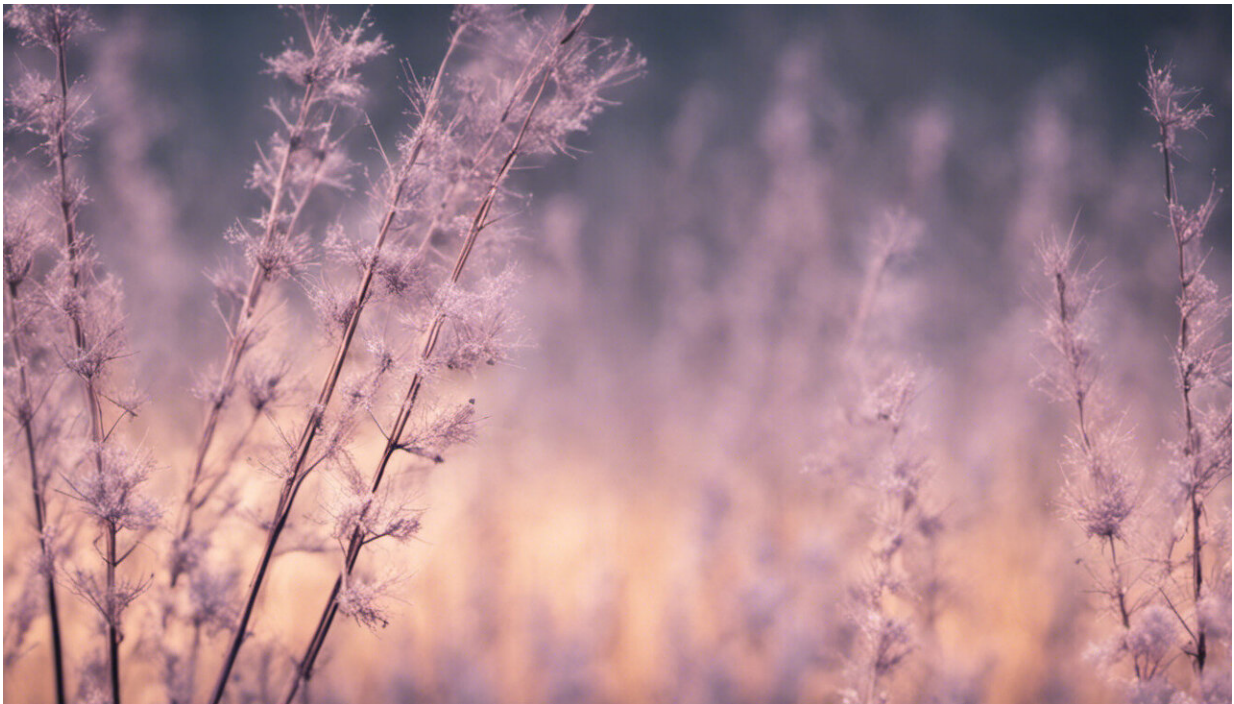


Man flu is real, but women get more autoimmune diseases and allergies

August 7 2017, by Gabrielle Belz And Cyril Seillet



Credit: AI-generated image ([disclaimer](#))

Men and women respond differently to diseases and treatments for biological, social and psychological reasons. In this series on Gender Medicine, experts explore these differences and the importance of approaching treatment and diagnosis through a gender lens.

We know that sex hormones drive characteristic male and female traits such as breast enlargement and hip widening in women, or increased muscle mass and growth of facial hair in men. But now we also recognise they have a major impact on the immune system - our body's inbuilt mechanism that helps fight and protect us against disease.

Research suggests this has an evolutionary basis: survival of the species may mean men are harder hit by viruses, but a woman's reactive immune system leaves her more susceptible to autoimmune diseases and allergies.

Viruses see men as weaker

Men die significantly more often from infectious diseases than women. For instance, men are 1.5 times [more likely to die](#) from tuberculosis, and [twice as likely to develop Hodgkin's lymphoma](#) following Epstein–Barr virus (EBV) infection. Men are also [five times more likely](#) to develop cancer after infection with human papillomavirus (HPV), than women.

This is because women's immune systems [mount a stronger response](#) against foreign invaders, particularly viruses. While the male hormone testosterone tends to dampen immune responses, the female hormone oestrogen increases the number of [immune cells](#) and the intensity of their response. So women are able to recover more quickly from an infection.

All this may reflect a sneaky evolutionary trick used by viruses to enable their survival. Women have developed multiple mechanisms to transmit infections; mainly through passing bugs from mother to child during gestation or birth, or through breastfeeding. So women are better vessels for viruses.

Meanwhile, viruses have singled men out as the weaker sex. While popular culture has come up with the term "man flu", suggesting men are

over-dramatising flu symptoms, [evidence suggests](#) they may in reality be suffering more due to this dampening down of their immune responses.

However, this increased susceptibility of men to infection may not be an advantage for the long-term (over tens of thousands of years) survival of a disease-causing organism (pathogen), if it induces such severe disease that it results in the death of the host.

Pathogens modify themselves so they can be transmitted by women during pregnancy, birth or breast feeding. Because of this, many have adapted to be less aggressive in women allowing wider infection, generally across a population.

However, this feature alone is not likely to be sufficient to ensure the ongoing survival of a virus. The fitness of both sexes is necessary to reproduce long-term and thus provide new hosts for invading pathogens. Thus, the hit to the male sex must somehow be balanced by other advantages to their immune system.

Autoimmune diseases

The most striking sex differences in the immune system are seen in [autoimmune diseases](#). Autoimmune disease affects about 8% of the population, but 78% of those affected are women. Women are [three times more likely](#) than men to develop these types of disease.

Autoimmune diseases occur when the immune system turns on and [attacks the body's own cells or tissues](#), initiating a chronic cycle that results in damage or destruction of specific organs. These diseases include type 1 diabetes, lupus, rheumatoid arthritis, multiple sclerosis, and up to 80 different diseases that affect systems such as the intestine, bones, joints and nervous systems.

In the case of lupus, the [immune system](#) mistakenly attacks the person's own DNA (the structure that carries a person's genetic code) causing damage to multiple organs that will lead to weight loss, anemia and eventually heart and kidney failure. Nine out of ten patients with lupus are women and [clinical observations suggest](#) that, again, hormones are the culprits.

These differences of susceptibility between males and females tend to appear after puberty, and flare-ups increase during pregnancy. On the contrary, menopause is associated with a lower disease severity.

Studies have linked oestrogen levels with the exacerbation of lupus. Oestrogens directly act on a [particular immune cell](#) (called the plasmacytoid dendritic cell) to promote their capacity to secrete inflammatory signals, which exacerbate lupus symptoms. Although these dendritic cells are generally important for fighting viral infections, in the context of lupus and [multiple sclerosis](#), they cause significant harm.

Hormones and allergies

One in nine Australians (more than 2.5 million in total) [suffer from asthma](#) – a disease that causes swelling and narrowing of the airways. This makes it difficult to breathe when we encounter environmental allergens such as pollen.

Twice as many women develop asthma compared to men. Interestingly, males are more susceptible to asthma before to the onset of puberty but, after puberty, females are more affected and develop more severe asthma than men. Until now, the reasons for this were not obvious, but hormones were speculated to play a role.

In a recent study, we showed that [high levels of testosterone](#) in males protect them against the development of allergic asthma. During puberty,

the level of testosterone increases.

Testosterone acts as a potent inhibitor of a recently discovered immune cell called an innate lymphoid cell (ILC2), which accumulates in the lungs and initiates asthma. ILC2 cells release inflammatory signals that drive the swelling and airway narrowing characteristic of asthma when people are exposed to pollen, dust mites, grass or other common allergens. Testosterone reduces the numbers of ILC2 in the lungs of males, while female hormones provide no protective effect.

Immunity and sex are far more intricately linked than we had previously appreciated. More research needs to be done to better understand the triggers involved in the different responses of males and females. But the recent discoveries open the door for tactics to potentially target hormonal pathways or receptors that are preferentially expressed on male or female immune cells.

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