## Y chromosome linked to male infertility

The Y chromosome was once considered a vast DNA wasteland, largely devoid of genes, says David C. Page of the Whitehead Institute of Biomedical Research in Cambridge, Mass.

In recent decades, however, researchers have realized that this masculine chromosome contains at least a few dozen genes, including one that enables a developing embryo to become male (SN: 7/28/90, p. 61). Page and his colleagues may soon add another vital gene to the Y chromosome's roster.

In two recent reports, including one in the May 11 LANCET, Page's group has presented evidence that some cases of male infertility result from specific deletions within the Y chromosome, a finding that suggests the deleted area contains a gene or genes crucial to the production of healthy sperm.

The new research adds another possible explanation, besides such factors as chemical exposure and infections, for why an estimated 3 to 4 percent of men generate either no sperm or so few that they are infertile.

"Male infertility is an extremely common problem, and until recently, we have not had solidly established examples of genetic causes," says Page.

The first suspicion that the Y chromosome has a role in fertility arose in 1976,

when two Italian researchers found, among more than 1,000 infertile men, a few who had major deletions of their Y chromosome. "They postulated the existence of one or more genes required for spermatogenesis [the creation of sperm]," says Page, a Howard Hughes Medical Institute investigator.

Last year, in the August Nature Genetics, Page and his coworkers reported that 12 of 89 men with azoospermia, the inability to make sperm, lacked the same small region of the Y chromosome's long arm. Yet their fathers had intact Y chromosomes, indicating that the deletions were new mutations and that these changes had caused the infertility.

In the LANCET report, Page's group discusses similar results from a study of 35 men with extremely low sperm counts—less than 1 million per milliliter—a type of infertility called severe oligozoospermia. When the scientists analyzed DNA taken from the men's blood cells, they found that two of the men had an identical region deleted from the Y chromosome. The missing region was the same one observed in the 12 men with azoospermia.

Page's group also looked at the sperm of one of the two oligozoospermic men with an obvious Y chromosome deletion. Investigators confirmed that his sperm has the same genetic defect as his blood cells, implying that fertility problems can pass from fathers to sons.

That remote possibility may become more common, says Page, as infertile men turn to techniques such as intracytoplasmic sperm injection, or ICSI. In this relatively new procedure, a physician needs only a single sperm to inseminate an egg.

"We need to tell fathers with very low sperm counts [considering ICSI] that there is a slight chance that male offspring may also have low sperm counts," says Norbert Gleicher of the Center for Human Reproduction in Chicago.

Adds Richard J. Sherins of the Genetics & IVF Institute in Fairfax, Va., "We've suspected there is a genetic component [to some male infertility] for a number of years. We've already been counseling couples [for whom] we think there is a likelihood that the husband's problem has a congenital basis."

How often azoospermia or oligozoospermia can be attributed to deletions or mutations of the Y chromosome remains unclear, says Page. His group has identified one gene, called *DAZ*, within the suspicious Y chromosome region. The scientists plan to examine infertile men for mutations in the gene to confirm that it is vital to sperm creation. Such research may eventually lead to a genetic test that would help physicians resolve the cause of a man's infertility. — *J. Travis* 

## Trauma syndrome traverses generations

Many survivors of World War II's Holocaust, who endured the horrors of Nazi concentration camps and in some cases hid for years from Hitler's minions, suffered painful emotional wounds that have never healed. This traumatic legacy has also seeped into the psyches of many of their children, according to a new study.

Holocaust survivors who developed post-traumatic stress disorder (PTSD) in response to wartime experiences tended to pass on to their children a vulnerability to the same condition, asserts Rachel Yehuda, a psychologist at Mt. Sinai School of Medicine in New York. Moreover, survivors' offspring diagnosed with PTSD often cite Holocaust-related thoughts or images as their primary traumas, Yehuda notes.

"This is the first good, empirical evidence that it's possible for someone else's traumatic experience to become one's own trauma," she holds. "It suggests that the effects of severe trauma may last for generations."

These findings, presented at the annual meeting of the American Psychiatric Association in New York last week, contribute to emerging evidence that certain biological and environmental factors ren-

der some people particularly susceptible to PTSD. The disorder, typically thought to result from direct confrontations with military combat or other traumatic events, features nightmares, repeated flashbacks of distressing incidents, and fear of situations or locales that might call to mind those experiences.

Yehuda and her coworkers studied 80 Jewish adults, most in their thirties or forties, born to Holocaust survivors and 20 Jewish adults of comparable age whose parents had not faced Nazi persecution. All of the volunteers lived in New York City. Most reported having had at least one traumatic encounter, such as getting mugged at gunpoint. The groups cited similar numbers and types of traumas.

At some time in their lives, 23 offspring of Holocaust survivors—29 percent of the total—had suffered from PTSD, whereas none of the controls had, Yehuda says. The disorder afflicts around 8 percent of the U.S. population at some point in their lives (SN: 12/23&30/95, p. 422).

"Children of Holocaust survivors often said that images of their parents' traumas intruded into their mental lives," Yehuda remarks.

Regardless of whether they had experienced PTSD, survivors' children more

often reported other psychiatric symptoms, including depression and anxiety. Offspring with PTSD had low concentrations of the stress hormone cortisol in their urine, Yehuda found. Similarly diminished cortisol characterizes Vietnam combat veterans suffering from PTSD, she says.

In another study, Yehuda and her colleagues interviewed 22 Holocaust survivors—11 of them diagnosed with PTSD—and one grown child of each survivor. The researchers found the disorder in six children, all of whom had a parent with PTSD.

Such children may carry a genetic vulnerability to that condition, in Yehuda's view. They may also learn or acquire some PTSD symptoms from their parents, she adds. Neurological disturbances in the womb or during childhood may influence PTSD as well.

"These are fascinating findings that need to be investigated further," comments Roger K. Pitman of the Veterans Affairs Medical Center in Manchester, N.H.

Aside from a parent with PTSD, other factors contributing to PTSD susceptibility may include low intelligence, extreme shyness, impulsiveness, and a family history of depression, according to several other studies presented at the meeting.

— B. Bower

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