A Review of Sex Differences: Glycobiology and Immunology

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Abstract

The biological differences between males and females are significant yet too often overlooked. In research and clinical studies, sex differences are often not taken into consideration. However, glycobiology and immunology are starting to shift. Recent studies in glycobiology show that male and female glycans are different; this causes differences in the immune system. These differences are affecting the quality of treatment received by females. Because research uses primarily male patients, the effectiveness of treatments on females is unknown and potentially dangerous. Therefore, we need better research on sex differences in biology.

Abstract Continued....

In this presentation I will be summarizing:

- How glycans affect the innate and adaptive immune systems
- Why it is important to study the differences between the male and female immune systems through general diagnostic and treatment related examples
- How research should move forward in specifically looking at males and females in research and clinical studies

Sex vs Gender

- Sex and gender are two different concepts, each important when defining health and in research. This presentation will be focusing on sex differences.
- Sex refers to biological factors. This includes chromosomal differences, physiological differences, and organ function besides reproductive purposes (Liu & Mager, 2016). The terms male and female will be used.
- Gender mirrors sociocultural factors. The self-representation, social, and cultural views on sex define gender (Liu & Mager, 2016). The LGBTQ+ community is considered under gender. Terms may include man, women, and non-specific gender pronouns.

Glycobiology and the Immune System

Glycobiology and the Immune System:

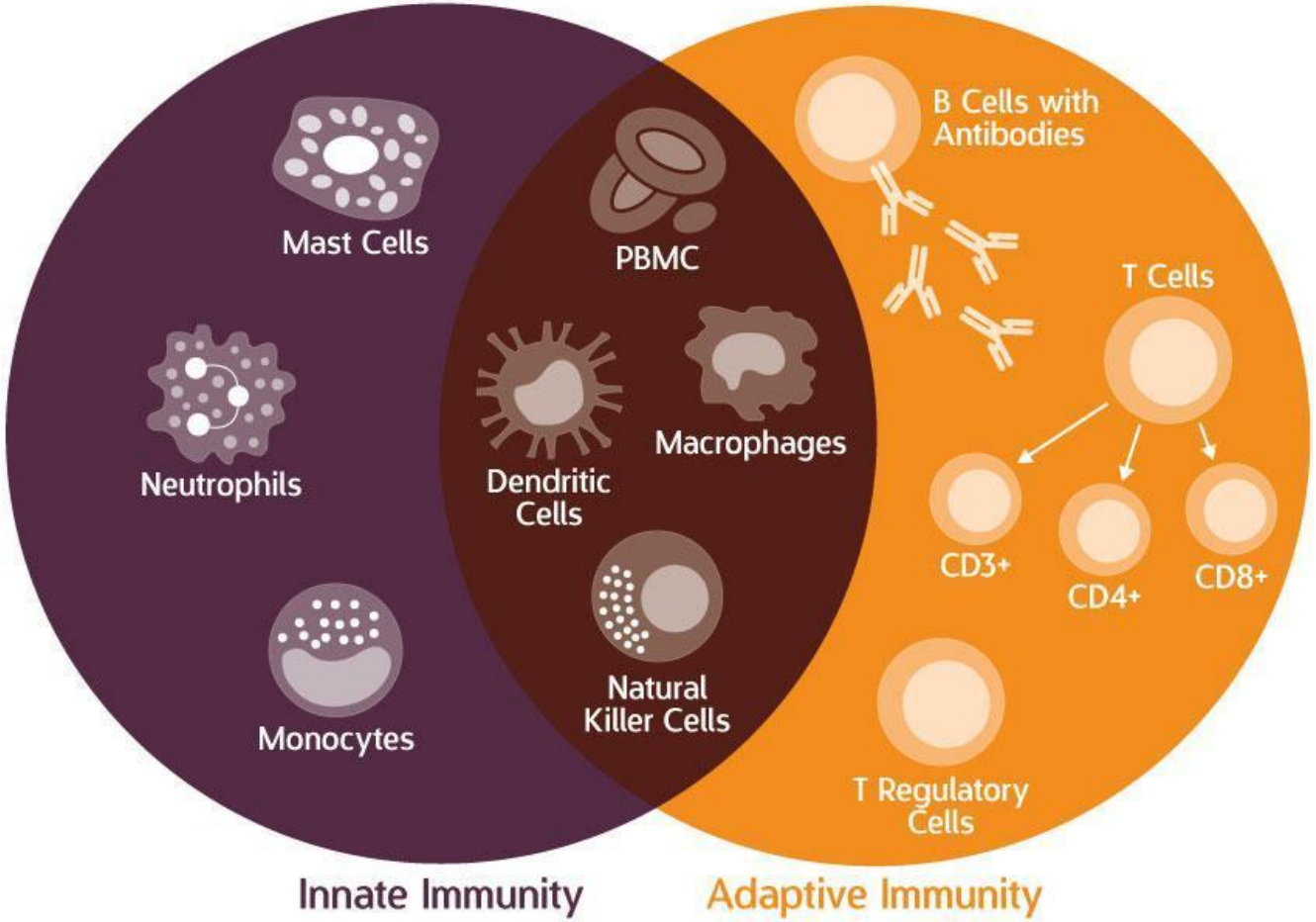
How glycans affect the innate and adaptive immune systems

The Immune System

Glycans control the immune system. For example, antibodies can specifically recognize glycans. Glycans can also internalize antigens through interactions with receptors. The internalization of antigens allows for glycans to regulate signalling events and immune responses. This is one way the innate immune system is affected by glycans.

Exposure to foreign pathogens is what develops your adaptive immune system. Specific immune cells, called T cells, respond to the pathogens when signalled by glycans. The T cells attack and remember pathogens creating a memory of said pathogen. T cell memory is what allows your body to fight the same pathogen efficiently and repeatedly (Gleeson, 2008).

Cells of the Innate and Adaptive Immune Systems



(Lodge et al., 2019)

Glycobiology and the Immune System:

The Importance in Studying Sex Differences in Glycobiology and Immunology

The Issue at Hand

Females are underrepresented in research and clinical studies. The lack of female representation has led to and will continue to lead to misdiagnosis and mistreatment of disease (L. Willis, personal communications, August 2021). The lack of knowledge of the effects of certain drugs, vaccines, and treatments is potentially life-threatening to females. Females, overall, have more adverse reactions consistently to prescription drugs. A lack of female patients in drug trials results in the general public experiencing infliction because the drugs were never properly assessed. An example is when organizations, like the FDA, take prescriptions off the market due to the harm they are causing.

The FDA

From 1997-2001, the Food and Drug Administration for the U.S. removed ten prescription drugs from the market. Eight of the ten were removed from the market because they pose a considerable threat for women compared to men. According to the GAO (2001), four of the eight resulted in higher adverse reactions in women due to prescription rates. The other four had equal prescription rates between men and women, but women experienced adverse reactions more commonly. The remaining two out of ten had equivalent risks between men and women (Office, 2001).

Implications of a Change in Research

By beginning to study sex differences in glycans and how sex affects the immune system, we can diagnose and treat a multitude of diseases more effectively. It is proven that males and females respond differently to medications and vaccines, and have different diagnostic indicators for illness. To this day, males are the primary patients in preclinical and clinical trials. The lack of female representation in studies results in females being misdiagnosed and mistreated. By looking at both sexes in studies, we are saving lives. Identifying the unique disease indicators between each sex is the solution (L. Willis, personal communication, July 2021).

Females are 20%-70% more likely to develop lung cancer as a male who smokes the same amount of cigarettes (Liu & Mager, 2016).

Studying Sex Differences in the Immune System

Studying Sex Differences in the Immune System:

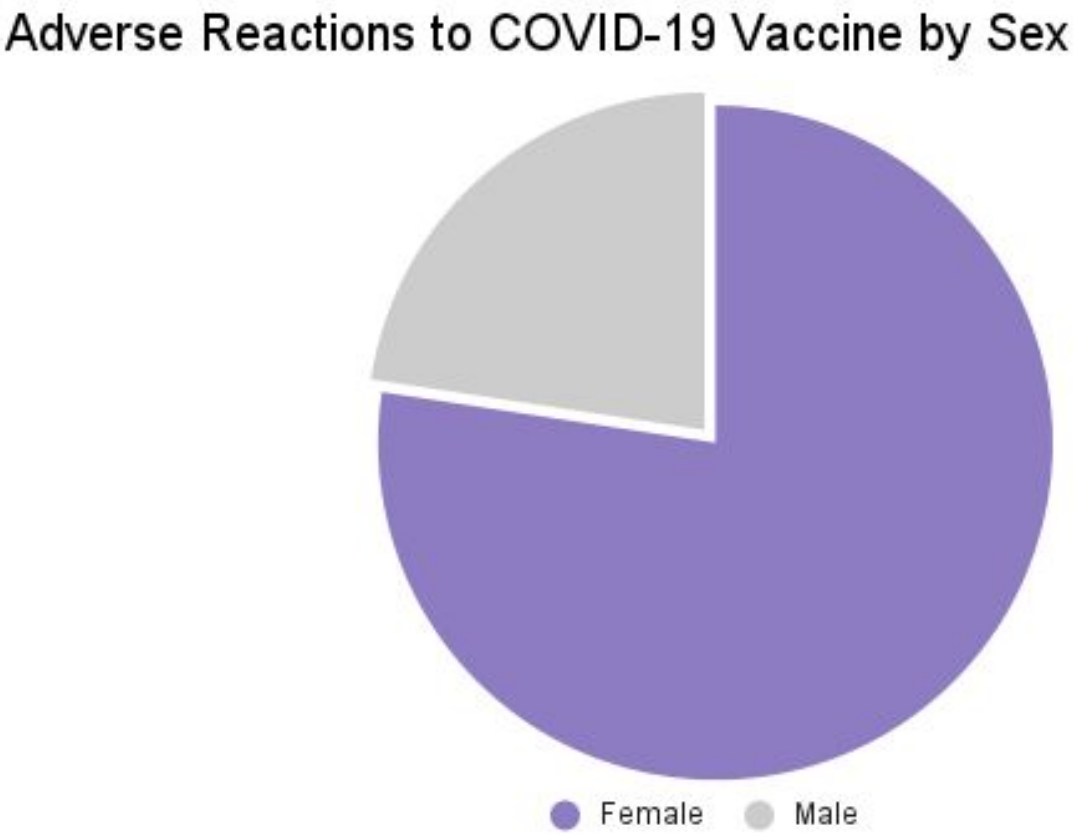
Better Diagnostic and Treatment Technology

Cardiovascular Disease (CVD)

- Many factors contribute to cardiovascular health including the environment, diet, activity levels, age, and genetics, however, sex is also a major factor.
- As science and diagnostics progress, concerns have been raised surrounding sex differences in CVD. Females do not respond to treatment as well as male patients do. This is likely due to the fact that males are more commonly used in animal preclinical trials and human clinical trials.
- Females have a higher risk of dying following a cardiovascular event due to the lack of effective treatment options (Mirabito Colafella & Denton, 2018).

Vaccines

At all ages, vaccine-induced immune response, adverse reactions, and overall protection vary between males and females. A higher antibody level and more adverse reactions are reported in females who get vaccinated compared to males. This superordinate immune response in females indicates that a dosage adjustment must be made between males and females to account for the over-active female immune system. However, sex has not always been considered in research, resulting in higher adverse reactions in females (Flanagan et al., 2017).



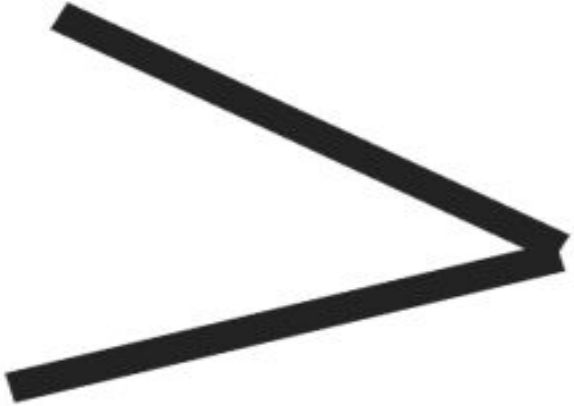
Females make up 77.4% of adverse reactions to a COVID-19 vaccine in Canada.

Similar statistics have been found in the United States, the United Kingdom, and other countries (Canada, 2021).

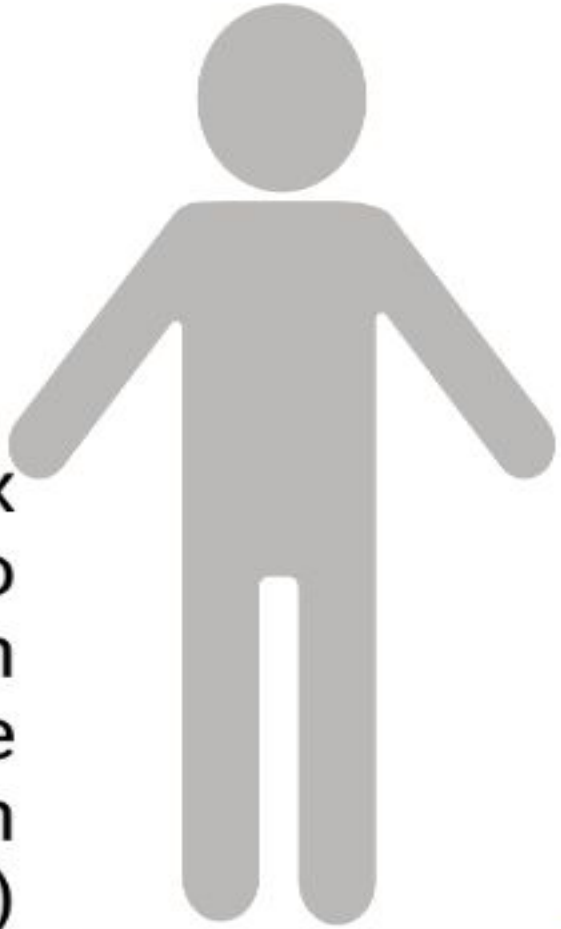
Data From Canada's Health Info Base

Dosage

Many genes related to immune function are located on sex chromosomes, specifically the X chromosome. Dosages are designed for the male body as the primary sex in clinical studies. This means that dosages are designed to stimulate one X chromosome and its corresponding immune genes. To try to mitigate this issue, an inactivator has been added to medications to prevent overexpression in females with XX chromosomes but it is only 70% effective at most. Furthermore, congenital lymphocytes that fight pathogens can stimulate X immune genes. The lymphocytes lead to the overexpression of X-linked immune genes and a more eminent immune response in females (Massey et al., 2021).



Females are 2.7x more likely to acciquire an autoimmune disease than males (NM;, 1997)



Studying Sex Differences in the Immune System:

Changes in Research

Next Steps

Moving forward, researchers and clinical studies need to use an equal amount of male and female patients and segregate the data based on sex. The results of this have the potential to be substantial. As mentioned earlier in the presentation, females have a higher likelihood of developing a disease and more adverse reactions to treatments. The statistics indicate that research must change. Females are not receiving proper and effective medical care.

Science must do better.

Conclusion

Male and female immune systems are different. The differences are observed in cardiovascular diseases, vaccination effectiveness, and adverse reactions. Also, how sex chromosomes affect the necessary dosage for effective treatment is an example. These are just a few cases of how sex differences affect immune responses.

The significance of researching sex differences is unmeasurable. Improving the quality of care given to females starts in the research. The use of females in clinical studies has the implications to be life-changing or potentially life-saving.

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CREDITS

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