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NEWS, VIEWS AND COMMENTS

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New wrinkles on aging and adolescence

Dr Darrick Antell, a New York City plastic surgeon, has been recruiting identical twins to study associations between life history events and aging. He is interested in identifying life history and life style factors accelerating aging in one monozygotic (MZ) twin, relative to the co-twin, as a way of understanding aging in the general population. His efforts, based on 34 MZ twin pairs, reveal that 'people may be more in control of the speed and degree of aging than is currently thought' (p 585).[1]

The notion that our actions may affect some aging processes is highlighted by the accompanying photograph (Figure 1). Depicted are identical female co-twins who look very much alike, except that one twin appears as an 'older version' (p 586) of the other. In my own interview with these twins I learned that neither one was sensitive to their different appearance.[2] Nevertheless, both twins were attracted to Antell's research program because it promised opportunities for adventure, scientific advancement and time together. The cost of the procedure is approximately $12 500 per individual, an expense subsumed by an anonymous benefactor. Twin participants are responsible only for the costs of an anesthesiologist and travel to New York City.[3]

Antell's efforts have attracted considerable attention within the medical community and in the popular press. His work has been featured in magazines such as Marie Claire[4] and Vogue,[5] and he has appeared on television talk shows including Good Morning America and the Today Show. The methods and details of his work are now available in the scientific literature.[1]

Participants in the study ranged in age from 45 to 75 years. They comprised 34 identical twin sets, as diagnosed by Nichols and Bilbro's (1996) standard physical resemblance questionnaire[6] and serological analysis. Skin samples from each twins were analyzed for thickness, distribution and ratio of elastin/collagen (elastin is a protein forming the main constituent of elastic tissue fibers; collagen is a protein that is the main component of white fibrous connective tissue) and changes due to the sun. Twins also completed extensive questionnaires concerning diet, health, medications, exercise and sun exposure. Sun exposure is believed to be responsible for over 90% of skin damage cases.

Results from this study have been promising to scientists and dramatic for twins. Patterning of wrinkles and hereditary blepharotosis (drooping of the eyelid) were similar within twin pairs. In contrast, the severity and depth of wrinkling, skin texture quality and degree of excess skin varied as a function of co-twins' life style differences. A compelling difference occurred in a 60-year-old male twin pair – the heavy smoking twin showed increased amounts of gray hair, relative to his non-smoking brother. Other than smoking habits, the twins' life styles appeared to be the same. Antell explained that smoking shrinks capillaries, reducing blood flow to the skin, causing it to become dry and to wrinkle. Smoking also has adverse affects on hearing via damage to the cochlea, hair cells, antioxidant processes and auditory system vessels.

The day I visited Antell's office a pair of identical female twins, Olvette Mahan and Ynette Sapp, had recently completed surgical procedures. Both twins had undergone a rhytidectomy (operation for reducing the visible signs of aging, commonly termed a face-lift). Neither twin smoked, but Ynette had experienced greater sun exposure and had lost some weight, factors which may have explained her more pronounced wrinkling. At age 71 the twins elected to undergo the surgery, to look more youthful and to look more alike. ('My sister's [Ynette's] smile went up and mine [Olvette]

Photo courtesy: Darrick Antell, MD

Figure 1

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went down'). Both twins were pleased with the outcomes: 'matching facelifts to make us alike again'. The wishes of some twins to restore their identical looks should interest psychologists representing diverse perspectives, especially social psychologists and evolutionary researchers. Future collaborations between plastic surgeons and behavioral scientists might enrich understanding of the significance of physical similarity among relatives.

Antell's naturally occurring co-twin control design is a significant addition to the literature which attempts to identify environmental factors associated with aging. It will be important to follow future outcomes as his twin sample increases. Fraternal twin comparisons would also be useful for revealing interactions between genetic predispositions and environments. It is conceivable that one fraternal twin might suffer greater skin damage than his or her co-twin, despite approximately equal periods of sun exposure. The protective factors in the co-twin, if identified, could contribute to devising appropriate means for resisting the sun's adverse effects. Meanwhile, existing twin studies have addressed other dermatological problems emerging at different points in the life span.

The contributions of twin studies to knowledge of skin conditions in adolescence and adulthood were the focus of a recent comprehensive review.[7] Concordance figures of 72% and 23% for MZ and DZ twins, respectively, were reported for atopic dermatitis (inflammation of the skin caused by an outside agent). Concordance figures of 65% and 23%, for MZ and DZ twins, respectively, were reported for atopic respiratory disorders (difficulty in lung/breathing function from exposure to a foreign substance or trauma). Both sets of findings demonstrate genetic influence on these conditions. Several other dermatological problems have been investigated via twin models, yet many have been limited to case studies of rarely occurring conditions. Fortunately, this is beginning to change as dermatological specialists become increasingly aware of twin research designs.

It is worth mentioning a twin study of acne, no doubt of interest to adolescent twins and their families. This British investigation, using 20 MZ twin pairs and 20 same-sex DZ twin pairs, suggested genetic influence on excretion of sebum (an oily substance reaching the skin through small ducts leading into the hair follicles).[8] In contrast, acne scores (indicating acne severity) did not demonstrate genetic effects. However, the modest size of the sample and qualitative nature of the data prevent firm conclusions concerning the onset and progress of this skin problem. More detailed, quantitative analyses are likely in the future and should allow earlier identification and intervention for individuals at risk. This information should be forthcoming from British researchers associated with the St Thomas UK Adult Twin Registry.[9] Results from 234 MZ twin pairs and 304 DZ twin pairs are indicating genetic influence on acne (as well as eczema and psoriasis). Further study may also check the frustration experienced by adolescents failing to find promising results even after forfeiting chocolates and other foods reportedly linked to acne. Of course, ingesting certain foods might exacerbate the condition in predisposed individuals.

Another new wrinkle on growing older comes from outside the dermatological field. Researchers have examined the X-inactivation patterns of MZ female twins participating in the Longitudinal Study of Aging Danish Twins.[10] DNA was derived from peripheral blood sampled from 71 MZ twin pairs between the ages of 73 and 93 years of age, as well as 33 individuals aged 100 years or more. A provocative observation was greater predominance of one of the two X-inactivated cell lines in elderly female twins, compared with younger female individuals. In other words, the degree of skewing (departure from a random 50:50 distribution of inactive paternally and maternally derived X chromosomes) was greater in the elderly twin sample than in the younger non-twin sample. The MZ twin intraclass correlation of 0.57 for patterning was significant, increasing to 0.84 when several outliers were omitted. This finding suggests genetic influence on human stem cell kinetics. It also raises the possibility that females' longer life span, relative to that of males, may be partly associated with their having two cell lines with different potentials. If true, associations between X chromosome patterning and longevity would require selection for females' more favorable X chromosome line. Males, in contrast, have only a single X-chromosome cell line.

Colleagues have viewed the Danish findings with a mixture of excitement and caution. The results have already raised many questions concerning parallel processes and outcomes in non-humans. The authors of the study noted that in non-human mammals, males (XY) do not live as long as females (XX), but that the reverse is true in birds in which females are heterogametic (ZW). These results offer some support for their twin study conclusions. However, a University of Idaho researcher proposed a more stringent test: paternally derived X chromosomes are always inactive in female marsupials, presumably eliminating effects of selection for the 'better' cell line.[11] Studying this population might reveal other clues concerning biological events tied to male–female differences in longevity.

It is surprising that other issues concerning the varieties of X-inactivation patterns among MZ female twins have not been raised. X-inactivation occurs between 6 to 8 days post conception, so greater differences in patterning may be expected between early rather than late-splitting twins.[12] Researchers have shown this to be the case. Analyses of buccal smears from two-chorion (presumably early-splitting) female twins revealed greater discordance in patterning than those from single-chorion (presumably late-splitting) female twins.[13] This finding suggests the following questions: Do two-chorion female twins show greater dissimilarity in longevity than one-chorion twins? Is the relatively greater predominance of a particular cell line in one co-twin associated with enhanced longevity of that twin? Research along these lines may help us evaluate the significance of these new findings.

Legal argument for common classrooms for twins

Are constitutional rights for placing twins in separate or common classrooms reserved for parents or educators in the USA? A new legal analysis – the first of its kind – grants this responsibility to parents. This significant document, written by Lana

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Larson Dean (an attorney and mother of identical female twins) promises to be a powerful tool for parents challenging mandatory school separation policies for young twins.[14] Many schools prefer assigning twins to different classes to enhance individuality but, as I have indicated elsewhere, these policies are not research based.[2] Researchers combining twin studies and developmental psychology concur that fixed school placement practices should be abandoned in favor of flexible plans that can accommodate the special needs of each twin pair.

Dean's law review article begins with reference to a hypothetical, but realistic portrayal of a couple raising identical twin daughters. The parents are beginning to observe some differences in the twins' personalities and preferences, but are keenly aware of how much the children enjoy each other's company. Their close relationship was underlined when one twin needed 2 days in hospital, causing her normally lively co-twin to become seriously withdrawn. The twins attended a common kindergarten and their parents anticipated continued success when the girls entered the first grade together. They were, however, unprepared for the news that, in accordance with school policy, the twins would be separated. There was no room for compromise or discussion. This is a situation many parents have experienced, but Dean's insightful analysis should reassign this decision-making ability to families.

Arguments cited in this article rest on two previous cases: Meyer vs Nebraska and Pierce vs Society of Sisters, which were tried in United States courts in the 1920s. Both cases are known for establishing the rights of parents to direct their children's education but, paradoxically, parents of twins are urged to avoid invoking these cases when attempting to affect school placement decisions. That is because outcomes of past cases have more narrowly defined the concept of parents 'directing education' (eg parental rights regarding children's schooling would be respected if the family's religious beliefs were jeopardized). Past cases have also restricted the settings in which parents' rights have prevailed (eg parents rights would more likely be upheld in non-educational contexts). Twins' school placement decisions do not involve parental religious practices, nor do they involve the choice of an educational setting. However, they do involve possible infringement on the family, specifically parents' knowledge of the optimal way to raise their twins and twins' trust in their parents to do so.

The concept of right to intimate association is the key to cases of separating twins in school. An intimate association, defined in 1980 by Professor Kenneth Karst, is 'a close and familiar personal relationship with another that is in some significant way comparable to a marriage or family relationship' (p 479).[14] According to Dean, twinship meets the criteria for such a relationship. Given the limited research support for separating twins in school, courts would be likely to decide in favor of parents' rights to choose. There are, of course, other legal complexities related to her analysis, but they are beyond the scope of this column. It will be important to follow a real-life legal application of the arguments in this review.

Medical reports: infections, formations, malformations and surgery

Ear infections Twin research on susceptibility to ear infections demonstrates what parents and physicians have suspected all along: there is genetic influence on the frequency and recurrence of otitis media.[15] Otitis media comes in several varieties, distinguished by the site of inflammation, type of symptoms and etiology.[16] For example, acute otitis media (AOM) refers to inflammation associated with viral or bacterial infection of the middle ear, accompanied by high fever and severe pain. Secretory otitis media is a chronic accumulation of fluid in the tympanic cavity, linked to loss of hearing.

Findings from a prospective analysis of 168 same-sex twin pairs and seven sets of triplets identified between 1982 and 1995 are reviewed. Investigators were from the Department of Otolaryngology and Otitis Media Research Center at Children's Hospital in Pittsburgh, PA.[17] Serological analysis available for 135 twin and 5 triplet sets classified 76 as MZ and 64 as DZ; 138 (99%) were followed for their first year of life (75 MZ and 63 DZ) and 126 (90%) were also followed for their second year (65 MZ and 61 DZ). Measures of interest included the proportion of time children experienced middle ear effusion (excess fluid due to inflammation), number of middle ear infusion episodes and occurrences of acute otitis media. The heritability estimate at age 2 for time with middle ear infusion was 0.73. MZ and DZ twin discordance estimates were 0.04 and 0.37, respectively, for three or more episodes of middle ear effusion, and 0.04 and 0.49, respectively, for episodes of AOM. (Methods for calculating discordance estimates are explained in a different source.[18]) Genetic influence on all three measures was thus demonstrated.

Implications of this study for the care and prevention of ear infections are many. At an early age more aggressive treatment may be provided for children showing initial symptoms, especially those whose older siblings are prone to ear infections. Improving environments, such as avoiding second-hand smoke and large crowds, may also decrease risk of infection.

Dentition Calcification of dental pulp (tissue located in the center of the tooth, or pulp cavity) is common, but its presence in every tooth is rare. Complete pulpal calcification has been associated with systemic or genetic conditions, such as dentinal dysplasia. (Dentinal dysplasia assumes various forms involving abnormal pulp development and root formation.) The first report of MZ twins concordant for multiple pulp calcifications appeared recently.[19] The patient, a 26-year-old identical female twin, showed nearly complete destruction of all pulp chambers, despite an unremarkable medical history. Her identical twin sister showed similar radiological and clinical results. Their symptoms fit most, but not all criteria, for dentinal dysplasia, a finding considered very unusual by the investigators. The fact that these atypical symptoms were present in both members of an identical pair may stimulate new thoughts and inquiries into the nature and progress of their condition.

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Keratoconus The first case of non-identical keratoconus in identical twins was reported in 1995.[20] (Keratoconus is an abnormality of the cornea such that it becomes a rounded apex in the center, rather than showing regular curvature; the 'cone' becomes sharper with age.) This condition occurs commonly in New Zealand (1/2000 in Hawke's Bay in the North Island), but is far less frequent in other nations (eg 1/10 000 in England; 1/40 000 in the Netherlands). Previous to this study only seven other cases of the condition in identical twins had been reported. Symptoms and progression were matched in one pair, but relevant information on the remaining cases was ambiguous. The authors of the present study believe it is the first to describe identical co-twin differences in severity and cone types.

The identical female twins were aged 35 when medically assessed. The pair was raised on a farm so both twins had been exposed to a dusty environment until they were teenagers. Both suffered allergic (atopic) conditions, consistent with observed associations between allergies and keratoconus. One twin was diagnosed with keratoconus as a teenager, whilst the other was diagnosed at age 20. Both twins experienced greater visual impairment during pregnancy and breastfeeding.

The twins showed very different cone types – round in one twin and oval in the other twin. This was the most interesting feature of this case because the presence of different cone types in the same person has never been reported; as such, identical twins would be expected to be concordant for this characteristic. Reasoning from their unique observations, the investigators proposed that whilst cases of keratoconus may be familial, specific cone shape may be affected by environmental events. One possible confound of which they are aware is that one twin wore rigid contact lenses for up to 12 hours a day, a factor that may have affected her corneal measures. One other problematic feature of the study, not mentioned by the investigators, also warrants attention.

It is unfortunate that the case studies of dentition and keratoconus failed to document the methods by which the twins were classified as monozygotic. The twins were, presumably, diagnosed as MZ on the basis of their identical physical appearance, but this cannot be known. Given that each report was a first in its respective field makes it especially important to be scientifically certain of twin type. Copies of this column will be forwarded to the investigators and their replies will be published in a future issue.

Breast reconstruction surgery Identical twins' genetic commonality offers them an ideal organ donor–recipient relationship. There are, however, other less obvious medical advantages that are now becoming evident, and some have significant implications for non-twins. Identical twin, Jane Culbreath, lost a breast to cancer at age 46 years, followed by two unsuccessful attempts at breast implants.[21] Rebuilding a breast from her own tissue was not an option because of her low weight and body fat. The problem was circumvented when her twin sister (who was 20 pounds heavier as a result of three pregnancies) offered to donate her own skin and fat for the procedure. The actual technique was a variation on a 'free TRAM' which involves removal of a small piece of abdominal muscle and fat with reattachment of small blood vessels after insertion of the material in a new location. In the twins' case, only skin and fat were removed from the donor twin and were nourished by a single artery and vein until new blood vessels could grow. Pain and risk were largely reduced by not cutting muscle. The success of this surgery highlights the well-known biological and psychological features defining identical twinship. It also underlies the unique medical benefits of the modified procedure for women undergoing breast removal.

Stranger than fiction

Chang and Eng Little is known of the private lives of conjoined twins. Given their complex biological constraints many conjoined sets do not survive; 40–60% are stillborn and 35% survive only a single day. The newborn survival rate varies between 5 and 25%, but not all pairs survive the first year.[2] Several child and adult twins have been interviewed recently in magazine articles and science programs, offering informative insights on what conjoined twinning means for twins and families. These brief exposés do not, however, adequately capture the daily thoughts, emotions, frustrations and dreams that are part of living under such extraordinary circumstances. In contrast, the recent film Twin Falls Idaho, while fictional, offered a more satisfying glimpse of conjoined twins lives because of the intimacy and detail allowed.

A fictionalized account of the lives of Chang and Eng Bunker, the well known conjoined twins from Siam (Thailand), is now available. Chang and Eng by Darin Strauss is a riveting view of the inner lives of these twins, told from the first person perspective of Eng. It is not intended as a history of their lives, but as an exploration of timeless human themes such as uncertainty, separation, acceptance and love. The twins' thoughts about their meeting with two sisters, Adelaide and Sarah Yates, in Mount Airy, North Carolina, and their evolving relationship and marriage, transforms the brothers from exhibits and oddities to husbands and fathers.

This book may inspire existing conjoined pairs to produce a non-fictionalized account of their lives. Information from multiple sources will help twins, families, physicians and others understand and come to terms with this variant form of twinning. Interested individuals may also contact Conjoined Twins International, PO Box 10895, Prescott, Arizona 86304-0895, USA, or visit the website at http://familyvillage.wisc.edu/lib_conjoined.htm.

Twin on the run Identical twin differences remind us that gene–behavior relationships are probabilistic, urging a search for environmental events that may be responsible. Twins' minor differences in behavioral features and physical form are not unexpected. A closer look is warranted when one co-twin leads a law-abiding life and the other goes from felon to fugitive. This question is debated from time to time in the popular and professional literature, most recently in 1996, in southern California.[22] Identical twin, Jeen Han, attempted an arranged murder of her twin sister, Sunny. Her alleged aim was to assume her twin sister's identity in order to eradicate

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her own crime-filled past. Some members of the press unfortunately turned this into a case of the 'good' vs the 'evil' twin. It turned out that Sunny was guilty of prior credit card fraud, diluting the differences between the twins.

Events surrounding the unusual case of Howard Mechanic were disclosed recently in the media and are briefly summarized below.[23] Individuals interested in additional details should refer to the original source.

Howard and Harvey Mechanic were born in 1948 and raised in Shaker Heights, Ohio, an affluent suburb of Cleveland. Both twins were finalists in the National Merit Scholarship competition. In the aftermath of the Kent State University demonstration against the Vietnam War, protests erupted in college campuses across the United States in the early 1970s. Howard was charged with tossing a cherry bomb toward firefighters at Washington University, in St Louis, a charge he denied. He was, nevertheless, convicted according to strict legislation introduced at about that time. Rather than serve a 5-year-sentence, he disappeared. During his disappearance, his twin brother was photographed repeatedly by the Federal Bureau of Investigation 'so they would know what the other looked like' (p 62, I assume from this statement that the twins are identical and have confirmed this with the author of the original article).

Mechanic was identified in February 2000 in Scottsdale, Arizona, where he had been living under the assumed name of Gary Tredway. His decision to run for Scottsdale City Council naturally attracted reporters interested in covering his campaign; however, this interest ultimately revealed his true identity. He faces an uncertain future.

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