For Some, SSIs Are In The Genes

An estimated 300,000 U.S. patients get surgical site infections every year, and while the causes are varied, a new University of Utah study suggests that some who get an infection can blame it partly on their genes.

In the Feb. 19, 2013, online edition of the journal Wound Repair and Regeneration, researchers from the University's School of Medicine show through a study of families in the Utah Population Database (UPD) that surgical site infections (SSI) appear to have a significant genetic connection, even in extended relatives. If further investigation bears out these findings, people who are genetically at risk for SSIs might be identified through personal genome analysis before surgery, according to Harriet W. Hopf, M.D., professor of anesthesiology at the University of Utah School of Medicine who is corresponding author on the study.

"Our research showed that people with surgical site infections are more likely to be related to one another than expected in the Utah population" Hopf says. "If that's the case, individual genome analysis might benefit many people if SSIs appear to run in their families. This type of personalized health care could be available in a few years, and with the unparalleled resource of the Utah Population Database (UPDB) and its world-class genetics research, the University of Utah is positioned to make it happen."

It's estimated that SSIs occur in approximately 5 percent of U.S. surgical procedures, resulting in longer hospitalizations and adding approximately \$1 billion a year to the nation's health care bill. Infections can occur on the outer layer of skin at the surgical site or in deeper tissue below the skin.

Hopf, who's also associate dean for academic affairs in the School of Medicine, conducted the research with Lisa A. Cannon-Albright, Ph.D., a genetic epidemiologist, professor of internal medicine and senior author on the study, and former U of U medical student and first author, James P. Lee, M.D.

Through the UPDB, a remarkable storehouse of genealogical records, public health data, and records from hospitals and ambulatory surgery centers, the researchers combed the records of 651 University of Utah Hospital patients who had suffered SSIs based on an internationally recognized medical code. (The researchers did not learn the names of the patients.) As controls, they used randomly selected U of U Hospital patients with the same birth year, birthplace, and sex as the group that did have infections. Only people with both parents, all four grandparents, and at least six of eight great-grandparents in the UPDB were analyzed in either group.

A test for excess familial relatedness, the Genealogical Index of Familiality (GIF), was performed to determine whether patients with SSIs were more related than expected, as measured by average relatedness in the randomly selected, matched controls. To rule out the possibility of shared environmental influences on

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predispositions to SSIs, the researchers also performed the analysis while ignoring first- and second-degree relationships (representing individuals who might be living together or in close proximity, such as parents, siblings, and offspring, and thus sharing non-genetic risk factors), according to Cannon-Albright.

The results might be considered surprising, showing that SSIs occurred more frequently than expected among, for example, third cousins and more distant relatives of individuals in the study. "People who'd had an SSI were significantly more related than we would have thought," she says. "The results indicate a strong genetic contribution to SSIs."

Hopf has researched SSIs for much of her career, suspecting that a mutation in a gene that makes superoxide, a compound released as part of the body's inflammatory response to invading pathogens, might cause a predisposition to the infections. The mutation could render this gene, p-47 phox, less efficient at making superoxide, leaving people more susceptible to SSIs.

Upon coming to the University in 2006, Hopf saw an ideal opportunity to investigate her hypothesis by taking advantage of the UPDB and the school's genetics expertise. "The chance to collaborate with people from different disciplines makes the University of Utah an exceptional place for this kind of research," she says.

For her next step, Hopf wants to draw blood samples from members of high-risk families identified in this study to investigate whether p-47 phox or other genes might predispose people to SSIs.

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