Naturally occurring higher order multiple births are high risk and rare. The rate of triplets+ (triplets, quadruplets and more) did, however, increase by 400% between 1980 and 1998, due to the increased availability of artificial reproductive technologies and advanced maternal age at conception. In contrast, the last decade witnessed a steady decline in the birth rate of triplets+. Statistics provided by the Center for Disease Control show a rate of 161.8/100,000 triplets+ births as of 2005, compared with 176.9/100,000 in 2004 (Martin et al., 2007). The birth rates of quadruplets, quintuplets and other higher order multiples, examined separately, also decreased. These downward trends have been explained by the American Society of Reproductive Medicine’s (ASRM) recommendations for limiting the number of embryos transferred in assisted reproductive procedures.

Medical professionals, developmental specialists and the general public are captivated by these extraordinary births, but not necessarily for positive reasons. Physicians emphasize the health risks to mothers and infants. Developmental specialists underscore the physical and behavioral delays suffered by many premature infants. The public points to the parental challenges posed by raising multiple birth children.

A pressing concern is the establishment of appropriate guidelines for embryo implantation. Revised recommendations, released in 2004 by the ASRM and the Society for Assisted Reproductive Technology (SART), favor the transfer of no more than one to two embryos in a single procedure for women under 35 years of age, barring unusual circumstances. The transfer of two to three embryos, at most, is advised for women between 35 and 37 years of age. Four embryos, at most, are advised for women between 38 and 40 years of age, and five embryos, at most, are advised for women above the age of 40 years (ASRM Guidelines, cited in Medical News Today, 2006). Establishing appropriate guidelines and prenatal counseling programs for families undergoing fertility treatments are important goals.

Reappraisal of assisted reproductive practices has received recent medical and societal attention, given the January 26, 2009 birth of octuplets to a 33-year-old Southern California woman. Nadya Suleman, a mother of six children all artificially conceived, had been implanted with her six remaining embryos. Not only were all six implantations successful, but two of the embryos divided to produce two monozygotic (MZ) twin pairs. The reproductive, developmental and rearing issues raised by this case have been extensively debated, and will not be revisited here. The present essay considers the unusual research possibilities posed by these octuplets and other higher order multiples. However, this exercise is not intended to detract from the serious physical and emotional issues associated with their birth.

Permutations and combinations are ways of organizing members of a set into separate subsets. Permutations are ordered sequences of elements, whereas combinations are unordered. For example, a pair of DZ triplets (A, B and C) would yield six permutations...
if the goal was to arrange them in subsets of two: AB, BA, AC, CA, BC and CB. In contrast, this same set of DZ triplets would yield only three unique pair combinations: AB, AC and BC. Twin researchers have often included triplets in their data files in the form of both permutations and combinations. Combinations yield unique pairs that are counted only once, whereas permutations would yield additional pairs, utilized in double entry data procedures.

The possibilities raised by organizing octuplets into smaller multiple birth sets are striking. The results are displayed in Table 1 below; formulas for computing these values and a website for calculating them are also provided. The number of permutations, especially for septuplets, is staggering. However, the most useful pairing for psychological and medical research would most likely be twins. Investigators could take advantage of the 56 twin pair permutations and 28 twin pair combinations yielded by the octuplets.

Other interesting pairings not displayed in Table 1 are also possible. It is known that four of the Suleman octuplets are members of two MZ twin pairs. Allowing attention to twins, the octuplets provide 26 unique DZ twin pairs, as well as two MZ twin pairs. At present, the gender of the four MZ pairs is unknown (although one MZ twin pair must be male because the octuplets include only two female infants). If zygosity is ignored, the yield is 16 same-sex pairs (15 male and 1 female) and 12 opposite sex pairs.

The 26 DZ twin pairs referenced above are unique with respect to individual pair members, but not with respect to pair relatedness. Consider that the octuplets include 4 individuals who are part of an MZ twin pair (A1, A2 and B1, B2), leaving four individuals who are fully DZ (C, D, E and F). A1 can be paired with C, D, E and F, yielding four genetically unique DZ twin sets. However, if A2 is paired with C, D, E and F this produces four genetically equivalent DZ pairings. Similarly, B1 can be paired with C, D, E and F, resulting in a different set of four genetically distinct DZ twin sets, while B2 paired with C, D, E and F yields genetically equivalent pairings. One other unique DZ twin pair can be derived by pairing A1 with B1; the remaining pair (A2 - B2; A1 - B1 and A1 - B2) are genetic replicas of A1 - B1. Other unique DZ twin sets include C - D, C - E, C - F, D - E, D - F and E - F, for a total of fifteen.

Comparing similarities in behavioral and physical development, both within and between related MZ and DZ twins raised together, is potentially very informative. One of us (NS) described this approach in *Indivisible by Two: Lives of Extraordinary Twins* (Segal, 2007) with reference to a naturally conceived MZ-DZ male quadruplet set. The two sets of MZ co-twins displayed similar eating and sleeping patterns as infants, whereas the DZ co-twins (created by pairing members from the two MZ sets) displayed striking differences. The quads’ mother intended to ‘decouple’ the twins by having each child room with a DZ co-twin, but this experiment failed; the children’s contrasting behaviors made this arrangement difficult. Consequently, the members of the MZ twin pairs were kept together. The quads’ parents saw these events as an important lesson in the how genetic factors shape early behaviors.

The future of the California octuplets is uncertain. Hospital personnel have decided against releasing the babies to their mother until their safety can be assured. It is unlikely that they will take part in behavioral-genetic studies any time soon. Hopefully, all eight babies will continue to thrive. Note: The last octuplet was released from the hospital in mid-April.

### Twin Research Reviews

#### Natural Twinning Rate

New data from Cardiff and Glamorgan in Wales, drawn from the Cardiff Birth Survey, indicate a rise in the natural twinning rate (Faisal et al., 2008). Pregnancy outcomes were inspected for eight 5-year periods, spanning 1965 and 2004. Total twinning rates (based on natural and assisted conceptions) declined from 13.1/1,000 (between 1965 and 1969) to 10.3/1,000 (between 1980 and 1985). A subsequent upswing was then observed, with a rate of 15.7/1,000 in the years 1995 to 1999, and 2000 to 2004. After excluding iatrogenic pregnancies (twin births due to fertility treatments), it was estimated that the natural age-adjusted twinning rate rose from 10/1,000 (between 1980 and 1984) to 13.3/1,000 (between 2000 and 2004). Factors thought to underlie this trend include advanced maternal age at conception and various nutritional factors, such as multivitamin use. It was emphasized that advanced maternal age alone was probably not responsible for the recent upward trend because the increase was observed across different age groups.

**Note**

The study by Martin et al. (2007) cited above found that the United States’ twinning rate remained stable from 2004 to 2005. Twins were born in 32.2/1,000 live births in both years. This figure includes twins from both natural and assisted conceptions.

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**Table 1**

Organizing Octuplets Into Smaller Birth Sets: Combinations and Permutations

<table>
<thead>
<tr>
<th>Group Size</th>
<th>Permutations</th>
<th>Combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twins</td>
<td>56</td>
<td>28</td>
</tr>
<tr>
<td>Triplets</td>
<td>336</td>
<td>56</td>
</tr>
<tr>
<td>Quadruplets</td>
<td>1,680</td>
<td>70</td>
</tr>
<tr>
<td>Quintuplets</td>
<td>6,720</td>
<td>56</td>
</tr>
<tr>
<td>Sextuplets</td>
<td>20,160</td>
<td>28</td>
</tr>
<tr>
<td>Septuplets</td>
<td>40,320</td>
<td>8</td>
</tr>
<tr>
<td>Octuplets</td>
<td>40,320</td>
<td>1</td>
</tr>
</tbody>
</table>

Note: Permutations: n! / (n - r)! Combinations: n! / r! (n - r)!

Calculations: [http://joemath.com/math124/Calculators/factorial.htm#Permutations](http://joemath.com/math124/Calculators/factorial.htm#Permutations)
Twin Survival at, or Before, 30 Weeks Gestation

Twins are more likely than non-twins to be born prematurely and to suffer greater physical risks. The nature of twins' health outcomes, relative to those of singletons born at, or before, thirty weeks gestation is of interest. British investigators examined the neonatal death rates of 479 twins and 1,538 non-twins between 1998–2001 and 2002–2005 (Ray & Platt, 2009). Mortality rates did not differ between the two groups when restricting the samples to births at thirty weeks. In contrast, twins born between 23-25 weeks gestation showed a higher rate of early and neonatal deaths than non–twins. However, this effect was noted only in the 1998–2001 cohort.

Unique Mirror-Imaging Effects

Mirror-imaging effects occur in approximately 25% of MZ twin pairs (Segal, 2000). Commonly observed reversed traits in MZ co-twins are handedness (left, right) and hair whorl (clockwise, counterclockwise). A recent report documented a rare instance of mirror-image reversal in a female MZ twin pair. The twins were born at 34 weeks with a single chorion and single amnion (Thacker et al., 2009). Each twin was diagnosed with heterotaxy syndrome (HS), a condition involving an abnormal arrangement of the usual left-right body axis. HS affects between 1/6,000 and 1/10,000 individuals in live births. Both genetic and environmental factors have been implicated in the etiology of this disorder. The co-

euros, were taken (Kulish, 2009). A
e rope ladder and a glove left at the
crime scene provided investigators with
DNA that they hoped would help identify
the three suspects. However, one DNA sample was traced to two
people — identical twins, Abbas and
Hassan O. This situation clearly com-
plicates the case because each twin can
claim that his co-twin was responsible
for the robbery. However, police inves-
tigators are now wondering if both
twins were involved since the possibili-
ty of four suspects has been raised.

The article stated that German
policies do not allow for the most
advanced tests that would enable dis-
crimination of the MZ co-twins.
Recent work has demonstrated the
presence of epigenetic differences
between MZ co-twins, as well as
greater epigenetic differences between
MZ than DZ co-twins (Kaminsky et
al., 2009). However, tests that would
allow the correct twin culprit to be
identified (if only one were involved)
are not available.

Twin Robbery at KaDeWe?

Kauhausen des Westens (KaDeWe) is a
famous Berlin department store, the
second largest in Europe after Harrods.
In January 2009, KaDeWe became
famous for a robbery in which watches and jewelry, worth up to 100,000

Twins with Mixed Race Parents

Fraternal twins, Lauren and Hayleigh,
were born in 2001 to Dean Durrant
and Allison Spooner of Great Britain
(Associated Press, 2009). The twins' strik-
ing physical differences attracted
worldwide attention. Lauren has light
skin, red hair and blue eyes, while
Hayleigh has dark skin, dark hair and
dark eyes. It turns out that both their
parents were born to couples from
mixed marriages. Researchers have,
therefore, speculated that the twin
children inherited different sets of rele-
vant genes from their mother and
father. In 2008, the couple made news
again when they delivered a second set
of fraternal female twins, Leah and
Miya. Leah is light-skinned like her
mother (and older sister Lauren),
while Miya is dark-skinned like her
father (and older sister Hayleigh). The
frequency of such twins is rare, yet
may be rising due to the increased
number of mixed marriages.

Twinning Rates in Candido Godoi

The name Josef Mengele is synony-
mous with evil. Mengele was the
infamous Auschwitz physician who
performed brutal medical experiments
on twins, dwarves and individuals
with genetic anomalies (Segal, 1985;
1992). He inflicted unimaginable pain
and suffering on many men, women
and children. The experiments had no
scientific merit, as determined by an
interdisciplinary panel in 1985, in
Jerusalem, at the conclusion of a
public hearing on Mengele's war
crimes. This event coincided with the
40th anniversary of the liberation of
Auschwitz.

News Highlights

Twins Born Together and Apart

Newborn twins from Rochester,
Michigan recently arrived on differ-
dent days, month and years. Tariq Griffin
was born on January 1, 2009 at 12:17
am, 26 minutes after his twin brother,
Tarrance, who was born on December
31, 2008 (Honolulu Star Bulletin,
2009). This event recalled a pair of
DZA female twins who participated in
the Minnesota Study of Twins Reared
Apart. The twins were born on differ-
dent days and in different months,
complicating their search for one
another and delaying their reunion for
some time. Note: I was born on the
same day as my twin sister, just 7
minutes earlier. However, now that we
live on opposite coasts our birth orders
have ‘reversed’ because she celebrates
her birthday 3 hours earlier.

Twins Born Together and Apart

Newborn twins from Rochester,
Michigan recently arrived on different
days, month and years. Tariq Griffin
was born on January 1, 2009 at 12:17
am, 26 minutes after his twin brother,
Mengele’s name surfaced recently in connection with the extraordinarily high twinning rate in Candido Godoi, a small Brazilian farming town (Barrionuevo, 2009). A survey identified thirty-eight sets of naturally conceived twins, born to eighty families residing in a one and a half square mile area. A recent book by Jorge Camaras (2008) (not reviewed by this author; it is published in Spanish) indicates that Mengele visited this region in the early 1960s. He fled Germany at the end of World War II to avoid capture for his horrific concentration camp activities (Evans, 2009). It has been suggested that Mengele conducted experiments that resulted in the town’s high twinning rate. This idea is supported by a local doctor who believes that the citizens (many of German descent) are withholding information. Others disagree, claiming that the explanation for the elevated twinning rate remains unknown.

Any link between Mengele and the high twinning rate in Candido Godoi is untenable for a number of reasons. According to reporter Barrionuevo, no one can prove for certain that Mengele conducted the alleged twinning experiments. Furthermore, the high twinning rate was widely noticed in the early 1990s, well past Mengele’s death in 1979. There is no known mechanism by which he, or anyone, could produce an effect on the twinning rate years beyond his death. The claim that Sao Pedro, an area of Candido Godoi, has the highest twinning rate in the world has not been confirmed. Finally, why would Mengele do anything to attract attention if he were on the run? Paulo Sauthier, a historian who runs a museum there, regretted any association between Mengele and the people of the town.

Note
The article by Barrionuevo wrongly dismissed genetic factors as possibly responsible for the town’s twinning rate. It stated that ‘a genetic predisposition to twins would be more likely if most of the twin pairs were identical’. Just the opposite is true.

References