

Identical Twin Parents; Research Reviews: Twin Pregnancy Risk Factors, a New Twin Type and a School Legislation Update; Twin Parents and Twin Researchers in the News

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Some legal and social complications that arise when identical twins have children are examined. The specific case presented concerns assignment of paternity. This section is followed by a review of recent studies of multiple birth pregnancy risk factors, namely mother to infant HIV transmission and congenital hypothyroidism. Honors given to recently recognized twin researchers are noted, as is the birth of twins to an older mother in the United States.

Identical Twin Parents

Twin-family designs are popular among behavioral and medical science researchers because they generate numerous genetically and environmentally informative kinships. The method itself is simple, yet elegant. When monozygotic (MZ) twins have children with unrelated partners, the children from the two families are biologically equivalent to half-siblings. It is also the case that twin aunts and uncles are biologically equivalent to the mothers and fathers of their nieces and nephews. In contrast, when DZ twins have children, conventional family relationships remain unchanged. There are also rare cases of MZ twins who marry MZ twins, generating two sets of 'genetic parents' and 'genetic full siblings' (Segal, 2005). These families represent a specific case of quarternary marriages (Casler, 1974).

Studies using twin-family designs (also known as MZ-Half-Sibling Families) have assessed sources of influence across a variety of human behavioral and physical characteristics. Recent

work includes studies of conduct disorder (Haber et al., 2005), developmental outcomes in childhood (D'Onofrio et al., 2006), age at menarche (Mendle et al., 2006) and social closeness (Segal et al., 2007). A less explored area concerns potential legal and medical consequences of situations posed by MZ twins who have children.

A recent case involving MZ male twins, Raymond and Richard Miller, from Missouri, is exemplary (Burke, 2007). It appears that both twins could be the alleged father of a 3-year-old girl. This is because both twins unknowingly had a relationship with the child's mother (within hours); and because the twins have identical DNA, they both have the same 99% chance of having fathered the child. (A 98% chance of paternity is required in the state of Missouri, so both twins qualify.) The judge, however, indicated that paternity could be assigned on the basis of other evidence, such as the mother's testimony as to the timing of the affairs. (This would seem highly debatable.) A difficulty is

that neither twin wishes to be responsible for child support, claiming that paternity cannot be conclusively determined. A curious twist in this case is that the twins' mother can be certain that she is the child's grandmother.

This case is an excellent example of how MZ twins' genetic identity can complicate legal proceedings. Of course, MZ twins can show genetic differences, due to somatic mutation, somatic recombination, different methylation patterns and differential X-inactivation (Martin et al., 1997; Machin, & Keith, 1999). Can MZ co-twin differences be transmitted to offspring? (see below).

The Miller twins' case is strangely reminiscent of another case I discussed in an earlier issue of this journal (see Segal, 2004). A woman in Portugal had conceived a child following sexual relations

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with both members of an MZ twin pair on the same day. Following DNA testing, the court was unable to assign paternity with complete certainty, as in the case of the Miller twins. Can research shed light on this case? Blewitt et al., (2002) observed that inbred mice show some allelic variability, despite their genetic homogeneity. This variable expressivity results from epigenetic processes (the turning on and turning off of genes due to changes in environments; see Wong et al., 2005). Raykan et al. have suggested that such processes occur during embryogenesis, and that such alleles may be more appropriately referred to as metastable epialleles — epialleles are alleles that can exist in multiple states, while metastable epialleles are alleles whose epigenetic state can change and be passed on genet-

ically (Raykan et al., 2002). Such effects would be hard to detect unless genetic and environmental differences between organisms were small, as with MZ twins. If such effects could be detected precisely, then it might be possible to distinguish MZ twin fathers/mothers from MZ twin uncles/aunts.

The biological relationship between MZ twins also offers unique advantages. Perhaps the most commonly known benefits concern organ transplantation. Given their biological compatibility, MZ co-twins are ideal organ donors for one another. Organ transplants should, therefore, proceed successfully, barring complications from infection. However, it seems less appreciated that MZ twins can also assist one another in the event of fertility problems. I described such a case

in which a fertile female twin conceived two children for her sister, via artificial insemination with her brother-in-law's sperm (Segal, 2005). (The fertile twin had already delivered two children of her own.) In this case, it is currently impossible to distinguish the mother from the aunt.

It is important to note that only one doctor of many that the twins contacted was willing to support their wishes. Many physicians whom the twins contacted worried that the attachment of the gestational mother to the newborn infant would interfere with the successful transfer of the child to her sister's care. However, these twins proved them wrong — and by doing so underline the importance of evaluating such situations on a case-by-case basis.

Research Reviews: Twin Pregnancy Risk Factors, a New Twin Type and a School Legislation Update

Twin Pregnancy Risk Factors

The greater physical risks to which twin pregnancies may be exposed, relative to non-twin pregnancies (e.g., increased rate of prematurity, increased frequency of congenital defects), are well known (Segal, 2000). New studies of some enduring problems bring focused attention to the management of multiple birth pregnancies.

Scavalli et al., (2007) examined trends in HIV-1 transmission from mother to fetus in twin and singleton pregnancies. The three targeted time periods were pre-1994, 1994 to 1996 and 1997 to 2004. The rate of transmission (until 1996) was 28.3% (15/53 pregnancies) among the twins and 13.5% (192/3,077 pregnancies) among the non-twins. In contrast, mother to child HIV-1 transmission was low between 1997 to 2003, and did not differ between twins

(1.0%) and singletons (1.8%). A higher proportion of first-born twins (8.5%) than second-born twins (2.4%) was affected.

A review of studies published in the 1990s revealed higher rates of HIV infection among twins than non-twins, and higher rates of HIV infection among DZ than MZ twin infants (see Segal, 2000). I suggested that the higher rate of affected DZ twins might be linked to an observed association between DZ twinning and increased frequency of sexual activity (Segal, 1992; also see James, 1992). Improved methods for managing multiple birth pregnancies and for treating HIV infection may have eliminated this association, but it would be worth exploring.

Congenital hypothyroidism (CM) is also of concern to families expecting multiple birth children. CM involves early reduced functioning of the thyroid gland, a

condition that can lead to nervous system damage and mental retardation if left untreated. Italian investigators Olivieri et al., (2007) compared the rates of congenital hypothyroidism (CH) among twin and non-twin infants between 1989 to 2000. The affected infants were part of The Italian National Registry of Infants with CM (INRICH), a neonatal screening program established in 1987.

The frequency of CH among the twins was over three times as high as that of the singletons. The estimated incidence of CH was 10.1:10,000 among the twins and 3.2:10,000 among the non-twins. Zygosity was mostly unknown for the 73 affected twins, so analysis was undertaken in which co-twins were classified as siblings. Results showed an increased risk of CM for these siblings (although the investigators warned that the estimated risk figure of 35.4% may

be too low). It was suggested that environmental factors may trigger the condition, given a predisposed genotype. It was also suggested that, while genetic factors may affect CM's onset and progression, sporadic cases may be linked to epigenetic changes and early somatic mutations. The elevated frequency of CH in twins is a concern because of recently increased twinning rates in western nations.

New Twin Type

A rare pair of twins who inherited identical genes from their mother, but different genes from their father, was recently described (Souter et al., 2007). The ambiguous genitalia of one of the twins attracted medical attention: One twin was a normal male, while his co-twin was a true hermaphrodite (an individual with both male and female sexual organs). Both twins had 46,XX/46,XY chromosomal complements in their peripheral lymphocytes (white blood cells), skin fibroblasts (widely distributed cells in connective tissue) and gonadal biopsies (microscopic examination of a sample from the reproductive organs).

The cellular events leading to these unusual twins (who are less alike genetically than typical MZ twins, but more alike genetically than typical DZ twins) are not definitive. The investigators proposed two pathways by which the twins may have originated:

Pathway I. Initial events would involve parthenogenic activation

and cleavage of an ovum. This would be followed by fertilization of the ovum by one X-bearing sperm and one Y-bearing sperm, and intermingling of the blastomeres (cells produced by cleavage of the fertilized egg) to form a chimeric embryo. A twinning event (with asymmetric division) would then lead to the twins in question.

Pathway II. A primitive egg cell would be fertilized by two separate sperm (one X-bearing and one Y-bearing), eventuating in an XXY zygote. Next, two post-zygotic diploidization events would occur, followed by the intermingling of blastomeres to form an XX/XY mosaic embryo (an embryo whose cells differ genetically). Asymmetric division would then create the twins under study.

The frequency of these unusual twins is currently unknown and is presumed rare. However, had two X-bearing or two Y-bearing sperm been involved, one wonders if the twins would have received the medical attention that they did. It is also likely that occasional cases like this one (classified as DZ) should not bias estimates of heritability if the pairs are part of a large research sample. However, the frequency of such twins and the frequency of other varieties of DZ twinning are unknown. As such, it could be argued that DZ twins and their parents should be extensively genotyped prior to research participation. For example, superfecundated twins — DZ twin who share mothers, but

not fathers — would elevate heritability calculations in classic twin studies in which they were highly represented. In recent years there have been closer associations between genomic studies and behavioral science investigations. This change in the research landscape may make mandatory genetic assessment and classification of DZ twins a future possibility.

School Legislation Update

On May 3, 2007 the Texas State Legislature voted 141 (Yeas) to 0 (Nays) to pass House Bill 314, giving multiple birth parents a significant voice in the classroom placement of their children. The bill, signed into law by Governor Rick Perry, will take effect on September 1, 2007. The bill allows for the following: (1) Parents who are displeased with having their children in separate classrooms may submit a written statement requesting that they be placed together; (2) Parents may appeal placement decisions made by their school's principal, in accordance with district policy; (3) If keeping twins together proves disruptive to the teacher and to other pupils, then the principal (in consultation with the twins' teacher) may determine the appropriate placement.

It is gratifying to see that parents of twins are able to affect their state's school policies by taking coordinated actions. Additional information about various state-wide movements to improve twins' school placement policies is available at www.twinslaw.com.

Twin Parents and Twin Researchers in the News

Delivering Twins at Age 60

A 60-year-old woman from Hackensack, New Jersey has become one of the oldest women to deliver twin boys (USA Today, 2007). The twins were conceived via in vitro fertilization at a South African clinic. The new parents

have three older children, but wished to have a near-in-age sibling for their youngest son who is six. The mother, Frieda Birnbaum, believes that she has opened the door to other women who wish to become mothers at older ages. Her decision will, no doubt, stimulate dialogue among

parents, children, psychologists and ethicists as to the benefits and difficulties of becoming an older parent. Note: Birnbaum is not the oldest mother in the world to bear twins — a 67-year-old woman, originally from Spain, delivered twins in December, 2006 (Reuters, 2007).

Dr Irving I. Gottesman

Dr Irving I. Gottesman is the recipient of the American Psychological Foundation's (APF's) 2007 Gold Medal for Life Achievement in the Science of Psychology. He will be recognized at the 2007 American Psychological Association Convention, in San Francisco, at a special session held on Saturday, August 18, at 4.00 pm. Dr Gottesman is currently at the University of Minnesota, in Minneapolis, as the Irving and Dorothy Bernstein Professor in Adult Psychiatry and as a Senior Fellow in Psychology.

The citation for this award and Gottesman's stunning academic biography are presented in a special section of the journal, *American Psychologist* (2007). The citation mentions his 'substantial contributions to schizophrenia, criminal behavior and personality', and his 'bringing psychology, psychiatry and genetics together in innovative ways'. Of course, Gottesman is famous for his work with twins — he used adolescent twins to study individual differences in personality, via the MMPI. He used the twin-family design to study the risk of schizophrenia and depression in the offspring of affected and unaffected MZ and DZ twins. He also used consecutively admitted British twins to study genetic predisposition to schizophrenia, in a classic collaboration with James Shields.

It continues to be my pleasure and privilege to know Irving I. Gottesman. He offers fresh answers, sharp angles and honest words on many topics — and with these words I consider his citation to be complete.

Dr Sandra Scarr

Dr Sandra Scarr was honored with a festschrift at the May 2007 American Psychological Society (APS) convention, in Washington, DC. The program was sponsored by the APS, Lawrence Erlbaum Publishers, Society for Research in Child Development, Behavior Genetics Association, Harvard Graduate School of Education,

the University of Minnesota's Institute of Child Development, and the University of Virginia's and Yale University's Departments of Psychology.

Dr Scarr's twin studies of personality and adoption studies of intelligence are legendary. Her work was remembered in approximately fifteen different presentations delivered by friends and colleagues.

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