Amish, Mennonite and Hutterite Genetic Disorder Database

Michael Payne (Meds 2010)
Faculty Reviewers: Dr. C. Anthony Rupar and Dr. Victoria Mok Siu

Clinical Example

A newborn baby girl presented with bowel obstruction. The possibility of cystic fibrosis was raised, particularly since there was a positive family history of cystic fibrosis in a deceased relative. CFTR mutation analysis was ordered using a panel that included ΔF508 and 28 other common mutations which account for 85% of all CF mutations. The results were negative for all mutations in the screening panel.

Since the parents were members of the Old Order Amish community, the Amish, Mennonite and Hutterite Genetic Disorder Database was accessed via the Internet and it was determined that a specific mutation (3905 ins T) had been described in the Old Order Amish. Further DNA testing confirmed that the baby was homozygous for the 3905 ins T mutation. Although the sweat chloride test is the gold standard for cystic fibrosis testing, it can be difficult to obtain sufficient sweat volume collection in the newborn period.1

Correct diagnosis of newborns with CF through mutation analysis is important as this will help direct therapies and improve overall outcomes.2 This case illustrates the usefulness of the Amish, Mennonite and Hutterite Genetic Disorder Database as it allows medical professionals to identify genetic disorders and specific mutations which otherwise may be rare in the North American general population.

Introduction

The Amish, Mennonite, and Hutterite Genetic Disorder Database was created in response to a paucity of resources for Canadian medical practitioners who treat “Plain People.” The database focuses on genetic diseases which are found with higher prevalence in these groups due to their unique cultural history. The database can be viewed at:

http://www.biochemgenetics.ca/plainpeople/

Common Background

The Amish, Mennonite and Hutterite populations share some similarities. They all arose in Europe during the Protestant Reformation in the 16th century.3 In contrast to other Protestants and Catholics, they are Anabaptists, believing that children should not be baptized at birth, but instead at an age when they can make a conscious decision to join the church. They also believe in the separation of church and state. These views were seen as heretical and led to their persecution in Europe by the Protestant and Catholic majority. The Anabaptists are also pacifists who do not engage in war and believe in segregating themselves from the general population.3 “Plain People” is a term which refers to their plain dress and restricted use of technology.4

History and Migrations

In order to understand present day genetic issues surrounding the Plain People it is important to understand where they originated and how they came to Canada and the USA. They can broadly be divided into 4 groups: the Hutterites, Old Colony Mennonites, Old Order Mennonites and Amish.
The Hutterites were followers of Jakob Hutter in Austria, and their colony was founded in 1528. They were persecuted for most of their history and were forced to migrate between settlements in Moravia, Romania, Hungary and, Ukraine. From 1874 to 1879, 443 individuals immigrated to the United States. They settled on the prairies and prospered until WW1 when they refused to accept conscription. Canada offered them land and exemption from military service. Many Hutterites immigrated to Canada during this period and settled in Alberta, Saskatchewan and Manitoba. There are also a few colonies in British Columbia. Their current population in the US and Canada numbers over 40,000. The Hutterites believe in communal ownership, with minimal personal possessions. They live in communal colonies, use modern farming and manufacturing techniques, and utilize modern health care.

Mennonites are named for their founding leader, Menno Simons. The Mennonites can be divided into two groups: Dutch-North German and Swiss-South German. The Dutch-North German (Old Colony) Mennonites originated in the low countries of Europe in the 16th century. As a result of persecution they were forced to move to Prussia and lived there in relative peace until the 18th century. With continued growth, land shortages forced emigration from Prussia to Russia. In 1870, 7000 Mennonites immigrated to Manitoba, while another 10,000 immigrated to the American Midwest. Another wave of Russian Mennonites came to Canada in 1920 following the Russian revolution.

In the 1920s, 7000 of the Canadian Old Colony Mennonites emigrated to Mexico, Belize and South America. Recently, many Old Colony Mennonites have returned to Canada from Mexico and South America, settling mostly in Southwestern Ontario, Alberta and Manitoba. Today, Old Colony Mennonites in Canada number over 27,000. They speak Low German at home, and High German for more formal occasions, such as church.

The Swiss-South German Mennonites were founded in the 16th century in Switzerland. In 1693, followers of Jakob Amman split from the Swiss-South Mennonites to form the Amish sect, a more conservative group. Both the Swiss-South German Mennonites and the Amish suffered persecution in Europe. Between 1683 and 1880, approximately 8000 Swiss-German Mennonites immigrated to the United States. With the onset of the revolutionary war in the USA, members of the Mennonite and Amish communities travelled to Canada, settling in the Kitchener-Waterloo and Aylmer-St. Thomas areas.

In 1824, Amish families began immigrating directly to the Waterloo and Perth County areas of Ontario from Europe. In the late 19th century, Old Order Mennonites (OOM) split from the other Swiss-Mennonite groups in the USA and Canada due differing opinions over Sunday school and higher education. OOM and the Amish are both quite conservative and can be seen driving buggies and wearing conservative clothes.

Suitability for Genetic Study

The unique history of Plain People groups makes them especially suitable for genetic research. They are socially isolated with little genetic inflow. They keep extensive genealogical records, maintained by local ministers. Their initial founder populations are well known. They have experienced many genetic bottleneck events caused by successive migrations over their history. Large families are common, with low rates of non-paternity. They have a relatively high standard of medical care.

The founder effect is quite pronounced in Plain People populations. For example, most of the over 40,000 Hutterites in North America can trace their ancestry back to a group of 89 founding members. The Amish and Mennonite populations of North America are similar with small founding populations and isolation resulting in genetic homogeneity. This can highly skew the prevalence of certain diseases in the isolated populations, particularly autosomal recessive conditions. For example, nephropathic cystinosis is a rare autosomal recessive lysosomal storage disorder affecting about 1 in 100,000 children in
the general population with a carrier frequency of about 1 in 150.\textsuperscript{10} In the Old Order Amish population of Ontario, the cystinosis carrier frequency is 1 in 4.5, predicting an extraordinarily high incidence of 1 in 78.\textsuperscript{11} The increased incidence of these otherwise rare conditions allow for linkage analysis and identification of causative genes.\textsuperscript{12}

These genetic studies are not only useful for Plain People, but also for the general population. Since 10-20\% of each generation of Old Order Amish and Mennonite children have chosen to leave their communities, many alleles have entered the general population.\textsuperscript{13} Also, many of the mutations causing disease in the Plain People can be found in Europe, where the founding populations originated.\textsuperscript{13} Genetic linkage studies in the Mennonites has led to the discovery of the genes for many conditions, such as hypophosphatasia and X-linked congenital stationary night blindness.\textsuperscript{3} The Clinic For Special Children in Pennsylvania specializes in care for Plain People and have been successful in isolating over 50 different mutations causing disease in the Mennonite and Amish communities over the past 5 years.\textsuperscript{14}

The Database

The Amish, Mennonite, and Hutterite Genetic Disorder Database is intended to be used as a resource to assist in research and diagnosis of genetic conditions for patients of Plain People ancestry. It has been compiled by researching published genetic conditions for Plain People. Literature searches were performed on PubMed. Some disorders and mutations were entered based on personal communication with other genetic researchers.

For each disorder, the group affected is recorded along with the geographic location (e.g. Amish, Ontario). This is important because disease prevalence can vary between locations, even within a specific group (e.g. Hutterite), as a result of differences in the founding populations.\textsuperscript{12} The specific gene and mutation(s) are also listed, if known. The journal articles detailing the illness with specific mutation(s) found in Plain People are listed along with the OMIM reference number. Finally, the clinical symptoms of each condition are listed, assisting healthcare providers in recognition and diagnosis.

In order to navigate the database, users 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 and is directed to the corresponding page. Alternatively, the user can input a specific gene and identify any disorders which are caused by mutations in that gene. Finally, the user can search the database by clinical manifestations of the genetic conditions. This is done using a drop-down menu divided by different body systems. The clinical search may be limited to one specific Plain People group and a geographic location. Finally, users are provided a link in order to communicate with the site administrator if they have questions or new information to add to the database.

Conclusion

Plain People have unique healthcare needs 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 the healthcare delivery to Plain People in Canada. We view it as an ongoing project, with continuing updates to the database with future discoveries.

References


