

Amish, Mennonite, and Hutterite Genetic Disorder Database

Michael Payne MD¹, C Anthony Rupa PhD FCCMG^{2,3,4}, Geoffrey M Siu BSc⁵, Victoria Mok Siu MD FRCPC^{2,3,4}

The Amish, Mennonite, and Hutterite Genetic Disorder Database was created in response to a paucity of resources for medical practitioners who treat these populations. The database focuses on single-gene Mendelian disorders and the specific mutations that have been reported in these groups. The database can be viewed at www.biochemgenetics.ca/plainpeople.

COMMON BACKGROUND

The Amish, Mennonite and Hutterite religious groups all arose in Europe during the Protestant Reformation of the 16th century (1). Collectively, they are known as Anabaptists ('rebaptizers') because they practice adult baptism rather than infant baptism. They also commit to pacifism and segregate themselves from the general population. Because the Catholic majority saw these views as heretical, the Anabaptists were persecuted in Europe, eventually resulting in the migration of many followers to North America (1). The Hutterite communities differ from the other two groups because they have a communal lifestyle and have embraced modern technology in their agricultural practices (2).

SUITABILITY FOR GENETIC STUDY

The history of the Anabaptist groups makes them especially suitable for genetic research. They are socially isolated with little genetic inflow. Some groups keep extensive genealogical records that are maintained by local ministers, and can identify their founder populations. They have experienced many genetic bottleneck events caused by successive migrations over their history. Large families are common, with low rates of nonpaternity (3). They have a relatively high standard of medical care (3).

The founder effect is quite pronounced in Anabaptist populations. For example, most of the more than 40,000 Hutterites in North America can trace their ancestry back to a group of 89 founding members (2). Small founding populations and isolation result in genetic homogeneity and can greatly skew the prevalence of certain genetic disorders, particularly autosomal recessive conditions (4). For example, nephropathic cystinosis is a rare autosomal recessive lysosomal storage disorder that affects approximately one in 100,000 children in the general population, with a carrier frequency of approximately one in 150 (5). In an Ontario Old Order Amish population, there is a population-specific mutation that causes cystinosis and is present with a carrier frequency of one in six people, predicting an extraordinarily high disease incidence of one in 144 people (6, and unpublished data). The increased incidence in isolated communities of otherwise rare conditions allows for linkage analysis and identification of causative genes (7,8).

Such genetic studies are useful not only for genetic health care for Anabaptists but also for the general population. Because 10% to 20% of each generation of Old Order Amish and Mennonite children have chosen to leave their communities, many rare disease alleles have entered the general population (9). In addition, many of the mutations causing disease in the Anabaptist groups can be found in Europe, where the founding populations originated (9). Genetic linkage studies of Mennonites have led to discovery of the genes associated with many conditions such as hypophosphatasia and X-linked congenital stationary night blindness (1).

THE DATABASE

The Amish, Mennonite, and Hutterite Genetic Disorder Database was created to serve as a resource to assist in research and diagnosis of genetic conditions in Anabaptist groups. It was initially compiled by performing PubMed and Online Mendelian Inheritance in Man (OMIM) literature searches on published genetic conditions in Anabaptist populations, using "Amish", "Mennonite" or "Hutterite" as key words. In addition, some of the disorders and mutations have been entered based on personal observation and communication with other genetic researchers. New disorders are added through periodic review of the literature.

For each disorder, the affected Anabaptist group is recorded along with the geographical location in which the disorder was described (eg, Amish, Ontario). This process is important because disease prevalence can vary between locations as a result of differences in the founding populations (7). The specific gene and mutation(s) are also listed, if known. The journal articles detailing the illness with specific mutation(s) are listed, along with the OMIM reference number. Finally, the clinical symptoms of each condition are listed, assisting health care providers with recognition and diagnosis.

To navigate the database, users can search by disorder, mutation, or clinical signs and symptoms. When searching by disorder, the user is able to input either the OMIM number or the name of the disorder, and is directed to the corresponding page. Alternatively, the user can input a specific gene and identify any disorders that are caused by mutations in that gene. Finally, the user can search the database by clinical symptoms. This feature is particularly useful when the diagnosis is unknown. The clinical search may be limited to one specific Anabaptist group and a geographical location. The user may also obtain a list of all genetic conditions found within each specific Anabaptist group. To do this, one would select "Search Database by Clinical" and enter the desired Anabaptist group, leaving the phenotype box blank. Users may communicate via a web link with the site administrator if they have questions or new information to add to the database.

¹Schulich School of Medicine and Dentistry; ²Department of Paediatrics; ³Department of Biochemistry; ⁴Children's Health Research Institute, University of Western Ontario, London; ⁵University of Toronto, Toronto, Ontario
Correspondence: Dr Victoria Mok Siu, Medical Genetics Program, London Health Sciences Centre, 800 Commissioners Road East, London, Ontario N5X 2V5. Telephone 519-685-8140, e-mail victoria.siu@lhsc.on.ca
Accepted for publication July 19, 2010

CONCLUSION

The Anabaptist groups have many unique genetic disorders as a result of small founding populations and cultural isolation. It is our hope that the Amish, Mennonite, and Hutterite Genetic Disorder Database will improve health care delivery to Anabaptists in Canada. It is an ongoing project, with continuing updates to the database as new discoveries are made.

ACKNOWLEDGEMENTS: Funding for the creation of the database website was provided, in part, by The Change Foundation. The site is maintained by the Biochemical Genetics Laboratory in London, Ontario.

REFERENCES

1. Orton N, Innes M, Chudley A, Torben Bech-Hansen B. Unique disease heritage of the Dutch-German Mennonite population. *Am J Med Genet A* 2008;146A:1072-87.
 2. Boycott K, Parboosingh J, Chodirker B, et al. Clinical genetics and Hutterite population: A review of Mendelian disorders. *Am J Med Genet A* 2008;146A:1088-98.
 3. Francomano C, McKusick VA, Biesecker L. Medical genetic studies in the Amish: Historical perspective. *Am J Med Genet C Semin Med Genet* 2003;121C:1-4.
 4. Puffenberger EG. Genetic heritage of the Old Order Mennonites of southeastern Pennsylvania. *Am J Med Genet C Semin Med Genet* 2003;121C:18-31.
 5. Shotelersuk V, Larson D, Anikster Y, et al. CTNS mutations in an American-based population of cystinosis patients. *Am J Hum Genet* 1998;63:1352-62.
 6. Rupar CA, Matsell D, Surry S, Siu V. A G339R mutation in the CTNS gene is a common cause of nephropathic cystinosis in the southwestern Ontario Amish Mennonite population. *J Med Genet* 2001;38:615-6.
 7. Arcos-Burgos M, Muenke M. Genetics of population isolates. *Clin Genet* 2002;61:233-47.
 8. Lahiry P, Wang J, Robinson JF, et al. A multiplex human syndrome implicates a key role for intestinal cell kinase in development of central nervous, skeletal, and endocrine systems. *Am J Hum Genet* 2009;84:134-47.
 9. Morton H, Morton C, Strauss K, et al. Pediatric medicine and the genetic disorders of the Amish and Mennonite people of Pennsylvania. *Am J Med Genet C Semin Med Genet* 2003;121C:5-17.
-
-