



NEWS, VIEWS AND COMMENTS

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Forgotten Twins

Recent, rapid increases in dizygotic (DZ) twinning rates, largely a product of the new assisted reproductive technologies (ART), have refocused attention on the pleasures and pitfalls of multiple births. Formerly childless couples are gratified by their 'instant families', while physicians grapple with developmental delays common to premature twins and triplets. Even while DZ twinning rates exceed monozygotic (MZ) twinning rates (a pattern that generally characterized natural twinning prior to ART), the majority does not rule! Fraternal twins remain the forgotten pairs in many scientific and non-scientific undertakings. For example, the three early reared-apart twin studies did not include DZA twin pairs in their samples.¹⁻³ The Minnesota Study of Twins Reared Apart, directed by Dr Thomas J Bouchard Jr, was the first investigation of twins reared apart to systematically include separated fraternal twins.⁴ Beyond the laboratory, identical twins have remained the preferred parties in documentaries and works of fiction.

These situations are understandable, but unfortunate. They are understandable because identical twin differences provide persuasive evidence of environmental effects on human developmental traits. Researchers are, however, documenting increasing numbers and varieties of genetic differences between some identical co-twins. These differences range from variations in X chromosome inactivation patterns in some identical (female) pairs⁵ to discordance for medical disorders⁶ and congenital anomalies in others.⁷ Rethinking the meaning of identical twin differences may be worthwhile in some cases. Fraternal twin differences reflect both genetic and environmental factors, so fraternal twin studies generally offer less clear conclusions as to influences affecting measured phenotypes. Case reports and formal investigations limited to fraternal twins are less plenti-

ful, so several insightful studies (both past and present) may escape notice. DZ twin investigations have explored associations between fraternal twins' blood group similarities and perceived zygosity,⁸ intellectual resemblance⁹ and physical appearance.¹⁰ More recent work on DZ twins includes genomic analysis for identifying regions with genes relevant to age-related chronic diseases, such as diabetes and osteoporosis.¹¹

The non-scientific world correctly perceives that most fraternal twins lack the striking behavioral and physical similarities of identical twins. Fraternal twins are, consequently, less captivating to general audiences than their identical counterparts. Almost exclusive attention to identical twins in educational programs and other public events undermines fraternal twins' crucial role in the scientific enterprise. We should never forget that identical twin resemblance is less meaningful than identical twin resemblance compared with that of fraternal twins. Furthermore, within the fraternal population is a wealth of exotic and undiscovered couples that may help solve persisting behavioral riddles. Reappraisal of selected twin research methods and findings may be warranted once the fraternal twin story fully unfolds.

Fraternal twins' complexities begin with superfecundation, the fertilization of two eggs by two spermatozoa at different times within the same menstrual cycle (usually three or four days apart).¹² Such co-twins are infrequently detected because their chronological age difference is slight, and because their behavioral and physical differences are easily associated with their genetic differences. It is, however, also possible for eggs to be released at somewhat greater intervals (eg 1-2 weeks), again allowing the possibility of separate conceptions. These twins are more likely to attract attention because their early developmental differences may be more pronounced. For example, the relatively greater prematurity of one twin

might amplify the twins' existing genetic differences.

Nevertheless, the twins' genetic heterogeneity would be the most common explanation for their diverging development. Few investigators raise superfecundation as an explanation because superfecundation is assumed to be rare. Contrary to conventional thought, I believe this remains an untested assumption, and urge renewed respect for the possibility that superfecundation occurs more frequently. Evidence from other sources supports this view. Estimated non-paternity rates range from 5-30%,¹³ fraternal twinning may be higher among illegitimate births than legitimate births¹⁴ and coital frequency may be higher among women bearing fraternal twins than among women bearing identical twins.¹⁵ It has been suggested that one in 12 fraternal twin pairs are superfecundated, and that bipaternity occurs in one in 400 pairs but these estimates are preliminary.¹⁶

Superfecundated twins attract undivided attention when different fathers are involved. The first scientific taste of these extraordinary pairs was provided by a famous 1810 report of twins whose contrasting appearances reflected their fathers' differing ethnicities. These remarkable pairs also occur in Greek mythology, although varied versions of these events exist.¹⁷ Zeus, taking advantage of Amphitryon's absence, assumed his likeness to court his wife, Alcmeme. When her real husband returned several hours later he was surprised by his wife's lack of enthusiasm and she was baffled by his ardor. Twins resulted from these unions, Hercules (son of Zeus) and Iphicles (son of Amphitryon). Zeus also transformed himself into a swan to seduce Leda, wife of Tyndareus. Two sets of twins were conceived on the same night, Pollux and Helen (children of Zeus) and Castor and Clytemnestra (children of Tyndareus), yielding several superfecundated sets. Medical science has never documented the birth of two pairs of twins

(quadruplets) in which different fathers were responsible for different pairs, but this is theoretically possible. Medical journals do describe intriguing superfecundated twin pairs that warrant further study.

Twins with different fathers were identified in 1982 when a Caucasian mother sought medical attention for her four-year-old fraternal twin girls who varied in appearance, complexion and features of fetal hydantoin syndrome.¹⁸ Fetal hydantoin syndrome, characterized by skeletal and craniofacial abnormalities, has been tied to prenatal exposure to phenytoin, a substance the twins' mother received for epilepsy treatment at age 13. Twins with different fathers were also identified in 1997 when the legal father requested paternity identification.¹⁹ The female twins, delivered at 35 weeks gestation, showed a 150 gram weight difference. The smaller twin (birthweight = 750 g) experienced anemia and septic risk due to her prematurity. When paternity was excluded for one twin and it was determined that neither infant had been released to the wrong family, the mother admitted to an extramarital relationship. This case was listed as the seventh occurrence of superfecundation involving separate fathers, but the number is actually higher. The 1982 study cited above documented 19 cases, 11 involving racial bipaternity, and more recent case reports are available. I have identified additional cases in the course of providing legal assistance to families with twins, and am unaware that these pairs have been appended to the scientific literature. The presumption that superfecundation is a rare twinning phenomenon seems unjustifiable in the absence of systematic study.

Consider, too, the difficulty of detecting superfecundated twins in populations with limited physical trait variation – superfecundation might easily escape notice because fathers would match across characteristics.²⁰ Superfecundation was suggested by ultrasonic examination of Japanese twins at 10 weeks' gestation, revealing a two-week discrepancy in co-twins' crown-to-rump length (CRL). The interesting feature of this case was that the twins' prenatal size difference, rather than their postnatal appearance, raised the possibility of superfecundation. The chance that

two fathers were involved was not addressed, but the investigators acknowledged the difficulties in finding superfecundated twin pairs in Japan's physically homogenous population. They urged first trimester measurement of CRL to discover the true frequency of this event.

Two bipaternal superfecundated twin pairs were identified in China in 1994, following paternity testing – a wife's extramarital affair and an illegitimate twin birth, rather than apparent twin differences, suggested different fathers, thus prompting genetic testing.²¹ I also recall a news report concerning black twins with different fathers, a finding revealed only because genetic analysis was needed to diagnose one twin's medical condition. Other superfecundated twins may well go unnoticed in the absence of marital or medical considerations that justify genetic testing.

What does superfecundation imply for twin studies? A concern is that discordance in seemingly ordinary fraternal twins might be associated with separate conceptions. Co-twins conceived apart could show greater differences for some traits than co-twins conceived together, even when fathers are shared. First, given a ten-day between-conception interval, one twin would enter the embryonic phase (at the start of the second gestational week) while the co-twin would be within the zygotic phase. Embryonic hearts, eyes and limbs are especially sensitive to teratogens during the third and fourth weeks of gestation.²² In contrast, zygotes are relatively unaffected by these agents unless effects are so severe as to be lethal. Secondly, ordinary fraternal twins share, on average, one-half of their genes, while twins conceived by different fathers share one-fourth of their genes (as do half-siblings). Ordinary fraternal twins can share dominance variance, while half-siblings cannot because they have only one common parent. The presence of superfecundated twins in modest size twin samples could increase identical–fraternal twin differences for some traits, thus inflating heritability.

Emergenesis is a term coined by Dr David Lykken at the University of Minnesota to describe traits influenced by complex configurations of genes across many loci, eg unusual musical talent and selected brain wave

patterns.⁴ High identical twin resemblance and low fraternal twin resemblance for measured traits may reflect emergenic effects. Emergenesis would not affect identical twin resemblance because identical twins share 100% of their genes. However, emergenesis would reduce fraternal twin resemblance given the low (but non-zero) probability of both co-twins inheriting the same unusual gene combination. Superfecundated twins with separate fathers differ, by descent, for paternally derived genes so their matching on emergenic traits is virtually impossible. Again, including such twins in small twin samples or single case reports could yield misleading estimates of genetic influence on complex phenotypes. Now that DNA analysis is becoming more common and less expensive it may be worth testing twins and their parents in future studies. Researchers may want to think seriously about whether and how to include such sets in ongoing studies.

How can superfecundated twins enhance understanding of human behavior? Evolutionary psychology suggests several important ways in which fraternal twin–superfecundated twin designs may yield new insights into social relations. There is abundant evidence that identical twins show closer social relations than fraternal twins.¹² Many proximal (immediate) explanations are available, such as identical twins' greater physical and behavioral similarities and/or greater opportunities for shared experiences. These explanations provide useful, but partial views of behavior that may be enriched with reference to evolutionary considerations. For example, findings on twins' social relationships are consistent with William Hamilton's (1964) theory of inclusive fitness.²³ Hamilton reasoned that natural selection favors alleles predisposing individuals to behave in ways favoring the transmission of those alleles into future generations. Alleles influencing individuals to favor others likely to carry replicas of these alleles is an indirect means by which these alleles can be represented subsequently: 'A gene causing its possessor to give parental care will leave more replica genes in the next generation than an allele having the opposite tendency. The selective advantage may be seen to lie through benefits conferred indifferently on a set of

relatives each of which has a half chance of carrying the gene in question' (p. 1).²³ Therefore, it pays (genetically speaking) to direct benefits toward close relatives. Recognizing who one's relatives are is essential and various mechanisms for doing so have been proposed. Comparing social relatedness between fraternal twins who share fathers and those who do not would allow further tests and applications of inclusive fitness theory.

Research shows that child abuse is elevated in families with step-children²⁴ and in families with twins.¹² Evolutionary psychologists Martin Daly and Margo Wilson have asserted that 'Investing resources in non-biological children may lead to "violent resentment" on the part of step-parents' (p. 304).²⁵ Twin researchers have linked increased family stress and reduced child health to increased abuse of twin infants and twin children, relative to non-twins. (Even while twins are overrepresented in samples of abused children, most parents do not abuse their multiples.) Ordinary fraternal twins can help test the hypothesis that paternity uncertainty may underlie differential bonding and/or abuse of one fraternal twin. Specifically, fathers may perceive reduced physical and/or behavioral resemblance to one twin, relative to the child's co-twin, thus affecting their evolving relationship. Such parental favoritism need not operate consciously – people may be predisposed to be sensitive to who their kin are since caring for kin improved survival throughout human history.

Superfecundated twins with different fathers offer a more stringent test of differential bonding between fathers and one twin. (Note that child abuse in families with twins more often involves one twin than both.²⁶) An advantage of using twins to understand differential child abuse is that family factors associated with abuse (eg financial concerns, marital difficulties) are held constant because twins enter the family at the same time.

Births of some superfecundated twins with different fathers have evolved into curious custody battles. These cases are rife with raw material for exploring evolutionary-based hypotheses surrounding paternity issues. An illustrative 1996 case concerned an Arizona woman who sus-

pected that her current and former husbands were each responsible for one twin.²⁷ Even from birth, the appearance of each infant girl suggested different fathers, a suspicion confirmed by genetic testing. The former husband initially sought custody of 'his twin'. He was eventually granted limited visitation rights and both twins remained in their mother's care. Similar events unfolded in a more recent case in which I provided expert testimony. The most curious feature of these cases was the effort made by fathers on behalf of their own twin children – had the birth involved their own single-born child they may have been less committed to the ensuing legal contest. Perhaps shame and lowered self-esteem from their partner's infidelity led to 'assertions of paternity' in the form of securing rights to their own child. Further evaluation of such cases and controls is needed to evaluate this notion.

An important caveat to much of the above is that the strikingly different appearances of some fraternal twins are not necessarily signs of superfecundation. The contrasting physical features of some twins born to interracial couples remind us that genetics underlies both similarities and differences among family members. I have encountered several such pairs over the years, one set the product of a Black mother and Caucasian father, and the other the product of a Black mother and White-Filipino father.

There are many other captivating varieties of fraternal twins that deserve careful study. They include polar body twins, superfetated twins, chimeric twins and male-female twins. Future columns of this journal will explore the biological and behavioral aspects of these sets and what their presence implies for twin data and designs.

Twins' Minds and Bodies

Theory of mind

Twin studies show that autism, a disorder involving severe social impairment and affecting 5–10 out of 10000 children, is influenced by genetic factors.²⁸ Autistic children appear to have abnormal development of their folk psychology (ability to understand other people's behavior by their intentions), while showing nor-

mal or superior folk physics (ability to understand physical objects with reference to their causal or mechanical properties).²⁹ The first twin study of early understanding of mind investigated genetic and environmental influences on young children's ability to comprehend the behavior and intention of others.³⁰ Participants included 61 monozygotic (MZ) and 58 same-sex dizygotic (DZ) three-year-old twin pairs enrolled in the TRACKS Twin Study in Great Britain. Twins completed eight false-belief tasks and two deception tasks, as well as the vocabulary and comprehension subtests of the Stanford–Binet Intelligence Scale.

A sample item for testing false belief required children to inspect a series of drawings: two children stand beside a basket and a box; one child places a ball in the basket; that child exits; the remaining child removes the ball from the basket and places it in the box; the first child returns. Twins are then asked: 'Where will Sally look for the ball?'

Genetic influence was indicated for both the theory of mind tasks (MZ $r_i = 0.66$, DZ $r_i = 0.32$) and verbal measures (tasks (MZ $r_i = 0.74$, DZ $r_i = 0.56$). Most of the genetic influence on understanding of mind (66%) proved independent of verbal ability. Non-shared environmental influences were also substantially implicated in the development of this behavior. The investigators concluded that genes may contribute to the development of social understanding, thus affecting many features of one's social interactions. It would be worth considering whether MZ twins show superior performance on understanding of mind tasks, relative to DZ twins and non-twins. This group difference would be reasonable, given some identical twins' nonverbal (gestural) communication patterns and exquisite sensitivity to their co-twins' intentions and feelings. MZ twins experiencing difficulties in these tasks might be less close socially to their co-twins than high-scoring twins.

Cerebral mirror-imaging

Ectodermally derived traits (eg hair whorl and dermatoglyphic patterns) show mirror-imaging effects in approximately 25% of identical twin pairs. Studies investigating cerebral mirror-imaging of cognitive function

in MZ pairs have produced a mixed picture. Lack of consistent findings may reflect failure to organize hand-d discordant pairs by source of left-handedness (ie birth trauma or delayed zygotic division)³¹ and/or ineffective methods for assessing mirror-imaging of cerebral function. A recent case report illuminates this issue and much more. A pair of hand-d discordant MZ female twins completed a language task and a mental rotation task, activities that differentially engage the left and right hemispheres.³² Brain activity was monitored by magnetic resonance imaging (MRI) while tasks were performed. The dextral co-twin showed pronounced left dominance during the language task while her sinistral co-twin showed the reverse pattern. The dextral twin showed greater right than left hemisphere activity during the mental rotations task, while her sinistral co-twin again showed the reverse pattern. These twins had experienced a nontraumatic birth so it is likely that their handedness discordance reflected embryological events.

The authors of this study raised the possibility that cerebral organization differences in MZ co-twins may explain differences in disorders such as schizophrenia, autism and dyslexia. A 1977 study by Boklage showed reduced concordance for schizophrenia in right-left and left-left MZ twins, compared with right-right MZ twins.³³ Colleagues' failure to replicate his findings directed attention away from this perspective on MZ co-twin differences in psychiatric syndromes. It may be time to revisit this issue in light of vastly improved experimental technologies.

Multiple review

(1) Eating disorders revisited. Twin studies of anorexia nervosa and bulimia have yielded a mixed picture with respect to the relative contributions of genetic and environmental influences. A recent comprehensive review reported widely ranging estimates of genetic influence for both conditions (anorexia: 0–70%; bulimia: 0–83%).³⁴ Inconsistencies across studies were variously explained by differences in sample size and representativeness, diagnostic criteria for bulimia, adherence to the equal environments assumption and ability to detect

shared environmental influence. Continued study of genetic, environmental and gene-environment interactions relevant to eating disorders is recommended. (Note: early reared-apart twin studies did not include discussion of eating problems; relevant data from ongoing analyses would be informative.)

(2) Language impairments. What twins tell us. This summary asserts that twins' language deficits are well known, yet their nature and complexity have been less appreciated.³⁵ The twin situation, ie growing up in close proximity to a same-age sibling, is regarded as the primary factor restricting twins' communicative abilities. Specifically, twins' rearing circumstances result in reduced verbal interaction with parents and atypical language forms. The author asserts that greater attention to individual cases would extend understanding of factors relevant to twins' speech development, such as prenatal and perinatal birth hazards, genetic predisposition for language disorders and specific features of twins' rearing situations.

Given the importance of good language skills for successful social and intellectual functioning, this language review is a welcome addition to the twin literature. The author recognizes that the different twin types undergo different speech-relevant experiences, although this point would have been more effective had it occurred earlier in the review. It will interest readers to learn that some investigators have identified language skills in which twins outperform non-twins, eg twins may understand one another better than do unrelated peers. Two recent-language studies not included in this summary showed increased turn-taking by twins in twin-mother triads than in single twin-mother dyads,³⁶ and superior quality and quantity of speech by twins than by singletons.³⁷ These contradictory, but encouraging findings should stimulate research efforts to clarify the complexity surrounding twins' language learning environments.

(3) Multiple birth risk and IVF. Researchers from the Division of Reproductive Health at the Centers for Disease Control and Prevention, in Atlanta, reported an extensive survey of associations between a number of embryos transferred during in vitro fertilization (IVF), and live birth and

multiple birth rates.³⁸ (Multiple births from one pregnancy were considered one live birth.) Assessing outcomes from these procedures is important for minimizing the well-known risks associated with multiple pregnancies. Some nations legally restrict the number of transferred embryos to three, but the United States has been reluctant to adopt a formal policy out of respect for the inviolability of patient-physician relationships.

Data were gathered from 300 United States centers, estimated to represent over 95% of all 1996 cycles reported for that year. (A cycle begins when a woman starts fertility medication or ovarian monitoring with the intention of transferring embryos.) Findings were stratified by maternal age and whether additional embryos (maintained through cryopreservation) were available. The risk of multiple birth following IVF varied with the mother's age and number of transferred embryos. Live birth rates were 43% and 36%, respectively, for women 20–29 and 30–34 years of age when two embryos were transferred. Live birth rates were consistently lower for women older than 35. Multiple birth rates were also higher for younger women and higher with increased number of embryos. For example, among women 20–29 years of age multiple birth rates were 22.7% and 45.7% with transfer of two and three embryos, respectively. In contrast, among women 40–44 years of age multiple birth rates were 10.8% and 25% with transfer of two and five embryos, respectively. Embryo quality was not associated with multiple birth risk, but was associated with increased live birth rates when fewer embryos were transferred.

Insights and Instincts

Parallel lives

Denise LaChance is the general manager of Live on Line, a company broadcasting events live on the Internet.³⁹ Her identical twin sister, Debra, is the chief operating officer of that company. The 46-year-old identical twins recently moved into adjoining New York City town house apartments with their respective spouses.

Their lives reveal striking parallels, as well as occasional detours. Both

twins graduated from Boston University, after which Denise remained there to attend law school, while her twin enrolled in New York University's business administration program. Denise relocated to New York upon completing her law degree and while the sisters grew closer socially, their careers took different tracks – Denise worked in health care (as an attorney) and Debra worked in fashion. When Denise sought a job change she joined her twin in the fashion world, after which Debra moved on to establish Live on Line in which both twins are now active. Their life history affirms once again that twin studies of occupational choice should focus on twins' last or 'best' positions for accurate assessment of job selection and satisfaction.

Guilty until proven innocent

Several years ago I was contacted by an attorney representing an identical twin whom the attorney believed was wrongly accused of a crime. His twin brother had been convicted of similar wrongdoings several years earlier, so the concern was that jury members in their small town would recall that event and be less than objective in rendering judgment. I am unaware of what eventually transpired in that case, but a similar scenario occurred in Los Angeles in December 1999.⁴⁰ Truck driver Ray Nugent was imprisoned for 13 days on charges of bank robbery and attempted murder – but police had mistaken him for his brother, Jay. The mistake occurred when an officer identified Ray as Jay after inspecting his driver's license photograph. The twins are believed to be fraternal, and while fraternal twins generally look less alike than identical twins, some look very much alike.

Nugent will receive \$150 000 compensation from Los Angeles County. His difficulty was not with his twin brother, but with law enforcement officials. 'They said that if I had a twin brother who did that [robbery and attempted murder], I must believe him, too. It is that mentality that disturbs me.' Enhancing public awareness of twin types and behavioral differences among twin types is necessary to avoid such errors in the future. This goal is becoming increasingly important, given multiple birth rates.

Searching for lost twinship

Many twins reared apart invest considerable time and expense in locating the twin sibling from whom they were separated in infancy. Unfortunately, not all separated twins are successful in this quest, a situation difficult for many to accept. Fraternal twin André Carmichael from Brooklyn, New York, is now at the center of a tragic case involving lost twinship. Childhood rumors of a twin sister, vague recollections of 'a baby' and commitment to finding a missing twin were ultimately responsible for his learning the difficult truth.⁴¹ In October 1999 it was revealed that his mother (who had placed him in foster care at age 9) had fatally beaten his twin sister, Lata-nisha, when she was only 3 years old. Carmichael is planning to file a lawsuit against the city for failing to protect his twin. This case generated enormous interest, making it likely that additional facts will be revealed in coming months. Attention will, hopefully, be directed to twin-related aspects of this case as well as the heinous crime.

Wonderful Websites

- A comprehensive medical dictionary is available on-line at: www.graylab.ac.uk/omd/index.html
- A group that performs zygosity diagnosis with many useful twin-related links can be found at: www.proactivegenetics.com/
- A listing of reared apart twins searching for their co-twins, and non-twins searching for twin relatives and friends is located at: www.twinsworld.com/reunite.html

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