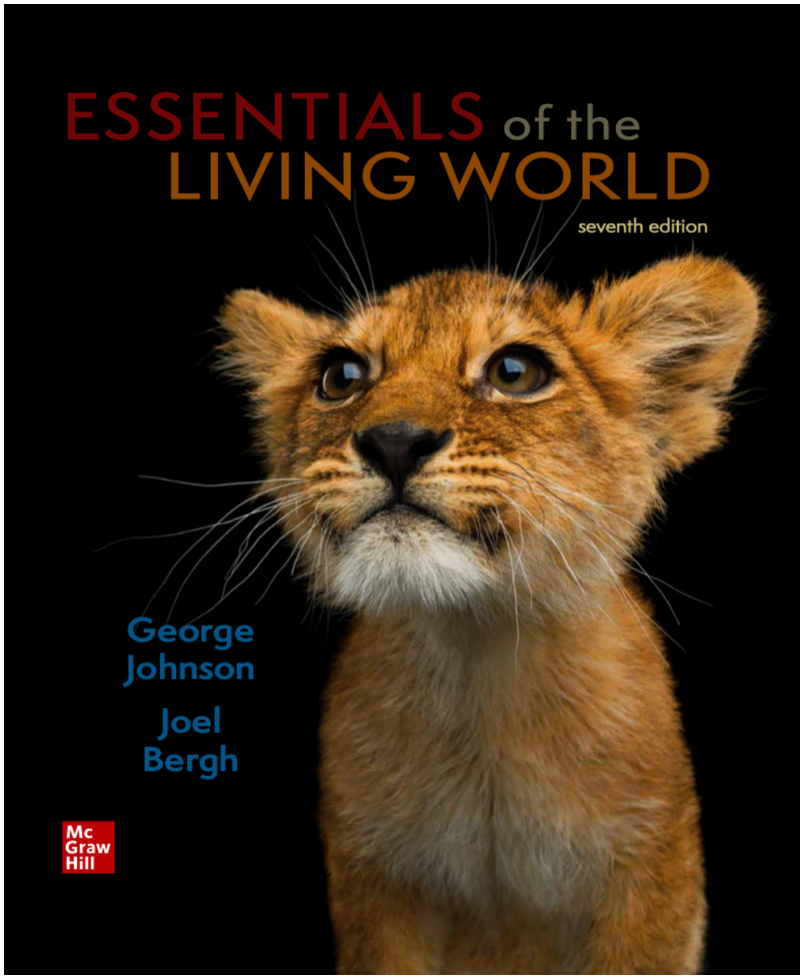
For my daughters: December 5, 2020

The Coronavirus Pandemic

A Murky Time

The COVID-19 news these last weeks has been disconcerting, some stories laced with hope, others with confusion. I'll try to walk you girls through a few of the more confusing items, sorting out fact from fancy. First a hopeful bit: The arrival of the cover for the new edition of my nonmajors biology text. I have always loved covers. For me, they are the funnest (actually, not a word) part of textbook writing. I found this image of a lion cub on the internet. The designer did a great job with it, with subtle touches like the cub's whiskers overlying my name to give the impression his face is projecting up at you like 3-D animation:

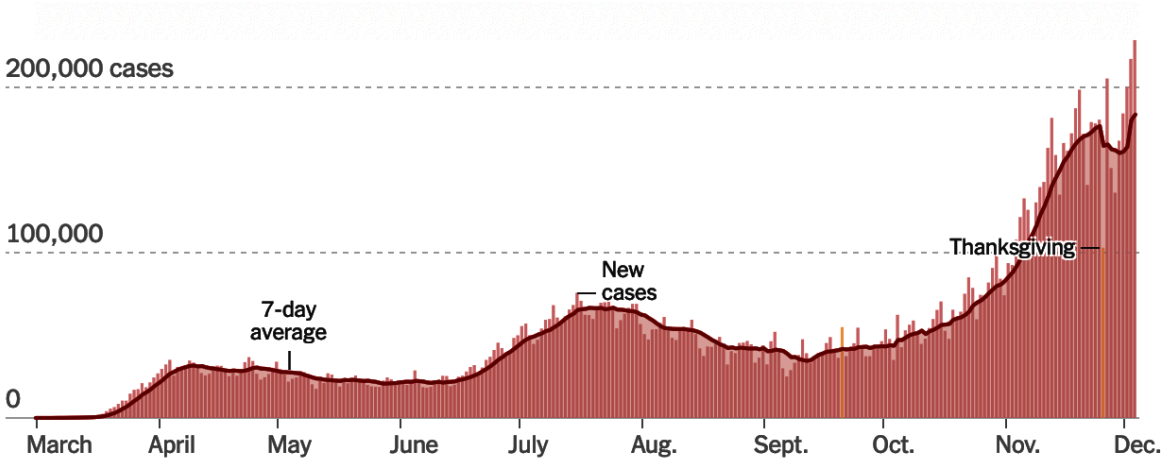


Nikki, you said *"This is a cover perfect for 2020 – he looks a little bit like he's faced obstacles but has the pluck to keep at it, venturing out into the world."* Exactly. So – starting with this image is my way to encourage you girls to see past a confusing week toward a more hopeful future.

A Confusing Thanksgiving: The Dip

Your mother, Caitlin, and I had tacos for Thanksgiving, and a full-size turkey for Sunday dinner (we are still eating it a week later). We missed the rest of the family, of course, but were glad our girls were sensible and did not travel home over this holiday. There will be other Thanksgivings. A lot of other families were less sensible, travelers crowding into airports and onto full planes all over the country; then together elbow to elbow with loved ones for large family dinners; then, a day or two later, a flight back. There is no way this traditional Thanksgiving is not bad news. All this close proximity of people from far and wide will surely lead to an explosion of new cases in about three weeks, say mid-December. The total number of COVID-19 cases in the United States passed 15 million this week; with this boost, it will zoom past 20 million by the end of the year.

While "not testing" created a big dip in the reported number of new COVID-19 case over the Thanksgiving weekend, the number of daily new infections has now renewed its acceleration upward past 200,000 a day:



So don't let the low Thanksgiving caseload fool you: the pandemic continues unabated. Nothing we are doing is slowing it's acceleration: 228,767 new cases were reported yesterday.

A Confusing Transition: Biden Begins

While the presidential election was November 3, the Trump administration did not release transition funds until three weeks later. In the meantime the federal response to the exploding COVID-19 caseload has been that of an ostrich. We have had to wait until last week for the new Biden administration to be able to get started with doing something other than waiting for a vaccine. I am encouraged with what I am hearing Biden doing in this short interval:

1. Naming a group of highly-respected professionals to head his COVID-19 response team;

2. Naming Dr Fauci as his high-level COVID-19 advisor;

3. Announcing he and Harris will get vaccinated publicly "*once Fauci says it is safe,"* to demonstrate their confidence in the vaccine;

4. mandating face masks "*for 100 days*."

So don't be confused by a slow start. This last item, a face mask mandate, is the most important thing Biden could do, in my judgement, as it will be at least three dark months (with over a million new COVID-19 cases each week) before most of us can hope to be vaccinated. In the meantime, we have to plan to keep safe –- it is sobering to think that 2,637 died of COVID-19 in one day yesterday.

A Confusing Vaccine: Oxford/AstraZenica

Much of the national press of late has been focused on the two recently-approved mRNA vaccines developed by Pfizer and by Moderna, both about 95% effective at blocking COVID-19 sickness. Both are being delivered to sites around the country, with vaccination of health care workers and those in homes for the elderly due to start within weeks.

Quietly, a third vaccine has cleared Phase Three clinical trials. Developed in England by Oxford/AstraZenica, it uses a very different approach, delivering the COVID-19 spike protein gene to a patient not in a fat bubble like Pfizer & Moderna, but rather as part of a disabled respiratory virus called adenovirus. This is actually a relatively new approach, first taken against Ebola only a few years ago, in 2019. A great deal of money has been invested in manufacturing millions of doses of the vaccine, so as to be ready to distribute world-wide as soon as the vaccine clears Phase Three trials. Like the mRNA vaccines, two doses are required, but the vaccine need not be stored at ultra-low temperature and so will be easier to use in third world countries.

It came as something of a surprise when the Phase Three trial results, made public last week, indicated the vaccine was only 62% effective. A much higher number has been hoped for. Even more surprising, in a small subgroup accidently given only a half-dose for the first of the two shots, the vaccine was fully 90% effective.

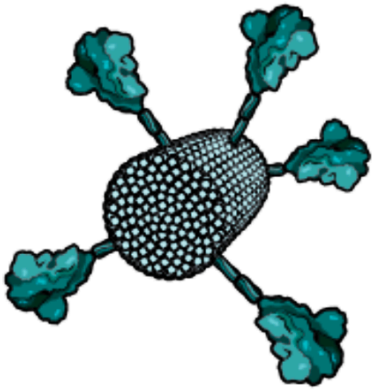
To understand what is going on here, you need to read the fine print. First, about that 60% number. It turns out the Oxford/AstraZenica Phase Three trials actually monitored each individual in the trial periodically via PCR for the presence of the virus. Thus EVERY virus infection was detected and duly noted. In the Pfizer and Moderna clinical trials, by contrast, only those patients self-reporting symptoms of COVID-19 were noted as infected. You see the point? The Pfizer and Moderna vaccines were 95% effective in blocking sickness -- but we know that 30% to 40% of COVID-19 infected individuals exhibit no symptoms! You reduce 95% by 35% and you get – wait for it – 60%. Said simply, had the Pfizer and Moderna clinical trials actually measured infection rather than sickness, they would in all likelihood have gotten the same result as Oxford/AstraZenica.

And the weird 90% half-dose result? Well, a major worry about this adenovirus vector approach has always been that the patient's immune system would react to the adenovirus particle itself as well as to the COVID-19 spike protein produced from the gene the adenovirus carried in. Were this to happen, the second injection would not be effective because of an immune defense against adenovirus, created in the patient by that initial shot. This is probably what happened to the bulk of the patients in the Oxford/AstraZenica clinical trial – except those who received only half a dose initially. It would seem that half a dose is not enough to elicit a strong immune response in the patient to the adenovirus, allowing the second shot to take full effect. Thus the Oxford/AstraZenica vaccine, to achieve its maximum 90% effect, should be administered in a half-dose/full dose series rather than as a series of two full doses. Simple.

When all is said and done, the Oxford/AstraZenica vaccine may be the best of the three -- not a conclusion you would draw from reading news accounts. Confusing indeed.

A Confusing Choice: Vaccines In the Pipeline

So which vaccine should you girls plan on taking? There is no hurry, as we will have to wait till Spring at the soonest. There are at least two others that I think even more promising than the three first out of the gate. Johnson & Johnson is developing a vaccine which takes the same adenovirus approach as Oxford/AstraZenica's. Its Phase Three clinical trials are due to complete in four weeks – and this vaccine only requires a single dose!



Even more exciting to me is the subunit vaccine being developed by Novavax. Rather than teaching a patient's cells to make covid-19 spike proteins as the other vaccines attempt to do, the Novavax vaccine simply injects the spike proteins themselves! The vaccine makers first manufacture huge amounts of COVID-19 spike protein in moth cells growing in tissue culture. They then harvest these spike proteins and attach them to tiny nanoparticles, dozens of spikes sticking out of each nanoparticle like spokes. This solution of spike-bearing nanoparticles is then injected into the patient, where the spikes evokes an immediate strong immune response. A single shot is all that is required, and there are no refrigeration issues. Phase Two clinical trials of the Novavax vaccine produced markedly more antibodies directed against COVID-19 than any other vaccine. Phase Three clinical trials only began in November, so it will be Spring before we will know what we have. My money is on this one.

A Confusing Fairy Tale: BCG

Over the last nine months all sorts of "re-purposed" medicines have been proposed to fight COVID-19. Their attraction is that these drugs have already cleared the FDA's regulatory hurdles and can be prescribed by any doctor. I have written you girls about some of the most widely-reported, like hydroxychloroquine (an anti-malarial drug promoted by the president) and remdesivir (a broad-spectrum antiviral agent). The latest entry in the re-purposed sweepstakes is the widely-used tuberculosis vaccine BCG, given to 100 million children worldwide each year. The germ of this recent re-purposing idea came from a study of blood samples collected from 6,000 health care workers in Southern California. The 30% of workers who had received BCG vaccinations as children were much less likely than others to test positive for COVID-19 antibodies. So, BCG vaccination blocks COVID-19 infection, right?

This is an example of what Kipling called "just so" stories -- it could be right, so it probably is right. But there is absolutely no evidence that it actually is. To quote the World Health Organization yesterday "*There is no evidence that the BCG vaccine protects people against infection with COVID-19 virus*." While two clinical trials to evaluate this possibility are underway, results will take many months.

It's important that you girls understand the faulty reasoning of "just so" stories like this one. It is a basic rule of logic, taught to every one of us in school: Correlation does not establish causation. A "just so" story like this BCG story simply points to a correlation, linking two items that may in fact be similar for totally unrelated reasons. The cause of one (a record of childhood BCG vaccination) may have nothing to do with the cause of the other (COVID-19 antibodies).

A Confusing News Story: Mink Rise From the Dead

When last I wrote you, we had left millions of mink in Denmark worried for their lives. The appearance in Denmark of COVID-infected mink had led the prime minister to order the culling (killing) of every mink in Denmark, some 15.5 million animals. Did you know that Denmark produces 40% of the world's mink fur? The industry, while large, is very decentralized, with much of it distributed among thousands of small farms scattered throughout the country. All of these folks let up a howl at the prime minister's culling order, creating a political firestorm that stopped the culling, but only after 2.8 million animals had died.

Well, the stop was soon stopped, and the killing resumed. Now Denmark is mink-less. Millions of their tiny carcasses have been quickly dumped into shallow graves in western Denmark. Those tiny red things in the photo are the mink being buried in long burial ditches, to be covered over with a meter of Jutland's light sandy soil.

But the story doesn't end there. Far from it. Last week the mink began to rise up from the dead! *Zombie Mink!* One local newspapers called 2020 "*the year of the zombie mutant killer mink.*" As the mink bodies decayed, you see, they released gases that caused their bodies to rise up from their graves through the light soil to the surface. Much confusion ensues. Dead mink everywhere. Millions of them. The government, embarrassed, has proposed reburying the mink in deeper ditches.

On that fantastical note I will leave you. Stay safe.

Dad