Study: Darwin was right to worry that marriage to his cousin affected his offspring

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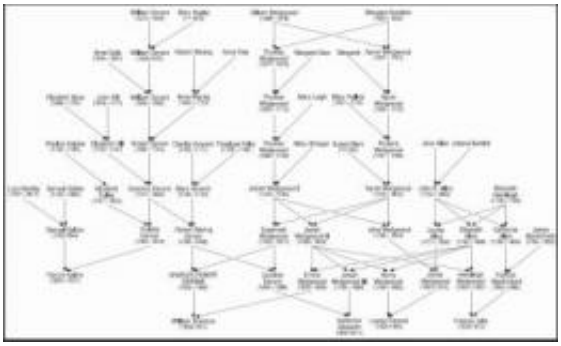

This is the pedigree of the Darwin/Wedgwood dynasty represented as chains of descent. Credit: Figure courtesy of Tim Berra, Ohio State University

New research suggests that Charles Darwin's family was a living human example of a theory that he developed about plants: that inbreeding could negatively affect the health and number of resulting offspring.

Darwin was married to his first cousin, Emma Wedgwood. They had 10 children, but three died before age 10, two from infectious diseases. And three of the six surviving children with long-term marriages did not produce any offspring - a "suspicious" sign, researchers say, that these Darwins could have had reproductive problems because of their lineage.

Studies have shown that susceptibility to infectious disease and unexplained infertility are risk factors of consanguineous marriage -

unions of people related by birth.

Scientists at Ohio State University and in Spain traced the genealogy of the Darwin and Wedgwood families for four generations. Darwin's mother and grandfather also were Wedgwoods, and his mother's parents were third cousins.

The researchers used these data to run calculations in a specialized computer program to determine what is called an "inbreeding coefficient," or the probability that an individual received two identical copies of a gene resulting from marriages among relatives.

The analysis showed a positive association between child mortality and the inbreeding coefficient for Charles Darwin's children and others in the Darwin/Wedgwood families, suggesting that matching damaging genetic traits from the blood-relative parents could have influenced the health of the offspring.

Darwin authored three botanical books showing that cross-fertilization was much more beneficial than self-fertilization for maintaining robust and plentiful plant species. He began to worry about the effects of Darwin-Wedgwood inbreeding on his own family after the death of his daughter, Annie, of tuberculosis at age 10 - the second of his children to die young.

"He fretted that the ill health of his children might be due to the nature of the marriage, and he came to that because of his work on plants. He realized that with breeding of any kind, it's better to cross-breed than to put close relatives together," said Tim Berra, lead author of the study and professor emeritus of evolution, ecology and organismal biology at Ohio State's Mansfield campus.

"We conclude that it may well be that he had some justification for his

worry about his offspring. But it's not all genetic doom and gloom - three of his sons were so prominent that they were knighted by Queen Victoria for their achievements."

The research is published in the current issue of the journal *BioScience*.

Berra became aware of Darwin's pedigree and the famous scientist's related worries about his children's health as he conducted research for a recent biography, Charles Darwin: The Concise Story of an Extraordinary Man (2009, Johns Hopkins University Press).

Darwin himself was sickly, and contemporary researchers have theorized that he suffered from Chagas disease inflicted by insects in South America during his voyage on the HMS Beagle.

He obsessively logged information about his own health, which may have influenced his interest in his children's health, Berra said. But he also recognized from his botanical research that the long tradition of intermarriage between the Darwins and the Wedgwoods - a common practice among prominent families in Victorian England - might have had the unintended consequence of harming the health of his children.

Darwin's third child, Mary Eleanor, lived for only 23 days and died in 1842 of an unknown cause. Annie, his first daughter and second child, died in 1851, and his last child, Charles Waring, died at 18 months of scarlet fever in 1858.

Shortly after he completed the book, Berra's co-authors on this paper, Gonzalo Alvarez and Francisco Ceballos of the Universidad de Santiago de Compostela, published a genetics study detailing how inbreeding led to the extinction of the Spanish Habsburg dynasty. The group then teamed to conduct a similar analysis of the effects of the Darwin-Wedgwood connections.

The researchers traced 25 families among four generations of the Darwin-Wedgwood dynasty, which included a number of consanguineous marriages. The families had 176 children, 21 of whom died before age 10.

They then entered the data into a computer program that documented gene flow across the generations and calculated the inbreeding coefficient for these families. The resulting number represents the probability that within one's genetic code, an individual receives two genes identical by descent as a result of the common ancestry of his or her parents.

Darwin's children had an inbreeding coefficient of 0.0630, meaning that there is a 6.3 percent chance that identical copies of a given gene will come from each parent. This figure is nearly identical to the already-known 6.25 percent chance that offspring of first-cousin marriages will experience the same genetic effect.

That means if both the mother and father have a deleterious allele - an allele is an alternate expression of a gene - there is a 6 percent chance that offspring will receive both of those deleterious alleles and the related damaging effects will occur. Statistically, this translates into a roughly 2 percent chance that the children of first cousins will develop a congenital defect, Berra noted - roughly the same order of difference in risks between a 30-year-old woman and a 41-year-old woman giving birth.

Darwin was concerned that his own ill health had been inherited by his children, though that was unlikely because he probably suffered from a parasitic disease rather than a genetic defect, Berra noted.

Instead, Berra and his colleagues suggest that Darwin's offspring might have had a higher chance of succumbing to such illnesses as TB and

scarlet fever - the cause of the children's deaths. Previous research has suggested that one consequence of inbreeding could be a higher susceptibility to infectious diseases.

Darwin didn't know about human genes, but he was such a good scientist, Berra said, that he was ahead of his time in linking his finding in plants to his own family.

"He was the one who developed this concept of inbreeding depression - a reduction in offspring - and therefore had enough information to begin to wonder about his own marriage and his children's health," Berra said.

The apparent infertility of three of the six surviving Darwin children will remain a mystery, Berra said. But population studies have suggested that statistically, offspring of consanguineous marriages are at higher risk for infertility.

"We can't really say they didn't leave offspring because they were the product of a cousin marriage. On the other hand, being the product of cousin marriage does have this infertility component. So one of six, you wouldn't worry. Two, there seems to be a chance this is the reason. Three out of six didn't leave offspring, so that's a fairly strong possibility," Berra said.

Provided by The Ohio State University

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