

News, views and comments

Quadruplets: Risks, Outcomes and a Set of Four/Twin Research Reviews and a Lawsuit: Antenatal Corticosteroids and Twins' Neonatal Outcomes; Fathers of Twins; Doppelgängers and Similarity; Monozygotic Co-Twin Difference in Asymmetric Pigmented Paravenous Chorioretinal Atrophy/In the News: Opposite-Sex Twin Holocaust Survivors; Twin Models at Gucci; Twins With Different Fathers; Reunited Twins Enter Same Convent; Death of a Twin Soldier During Training; Surgical Separation of Conjoined Twins

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Abstract

Quadruplets are at elevated physical risks at prenatal, perinatal, and postnatal levels, relative to twins. A brief review of this area is followed by discussion of a female quadruplet with three co-quadruplet brothers. Next, several timely twin research reports are examined. The topics include antenatal corticosteroids and twins' neonatal outcomes, the meaning of fatherhood in families with twins, what doppelgängers (look-alikes) reveal about physical and behavioral similarity, and monozygotic (MZ) co-twin discordance for asymmetric pigmented paravenous chorioretinal atrophy. A lawsuit involving alleged cheating on a medical school examination by identical twins is also reviewed. General interest stories cover opposite-sex twin Holocaust survivors, twin models at a Gucci fashion show, twins with different fathers, reunited female twins who entered the same convent, the death of an MZ female twin soldier during training, and the surgical separation of conjoined twins in Brazil.

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Quadruplets: Risks, Outcomes and a Set of Four

During the first week of each semester, I ask my students if anyone in the class is a twin. I usually identify one or two pairs (or partial pairs) in this way and encourage them to participate in my ongoing research. This year a female student, Gabriela, approached me at the end of class to say she is a quadruplet, but was reluctant to announce her life history information publicly. She explained that two of her three brothers are legally blind — when she was younger, she would hold up different numbers of fingers to gauge how far they could see. The brothers also variously suffer from physical effects associated with their premature birth and very low birth weight, such as cerebral palsy and cognitive deficits. In contrast, Gabriela developed into a healthy individual, possibly because

she was female and better able to withstand prenatal, perinatal and prenatal adversities — male infants born before the 30th gestational week showed faster declines in mortality, respiratory distress syndrome and chronic lung disease than female babies over an 11-year period (Boghossian et al., 2018).

I invited Gabriela for a Zoom interview during which we discussed her birth history, growing up years and present circumstances relating to her multiple birth status. I was intrigued and inspired to look more closely at the literature on higher order multiple births and to tell the story of these quadruplets. I also obtained information about the quadruplets from their mother, Nellie. I will begin with a brief overview of quadruplet conceptions, deliveries and outcomes.

Quadruplet Births

Higher order multiple births result mostly, but not exclusively, from ovarian stimulation and in vitro fertilization (IVF). A recent study of seven women carrying quadruplets was conducted by a pair of Russian investigators (Kalashnikov & Kudratova, 2021). Extensive examination indicated that this subset of women faces increased risk of gestational complications, such as cervical incompetence (85.7%), fetal growth retardation (71.4%) and premature

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birth (100%). Constant monitoring and delivery at a level 3 facility were recommended; a level 3 facility is usually a trauma hospital that provides all medical services (McLaren, 2021).

Some developmental outcomes are less favorable for quadruplets than triplets, and less favorable for triplets than twins (Sellier et al., 2021). A cross-sectional Australian study examined the prevalence of cerebral palsy (CP) for 1033 twins, 81 triplets and 11 quadruplets who were minimally 4 years of age. The children were drawn from a European network of CP surveillance and the Australian CP Register. Clinical data were obtained for multiple birth children registered in all participating registries. The birth prevalence of CP was greatest for quadruplets (50.7/1000 births), followed by triplets (17.1/1000 births) and twins (6.5/1000 births). In contrast, prevalence by gestational age did not show group differences. The prevalence of CP among twins, but not triplets or quadruplets, decreased over time. It was concluded that premature birth poses a salient risk for CP, consistent with the diagnoses of Gabriela's quadruplet brothers.

The need for targeted support for mothers of twins and higher order multiples was highlighted in research by Wenze et al. (2020). Twenty-eight women carrying twins, triplets or quadruplets were recruited online to complete self-report measures and telephone focus groups aimed at identifying their treatment preferences. All participants were to be first-time mothers. Negative responses, such as anxiety, depression and insomnia, were reported. Interest in online support was indicated, sometimes by women who were already receiving such services. The researchers proposed employing healthcare professionals familiar with multiple birth and offering delivery care at home.

It should be noted that many women celebrate multiple pregnancies, so it is possible that the 28 participants were especially in need of support, and so were somewhat unrepresentative of the population of multiple birth mothers, in general. Given that current assisted conceptions are more successful with single embryo implantation than in the past, it is likely that the frequency of higher order multiples will continue to show the recent declines reported by the Center for Disease Control (Osterman et al., 2022).

Gabriela and Her Brothers

The quadruplets were born on April 16, 1998, so are currently 24 years of age. They were conceived via IVF after their parents attempted to have children for four years, but were unsuccessful — their mother and father (José) were 28 and 30 years of age, respectively, when the babies were born. Nellie had completed three years of college; their father had completed two years of college before receiving training to become a corrections officer. The couple had been informed that implanting multiple embryos could result in twins, triplets or more, but chose to proceed. They felt both excited and scared. 'We didn't really understand the extent of the consequences that would follow a premature birth,' Nellie admitted.

When quadruplets were detected, the family's physician suggested selective termination of one or more embryos to increase the survival chances of a smaller number, but both parents were against the procedure. Nellie explained that they had had a difficult time conceiving and did not wish to risk losing all four fetuses. She also felt that the physicians had not fully explained the consequences of premature birth, and that she and José were somewhat naive on the subject. 'In our minds premature birth was not going to happen to us.' Interestingly, their mother conceived naturally after their birth, delivering her fourth son, Adrian, two years later.

The infants were delivered early by Cesarean section at 24 weeks of gestation. The pregnancy went well at first. 'I had a fabulous pregnancy. I was fat and happy! I loved being pregnant up until the very end when I started having cramps and got preeclampsia.' (Preeclampsia is a serious condition involving high blood pressure, protein in the urine, swelling, headaches and blurred vision. It may occur at about 20 weeks into a pregnancy; see Cleveland Clinic, 2022). As a result, Nellie was airlifted from her local hospital to a better equipped facility. The quadruplets' birth order was Michael, Joseph, Gabriela and Erik. Their birth weights were exceedingly low, ranging from 1 pound, 1 ounce (Gabriela) to 1 pound, 12 ounces (Michael). During their hospital stay, one of the male babies was especially ill, prompting the doctor to ask the parents if he should be revived — they insisted that the medical staff do everything possible to keep him alive.

Each month a different baby came home, but the first one to be released did not leave the hospital until approximately six or seven months of age, and all four were discharged with breathing tubes. In the hospital they had received oxygen and small doses of caffeine intended to help them survive; caffeine helps premature babies' lung development (Kehoe, 2016). There was some worry that one or more of the babies was deaf — but when Gabriela's mother threw a bottle away it 'clinked', scaring Gabriela. It was a relief to her mother to know her daughter's hearing was normal. A picture of the infant quadruplets with their parents is shown in Figure 1.

Nellie explained that the problems persisted. 'All four infants required oxygen at birth, which affected their vision and had long-term consequences. I have two sons who are legally blind and two that require glasses. Of the four, two (sons) have cerebral palsy — one is spastic, one is floppy. Their mental health is also affected — the oldest (Michael) has schizoaffective disorder, and two of the others have issues with anxiety and depression.'

The quadruplets were kept together in preschool, but when they advanced to kindergarten Gabriela was placed in a class apart from her brothers. She recalls crying out for them. Her brothers required special needs classes from the start, and she was diagnosed with attention-deficit/hyperactivity disorder (ADHD) in second grade; the last-born brother (Erik) also has ADHD. Gabriela's memories from those years are mostly of checking in on her brothers during each school day. Courses of action, known as 504 plans, were developed for all four quadruplets — 504 plans enable adjustments and accommodations for children with special needs (Mauro, 2022). Then, as time passed, one of the brothers developed Tourette's disorder (TD), a condition involving vocal tics, facial tics and various repetitive movements (Greydanus & Tullio, 2020). TD has a known familial component, but the family is unaware of any immediate or distant relatives having been diagnosed with the condition.

Gabriela benefitted greatly from the educational resources provided to her. She completed high school and junior college and is now enrolled in a four-year university that is a five-hour drive from her home. She and her younger brother help care for their three other brothers whenever they can. Prior to the COVID-19 pandemic, the brothers were receiving educational assistance, but that has ended. Currently, they are unable to work, but assist on the family's ranch that their parents purchased two years ago.

We discussed Gabriela's reluctance to call attention to herself when I asked who among my students is a twin. She understands why people are curious about her multiple birth status, but because her situation is painful and personal, she rarely discloses this birth event to anyone. Gabriela has never known another set of triplets or quadruplets, but she has known pairs of twins. She remarked



Fig. 1. The four infant quadruplets at age eight months with their parents, José and Nellie, at Christmas time. From left to right the babies are: Joseph, Michael, Gabriela, and Erik. Photo courtesy: The quadruplets' mother Nellie, and her daughter Gabriela.

that when one or both twins reveal their twinship to someone for the first time, she prefers 'not to steal their thunder'. Knowing someone is a twin is exciting, but knowing someone is a quadruplet would overshadow that news and invite considerable commentary and questioning, not always sensitive.

Final Remarks

Gabriela feels lucky to have escaped the physical deficits associated with higher order multiple births, but she also feels slightly guilty. Perhaps that partly explains why she is so committed to caring for her brothers whenever she can. 'They are just such a light in my life. If anyone is going to care for them, I would rather it be me and my younger brother.' There is some available literature on the negative impact of care provided by a healthy twin to a co-twin with special needs and circumstances. For example, reduced parental attention and forfeited opportunities are likely to result, causing jealousy and resentment (see Segal, 2017). However, many able-bodied twins take pleasure and pride in assisting their co-twins and watching them thrive—to deny them that opportunity would be unjust. Increased research along these lines, as well as finding ways to provide better information and support for families with quadruplets, are clearly warranted. Nellie can attest to that:

'Caring for the quads has been a full-time job! IEPs [Individualized Education Plans], doctors' appointments, appointments with specialists and day-to-day life have been a challenge. I feel like had I been better informed I would have been better prepared to deal with all the challenges. A lot of what I've learned has been hands on and learning online — educating myself online because each child is so different, and their care requires different approaches.' At the same time, Nellie acknowledged her family as an incredible support system. She also received valuable assistance from a regional center near her home, calling the staff 'a great source of support'.

Moreover, the pleasures of motherhood are not lost on Nellie. She had always wished to become a mother and now receives 'four times the love back'. She continued, 'It's taught me how to be independent — I had to learn how to be assertive, and it taught me

compassion.' She conceived another child "the good old-fashioned way" after being sleep deprived, stressed out and broke. Had we been able to, we would have had even more children!! The only time I was afraid was when the doctor put [the fifth single child] on my chest right after birth and I didn't know what to do.'

Nellie discussed the future prospects of her three quadruplet sons. 'Michael and Joseph will live with us for the rest of their lives. They attend an adult program that they love! They are happy on the ranch, and they love the animals we have. Erik is legally blind, but he has goats that he tends to, enjoys social media, and looks forward to having a girlfriend!' She also encourages prospective quadruplet mothers to educate themselves about multiple birth risks. Nellie does not advocate selective reduction, but respects everyone's individual choice in the matter. She added, 'You definitely have to be a spur of the moment type of person because planning a routine is *very* difficult when you have four individuals with different needs — even if they are all healthy, it's definitely a challenge!' Nellie also noted that she and her husband José have weathered great challenges, but their strong relationship pulled them through with success. She ended by emphasizing that, 'It is important as a mom to take care of yourself, to not burn out. You are no good if you put everyone before yourself. You need to set aside time for yourself and fight feelings of being selfish. Sometimes we let guilt get to us . . .'

Twin Research Reviews

Antenatal Corticosteroids and Twins' Neonatal Outcomes

Improving the developmental outcomes of twins is a high priority among the medical community. A collaborative effort on the effects of antenatal corticosteroids on the outcomes of multiple birth babies was undertaken by researchers in Canada, Australia and the United Kingdom (Socha et al., 2022). Records from MEDLINE, PubMed, EMBASE, and the Cochrane Library were reviewed from inception through August 12, 2021, and a meta-analysis was presented. It was found that administering antenatal corticosteroids was linked to reduced odds of infant mortality and respiratory distress syndrome in preterm twins; however, results

were inconclusive for other outcomes — for example, retinopathy of prematurity and intraventricular hemorrhage. Noting that studies on the effects of antenatal corticosteroids are limited, it was recommended that future studies along these lines continue, especially using nonrandomized trials — the data analyzed here came from randomized studies.

Fathers of Twins

Relative to mothers, little systematic research has been directed toward uncovering the parenting experiences of father of twins. Consequently, it was gratifying to find a recent analysis along these lines by a Norwegian investigator (Heinonen, 2022). Six fathers participated in response to a notice about the study posted on the Multiple Birth Association's website. The six fathers provided written descriptions of their experiences and took part in a parenting discussion that followed. Fathers ranged in age from 31 to 50 years of age, and twins ranged in age from 2 to nearly 9 years.

The data were analyzed by qualitative methods, yielding several key themes: twin fatherhood grows naturally; strengthening of twin fatherhood occurs by fathers being present and involved; fathers develop a relationship with each twin and with both twins; and making space for multiple fatherhood. Heinonen (2022) focused on the last two themes. It was concluded that (1) fatherhood is a special time and affects children's health and wellbeing; (2) fathers wish to create a close bond with their twins by being present and involved; and (3) father look to the future with respect to their relationship with their twins. Closer associations between healthcare providers were viewed as essential for facilitating fathers' role in their evolving relationship with their twins. Missing from this analysis was the zygosity of the twin pairs and whether there were other children in the family. Both of these variables may have affected the themes that emerged from this study. The study was also very limited in terms of the sample size, raising the possibility that it was unrepresentative of the population of twin fathers.

Doppelgängers and Similarity

In 2022, a research team from Spain, headed by Manel Esteller (Joshi et al., 2022), examined the genetic and behavioral similarities of unrelated look-alikes or doppelgängers (DGs). I have been interested in such pairs and have reported the following findings: (1) DGs show negligible personality resemblance, compared with MZ twins reared together or apart, indicating that MZ twins' personality similarity is linked to their shared genes, not to their common treatment by others; and (2) Unlike MZA twins, DGs do not generally form close attachments when they meet, underlining the importance of shared traits (and probably perception of those traits) in evolving social relations (Segal et al., 2018).

The Spanish team looked at associations between shared genetic variants and various measured and self-reported traits. They found that unrelated individuals with unusual facial resemblance share common genotypes, but differ at their epigenome and biogenome. Within-pair correlations were found for height, weight, smoking and education. It was suggested that 'These findings do not only provide clues about the genetic setting associated with our facial aspect, and probably other traits of our body and personality, but also highlight how much of what we are, and what defines us, is really inherited or instead is acquired during our lifetime' (Joshi et al., 2022, p. 2). It will be of interest to follow this study as it (hopefully) continues. Recall, however, that I found little personality similarity in the DGs I studied, so perhaps the Spanish

study can shed light on this lack of resemblance; the research team did not gather data or compare resemblance in the DGs' personality traits. Personality is a complex trait with a demonstrated genetic component (Knopik et al., 2017). It is also appropriate to recall a comment from my late colleague Dr David Rowe (1994), who stated, 'Personality and temperament reside in the brain, not in a face' (p. 48).

Monozygotic Co-Twin Difference in Asymmetric Pigmented Paravenous Chorioretinal Atrophy

Researchers at the Moorfield Eye Hospital and Institute of Ophthalmology in London presented a case study of MZ co-twin discordance for asymmetric pigmented paravenous chorioretinal atrophy (PPCRA; Fischer et al., 2022). PPCRA is a rare eye disorder in which pigments accumulate along the retinal vein of the eye. Symptoms are not displayed in some cases, while blind spots or night blindness affects other individuals. Males are more frequently affected than females. The underlying cause of the condition is unknown, but appears to involve both genetic and nongenetic factors (DoveMed, 2022). Only one previous case of MZ co-twin discordance has been reported (Small & Anderson, 1991).

The pair in question included 48-year-old MZ male twins whose zygosity was confirmed by short tandem repeat analysis. The proband had experienced reduced near vision when reading and difficulties driving at night for the past two years. Examination revealed 20/20 visual acuity, normal color vision and outer retinal atrophy with intraretinal pigment migration along the retinal vein, consistent with PPCRA. His co-twin showed no visual impairments, nor did his parents, three nontwin siblings or five children. His maternal grandmother had had glaucoma and his late maternal aunt had experienced blindness due to an unknown cause. Previous case studies have suggested that PPCRA may be explained by X-linked inheritance, mosaicism due to germline mutation or somatic mutation, or unspecified nonhereditary events.

Lawsuit

MZ female twins, Kayla and Kellie Bingham, were accused of cheating on a medical school examination, based largely on their high degree of matched multiple-choice responses. I was interviewed about this case beginning in 2016 and served as an expert witness in their November 2022 trial. The evidence I cited consisted of the wealth of studies showing MZ twins' consistently higher concordance on tests of general intelligence, special mental abilities, speed of response, interests and related behaviors, compared with all other kinship pairs. I also described other examples of MZ twins who performed alike, despite taking tests in separate locations. Happily, the jury decided in favor of the twins whose reputations have been restored — the situation forced the twins to leave medical school and to change fields; they recently completed law school at another institution. Additional information about this case is available in Smith (2020). My December 13, 2022 CNN Evening News interview about this case can be viewed at https://us.vocuspr.com/ViewNewsOnDemand.aspx?Email=ckeung%40fullerton.edu&date=12%2f14%2f2022+10%3a50%3a46+AM&ArticleID=3523961_28521_119763809.

I have been involved in previous cases involving twins accused of cheating (Segal, 2017). It is important to bring these cases to attention to prevent them from recurring. Educating both behavioral science and medical science professionals, and the general

public with respect to MZ twins' matched intellectual abilities is a high priority.

In the News

Opposite-Sex Twin Holocaust Survivors

I have heard many extraordinary stories of events leading to the reunions of separated twins, but none as riveting as the one reported in *The Australian* (Stewart, 2022). Philip Maisel and his twin sister Bella were from Vilna, which was a part of Poland before the outbreak of World War II. German soldiers entered their town, placing Phil and his father in a Jewish ghetto. Bella was arrested and charged with belonging to the Polish underground. Both twins were put into concentration camps. After the war, Phil was in Germany and in conversation with a man who commented on his unusual accent, saying that he had heard the same accent from a woman in a displaced persons camp. Despite the slim chance that the woman could be his twin, Phil motorcycled approximately 90 miles to the camp in Landsberg to find out. Bella, who had assumed her twin brother was dead, described her reaction when she saw him again: 'I couldn't believe it. We looked at each other and we couldn't talk. I was just so incredibly happy.' The twins now live in Melbourne, Australia. Phil is an active member of the city's Holocaust Center and has recorded 1400 testimonies from survivors.

Twin Models at Gucci

Sixty-eight pairs of identical twins modeled Gucci dresses as part of Milan's Fashion Week, held in September 2022 (Cartner-Morley, 2022). The twins were recruited at the annual Twins Days Festival, which takes place in Twinsburg, Ohio. During the show, the audience was divided and seated in two separate rooms, unaware that they were watching twins. As the show ended, the screen that divided them was lifted and each twin joined hands with their co-twin. The creative director, Alessandro Michele, believes that fashion speaks to 'otherness'. I have noted that only identical twins truly know how they look in a particular outfit, or how they appear as a thinner or heavier version of themselves. Michele dedicated the program to his mother, Eralda and her identical twin sister, Giuliana, whom he calls his 'twin mums'.

Twins With Different Fathers

A 19-year-old woman from Mineiros, Brazil was stunned to discover that she had delivered heteropaternal twins — twins with different fathers (Steinberg, 2022). Knowing she had had sexual relations with two men on the same day, she was eager to know the identity of the father. Her interest increased as the twins approached their first birthday — she began to question who the real father was, most likely based on the twins' physical features. She obtained a DNA sample from one of her partners, but he was related only to one of her twins. The twins are now 16 months of age and are being cared for by one of the fathers — the other father does not appear to play a role in their lives. The identity of the mother and the sex of the children have been kept confidential.

Reunited Twins Enter Same Convent

Identical twin sisters, Elizabeth and Gabriela, born in 1962, were separated at birth when their mother, Cecilia, passed away during the delivery. One twin was raised by the twins' biological father,

while the other twin was raised by their mother's sister. The twins were registered as cousins and their deceased mother was known as their 'Aunt Cecilia' (Cicha & Devoud, 2019).

Because the twins grew up in neighboring towns, they attended the same school. They dressed alike, enjoyed similar activities — both were very spiritual — and suffered from vision problems. They played together often. Given their physical and behavioral similarities, people thought of them as twins, rather than as cousins. Gabriela learned they were twins at age 10 when she overheard a conversation, while Elizabeth learned the truth shortly thereafter. When they decided to enter the Sisters of St. Elizabeth together, the twins' father who had raised Elizabeth agreed, but the man who raised Gabriela was strongly against their plan and prevented the twins from meeting. Eventually, Gabriela conceived a plan to reunite with Elizabeth and her rearing parents finally gave their approval.

Death of a Twin Soldier During Training

Brianna and Alyssa Cahoon were 17-year-old identical twins when they joined the 1st Battalion 34th Regiment at Fort Jackson, South Carolina. Approximately half of all soldiers entering the army undergo training at that site. On August 25, 2022, Alyssa passed away after collapsing five days earlier during a training session. Her cause of death was not immediately determined (Miller, 2022a, 2022b).

Surgical Separation of Conjoined Twins

Three-year-old Brazilian twin boys, born with fusion of their brains, were separated during a 33-hour operation in Rio de Janeiro (*Sky News*, 2022). The twins, Bernardo and Arthur Lima, underwent seven surgeries in total, led by British surgeon, Noor ul Owase Jeelani, from London's Great Ormond Street Hospital. The medical procedures were financed, in part, by Gemini Untwined, an organization that relies on public donations. The charity was founded by Dr Jeelani to further research and treatment of craniopagus twins — conjoined twins connected at the head. The twins are progressing well and are receiving approximately six months of rehabilitation.

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