		Low urine volume (<1L/24h) promotes calculi formation.
pH	5.40		5.00-7.50	Acidic urine (pH<5.5) promotes precipitation of UrA. Alkaline urine (pH>7.2) promotes formation of CaHPO4 stones.
Calcium	305	mg/d		Hypercalciuria (>200 mg/d) promotes formation of CaOx and CaHPO4 stones.
Oxalate	12	mg/d	4-31	Hyperoxaluria (>40 mg/d) promotes formation of CaOx stones.
Phosphorus	608	mg/d	400-1300	Forms insoluble complexes with calcium.
Sodium	94	mmol/d	51-286	Increased sodium promotes formation of CaOx and CaHPO4 stones.
Sulfate	12	mmol/d	6-30	Normal to high sulfate promotes precipitation of CaOx and CaHPO4 stones.
Urate	369	mg/d	250-750	Hyperuricosuria (>600 mg/d) promotes formation of UrA stones.
Citrate	546	mg/d	320-1240	High citrate inhibits formation of CaOx and CaHPO4 stones.
Magnesium	58	mg/d	12-199	High magnesium inhibits fomation of CaOx and CaHPO4 stones.
Potassium	21	mmol/d	25-125	Forms soluble complexes and inhibits stone formation.
Chloride	85	mmol/d	140-250	Forms soluble complexes and inhibits stone formation.
Creatinine	704	mg/d	500-1400	Excretion provides a measure of completeness of 24h urine collection.

Future: Assay Improvement and Development

Currently On-Line:

- Latest adrenal steroid panel
  - Corticosterone
  - 11-Deoxycortisol
  - 11-Deoxycorticosterone
  - 17-Hydroxyprogesterone
  - Progesterone
- Pico AMH assay
  - Newly established reference intervals (n = 1,324), lower sensitivity (0.003 ng/mL)

Currently In Development:

- 17-Hydroxypregnenolone, pregnenolone
- Ultrasensitive luteinizing hormone
- Aldosterone by LC-MS/MS

Future Development:

- Free testosterone in women and children
  - Equilibrium dialysis
- IGF-II
- IGFBP-1

Outline

ARUP: Background, Resources, Research and Development

Pediatric Reference Intervals: Challenges and Concerns

CHILDx Initiative

Current Improvements and Future Developments

Conclusions and Questions

Conclusions:

- Establishing quality reference intervals in pediatric populations can be challenging.
  - Sources
  - Sample numbers
  - Healthy definitions
- ARUP is invested in serving the needs and missions of pediatric-focused institutions.
  - R&D efforts
  - Automation
  - Publications
  - CHILDx repository
  - www.aruplab.com/pediatrics




End Goal:
Quality results for each and every patient, large or small.




ARUP Gateway

ARUP Consult