DDC Clinic
Center for Special Needs Children
Middlefield, Ohio

Presentation for July 17, 2013

DDC Clinic – Started with a Family Story

- An Amish family with four children with a devastating condition tried to find the answer after visiting many major medical centers
- In 1998, five families traveled hundred miles to PA to see Dr. Holmes Morton

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DDC Clinic – History

- Inspired by Dr. Holmes Morton's clinic in Lancaster, PA
- Community-based initiative for a dream of
  - A gathering place
  - A place of love, compassion, and caring where our children and families are respected
  - A place where people take time to listen and share
  - A place of faith and hope

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DDC Clinic – Setting

- A 501(c) (3) non-profit organization located in Middlefield of Ohio, Geauga Amish settlement
  - Total population ~95,000, Amish ~14,000 (15%)
  - 50% of developmental disabilities are from Amish
  - One hour (but a world) away from world class healthcare
- A collaboration of families, Amish communities, medical professionals, and research scientists
- Unique primary care facility for
  - Comprehensive patient care
  - Patient-oriented translational research
  - Community-based education

DDC Clinic – Mission and Vision

- ***Our Mission***

  To enhance the quality of life for people with special needs caused by rare genetic disorders

- ***Our Vision***

  DDC Clinic is a world-class medical home


THANK YOU!

DDC Clinic's LEED Gold Facility Opened in 2009

LEED: Leadership in Energy & Environmental Design

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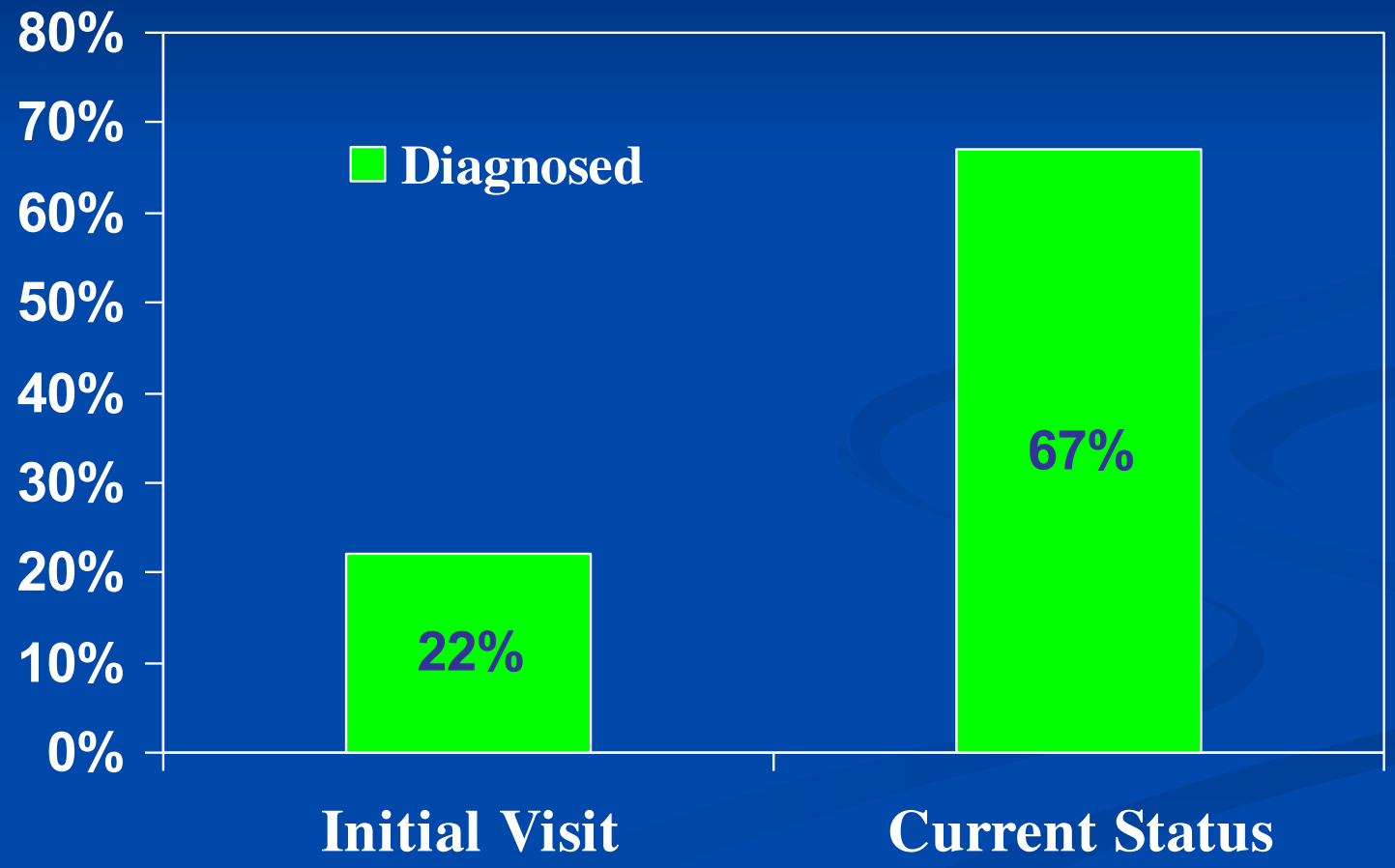
Medical Home Approach

- A family-centered medical home is not a building, house, hospital, or home healthcare service, but rather an approach to providing comprehensive primary care
- "A medical home is defined as primary care that is accessible, continuous, comprehensive, family centered, coordinated, compassionate, and culturally effective."

The American Academy of Pediatrics (AAP)

We Can Make a Difference



DDC Clinic – A Unique Collaboration

- Serves over 600 patients, no family is turned away based on their ability to pay
- Partnership with the community for translational research
- Focus on rare genetic diseases

List of Genetic and Metabolic Diseases in DDC Clinic (2007)

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Disease	OMIM Number
Adenylosuccinase (adenylosuccinate lyase, ADSL) deficiency	103050
Alagille syndrome	118450
Amish albinism	606952
Amish brittle hair syndrome	234050
Autism spectrum disorders	209850
Beal's syndrome	121050
Byler disease	211600
Cartilage-hair hypoplasia dwarfism	250250
Celiac disease	212750
Cerebral palsy with late onset Ig A nephropathy (?)	
Charcot-Marie-Tooth disease	214400
Chicken breast disease (Amish nemaline myopathy)	605455
Chromosome 8p duplication	
Cockayne syndrome	216400
Cohen syndrome	216550
Cortical dysplasia and focal epilepsy syndrome	
Crigler-Najjar syndrome Type I	218800
Down syndrome	190685
Duchenne muscular dystrophy	310200
Factor V deficiency	227400
Familial cleft lip with or without cleft palate (?)	
Familial craniosyostosis (?)	
Familial deafness (?)	
Familial seizure with mental retardation (?)	
Ganglioside GM3 synthase (alpha 2,3-sialytranserase) deficiency	609056
Glucose/galactose malabsorption	606824
Glutaric acidemia I (glutaryl-CoA dehydrogenase deficiency)	231670
Hemophilia B – Factor IX deficiency	306900
Hypertrophic cardiomyopathy	115197
Hypotonia, ataxia and developmental delay (?)	
Hypotonia, excessive height, pectus excavatum & mental retardation (?)	
Hypertriglyceridemia – lipoprotein lipase deficiency or apolipoprotein C-II deficiency	238600
Infantile lethal cardiomyopathy	115197
Juvenile glaucoma, failure to thrive and leukodystrophy (?)	
Leigh syndrome	256000
Leri-Weill dyschondrosteosis	127300
Maple syrup urine disease	248600
Maternal phenylketonuria (PKU)	
McKusick-Kaufman syndrome	236700
Metachromatic leukodystrophy	250100
Microcephalic osteodysplastic primordial dwarfism, Type I	210710
Mitochondrilal respiratory chain complex IV deficiency	220110
Phenylketonuria (PKU) – phenylalanine hydroxylase deficiency	261600
Prolidase deficiency	170100
Propionic acidemia – propionyl-CoA carboxylase deficiency	606054
Pyruvate kinase deficiency of red cell	266200
Rett syndrome	312750
Tarsal coalition	186570
Troyer syndrome	275900
Usher syndrome, Type II	276901

OMIM: Online Mendelian Inheritance in Man, ?: under study

More Than Seventy Rare Genetic Diseases at DDC Clinic

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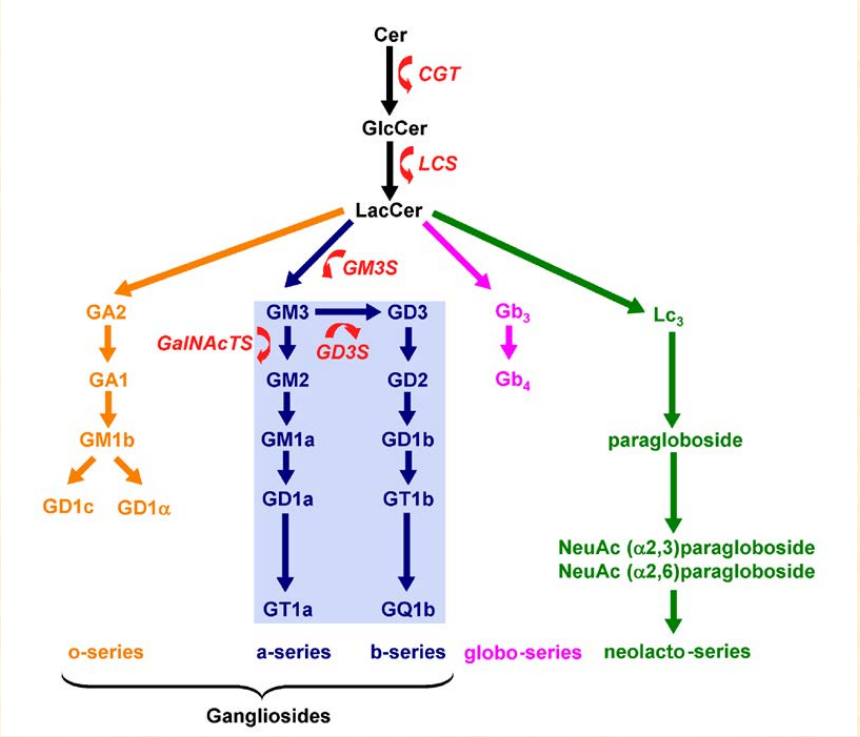
- Community specific –
  - Cohen syndrome (43) + (11)
  - Glucose-galactose malabsorption (33)
  - Prolidase deficiency (11)
- Although found in other communities, we may be serving more patients than other clinics
  - Ganglioside GM3 synthase deficiency (39)
  - SAMS association (25) + (4)
  - TMCO1 defect syndrome (11)
  - Yoder dystonia (9)
  - Byler disease (12)
- A few notable autosomal dominant conditions – we are currently not following up with most heterozygous carriers
  - Hypertrophic cardiomypathy
  - Long QT syndrome

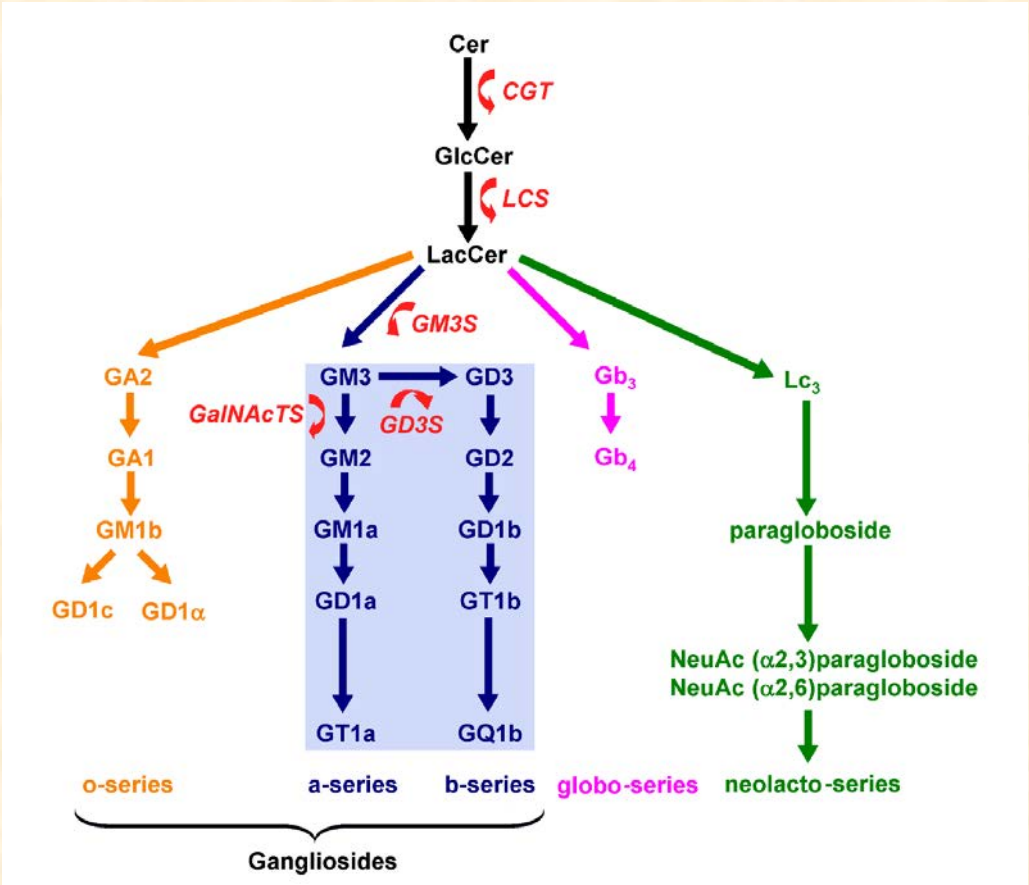
Ganglioside GM3 Synthase Deficiency (Nat Genetics 2004)

- An autosomal recessive disease
- A complete lack of ganglioside GM3 and its biosynthetic derivatives
- Over 50 patients from OH, IN, KY, MI, NY and PA have been identified
- It has been recently reported in African American and European
- Clinical manifestations: severe infantile irritability, intractable seizures, profound psychomotor developmental delay, completely caregiver dependent



GM3 Deficiency - Potential Treatment and Its Implications

- Providing an adequate amount of GM3 might be effective treatment
  - Cronassial and Sygen – Fidia of Italy
  - Pig brain formula - DDC
  - G500 – Fonterra of New Zealand
- The therapeutic implications might be much broader
  - Parkinson's disease
  - Brain and spinal cord injury
  - Stroke



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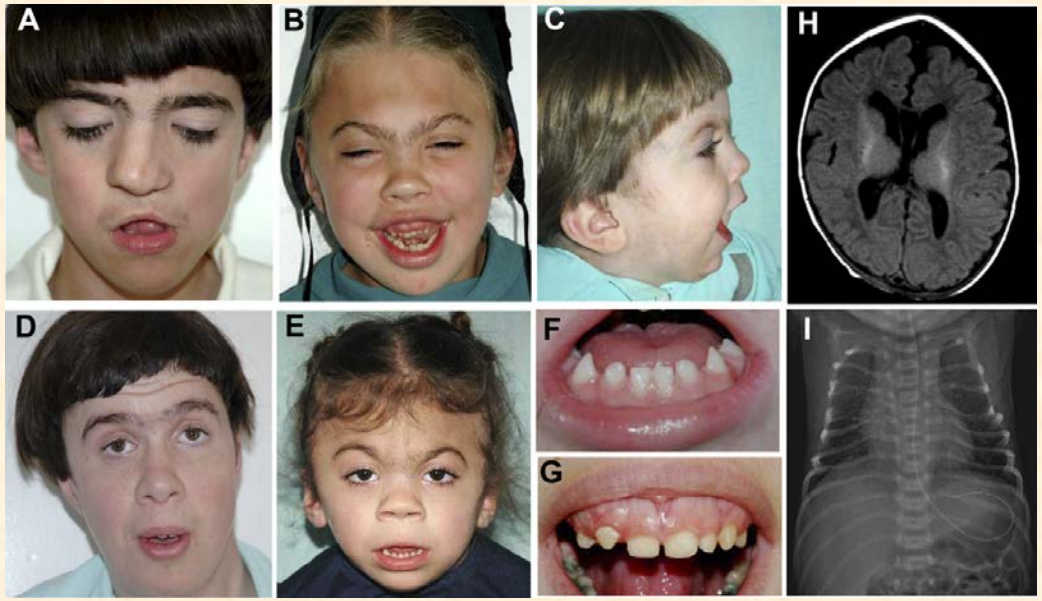
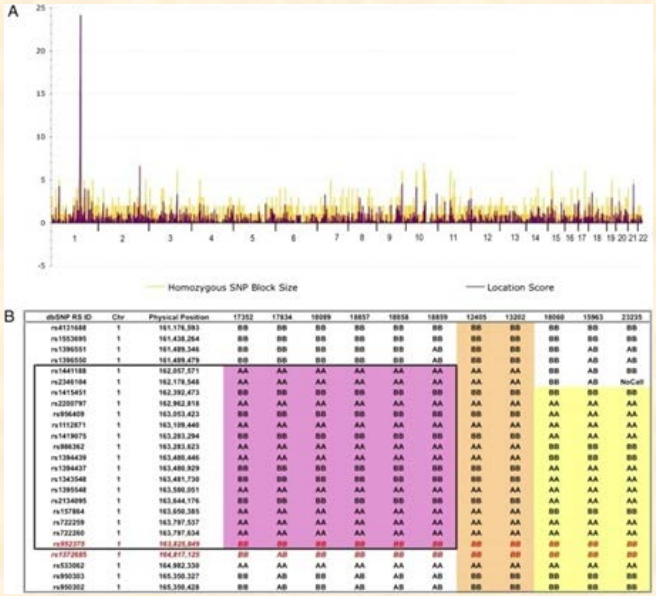
TMCO1 Defect Syndrome

- Autosomal recessive disorder
- Characterized by distinctive craniofacial dysmorphism, skeletal anomalies, mental retardation and frequent sinus infections
- "TMCO1 defect syndrome" is proposed as name of the disease





Xin B et al. PNAS 2010;107:258-263

PNAS

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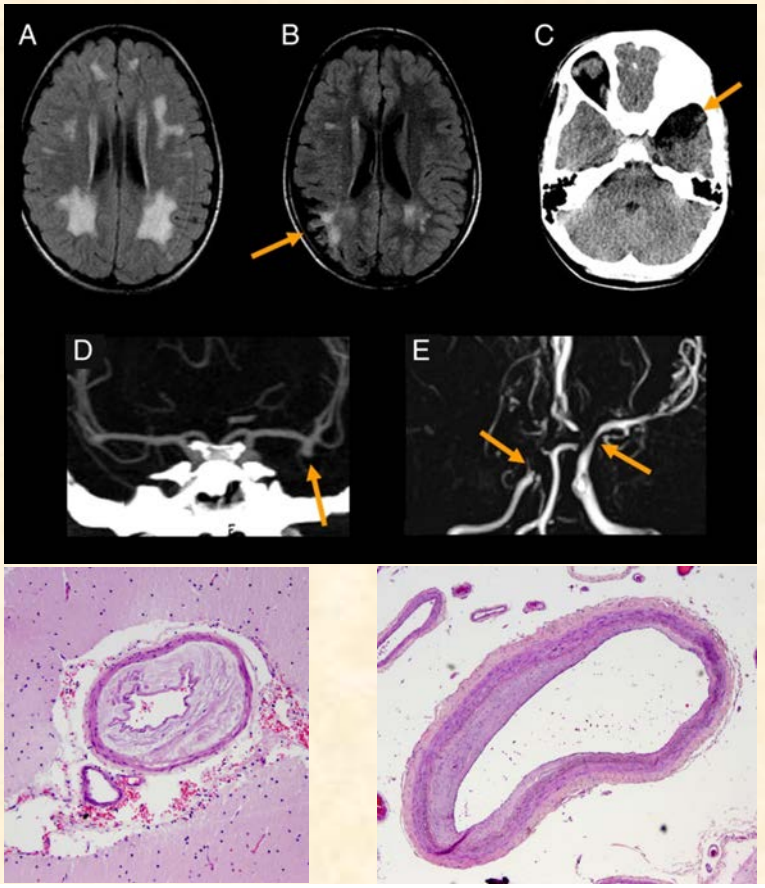
SAMS Association

- Another novel condition we described recently
- An acronym (first 3 letters of gene SAMHD1 as well) is used to name the disease
  - ***S***tenosis
  - ***A***neurysm
  - ***M***oyamoya
  - ***S***troke
- The gene may be associated with stroke, its implications are broad



Xin B et al. PNAS 2011;108:5372-5377

PNAS

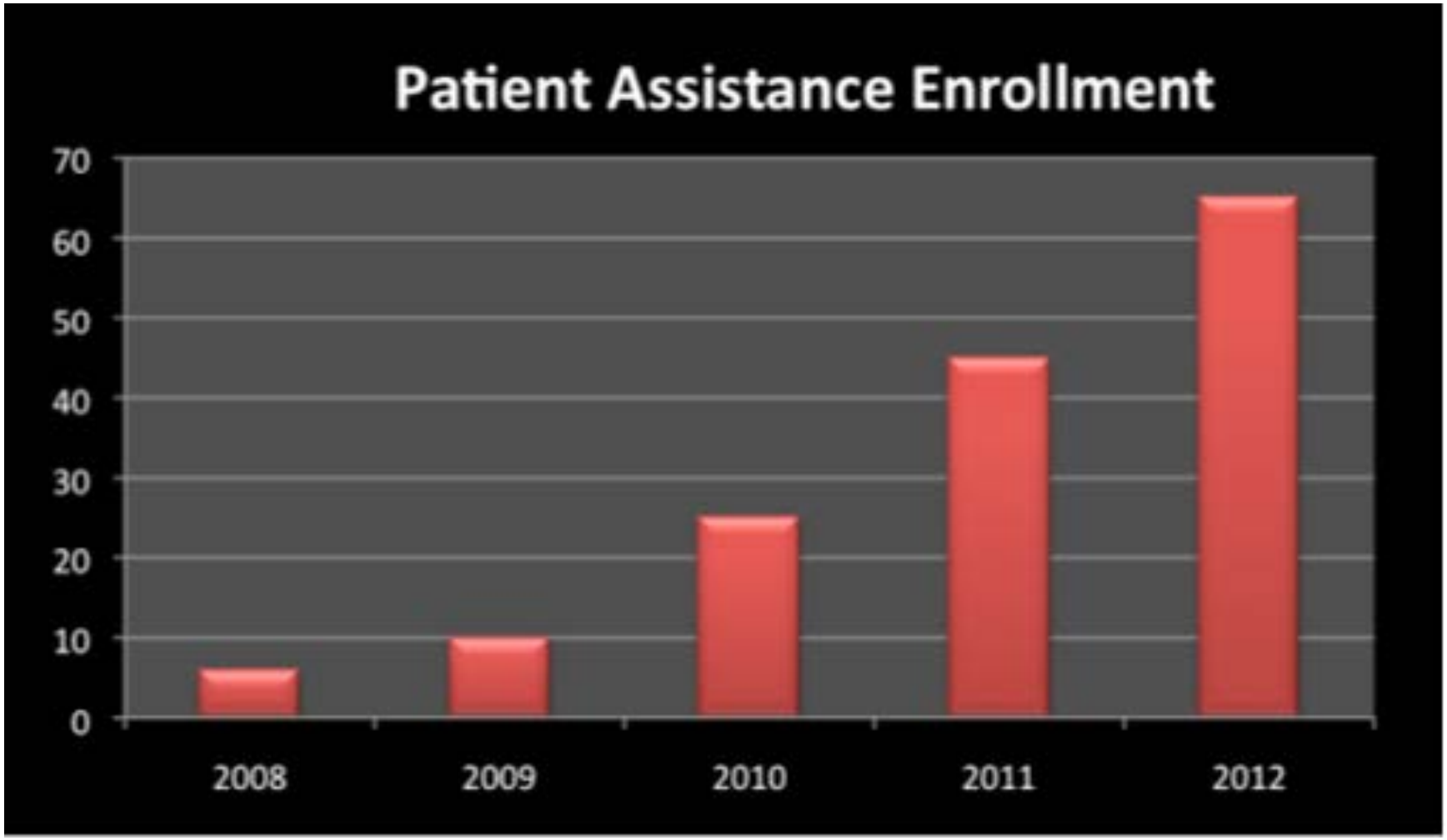
What are the greatest needs of families affected by genetic disease?

- Transportation
- Subspecialty care and therapy
- Medical supplies
- Information about genetic disease

Healthy Tomorrow Program

- Provide direct transportation to DDC Clinic
- House calls for high needs, high risk patients
- Monthly outreach clinics to Holmes County, OH
- A total of 13,644 miles have been logged during last 12 months
- Onsite specialty clinics to minimize long distance travel to major medical centers
  - Hemophilia Programs (pediatrics and adults)
  - Pediatric Neurology Program
  - Dental Program

Patient Assistance Program



Parent Support Groups

- DDC Clinic Family Newsletter

Love, Faith, and Family

The DDC Clinic Newsletter for the Amish Community

Winter 2012 - 2013

DDC Clinic Genetics Laboratory Is CLIA Certified

Dear Families and Friends,

We have some good news we want to share with you. Our application for CLIA certification for genetic testing has been approved. That means our genetics laboratory will become one of the few

- Disease-specific family gatherings
  - Prolidase deficiency, GM3 deficiency, TMCO1 defect syndrome, Cohen syndrome etc.

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Building a Sustainable Future

- To sustain our achievements and further our mission, DDC Clinics strategic plan has three priorities
  - Increase financial sustainability
  - Increase scope of genetic research
  - Enhance programs and services

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Molecular Diagnostics Lab

- Successfully passed CLIA Inspection
- Officially certified as a clinical diagnostic lab to provide high complexity genetic testing services

Diseases	Gene symbol
Amish brittle hair syndrome	MPLKIP (TTDN1)
Amish nemaline myopathy	TNNT1
Byler disease	ATP8B1
Cartilage-hair hypoplasia dwarfism	RMRP
Charcot-Marie-Tooth disease	GDAP1
Cockayne syndrome	ERCC6
Cohen syndrome	VPS13B (COH1)
Cortical dysplasia and focal epilepsy syndrome	CNTNAP2
Crigler-Najjar syndrome Type I	UGT1A1
Ganglioside GM3 synthase deficiency	ST3GAL5 (SIAT9)
Gaucher disease	GBA
Glucose/galactose malabsorption	SLC5A1(SGLT1)
Glutaric acidemia type I	GCDH
Hallervorden-Spatz syndrome	PANK2
Hemophilia B – Factor IX deficiency	F9
HERC2 disorder	HERC2
Homocystinuria due to MTHFR deficiency	MTHFR
Hypertrophic cardiomyopathy	MYBPC3
Maple syrup urine disease	BCKDHA
McKusick-Kaufman syndrome	MKKS
Microcephalic osteodysplastic primordial dwarfism type 1	RNU4ATAC
Osteopetrosis	TCIRG1
Phenylketonuria (PKU) (261600)	PAH
Prolidase deficiency (170100)	PEPD
Propionic acidemia (606054)	PCCB
Pyruvate kinase deficiency of red cell	PKLR
SAMS Association	SAMHD1
Spastic ataxia	MTPAP
Thrombophilia-Factor 5 Leiden	F5
TMCO1 defect syndrome	TMCO1
Troyer syndrome (275900)	SPG20

Holmes County Outreach

- There has long been a need for similar services
- A monthly outreach clinic started in 2005
- Supported by Robert Wood Johnson Foundation, Ohio Developmental Disabilities Council, and a family association from inside of the community
- Our work there has been fruitful as rare genetic disorders we see in Holmes County mirror much of what we see and have learned in our main clinic
- But the need is great and growing

Holmes County Outreach

- Many informational meetings held by families, community leaders, and potential partners
- A thoughtful process to engage diverse Amish communities to develop best model in Holmes County
- With Dr. Olivia Wenger's commitment and local community support, New Leaf was launched in 2013
- As New Leaf was coming together, their staff have made a number of trips to visit DDC Clinic and vice-versa
- We all have much to learn - it's critical to share thoughts, ideas, and strategies as we develop a growing network of community clinics for special children

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The New York Times

…"It may be too late for us, but if we can help others with this center, we'll gladly do that" …

From an Amish father with 4 special needs children

(New York Times 6/20/2002)