

## **What Happens Next in 6 Minutes – February 27, 2022**

### **Limitations of Scaling a Business or Idea & Ivermectin**

#### **Ari Ciment Q&A**

#### **Larry Bernstein:**

Ari. Welcome back to the show. Today's topic is ivermectin. Ari, what is ivermectin?

#### **Ari Ciment:**

Ivermectin is an anti-parasitic drug used for scabies in the past that has been repurposed for COVID-19.

#### **Larry Bernstein:**

Why did we think of using ivermectin for Covid19?

#### **Ari Ciment:**

It does have in vitro activity at higher doses against COVID-19.

They did initial in vitro experiments with a whole variety of medicines and ivermectin showed potential antiviral activity. A lot of the drugs that were seen to be effective versus malaria were studied against COVID. So if you went on the CDC website, looked for malaria drugs, they'll find alternative therapies besides quinine. You'll find hydroxychloroquine, doxycycline, ivermectin, and it's interesting that all those drugs turned out to be possible therapies for COVID.

#### **Larry Bernstein:**

There was a meta-study of all the major global ivermectin trials. And Dr. Richard Hill found that ivermectin reduced mortality by 56%, but the results were dependent on two studies which were later found to be fraudulent.

#### **Ari Ciment:**

The initial meta-analysis had two studies from Egypt and Lebanon, and both studies basically had duplicate data and was fraudulent, then when you take away 20% of your effectiveness you're left with nonsignificant.

#### **Larry Bernstein:**

Why were these medical trials fraudulent, what happened?

#### **Ari Ciment:**

What is causing people to publish fraudulent data? I think that it's the same problem that we've had in the past with the anti-vaxxer who was published in Lancet. They figure that's the fastest way to become famous is to publish something that is a hot topic, even if it means fabricating data. At the time that all these studies are coming out, there's an excitement, what can we do? And some of the investigators really believe in ivermectin and they wanna get it out. So, they do less than honest approaches.

**Larry Bernstein:**

During the beginning of the pandemic, doctors and scientists had no idea about the disease and the medications. So, they followed their intuition and provided patients with a cocktail. Some worked and some didn't. Is that to be expected?

**Ari Ciment:**

Well, that's a great question. Initially in a pandemic, there was a lack of medicine, if the medicines made sense, then it was appropriate to at least try because nothing else seemed to work. Ivermectin doesn't have a very clear mechanism of action, but there were anecdotal stories by physicians. So, it made sense to try it, because the risk benefit ratio was favorable.

You rely on anecdotal medicine when you have a new disease. And then over time, you start seeing some of these articles being published. But the key takeaway is to rely on people like from the New England Journal of Medicine, someone like Eric Topol.

**Larry Bernstein:**

Medical information in a pandemic is evolving, how do you change your choice of medications?

**Ari Ciment:**

I think the key is to react and adapt. We used high dose Plaquenil in the beginning and HIV medicine, but when we saw it wasn't helping and potentially hurting, we stopped it. The flip side is there was a medicine called Tocilizumab that everybody was saying that it's dangerous to use along with steroids, but we saw in our patients that it seemed to dramatically help. So even though it was against the initial randomized control trials, we saw it with our own eyes that it helped and we continued to use it, and eventually there was a randomized control trial that showed benefit. Reacting and adapting is the key.

**Larry Bernstein:**

Ari, I was your patient in the hospital in December 2020 when I had the Cytokine Storm and you gave me that cocktail.

**Ari Ciment:**

You reacted excellently to Tocilizumab and steroids. And you had the variant where we were most concerned with the cytokine phase and I believe that's what helped you turn around.

**Larry Bernstein:**

The meta-study for ivermectin comes out two years after the outbreak of COVID, and it relies on studies from Egypt and Lebanon. This is the most important medical event of our lifetime, why did it take so long?

**Ari Ciment:**

It takes time to do a study. I was just involved in a COVID study and it took a year and a half to get it going, and it seemed like a pretty straightforward, easy study. It takes a while to develop protocols and methods and to do things the right way. There were over 80 trials, randomized control trials that were in the works. I don't know how many of them actually ended up completed, but for ivermectin, there were many. And also for Plaquenil, there were many, many studies.

**Larry Bernstein:**

When you think about experimental design for these COVID drugs, there are so many variables, when to take the drug, the dosage, as a cocktail with other drugs, which ones? How does these variables complicate matters?

**Ari Ciment:**

it's a matter of the timing. That's number one. Number two all those ivermectin studies used different drug doses. Nevertheless, whichever dose they used, it was never a rip-roaring positive randomized control trial.

**Larry Bernstein:**

I want to explore varying dosage of ivermectin. Some of these studies were using 20x the recommended use. How do you think about radical increases in the dosage amounts and your concern about possible side effects?

**Ari Ciment:**

I think that's the reason why the CDC and the NIH sort of clamped down on the ivermectin. Ivermectin does have a Nobel Prize associated with it. It's a safe drug, it's a very effective good drug for what it's purposed for, but we're talking about doses that needed to be that high based on the in vitro studies that showed that it was only effective at high doses.

**Larry Bernstein:**

The most positive ivermectin study was done in Brazil by Pierre Kory. Ivermectin was used as a prophylactic, so people were taking it who did not have COVID. The size of the study was gigantic. 160,000 subjects in the study with 113,000 taking ivermectin and 47,000 taking the placebo. The results were beyond impressive, mortality was reduced by 68% for ivermectin users from 2.6% mortality to 0.8%.

This study was not peer reviewed but it showed great promise when it was released. In retrospect, how do you think about this particular study?

**Ari Ciment:**

That study was definitely thought-provoking and you really have to investigate not what you're reading only, but also where it's coming from. Some of the authors listed are Flavio Cadegiani, and Juan Chamie, C-H-A-M-I-E, and Pierre Kory. These people are members of the Front Line

COVID Critical Care Alliance, and Cadegiani is a PI of a trial that's being investigated for violations of medical ethics by Brazil's National Health Council. And Lucy Kerr works for a company that produces ivermectin.

So even before you start reading the paper, is it reliable? The numbers look good. It's definitely thought-provoking and it looks positive. But the flip side is it's an observational study. Did these patients assigned to the ivermectin, did they really pick up the medicine? Were they really taking it? I think it comes down to design differences. A meta-analysis that has many, many randomized control trials that's on the top. Then you have a randomized control trial. Then below that you have observational studies like cohort studies, case control studies, cross-sectional surveys, right?

You really wanna see a robust randomized control trial that would yield you the best information. What they were employing was an observational study, but they were doing such dramatically high numbers that it should blow you away. But then you have to look at where they're getting their information, if it's accurate and see if they're really trustworthy.

At this point because of the people involved in it, I say, wow, that's cool, but I don't give it any credence personally.

**Larry Bernstein:**

Do you view yourself as impartial on ivermectin?

**Ari Ciment:**

I promise you, I wanna believe that ivermectin works. I was hoping to see a positive trial, honestly, but there hasn't been one large randomized control trial without credibility issues that have been positive.

**Larry Bernstein:**

What lessons can we learn from this ivermectin experience?

**Ari Ciment:**

We went for it because it inhibited the replication of SARS-CoV-2 and cell culture, so it made sense, because it has a good track record of safety. There hasn't been any major randomized control trials that have shown positive benefit. And these trials that have been done that have been beneficial are either published by people with credibility issues or have some problems in the makeup of this study.

**Larry Bernstein:**

Ari, I end each episode on a note of optimism. What are you optimistic about this week?

**Ari Ciment:**

I'm optimistic that COVID just seems to be going away.

**Larry Bernstein:**

Thanks to John and Ari for joining us today.

That ends today's session. I want to make a plug for next week's show.

Our first speaker will be Heather Mac Donald who will speak about her recent article in The City Journal entitled The Guardians in Retreat. And the topic is the rise of wokeness in art museums and The Art Institute of Chicago in particular. This will be a very provocative discussion.

Our second speaker will be Rosemary Salomone who is the Kenneth Wang Professor of Law at St. John's University. Rosemary has a new book entitled The Rise of English: Global Politics and the Power of Language. Rosemary is interested in the reaction to the growing dominance of English in the world of business and science. And how this is impacting millions of youngsters' choice of a second language. In addition, we will discuss the growing influence of Mandarin and Hindi as competing languages in global commerce.

Please email me your questions for next week's session, if you want to participate at [larrybernstein1@gmail.com](mailto:larrybernstein1@gmail.com).

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Thanks to our audience for your continued engagement with these important issues, good-bye.