

NEWS, VIEWS AND COMMENTS

Tribute to Dr Louis Keith: Twin and Physician Extraordinaire/Twin Research Reports: Influences on Asthma Severity; Chimerism Revisited; DNA Strand Break Repair/Media Reports: Twins Born Apart; Elevated Twin Frequencies; Celebrity Father of Twins; Conjoined Twinning

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The International Society for Twin Studies has lost a valued friend and colleague. Dr Louis Keith, Emeritus Professor of Obstetrics and Gynecology at Northwestern University, in Chicago, passed away on Sunday, July 6, 2014. His life and work with twins will be acknowledged at the November 2014 International Twin Congress in Budapest, Hungary. Next, twin research reports on the severity of asthma symptoms, a case of chimerism, and factors affecting DNA breakage and repair mechanisms are reviewed. Media reports cover twins born apart, elevated twin frequencies, a celebrity father of twins, and a family's decision to keep conjoined twins together.

Tribute to Dr Louis Keith: Twin and Physician Extraordinaire

The *International Society for Twin Studies* (ISTS) has lost a valued friend and colleague. Dr Louis Keith, Emeritus Professor of Obstetrics and Gynecology at Northwestern University, in Chicago, passed away on Sunday, July 6, 2014.

Louis Keith was a founding member of ISTS (1974), a society he nourished and treasured throughout his lifetime. Together with his identical twin brother Donald, Louis was a familiar presence at every triennial (and now biennial) meeting. He offered marvelous insights into many areas of twinning, in addition to his particular areas of expertise, namely the biological bases and gynecological aspects of twinning.

One of my earliest associations with Louis was in Chicago where, in September 1988, he organized the VI Working Party on Multiple Birth as part of the ISTS. It was a terrific event, bringing together many experts who addressed a di-

verse array of topics. Some years later, I appeared with him on a television talk show where we disagreed over twins' ability to communicate telepathically. Louis believed that twins could exchange information in this way, but I never saw credible scientific evidence to support that claim. The audience, composed almost completely of identical twins, sided with Louis. I held to my view and Louis respected my position.

Louis's life and work touched those of many of our colleagues. Professor Paolo Parisi, in Italy, wrote:

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**FIGURE 1**

Louis Keith.

I first had the privilege of meeting [Louis] at the First International Congress on Twin Studies in Rome in 1974, and our encounter gave start to a collaboration, and above all a friendship that was to last ever since. He supported from the beginning our efforts to promote twin research, and was in fact greatly appreciated by Luigi Gedda and other founding fathers, and he was one of the main forces behind the establishment and subsequent development of the *International Society for Twin Studies*, with a commitment that characterized his entire life. With him goes an important part of our professional life and scientific history.

Louis was a prolific writer and his books on the biology of twinning are among the best sources available. In my view, one of his best works is *An Atlas of Multiple Pregnancy: Biology and Pathology*, coauthored with Geoffrey Machin (Machin & Keith, 1999). Another source that I frequently consult is *Multiple Pregnancy: Epidemiology, Gestation and Perinatal Outcome*, coedited with Isaac Blickstein (Blickstein & Keith, 2006); Louis's twin brother Donald served as an Associate Editor on that volume and David Teplica contributed his marvelous photographs.

With the next Twin Congress occurring in November 2014, I am reminded of a photograph taken at one of the final sessions at the 2012 meeting in Florence, 'Books, Media and Twins'. The entire front row was filled with twins: two intact twin pairs (Adam and David Tárnoki; Louis and Donald Keith) and three single twins (art student Mònica del Rey Jordà, filmmaker Anna Van der Wee, and myself). That unposed picture underlines the great interest and personal investment that twins share in research and in friendship, both within and between pairs. This particular photograph may also be the last one taken of the Keith twins together at an ISTS event. It was published in *Twin Research and Human Genetics* (Segal, 2012).

My ongoing studies of twin loss have highlighted the many unique consequences of losing a twin, for the surviving co-twin and for family and friends. These studies did not, however, prepare me for the loss of Louis Keith.

Twin Research Reports

Influences on Asthma Severity

It is well known that asthma tends to run in families, demonstrating a genetic component. However, factors affecting the severity of the overall condition, as well as the severity of specific symptoms, are less well understood. A Danish twin study investigated this issue using 256 intact twin pairs (89 MZ, 167 DZ) and 63 individual twins (Thomsen et al., 2012). Participants were among the 21,133 individual twins who filled out a health and lifestyle inventory, indicating that at least one co-twin was affected with asthma. Twins in the final sample completed a clinical interview addressing their symptom severity, and underwent various allergy tests and respiratory measurements.

It was found that the symptom severity of asthma overall appears to be genetically influenced, estimated at 26%. The remaining variation was explained by non-shared environmental factors. These figures remained constant after controlling for age, sex, current airway infection, smoking, and body mass index. In addition, the severity of specific symptoms (e.g., wheezing and shortness of breath) was associated with genetic factors (12% and 17%, respectively). These two symptoms did, in fact, show a shared underly-

ing genetic component. However, genetic influence on the severity of asthma, in general, was not demonstrated.

Chimerism Revisited

Chimerism refers to the presence of cells in an individual that originate from more than one zygote. An update on a previously studied pair of monochorionic dizygotic (MC/DZ) twins, and a review of chimerism in such pairs, was presented by Chen et al. (2013).

The MC/DZ twins in question were studied in 2010 because of their discordant chimerism and twin-to-twin trans-fusion. Only three other such cases (out of nine MC/DZ twin pairs) have been described in the literature. The male twin showed 30% 46.XY cell lines and 70% 46.XX cell lines at birth, while his female co-twin showed 18% 46.XY cell lines and 82% 46.XX cell lines. Buccal smears taken when the twins were 6 months of age showed consistent findings. Neither twin showed congenital abnormalities, and at age 9 months, their external genitalia appeared normal. A 2010 report of another MC/DZ twin pair showing aplasia (defective development) of the uterus and fallopian tubes prompted a comprehensive updated evaluation, when the

twins in the present report were young children. Both twins showed normal physical development, although both exhibited below average language expressivity. Both twins also showed more XX than XY cells in their peripheral blood samples, with no evidence of chimerism in their somatic cells, based on buccal smears.

The authors concluded by noting that (1) blood chimerism may persist from birth until at least 2 years of age, (2) chimerism in humans most likely occurs more frequently than is suspected, and (3) the risk for MC/DZ twins appears to be enhanced following assisted reproductive technology.

DNA Strand Break Repair

Environmental sources, both exogenous and endogenous, can damage DNA. Understanding the extent to which genetic and environmental factors affect DNA repair mechanisms has been lacking. A twin study designed to fill this knowledge gap was recently undertaken by researchers in Denmark (Garm et al., 2013). Twin participants were 198

pairs (94 MZ, 104 DZ) drawn from the Danish Twin Registry. The same individual performed all analyses to minimize experimental variability.

Four strand break repair measures were assessed: endogenous single strand break (SSB), single strand break repair (SSBR), double strand break repair (DSBR), and γ -H2Ax response (DNA damage signaling response). Intraclass correlations for these measures did not demonstrate genetic effects on the SSB measures. However, moderate genetic effects on the DSB measures were suggested. Biometrical models specifying shared and non-shared environmental effects showed the best fit to the repair variables, with the exception of SSBR. The best-fitting model for SSBR was an E model, specifying non-shared environmental variance. The researchers noted that environmental events, measurement errors, and batch effects may have masked genetic factors relevant to the DNA repair mechanisms under study. They urged future studies to consider factors affecting repair mechanisms in response to specific environmental events.

Media Reports

Twins Born Apart

Twins are sometimes born days or even weeks apart, as were twin boys, Alexandre and Ronaldo da Silva (Moisse, 2014). Their mother, Lindalva Pinheiro da Silva, age 35, delivered Alexandre at 24 weeks gestation when her waters broke. It is estimated that 50% of infants born this early do not survive and those who do often experience health difficulties. Alexandre weighed 1 pound, 10 ounces at delivery and while he survived, he will most likely require corrective surgery for a hernia and for eye problems. However, following Alexandre's delivery, the pregnancy continued because da Silva's contractions eased and her cervix closed. This allowed the other twin, Ronaldo, to be born 3 weeks later, weighing 3 pounds, 3 ounces.

The da Silva twins will not be entered into the *Guinness Book of Records*. The longest recorded birth interval for twins is 87 days (Bennell-Smith, 2013).

Elevated Twin Frequencies

John F. Kennedy High School in Plainview–Old Bethpage, New York included nine sets of twins and one set of triplets in their 2014 graduating class (CBS News, 2014). The multiples included a mix of MZ and DZ pairs, as well as males and females. A tenth set of twins would have been present had they not moved from the area. Ten twin pairs and one triplet set out of a class of 371 means that 6% of the students had multiple birth status, approximately double the 3% figure among western nations. This increase is most likely tied

to the increased use of assisted reproductive technologies and delayed child bearing by mothers (Martin et al., 2012).

Celebrity Father of Twins

Actor Neil Patrick Harris won the 2014 Tony award for his leading role in the Broadway production of *Hedwig and the Angry Inch*. In addition, he has starred in the Los Angeles-based sitcom *How I Met Your Mother*, the *West Wing*, and *A Very Harold & Kumar 3D Christmas*.

Harris is also known for being the father of 3-year-old twins, Gideon and Harper, and will be relocating to New York with his partner and young children (Kindelan, 2014). The twins have visited his dressing room on many occasions and have witnessed his transformation from father to the character he plays. (Hedwig is a transgendered woman from East Berlin who underwent unsuccessful sex reassignment surgery.) Harris's twins pose a lot of questions about his career and he wants them to understand exactly what he does for a living.

Conjoined Twinning

Conjoined twins, Andrew Donovan Lee and Garrett Lee Donovan, were born on April 10, 2014 to an Indiana, Pennsylvania couple, Kody Stancombe and Michele Van Horne (Christensen, 2014). The twins' parents have decided against surgical separation for their omphalopagus twins, who share a heart and liver. Surgery would pose a great risk for the twins' survival, given the particular organs that they share.

The article noted that conjoined twins are rare, occurring in approximately 1/200,000 births. Conjoined twins also represent 1/200 MZ twin births (see Segal, 2000). A recent study from Spain reported a conjoined twinning frequency of 1/152,107, based on data collected between 1976 and 2006 (Martinez-Frias et al., 2009). Male conjoined twins are especially rare, probably due to the generally greater vulnerability of male fetuses to adverse birth events.

This article reminded me of the famous Chulkhurst twins, Elisa and Mary, born in 1100 in Biddenden, England; thus, the name the 'Biddenden Maids'. The twins lived until age 34 at which time Mary became ill and died, and Eliza passed away 6 h later. During that interval, Eliza refused to be separated from her sister to whom she was joined at the shoulders and hips. The image of these sisters lives on in the cakes baked in their town that bear their impression (M. C., 2014). I am grateful to Dr Irving I. Gottesman for giving me a marvelous print of the twins that also includes a bit of their history.

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