

The Mortar & Pestle:

MD Custom Rx's monthly e-newsletter

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Greetings!

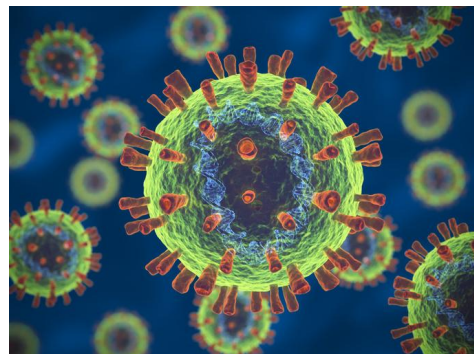
Thank you for entrusting in the compounding services at MD Custom Rx to help meet the unique medication needs of your patients. We are excited to share our monthly newsletter with you and look forward to continuing to be your medication problem solvers. Please don't ever hesitate to let us know how we can be of further assistance to you and your practice.



Sincerely,
Dan, Monica and John

The Role of Hormones in COVID and Immune Response

Across the world, why are men so much more susceptible to severe outcomes from COVID-19 than women? It has been suggested that estrogen may be protective against COVID-19 in females and/or that androgens worsen COVID-19 outcomes in men. Androgen sensitivity would explain severe cases in female patients who present with metabolic syndrome or polycystic ovary syndrome (PCOS) or who are using birth control methods with progestogen hormones that bind to an androgen receptor. Several studies have demonstrated that androgen sensitivity is associated with the CAG repeat in the first exon of the androgen receptor gene. Shorter CAG repeat length predisposes men to develop androgenetic alopecia, acne and oily skin; therefore, it's believed that CAG repeat in the AR gene may be associated with increased COVID-19 disease severity and mortality. This can also explain the disproportionate mortality rate observed in African American COVID-19 patients, because African Americans tend to carry a shorter version of the CAG repeat in the androgen receptor gene.



Do Androgens Worsen Outcomes?

The first biological step required for viral infectivity of the SARS-CoV-2 virus is priming of the spike proteins by transmembrane protease, serine 2 (TMPRSS2). TMPRSS2 is expressed on the surface of type II pneumocytes in human lung tissue, and TMPRSS2 activity is regarded as essential for viral entry and replication in infected hosts. TMPRSS2 is an androgen-regulated gene. This has led researchers to speculate that ADT (Androgen Deprivation Therapy) may be protective against COVID-19 in male patients.

In an Italian study published online May 7 in *Annals of Oncology*, researchers found that while men with cancer had an almost twofold higher risk of becoming infected with COVID-19, patients with prostate cancer being treated with androgen deprivation therapy (ADT) were significantly less likely to become infected with COVID-19 and die from the disease than other groups. ADT involves the use of medications that temporarily target androgen activity, such as androgen receptor inhibitors, steroidogenesis inhibitors, and 5-alpha reductase inhibitors. Only four out of 5273 patients receiving ADT developed SARS-CoV-2 infection and none of these patients died.

Data from 9280 patients (4532 males) with laboratory-confirmed COVID-19 infection in 68 hospitals in the Veneto region (Italy) was analyzed. "Women in the region were slightly more likely to be infected with COVID-19 than men, 56% vs 44%. However, men were more prone to develop more severe forms of the disease: 60% of men vs 40% of women required hospitalization, rising to 78% of men vs 22% of women who required intensive care. More men died than women (62% vs 38%)".

Because ADT is known to decrease TMPRSS2 levels, it has been suggested that androgen receptor antagonists could be used to block or decrease the severity of SARS-CoV-2 infection in male patients, and that men without prostate cancer at high risk for COVID-19 could take ADT to prevent infection. For men who do become infected with COVID-19, ADT might also help reduce symptom severity. Given that the effects of androgen receptor antagonists are reversible, they could be used short term (e.g., 1 month) in patients affected by SARS-CoV-2, thereby reducing the risk of side effects caused by long-term administration.

Benign prostate enlargement is caused by a very potent androgen hormone, called DHT. This is the most potent natural androgen and it binds with great affinity to the androgen receptor, making it express proteins like TMPRSS2, which has been studied for decades in prostate health and prostate cancer research and is now known to open the door to novel coronavirus.

Women also produce DHT and testosterone, though at much lower levels than men. However, due to ovary diseases such as PCOS or ovary adenomas, women can produce very high levels of male hormones. We know PCOS is related to obesity and diabetes, so women with these conditions and post-menopausal women are likely more susceptible to severe infections, following the androgen vulnerability rationale.

Is Estrogen Protective?

Another host-cell receptor, Heat Shock Protein A5 (HSPA5) also termed GRP78 or BiP, is reported to be recognized by the viral spike protein. Upon viral infection, HSPA5 is upregulated, then translocating to the cell membrane where it can be recognized by the SARS-CoV-2 spike. Phytoestrogens and some physiological hormones such as estrogens, progesterone, and testosterone show moderate to high binding affinity for HSPA5 substrate-binding domain β (SBD β), which may interfere with SARS-CoV-2 attachment to the stressed cells. These substances may be helpful as anti-COVID-19 agents for people with a high risk of cell stress like the elderly, cancer patients, and front-line medical staff.

Sharon Nachman, MD and Antonios Gasparis, MD of the Renaissance School of Medicine, Stony Brook University in New York are conducting a randomized trial with a placebo-controlled arm. They are recruiting male and female patients who present to their

emergency department with signs and symptoms of COVID-19 to determine if the use of a transdermal estrogen patch for 7 days in patients with COVID-19 might reduce the need for intubation in men and women infected with COVID-19.

Possible Immune Effect of Progesterone

“Cytokine storm” is the body’s overactive immune response to a viral infection and is one of the most devastating complications of COVID-19 infections. Researchers have looked at the anti-inflammatory properties of progesterone based on a significant amount of data in preclinical literature describing how progesterone affects immune response. “There’s a striking difference between the number of men and women in the intensive care unit, and men are clearly doing worse,” said Dr. Sara Ghandehari, a pulmonologist and ICU physician at Cedars-Sinai in Los Angeles who is the principal investigator for a proof-of-concept progesterone study. Pregnant women, who are usually immunocompromised but have high levels of estrogen and progesterone, tend to have mild courses of COVID-19. Ghandehari’s study will assess the use of a short course of hormone therapy in hospitalized men diagnosed with the novel coronavirus.

References

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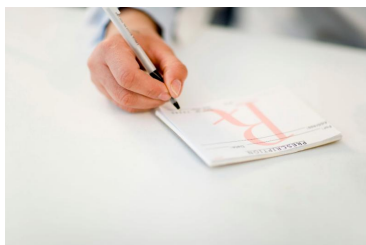
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For the reasons discussed above, it is essential that women continue their hormone therapy and that the hormonal status of both men and women is optimized to potentially reduce their risk of serious consequences of COVID-19.

MD Custom Rx Educational Events

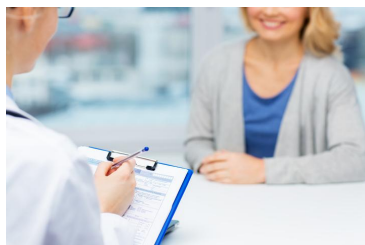
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