THE VALUE OF A GENETIC DIAGNOSIS FOR INDIVIDUALS WITH INTELLECTUAL DISABILITIES: OPTIMISING HEALTHCARE AND FUNCTION ACROSS THE LIFESPAN

Elena Lopez-Rangel, Elizabeth C. R. Mickelson and M. E. Suzanne Lewis

Introduction

An intellectual disability (ID) is defined as a significant limitation in both intellectual functioning (IQ < 70) and concurrent limitations in conceptual, social and practical adaptive skills, originating before the age of 18 (American Psychiatric Association, DSM IV, 2000). IDs manifest with limitations in the ability to cope with common life demands and to meet standards of personal independence expected for the individual in at least two of the following domains: Communication, Self-care, Domestic skills, Social skills, Self-direction, Community, Academic skills, Work, Leisure, and/or Health and Safety (American Psychiatric Association, DSM IV, 2000). This definition of ID incorporates a multidimensional approach, with emphasis on functioning and environmental considerations, rather than previously used medical or statistical frameworks. The goal in management is to optimize the individual’s personal functioning, the environment and health status so that there is maximal participation, activity and functioning in life by focusing on skill development that is in context and of value to the individual and family.

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IDs are estimated to occur in 1–3% of the population and represent a heterogeneous manifestation of central nervous system dysfunction that can result from a multitude of diverse causes, both congenital and acquired. Despite the clinical importance of IDs to medicine, public health, educational systems and society, their causes remain poorly understood. The variable manifestations and causes of IDs make it very difficult to establish a definitive etiology in most cases; this is particularly true in cases of mild ID (IQ 55-70). In cases of ID that are moderate (IQ 40-55), severe (IQ below 25-40) and profound (IQ less than 25) it has been estimated that at least 60% have an underlying genetic aetiology (Battaglia and Carey, 2003). Results from clinical studies coupled with recent advances in analytic genetic technology and tools have provided new and substantial insights into the genetics of ID. Increasingly such knowledge will contribute to a better understanding of the genetic factors involved in the etiology of ID and means for improved diagnosis and anticipatory care of the individual across their lifespan.

In the past, the genetics field has focused primarily on a medical model of care for persons with an ID, a perspective divergent from the philosophies embraced by non-medical workers who are the most populous workers in the ID field (special educators, speech and language therapists, occupational and physiotherapists, psychologists, social workers, recreation therapists and others), thus creating a medical versus functional dichotomy of care. Such division is further potentiated by residual skepticism and controversy persisting from the eugenic campaigns of the early 1900’s that promoted social exclusion of individuals with ID from the community (Elks, 2004; Carlson, 2001). More recently, other issues of relevance to individuals with ID have evolved from genetic knowledge gained since completion of the Human Genome Project (Munger et al., 2007). Possibilities include the risk of insurance and employment discrimination against people with IDs and their families, as well as their growing need to balance such burdens with acceptance and understanding of genetic test results, their implications and impact on other family members, health management and anticipatory planning. Because of past history and ongoing concerns, genetic research and genetic investigations of individuals with ID has been seen by some advocates as a means to prevent disability and perpetuate exclusion. In marked contrast, there have also been numerous studies that show that families with a child with ID welcome a genetic diagnosis even if this comes with some uncertainty regarding unknown or probabilistic effects (Whitmarsh et al., 2007).

Today, an individual with ID ideally liaises with an interdisciplinary team of caregivers including physicians, allied health professionals, educators, social workers, and community intervention specialists. It is within this team that the Medical Geneticist and Genetic Counselor increasingly play a key role. Knowing the cause of a condition is essential to its management and its foundation for health optimization (by employing interventional, preventative and health screening approaches), a role in which medical geneticists and genetic counselors are educated, skilled and experienced in working with patients, families and caregivers to maximize the benefits, and minimize potential pitfalls, of uncovering a previously unknown cause of ID.

Parents of children with ID of unknown aetiology find “not knowing”
one of the greatest challenges, as they continuously search for explanations that might lead them to the best treatments and ascertainment of resources. Early diagnosis of ID in children is important for prognosis, recurrence risk counseling, early application of therapeutic and educational interventions, aiding family grieving and adaptation, as well as facilitating connections with groups/families with similar disorders. Determining the genetic aetiology of an unknown cause of ID is pivotal in generating and translating knowledge relevant to the anticipatory healthcare needs of the individual and their family, and minimizing gaps or disparities in care. Moreover, a definitive diagnosis also provides a means for improved recognition and understanding of related behavioural and functional phenotypes that allows for overcoming personal and environmental challenges for those with an ID. Overall, the future holds great promise to be derived from the current exponential growth in genetic information that will lead to improved diagnosis, understanding of the causes, treatment, and quality of life for persons with IDs and their families.

**Common Genetic Etiologies of Intellectual Disability**

The etiology of ID is complex, resulting from heterogeneous environmental, chromosomal and monogenic causes (TABLE I). Although the causes for some IDs are well-known (e.g. Down syndrome, Fragile X, TORCHES infections, structural brain anomalies), causes for 30-50% of the remainder are not (Battaglia et al., 1999; Hunter, 2000; Battaglia and Carey, 2003). The comprehensive assessment of individuals with ID represents one of the most difficult challenges faced today by clinicians and geneticists. The diagnosis underlying the cause of idiopathic ID cannot be achieved through a single practice guideline, nor viewed as a single measurement process at one point in time. Despite ID being unexplained in a large proportion of cases, several clinical series suggest that a diagnosis or cause of ID can be determined in 40-60% of all patients undergoing neurodevelopmental evaluation (Curry et al., 1997; Battaglia and Carey, 2003).

Evidence based recommendations for the genetic evaluation of an individual

<table>
<thead>
<tr>
<th>The Causes of Intellectual Disability</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome abnormalities</td>
<td>4 - 34</td>
</tr>
<tr>
<td>Recognisable syndromes</td>
<td>3 - 7</td>
</tr>
<tr>
<td>Known monogenic conditions</td>
<td>3 - 9</td>
</tr>
<tr>
<td>Structural central nervous system abnormalities</td>
<td>7 - 17</td>
</tr>
<tr>
<td>Complications of prematurity</td>
<td>2 - 10</td>
</tr>
<tr>
<td>Environmental/teratogenic causes</td>
<td>5 - 13</td>
</tr>
<tr>
<td>“Cultural-familial” mental retardation</td>
<td>3 - 12</td>
</tr>
<tr>
<td>Provisionally unique monogenic syndromes</td>
<td>1 - 5</td>
</tr>
<tr>
<td>Metabolic/endocrine causes</td>
<td>1 - 5</td>
</tr>
<tr>
<td>Unknown</td>
<td>30 - 50</td>
</tr>
</tbody>
</table>

(Adapted from Curry et al., 1997)
with an ID have been extensively reviewed in the past (Curry et al., 1997; van Karnebeek et al., 2002; van Karnebeek et al., 2005; Shevell et al., 2003). In general, recommendations include a thorough family, pregnancy and medical history as well as a detailed physical, neurological and dysmorphology exam. If a recognizable diagnosis is not apparent, first-line ancillary testing involves various investigations including high resolution karyotype (>550 band level resolution), testing for Fragile X syndrome, neuroimaging and in some cases, a screening metabolic workup, particularly if there is evidence of neurodevelopmental regression or metabolic decompensation. The diagnostic yield of these investigations will vary depending on the ascertainment of the patients and the severity of the ID.

Overall, the main genetic causes of IDs are chromosome abnormalities, including submicroscopic microdeletions and microduplications, and single gene mutations. Data on 16 worldwide-published series show that, overall, chromosomal abnormalities are found in 4-34.1% of individuals with ID (Xu and Chen; 2003), with newer and more sophisticated technologies leading to a better understanding of the contribution of such abnormalities to the aetiology of ID. In contrast, single gene mutations associated with ID underlie only 1-5% of cases, for which males with Fragile X syndrome and other X-linked disorders of idiopathic ID predominate.

Relatively small chromosomal microdeletions or microduplications are found in at least 1/1000 births (Ji et al., 2000) and include Prader Willi syndrome (PWS), Angelman syndrome, Velocardiofacial or 22q11 deletion syndrome, Williams-Beuren syndrome, Smith-Magenis syndrome, and chromosome 1p36 as well as 22q telomere deletions (Vogels and Fryns, 2002; Greenhalgh et al., 2003 and Rauch et al., 2006) (see TABLE II for respective frequencies in ID and associated clinical features). They are routinely identified using targeted molecular cytogenetic methods such as fluorescence in situ hybridization (FISH), aimed to directly detect rearrangements of specific chromosomal regions. Subtle subtelomeric rearrangements resulting in gene-dosage imbalance are also the cause of idiopathic ID with or without congenital anomalies in at least 2-5% of cases (Joyce et al., 2001).

More advanced genetic technology, such as microarray comparative genomic hybridisation (array CGH) that allows for detection of submicroscopic chromosomal abnormalities invisible to routine karyotype or FISH analyses, is emerging as a very valuable tool in the etiologic investigation of individuals with ID. Studies have estimated that approximately 8-10% of individuals with undiagnosed ID have hidden submicroscopic (cryptic) chromosomal changes not detectable with standard karyotype investigation (Shoumans et al., 2005). This technology also facilitates the detection of previously unrecognized somatic chromosomal mosaicism in some cases of idiopathic ID (Cheung et al., 2007) including recognizable syndromic disorders.

The Value of Determining a Genetic Diagnosis

The goal of establishing a genetic diagnosis for an individual with ID is to provide information to the individual, his/her family and to their health care providers (Curry et al., 1997). Individuals with ID of varying aetiology can exhibit distinctive natural histories in which the evolution of symptoms offers
opportunities for the development of improved prospective medical, educational, functional and behavioral management strategies.

For the physician, a genetic diagnosis clarifies the aetiology of the condition, provides a general prognosis, and treatment options as well as allowing the opportunity to counsel the individual/family regarding prospective health care needs and reproductive planning. In complicated cases it also allows for a multidisciplinary medical management approach that may avoid unnecessary, invasive and costly investigations and testing. For other health care providers it

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Rearrangement</th>
<th>Chromosomal Location</th>
<th>Size (Mb)</th>
<th>Frequency in the ID population</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGS/VCFS</td>
<td>Deletion</td>
<td>22q11.2</td>
<td>3</td>
<td>2.4%</td>
<td>ID, speech and language delay, cleft palate, cardiac defects.</td>
</tr>
<tr>
<td>WBS</td>
<td>Deletion</td>
<td>7q11.23</td>
<td>1.6</td>
<td>1.3%</td>
<td>Supravalvular aortic stenosis, multiple peripheral pulmonary arterial stenosis, elfin face, intellectual and statural deficiency, characteristic dental malformation and infantile hypercalcaemia.</td>
</tr>
<tr>
<td>Monosomy 1p36</td>
<td>Deletion</td>
<td>1p36.3</td>
<td>3-10</td>
<td>0.6%</td>
<td>ID, hearing impairment, seizures, growth retardation, hypotonia, heart defects, microcephaly, distinctive craniocyes with deep set eyes, flat nasal bridge, pointed chin.</td>
</tr>
<tr>
<td>PWS</td>
<td>Deletion</td>
<td>15q11-q13</td>
<td>4</td>
<td>0.4%</td>
<td>Decreased fetal activity, obesity, muscular hypotonia, ID, short stature, hypogonadotrophic hypogonadism and small hands and feet.</td>
</tr>
<tr>
<td>AS</td>
<td>Deletion</td>
<td>15q11-q13</td>
<td>4</td>
<td>0.4%</td>
<td>Severe motor and intellectual retardation, ataxia, hypotonia, epilepsy, absence of speech and unusual facies characterised by a large mandible, mouth and protruding tongue.</td>
</tr>
<tr>
<td>Inv dup (15)</td>
<td>Duplication</td>
<td>15q11-q14</td>
<td>4</td>
<td>0.4%</td>
<td>ID, autism, epilepsy, hypotonia and non-specific craniofacial dysmorphic features.</td>
</tr>
<tr>
<td>SMS</td>
<td>Deletion</td>
<td>17p11.2</td>
<td>5</td>
<td>0.3%</td>
<td>Brachycephaly, midface hypoplasia, prognathism, hoarse voice, speech delay, psychomotor and growth retardation, behavioural problems.</td>
</tr>
</tbody>
</table>

Abbreviations are defined as follows: DGS/VCFS - DiGeorge and Velocardiofacial (22q11 Deletion) syndrome; WBS - Williams-Breuren syndrome; PWS - Prader-Willi syndrome; AS - Angelman syndrome; Inv dup (Inversion duplication) Chromosome 15q11-q13; SMS - Smith-Magenis syndrome.
can help provide anticipatory guidance of an individual’s educational, behavioural and functional needs. Educational specialists may access additional resources, including an in class assistant or resource teacher for children/youth with ID, based on a specific diagnosis and known developmental and medical profile. Community agencies may be able to provide access to therapeutic recreational programmes, social programmes and group support for affected individuals and their families when there is clarity of diagnosis and function, and concordant guidelines for management.

For the family, a genetic diagnosis identifies the cause and allows explanation and understanding of specific health management and surveillance needs, as well as providing the ability to plan, and advocate for, the educational and functional needs of an individual. In addition, a genetic diagnosis may allow the family the opportunity to establish a connection with a peer support group and with other families of similarly diagnosed individuals. Furthermore, there may be financial savings for families based on their local and government tax structure. More importantly for the individual with an ID, a genetic diagnosis establishes a general blueprint of their medical, cognitive and behavioural profile that provides crucial knowledge to address specific functional needs.

There are many examples where a genetic diagnosis has informed the understanding of the developmental and cognitive profile of an individual with ID. A few examples include Fragile X syndrome, Angelman syndrome, PWS, amongst others. When the diagnosis is made parents draw on various resources that describe the related medical and cognitive needs of a specific disorder in order to make sense of the diagnosis for their child and family (Whitmarsh et al., 2007). Novas and Rose (2000) point out that an individual with a genetic diagnosis is better enabled to optimize health by gaining knowledge about what the diagnosis implies. By expanding the potential to identify distinct genetic disorders and syndromes of ID we similarly expand the opportunity to follow and better understand their respective natural histories, evolution of symptoms and medical needs, such that related complications can be anticipated and prevented.

In many instances, knowledge and understanding of genetic causes of ID has led to the implementation of specific health surveillance guidelines. In the example of Down syndrome, the American Academy of Pediatrics has developed very detailed guidelines regarding Health Supervision for Children with Down syndrome (American Academy of Pediatrics, Committee on Genetics, 2001). Similar guidelines have also been established for children with Turner syndrome (Frias and Davenport, 2003), some of whom can have ID and/or learning disabilities, as well as for children with Fragile X syndrome (American Academy of Pediatrics Committee on Genetics, 1996). These guidelines include both medical and developmental surveillance recommendations that physicians, allied health care providers and families can access in order to provide optimal care.

The Importance of Genotype-Phenotype Correlations

Genotype-phenotype correlations are used in medical genetics to describe the clinical findings associated with a specific
chromosomal or gene change. Major breakthroughs have been made by first recognising unique commonalities shared between individuals with developmental disabilities based on a variety of phenotypic features. An excellent example of how a specific disorder was characterised through a combination of clinical studies and subsequent genetic studies is the Fragile X syndrome, the most common inherited cause of ID. Prior to identification of the fragile site on the X-chromosome, individuals with this syndrome were said to have “non-specific X-linked mental retardation” (XLMR) and were considered together with individuals with other forms of XLMR. The discovery of X chromosome fragility allowed the grouping of persons together, and defining the distinct clinical features of the syndrome (i.e. long face; large jaw; large, cupped ears; large testes; etc) and a common morphology was suddenly evident. The fragile site also pointed to the gene involved, facilitating its cloning. Discovery of the gene led to a better understanding of the novel genetics, neurodevelopmental phenotype and related medical issues for this disorder in those affected (risk of autism for example) and in carriers (risk of premature ovarian failure and fragile X-associated tremor/ataxia syndrome), as well as the development of a diagnostic test which can be done for less than $10. The fragile X syndrome did not change, but the means for identifying individuals with it did, together with the means for improving anticipatory care for persons and families with this disorder.

Phenotype-genotype correlations have been used mostly to subgroup characteristic facial features, minor physical variations and/or major congenital malformations associated with a specific diagnosis. The phenotype described for a specific disorder often represents the first recognized or the most severe cases. However for each chromosomal or gene change it is important to emphasize that there can be a wide spectrum of clinical features ranging from mild to severe.

An example of a disorder manifesting a wide clinical phenotypic spectrum is illustrated by the 22q11 deletion syndrome (previously known as DiGeorge or velocardiofacial syndrome (VCFS)). Although it is one of the most common microdeletion syndromes, with an estimated prevalence of 1 in 3000 live births and 2.4% prevalence in persons with ID (Rauch et al., 2006), it often remains unrecognized. The clinical variability, multisystem involvement, subtle features and wide spectrum of cognitive and behavioural phenotypes contribute to its delayed diagnosis (Oskarsdottir et al., 2005; Hay, 2007). The knowledge of this diagnosis provides support and up to date information for families and professionals, relieves parental guilt or blame and can facilitate access to special programmes and funding opportunities (Basset et al., 2005). Since this condition is known to be associated with an increased risk of schizophrenia and other psychiatric disorders the knowledge of the diagnosis also allows for the provision of mental health surveillance and services (Basset, 1999).

In addition to physical phenotypes, behavioural phenotypes are also an important feature of specific genetic disorders of ID (Feinstein and Singh, 2007). For example, for persons with PWS (food-seeking behaviour) (Gunay-Aygun et al., 2001), Williams syndrome (loquacious personality) (Carrasco et al., 2005) or Smith-Magenis syndrome (aggressive, self-injurious behaviour) (Gropman et al., 2006), it is often their well described behavioural phenotype that first raises
suspicion for the diagnosis. In Phelan-McDermid syndrome or 22q13 deletion syndrome (Phelan et al., 2001), most individuals do not have any characteristic dysmorphic features but can have a characteristic behavioural phenotype marked by ID, significant expressive language deficits (verbal apraxia) in addition to an autism spectrum disorder (Cusmano-Ozog et al., 2007).

**Genetics and the Medical and Functional Models of Disability**

The medical model of disability is a model in which illness or disability is the result of a physical condition, intrinsic to the individual which may disadvantage the individual and reduce quality of life. As a result, curing or managing illness or disability revolves around identifying the illness or disability, understanding it and learning to control and alter its course. Thus the medical model of care for disability and, by extension, ID emphasizes “medical facts” and is based on assessments of impairments from a deficit point of view, i.e. what one cannot do, instead of what one can do (Brisenden, 1986). Needless to say, this model leads to a very partial view of an individual’s abilities.

In contrast, the functional model of care recognizes that, although a diagnosis is important for defining cause and prognosis, limitations of function are often the most important information necessary to implement intervention strategies. In other words it stresses the importance of assessing and understanding an individual’s functional abilities and participation in his/her environment. This assessment will often identify needs beyond the health condition and calls for the inclusion of other disciplines in treatment planning including therapies, education and social welfare.

In 2005, Lollar and Simeonsson wrote a comprehensive review of the World Health Organization framework and classification system for human functioning that summarizes the current conceptions of disability. The aim of this classification is to describe components of health rather than having a disease perspective and is based on interactions that occur between the person, his or her abilities (rather than disabilities), that particular person’s environment and society (FIGURE 1).

It is within this framework that knowledge of an individual’s genetic diagnosis and clinical phenotype (including both physical congenital limitations leading to disability and general behavioural phenotype) can prove very valuable. Recognizing and applying tools to tease out the complete spectrum of neurodevelopmental and physical features relating to a known diagnosis can better guide and inform functional assessments that incorporate both the medical and the functional models of care synergistically.

**The Link Between Genetic Diagnosis and Function**

“Mental retardation [intellectual disability] is not something you have, like blue eyes or a bad heart, nor is it something you are, like short or thin. It is not a medical disorder or a mental disorder... Mental retardation [intellectual disability] reflects the ‘fit’ between the capabilities of individuals and the structure and expectations of their environment” (Luckasson et al., 1992).

This quote has been cited in many
published articles, perhaps because it best describes the need to see a person with an ID as an individual with specific strengths and weaknesses. In the past, assigning a medical diagnosis to an individual with an ID may have revealed little about the functional characteristics of a child or adolescent. Diagnoses were thought to be associated with symptomatology, and were often unrelated to function (McLaughlin and Bjornson, 1998).

In 2006, Johnson et al., recommended three steps essential to the evaluation of individuals with ID that integrate functional measures. These include:

1) Testing to obtain standardized measurement of intelligence and adaptive skills;
2) Defining the individual’s strengths and needs across five dimensions: (i) intellectual abilities; (ii) adaptive behaviours; (iii) social roles, participation, and interventions; (iv) health concerns; and (v) contextual considerations and;
3) Developing a plan to provide the supports and services consistent with the level of need.

In order to address these points the International Classification of Function (ICF) was developed by the World Health Organization (ICF-WHO, 2001). This classification provides a standard language and framework for the description of health and health-related domains that accommodates changes in body functions and structure by identifying specific impairments, activity limitations and participation restrictions for a health condition.

The recognition of a clinical genetic diagnosis, but more importantly the identification of physical and/or behavioural features of genetic disorders that present with ID, can support the above functional template (see TABLE III and clinical examples). In the case of PWS, for example, awareness of co-

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**FIGURE 1**

Conceptual framework for international classification of functioning, disability and health (ICF) (from Lollar and Simeonson 2005)

- Health condition
  - (disorder or disease)
  - Body Functions & Structure
  - Activity
  - Participation
  - Environmental Factors
  - Personal Factors
  - Contextual factors
### TABLE III
Genetic disorders and levels of functioning

<table>
<thead>
<tr>
<th>Health Condition</th>
<th>Features</th>
<th>Impairment</th>
<th>Activity Limitation</th>
<th>Participation Restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td>22q11 deletion</td>
<td>Cleft palate</td>
<td>Velopalatal insufficiency</td>
<td>Speech difficulties</td>
<td>Difficulties in social interactions</td>
</tr>
<tr>
<td></td>
<td>Cardiac defects</td>
<td>Cardiac insufficiency</td>
<td>Exercise and fitness</td>
<td>Limited participation in social sports</td>
</tr>
<tr>
<td></td>
<td>Anxiety disorder</td>
<td>Anxiety</td>
<td>Difficulties with transitions</td>
<td>Unable to adapt to new environments leading to social isolation</td>
</tr>
<tr>
<td></td>
<td>Mild ID</td>
<td>Cognitive</td>
<td>Academic and employment opportunities</td>
<td>Stigma of ID may lead to unemployment</td>
</tr>
<tr>
<td>PWS</td>
<td>Hypotonia</td>
<td>Neuromuscular</td>
<td>Difficulties with joining non-adapted recreational sports</td>
<td>Unable to participate in physical activities impacting overall health</td>
</tr>
<tr>
<td></td>
<td>Excessive eating</td>
<td>Behavioural</td>
<td>Need for monitoring of food intake/supervision</td>
<td>May limit socialising around food based activities including family meals</td>
</tr>
<tr>
<td></td>
<td>Moderate ID</td>
<td>Cognitive</td>
<td>Academic, social and employment opportunities</td>
<td>Limitations re: employment, peer activities due to lack of support in the workplace/recreational programmes</td>
</tr>
<tr>
<td>Angelman syndrome</td>
<td>Ataxia</td>
<td>Neuromuscular</td>
<td>Difficulties with walking</td>
<td>Limitation in independent mobility safety concerns given ataxia/poor balance</td>
</tr>
<tr>
<td></td>
<td>Moderate-Severe ID</td>
<td>Cognitive</td>
<td>Academic</td>
<td>Limitations re: employment, peer activities due to lack of support in the workplace/recreational programmes</td>
</tr>
<tr>
<td></td>
<td>Seizures</td>
<td>Physical</td>
<td>Difficulties with joining recreational sports/close supervision required given seizures</td>
<td>Potential impact on overall fitness, peer social interactions, family outings</td>
</tr>
</tbody>
</table>

The advantage of the International Classification of Function (ICF) system is it allows for the determination of function, disability and health of an individual at a societal and institutional level. Clinical examples include:

**Prader-Willi Syndrome**
A child with PWS entering school would need a programme designed to meet their educational level of functioning, adaptation to physical activity for gym class given some restrictions based on the hypotonia, coordination status and a management strategy for food access/sharing at school with direct supervision during lunch/recess breaks to optimise health status.

**VCFS or 22q11 deletion syndrome**
A child with 22q 11 deletion may be stable from the health point of view, post cardiac surgery with no cardiac/respiratory impairment yet be unable to participate in a school field trip due to anxiety in unfamiliar situations and problems in understanding an "abstract" school activity given their ID. To plan for this a transition strategy could be employed with an identified assistant to make the field trip a success.
existing gross and fine motor delays due to hypotonia can be identified early and appropriately managed, especially in relation to feeding issues and mobility concerns in early infancy and toddlerhood. However, the greatest problem affecting the ability for one with PWS to function in their environment relates to the behavioural ramifications of this disorder. Young school age children as well as older individuals with PWS manifest well described behavioural patterns that include obsessions, compulsions and perseverative behaviours. They also present with cognitive challenges due to educational profiles that range from moderate to borderline ID and in a few cases normal cognitive skills but with a learning disability profile. Also during these later years individuals with PWS engage in excessive eating and gradually develop morbid obesity with associated health complications such as Type 2 diabetes and sleep apnea. Understanding the genetic and biologic liability of persons with PWS toward these difficulties allows for earlier behavioural and environmental modifications around dietary education, availability of food and a good exercise/recreational programme that can change not only their long term medical outcome but most importantly allows them to be engaged in everyday home, school and work activities.

**Summary**

Collaborations amongst professionals caring for persons with ID are increasingly challenging the deeply rooted historical differences that have divided its medical/biologic and functional domains. The benefits of finding a medical etiology are obvious to genetic professionals, including understanding of presentation, recurrence risk, anticipatory medical guidance and family supports (Curry et al., 1997). To those working on the front lines of education and behaviour management, recognition of an aetiology offers insights to address the functional life needs of children and adults with ID.

The medical and functional models of ID needn’t be mutually exclusive, but conjoined to synergize advances from both biomedical and functional research in ID to the translation of improved management and anticipatory care for individuals with ID and their families. It is essential to emphasize the critical need for reciprocal cultural enrichment and cross-fertilization of ideas and action between physicians and all professionals dedicated to the care of the individual with ID, an issue pivotal to broadening the evaluation and practical application of genetic and functional research to the needs of individuals with ID.

**Glossary**

**TORCHES infections**: An acronym for a group of infections that in a pregnant woman can lead to severe fetal anomalies or even fetal loss. These include Toxoplasmosis, Rubella, CMV, Herpes simplex and Syphilis.

**Karyotype**: A photographic representation of the chromosomes of a single cell prepared according to a standard classification to define human chromosome complement.

**Congenital**: Conditions that are present at birth, regardless of their causation.

**Monogenic**: Genetic disorders that occur as a direct consequence of a single altered gene.

**Phenotype**: Any observed quality of an organism, such as its morphology, development, behavior or biochemical characteristics.
Genotype: The inherited genetic constitution of a cell or organism.

Cloning of gene: Isolation and copying of a gene (i.e. genetic information)

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