FROM THE DESKS OF
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June 26, 2020

To Our Patients,

In a recent newsletter, we wrote about how much we enjoy teaching. Then a patient gave us this poem.

"Namaste
The Light and Teacher in me
Bow and Honor
The Light and Teacher in you"

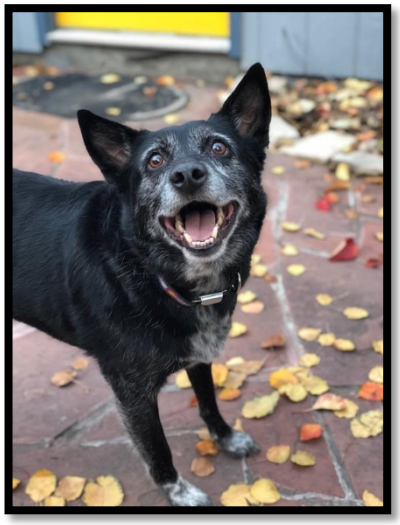
We realized that we didn't emphasize or acknowledge enough just how much our patient community teaches us every day and how much we have grown from your teaching. Thank you! We are truly honored and humbled.

If it had been any other year Dave would be spending this week in England, perhaps even testing out his golf swing at the historic St. Andrew's. I'd be packing my bags, and joining friends on our first Africa safari. But alas, we like many of you have cancelled our trips due to COVID-19 and are awaiting a vaccine to return to travel. As we dream of future adventures, we are dedicating this issue to the development of a COVID-19 vaccine!

<u>Office Updates</u>

- In order to serve our patients more efficiently and to get patients back into rooms more quickly, Dave and I will have our own staff at the Front Desk separate from the other doctors. You will be greeted by either Luke or Kris. Many of you know Kris, but they both look forward to getting to know you better!
- Murphy provided much needed pet therapy at the office today.

- With two new staff members, 2 new dogs have joined the practice family for social events – Beau and Howard.
- Nancy's baby, Riley, finally got a haircut!


- For the cat lovers…despite all of the big dogs(8 in total), guess who will always be in charge? The one and only cat in the bunch, Little Miss Francesca

<u>Kelly Dwyer's Update On Grocery Ordering</u>

In addition to the previous food delivery options, Altamira Foods, a local wholesale restaurant supplier, has added a home grocery delivery service. You can place an order online or call it in. Altamira's menu is smaller than large groceries, but the company stocks a good number of high-quality items.

To order by phone … or if you want help setting up online ordering, call Caroline at 720-473-4510. You can also email her at caroline@altamirafood.com. If Caroline is busy when you call, another staff member will take your order, or you'll get a call back shortly. **Phone orders are taken 9 a.m. - 5 p.m. Monday-Friday.**

To order online, go to www.altamiradoorstep.com.
You can **place online orders up until 10 p.m. for next-day delivery** in Denver and the suburbs inside the 470 corridor.

Notes:
- **No deliveries on Sundays**
- Altamira delivers to Boulder, Lafayette, Louisville and Superior on Tuesdays and Thursdays
- Altamira delivers to Parker, Castle Rock and Colorado Springs on Tuesdays

Delivery fees:
- Free for orders $50 and above
- $25 delivery fee on orders under $50

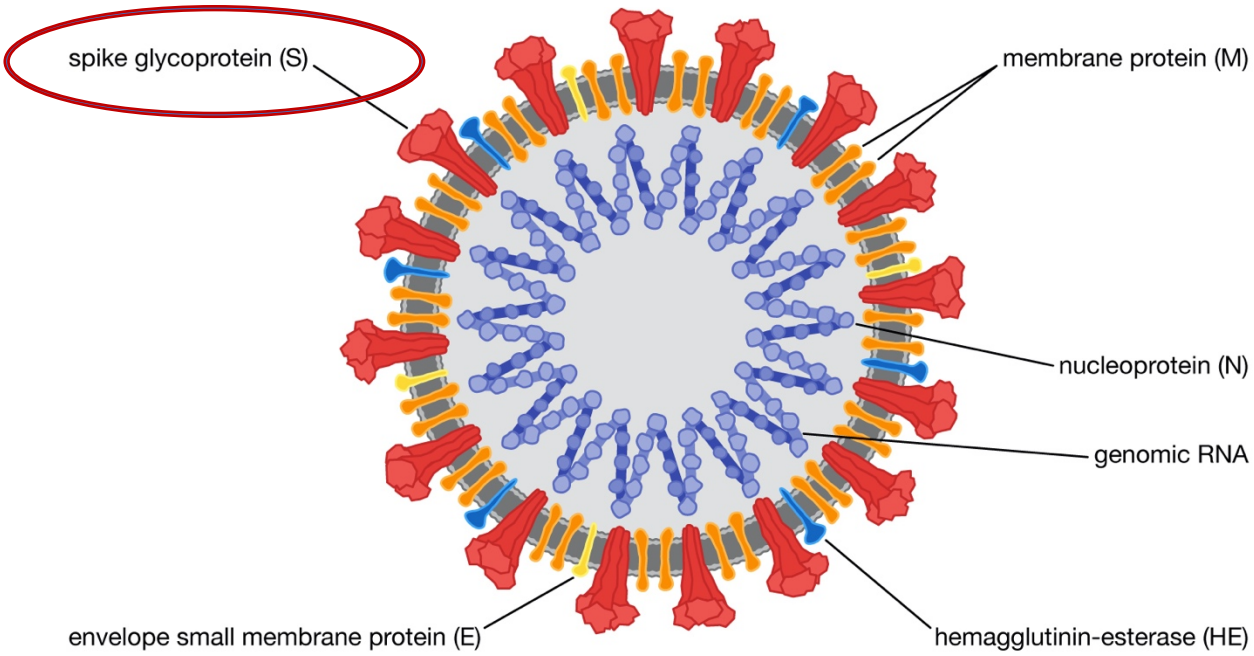
COVID-19 vaccine

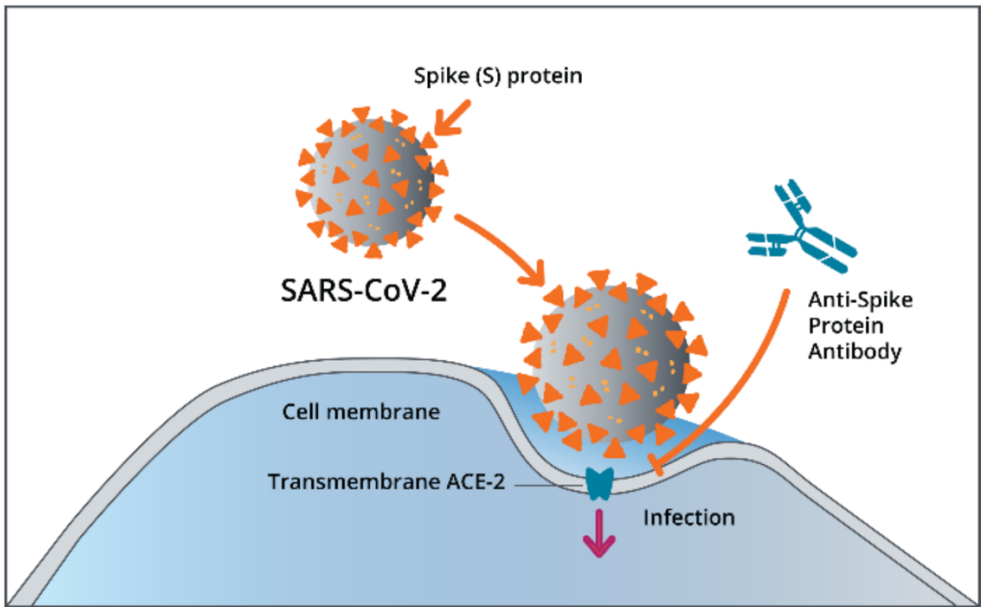
1. **When did COVID-19 vaccine research begin?**
   . In January of 2020, the COVID-19 virus was genetically sequenced. This is the first step that allows for research and development of a vaccine.

2. **Who is doing COVID-19 vaccine research?**
   As of April 8 2020, there were 115 vaccine research groups deemed eligible to begin research, 78 with confirmed active projects. 72% were from private/industry development companies and 28% were from academic/public sector/nonprofit organizations. While many of the studies are conducted across states and countries, 46% of the research originated out of North America, 18% from China, 18% from other parts of Asia (not China), and 18% from Europe.

   The most advanced companies in clinical development include mRNA 1273 Moderna, Ad5 from Can Sino Biologics, INO-4800 from Inovio, and LV-SMENP-DC and pathogen-specific aAPC from Shenzhen Geno-Immune Medical Institute. Many vaccine developers have indicated plans to initiate human testing soon.

3. **Shouldn't we know more about the COVID-19 vaccine research by now?**
   Below is a picture of the COVID-19 virus. Take notice of the spike proteins.





In order for the virus to enter human cells it must bind to the ACE-2 transmembrane protein. If scientists can block this attachment then humans won't be able to be infected by COVID-19 (also called SARS-CoV-2 and coronavirus).

We know that most of the vaccines are aimed at the viral spike protein with the goal of preventing the binding and uptake of the virus into human cells via the ACE-2 receptor.

We also know some companies are researching molecules called adjuvants. Adjuvants are chemicals that enhance the effectiveness or immunogenicity of a vaccine. Adjuvants

allow vaccines to work at lower doses or with less doses. This would enable healthcare professions to vaccinate more people and to do so more quickly without compromising protection. Companies like GlaxoSmithKline, Seqirus, and Dynavax are currently working on adjuvants.

While it may sound like I just gave you a lot of information, for a doctor or scientist that is not very specific information. The available details regarding how vaccines and adjuvants are being made and their exact molecular targets have been very limited, perhaps to protect proprietary interests.

4. **Has a COVID-19 vaccine been tested on humans?**

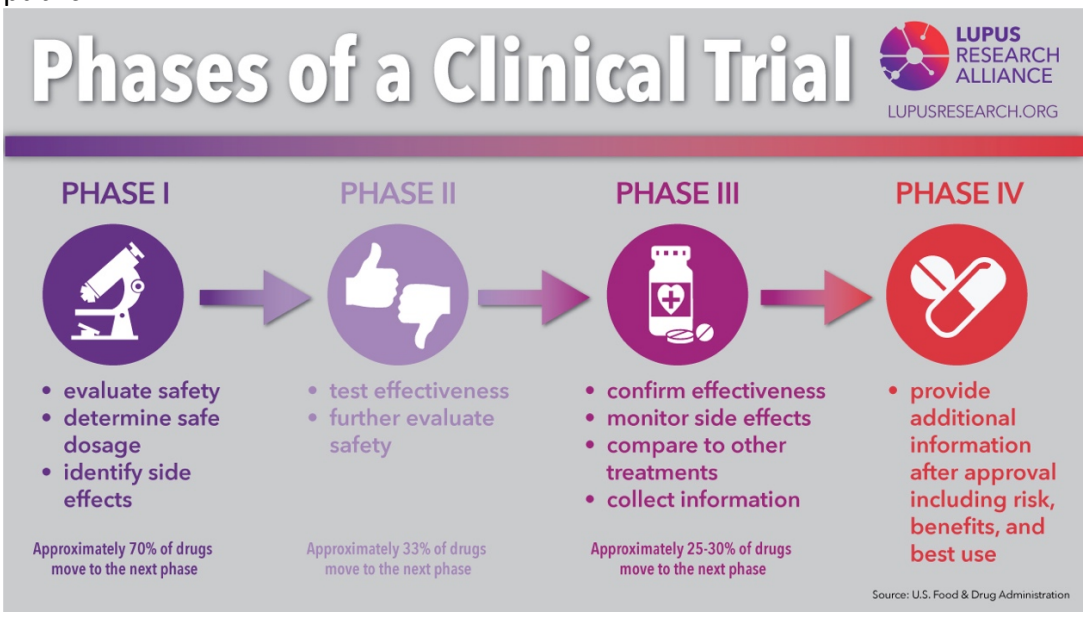
First, vaccines are tested on animal models: mice, hamsters, ferrets and non-human primates. The most common non-human primate is the Rhesus macaque monkey.

Vaccines also come in many different types thanks to a range of technologies that have been developed over the years: DNA and RNA vaccines, virus like particles, viral vectors, recombinant proteins, live attenuated virus and inactivated virus vaccines.

Here are three studies that have been published so far.

Study 1: 35 Rhesus macaque monkeys were given a DNA vaccine that targeted the COVID-19 spike proteins. 35 is a very small number in research. As hoped, those monkeys were able to produce viral COVID-19 mRNA and proteins that did not make them sick but allowed their bodies to produce antibodies. Most vaccinated monkeys made various types of antibodies (humoral and cellular, including *neutralizing antibodies*.) The scientist then tried to give the vaccinated monkeys COVID-19 to see if the antibodies worked. When confronted with the real COVID-19 virus to see if they had immunity, the number of viral particles in bodies was lower in vaccinated animals, resulting in only mild clinical symptoms. The more *neutralizing type* of antibodies the monkeys had, the less symptoms they developed.

Study 2: Vaccines go through 4 phases before they can be released to the public.



In March, an mRNA vaccine was tested on 45 human participants in a phase 1 trial. In this study, all 45 participants developed antibodies 2 weeks after the 2nd dose of the vaccine. Their antibodies were at the same levels as recovering patients. The first 8 participants in the study developed neutralizing antibodies (nothing was said about the remaining). Adverse events were rare. The same vaccine was shown to block viral replication in the lungs of mice infected with SARs-CO-V-2. Phase 2 was scheduled to start in June and, phase 3 in July.

Study 3: Adenoviruses have been used in the past as a vector (carrier) for human vaccines to transport the vaccine into the body, like a capsule brings medicine into the body in a pill form. Research scientists have evaluated the safety and effectiveness or immunogenicity of an adenovirus type 5 (Ad5)-vectored vaccine expressing the COVID-19 spike protein. This vaccine has been given to 87 people. 81% had side effects – pain at the injections site and fever. 94-100% of participants had a 4-fold rise in antibodies at 28 days and 4 fold rise in *neutralizing* antibodies at 28 days in 50-75%. Remember from study 1, neutralizing antibodies are the most effect at preventing disease symptoms! Unfortunately, pre-existing immunity to the adenovirus type 5 decreases the likelihood of neutralizing antibody titers post vaccination. This means that if you have had the adenovirus, which is a cold virus, before you are less likely to develop an adequate immune response to this vaccine. If this vaccine is only 50-75% effective, that would make it about as effective as the flu vaccine.

5. **When will a COVID-19 vaccine be available?**
   Globally, the goal is to have a vaccine available in early 2021. This would be a record as prior vaccines have averaged 10 years and even the recent Ebola vaccine took 5 years to develop. But, as we mentioned earlier there are many new technologies now available

for developing vaccines. Specifically, the DNA and mRNA vaccines are new. They are much more flexible, allow for much quicker development and higher production capacity. We will still need many companies to develop vaccines and several different types of delivery systems, such DNA and RNA vaccines, virus like particles, viral vectors, recombinant proteins, live attenuated virus and inactivated virus vaccines. Some platforms for delivery of the vaccine may be better for different populations: babies vs. adults, those with access to refrigeration vs those without, etc. There are rumors that Astra Zeneca may have a vaccine available by October at a cost of $3-4 dose…

6. **Anything else interesting in the pipeline?**
   Researchers identified an antibody in a patient who was infected with SARS-CoV (the original SARS) in 2003 that effectively neutralized COVID-19, which may work as prophylaxis or post exposure therapy to limit or treat severe disease.

Patient Questions

1. **What is known about blood type and COVID-19?**
   Patient with blood group A+ were more likely to get COVID. O+ was the least likely. (For the scientists reading this… the difference was only significant between A+ and O+). But, people with A+ blood did not get sicker than others. They were *no* more likely to end up on a ventilator or breathing machine and were *not* more likely to die.

2. **Do you have my blood type in my medical record?**
   Unfortunately not. Blood type is not a routine test. When a patient needs a blood transfusion, blood type can be determined on the spot and is done so to ensure accurate blood type matching.

We hope you continue to enjoyed the variety of newsletters as we try to meet the needs of our audience that span ten decades and an even wider spectrum of interests. Keep the questions and topic requests coming.

Take care, be well, wash your hands and wear a mask!

Jeannette and Dave

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