Shocking News: Imprinting Disorders Are Not Included on RUSP. But They Could.

Chromosome Imprinting Disorders? The Basics.

- Chromosome imprinting disorders which are a group of congenital diseases characterized by molecular changes affecting chromosomal regions and genes [2].
- Imprinting disorders (ID) are often characterized by clinical features affecting growth, development, and metabolism. Many imprinted genes are growth factors such as insulin-like growth or as regulators of gene expression controlling [2, 4, 5, 6, 7].
- The number of human diseases or disorders, due to genomic imprinting may be greater than 100 conditions [2].
- Widely known and studied IDs include Prader-Willi syndrome (PWS), Angelman syndrome (AS), Silver-Russell syndrome (SRS), Beckwith-Weidemann spectrum (BWS).

Problem Statement

- Many imprinting disorders require early intervention to increase success and progression of growth and cognitive development. Studies have concluded that infants born with congenital imprinting disorders, such as PWS, benefit from early intervention like growth hormone treatment, diet management, and physical therapy [6]. Late identification and intervention are common because of limited screening of newborns [2, 3].

Research Purpose

- To examine the current protocols and recommendations on newborn screening and the need for screening of congenital imprinting disorders in newborns.

Newborn Screening

Recommended Uniform Screening Program (RUSP) from the Advisory Committees on Heritable Disorders in Newborns and Children of the Health Resources and & Services Administration [1]

- Basic criteria to be included to RUSP –
  1. evidence that supports the potential net benefit of screening;
  2. the ability of states to screen for the disorder;
  3. the availability of effective treatments.
- Newborn Screening (NBS) timeliness goals - to effectively reduce disability, morbidity and mortality, the newborn screening (NBS) process from specimen collection through diagnosis and treatment must occur within the short window of opportunity between birth and the onset of symptoms [1].
- Health plans are required to cover screenings included in RUSP without charging (plan years beginning on or after the date that is one year from the Secretary's adoption of the condition for screening) [1].
- Committee uses decision matrix to steer review process, after nomination requirements are met [1].

Current NBS methods

- Blood tests. A few drops of blood are taken from the baby's heel. The blood is sent to a lab for analysis.
- Hearing test.
- CCHD screen with oximeter. The oximeter will measure the baby's oxygen levels in the hand and foot.

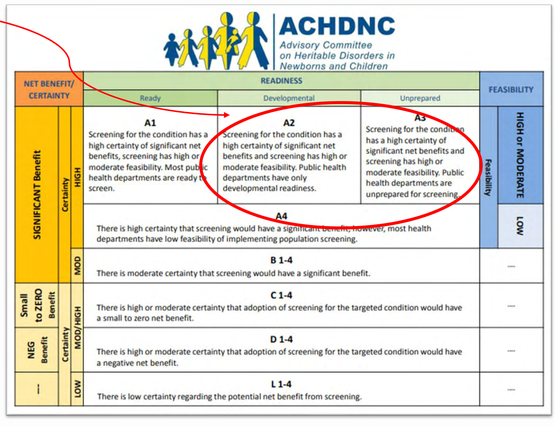
Discussion

RUSP inclusion criteria fails children with imprinting disorders and their families.

- If most health departments have a low feasibility of implementing population, then the condition will not be added (despite there being some health departments that could implement the screening and there being a high certainty of significant net benefit)
- There is potential for missing out on identification of other disorders/diseases that are often co-morbidities

Newborn screening for imprinting disorders may lead to benefit from early diagnosis and treatment.

- For PWS, diagnosis in infancy allows for early initiation of growth hormone treatment to improve long-term outcomes [6].
- For AS, early diagnosis could prevent the diagnostic odyssey, reducing medical costs and the significant stress and anxiety currently experienced by families while they await a diagnosis [4].
- RSS remains difficult to diagnose based on clinical findings because many of the symptoms are nonspecific. Early diagnosis and intervention can help improve growth and ensure that affected children reach their highest potential [7].
- Patients with BWS can be diagnosed prenatally and postnatally either by physical evaluation (clinical diagnosis) and/or genetic testing (molecular diagnosis) [5].



Quantitative Methylation Analysis (QMA)

One feature common to virtually all imprinted genes is parental-specific methylation. For genes such as H19 and SNRPN, there is substantial methylation at the 5′ end of the gene on the repressed allele, and methylation may inhibit transcription directly.

Methylation-specific quantitative melt analysis (MS-QMA) can be implemented as a first-tier screening test [3]

- high-throughput
- low-cost
- population scale
- can use the same blood sample already collected via heel stick

References

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