

# Dramatically Different Dizygotic Twins: Will We Include Them in Research?

## Twin Research Reviews: Congenital Anomalies, Mirror-Image Effects in Conjoined Twins, Older Mothers of Twins; Twin Statistics: ‘Massachusetts, Land of Twins’; Tribute: Dr Victor A. McKusick

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The increased frequency of interracial marriage is a likely source of unusual-looking dizygotic (DZ) twins. Some members of DZ twin pairs born to mixed-race couples inherit very different physical features from their parents. This raises several questions, such as: Will researchers wish to include such twins in their ongoing studies? Next, new twin research concerned with congenital anomalies, mirror-image effects in conjoined twins and older mothers of twins will be reviewed. New statistics on twinning rates in Massachusetts will also be summarized, followed by a tribute to the late medical geneticist Dr. Victor A. McKusick.

**Keywords:** DZ twins, mixed couples, mirror-image effects

## Dramatically Different Dizygotics: Will We Include Them in Research?

There has been a dramatic increase in the number of interracial marriages in the United States. The number has gone from 310,000 in 1970 to 2,669,558 in 2000 (Wikipedia, 2008). This changing trend has had unforeseen consequences for dizygotic (DZ) twinning. Specifically, some DZ co-twins born to mixed-race couples inherit very different physical features from their parents. In some cases, the twins even appear to represent different ethnic groups. This situation poses challenging questions for twin researchers, such as: How different are the experiences of these DZ twins? Behavioral geneticists study phenotypic variations within groups, not between groups — so while the twins technically share their ethnicities, they

may not share them in a practical, everyday sense. Will researchers wish to include such twins in their ongoing studies? If they hesitate to do so, then perhaps there is a need for standard criteria for deciding which twins are ‘too different’.

I became aware of ‘mixed-race’ twins a number of years ago. A colleague had forwarded a British newspaper clipping showing a mixed-race couple (Black mother and Caucasian father) holding up what appeared to be a Caucasian child and a Black child — but the two boys were ordinary DZ twins. The extent to which the rearing circumstances of such co-twins could be markedly different was underlined several years ago by a student in one of my classes. The

young woman, who looked Hispanic, revealed that she had a Hispanic father and a Caucasian mother, and that her fraternal twin sister looked completely different — Caucasian. When I saw the sisters together, I was struck by their physical difference. I also learned that one of them (the Hispanic-looking twin) had experienced some ethnic discrimination that her twin sister had not; their picture appears in an earlier issue of this journal.

To my knowledge, no one has studied the psychological similarities,

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differences and experiences of 'mixed-race' DZ twins. Such a study could make a significant contribution to our understanding of group identity, racial bias and family dynamics. A number of such cases have recently been reported in the media. The media often incorrectly refers to some of them as 'Black-White twins.' However, these twins are quite ordinary in the sense that their conception did not differ from that of couples of the same ethnic background. They are, however, extraordinary in the sense that they differ physically in a fundamental way. The stories behind these pairs are illuminating.

Tracey-Ann and Andrew Balasco recently became the parents of opposite-sex twins, Orlando and Natalia (Irvine, 2008). Orlando resembles his Black mother, while Natalia resembles her Caucasian father. The twins' physical differences seem to have deepened during the first few months of their lives. However, as their father correctly observed, the twins are both half-Jamaican, one-quarter English and one-quarter Italian. Apparently, there was a history of racial admixture on both sides of the family. Their mother seemed relieved that one child had acquired her darker color; '... other-

wise I would have gone through all the effort of having them only for them both to look completely unlike me'. It is possible that parents will identify (knowingly or unknowingly) with the twin whom they resemble, affecting relations within the family. Perhaps researchers need to make note of such circumstances,

Another set of mixed-race twins was born to a German couple in early July 2008 (*Daily Voice*, 2008). Florence Addo-Gerth (from Ghana) and her husband Stephan Gerth (from Germany) became parents to DZ twin boys, Ryan and Leo. Ryan is light-skinned with blue eyes, while Leo is dark-skinned with brown eyes.

The biological processes giving rise to these pairs have not been fully confirmed. A published interview with Dr Peter Propping, former director of the Institute for Human Genetics at Bonn University, brings some insight into this situation (Dahlstrom, 2008). He speculated that the black mother in this last case may have had some white ancestry or that the Caucasian father may have had some black ancestry. The transmission of certain genes from parent to child could cause a child of biracial parents to inherit genes coding for only one skin color.

Other cases of mixed-race twins could be described, but they all present the same hard question: how different in appearance must DZ co-twins be in order to justify their exclusion from a study? Of course, a similar question could be raised with respect to some ordinary DZ twins whose appearances match with respect to ethnicity. For example, if one twin was very tall in a society that valued height, while the co-twin was very short, it is likely that these twins would have had very different social experiences, both within their family and at school. If one twin had an illness or condition that the other twin did not have, this difference might have a similar effect, associated with societal beliefs about affected individuals. I recently described an exemplary case in which one DZ twin suffered a limp due to childhood polio, while his twin brother did not (Segal, 2000). Perhaps decisions to include or exclude such twins should be made on a case-by-case basis, based on the measures in question. Analyzing data both with these pairs and without them offers another solution. Of course, in very large twin samples, the inclusion of such cases is unlikely to make a meaningful difference in the results or interpretation.

## Twin Research Reviews

### **Congenital Anomalies**

The greater risk of congenital anomalies among twins than non-twins is well known. However, reports of such occurrences with reference to chorionicity have been less frequent. Glinianaia, Rankin & Wright (2008) have provided such an analysis, using data from the Northern Multiple Pregnancy Register and Northern Congenital Abnormality Survey. Both databases are population-based sources located in the northeast of England. The need for such a study was prompted, in part, by the increased twinning rate in that part of the country: from 9.8/1,000 maternities in 1990 to 16.7/1,000 maternities in 2002.

As expected, the twins had a higher rate of congenital anomalies than did the non-twins (405.8/10,000 twins vs. 238.2/10,000 non-twins). The preva-

lence of congenital anomalies was also higher among monochorionic pairs than dichorionic pairs (633.6/10,000 vs. 343.7/10,000). The sample size was, however, too small to allow comparison of specific anomalies between twins with different chorion types.

### **Mirror-Image Effects in Conjoined Twins**

A case report by Brazilian investigators suggests an explanation for mirror-image effects in conjoined twins (da Silva Dalben et al., 2008). Male thoracopagus twins were delivered stillborn to a 20-year-old mother. (Thoracopagus twins represent the most common form of conjoined twinning. They are situated face-to-face and are connected through the upper half of the trunk, through the chest wall from the thorax to the umbilicus. They always share a

heart, and have four arms, four legs and two pelvises; Fierro, 2008). She had delivered two other children without complications. The twins were concordant for cleft lip and palate, with mirror-imaging. This is the sixth reported case of conjoined twins with such structural defects.

The authors argued that mirror-image clefts in conjoined twins suggest 'difficulty in the replacement, duplication, and distribution of blood vessels that interferes with the formation and normal development of facial structures' (p. 317). They explained that circulatory problems may be key contributors to cleft lip and palate in the absence of a family history of such defects. Cleft lip and palate tend to occur more often on the left side of the face because of the greater blood supply to the right side of the face

during embryogenesis. According to da Silva Dalben et al., this is consistent with the mirror-image occurrence of cleft lip and palate in thoracopagus twins, because they face each other and their opposite sides are exposed to the weaker blood supply. Given their findings, the investigators also favor fission as an explanation for conjoined twinning, as opposed to fusion.

### Older Mothers of Twins

Older mothers may seek fertility treatment in order to have children, increasing their risk of DZ twinning. This raises the question of when fertility specialists may refuse to provide such interventions (Check, 2007). This paper reviews six cases in which women between the ages of 33 and 59 years sought medical assistance due to ferti-

lity problems. Reasons for infertility included hypertension and intramuscular fibroids (muscular tumors that grow on the walls of the uterus), Graves' Disease (a type of autoimmune disease that causes hyperactivity of the thyroid gland), intrauterine exposure to diethylstilbestrol (a drug with teratogenic effects on fetuses), unicornuate uterus (a rare anomaly in which the womb is underdeveloped and there is only one fallopian tube), chronic amenorrhea (abnormal absence or cessation of menstruation) and oligomenorrhea (light menstrual periods in women of child-bearing age). Fertility treatment was provided in all cases with the exception of a 59-year-old woman with hypertension and intramuscular fibroids. Children were delivered in all five cases, although there were some

complications. Two women delivered healthy twin pairs, one male set and one opposite-sex set.

The author concluded that infertile couples should be allowed to receive fertility treatments as long as they understand that the odds of conception and delivery are slim and the physical risks to the mother and/or infants can be great. He also asserted that physicians have the right to deny fertility treatment to patients if they are concerned with lawsuits in response to unfavorable results. In such cases, he urges physicians to be forthcoming with their patients about their reservations, and to suggest that they obtain other opinions. Attention to such issues is likely to become more common, given improved methods for assisted conception, albeit still with degrees of risk.

## Twin Statistics: 'Massachusetts, Land of Twins'

Twin births, especially DZ twin births, have escalated in recent years. This has been explained by the combined effects of more frequent pregnancies among older women and the greater success of artificial reproductive technology (ART). In the United States, the state of Massachusetts leads the nation with respect to its twinning rate (Schweitzer, 2008). The twin birth rate is 4.5/100 live births, as compared with 3.2/100 live births in the rest of the country. Massachusetts also leads the nation in the frequency of triplets and other higher order multiple births. Following Massachusetts are the states of New Jersey and Connecticut.

Twins in Massachusetts do not occur with equal frequency across the state; instead, they are concentrated in affluent suburbs outside major cities. Residents of such neighborhoods are wealthy and well educated because the women have delayed their child-bearing years to attend school and to establish careers. They are, therefore, more likely to seek ART to overcome fertility problems when they do decide to start a family. They also have the financial means to obtain reproductive assistance, although state insurance will cover the costs.

Hospitals and schools have been significantly affected by Massachusetts' elevated twinning rate. Neonatal inten-

sive care units have been forced to expand, and services have been extended beyond the early weeks because many twins suffer physical difficulties due to their premature birth. Schools must find ways to accommodate families who wish to separate twins and triplets — sometimes there are not enough classrooms available to allow for this. However, Massachusetts is one of several states to have recently sponsored a bill giving parents a significant voice in deciding whether to keep their young twins together or apart in school. Many parents favor keeping young twins together in the early years, so the question of separate classrooms may not become important until the twins are older.

## Tribute to Dr Victor A, McKusick

### 1921–2008

Dr Victor McKusick was a familiar name to anyone who has studied the genetics of disease transmission. His recent death at the age of 86 years brought up the memory of his seminal 1966 work, *Mendelian Inheritance in Man* (McKusick, 1966). I have a copy — endless rows of X's (presumably X

chromosomes) run across the cover. That book provided preferred designations, phenotypic descriptions and key references for 837 dominant genetic conditions, 531 recessive genetic conditions and 119 X-linked genetic conditions. His 12th edition, published in 1998, included many more. A recently updated database is now available online (Maugh, 2008).

Dr McKusick may be best known for recognizing the symptoms of Marfan's disease (MD). MD is a connective tissue disorder with characteristics variously including increased stature, long bones, skeletal anomalies, structural eye defects, cardiac anomalies, skin problems and lung difficulties. MD may vary in severity across individuals. In 1991, McKusick identified the gene

(FBN-1) responsible for this disorder. He also advocated using mice as a model for studying human genetics. As early as 1969, McKusick urged scientists to sequence the human genome, but the idea was not widely accepted at that time.

Dr Victor A. McKusick was an identical twin, perhaps explaining his interest in human genetics. His twin brother, Vincent, became a lawyer, then chief justice of the Maine Supreme Judicial Court, a position from which he retired in 1992. Vincent has survived his brother.

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