Advances in Genetic Testing

Professional & Consumer Perspectives

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Impressions & Questions

- This presentation is based on my impressions as a parent and a professional and not on formal research.
- Parent… Genetic Counseling across the decades
- As a professional, working with children and adults with severe disabilities and their families since the 1960. International Rett Syndrome Foundation Professional Resource, MECP2 parents groups.

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Testing & CMA

- This presentation is partly about CMA (Chromosomal Microarray Analysis) BUT it is not intended to be just about this specific procedure…
- New tests…
  - … based on genomic information
  - … can find much (about 100 times) smaller deletions and duplications
  - … test concurrently for large number of possible conditions
    - currently about 1700 possible deletions or duplications can be assessed in a single test

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About Testing & CMA

- CMA is currently expensive and used sparingly
- Cost per procedure is coming down and CMA use is expanding
- Newer versions of the test are increasing the number of genes that can be probed
- "During his progress report on the evolution of testing for genetic abnormalities, Arthur Beaudet, M.D., chair of molecular and human genetics at BCM, pointed out that these tests represent a double-edged sword. While they reveal a wealth of information about individuals, they also introduce complex ethical quandaries." Tomin, 2006

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2010 Consensus Statement

- Consensus Statement: Chromosomal Microarray Is a First-Tier Clinical Diagnostic Test for Individuals with Developmental Disabilities or Congenital Anomalies –
  - Miller et al. *Am J Hum Genet.* 2010 May 14; 86(5): 749–764.
- August, 2009 -The case for offering all women amniocentesis and chromosomal microarray analysis – Beaudet, 2009.

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Concerns

- "… molecular genetic testing represents more than a single discrete research or clinical intervention, since the information obtained may predict future events or affect the lives of others besides the person consenting to be tested." – Grody, 2003
- "As this sort of testing continues to proliferate, referral of all such cases to a medical genetics clinic for proper interpretation becomes less of a practical option, as there are not enough genetic counselors in the entire country to handle the anticipated case load of even a single large program, such as nationwide carrier screening for cystic fibrosis mutations" – Grody, 2003

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Concerns

- "Clearly our ability to add more and more mutation probes to an array will rapidly outstrip our ability to clinically validate each of them." - Grody, 2003
- "If the DNA alteration detected has not been reported before in the context of the disease phenotype, it may be difficult or impossible to decide whether it represents a pathologic mutation or merely a benign polymorphism." - Grody, 2003

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A Personal Perspective

- This presentation is partly from the perspective as the parent of a 20-year-old son with MECP2 Duplication syndrome.
- Diagnosed at age 18 through CMA
- As a family, we were glad to finally get a diagnosis for our son… but we were also happy to get it at age 18 and not when he was an infant or even before he was born.
- While this syndrome serves as an example, it is just one of many that will be identified for the first time or diagnosed in much larger numbers in the recent past and near future.

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Our Perspective

Pros

- Provided an explanation
- Did help with a few decisions about treatment
- Put us in touch with other families for support

Cons & Nons

- Little value in directing treatment at present
- Presents a bleak outlook
- Tended to become an all encompassing explanation

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MECP2 Duplication Syndrome

- First identified syndrome in 2005
- About 300 cases have been diagnosed worldwide
- Progressive
- Characterized by severe developmental disability, autism, hypotonia, immune compromise, intractable seizure disorder, GI symptoms.
- Discovered in mice before humans.

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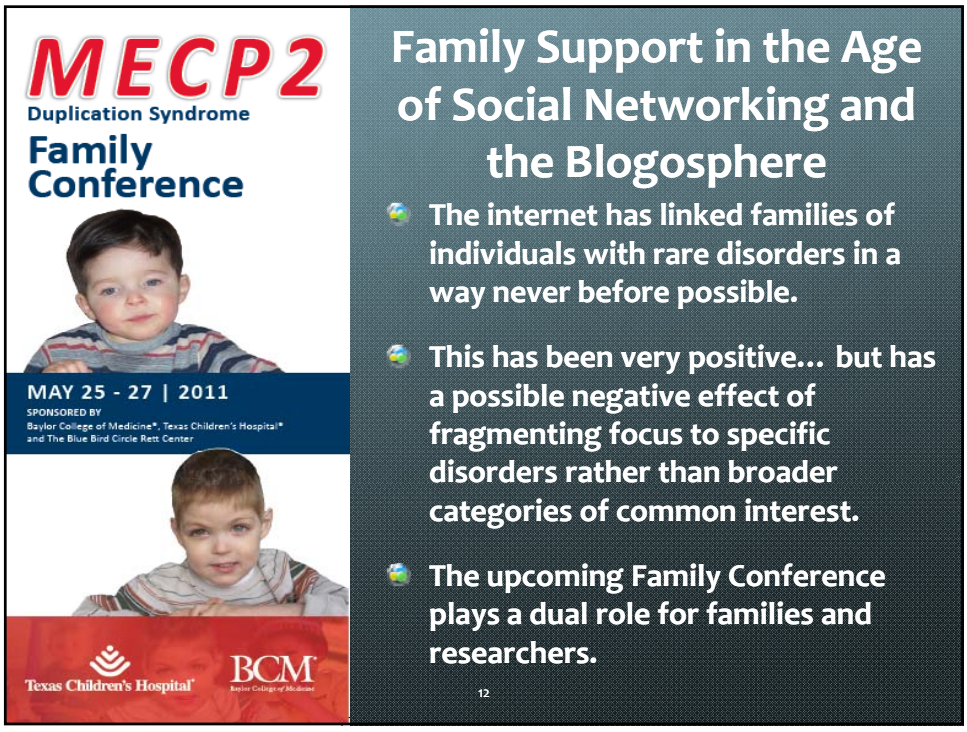
MECP2 Duplication Syndrome
Home
About MECP2
Families
News & Events
Community
Join The Fight!
The site for families affected by MECP2
MECP2 Duplication Syndrome
facebook
Search
MECP2
Family Talk
MECP2 Duplication Syndrome Family Talk
Wall
Info
Discussions
Photos
Video
Events
Share:
Status
Photo
Link
Video
Write something...
Settings


MECP2
Duplication Syndrome
Family Conference
MAY 25 - 27 | 2011
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Baylor College of Medicine*, Texas Children's Hospital* and The Blue Bird Circle Rett Center
Texas Children's Hospital
BCM
Family Support in the Age of Social Networking and the Blogosphere
The internet has linked families of individuals with rare disorders in a way never before possible.
This has been very positive… but has a possible negative effect of fragmenting focus to specific disorders rather than broader categories of common interest.
The upcoming Family Conference plays a dual role for families and researchers.
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Impressions of Family Attitudes

- As a result, I have had contact with what is probably the majority of families with diagnosed sons and daughters.
- Many have already lost a previous child or relative… others have two affected children
- There is a very high level of satisfaction with the diagnosis among families.
- There has been significant misinformation given to some families.
- There are some very high (unrealistic?) expectations for cures and treatment.

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Positive Aspects of Dx and Counseling

- Families are glad to have an explanation.
- Some help in getting better treatment (will probably improve over time).
- Provides families, including extended families, with useful information for family planning.
- Puts families in touch with each other for practical and emotional support.

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Problems Encountered with Counseling

- Much of the genetic counseling received has come from health care counselors who were neither geneticists nor counselors.
- In a few cases, even "genuine" genetic counselors did not appear to understand the genetics of the syndrome.
- In some cases the information available to counselors was incorrect or misinterpreted. For example, information on life-expectancy and frequency of seizure disorders.

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Social and psychological information

- Many families reported that they were told there would be severe negative effects on their marriage and other children.
- Research does not actually support the myth of very high rates of divorce among parents of children with disabilities.
  - About twice as many parents report that having a child with a disability strengthened their marriage as report negative effects.
- Research suggests that there are positive effects on siblings of children with disabilities.
  - "Results indicated that siblings of children with intellectual disabilities evidence higher levels of growth..." including personal, social, and spiritual growth." Findler, L., & Vardi, A.2009.

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Issues

- What constitutes a significant atypicality for which genetic counseling and intervention may be appropriate?
- Testing may be undertaken to look for a specific disorder but other atypicalities may be found with known or unknown consequences. Should all findings be recorded and communicated?
- When is it appropriate to order CMA testing?

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Issues

- What happens when we identify deletions or duplications for which the clinical implications are unknown or only partially understood?
- Are enough appropriate genetic counseling services available to support the potential coming widespread use of CMA testing?
- How can informed consent be appropriately obtained when a single array may involve the potential for such large numbers of diagnostic and predictive tests.

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Issues

- How will the results of diagnostic, carrier, or predictive testing affect access to health, life or disability insurance, employment, etc?
- Should CMA predictive or carrier testing be undertaken on children? … The general consensus has been NO, but there seems to be a growing second opinion.
- How is confidentiality maintained?

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Issues

- When should CMA and other such tests be covered as a legitimate healthcare costs?
- Does CMA and similar testing promote a new eugenics?
  - "Is this a new eugenics? I think it is." Margaret Somerville (quoted in Collier, 2009)

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Readings

- Al-Mulla, F. (2007). Utilization of microarray platforms in clinical practice: an insight on the preparation and amplification of nucleic acids from frozen and fixed tissues. Methods *Mol Biol, 382*, 115-136.
- Ball, C., Brazma, A., Causton, H., Chervitz, S., Edgar, R., Hingamp, P., et al. (2004). Standards for microarray data: an open letter. *Environ Health Perspect, 112*(12), A666-667.
- **Beaudet, A. (2009), "The case for offering all women amniocentesis and chromosomal microarray analysis", in Scherer, S. (ed.), *Copy Number Variation: , The Biomedical & Life Sciences Collection, Henry Stewart Talks Ltd, London (online at http://hstalks.com/bio)***
- **Collier, R. (2009, March 31).** Prenatal DNA test raises both hopes and worries, *CMAJ,180* (7), http://www.cmaj.ca/cgi/content/full/180/7/705
- Grody, W. W. (2003). Ethical issues raised by genetic testing with oligonucleotide microarrays. *Molecular Biotechnology, 23*(2), 127-138.
- Manamperi, A. (2008). Current developments in genomics and personalized health care: impact on public health. *Asia Pac J Public Health, 20*(3), 242-250.
- **Shuster, E. (2007). Microarray genetic screening: a prenatal roadblock for life? *Lancet, 369(9560), 526-529*.**
- **Tomlin, R. (2006, November). The ethics of genetic testing. FINDINGS, 4(10), retrieved from http://www.bcm.edu/findings/vol4/is10/06nov_n1.html on 15 February 2011.**
- Wilcken, B. (2003). Ethical issues in newborn screening and the impact of new technologies. *Eur J Pediatr, 162* Suppl 1, S62-66.

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