**Medical Genetic Studies in the Amish: Historical Perspective**

Medical genetics studies in the Amish began in 1962, when two events sparked the interest of one of the authors (V.A.M.). As a member of the faculty committee advising the Johns Hopkins Press, he was asked to read the manuscript *Amish Society* submitted by John Hostetler. It was apparent that many characteristics of Amish society made it an excellent community in which to study genetic traits, particularly recessive conditions. In the preface to the 1978 book, *Medical Genetic Studies of the Amish*, he writes:

> Actually, my medical genetic interest in the Amish had been piqued a few months earlier in 1962 by an article about a country doctor, David Krusen, who had an extensive practice among the Amish in Lancaster County, Pennsylvania. He indicated to the author of the article—in a slick-paper, pharmaceutical company “throw-away”—that achondroplasia is frequent among the Amish. On the basis of this tip, dwarfism was the first entity we studied systematically among the Amish, and my first field trip, with visits to Amish homes, was made in the company of Dr. Krusen. [McKusick, 1978]

The early studies on dwarfism in the Amish, which was, in fact, not achondroplasia, led to the recognition of two recessive conditions: Ellis-van Creveld syndrome [McKusick et al., 1964a], which had been previously reported [Ellis and van Creveld, 1940], and cartilage-hair hypoplasia [McKusick et al., 1965], a newly recognized disorder that was eventually given the formal name of metaphyseal chondrodysplasia, McKusick type. Systematic investigations were undertaken on a number of other disorders, including mental retardation, neurologic conditions, and deafness [Mengel et al., 1969]. Several disorders were initially described in publications resulting from this work, including the Troyer [Cross and McKusick, 1967a], Mast [Cross and McKusick, 1967b], and Amish microcephaly syndromes [Kelley et al., 2002]. In addition, much was learned about previously described genetic conditions, including ataxia-telangiectasia [Ginter and Tallapragada, 1975; Rary et al., 1975; Gatti et al., 1988], epidermolysis bullosa [Cross et al., 1968], hereditary spastic paraplegia [Thurmon and Walker, 1971], and pyruvate kinase deficiency [Bowman et al., 1964], among others. Other investigators exploring genetic conditions among the Amish in the 1960s and 1970s included D. Bernard Amos, Herbert S. Bowman, Joe C. Christian, C.E. Jackson, Richard C. Jurgib, Walter E. Nance, and John M. Opitz. Many of these studies were published in scientific journals and later compiled in the book *Medical Genetic Studies of the Amish* [McKusick, 1978].

In a paper entitled “Genetic Studies of the Amish: Background and Potentials” [McKusick et al., 1964b], the authors listed 15 advantages to performing genetic studies in the Amish community (Table I). In addition to these intrinsic attributes, the Amish were surprisingly open to participation in genetic studies. It was speculated that their receptivity stemmed from approaching them as a physician, genuinely concerned about those among them who were physically and mentally handicapped [McKusick et al., 1964b]. In our experience, most Amish families have been welcoming of physicians who come with information about the disorders that affect their children or family members.

The initial studies of Amish in Pennsylvania, Ohio, and Indiana were facilitated greatly by the assistance and introductions from the late John Hostetler, PhD, a rural sociologist whose parents were Old Order Amish. In Lancaster County, Pennsylvania, a local Amish liaison has worked with us and other clinical researchers for many years. She, and eventually others who followed, fulfilled a critical role for the research efforts. She personally knew many of the families, spoke the local

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*Several disorders were initially described in publications resulting from this work, including the Troyer, Mast, and Amish microcephaly syndromes.*

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TABLE 1. Advantages of Studying Genetics in the Amish [McKusick et al., 1964b]

<table>
<thead>
<tr>
<th>Number</th>
<th>Advantage Description</th>
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<tr>
<td>1.</td>
<td>The Old Order Amish are a defined, indeed self defined, population.</td>
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<td>2.</td>
<td>It is a closed population; gene flow is almost exclusively centrifugal.</td>
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<td>3.</td>
<td>The western European origins of the population are well known.</td>
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<td>4.</td>
<td>Genealogic records are extensive.</td>
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<td>5.</td>
<td>The standard of living is high.</td>
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<tr>
<td>6.</td>
<td>The standards of medical care are relatively high.</td>
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<tr>
<td>7.</td>
<td>An interest in illness is evident.</td>
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<td>8.</td>
<td>There is a high coefficient of inbreeding due to the relatively small number of founder couples.</td>
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<td>9.</td>
<td>The illegitimacy rate is apparently low.</td>
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<tr>
<td>10.</td>
<td>The Amish are interested in and knowledgeable about the health of their relatives. They seek out information on rare disorders shared by other Amish families.</td>
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<tr>
<td>11.</td>
<td>Socio-economic and occupational circumstances are notably uniform.</td>
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<td>12.</td>
<td>Because of constraints on transportation, the Amish are relatively immobile.</td>
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<td>13.</td>
<td>Most Amish families are large, with an average of seven to nine children.</td>
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<td>14.</td>
<td>Children with birth defects or genetic disorders are usually kept at home rather than institutionalized.</td>
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<tr>
<td>15.</td>
<td>The existence of several Amish isolates makes comparisons of sub-populations possible.</td>
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To a large degree, the advantages of studying genetic disease in the Amish (and other Anabaptist communities) are as true today as they were in 1964.

[These references are not listed here but should be included in the final document.]
1987; Kelsoe et al., 1989; Ginns et al., 1998] shows that genetic research in the Amish is not immune from problems that plague complex genetics in general, and psychiatric genetics in particular.

This rich history and the many successful ongoing studies of Amish and other Anabaptist communities in North America (e.g., Mennonites and Hutterites) are a testament to the generosity of those communities, and the vision and hard work of the early proponents of this research. However, genetics research is not the same enterprise it was in 1964. Formal requirements for the protection of human subjects and concerns about the protection of communities [Weijer et al., 1999] have changed the landscape of family studies in the Amish. Whereas in the past it was sufficient for the investigators to treat the community with respect and sensitivity, today detailed Institutional Review Board (IRB) protocols and informed consent are required. Although these regulatory approaches may assure a certain kind of protection for the Amish, they are no substitute for respect and sensitivity. There have been unfortunate examples of researchers entering the community without its support. In these cases, a researcher should expect to be treated coldly and fail to meet the research goals. In spite of the infrequent use of telephones, word travels fast among the Amish, and the community is capable of making a determination that cooperation is not in their best interests.

A frequent misconception among the “English” is that the Amish and Mennonite cultures are monolithic and uniform because of their consistent outward appearance and customs. In fact, the community represents substantial variance in their opinions regarding the utility and appropriateness of genetics research, appropriate clinical uses for genetics, and their involvement in modern technically oriented health care. In our studies (L.G.B. and C.A.E.), a large majority of families whom we visited agreed to participate in research following an explanation of the study during a house call. In spite of that high uptake, a significant portion of the families declined to participate, suggesting that we were interfering with God’s will, developing technological health care that would not clearly benefit Amish children, and other reasons. Any researchers who treat Amish persons as anything but intelligent and thoughtful individuals are likely to fail in their research endeavors.

In the more than 40 years since this research has started, there have been notable changes among the Amish as well. These days it is not unheard of to reach an Amish farmer on his cell phone. In addition, the pressure of encroaching suburbs is slowly eroding the farmland of Lancaster County, causing families to disperse to settlements farther west where land is less expensive and where cities do not loom. But one attribute has not changed, which is a people who strongly value a communitarian spirit that itself springs from their deeply held religious beliefs. The primary reason why the Amish share medical information with each other and with doctors and researchers is a commitment to help those in need and to provide the most help to those in greatest need. This is another manifestation of their attitude and commitment to the special children who are the subjects of this research. This cultural value is most readily recognized in the Lancaster community by the barn raisings that follow the unfortunately frequent barn fires. Without hesitation, families put aside their own needs and rally to those with greater needs. The willingness of the community to share medical and genealogic information must be reciprocated by a commitment of the medical and research communities to provide improved medical care to those studied in this community who are affected by the disorders. Furthermore, researchers must endeavor to avoid perturbing or altering the culture that makes the Amish unique. There can be no greater manifestation of this commitment than the Clinic for Special Children. Dr. Morton and his colleagues are unwavering in their commitment to the advancement of knowledge and the application of this advanced and appropriate medical care for the special children. By respecting the culture of the Amish, physicians and geneticists can improve the health of the special children, provide new insights into genetics and biology, and preserve the unique cultural heritage of these generous and peaceful people.

REFERENCES


A genome-wide search for chromosomal loci linked to mental health wellness in relatives at high risk for bipolar affective disorder among the Old Order Amish. Proc Natl Acad Sci USA 95:15331–15336.


