Pocket Guide to Alaska Native Pediatric Diagnoses

Review of diagnoses rarely seen in other populations

ALASKA NATIVE MEDICAL CENTER

VERSION 1 : SPRING 2016

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Pocket Guide to Alaska Native Pediatric Diagnoses:

Review of Diagnoses Rarely Seen In Other Populations

Version 1: Spring 2016

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Disclaimer:

Contents

Directory of Pediatric Specialists & Clinics

For urgent/emergent pediatric questions:

Call ANMC Paging Operator at
907-563-2662
Ask for the on-call pediatrician

This is a list of current (as of May 2016) pediatric sub-specialties available in Alaska for Alaska Native patients. If you feel your patient needs sub-specialty care, please consider referring them to a local pediatrician, an ANMC Pediatric Field Clinic, or ANMC/Southcentral Foundation Pediatrics Clinic in Anchorage for further evaluation of sub-specialty needs.

Ped. Cardiology *(non-ANMC affiliated)*
Ped. Dermatology *(non-ANMC affiliated)*
Ped. Endocrinology
Ped. Gastroenterology
(non-ANMC affiliated)

Genetics
(visiting from Oregon Health & Science Univ.)
Metabolic Genetics
(visiting from Oregon Health & Science Univ.)
Ped. Nephrology *(non-ANMC affiliated)*
Neurodevelopmental Pediatrics
(non-ANMC affiliated)
Neurosurgery
(general neurosurg based at ANMC)
Ped. Neurology
Ped. Ophthalmology
(non-ANMC affiliated)
Orthopedics
(general ortho based at ANMC)
Otolaryngology/ENT
(general ENT based at ANMC)
Ped. Pulmonology
(visiting from Seattle Children's Hosp. and non-ANMC affiliated)
Ped. Rheumatology
(visiting from Seattle Children's Hosp.)
Ped. General Surgery
Ped. Urology

Carnitine Palmitoyl Transferase, Type 1A Arctic Variant *(CPT1A Arctic Variant)*

Pathophysiology: Fatty acid oxidation disorder; difficulty breaking down fatty acids from both food and body fat

Inheritance: Autosomal recessive

Demographics:

- Considered to be the wild-type (normal) gene in Inupiaq and Yu'pik populations in Alaska (50% are homozygous for the Arctic Variant)
  - Inupiaq = northern Alaska = Barrow, Kotzebue, Nome areas
  - Yu'pik = Yukon-Kuskokwim Delta = Bethel, Dillingham areas
- Total incidence per year in newborns in Alaska = 7%
- Found at a higher rate in all circumpolar coastline populations

including Inuit populations in Canada and Greenland and indigenous populations of northern Siberia
- General population = <1/1,000,000 (general CPT1A deficiency)

Signs/Symptoms: Most children never have symptoms, but if they do, symptoms are more likely to be seen in children <2 years old
- Initial signs of metabolic crisis:
  - Sleepiness
  - Irritability
  - Poor appetite
- Metabolic crisis:
  - Hypoglycemia (hypoketotic)
  - Seizures due to hypoglycemia
  - Death, especially associated with a concomitant infectious disease

Diagnosis:
- Alaska Newborn Screen (processed in Oregon) – added to screen in the fall of 2003

Management: Avoid fasting states

- When healthy, children with CPT1A Arctic Variant should eat like any other child their age.
- When sick, if infants and toddlers with CPT1A are unable to tolerate glucose-containing fluids (Pedialyte, juice, sports drinks) or food for more than 6 to 8 hours, they should see a health care provider immediately for IV or NG glucose-containing fluids.
- Children with CPT1A Arctic Variant who are NPO on IV fluids should always be on dextrose containing fluids (D5-NS or D5-1/2NS). A normal maintenance rate is all that is needed.

Critical Times for Affected Patients:

- Fasting or illness during first 2 years of life
  - Fever
  - Infection
  - Dehydration
  - Surgery

For further questions (non-urgent):

- Matt Hirschfeld, MD (Pediatrician, ANMC)
  MHirschfeld@southcentralfoundation.com
- Charlene DiFilippo, RD (Dietician, SCF Pediatrics)
  CDiFilippo@southcentralfoundation.com

For any urgent/emergent issues, page the ANMC on-call pediatrician: 907-563-2662.

Other resources:

- Newborn Screening Information for Parents
  http://www.newbornscreening.info/Parents/fattyaciddisorders/CPT1AV.html
- YouTube: "The Other Energy Crisis: Arctic Variant CPT1A"
  https://www.youtube.com/watch?v=g-JRZ7PO3yk

Congenital Adrenal Hyperplasia (CAH)

Pathophysiology: Inherited disorders of adrenal steroidogenesis resulting from deficiency in 1 of 5 enzymes necessary for normal cortisol synthesis

- 21-hydroxylase deficiency accounts for 90% of CAH:
  - Classic Salt Wasting (2/3) and Classic Simple Virilizing (1/3)
    - Prenatal androgen excess causes external genital ambiguity in female fetuses
    - Progressive postnatal virilization
    - Aldosterone deficiency seen in salt-wasting variant
  - Mild, non-classic
    - Mild deficiency of 21OHD
    - No genital ambiguity at birth; variable signs of androgen excess at any phase of postnatal

development, can present from birth to teen years

Inheritance: Autosomal recessive

Demographics:

- Yu'pik Eskimos = 1:280 live births
  - Yu'pik = Yukon-Kuskokwim Delta = Bethel, Dillingham areas
- Alaska = 1:4,000 live births
- General = 1:15,000 live births (classic CAH)

Signs/Symptoms of initial presentation by age:

- Newborn:
  - Ambiguous genitalia (females, classic)
- 1 to 2 weeks old:
  - Adrenal crisis (males, classic salt-losing): Failure to thrive, dehydration, hyponatremia, hyperkalemia
- 2 to 4 years old:
  - Early virilization with pubic hair,

growth spurt, adult body odor (males, classic non-salt-losing)
- School age:
  - Hirsutism, menstrual irregularity, early pubarche, sexual precocity (non-classic, school age children)

Diagnosis:
- Newborn Screen – looks for high levels of 17-OH-progesterone seen in classic CAH
- If NBS(+): check levels of 17-OH-progesterone (by mass spectroscopy) and electrolytes
- If concerns for non-classic CAH, consult Peds Endocrinology at ANMC
  - ACTH Stimulation Test (measures serum concentrations of 17-OHP after giving ACTH)
  - 90-95% sensitive (not necessary for classic CAH)

Management:
- Refer to Pediatric Endocrinology

(see below) if not an emergency for long term follow-up when diagnosed clinically or on the NBMS

- If genital ambiguity and nonpalpable gonads, run diagnostic tests and then treat empirically in discussion with Peds Endocrinology. Draw blood for diagnostic tests before treatment. Treat with:
  - Hydrocortisone
  - Fludrocortisone
  - Sodium Chloride
- Adrenal Crisis management (discuss with Endocrinology or ANMC Pediatric Hospitalist on-call in an emergency)
  - Fluids (20mL/kg NS then D5NS or D10NS at 1.5x maintenance)
  - Monitor glucose and electrolytes
  - Stress-dose hydrocortisone (IV or IM)
    - <3yo: 25mg bolus followed by 30mg/day
    - 3-12yo: 50mg bolus followed by 60mg/day

- >12yo: 100mg bolus followed by 100mg/day

Critical Times for Affected Patients:
Any time that could trigger adrenal crisis (hypotension, hyponatremia, +/- hyperkalemia, metabolic acidosis, hypoglycemia)

- First 1 to 4 weeks of life (if undiagnosed)
- When ill or severely stressed (e.g. infectious diseases, surgical procedures, etc)

For further questions:

- Rachel Lescher, MD (Pediatric Endocrinologist, ANMC)

Office phone: 907-729-1000

Admin (Agnes Hunt):
907-729-8822

Case Manager (Sherry Hammock):
907-729-8803

Paging operator:
907-563-2662, ask for pediatric endocrinologist on call

For any urgent/emergent issues, page the ANMC on-call pediatrician:
907-563-2662.

Congenital Sucrase-Isomaltase Deficiency (CSID)

Pathophysiology: Lack intestinal brush border enzyme to breakdown di- and oligosaccharides including sucrose & isomaltose

Inheritance: Autosomal recessive (potential mild form in carriers)

Demographics:

- Likely 3-10% of Alaska Natives (exact numbers not known)
- 3% of Canadian Inuit (28.5% are

carriers)
- 5-10% of Greenland Inuit
- 0.2% of European-descended North Americans

Signs/Symptoms: Watery diarrhea when fed sucrose-containing food (breast milk and many infant formulas have only lactose)

Diagnosis: Genetic screen (blood), run at University of Washington:
- http://depts.washington.edu/moleclab/available/csid.html
- Test: "Circumpolar 5-mutation panel" ($1,091 as of 01/2016)

Management:
- Dietary Modification: Avoid sucrose, isomaltose and maltose (corn syrup is sucrose).
- Enzyme Replacement: Sucraid (sucrose digestion only), costs ~$2000/month, not covered by Alaska Medicaid at this time.

Critical Times for Affected Patients:
When first exposed to sucrose (some formulas; most often when starting solids around 6mo old)

Consider this diagnosis when you have an infant or toddler with chronic diarrhea who has recently started solids or transitioned from breast milk or formula to whole milk and other foods.

For further questions:

- Charlene DiFilippo, RD (Dietician, SCF): CDiFilippo@southcentralfoundation.com
- Sam Maloney, RD (Dietician, ANMC): SMaloney@anthc.org
- Matt Hirschfeld, MD (Pediatrician, ANMC): MHirschfeld@southcentralfoundation.com

Other resources:

- http://www.adn.com/article/20150119/sugar-intolerance-

northern-populations-linked-specific-gene-researchers-say

- http://csidcares.org/

Sucrose-Free Infant Formulas:
Enfamil Enfacare
Similac Advance

Other options:
http://csidcares.org/treatment/infants/

CSID Dietary Recommendations from http://csidcares.org/treatment/diet/

Each patient with CSID responds to foods variably. If a patient tolerates a food listed below without diarrhea, then there is no reason to limit intake.

Fruits to Avoid:
apples
apricots
bananas
cantaloupe (rockmelon)
dates
grapefruit
guava
honeydew melon
mango
nectarine
oranges
passion fruit
peaches
pineapple

tangelos
tangerines
(mandarin
oranges,
clementines)

Fruits Generally Tolerated:
avocado
blackberries
blueberries
boysenberries
cherries
cranberries, fresh
currants
grapes
kiwifruit
lemons/limes
olives
papaya
pears
pomegranates
prunes
raspberries
rhubarb
strawberries

Vegetables to Avoid:
beets
black beans
black-eyed peas (cowpeas)
butternut/ buttercup squash
carrots
cassava (yuca)
carrots
chickpeas (garbanzo beans)
corn
garlic
green peas
lentils
kidney beans
lima beans
navy beans
onions
parsnips
pinto beans
potatoes

soybeans
split peas
sweet potatoes
yams

Vegetables Generally Tolerated:
collard greens
cress
cucumber
eggplant
endive
green beans
kale
lettuce
mung bean sprouts
mushrooms
mustard greens
okra
peppers (red, yellow & green)
radishes
rutabaga
snow peas
spaghetti squash
spinach
tomatoes

turnips
yellow squash
zucchini (courgette)

Kuskokwim Syndrome (Arthrogryposis-like syndrome)

Pathophysiology: Mutation in the FKBP10 gene resulting in impaired collagen cross-linking and disorganization of collagen molecules causing congenital joint contractures

Inheritance: Autosomal recessive

Demographics:

- Rare, incidence unknown
- Found only in Yu'pik population in Kuskokwim River Delta
    - Yu'pik along Kuskokwim River = Bethel area

Signs/Symptoms:

- Range and severity of contractures varies greatly
- Contractures are generally present at birth, worsen during childhood, then stabilize
- Often contractures of large joins, especially knees and elbows
- Other joints may also be involved, especially in lower extremities
- Milder skeletal features are common including:
    - Spine: scoliosis, lordosis, spondylolisthesis
    - Feet: bunions (hallux valgus), flat feet (plano valgus), club feet (talipes equinovarus)

Diagnosis:

- Genetic testing – discuss with ANMC On-Call Pediatrician and ANMC Orthopedics

Management:

- Bracing and surgical correction of

lower extremity contractures to allow ambulation
- Occupation Therapy and Physical Therapy to enhance upper limb movement for self-care and lower limb movement for ambulation

For further questions:
- ANMC Orthopedics
  ANMC Paging Operator:
  907-563-2662

For any urgent/emergent issues, page the ANMC on-call pediatrician: 907-563-2662.

Other resources:
- NIH Genetic and Rare Diseases Information Center

https://rarediseases.info.nih.gov/gard/3150/kuskokwim-disease/resources/1
- National Library of Medicine Genetics Home Reference
  http://ghr.nlm.nih.gov/condition/kuskokwim-syndrome

Metachromatic Leukodystrophy (MLD)

Pathophysiology: Lysosomal storage disease causing progressive demyelination of central and peripheral nervous system, also affecting kidneys and other visceral organs due to accumulation of cerebroside sulfate
Inheritance: Autosomal recessive

Demographics:

- 1:2,500 in Navajo (closely related to Athabascan)
    - Athabascan = interior Alaska = Anchorage, Fairbanks, Mat-Su Valley, Wrangell, etc. areas
- 1:40,000-1:100,000 in northern Europe and North America

Signs/Symptoms: Children have normal development until onset of disease

- Late infantile onset = 6mo – 2yr (up to 4yr)

    - regression of motor skills
    - gait difficulties
    - seizures
    - ataxia
    - hypotonia
    - extensor plantar responses
    - optic atrophy
    - fussiness/pain/distress – thought to be due to neuropathy or dystonia
- Juvenile and adult onset = >4yrs
    - gait disturbance
    - ataxia
    - seizures
    - intellectual impairment
    - behavioral difficulties
    - upper motor neuron signs
    - peripheral neuropathy

Diagnosis:

- Brain MRI
    - symmetric white matter lesions with periventricular predominance (early) and cortical atrophy (late)

- Genetic testing for deficient ARSA (arylsulfatase A) gene activity
  - Option 1: blood draw 6-8mL green top (min 2mL) plus optional 1-2mL lavender top for DNA extraction if worried about aged specimens
  - Option 2: blood spots on PKU card
  - Send-out to:
    Lysosomal Diseases Testing Laboratory
    Thomas Jefferson University
    Dept of Neurology, Dr. David Wegner
    1020 Locust Street, Rm 346
    Philadelphia, PA 19107

Management:

- No curative treatment
- Bone marrow transplant, gene therapy and hematopoietic stem cell transplant are all investigational with goal of slowing the disease course
- Prognosis for late infantile and early

juvenile onset is poor (death within 5 to 6 years)

Critical Times for Affected Patients:

- Recognition of symptoms and accurate diagnosis

For further questions (non-urgent):

- Rod Smith, MD (Pediatric Neurologist, Anchorage)

Contact ANMC Consult Pediatrician via ANMC Paging Operator: 907-563-2662

For any urgent/emergent issues, page the ANMC on-call pediatrician: 907-563-2662.

Other resources:

- National Library of Medicine Genetics Home Reference http://ghr.nlm.nih.gov/condition/metachromatic-leukodystrophy

Micro-aspiration in Apparently Neurologically Typical Children

Pathophysiology: Unknown
Demographics: Unknown, but appears to be a significant number of otherwise normal children under age 3 from Western or Northern Alaska

Signs/Symptoms: Overt signs/symptoms not always present

- frequent cough
- aspiration with feeds during URIs
- frequent (or any) pneumonia, especially right upper lobe

Diagnosis: Clinical vs Video Fluoroscopic Swallow Evaluation
The radiation exposure from video fluoroscopic swallowing study as well as the cost of transporting patients to Anchorage are higher risk and cost than initially treating symptomatic patients.

Management: Slow-Flow Nipples, then Proactive Thickening

This requires close follow-up to document improvement versus unchanged or worsening lung disease which would require a swallow evaluation.

- Change nipple to Dr. Brown Level 1 or Dr. Brown Preemie nipple to slow down flow rate. Ensure that families do not cut or alter nipples in any way.
- Thicken liquids to nectar thick (using Thick-It). If flow is too slow once feeds are thickened, try Dr. Brown's Level 2 or 3.
- If still experiencing overt symptoms of aspiration or if no resolution of lung disease within 3 months of proactive thickening, child should be referred to ANMC for a video fluoroscopic swallow study/modified barium swallow study.
- Continue thickened liquids until the patient experiences 12 symptom free months, then gradually wean off

thickener. If child does not tolerate wean, refer to ANMC for swallow evaluation.

Risks of Proactive Thickening:

- Child's swallow pattern may not change; child may still be aspirating but with reduced signs and symptoms.
- If this is the case, child is now aspirating corn starch and additional sugar from thickener.
- If still aspirating, the heavier consistency of thickened liquids make them more difficult to clear via spontaneous cough.

Critical Times for Affected Patients:
Respiratory illness in infancy

For further questions:

- Matt Hirschfeld, MD (Pediatrician, ANMC): MHirschfeld@southcentralfoundation.com
- Alee Glass (Speech/Language Pathology, SCF): AGlass@

southcentralfoundation.com
Office phone: 907-729-3124
- Sam Maloney, RD (Dietician, ANMC): SMaloney@anthc.org

Other resources:
- http://www.ncbi.nlm.nih.gov/pubmed/21618720
- http://www.ncbi.nlm.nih.gov/pubmed/16933218

Optic Nerve Hypoplasia (ONH)

Also known as Septo Optic Dysplasia (SOD) and de Morsier Syndrome

Pathophysiology: Disorder of early brain development resulting in wide variation of findings including hypoplasia of optic nerve, agenesis of corpus callosum and septum pellucidum, and/or pituitary hypoplasia

Inheritance: Usually sporadic; occasionally autosomal recessive

Demographics:

- 1:10,000 live births
- Unknown but anecdotally higher incidence for Alaskan Native populations

Signs/Symptoms:

- Hypoplasia of optic nerve
  - impaired vision (one or both eyes)
  - nystagmus
- Abnormal midline brain structure formation (corpus callosum)
  - intellectual disability
  - other neurologic problems including seizures
- Pituitary anomalies (hypoplasia, ectopia, etc.)
  - growth hormone deficiency (most common)
  - pan-hypopituitarism (also possible)

- Occasionally can have seizures, developmental delay, abnormal movements

Diagnosis:
- Brain and Pituitary MRI
  - Thinning of optic nerves & chiasm
  - Absence of septum pellucidum
  - Agenesis of the corpus callosum
  - Pituitary hypoplasia or posterior pituitary ectopia
- Ophthalmology exam
- Endocrinology evaluation
- Can be suspected initially based on prenatal ultrasound

Management: Varies depending on individual
- Refer to Pediatric Endocrinology for regular endocrine evaluations
- Refer to Ophthalmology
- Refer to Infant Learning Program/ Birth to 3
- Refer to Pediatric Neurology in

setting of seizures and neurologic deficits

Critical Times for Affected Patients:
Vary depending on individual

- If hypopituitarism, times of stress (fasting, illness, surgery, trauma) are high-risk as well as newborn period due to:
  - ACTH/Cortisol deficiency can present with adrenal crisis in the first week of life (similar to CAH). This is NOT picked up on the newborn screen.
  - Thyroid deficiency (can show up on newborn screens as low T4)
  - GH deficiency and ACTH deficiency can present with hypoglycemia

For further questions (non-urgent):

- Rachel Lescher, MD (Pediatric Endocrinologist, ANMC)
  Office phone: 907-729-1000
  Admin (Agnes Hunt): 907-729-8822

Case Manager (Sherry Hammock): 907-729-8803
Paging operator: 907-563-2662, ask for pediatric endocrinologist on call

- Kevin Winkle, MD (Pediatric Ophthalmologist) 907-561-1917; rkwinkle@anthc.org
- Rod Smith, MD (Pediatric Neurologist, Anchorage) Contact ANMC Pediatric Hospitalist via ANMC Paging Operator: 907-563-2662

For any urgent/emergent issues, page the ANMC on-call pediatrician: 907-563-2662.

Other resources:

- National Library of Medicine Genetics Home Reference http://ghr.nlm.nih.gov/condition/septo-optic-dysplasia

Notes

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