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## Revealed: the inbreeding that ruined the Hapsburgs

By Steve Connor *the independent*

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*Dynasty that dominated Europe for more than 500 years was undone by incest, study finds*

The Hapsburg dynasty was one of the most important and influential royal families in Europe dating back more than 500 years and producing rulers in Austria, Hungary, Belgium, the Netherlands and the German empire. Then, in 1700, it suffered a sudden demise of its Spanish branch. Now scientists believe they have come up with a definitive explanation.

A study of the extended family tree of the House of Hapsburg has found that the last Spanish Hapsburg king, Charles II, was the offspring of a marriage that was almost as genetically inbred as an incestuous relationship between a brother and sister or parent and child.

Scientists have found that the Hapsburg fashion of marrying their relatives to keep their dynastic heritage intact had dire consequences for subsequent generations, which culminated in the last heir to the Spanish throne being sickly and impotent.

Charles II of Spain was nicknamed El Hechizado – The Hexed – because people at the time thought that his physical and mental disabilities were the result of sorcery. Now a study into the genetics of his immediate ancestors has found that he was so inbred that he probably suffered from at least two inherited disorders.

Despite his deformities and severe health problems, Charles had married twice in the hope of continuing the rule of the Hapsburgs, but he was incapable of fathering an heir and died childless at the age of 39. He was the last of a long line of Hapsburgs and it spelled the end for the Spanish branch of the dynasty.

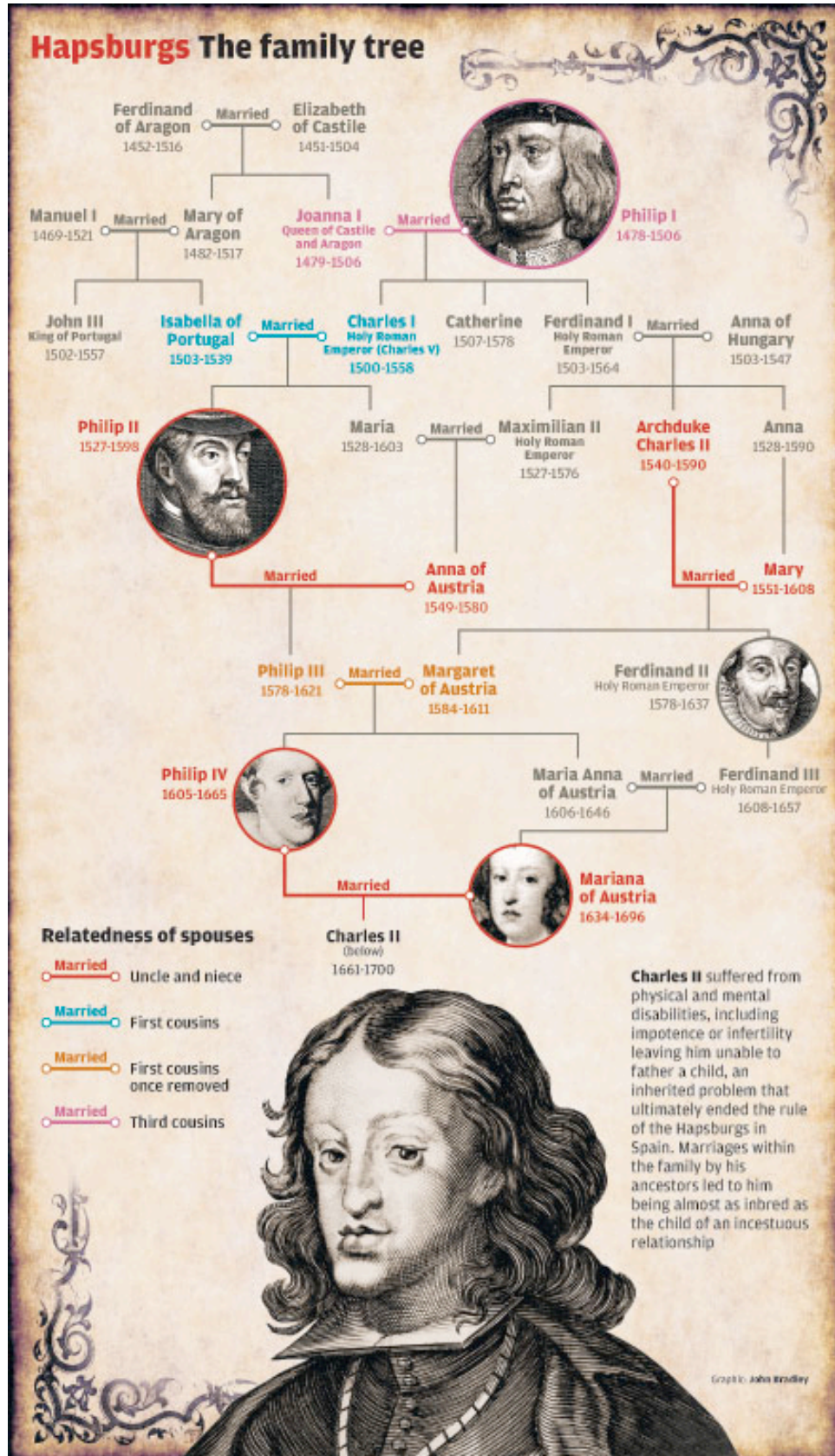
Scientists believe they can show just how inbred Charles was following a study of more than 3,000 relatives of the Hapsburg family extending over 16 generations. The researchers found that his "inbreeding coefficient" – a measure of the proportion of inbred genes he had inherited from his parents – was on a par with that of the offspring of an incestuous marriage.

Professor Gonzalo Alvarez, of the University of Santiago de Compostela in Spain, found that the Hapsburgs suffered a far higher child mortality than the general population, even though the family was immensely wealthy and did not experience the poverty related health problems faced by many people at the time.

They also suffered a higher incidence of physical deformities, which were best exemplified by the famous "Hapsburg lip", a disfiguringly prominent lower jaw caused by an inherited medical condition called mandibular prognathism, when the lower jaw grows faster than the upper jaw.

Charles II not only suffered an extreme version of the Hapsburg lip, his tongue was said to be so big for his mouth that he had difficulty speaking and drooled. He also suffered from an

oversized head, intestinal upsets, convulsions and, according to his first wife, premature ejaculation.



"He was unable to speak until the age of four, and could not walk until the age of eight. He was short, weak and quite lean and thin. He was described as a person showing very little interest in his surroundings," Professor Alvarez said. "He looked like an old person when he was 30 years old, suffering edemas [swellings] on his feet, legs, abdomen and face. During the last years of his life he could barely stand up and suffered from hallucinations and convulsive episodes," he said.

The medical problems of Charles II of Spain were not the random consequences of life, but the direct result of many generations of interbreeding between close relatives within the extended Hapsburg dynasty, according to the study published in the online journal *Plos One*.

The motto of the Hapsburg dynasty – "Let others wage wars, but you, happy Austria, shall marry" – extolled the tendency of family members to marry within their ranks. Charles' father, Philip IV, was the uncle of his mother, Mariana of Austria; his great-grandfather, Philip II, was also the uncle of his great-grandmother, Anna of Austria; and his grandmother, Maria Anna of Austria, was simultaneously his aunt.

There were many marriages between first and third cousins within the Hapsburg family, as well as between uncles and nieces and more remote family members.

This meant that down the generations, with no let up on the amount of intermarriage, the degree of genetic inbreeding gradually built up. The founder of the Spanish dynasty, Philip I, is calculated to have an inbreeding coefficient of 0.025, which meant that just 2.5 per cent of his genes were likely to be identical by common descent. But 200 years and seven generations later, the coefficient had leapt ten-fold to 0.25 in the genome of Charles II, meaning up to one in four of his genes might have been identical.

The medical dangers of such a high level of inbreeding is that dangerously defective genes, which are usually recessive, can come together in one individual and so manifest themselves as an ailment. This is why the offspring of first-cousin marriages are at higher risk of inherited disorders.

Professor Alvarez and his colleagues believe that Charles II suffered the consequences of a high level of marriage between biological relatives. Nine of the 11 marriages over 200 years that preceded his birth were consanguineous, including two uncle-niece marriages and two first-cousin marriages.

Professor Alvarez suggested that Charles II had inherited genes that caused two genetic disorders. One was a hormone imbalance called pituitary hormone deficiency, which would have affected his growth and development, and the other was a kidney problem that led to a metabolic disorder which caused impotence and infertility. "His muscular weakness at a young age, rickets, haematuria [blood in the urine] and big head relative to his body size could be attributed to this genetic disorder," he said. "In this way, we may speculate that most of the symptoms showed by Charles II could be explained by two genetic disorders."