The X-Chromosome and its Effect on Disease Susceptibility

Men and women vary due to their hormones, such as estrogen and testosterone. However, according to Dr. Carolyn Bondy and her associates in the 2013 study, *The X-Chromosome and Gender Effects in Physiology, Pathophysiology and Longevity*, these hormones do not adequately account for differences in susceptibility to disease and longevity between men and women. Instead, this study focused on the X-chromosome gene to uncover biological differences between males and females. For example, Turner Syndrome indicates that the second X-chromosome is in fact important for normal female development. By studying Turner Syndrome women and girls, the researchers were provided a unique opportunity to explain the effect of the X-chromosome gene, while simultaneously broadening the scientific understanding of Turner Syndrome.

**X-Chromosome and genomic imprinting**

Genomic imprinting denotes the selective transfer of certain genes from parent to child. Genomic imprinting of the X-linked genes causes differences between males and females. For example, women are less likely to experience ischemic heart disease because their fat distribution is generally concentrated in the hip area. Conversely, men’s fat distribution is generally around the abdomen.

**Congenital cardiovascular defects in Turner Syndrome**

This study notes that congenital cardiovascular disease “may be the most serious medical problem in monosomy X or TS.” Fifty percent of study participants had cardiovascular anomalies, most commonly an elongated transverse arch of the aorta. This abnormality can be predictive of aortic complications; therefore, aortic dimensions of patients should be under close surveillance, even if they do not experience symptoms. Three women with TS during the course of this study did qualify for prophylactic intervention (aortic diameter less than 5 cm) and as a result suffered aortic dissection. Thus, the research team established a new standard for evaluating aortic dilation: “If the ASI (Aortic Size Index) is equal to or greater than 2.5 cm/m², the patient should be evaluated for prophylactic intervention.” It has also been concluded that aortic valve defects are directly linked to the deletion of the X-chromosome “short arm distal to Xp11.”

The immune system was also studied, concluding that 40% of the studied TS population had autoimmune thyroiditis, compared to 5% of the general female public. All women studied that experienced aortic complications resulting in surgery or death had both autoimmune thyroiditis and bicuspid aortic valves (BAV). The combination of the two indicates a 66x greater risk of complications than groups with one or neither.
The X-chromosome, ovarian failure, and psychosocial function

Past surveys have indicated that TS girls and women experience shyness and social anxiety due to a “shyness trait” linked to stigmatization of short stature. However, recent scientists have proposed that social difficulties are actually the result of genomic imprinting of X-linked genes involved in processing social information. The findings of this study suggest that social concerns, such as anxiety and depression, are related to “gender identity” issues due to infertility and ovarian failure.

To examine this, the researchers compared TS women and average women who experienced premature ovarian failure. They expected that behavioral outcomes would be similar amongst the two groups. The two groups experienced increased levels of shyness and social anxiety and lower self-esteem compared to women with normal ovarian function. The study denotes these feelings of “social inadequacy” to “social isolation, difficulty in partnering, and very limited sexual functioning.”

Finally, the researchers studied the impact of the single parental X-chromosome on educational and occupational outcomes. Of the 250 study participants, 70% had a bachelor’s degree or higher and 80% were employed outside the home. Both of these numbers are higher than the general female population. Turner Syndrome women were more drawn to legal, healthcare, and social services occupations.

Overall, this study clearly shows a connection between X-linked genomic imprinting and susceptibility to disease. This is made especially apparent in Turner Syndrome women and girls’ increased rate of various diseases, such as congenital cardiovascular disease. Health care providers should be aware of this link and also take note of the improved care guidelines mentioned by the research team.

The full article can be found at: http://2013annualreport.nih.gov/bondy.html.