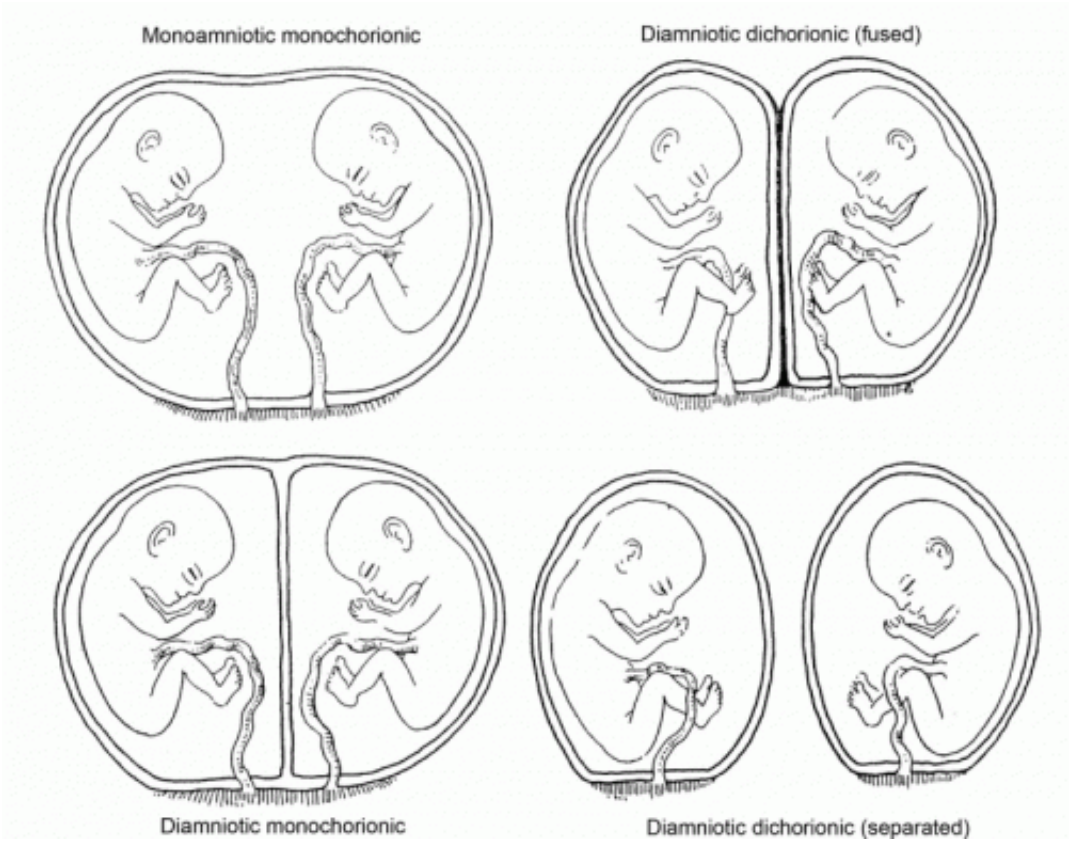
The origin of twins

April 2 2014, by John Hewitt



Kinds of Twins. Credit: babymed.com

(Medical Xpress)—The egregious presumption of universal fact has a long history in science. The ever popular Giordano Bruno was burned at the stake in the year 1600 for crimes against the state; namely, declaring not only that our life-bearing earth is just one among many planets in orbit about a Copernican sun, but also that our sun itself is just one

among so many equivalent stars. In hindsight, it is clear that unconditional acceptance of "scientifically proven" accounts of reality, does the entire field a disservice. Take for example, the highly successful theory of the symbiotic origin of mitochondria. Given what we know today about cells, this concept is consistent with the greatest preponderance of accepted facts, and therefore appears to us as the best explanation of them.

Yet in completely discarding the old ideas that the new theory displaces—that cells could have produced mitochondria from their own internal tissues—we jettison several unexplained kernels of truth we might otherwise keep handy for application to future conundrums. One old idea, and by old I mean at least a century, is a commonly held view pertaining to the origins of twins—the double ovulation hypothesis of dizygotic twinning. As we shall see, like the Copernican sun, the idea that monozygous (identical), and dizygous (nonidentical) twins arise by completely different mechanisms in the womb suffers from narrow perspective.

Dizygotic twins, by definition arise from separate eggs and are therefore not identical. That idea was good enough for me, until I received a comment from a British woman named Lorraine Moss. There had been some ongoing debate on twitter as to the safety of new mitochondrial transplantation techniques with regard to creating so-called three-parent embryos. From her mentions, it was clear that Lorraine had a peculiar insight into reproductive events. After talking to her, I learned that not only is she the mother of an intersex child, but has become a remarkable observer of the condition as it pertains to the phenomena of chimerism.

Lorraine's child has a karyotype of 46,XX/46,XY. Chromosome rations like that generally result in hermaphroditism, and are often accompanied by anomalies resulting from midline and neural tube closure effects. There are many ways this karyotype can occur depending on the genetic

contributions of mother and father, and also on subsequent events in utero. Geneticists have traditionally drawn a sharp distinction between chimerism, and a related phenomenon known as mosaicism. However in many cases, like 46XX,XY hermaphroditism, this distinction is not always so simple to draw.

The term "mosaic" has been applied to individuals that have developed from a single fertilized egg but nonetheless have two or more populations of cells with different genotypes. A somatic (or body) mosaic can result if genetic recombination events normally seen in meiosis also happen during mitosis. It can also result from mutations during development. One possible way, for example, to arrive at the 46XX,XY mosaic karyotype would be to have to nondisjunction events resulting in the loss of 47,XXY cells early on. A child having some cells with XX chromosomes and others with XY might then develop with intersex features.

The term chimera, on the other hand, has been reserved for those cases where two or more genotypes arise from fusion of more than one fertilized zygote. These definitions can sometimes run into trouble because inside the womb there are many different times and places that fusions, and even divisions, can occur. Not only can individual cells fuse, but there can also be various levels of exchange and fusion of cells and tissues across placenta, chorion, amnion, or blood vessel anastomses. There are also other incompletely understood phenomena that can be involved including double fertilizations, or internal divisions of a second meiotic spindle with no production of a second polar body (retention of the second polar body, not to be confused with Barr-Bodies and X chromosomes).

Lorraine has been investigating the origins of chimeras together an unorthodox researcher from East Carolina University named Charles Boklage. Over the course of a substantial career, Blokage has distilled

the vast literature on the epidemiology twins into a delightful compendium of a book titled, "How Humans are Made." It is probably fair to say that origin of twins has fascinated folks as long as they have been making them. The accumulated anecdotes regarding twins comprises not only one of the most exhaustive collective records in our scientific heritage, but also perhaps the most methodical. While studies addressing the incidence of handedness, schizophrenia, birth defects, and cultural variances abound, there appears to be no evidence that an actual double ovulation has ever been observed and reported in direct association with an event of spontaneous human dizygotic twinning. We are also informed, to great effect in the book, that not all monochorionic twins are monozygotic, and not all dizygotic twins are dichorionic.

Boklage reaches the startling conclusion that identical and nonidentical twins can not be the result of a fundamentally different form of embryogenesis, because statistically they differ from normal "singletons" in nearly every case, in the exact same way. For example, monozygous twins do not in fact have any higher incidence of nonrighthandness (ie. lefthanders and mixed state handedness) than dizygotic twins, but both have incidence significantly higher than observed for singletons. Boklage suggests that the idea that "each of us was once a single cell is just a theme on which the truth is a fascinating variation," and that an astonishing fraction of us never were contained within a single cell. No less dramatic, is Boklage's conclusion that twinning is far more common than we have given it credit, and that most or many of us may have had a lost twin in utero with whom which we likely exchanged cells.

Crucial to our understanding of embryogenesis, particularly as it may pertain to things like handedness, is the process of establishing symmetry. While Boklage traces the earliest possible original signal to DNA itself he does not here make much mention of other fairly well established mechanisms that eventually come into play—like for example, the mechanical actions of cilia and the redistribution of

diffusible components. In the language of the embryo, when one embryo decides for whatever reason that it needs to become two, or vice-versa, the proper re-establishment of body axis and re-apportionment of cells is critical.

Boklage discusses other anomalies like the incidence and viability of triploidy (three copies of each chromosome) or even tetraploidy. Survival beyond embryogenesis is rare in both cases and if the conceptus does manage to come to term, it does not live for more than a few hours. In the same fold Boklage also discuss asynchrony of cell division, noting that in the first few division cycles only one cell divides at a given time. One could take a look at normal human early cleavage and know that the largest cell remaining will be the one to divide next. Similarly, he notes that the mechanical ability to conduct cell division depends upon the pair of centrioles brought in by the sperm to form a microtubule organizing center. This paternal structure conducts chromosome segregation in all subsequent cell mitotic cell divisions.

Boklage draws on many examples from other species including observations from animal husbandry. In cattle the female member of a male-female twin pregnancy usually has an incomplete or ambiguous sexual development. These "freemartins" as they are called, are typically infertile. Boklage discusses the occasional ability of some animals to reproduce by parthenogenesis (ie. the development from the egg cell without fertilization, ie. virgin birth). In humans, he notes that genomic imprinting during the construction of sperm and egg cells would appear to assure the impossibility of phenomena like parthenogenesis. Tantilizingly however, amidst the proliferation of in-vitro fertilization (IVF) techniques, odd things have been reported. In one claim for example (not from the book), it appears that a single unfertilized egg in culture became seven cells overnight. Boklage also makes peripheral mention with dtandard flair throughout the book of the idea of slowing of female embryogenesis by the paternally-imprinted X-chromosome.

Although lacking a complete mechanism, this is an intriguing concept as it relates to gender and handedness.

In the course of evolution, Boklage notes that humans gave up the protections of estrus timing, in exchange for constant sexual availability in "service of the pair bond." With some speculation, he suggests that like the pig, humans may have some capability for "facultative reflex ovulation." He notes that the sow's ovulation can be advanced by insemination to occur a few hours before spontaneous ovulation is expected. While curious, any ability for discretionary ovulation in humans, awaits more rigorous verification.

The book obviously does not have all the answers and in light of our limited knowledge is incomplete in many ways. Boklage observes that, "By mechanisms we have not yet been able to see clearly, the process of recombination does its wonderful job of generating our genetic diversity as a side issue or byproduct of some other function that is essential to proper performance of gametogenesis." The fuller nature of these and other functions are is a topic for another day, but for now fertility researchers are starting to take notice of some of the flaws with the double ovulation theory that Boklage has pointed out.

In other fields of science where popular consensus appears to hold sway, minority voices continue to have appeal. For example, hybrid origins in the evolutions of several cryptic species, or the vibrational theory of olfaction, while not proven, can explain some observations the prevailing theory cannot. For more contentious agendas, like anthropogenic CO2-based extremization of the climate, dissenters today are often vilified publically. In looking across the range of science, certainty is often sweeter when the uncertain is still held dear.

More information: Study paper: www.ncbi.nlm.nih.gov/pubmed/19252194

How New Humans Are Made: Cells and Embryos, Twins and Chimeras, Left and Right, Mind/Self/Soul, Sex, and Schizophrenia... by Charles E Boklage (Mar 31, 2010)
www.amazon.com/Charles-E.-Boklage/e/B00300LI12