

News, views and comments

Twins Reared Apart: Zygotic Division After Artificial Insemination/ Twin Research Reviews: Selective Resuscitation of Premature Twins; Scientist Jailed for Editing Twins' Genes; Sexual Arousal Patterns in MZ Twins Discordant for Sexual Orientation; MZ Twins With Jejuno- Ileal Atresia/Media Reports: Twin Girls' Search for a Bone Marrow Donor; Puppy with a Possible Parasitic Twin; Twins in Silicon Valley; Surgical Separation of Craniopagus Twins; Twin-Based *New Yorker* *Magazine* Cartoon; Twin Tragedies

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Abstract

This article opens with the brief life histories of reared-apart monozygotic (MZ) male twins. A New York City program that helped childless couples conceive via artificial insemination from the 1930s to the 1950s is examined as it related to these twins. The frequency with which pregnancies following assisted reproductive technology resulted in MZ twin pairs is also provided. Next, summaries of twin research concerning selective resuscitation, gene editing, sexual arousal and jejuno-ileal atresia are presented. The article ends with media reports of twin girls' efforts to find a bone marrow donor for their father, possible parasitic twinning in a puppy, identical female twins' business venture, the surgical separation of craniopagus twins, a twin-themed magazine cartoon and tragic events involving identical male twins.

Twins Reared Apart: Zygotic Division After Artificial Insemination

Monozygotic (MZ) male twins Lyle Rosenbaum and Steven Leventhal were born in the New York City area in August 1946. Separated at birth and reunited at age 26, they were assigned different dates of birth: August 4 (Lyle) and August 13 (Steven). According to Steven, this was done to keep their birth as twins off the record. Prior to the twins' chance reunion, they were confused for one another on several occasions. A house painter who worked for both families saw photographs of a son in each home that looked exactly alike. Steven's mother, who worked in real estate, had rented an apartment to Lyle's sister. When Lyle brought the key to her office, Steven's mother planted a kiss on his cheek. Other events occurred in which people were puzzled by encountering two identical individuals in different locations, or by mistaking one twin for the other. For example, Steven was fired from his job at

Alexander's department store after he called in sick and Lyle was seen shopping. However, no one pursued these incidents seriously until the twins were young adults, thereby delaying knowledge of their twinship and their eventual meeting.

The encounter that led to the twins' reunion happened when Lyle's Uncle Ruby visited a restaurant and noticed Steven seated at a table with his new bride, wearing a wedding band. The uncle became upset, thinking he and his wife had not been invited to the wedding — until Steven explained that he was *not* the man's nephew. Ruby gave Lyle's telephone number to Steven and Lyle received a call from Steven's mother. She first asked him about the events surrounding his adoption — both twins had been adopted privately, rather than through an agency. She also asked him about his hair — both twins turned gray at a very early age.

Today, at age 73, Lyle and Steven live close to one another in Florida. They are both six feet tall, have a full head of the same gray hair and look remarkably alike. In this regard, they exemplify twin research findings showing that many aging processes are influenced in part by genetic factors (McCleary et al., 1994; Segal, 2012), including height (Silventoinen et al., 2000) and premature graying of the hair (Trüeb, 2005). They see each other often and speak on the telephone nearly every day. They sometimes call each other at the same time so that neither telephone rings. And one time, Lyle was driving down an empty highway in the rain at

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Fig. 1. (a) Identical twins, Lyle Rosenbaum (right) and Steven Leventhal, with Phil Donahue. (b) Identical twins, Lyle Rosenbaum (left) and Steven Leventhal, with their wives. (c) Identical twins, Lyle Rosenbaum (right) and Steven Leventhal, as they are today. Courtesy of the twins.

10:00 pm and had a feeling that his twin brother Steven was also on the road. Three minutes later he noticed a car, pulled over and rolled down his window as the other driver rolled down his window. It was Steven and he had run out of gas.

Following their reunion, Lyle and Steven appeared on the *Phil Donahue Show*, broadcast from Denver. In 1980, they appeared on the *Today Show* where they met Dr Thomas J. Bouchard, Jr., Director of the Minnesota Study of Twins Reared Apart (MISTRA). By then, the MISTRA had been in progress for a year and new twins were being identified and assessed. However, Lyle and Steven were not part of the study because they had had extensive contact as adults for a period of 8 years. Photographs of the twins are displayed in Figure 1.

Years later, Lyle's Uncle Ruby was still so delighted that the twins had found each other. Lyle recalls, 'He would start crying, he was so happy for me. He was a very special person, Uncle Ruby.'

The circumstances surrounding Lyle and Steven's separation at birth are unknown, but events leading to their conception have been well documented. In the 1930s–1950s, Dr Frances Seymour and her husband, Dr Alfred Koerner, were specialists and pioneers in the field of reproductive medicine, based in New York City. Seymour was a gynecologist with interests in infertility and eugenics. Using artificial insemination (AI), in which sperm are injected into the uterus during ovulation, Seymour, Koerner and their associates helped countless childless couples to create families of their own (*New York Times*, 1954). (Note that AI is often referred to as intrauterine insemination or IUI; see attainfertility.com, 2019.) AI was not a new method at that time — according to Dr Iago Galdston, interviewed in 1934, the idea was at least 2000 years old and had been used for at least 130 years (*The Atlanta Constitution*, 1934). In fact, the first documented case of AI resulting in a pregnancy was in 1785, when Scottish surgeon John Hunter advised an infertile husband to collect his semen and inject it into his wife's vagina (Wagoner, 2017).

By 1934, Seymour's treatment was responsible for eight births and five pregnancies. Two of the women who had sought her assistance were prominent businesswomen. Seymour is known for introducing an innovative procedure as part of the process, namely obtaining an X-ray of the uterus with an opaque medium, and evaluating the use of the frog test for determining pregnancy (*New York Times*, 1954). An X-ray was useful for identifying blockages that could prevent eggs from moving through the fallopian tubes into the uterus for fertilization and implantation (attainfertility.com, 2019). The frog test involved injecting female African clawed frogs with a woman's urine. If the frog ovulated it meant that the woman was pregnant, because the human chorionic gonadotropin in her urine would have triggered ovulation in the frog. The frog test may be better known as the Hogben test, after

Lancelot T. Hogben who developed it in 1930 (Hogben, 1946). This test was replaced by immunological test kits in the 1960s, followed by over-the-counter home kits in the early 1970s and the current single-step kit in 1988 (Nuwer, 2013).

In 1934, over 150 children in the USA were conceived via AI (*Newsweek*, 1934). Seymour noted that parents generally do not wish to publicly reveal that their child was created in this way. However, the birth of twin girls in May 1934 was such an overwhelming joy to Salvatore Lauricella and his wife Lillian, of Lawrence, Long Island, in New York that they agreed to tell their story to the press. The twins, Victoria and Marilyn, weighed five and half pounds and seven and a half pounds, respectively. The couple had been trying to have children for 8 years until they were assisted by Seymour. Their success encouraged Seymour to speak more publicly about the details and success of her reproductive program.

Seymour brought a eugenic perspective to her work. She chose sperm donors who had excellent health, held a professional position and had undergone physical examinations to rule out structural defects and various diseases. IQ testing of potential sperm donors was considered unnecessary, given the health and occupational requirements. Donors were paid \$100–\$150 (*The Atlanta Constitution*, 1934). Interestingly, Seymour attempted to match sperm donors' physical and temperamental traits to those of the eventual rearing father. She reasoned that doing so would help the child adapt to the family, due to observed similarities. She was against using the same donor on repeated occasions, both because the wife might object and the existence of a child's half-siblings might prove problematic (Seymour, 1936).

An essay by a child conceived with Seymour's assistance is insightful and informative (Atallah, 1976). She begins by presenting an historical overview of the procedure and then segues into her personal story. Both she and her younger sister, also conceived via AI, did not learn about their biological origins until they were young adults. After feeling 'incredulous', she decided that her parents' choice made perfect sense. Her mother and father were Arab immigrants in the USA, but in their culture the inability to have children brought forth others' contempt and pity for such couples. Adoption was also not an option for her parents because it would have been a clear signal of their infertility.

Throughout her growing up years, Allah recalled no 'irregularities' in her family structure. However, there were some 'unexplained incidents'. She recalls visiting Seymour's office and taking various psychological and intelligence tests. Seymour praised her 'lavishly' for her performance. She also recalled that Seymour fussed over her and beamed like a surrogate parent. Lyle, one of the reared-apart twin brothers mentioned above, remembers taking tests in an office, some of which involved 'fitting in blocks'. His twin brother Steven does not share this particular memory, but he might have been

similarly tested. Steven does recall that he was observed while out playing basketball.

There is no available information as to how many children conceived with Seymour's assistance were tested, why they were tested and what was done with their data. The number of twins that resulted from Seymour's efforts was also not reported. She did present her material at conferences, but whether or not she discussed the children's test findings is unknown. Her 1944 exhibit at the Medical Society of the State of New York involved '110 elaborately authenticated cases'. The material included complete records (except for names), but dates, notarizations, letters, canceled stamped envelopes from patients and physicians, some original birth notices and X-ray films were on display (*New York Times*, 1944). I tried to determine the current location of these materials, but my efforts were unsuccessful (A. Shaner, personal communication, October 22, 2019).

The more recent frequency of conceiving twins and higher order multiples via AI (IUI) is of interest. In a sample of 353 couples studied between 2002 and 2005, French researchers Merviel et al. (2010) reported 153 pregnancies out of 1038 IUI cycles. Nineteen of the pregnancies (13.5%) were twins, but none were triplets or more. The proportion of twins declined with age, with the highest number delivered by women aged ≤ 30 (20%), followed by women aged 31–35 (10.3%), 36–40 (5.2%) and >40 (0%). Twinning was higher among women with cervical or anovulatory indications (21% and 22%, respectively) than among women without such conditions. Twinning did not occur in cases of endometriosis (growth of tissue outside the uterus instead of inside; Berkley et al., 2005), ovarian insufficiency or unexplained infertility.

The zygosity of the twins identified by Berkley et al. (2005) was not reported. Ovarian stimulation typically precedes AI, so the release of more than one egg, resulting in DZ twins is likely. The zygosity of the Lauricella twins, whose conception was assisted by Dr Seymour, was not indicated, and the lack of detail available in the only photograph does not allow an opinion. Cellular events behind the zygotic division that gave rise to MZ twins Lyle and Steven are unknown. Speculation suggests that they were born to a relatively young mother who may have had a family history of MZ twinning, known to have a partial genetic component (see Segal, 2017). Future research in reproductive medicine will, hopefully, provide information that will inform our knowledge of all twinning processes.

Twin Research Reviews

Selective Resuscitation of Premature Twins

Selective resuscitation (SR) refers to the provision of resuscitative procedures to one, or some, members of a multiple birth set, but not to all. Resuscitation is typically necessary in the event that infants are born at 23 weeks' gestation and one twin has a serious anomaly. Parents may be offered the choice as to which child to resuscitate, but as Bizzarro and Mecurio (2009) note, physicians may not feel that parental choice is ethical. To illustrate, opposite-sex twins were delivered at 23 weeks, with the female weighing 650 g and the male weighing 510 g. An online Outcome Estimator to help determine infant outcome was made available by the National Institute of Child Health and Human Development's Neonatal Research Network. This tool combines birth weight, gender, gestational age, birth status (single vs. multiple) and receipt of antenatal steroids to yield a likely

prognosis. In the present case, the female and male co-twins were given chances of survival and survival without impairment of 51% and 35%, and 24% and 13%, respectively. The parents received this information and decided to resuscitate their daughter, but not their son. However, the medical team was uncomfortable with denying care to one twin, a decision that the parents fully accepted. Both twins received treatment.

This article explores a number of interesting and important ethical issues. The authors' conclusion is that there is no ethical justification for denying parental wishes, despite discomfort on the part of their physicians. The question of when to provide SR for both twin and nontwin babies is not new and will likely be examined further in years to come.

Scientist Jailed for Editing Twins' Genes

Chinese scientist He Jiankui was sentenced to a 3 years' prison term and fined the equivalent of \$430,000 for editing the genes of a pair of female twins (Baert, 2019). He had allegedly performed the procedure to provide the twins with immunity to HIV infection. Two of his colleagues were also sentenced. The court found that none of the three were qualified to work as doctors and that all three had violated China's regulations and ethical principles. In fact, they had forged ethical review materials and recruited couples in which the husband was HIV positive.

The technology behind gene editing is considered unsafe and unpredictable in that it can cause mutations in genes situated close to the genes of interest. Therefore, it is illegal in most countries for use in human reproduction, although permissible for some research-related purposes. For example, Great Britain allows scientists studying the causes of miscarriage and infertility to edit the DNA of embryos.

Sexual Arousal Patterns in MZ Twins Discordant for Sexual Orientation

There is concern that self-report measures of sexual arousal may have limited validity. As such, Watts et al. (2018) conducted a twin study of sexual arousal that used two physiological measures, namely genital arousal and pupil dilation, when viewing sexual stimuli showing males or females. The sample included six MZ male twin pairs and nine MZ female twin pairs, all discordant for self-reported sexual orientation. Zygosity determinations were made by DNA analysis.

The researchers found that homosexual twin males responded more strongly to men than to women, whereas the reverse was true for their heterosexual co-twins. However, co-twin differences were significant for pupil dilation only. In contrast, homosexual twin females responded somewhat more to women than men, whereas their heterosexual co-twins responded equally to both sexes. The twins showed the same pattern as nontwin homosexual and heterosexual males and females. Finally, the results from the physiological measures aligned with the twins' self-reported sexual preferences. Watts et al. (2018) speculated that a combination of epigenetic and prenatal hormonal influences might explain their results.

It is important to note that the sample was small and that the twins were recruited via university newsletters, social media sites, online news sites for heterosexual individuals and gay pride festivals. It is therefore possible that these methods attracted an unrepresentative sample of discordant twin pairs. It would be

worth repeating this study with larger samples drawn from population-based registries.

MZ Twins with Jejuno-Ileal Atresia

Jejuno-ileal atresia is a congenital condition characterized by discontinuity of the bowel lumen (opening inside the bowels) and consequent intestinal obstruction in newborns. The present case study from Zimbabwe adds to the available case reports of 17 twin pairs concordant for intestinal atresia, 15 of whom are MZ and 1 of whom is DZ, consistent with genetic influence; zygosity determination was not provided for one pair. The twin type classification of the male twins in the present report was MZ, based on 'zygosity tests' (Mazingi et al., 2019).

The twins in question were born to a 21-year-old mother at 34 weeks' gestation. The pregnancy was uneventful and the twins appeared healthy at birth. On their second day of life, neither twin had passed meconium and they exhibited bilious vomiting and jaundice. The twins were referred to the University of Zimbabwe's Parirenyatwa Hospital at day 9. Supine radiographs suggested intestinal atresia in Twin 1 and jejunal atresia in Twin 2; they survived until days 19 and 18, respectively. Their parents were advised to discuss future fertility plans with the obstetric and surgical team for appropriate monitoring and treatment. The investigators noted that prompt diagnosis and referral for intestinal atresia can improve the chance of a positive outcome, but they noted that that goal is challenging to achieve in a developing country.

Media Reports

Twin Girls' Search for a Bone Marrow Donor

Nine-year-old identical twin girls Ava and Leah Clements have been labeled the most beautiful twins in the world (*Inside Edition*, 2019; Wanjiru, 2019). These popular twins have been modeling children's clothing for the last 2 years, but they recently embarked on a different quest. Their father, Kevin Clements, once a close qualifier as an Olympic swimmer, has been diagnosed with leukemia and needs a bone marrow donor. The twins and their family have joined with DKMS.org and are using social media to identify a suitable donor.

Puppy with a Possible Parasitic Twin

A puppy named Narwhal has become famous due to the unusual outgrowth of skin on his forehead. He was named after a marine animal that has a tusk coming out of its face (Preston, 2019). Dr Margret Carsal, a professor of veterinary medicine at the University of Pennsylvania, suspects that Narwhal is a parasitic twin, resulting from asymmetrical division of a fertilized egg. She noted that the fur above Narwhal's facial appendage grows in a backward direction, suggesting that the extra body part comes from the rear end of the parasitic twin. Dogs are typically born in litters, similar to fraternal twinning, in contrast with identical twinning, which is extremely rare. However, a previous example of possible parasitic twins concerned a puppy with extra hind legs protruding from its belly. These cases are consistent with parasitic twinning, but they are difficult to prove. Parasitic twinning does occur in humans. A comprehensive review of the different types of twins, including parasitic twins, is available; see Spitz et al. (2018).

Twins in Silicon Valley

Kerry and Anna Wang are identical twins and the co-founders of *Searchlight* (Chan, 2019). Their company develops software designed to help employers assess a job candidate's references, leading to more diverse teams. By doing so, greater emphasis is placed on candidates' references, relative to resumes. Their idea came from their own personal experiences. The twins graduated from Stanford University in 2018 with BA and MA degrees. While attending school, they interned at McKinsey & Co., but their assignments were in computer interaction design (Kerry) and artificial intelligence and machine learning (Anna). Despite these different internships, their resumes were extremely similar, but their references set them apart. This observation inspired them to take their product to Silicon Valley, for which they were able to raise \$2.5 million. Their claim is that hiring managers can gain more information from references than from a 45-min interview.

The Wang twins are first-generation Chinese-Americans. They believed it was important for them to repair a problem that they had experienced during the process of interviewing for jobs.

Surgical Separation of Craniopagus Twins

A 50-h surgical session successfully separated conjoined twin girls Safa and Marwa Ullah (Hein, 2019). The 2-year-old twins were born in Pakistan, but in October 2019 they were flown to London for an operation at the Great Ormond Street Hospital. The medical team included craniofacial specialists, neurologists, psychologists, nurses, radiologists, and physical therapists. The twins, known as craniopagus twins, were joined at the head. Following 3-D technology to determine the best way to conduct the surgery, the team separated the brains and blood vessels, then inserted a piece of plastic between them. The twins were released from the hospital on July 1, 2019, and will remain in London for continuing care.

Twin-Based New Yorker Magazine Cartoon

An eye-catching cartoon shows an embryo about to divide into two mirror-image portions, eventuating in identical twins (Schwartz, 2019). The caption reads 'I think we should be other people'. Of course, identical co-twins *are* other people — they are never exactly alike in appearance or behavior, but they are more alike than any other pair of people (Segal, 2017).

Twin Tragedies

Two recent tragedies involving twins have been reported. In northern California, 16-year-old identical male twins Anthony and Michael Angelo Urista were visiting a friend in need on Christmas night (Calicchio, 2019). The driver lost control of the car, which then hit a tree and a utility pole. Another passenger, their Dublin High School classmate Javier Ramirez, was also killed. The deaths of the three young men are understandably difficult for their families and their community.

In Sevenoaks, England, law enforcement officers reported that 32-year-old identical male twins Billy and Jose Smith were found hanging from a tree (TMZ, 2019). The Smith twins had starred in *My Big Fat Gypsy Wedding*, a series broadcast on TLC. The show follows the lives of Irish traveler families. It appears that the twins made a suicide pact after Joe was diagnosed with cancer, and Billy claimed he could not live without his brother. Joe had told his family that as of 2 months ago, he was declared healthy. It is possible that this was not the case, or that the cancer had recently returned.

Suicide has a demonstrated genetic component (Voracek & Loibl, 2007), but the frequency of joint suicide in twins and siblings is unknown. However, such cases have been reported in the psychiatric literature (Berman, 1996; Kallman & Anastasio, 1947) and in the media (Kleiman, 1975; Schmidt, 2018). Journalists identified the two sets of twins as identical, and both sets appear to be identical, based on my inspection of their photographs.

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