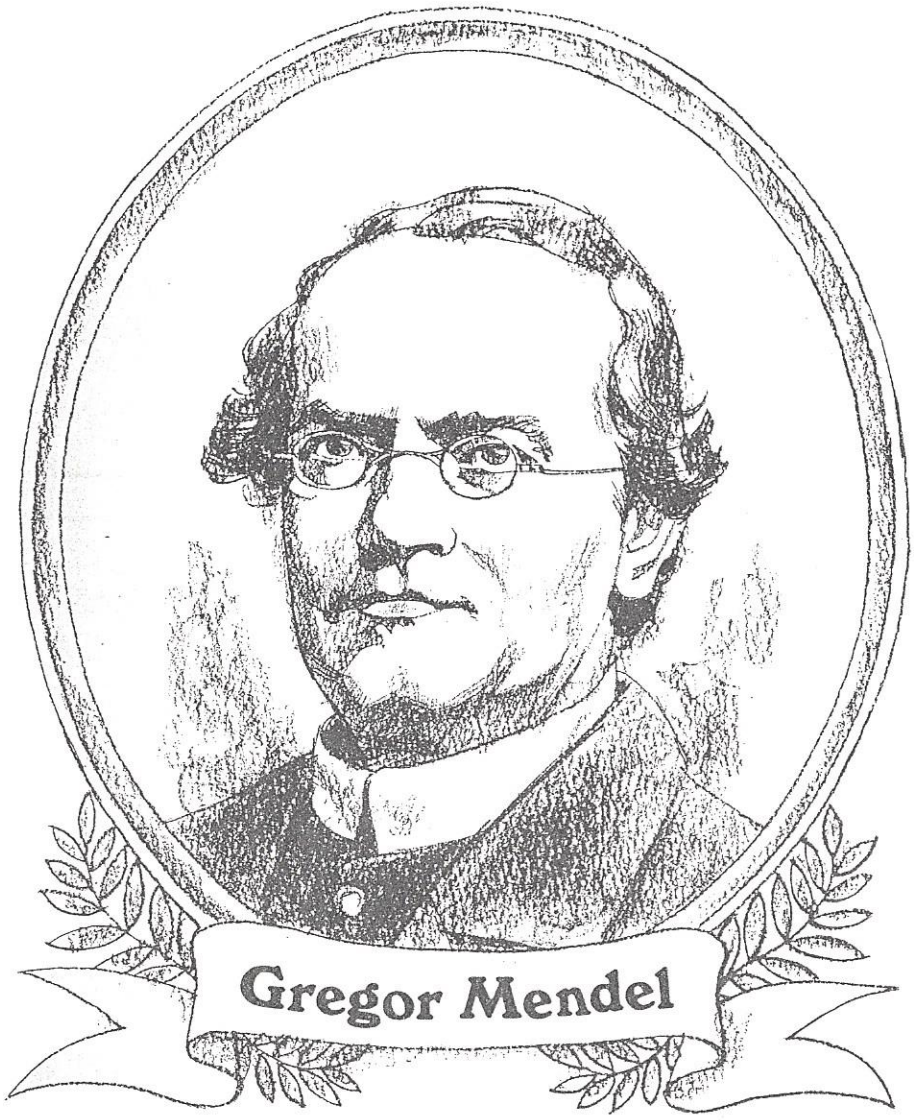



# THE GOOD MONK THE BAD MONK THE TSAR AND THE QUEEN

## A story of Hemophilia, the "royal" disease

by Mary Olsen

From the diary of Tsar Nicholas II come these words, written in the early fall of 1904, six weeks after the birth of his son, heir to the Russian empire:

"Alix and I have been very much worried. A hemorrhage began this morning without the slightest cause from the navel of our small Alexis. It lasted with but a few interruptions until evening."

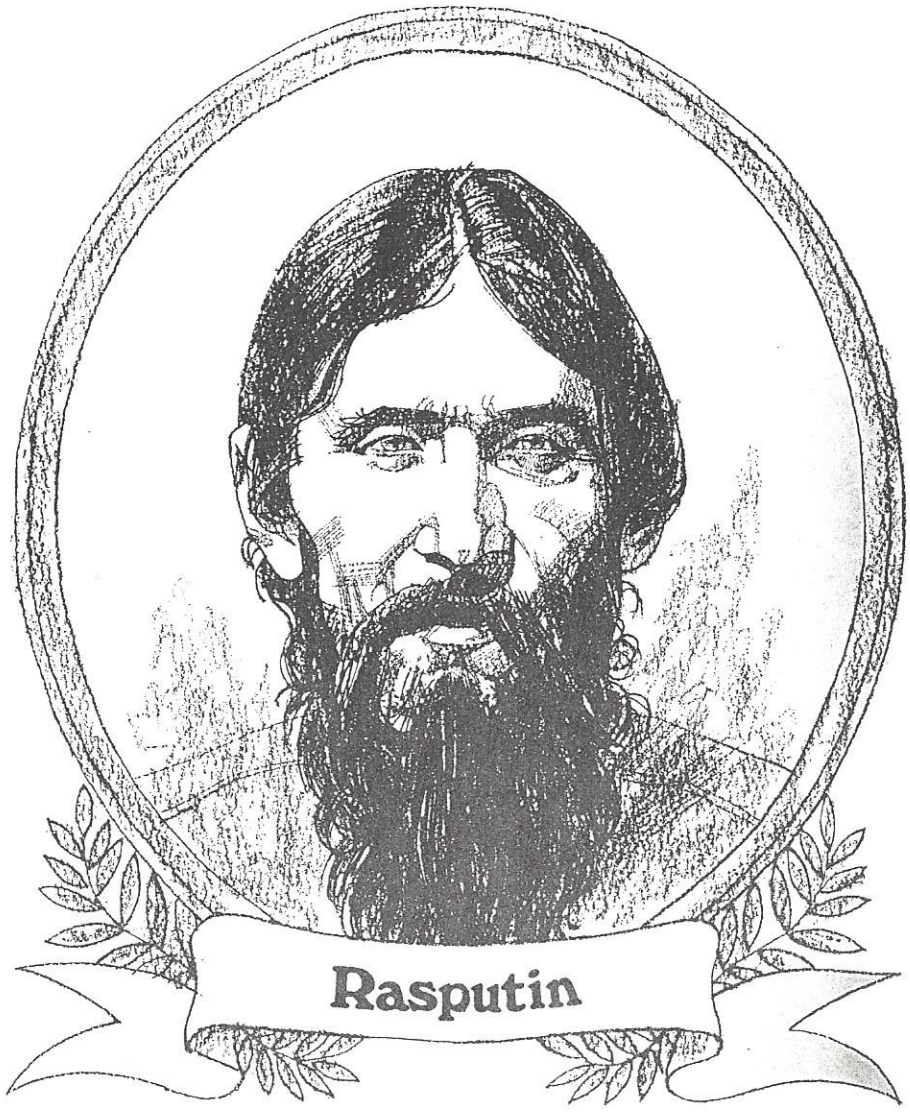
The bleeding actually went on for three days. It was not, however, entirely unexplained. To Nicholas and Alexandra, whom the family called Alix, it brought the unwelcome realization that she had not escaped her family's heritage: hemophilia. Hemophilia is a defect of the blood clotting mechanism, and it often involves painful and debilitating hemorrhages into joints or other body tissues.

The reluctance of the Tsarevich Alexis' blood to clot traces back to an infinitesimal change that occurred in the genetic makeup of one of his distinguished forebears, either his great grandmother, Queen Victoria of England, or Victoria's mother. As a female, Victoria herself was not affected by the genetic disorder nor were the two of her daughters, Beatrice and Alice, who inherited it. But her son Leopold died at age 31; a minor bump on his head produced a fatal hemorrhage. All three of Victoria's affected children passed on the errant gene. Through their children and their children's children, hemophilia travelled to the royal houses of Spain, Germany, and Russia (see diagram, page 6).

### The Bad Monk

For Russia, the consequences of little Alexis' hemophilia were more than medical. In fact, the Tsarevich's rare bleeding disorder became one of the forces that helped change the course of history. The story is a bizarre one. Alexis' mother, the Tsarina, despairing at the illness that was destroying her only son, turned for help to a peasant monk, Gregori Rasputin, whose hypnotic presence, she believed, held mystical powers to stop the little Tsarevich's bleeding.

Convinced that God had sent "Father Gregori" to save her child, Alexandra refused to credit rumors of the alcoholic and sexual excesses of Rasputin — his very name translates as "dissolute." Alexandra reportedly even urged her husband the Tsar to rely on Rasputin in matters of state. While Rasputin can scarcely be said to have precipitated the political upheaval that was about to occur, the Tsarina's blind devotion to the debauched "holy man"




illustrated the widening gap between the aristocracy and the Russian people, who — kept in ignorance of the young heir's disease — interpreted Rasputin's presence and influence in court as one more sign of royal decadence and the need for radical change. Rasputin was killed by a desperate group of aristocrats at the end of 1916, but matters had already gone too far, and in 1917 the Russian people rose up against their Tsar and his family in the Bolshevik Revolution that produced today's ruling regime. The bad monk, Rasputin, thus provides a colorful footnote to the cataclysmic events of that time.

Much has been learned about hemophilia since 1917. It was discovered in the 1960s that injections of a plasma derivative called "anti-hemophilia factor" can be used to provide the missing clotting factor to control bleeding and permit persons with hemophilia to live longer and more productive lives. It is not, however, a cure, and there are some 40,000 carriers in the United States today who are at high risk for producing hemophilic sons.

With the advent of recombinant DNA techniques, geneticists have made tremendous strides toward detecting who within a family carries the defective piece of hereditary information. A new test to analyze the gene affecting blood clotting has been developed. The test is almost always more accurate than the previously available test, though its accuracy can vary among families.

Work with this test in the laboratory of Dr. Steve Sommer at Mayo offers hemophilia carriers a number of options in planning their families. These options weren't open to Russia's royalty, who really had no information about the mechanism by which the disease travelled from mother to child.

"Hemophilia was something that was in Alexandra's family," comments Dr. Sommer, "but it was viewed as a fluke or a curse. There was no understanding of what was going on."

### The Good Monk

Although Nicholas and Alexandra — like almost everyone else at that time — were ignorant of the rules of hereditary transmission, the germ of the crucial knowledge already existed. More than 40 years before Alexis' birth in 1904, an Austrian monk named Gregor Mendel began a science project as part of a

teaching examination. He bred hybrid peas — lots of them — and found that traits can travel from one generation to the next in discrete packages, so to speak; each offspring was not, as had been previously thought, solely a blending of parental traits.

Eventually, Mendel's work opened up the study of genetics: the passing of heritable traits from parent to child. But at the time, his discoveries remained obscure. Though Mendel published his findings in 1865, few scientists knew of them, or appreciated their importance.

### Role of Chromosomes

A generation later, however, scientists were starting to make effective use of dyes to look at cells under the high-powered microscope. In 1873, eight years after Mendel's publication, they identified what came to be called chromosomes, cell components crucial in carrying hereditary traits from generation to generation. It was much later found (in 1956) that 23 pairs of chromosomes inhabit every human cell, making copies of themselves in the creation of new cells. With this knowledge, it was possible to describe exactly how hemophilia was transmitted.

The members of each pair of chromosomes in a cell, Dr. Sommer explains, are similar in size and shape, with one important exception: the pair that signifies gender. For that one pair, males have a large chromosome known as the X chromosome and a much smaller one known as the Y chromosome; females have two Xs. On every X chromosome lies the gene controlling the blood's clotting ability. Women, then, have two of these genes; men have only one. (See page 8, The X-Linked Inheritance of Hemophilia.)

For female relatives of a person with hemophilia, knowing whether an X chromosome with the defective gene has been inherited is important information. If the defective gene has been inherited by a female, it can be passed on to her son and cause hemophilia. The team in Dr. Sommer's laboratory addresses the question: which female relatives of a person with hemophilia also have the defective gene and are therefore carriers? Today, odds are that Dr. Sommer would be in a position to answer that intriguing question: 'Was Anastasia in fact the youngest daughter of the Romanovs, or a fortune-seeking impostor?' MAYO