MEDICAL BREAKTHROUGHS
RESEARCH SUMMARY

TOPIC: PATIENT #1: A NEW BATTLE AGAINST CYSTINOSIS
REPORT: **MB #4770**

BACKGROUND: Cystinosis is a rare genetic disease caused by a buildup of cystine in the body. This buildup causes crystals to form and harm the body. It affects about 500 to 600 children and adults in the United States. Cystinosis is a genetic disorder, which means a person is born with it. It occurs when both parents pass down a specific gene that doesn't work right. In people with cystinosis an amino acid called cystine gets trapped inside the cells, builds up, and forms crystals. People with cystinosis cannot feel the rise in cystine levels. But over time, the buildup of crystals causes damage to every cell and organ in the body. Signs of damage usually start in the kidneys and eyes. Damage cannot be undone but it can be slowed down. Keeping cystine levels low is the main way to slow this damage. There are three types of cystinosis. Nephropathic Cystinosis or Classic Infantile Cystinosis is the most common form of the disease and is also the most serious. About 95% of people with cystinosis have this type. Symptoms usually appear early in the first year of life, and it's a lifelong disease. Intermediate cystinosis or juvenile cystinosis is a less serious form of the disease and may not be diagnosed until a person is a teenager. Ocular cystinosis or nonnephropathic cystinosis is the least serious form of the disease and only affects the eyes.
(Source: https://www.cystinosisunited.com/what-is-cystinosis)

DIAGNOSING: A diagnosis of cystinosis is based upon characteristic symptoms, a detailed patient history, a thorough clinical evaluation and a variety of specialized tests. A diagnosis of cystinosis can be confirmed by measuring cystine levels in certain white blood cells. Urinary examination may reveal excess loss of nutrients including minerals, electrolytes, amino acids, carnitine and water, which is indicative of renal Fanconi syndrome. A physician may use a special microscope called a slit lamp to view the eyes through high magnification, which can reveal cystine crystals in the cornea. A diagnosis of cystinosis can be confirmed by molecular genetic testing, which can identify the characteristic *CTNS* gene mutation that causes the disorder. Prenatal diagnosis is also available for families with a known risk for having a baby with cystinosis. Cystine levels can be measured in cells obtained from the amniotic fluid that surrounds the developing fetus. A test known as chorionic villus sampling can also be used to obtain a prenatal diagnosis of cystinosis. Chorionic villi are thin, hair-like structures found on the placenta. These cells can be examined to detect elevated levels of cystine. There are three treatment options. One is *cystine depleting therapy.* Cysteamine is a cystine-depleting agent that can greatly lower cystine levels within cells. Therapy with cysteamine slows the development and progression of kidney damage and enhances growth in children. There is also symptomatic therapy which is when Renal Fanconi Syndrome is treated with a high intake of fluids and electrolytes to prevent excessive reduction of body water (dehydration). Finally, there is renal transplantation. Individuals with infantile and intermediate cystinosis eventually develop end stage renal disease (ESRD), requiring a kidney transplant.
(Source: https://rarediseases.org/rare-diseases/cystinosis/)

NEW TECHNOLOGY: In October 2019, Dr. Stephanie Cherqui, Associate Professor of Pediatrics and her team at University of California - San Diego School of Medicine, developed a clinical trial gene therapy approach to treat cystinosis. It involves genetically modifying the patients own stem cells. Doctors obtain hematopoietic stem cells from the patient's bone marrow. The scientist then re-engineer the stem cells in a lab using gene therapy techniques to introduce a normal version of the cystinosin gene. Then they reinfuse the patient with their new cystinosin-producing cells. Like a bone marrow transplant the patient is both the donor and the recipient. The gene-modified stem cells embed themselves into the bone marrow, where they divide and differentiate to all types of blood cells. Those cells are then circulated throughout the body and embed in tissues and organs, where they produce the normal cystinosin protein. Then, the cystinosin protein will be transferred to the surrounding diseased cells. At that point, the patient's cells should be able to transport cystine for disposal—potentially alleviating the symptoms.
(Source: https://ucsdnews.ucsd.edu/feature/a-tornado-at-the-front-door-a-tsunami-at-the-back-door)

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If this story or any other Ivanhoe story has impacted your life or prompted you or someone you know to seek or change treatments, please let us know by contacting Marjorie Bekaert Thomas at mthomas@ivanhoe.com