



Joint meeting of the
**Newborn Screening and
Genetic Testing Symposium**
and the
**International Society for
Neonatal Screening**

May 5-10, 2013

Atlanta, GA

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New England Newborn Screening Program
Associate Professor, Pediatrics

Case Definitions

Pulmonologist report of a missed CF case

<1 yr old

Lung disease, bowel resection, liver transplant

Sweat Cl: 105 mEq/l

Sweat Cl: 92 mEq/l

One copy of 5t

Pulmonologist report of a missed CF case

IRTpercentiles: 41, 24, 58

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One copy of 5t

NOT CF

Even the best case definitions
(two independent sweat tests)
can fail.

When things don't add up.....

Pulmonologist report of a missed CF case

4 month old

Failure to thrive

Sweat Cl: 60 mEq/l

Pulmonologist report of a missed CF case

IRT percentile: 61.4

5 month old

Failure to thrive

Sweat Cl: 60 mEq/l

Full seq: 711+1G>T; 7t7t

Pulmonologist report of a missed CF case

IRT percentile: 61.4

>6 month old

Failure to thrive

Sweat Cl: 60 mEq/l

Sweat Cl: 35 mEq/l

Full seq: 711+1G>T;7t7t

Pulmonologist report of a missed CF case

IRT percentile: 61.4

>6 month old

Failure to thrive

Sweat Cl: 60 mEq/l

Sweat Cl: 35 mEq/l

Full seq: 711+1G>T;7t7t

NOT CF

In this case,
Specialist continues to follow the child in
clinic...

It's not a missed case of CF.

How to characterize this child?

Should newborn screening be trying to find
infants with these characteristics?



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home > healthy kids center > healthy kids a-z list > newborn screening may miss adrenal-gland disorder article

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Newborn Screening May Miss Adrenal-Gland Disorder



Adult Skin Problem
Recognize These Skin Cond



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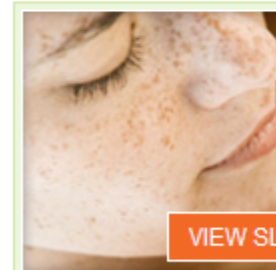
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TUESDAY, June 12 (HealthDay News) -- Routine [newborn screening](#) failed to identify about one-fifth of infants with an [adrenal gland](#) disorder called congenital adrenal [hyperplasia](#), a new study has found.

This genetic disorder is characterized by a

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ADUE

Who are these 20% CAH infants not found by newborn screening?

What do they have – and should we be trying to identify those with these conditions?

Babies' blood tests can end in false-positive screening scares

Newborn panels can save lives, but about 200,000 a year aren't accurate.

Recommend 15

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By JoNel Aleccia
Health writer

msnbc.com
updated 5/9/2011 8:33:12 AM ET

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After seven years of unexplained infertility, Ann Najdek-Andrada finally had a son, a baby boy who seemed as perfect as she'd always imagined.

But that fantasy was shattered when Gianni was two weeks old. That's when the call came saying the child had tested positive for cystic fibrosis — and that it would take nearly four months to find out for sure.



of the babies we do identify.....some will not have the condition...but do they have something related to it?

Where does “it” end and “related” begin?

What are the characteristics of infants with RUSP and related disorders...

Additional Acknowledgements

Melissa A Parisi, NICHD

Jelili A Ojodu, APHL

Cindy Hinton, CDC

Marci K Sontag, Newsteps, CO SPH

Inderneel Sahai, UMass

Surveillance Case Definitions

for newborn screening

Decision-making

To screen or not to screen
Choice of algorithm

Quality assurance

Quality monitoring of screening

Evaluation and Research

Clinical utility of screening

Defining Surveillance Case Definitions

1. To be developed for each RUSP condition,
2. To be used primarily by newborn screening programs,
3. To be based on clinical and laboratory information available by one year of age,
4. To be assigned based on the fit with pre-determined criteria,
5. To encompass a measure of certainty.

6. NOT to determine whether an infant is treated or followed at a clinic.

Minimum Criteria

Simple format

Outline each set that meet minimum criteria

Clarity relative to ands and ors

Intuitive search...

When NBS receives a STFU diagnosis, where does it fit and how certain is it?

Process

Convene clinical working groups for draft definitions

Standardize formats

Incorporate in a REDCap system at NewSTEPs

Pilot preliminary evaluations in state NBS programs

Case Definition Development

- Clinical Experts –
Celia Kaye, Bob Zori, Cary Harding, Nancy Leslie, Maddy Martin, Steve Kahler, Jose Abdenur, David Kronn, Janet Thomas, Anne Comeau, Lorenzo Botto, Susan Berry, Kathy Hassell, Jim Eckman, Ferdane Kutlar, Kim Smith-Whitley, Elliott Vichinsky, Phil Farrell, Frank Accurso, Hank Dorkin, Mike Rock, Drucy Borowitz, Richard Parad, George Retsch-Bogart, Laurie Varlotta, Michelle Howenstine, Vincent Bonagura, Francisco Bonilla, Becky Buckley, Sean McGhee, Jennifer Puck, John M. Routes, Kupper Wintergerst, Marvin Mitchell, Chanika Phornphutkul, Dan Hale, Phyllis Speiser, Susan Rose, Stephen LaFranchi
- Federal and National Partners – CDC, NICHD, NLM, NHLBI, NIH/ORD, ACMG, APHL, NNSGRC

2012 Case Definition Meeting

Swapna Abhyankar
Cindy Ashley
Becky Bailey
Lou Bartoshesky
Linda Beischel
Stan Berberich
Natasha Bonhomme
Bob Bowman
Amy Brower
Michele Caggana
Colleen Clarke
Anne Comeau
Sara Copeland
William Cramer
Hank Dorkin
Roger Eaton
Lisa Feuchtbaum
Bryant Fortner
Lucy Fossen

Debra Freedenberg
Michael Glass
Aaron Goldenberg
Art Hagar
Alaina Harris
Kathryn Hassel
Cindy Hinton
Amy Hoffman
Phillis Hoggatt
Patrick Hopkins
Cindy Ingham
Ward Jacox
Carol Johnson
Jamey Kendall
Janice Kong
Michelle Lewis
Sharon Linard
Jennifer Macdonald
Mark McCann

Susan Oliver
Richard Parad
Melissa Parisi
Julie Raburn-Miller
Deborah Rodriguez
Inderneel Sahai
Scott Shone
Susan Tanksley
Laura Taylor
Lois Taylor
Patricia Terry
Tiina Urv
Sheila Weiss
Kupper Wintergerst
Alan Zuckerman

Pilot Study Participants

Alabama	Cindy Ashley	Missouri	Jami Kiesling
Arizona	Sondi Aponte	Nebraska	Julie Luedtke
Delaware	Lou Bartoshesky		Krystal Baumert
Florida	Lois Taylor		Karen Eveans
Hawaii	Janice Kong	New York	Beth Vogel
Illinois	Claudia Nash		Michele Caggana
Iowa	Carol Johnson		Deborah A. Rodriguez
Kansas	Jamey Kendall	South Dakota	Lucy Fossen
Louisiana	Colleen Clarke	Utah	Kim Hart
Maryland	Johnna L. Watson	Vermont	Cynthia Ingham
Massachusetts	Anne Comeau	Virginia	Jennifer MacDonald
	Neela Sahai		

RUSP CONDITION	# STATES PILOTING	# CASES CONTRIBUTED
CAH	8	48
CONGENITAL HYPOTHYROIDISM	6	68
CYSTIC FIBROSIS	6	60

Congenital hypothyroidism

Primary Congenital Hypothyroidism	Category	Serum TSH mU/L*	Serum Total or Free T4*
	Definite	TSH > 10	< age established reference range
	Probable	TSH > 10	normal T4/total T4
	Probable	TSH > 10	Untested or unknown
	Possible**	TSH 6-10	< age established reference range
	Possible **	TSH 6-10	Normal
	Possible **	TSH 6-10	Untested or unknown
	Incomplete	Untested or unknown	Untested or unknown
Incomplete	Untested or unknown	< age established reference	

Secondary Congenital Hypothyroidism	Category	Serum TSH mU/L*	Serum Total or Free T4*	Other studies
	Definite	TSH < 10	< age established reference	documentation of other pituitary hormone deficiencies or midline defects
	Probable**	TSH < 10	< age established reference range	no other pituitary hormone deficiencies or midline defects
	Possible	Untested or unknown	< age established reference range	Documentation of other pituitary hormone deficiencies or midline defects
	Possible	TSH<10	Untested or unknown	Documentation of other pituitary hormone deficiencies or midline defects
	Incomplete	Untested or unknown	Untested or unknown	Documentation of other pituitary hormone deficiencies or midline defects
	Incomplete	TSH<10	Untested or unknown	no other pituitary hormone deficiencies or midline defects
	Incomplete	Untested or unknown	< age established reference range	no other pituitary hormone deficiencies or midline defects

Congenital Hypothyroidism

Please Choose One:			
Hypothyroidism type	Frequency Reported	Percent	
A. Primary Congenital Hypothyroidism	66	97.06	
B. Secondary Congenital Hypothyroidism	1	1.47	
Does not match A or B	1	1.47	

68 RECORDS

66 listed as Definite Primary Congenital Hypothyroidism

- 28 Definite (TSH>10 and fT4< age adj ref range)
- 28 Probable (TSH>10)
- 3 Possible (TSH 6-10)
- 7 Incomplete – no data

1 listed as Secondary Congenital Hypothyroidism

- 1 Incomplete (TSH<10)

1 no diagnosis available.

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Position Wrap Text Bring Forward Send Backward Selection Pane Rotate

Classification	Clinical	Sweat Chloride	Non Newborn Screen Molecular	Newborn Screen Molecular	NBS Result
Definite		>=60 mmol/L (regardless of age)		2 CF disease-causing mutations	
Definite		No valid sweat chloride result available	2 CF disease-causing mutations <i>in trans</i> –	2 CF disease-causing mutations <i>in trans</i>	
Definite		<60 mmol/L	2 CF disease-causing mutations <i>in trans</i> and 1 or both have been previously shown to have lower chlorides, (e.g., L206W or 3849+10kbC>T)	2 CF disease-causing mutations <i>in trans</i> and 1 or both have been previously shown to have lower chlorides, (e.g., L206W or 3849+10kbC>T)	
Definite	No known medical condition associated with false	>=60 mmol/L x 2 (regardless of age, two independent results)			

Discordant certainties

listed as type: CF definite

Based on the information above please categorize your level of c	Complete?	Field25	annes determination
A. Definite	Complete	2 nbs mut, 1 96	definite
A. Definite	Complete	2 nbs, 1 101, 1 98	definite
A. Definite	Complete	2 nbs, 1 93, 1 92	definite
A. Definite	Complete	2 nbs mut, 1 68 and 1 92	definite
A. Definite	Complete	1 mut 1 95	incomplete
A. Definite	Complete		incomplete
A. Definite	Complete	1 nbs mut, 1 99	incomplete
A. Definite	Complete	1 nbs mut, 1 dx mut, 1 94	no fit
A. Definite	Complete	1 nbs, 1.5 dx, 1 92	no fit
A. Definite	Complete	1 nbs mut, 1 81	no fit

Cystic fibrosis

- 45 Listed as typical CF definite
 - 28 met criteria
 - 5 better fit is probable
 - 3 better fit is incomplete
 - 1 better fit is CRMS
 - 8 no good fit- want to avoid judgment calls

Status

Still have some work to do.
Data elements may need more clarity.
All permutations need to be available.
Training of Programs and Clinicians to ensure
quality data.

Thank-you
Looking forward to your comments!

Thank-you