Short Term Follow-Up for New Conditions: What we can learn from the present and needs for the future

Amy Gaviglio, MS, CGC | Follow-Up Supervisor

Setting Up a Short Term Follow-Up System

- **Follow-Up Considerations**
  - **Pre-Analytical**
    - Improving information dissemination prior to testing
  - **Analytical**
    - Understanding of testing approach
      - Psueudodeficiency; Molecular variants; Females with XALD
      - Typical molecular terminology (protein vs cDNA)
      - Do you need a 2nd tier and does it need to be molecular?
  - **Post-Analytical**
    - Equipping primary care providers to communicate results with families
    - Establishing follow-up protocols and diagnostic forms (keeping long term follow-up needs in mind)
    - Thinking outside the box

Reassessing Informational Needs for Parents

- **Parents still report being underinformed and overwhelmed upon receiving newborn screening results**
- **Why?**
  - Is there a lack of workflow to provide information to parents in birth facilities?
  - Is there a language or cultural barrier?
  - Does the family have low health literacy?
  - Is the family too overwhelmed to process information?
  - Is there poor recall by the family of the information provided?

Memory for medical information is a prerequisite for a good experience and ongoing adherence.

Kessels, Roy. J Royal Society of Medicine. 2003;96:219-222

From Parents with Out-of-Range Results…

"As I look back now, I think that [hospital staff] probably should have talked to us a little bit more about it rather than just handing me a booklet."

"…I think the information is the thing that should be required… my main concern is that parents are not given the information, [and] all of a sudden they get a call saying, oh, your child might have [X]."

From work by Jeff Botkin and Erin Rothwell

Setting Up a Short Term Follow-Up System

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Robust Communication Between Follow-Up and Lab

- **Follow-Up Staff need to:**
  - Understand testing algorithm
    - Enzyme only? Biochemical 2nd tier? Molecular 2nd or 3rd tier? Sequencing vs Mutation Panel?
      - Informational materials developed will depend upon testing process
  - Understand reporting (and contribute to interpretation writing, if possible)
    - What will be included on report? What is plan for females/pseudodeficiencies?
    - What are follow-up recommendations?

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Keeping the Family Experience at the Forefront

We need to equip physicians with discussing this information with parents in order to improve understanding, satisfaction with experience, and adherence to ongoing monitoring

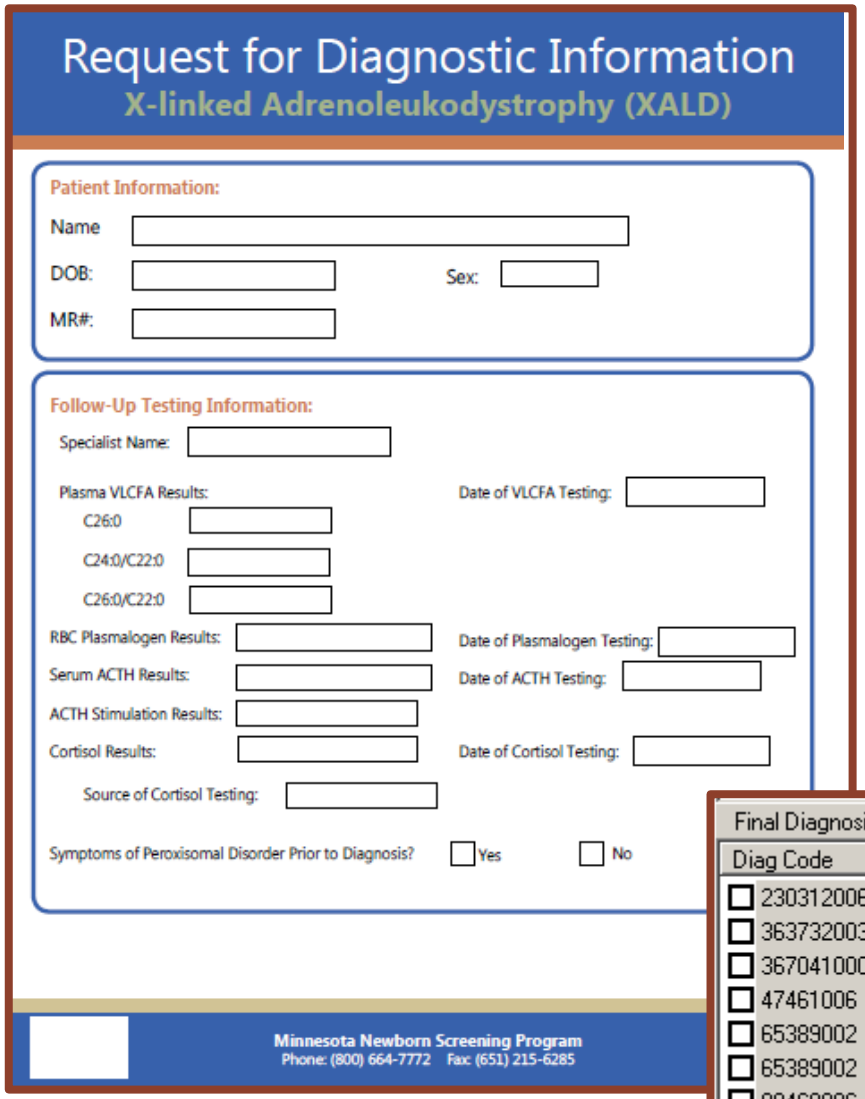
Ley's model on effective communication in medical practice

Ley P. Communicating with Patients: Improving Communication, Satisfaction, and Compliance . New York: Croom Helm, 1988.

What is follow-up algorithm and what labs are needed?

- **Work with subspecialists**
  - What labs will be ordered upon an abnormal screen?
  - What is the TAT for those labs?
  - What, if any, labs can be done locally prior to specialist visit?
  - Can the LBW protocol be followed (e.g., no referral until 2nd or 3rd specimen?)

Obtaining the Diagnosis



Request for Diagnostic Information

X-linked Adrenoleukodystrophy (XALD)

Patient Information:

Name

DOB: Sex:

MR#:

Follow-Up Testing Information:

Specialist Name:

Plasma VLCFA Results: Date of VLCFA Testing:

C26:0

C24:0/C22:0

C26:0/C22:0

RBC Plasmalogen Results: Date of Plasmalogen Testing:

Serum ACTH Results: Date of ACTH Testing:

ACTH Stimulation Results:

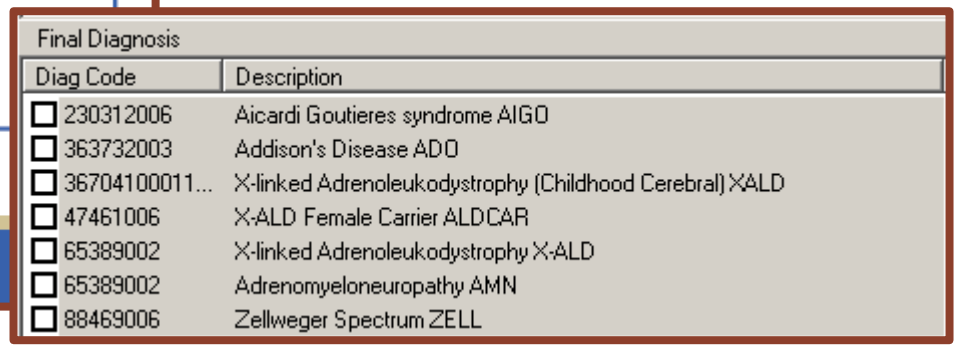
Cortisol Results: Date of Cortisol Testing:

Source of Cortisol Testing:

Symptoms of Peroxisomal Disorder Prior to Diagnosis? Yes No

Minnesota Newborn Screening Program

Phone: (800) 664-7772 Fax: (651) 215-6285



Final Diagnosis

Diag Code	Description
230312006	Aicardi Goutieres syndrome AIGO
363732003	Addison's Disease ADO
36704100011...	X-linked Adrenoleukodystrophy (Childhood Cerebral) XALD
47461006	X-ALD Female Carrier ALDCAR
65389002	X-linked Adrenoleukodystrophy X-ALD
65389002	Adrenomyeloneuropathy AMN
88469006	Zellweger Spectrum ZELL

- **Forward Thinking:**
  - What fields do you need to confirm a case?
    - Nice to know vs Need to know
    - NewSteps Cases?
  - Capturing Discrete Fields and Utilization of Web Portals
  - Keep in mind possible Electronic Reporting (LOINC)

When is a Diagnosis a Diagnosis? When are you "done"?

- **Subtype may not be known right away**
  - Child has X-ALD or Pompe or MPS1, but what subtype?
  - Will you continue to follow until a subtype is determined?
  - Siblings may also be detected (X-ALD particularly)

- **How will you classify outcomes?**
  - Which are considered False Positives?
  - Which will receive long term follow-up (if applicable)
  - Will you re-classify outcomes? How frequently?

Obtaining Information to Aid in Ongoing Short Term and/or Long Term Follow-Up

- **Language information**
  - Are interpreters needed? Translated materials?
- **Psychosocial information**
  - Does family have potential barriers to ongoing follow-up/monitoring?
- **Parental awareness of diagnosis**
  - Have parents been given diagnosis and what do they understand of the diagnosis? Did they receive genetic counseling?
- **Preferred contact modality?**

Is there an App for That?

- **Utilization of mobile technology**
  - Published studies in chronic disease literature suggest mobile technology improves understanding, self-management, communication, and adherence to appointments/medications

- **Is it time for newborn screening to follow suit?**
  - Yes.
    - Baby's First Test has an App!
    - Is this also a potential solution for ongoing follow-up?

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Reassessing Short Term and Long Term Follow-Up: The Example of SCID

CQI in the Laboratory

- **Started by reporting TREC values**
  - A lot of variation
- **Moved to reporting Cq values**
  - Allows for fixed cut-off
- **Now reporting Cq and MoM values**
  - Accounts for variation in reagent lots
  - Adds stability to numbers
  - 1% repeat rate and 0.1% positive rate

CQI in Follow-Up

- **Data Definitions/Classifications**

Previous Classifications	Current Classifications
• Classic SCID • Variant SCID • 22Q11.2 Deletion Syndrome • Trisomy 21 • Non-SCID T cell lymphopenia • Idiopathic T cell lymphopenia • Transient T cell lymphopenia (excluding preterm birth alone) • Other	• Typical SCID • Leaky SCID • Omenn Syndrome • Syndrome with low T cells • Secondary low T cells • Preterm birth alone* • Idiopathic T cell lymphopenia (numerical deficiency only)** • Idiopathic T cell lymphopenia (numerical and functional deficiency)**

SCID Diagnostic Form… Version 1,698

Request for Diagnostic Information
T-Cell Lymphopenia (SCID)

Follow-Up Testing Information:

Additional Immunological Studies:

Center where additional testing was done: (Please Select Center)

TREC Analysis Done: **Yes** ☐ **No** ☐

Date of Testing:

TRECs: ____ copies per million CD3+ T cells (Please Select Interpretation)

CD4RTE Analysis Done: **Yes** ☐ **No** ☐

Date of Testing:

CD4+CD45RA+ of total CD4+ T cells (naive): ____ % (Please Select Interpretation)

CD4+CD45RO+ of total CD4+ T cells (memory): ____ % (Please Select Interpretation)

CD4+CD45RA+CD31+ of total CD4+CD45RA+ T cells (CD4RTE): ____ % (Please Select Interpretation)

False Positive Result? Yes ☐ **** If False Positive, please stop here ****

Request for Diagnostic Information
T-Cell Lymphopenia (SCID)

Diagnostic Information:

Center where additional testing was done: (Please Select Center)

Lymphocyte Proliferation to Mitogens (PHA) Done: **Yes** ☐ **No** ☐

Date of Testing:

% of maximal PHA response, CD45+: ____ (Please Select Interpretation)

% of maximal PHA response, CD3+: ____ (Please Select Interpretation)

Molecular Testing Done: **Yes** ☐ **No** ☐

Targeted Mutation Analysis: Yes ☐ No ☐

Whole Exome Sequencing: Yes ☐ No ☐

Mutation(s) Identified? Yes ☐ No ☐

Gene:

Allele 1 Allele 2

Chromosomal Array Done: **Yes** ☐ **No** ☐ **FISH Done:** **Yes** ☐ **No** ☐

Diagnosis: (Please Select Diagnosis) **Syndrome:** (Please Select Syndrome, i

If Secondary low T cells, please specify findings: (Please select findings, if applicabl

Are Parents Aware of Diagnosis? Yes ☐ No ☐

When does STFU end and LTFU begin?

- Typically STFU ends and the case is sent to LTFU upon a confirmed diagnosis…

…However…

- Supposed idiopathic T-cell lymphopenia can take a long time to resolve or to determine the underlying cause
  - Infants were “aging” out of services they qualified for based on T-cell lymphopenia finding alone

When does STFU end and LTFU begin?

- Now, we work with LTFU on lengthy cases to ensure that these children still receive the services they qualify for and often really need… even if a diagnosis has not yet been made.

- Recontact Immunology specialists every 6-12 months to assess whether case has been re-classified (e.g., from idiopathic to syndrome)

Concluding Thoughts

- A robust follow-up system considers the entire newborn screening process
- Consideration of follow-up data needs should take into account what your program's endpoint will be
- Continuous Quality Improvement is as important in follow-up as it is in the laboratory
- The family experience should dictate practices – not "arbitrary" stop points

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Thank you!