

COVID-19 - Our Wildest Ride Yet

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Have you ever sat in the passenger seat of a car and pressed down on an imaginary brake because you were increasingly uncomfortable by the driver's speed and their brazen flirtation with disaster? In the past week, life as we know it has been unprecedentedly disrupted by COVID-19. Right now, we are all riding shotgun and COVID-19 is behind the wheel. The question is - are we all wearing our seatbelts?

So why are a frontline emergency medicine physician and a business CEO teaming together to write about COVID-19? Because we are both experts in how biological sex and gender influence our bodies and behavior and we realize that the actions people take or don't take in the next few weeks will heavily impact the overall mortality rates of this virus. So, we think it's time we have a frank talk about sex, gender and COVID-19.

From the data we have so far, physiologically males appear to be at greater risk of having symptoms, and of dying from [COVID-19](#). In Italy, currently [58% of confirmed](#) cases are male, and in China sources have shown the death rate to be between [2.8%- 4.7%](#) in men versus 1.7% - 2.8% in women. Of note, previous coronavirus outbreaks including Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) also killed more men. Some of this gap is due to differences in gender-based cultural habits, for example in China, far more men than women smoke. However, there also appears to be a biological sex-based difference in immunology. Detailed [basic science research](#) on SARS showed that after being inoculated with similar amounts of virus, male mice experienced higher viral titers and greater inflammatory changes in their lungs. Importantly, their findings correlated with age. In those at the extreme of age there were no significant differences, but for those in between it was quite pronounced with a group of middle-aged mice infected with a moderate amount of virus showing a 90% mortality in the males but only a 20% mortality in females.

Sex-based differences in COVID-19 death rates are likely due to both sex chromosomes and hormones. Men and women may share over 98% of the same DNA but we now know *which* genes get turned on and off after an environmental trigger like an infection can be quite [sex specific](#). Although we once thought our X and Y chromosomes were mostly involved with hormonal reproductive housecleaning tasks, recent research suggests that these chromosomes also contain [genes](#) that regulate our immune response and actually influence which genes on other chromosomes get read. Interestingly, there is now evidence that COVID-19 infects lung tissue via attaching to the angiotensin converting enzyme 2 (ACE2) receptor, the gene for ACE2 is on the [X chromosome](#).

Concerning sex hormones, although both men and women have estrogen, progesterone and testosterone in their bodies, their ratios are sex specific. Testosterone can suppress immune responses while estrogen effects are more complicated and vary depending upon circulating levels and interactions with different pathways of the immune system. A [recent](#) study showed that when nasal cells infected with a flu virus were exposed to estrogen they had smaller viral replication rates, suggesting that compared to women, men might require a smaller viral load to get sick. Plus, men may be at greater risk of dying from COVID-19 because in some cases they

may have an *overly* exuberant inflammatory response that ends up suffocating their lungs and preventing adequate oxygen exchange. Women may be somewhat protected from this inflammatory overdrive due to certain estrogenic effects that dampen it.

When considering big picture numbers as to who and how many might actually die from this pandemic, our biological sex, however, is probably far less of a factor than how we as a society collectively manage these next few weeks. This is where the “gender” part comes in. In general, women historically tend to be more focused on medical [issues](#), are less likely to take [unnecessary](#) health-related risks and are more likely to [wash](#) their [hands](#). As it has just been reported that *Doctor* Rand Paul was working out in a communal gym just hours before his positive test came back, now is a good time for us all (and perhaps especially risk tolerant men) to consider the following:

1. Respect this virus. As an emergency medicine physician who has weathered the HIV, SARS, H1N1 and Ebola scares, Dr. Wolfe can say that COVID-19 is a different creature. This virus is very contagious and spreads even before someone is [symptomatic](#). [Personal accounts](#) of its impact from Italian medical colleagues are chilling and hint to the chaos that will likely hit our health care systems soon.

Fortunately, there are lessons from other pandemics that can help us get ready for COVID-19, such as those learned over a hundred years ago when the Spanish Flu that killed upwards of 100 million people. During that [pandemic](#), cities that supported aggressive early interventions like voluntary quarantines, school closures and bans on public meetings seemed to avoid a significant bolus of people getting critically ill, compared to communities with less restrictive policies. Social distancing works, and for those of you who may still be muttering “*Yeah, but don’t you think we pulled this trigger just a little too early*”, unfortunately the answer is a definitive “no”.

Once even a small amount of a community gets [infected](#), isolation strategies don’t work as well and the number of people getting sick all at once can quickly exceed the amount of available hospital and intensive care beds. COVID-19 makes things even trickier, however, as it appears that patients who survive have longer [recovery times](#) compared to patients with more common types of pneumonia. This creates a double logjam - more sick patients coming in and fewer patients going home.

Further confounding things are the very real shortages that have already started happening. By now most people are likely aware of the critical mask shortage. In another time, the idea that hospital administrators would be constructing do-it-yourself masks using [Home Depot](#) supplies to protect their frontline workers would have been simply absurd. Yet, we are now in a new reality and this is only the beginning. With hospitals modifying common practices to minimize the spread of virus between patients and staff, many are quickly running out of certain types of [asthma](#) medications. In addition, due to the impact of COVID-19 on suppliers, the restocking of other commonly used medications, like those used in heart failure, are being negatively effected. This is a long domino chain.

2. Be a Modern-Day Hero. If COVID-19 was a psychopathic killer hiding out in an empty warehouse with a dirty bomb pointed at a medium sized American city, there would be a 100-mile-long line of men waiting and willing to fight it with their lives. This virus is just as lethal as that psychopath but to defeat it will require different weapons and a different mindset. The heroes of this outbreak will be the ones willing to bunker down into the trenches of their living rooms and sacrifice their everyday conveniences to put the health of their families and the most vulnerable in their communities first. Social isolation will only work if people do it. To quote one of my fellow emergency medicine colleagues, "So, you can stay home and NOT be responsible for grandma's death, or you can ignore my advice and kill innocent people - what are your priorities?"

3. Worship the altar of Mr. Clean. In a freakishly timed release, this past [December](#) a group of researchers published a data-driven simulation model showing how pandemics might be mitigated by having more travelers at airports simply wash their hands. Their modeling suggested that by increasing hand hygiene at 10 core airports, the risk of a pandemic could be decreased by 37%. Although we can't roll back the clock and just donate a couple of barrels of hand sanitizer to those airports, there is still great value in deciding right now that having clean [hands](#) will be your new super power. Besides handwashing, here are 5 other easy ways to slow COVID-19's spread: cough into your elbow, clean your [cell phone](#), [flush](#) the toilet with the seat down, use [hand sanitizer](#) after touching shared public surfaces and..... wash your hands again. Importantly if you have kids at home, remember that your optics matter. What you do, will likely influence whether or not they adopt or discard their own COVID-19 prevention [habits](#).

4. Secure a sanctuary. With social distancing guidelines and public closures, many families will find themselves spending an uncomfortable amount of time together over the next many weeks. Cabin fever peppered with real concerns about physical risks and financial uncertainties can be a set up for sparks. Know your limits, and when you [need a break](#) separate yourself from those you love. If you don't have a cough or a fever and live in an area where there is adequate space to safely go outside, get some fresh air and exercise. Otherwise, identify an inside place where you can escape to re-center. Use technology to your advantage: play a game, listen to some music or download a relaxation [app](#). If things get overwhelming, know the resources to get you or your family members [help](#).

5. Use your Status. Somewhat ironically, the population most at risk in this pandemic - older men - are also the ones who are making many of the [key decisions](#) in how government, business and health care systems are reacting to this crisis. If you are fortunate to be in this group, use your influence wisely. This virus is quickly redefining how we do "work", and policies that are made now will influence not only your own personal exposure risk, but those of your colleagues and employees. For our economy to stay afloat during this uncertain time, you will need to be nimble and creative in ways to keep the population who can work, working. Of note, please pay

particular attention to meeting the needs of our most vulnerable workers - single parents who are supporting their family paycheck to paycheck.

For those of you who are literally in the public's eye, consider the following:

- Bring senate and congressional policies into the 21st century
 - Currently six-year-olds are being asked to do their work online, isn't it reasonable to expect Congress to do the same? From a medical lens this is even more critical because those six-year-olds are statistically going to weather this pandemic just fine - but our aging politicians? Maybe not so much.
- Modify press conferences. Sacrifice the mobbed photo op for a one podium, one-person rule. Have everyone else stand at least six feet apart or better yet, put up large screens behind the podium and connect key contributors remotely. Also reconsider the press seating area- cramming a large group of reporters into a small space in the middle of a pandemic is a bad idea. Set up an online question forum.
- Take care of first responders. Follow through on promises for increased personal protection equipment and hospital equipment. Please don't send the individuals willing to risk their own physical and emotional health to fight this battle with arts and crafts from Home Depot.
- Message responsibly. Since the start of COVID-19 there have been many instances in which there has been a major disconnect between public expectations and the reality of what health care providers and hospital systems can offer. This creates unnecessary stress for everyone. Now more than ever we need clear, coordinated information based on real data to keep everyone on the same page.
- Finally, if you are a prominent athlete, actor, gamer; if you're a business leader, a CEO or key influencer, please use your social influence to save lives by better engaging the Millennials and Generation Z in this conversation. Again, social isolation only works if we actually do it.
#StayAtHome #GetMePPE

This is it. COVID-19's foot is on the gas and we are all in for one wild ride. Click in that seatbelt.

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