DSHS Grand Rounds

October 5

Down Syndrome Today: New Information and New Obligations for Clinicians

Presenters:

Suzanne Shepherd, Healthcare Chair and Past President, Down Syndrome Association of Central Texas (DSACT)

Adam Barta, MD, Attending Physician Blackstock Family Health Center and Clinical Assistant Professor, UT Austin Dell Medical School

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Peer-Reviewed Articles

- Bull MJ; Committee on Genetics. Health supervision for children with Down syndrome. Pediatrics. 2011 Aug;128(2):393-406. doi: 10.1542/peds.2011-1605.
- National Society of Genetic Counselors. Abnormal prenatal cell-free DNA screening results, 2015. Available at http://nsgc.org/page/abnormal-non-invasive-prenatal-testing-results.
- Skotko BG, Kishnani PS, Capone GT; Down Syndrome Diagnosis Study Group. Prenatal diagnosis of Down syndrome: how best to deliver the news. Am J Med Genet A. 2009 Nov;149A(11):2361-7. doi: 10.1002/ajmg.a.33082.
- Skotko BG, Capone GT, Kishnani PS; Down Syndrome Diagnosis Study Group. Postnatal diagnosis of Down syndrome: synthesis of the evidence on how best to deliver the news. Pediatrics. 2009 Oct;124(4):e751-8. doi: 10.1542/peds.2009-0480.
- Texas Department of State Health Services. Information about Down syndrome for new and expecting parents, 2016. Available at http://www.dshs.texas.gov/birthdefects/downsyndrome/.

John Hellerstedt, MD
DSHS Commissioner

Introductions

John Hellerstedt, MD
DSHS Commissioner is pleased to
introduce our DSHS Grand Rounds speakers

Down Syndrome Today: New Information and New Obligations for Clinicians

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Program Objectives

To provide healthcare professionals with:

- Insight into the current range of developmental and medical outcomes of individuals with Down syndrome.
- Current information about best practices, professional guidelines and new Texas law (Texas Down Syndrome Information Act) related to delivering the diagnosis of Down syndrome prenatally or postnatally.
- Current information about resources for parents.
- Awareness of latest Down syndrome cognition research.
- Current information on cell-free DNA tests for Trisomy 21.

More Alike Than Different

Medical Considerations

The child with Down syndrome generally requires the same medical care as any other child.

Common medical considerations for individuals with Down syndrome occur at the following frequency (many of which are correctible through surgery and/or medical treatment):

- 60 to 80% have hearing deficits
- 40 to 45% have congenital heart disease
- 8 to 12% have intestinal abnormalities
- 3% have cataracts, and children with DS often have other eye problems
- 15 to 20% have hypothyroidism
- 15% have atlantoaxial instability
- 45% have sleep apnea

Medical Considerations (cont.)

- Other important medical aspects include hypotonia, frequent respiratory infections (early years), immunologic concerns, leukemia, Alzheimer's disease (including early-onset), seizure disorders, celiac disease, skin disorders, nutritional concerns, and other skeletal problems.
- Parents need to know it is very unlikely their child will develop all or even most of these conditions, and need to understand many are highly treatable.
- Life expectancy is now 55-60 years with some individuals living into their 70's.
- Lower than average risk of developing solid tumors.
- Health Supervision for Children with Down Syndrome, American Academy of Pediatrics, 2011.

Development

- The majority of individuals with Down syndrome function in the mild to moderate range of intellectual disability; however, there are exceptions at both ends of the spectrum, with the degree of cognitive impairment extending from minimal to severe.

- Most learn to read; reading instruction should begin in preschool. Teaching methods should adapt to the learning strengths and cognitive profile of a student with Down syndrome.
  dseinternational.org is an important educational resource.

- Individuals with Down syndrome attend school, establish friendships, pursue interests, and are included in community activities.

- Receptive verbal abilities often exceed expressive verbal abilities.

- High parental expectations with good early childhood intervention and educational resources can produce remarkable outcomes. No one knows what any child will be capable of when the child is born.

Development

- Developmental skills may not easily blossom on their own - but they do develop.
- Parents search for the right development and therapy resources - speech, PT, OT, behavior, orthoptist.
- Parents need to find the time/energy to incorporate therapy appointments and homework into the day.
- Parents may have to pick which skills are most important and focus on those.
- Clinicians can help find the right therapists and advocate for the child's development.

Terminology

Down syndrome is named after Dr. John Langdon Down, an English physician who in 1866 first described the characteristic features of Trisomy 21.

People now use the term “Down syndrome” as opposed to “Down’s syndrome.”

Use “people first” language : “a child with Down syndrome.” Do not equate a person with a disability.

2010 federal law and 2011 Texas law adopt “intellectual disability” rather than “mental retardation” in new regulations/statutes, and use of “person first" language.

Development – The Payoff

Assume Ability

Assume Ability

ruby's rainbow
rockin' that extra chromosome!

The University of Texas at Austin
Informal Classes

think COLLEGE!
College Options for People with Intellectual Disabilities

AUSTIN COMMUNITY COLLEGE
CONTINUING EDUCATION

Assume Ability

Incidence

- Down syndrome occurs once in every 700 to 800 live births, and is not related to race, nationality, religion or socio-economic status.

- There are 350,000 Americans with Down syndrome.

- While the age of the mother can be a factor, 80% of people with Down syndrome are born to parents under the age of 35 (the average age is 26).

Diagnosis of Down Syndrome

- Diagnosis can be either prenatal or postnatal and currently can only be confirmed with a karyotype.
- Non-invasive screening tests currently yield only a probability. New non-invasive cell-free “fetal” DNA tests offer greater accuracy, with questions about their use in low-risk populations.

Current Diagnostic Practices and Pregnancy Outcomes

- 2005 study by Brian Skotko, M.D. “Mothers of Children with DS Reflect on their Postnatal Support,” *Pediatrics*, found that the majority of mothers reported being frightened or anxious after learning the diagnosis, and rarely received current materials about DS or contact information for other parents of children with DS.
- 2007 American Journal Obstetrics/Gynecology article cites reasons for termination: belief that child would not function independently, that abnormality was too severe, concern about child’s care after parents’ death.
- In January 2007, ACOG Practice Bulletin 77 called for prenatal testing for all pregnant women regardless of age.
- In December 2007, PB 77 was revised to include a recommendation to provide information about DS to parents.

Current Pregnancy Outcomes

- Current research indicates a prenatal diagnosis termination rate between 70-85%

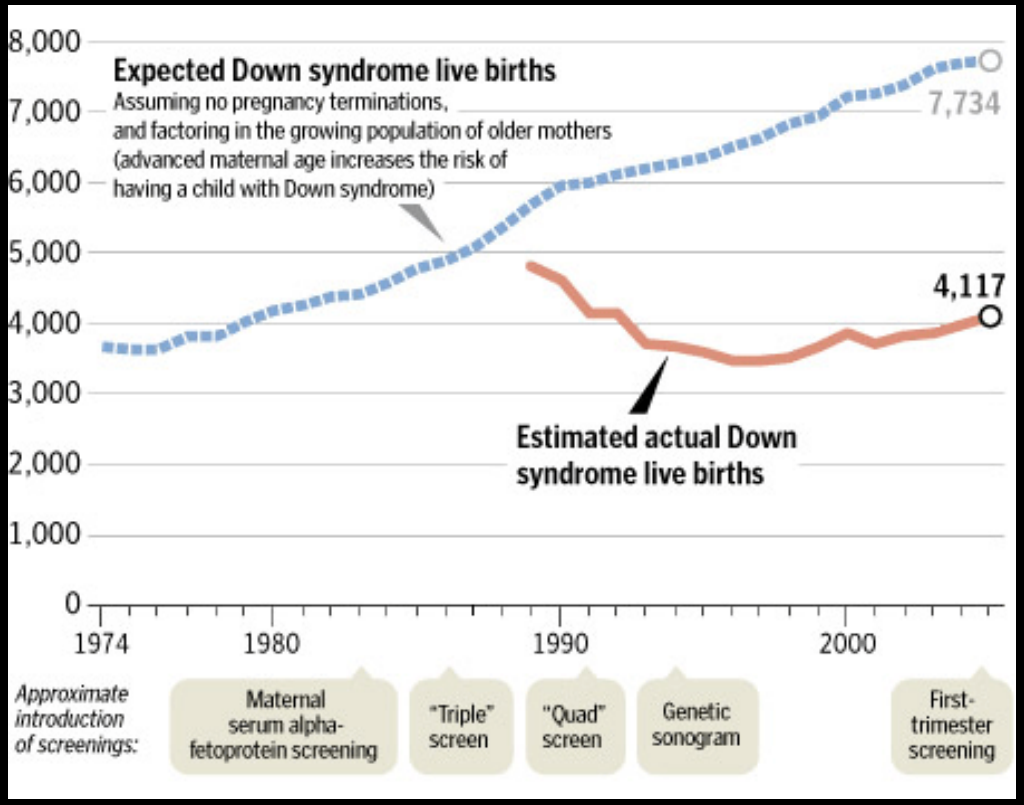
  -Amy Julia Becker, Feb 21 2013, The Atlantic

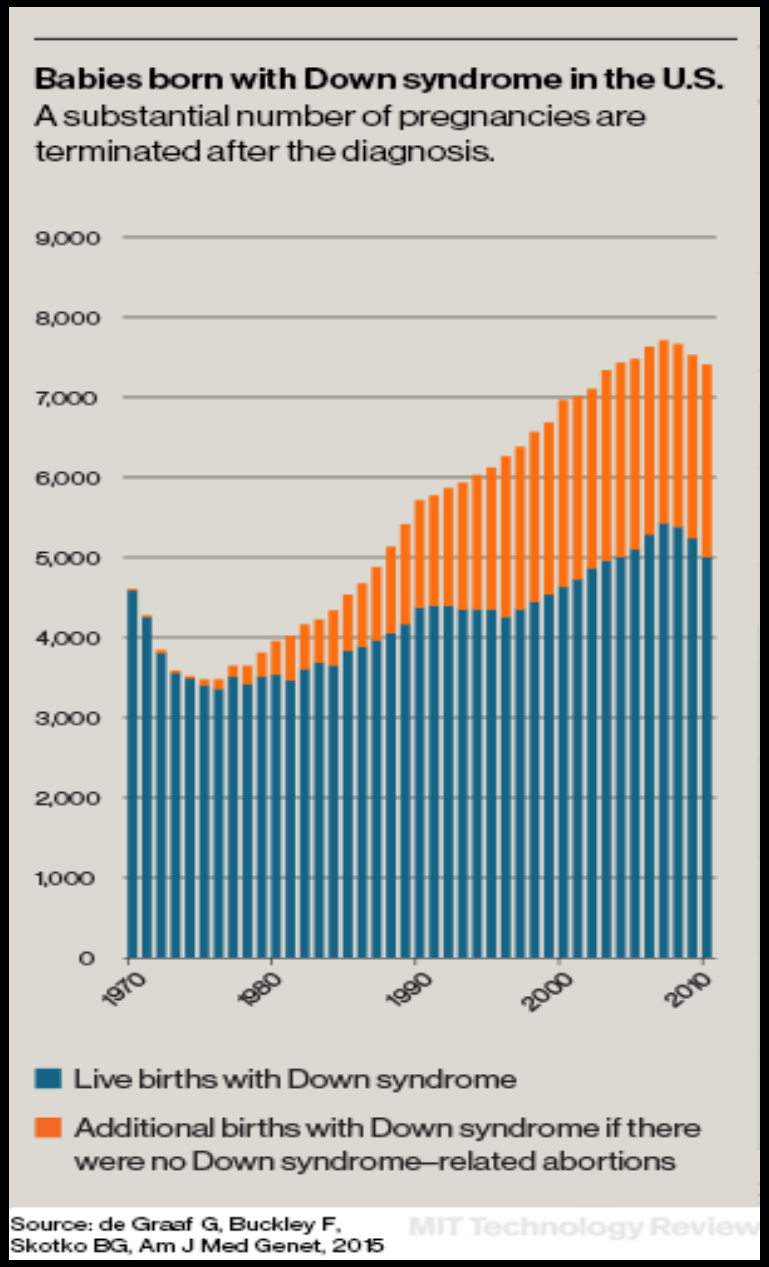
  Pregnancy continuation as well as adoption are the other options.

  There are waiting lists to adopt babies with Down syndrome.

Current Pregnancy Outcomes

James Egan, University of Connecticut | The Washington Post - February 24, 2009





Recent Professional Guidelines Call for Use of Best Practices in Providing a Diagnosis

- 2011 Guidelines of the American Academy of Pediatricians “Health Supervision for Children with Down Syndrome” calls for pediatricians who discuss a DS diagnosis to convey the **wide range of variability in outcomes**, family options, and current treatments and interventions.
- 2011 Practice Guidelines for Communicating a Prenatal or Postnatal Diagnosis of Down Syndrome: Recommendations of the National Society of Genetic Counselors. “Non-directiveness is a central tenet [of genetic counseling]… Genetic counselors should balance the negative aspects of DS, such as birth defects, medical complications and developmental delays, with positive aspects like available treatments, therapies, and the ability for people with DS and their families to enjoy a high quality of life… **Each baby with DS is different and physical and cognitive development cannot be predicted prenatally**. “

Best Practices – Providing a Diagnosis

- Skotko, B., Kishnani, P., & Capone, G. for the Down Syndrome Diagnosis Study Group (2009). **Prenatal diagnosis of Down syndrome: How best to deliver the news.** *American Journal of Medical Genetics.*

Mothers emphasized that at the time of receiving a definitive prenatal diagnosis, they should be provided with up-to-date information about what DS is, what causes DS, and what are the expectations for a child with DS living today.

Delivering the Diagnosis: Prenatal Best Practices

- Results of screening should be clearly characterized as risk assessment.
- Prior to invasive diagnostic test, discuss reasons for test.
- Healthcare professionals knowledgeable about DS should provide the diagnosis to parents together, in person if possible and in private. If necessary, provide the results on the phone at a pre-arranged time.
- Be factual and clear, discuss what Down syndrome is. Discuss child's potential and abilities as well as possible limitations and disabilities.
- Distinguish between a clear diagnosis and the uncertainty of what the developmental outcome will be for a particular child, especially given the wide variability of outcomes with Down syndrome.

Delivering the Diagnosis: Prenatal Best Practices

- **Provide information about Down syndrome from the Texas Dept. of State Health Services website (legal obligation).** Also provide "Understanding a Down Syndrome Diagnosis" booklet.
- Provide information about a local Down syndrome organization to allow parents to connect to New Parent Outreach (trained volunteer parents of children with DS). In Central Texas, www.dsact.org or 512-323-0808. Full list of Texas Down syndrome organizations: https://www.dshs.state.tx.us/birthdefects/downsyndrome/.
- Encourage parents to watch DVD "Down Syndrome in the 21st Century." www.dsact.org.
- Expect parents' emotional reaction of surprise, grief and upset.
- Allow time for the parents to absorb the news. Respect whatever choice is made going forward and remain engaged with them as a resource for questions going forward.
- www.downsyndromepregnancy.org offers support to expectant parents who have received a prenatal Down syndrome diagnosis and are moving forward with their pregnancy.

Delivering the Diagnosis: Postnatal Best Practices

- Provide the diagnosis or suspicion to parents together, in person, privately and as soon as possible following delivery.
- Congratulate parents on baby's birth.
- Touch the baby, use his/her name.
- Evaluate their understanding of the diagnosis.
- Stress that their child is a BABY first and foremost.

Delivering the Diagnosis: Postnatal Best Practices

- Be factual and clear, discuss child's potential and abilities as well as possible limitations and disabilities. Avoid words that imply tragedy or pity.
- Align communications from all members of the healthcare team.
- Remember no one can predict a precise outcome for any child. Limit discussion of medical complications to those the infant has or might develop in 1st year.
- Provide information about Down syndrome from the Texas Dept. of State Health Services website (legal obligation). Also provide "Understanding a Down Syndrome Diagnosis" booklet.
- Provide information about a local Down syndrome organization to allow parents to connect to New Parent Outreach (trained volunteer parents of children with DS). In Central Texas, www.dsact.org or 512-323-0808. Full list of Texas Down syndrome organizations: www.dshs.state.tx.us/birthdefects/downsyndrome/.
- Encourage parents to watch DVD "Down Syndrome in the 21st Century." www.dsact.org.

Impact of the Diagnosis; Impact of the Child with DS

- The initial reactions of healthcare providers can have a profound and lasting impact on parents. Choice of language is key. “I’m so sorry, must be your worst nightmare” vs “Congratulations, you have a beautiful baby. This is probably unexpected news, you’ll need some time to process it. Many of these kids do very well.”
- While the birth of a child with Down syndrome may initially be viewed as unwelcome, this interpretation often changes dramatically over time.
- Families and friends of children with Down syndrome have reported that their lives have been profoundly and positively influenced by the experience of having or knowing a child with Down syndrome.
- All members of the healthcare team can have an important role with families.

Delivering the Diagnosis - Simulation

- www.brighter-tomorrows.org - an interactive simulation with video scenarios/ questions for the healthcare professional about the scenarios.
- Using the simulation has been demonstrated to increase level of comfort in providing a diagnosis.
- www.ndsccenter.org - “A Physician’s Guide: Delivering the Diagnosis” provides brief video clips offering expert advice for a variety of scenarios (prenatal/postnatal, suspected/confirmed).

National Gold-Standard Parent Resource for Prenatal and Postnatal Diagnosis

- “Understanding a Down Syndrome Diagnosis” booklet published in 2011.
- Represents consensus of ACOG, American College of Medical Genetics, National Society of Genetic Counselors, National Down Syndrome Congress, and National Down Syndrome Society.
- Content is designed to answer questions about Down syndrome for expectant parents, and is appropriate for new parents as well.
- 10,000 copies distributed nationally.
- Clinicians are welcome to give a copy of this booklet (lettercase.org) to new parents at the time of diagnosis, as well as the mandatory information about Down syndrome from Texas Dept. of State Health Services website. https://www.dshs.state.tx.us/birthdefects/downsyndrome/

Legal Requirements

Texas Down Syndrome Information Act, effective September 1, 2015.
Texas Health & Safety Code, Sections 161.651-653.

- Requires physicians and genetics counselors to provide current, evidence-based information about DS to new/expectant parents at the time of initial diagnosis OR positive test result.
- The mandatory information addresses physical, developmental, educational and psychosocial outcomes, life expectancy, clinical course, intellectual/functional development, treatment options and contact information for national and local Down syndrome organizations.
- As of February 2016, the mandatory information is housed on the Texas Department of State Health Services website dshs.state.tx.us/birthdefects/downsyndrome/.

From this link, download the 4-page brochure "Information about Down Syndrome for New and Expecting Parents" in English or Spanish. DSHS website information may not mention termination as an option.

Legal Requirements

Information about Down Syndrome for New and Expecting Parents

Your baby has or may have Down syndrome. It is natural for you to have questions, concerns or fears. You are not alone in your feelings or on the journey ahead of you. Know that the outlook for people with Down syndrome has improved over time because of advances in medical care, education and public attitudes. This brochure has facts about Down syndrome and a list of places where you can go to find more information and support.

About Down Syndrome

Each cell in the human body has 23 pairs of chromosomes; babies get half of each pair from their mom and the other half from their dad. Down syndrome is a genetic condition that is usually caused by an extra copy of the twenty-first chromosome. It is not caused by anything either parent did or did not do.

About 250,000 people in the United States have Down syndrome. Down syndrome does not usually run in families.

Children with Down syndrome will grow and develop like other babies, but may meet milestones later than a typical child. The mental, behavioral and developmental progress of people with Down syndrome varies widely and cannot be predicted before a person is born. Currently, the average life expectancy for people with Down syndrome is about 60 years.

Your Child with Down Syndrome

You can help your child fulfill his or her potential by having high expectations. Nurture and relate to your child like any other, and create a supportive and caring environment to help your child thrive.

People with Down syndrome are active and valued members of their community. This includes children who are involved in social and school programs, and adults who have jobs and live independently or with some support.

- Children with Down syndrome are more like other children than they are different.
- Babies with Down syndrome usually have developmental delays. Early intervention like occupational and speech therapy helps babies meet their milestones.
- Most babies with Down syndrome have low muscle tone at birth. This usually improves with time, and physical therapy can help.
- Half of babies with Down syndrome will have health issues. This could include heart or gastrointestinal conditions that may require surgery. Babies with Down syndrome have higher chances for feeding and digestive issues, hearing loss, vision impairments, and respiratory infections. Most of these conditions can be treated with good health care.
- People with Down syndrome can do all the things a typical person can do, including participate in sports and have a job.
- People with Down syndrome usually have a mild to moderate range of intellectual disability.
- Children with Down syndrome often attend regular schools in regular education classes with differing levels of support. There are now many college programs for people with intellectual delays.
- People with Down syndrome can have regular jobs or ones with support.
- People with Down syndrome can live independently or in a group home, and have friends and intimate relationships.

Legal Requirements

- Under the Down Syndrome Information Act, providers are explicitly allowed to give parents *additional* DS information that is current, evidence-based and reviewed by medical experts and national DS organizations (such as “Understanding a Down Syndrome Diagnosis”).

- The obligation under the DSIA does not impose a standard of care or create an obligation or duty that provides a basis for a lawsuit against a provider. A provider may not be held civilly or criminally liable for failing to provide the mandatory information under the DSIA.

Legal Requirements

- Other healthcare professionals can play an important role in supporting the family at the time of diagnosis or positive test result, but there is no provision in DSIA allowing a physician to *delegate* to another clinician provision of the mandatory information to the parents.

- Down syndrome organizations in Texas capture compliance data, in service to their members

Impact of the Person with DS on the Family

3 Studies (Parents, Siblings and Self Perceptions about DS), Skotko, Levine and Goldstein, American Journal of Medical Genetics, Oct 2011.

- Parents: 79% said their outlook on life more positive. 4% regretted having the child.
- Siblings: 94% proud. 88% felt they were better people because of their sibling. 4% would trade him in.
- Self: 99% happy with their lives.

Joy as well as Disability

Down Syndrome Cognition Research

Down syndrome cognition research is making great strides to:

- identify the genes on chromosome 21 that cause medical problems in Down syndrome;
- develop treatments for the cognitive effects of Down syndrome;
- transfer therapies developed for Alzheimer's disease to Down syndrome (both conditions exhibit beta-amyloid plaques made by the APP gene on 21st chromosome); and
- identify and treat additional medical problems related to Down syndrome.

Down Syndrome Cognition Research (cont.)

- 2003 founding of Down Syndrome Research and Treatment Foundation, funding research at Stanford, Johns Hopkins, UCSD, Univ. of Arizona, and UT. Now called Lumind Foundation.
- September 2011 formation of NIH Down syndrome consortium.
- 2013 launch of national Down Syndrome Patient Registry.
  dsconnect.nih.gov
- 2014 release of "Down Syndrome Directions: NIH Research Plan on Down Syndrome."
- Two clinical trials are now underway in 2016 by Transition Therapeutics and Balance Therapeutics.
  - https://www.lumindrds.org/research/clinical-trials
  - https://clinicaltrials.gov/

Down Syndrome Cognition Research (cont.)

Pharmacotherapy in Down's syndrome: which way forward?
The Lancet Neurology, Vol. 15, No.8, p776–777, July 2016.

- A team of scientists led by doctors Rafael de la Torre at Hospital del Mar Medical Research Institute (IMIM) and Mara Dierssen at the Centre for Genomic Regulation (CRG) have shown that epigallocatechin gallate together with a cognitive stimulation protocol, might improve some cognitive domains in individuals with Down's syndrome.
- The findings suggest that participants who had received the treatment had better scores in the visual memory recognition and inhibition tasks, and improvement in adaptive behavior than those in the control group (placebo and cognitive training).

Down Syndrome Cognition Research (cont.)

Pharmacotherapy in Down's syndrome: which way forward? The Lancet Neurology, Vol. 15, No.8, p776–777, July 2016.

- Epigallocatechin gallate was known to inhibit the excess of the DYRK1A gene, and the success achieved in previous studies with mice suggested that the treatment could also work for human beings. The scientists studied more than the cognitive effects on the study participants. They also conducted neuro-imaging tests to determine whether the improvement was attributable to physical or neurophysiological changes in the brain. "It was surprising to see how the changes are not just cognitive--in the reasoning, learning, memory and attention capacities--but suggest that the functional connectivity of the neurons in the brain was also modified" says Dr. de la Torre.

EurekAlert, Public Release: June 6, 2016.

Down Syndrome Cognition Research (cont.)

Multiple organizations now support Down syndrome cognition research.

Down Syndrome Cognition Research
Lumind™ FOUNDATION

Jerome Lejeune
FOUNDATION USA
Research Care Advocacy

GLOBAL DOWN SYNDROME FOUNDATION®

Dedicated to significantly improving the lives of people with Down syndrome through Research, Medical Care, Education and Advocacy

New Non-Invasive Prenatal Screening: Questions Abound

- Sequenom, Inc. 10/17/11 announced the immediate launch of a new noninvasive Down syndrome screening test using cell-free DNA with a high degree of accuracy (MaterniT21) in 20 U.S. cities, to be used in 1st or 2nd trimester.

- Ariosa, Verinata (Illumina), Ravgen and Natera(Panorama) now also offer NIPS.

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

- Tests of cfDNA appear to be highly sensitive and specific in detecting trisomies, but two problems plague the evidence base. First, the sensitivity and specificity of the tests derive from studies done on collections of archived samples with known karyotypes that intentionally included a large proportion of specimens from women with known aneuploid fetuses. Evidence concerning the performance characteristics of the testing in the general population and for multiple gestations is limited… Second, cfDNA-testing companies have not reported information about their tests' positive predictive value (PPV), and there is reason to question the tests' performance on this measure…Arguably, PPV is more important than sensitivity and specificity to patients undergoing testing: it indicates the probability that a positive test result indicates a true fetal aneuploidy. Thus, PPV should be discussed in study reports and marketing materials but isn't.

  – A New Era in Noninvasive Prenatal Testing, Stephanie Morain, M.P.H., Michael F. Greene, M.D., and Michelle M. Mello, J.D., Ph.D.,

    New England Journal of Medicine, August 8, 2013.

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

Risk assessment is limited to specific fetal aneuploidies (trisomy 13, 18, and 21) at this time. Some platforms also screen for sex chromosome abnormalities. Approximately 50% of cytogenetic abnormalities routinely identified by amniocentesis will not be detected when trisomy 21, 18, and 13 are the only aneuploidies being screened. When patients <35 years or >35 years are considered separately, 75 and 43% of cytogenetic abnormalities will be missed, respectively.

ACMG Policy Statement, Genetics in Medicine: ACMG statement on noninvasive prenatal screening for fetal aneuploidy, 2013.

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

In general obstetrical population, prenatal testing with the use of cfDNA had significantly lower false positive rates and higher positive predictive values for detection of trisomies 21 and 18 than standard screening….the positive predictive value for cfDNA testing was significantly higher than that for standard screening, for both trisomy 21 (45.5% vs 4.2%) and trisomy 18 (40% vs 8.3%).

-DNA Sequencing versus Standard Prenatal Aneuploidy Screening, Diana W. Bianchi, M.D., R. Lamar Parker, M.D., et al., New England Journal of Medicine, February 27, 2014. Study funded by Illumina.

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

Two recent industry-funded studies show that test results indicating a fetus is at high risk for a chromosomal condition can be a false alarm half of the time. And the rate of false alarms goes up the more rare the condition, such as Trisomy 13….Two Boston-area obstetricians, with funding from a testing company, recently sent samples from two nonpregnant women to five testing companies for analysis. Three companies returned samples indicating they came from a woman who was carrying a healthy female fetus. "Oversold and Misunderstood," Beth Daley, New England Center for Investigative Reporting, December 14, 2014.

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

How accurate is an abnormal result?

- These tests are often advertised to patients and healthcare providers as being >99% accurate. It is important to recognize that this is a population-level statistic and applies to all women screened. Since most pregnancies are unaffected and most results are "low risk" this test is correct 99% of the time for all women. However, the chance that a high risk result indicates an affected fetus is not 99% in the majority of cases. In order to determine the chance for a high risk result to be a true positive, one must calculate the positive predictive value.

Positive Predictive Value	Wang et al.	Bianchi et al.	Choy et al.	Meck et al.	Norton et al.
Trisomy 21	38/41 (93%)	5/11 (45.5%)	52/55 (95%)	29/30 (97%)	9/47 (80.1%)
Trisomy 18	16/25 (64%)	2/5 (40%)	6/12 (50%)	3/5 (60%)	9/10 (90%)
Trisomy 13	7/16 (44%)		4/7 (57%)	1/4 (25%)	2/4 (50%)
Sex Chromosome Aneuploidy	6/16 (38%)		4/6 (67%)	1/7 (14%)	

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

- You can explain these results similarly to how you would explain other screening tests, taking into consideration cfDNA screening has fewer false positive results than traditional screening. While an abnormal result greatly increases concern, it does not provide a diagnostic answer and further testing is necessary for confirmation.
- Confirmatory testing via CVS or amniocentesis should be offered to all women with an abnormal cfDNA result.

Fact Sheet for Medical Professionals. A product of the National Society of Genetic Counselors (NSGC) Prenatal Special Interest Group, June 2015. Endorsed by the American College of Obstetricians and Gynecologists (ACOG), June 10, 2015, and should be construed as ACOG clinical guidance.

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

Table 1. Cell-free DNA Test Performance Characteristics in Patients Who Receive an Interpretable Result*

			Age 25 years	**Age 40 years**
	Sensitivity (%)	**Specificity (%)**	**PPV (%)**	**PPV (%)**
Trisomy 21	99.3	99.8	33	87
Trisomy 18	97.4	99.8	13	68
Trisomy 13	91.6	99.9	9	57
Sex chromosome aneuploidy	91.0	99.6	--†	--

American College of Obstetricians and Gynecologists Committee Opinion Number 640, September 2015. Committee on Genetics, Society for Maternal–Fetal Medicine. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

- Given the performance of conventional screening methods, the limitations of cell-free DNA screening performance, and the limited data on cost-effectiveness in the low-risk obstetric population, conventional screening methods remain the most appropriate choice for first-line screening for most women in the general obstetric population.
- Although any patient may choose cell-free DNA analysis as a screening strategy for common aneuploidies regardless of her risk status, the patient choosing this testing should understand the limitations and benefits of this screening paradigm in the context of alternative screening and diagnostic options.
- *American College of Obstetricians and Gynecologists Committee Opinion Number 640, September 2015. Committee on Genetics, Society for Maternal–Fetal Medicine. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.*

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

- The cell-free DNA test will screen for only the common trisomies and, if requested, sex chromosome composition.
- Given the potential for inaccurate results and to understand the type of trisomy for recurrence-risk counseling, a diagnostic test should be recommended for a patient who has a positive cell-free DNA test result.
- Management decisions, including termination of the pregnancy, should not be based on the results of the cell-free DNA screening alone.

American College of Obstetricians and Gynecologists Committee Opinion Number 640, September 2015. Committee on Genetics, Society for Maternal–Fetal Medicine. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

New Non-Invasive Prenatal Screening: Questions Abound (cont.)

- FDA Considers Regulating NIPS
- 12/2014 announcement of 2/15 workshop of "Optimizing FDA's Regulatory Oversight of Next Generation Sequencing Diagnostic Tests."

"In order to continue to support the development of useful medical information, FDA believes the most efficient possible approaches to regulating NGS (Next Generation Sequencing) tests should be considered. Among the possibilities, a standards-based approach to analytical performance of NGS tests and the use of centralized curated databases containing up-to-date evidence to support clinical performance are under discussion. "

FDA Discussion Paper

National Resources

- National Down Syndrome Society (NDSS)
  666 Broadway, Suite 810
  New York, NY 10012
  (800) 221-4602 *www.ndss.org*

- National Down Syndrome Congress (NDSC)
  7000 Peachtree-Dunwoody Road
  Atlanta GA 30328
  (800) 232-6372 *www.ndsccenter.org*

Texas Resources

Texas Down syndrome organizations are listed in https://www.dshs.state.tx.us/birthdefects/downsyndrome/.

Central Texas:

Down Syndrome Association of Central Texas
(DSACT)
3710 Cedar Street, Box 3
Austin TX 78705
www.dsact.org
512-323-0808
Fax: 512-451-3110

Programs, services, social groups and events, website, educational resources, new parent outreach, speech therapy and a wealth of information and resources for families.

Healthcare Resources

- Clinical Report – Health Supervision for Children with Down Syndrome. Bull et al., *Pediatrics*, 2011. *http://pediatrics.aappublications.org/content/early/2011/07/21/peds.2011-1605.*
- Growth Charts for Children with Down Syndrome in the U.S. Zemel BS, et al., *Pediatrics*. Oct. 26, 2015. *http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2015-1652*
- www.ndss.org/Resources/Health-Care/Health-Care-Providers/ - Map of US Down syndrome clinics
- *http://downsyndrome.nih.gov/Pages/default.aspx* - NIH Down syndrome consortium
- *https://dsconnect.nih.gov/* - DS-Connect, the national Down syndrome patient registry

References and Resources

- dseinternational.org (Down Syndrome Education International; leading education research organization)
- Txp2p.org (Texas Parent to Parent, support and information to families of children with disabilities)
- Ndsccenter.org ("Delivering a Diagnosis: Physician Guide")
- lumindfoundation.org (Down Syndrome Research)
- http://dsresearch.stanford.edu (Stanford CRTDS)
- http://pediatrics.aappublications.org/cgi/content/full/115/1/64 (2005 Skotko study).

References and Resources (cont.)

- Prenatal Diagnosis of Down Syndrome: How Best to Deliver the News. Skotko et al., *American Journal of Medical Genetics*, 2009. www.brianskotko.com
- Lettercase.org (Publisher of *Understanding a Down Syndrome Diagnosis*)
- Parent video, *Down Syndrome in the 21st Century* at www.youtube.com/watch?v=I13KxRYqoo0 or search for "Down syndrome"
- Practice Guidelines for Communicating a Prenatal or Postnatal Diagnosis of Down Syndrome: Recommendations of the National Society of Genetic Counselors. Sheets et al., *Journal of Genetic Counseling*, 2011.

References and Resources (cont.)

- *ds-health.com*
- Three Studies (Parents, Siblings and Self Perceptions about DS). Skotko, Levine and Goldstein, *American Journal of Medical Genetics*, October 2011.
- A Drug for Down Syndrome. Dan Hurley, *New York Times Magazine*, July 31, 2011.
- *www.downsyndromepregnancy.org* for parents who have decided to continue a pregnancy following diagnosis of Down syndrome.
- Jon's Worms. S. Kirk Walsh *Alcalde*, September/October 2011.

Resources for Parents

- The Right Parent Resources Make the Difference
  - DSACT, Texas Parent to Parent, ARC of Texas
  - Inclusion Works Conference
  - Down Syndrome Education International
  - Early Childhood Intervention

- The Right Education Resources Make the Difference
  - Inclusion Works Conference (ARC of Texas)
  - Down Syndrome Education International
  - *www.udlcenter.org/aboutudl/udlguidelines*

Books

Kumin, Libby: *Early Communication Skills for Children with Down Syndrome: A Guide for Parents and Professionals*, Bethesda, MD: Woodbine House, 2012.

Winders, Patricia PT: *Gross Motor Skills in Children with Down Syndrome: A Guide for Parents and Professionals*, Bethesda, MD: Woodbine House, 2013.

Bruni, Maryanne: *Fine Motor Skills for Children with Down Syndrome: A Guide for Parents and Professionals,* Bethesda, MD: Woodbine House, 2016.

Parents of a child with Down syndrome never forget their first contact with healthcare professionals

Courtney Dezendorf, Director
Office of Academic Affairs
Q & A Moderator

Questions and Answers

Remote sites can send in questions by typing in the *GoToWebinar* chat box or email GrandRounds@dshs.state.tx.us.

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October 12

Obesity and Distress: The "Second Brain" Connection

Presenter:
Karen Williams, MSSW, Williams Group