Education and Training Subcommittee

Don Bailey, Chair
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DACHDNC MEETING
JANUARY 16, 2014

AGENDA

- Introductions and “2-minute updates” from committee members
- Wilson’s Disease – issues and considerations for childhood screening -Sihoun Hahn, MD, PhD, University of Washington
- Discussion of nomination guidance, available materials, next steps

Six Questions for Each Condition

- What is the typical pattern of identification of children with this condition?
- What problems exist with the current pattern of identification, problems that could be ameliorated to some extent by earlier identification?
- Would population screening outside of the newborn period be at all feasible or desirable?
- In the absence of population screening, what could be the likely best case scenario for earlier identification?
- What level of effort would be required to substantially change the current paradigm – minimal, moderate, substantial, or heroic?
- Which stakeholder groups would need to be engaged in any discussions about altering current practice?

What is the typical pattern of identification of children with this condition?

Fragile X Syndrome	Long QT	Wilson's Disease
• Parents begin noticing problems around 9-12 months • Boys are typically diagnosed with a developmental delay around 24 months • Average age of FXS diagnosis is around 36 months for boys • Girls, especially those who are mildly affected with no affected male siblings are identified later or not at all	• ECG done in asymptomatic individual • Syncopal event • Unexplained sudden death in a young individual • Identification of a family member • Suspicious family history (e.g., SIDS, seizures, syncope)	• Most likely to be diagnosed by pediatricians if jaundice, then would order liver enzyme tests, vital marker tests, then refer to GI/renal specialists. • Begin noticing symptoms between 6-20yrs. • Neurological symptoms, eye abnormalities within adolescence, 15-25yrs.

What problems exist with the current pattern of identification,?

Fragile X Syndrome	Long QT	Wilson's Disease
• Parents experience a lengthy, costly, and frustrating diagnostic odyssey • Children miss the opportunity to participate in early intervention programs • About 30% of families have a second child with FXS before the first child is diagnosed	• First presentation can be sudden death	• Variable and non-specific symptom presentation often means a long diagnostic process and many individuals are never diagnosed (possibly 50%) • With the current delay in diagnosis, liver damage and other serious conditions.

Would population screening outside of the newborn period be at all feasible or desirable?

Fragile X Syndrome	Long QT	Wilson's Disease
• Full population screening at another age would be very challenging, especially if the test were a stand-alone test. The most likely scenario would be if it became standard practice to do a population-based panel screen for a variety of disorders at some other point during childhood.	• Yes IF predictive of clinical severity	• Feasible, but would require a higher level of effort.

In the absence of population screening, what is the best case scenario for early identification?

Fragile X Syndrome	Long QT	Wilson's Disease
• All pediatricians follow the APA guidelines for screening at 9, 18, and 30 months • Any questionable screen is immediately followed by a complete evaluation • Any child with a documented delay is immediately referred for genetic testing • Best case scenario is 16-18 months diagnosis for most severely affected males	• Screening for symptoms in individual • Reviewing family history	• Increasing the awareness so that any patients with unexplained liver or neurological problems get tested for Wilson's. • Goal, to reduce the time between first symptoms and diagnosis.

What effort would be required to substantially change the current paradigm?

Fragile X Syndrome	Long QT	Wilson's Disease
• Substantial – the main way this would work is if pediatricians themselves requested genetic testing, rather than referring to specialists (e.g., neurologist, developmental behavioral pediatrician, medical geneticist)	• Substantial	• A substantial effort, involving training pediatricians/family practitioner to pay attention to these signs and get testing. • Neuropsychiatric problems would be harder, clinicians wouldn't look to Wilson Disease as the initial issue. • Develop a gene-based panel based on symptomology.

Which stakeholders would need to be engaged in discussions about altering current practice?

Fragile X Syndrome	Long QT	Wilson's Disease
• Pediatricians • Early intervention programs • Developmental evaluation centers	• Cardiologists • Geneticists • Primary care physicians • Patients and families	• 1st line: pediatricians, general practitioners, 2nd line: ophthalmologists, neurologists, psychiatrists.

Next Steps

- Finalize tables comparing the three conditions
- Summarize major issues/themes that have emerged from this work
- Final report to Committee in May

Priority C: Provide better guidance for advocacy groups and others regarding the nomination and review process

- Problems to be solved
  - Increase public transparency for what we do and the rationale for decisions made
  - Support future nominators in preparing successful application packages

Condition Review Guidance Timeline

- Summer, 2012 — SACHDNC report of activity timeline
- Fall-Spring, 2013 — Draft documents prepared by Atlas Research
- Summer, 2013 — CRW and E&T document revision
- September, 2013 — Further discussion of draft document
- September, 2013 — Atlas conducted interviews with 4 advocates

Themes from advocate interviews

- Great appreciation for the work of the committee and the systematic approach to decision-making
- The nomination form and the matrix portray a deceptively simple process and decision guidelines, behind which is enormous complexity and work
- A big challenge for everyone is that we have a standardized process that in reality has to be individualized for each condition
- Advocates need to realize how much work they need to do, the most important being to have a steering committee of experts and stakeholders, and a champion who will guide and lead the process

Themes from advocate interviews (continued)

- There are terms that advocates do not know (e.g., “analytical validity”) and concepts that advocates and researchers might see differently (e.g., “treatment” or “benefit”) – clear definitions would help
- An instruction manual would be useful
- Ideally, advocates and nominators would have someone available to to guide them, including specific advice on next steps and data needed
- Especially needed is advice on whether the nominated condition is “truly ready to be competitive.”
- Lack of clarity on sources of funding to do the work needed to provide the evidence required
- The process takes too long and the committee will not be able to conduct reviews with sufficient expediency as the number of nominations increases

So where are we?

- What do we have right now?
  - Web site description of process
  - Nomination form
  - Kemper et al. article
- What do we need now?
  - "Navigator" to respond to questions and help provide guidance for nominators
  - Hyperlinks on the nomination form to explain terms and provide further details about what is needed
- Who will do it?