Bret and Heather 58th DarkHorse Podcast Livestream\_ A Vaccin...

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**SPEAKERS**

Bret, Heather

**Bret** 00:15

Hey folks, welcome to the Dark Horse podcast live stream number 58. I am alerted 58 live darkness podcasts in a row, right in a row, right? Almost immediately in a row if you count only the live ones. Yes, yeah, that's circular, but let's just go. So a very Happy Hanukkah to you all Hanukkah is ongoing. I remember Maybe you remember, you and I both grew up in LA, obviously. Do you remember our local stations? Had a broadcast during Hanukkah? And they would say Happy Hanukkah, to our Jewish friends? Do you remember that? I remember I felt like it. Is that a threat? I mean, it seems friendly. But there was just a little talking about like, I don't know, it was. I think it was all of the local ones had some version of that.

**Heather** 01:05

Okay. To our Jewish friends.

**Bret** 01:08

Exactly. And the thing is, because you couldn't see the person saying that you didn't know if they were raising an eyebrow, which of course tells you whether it's to be taken ironically, you're talking about radio stations? No, no, this was television. I think it was just they had an image of a menorah. I don't know what it was. And then the voiceover would say that. Sure. Or possibly I imagined it. That's why I was hoping that you might have remembered it as well.

**Heather** 01:30

I don't know, I guess but you know, it wasn't targeted at me. I wasn't one of their Jewish friends. Exactly. Exactly.

**Bret** 01:35

So yes, it would have been less significant, I would imagine. Yeah. So this does raise a question though. I was wondering, why is it that Energizer is not the official battery of Hanukkah.

**Heather** 01:51

You were wondering this I was wondering this yesterday. Was this been plaguing you while you're out on your nighttime midnight bike ride? Yeah, in December, Chile, Chile, Chile bike, dry, and you're wondering why Energizer batteries are not the official battery of Hanukkah. Is there an official anything of Hanukkah?

**Bret** 02:09

No, but we're I energiser. I would at least note that you could avail yourself of something like you know the slogan. It's like McCabe lamp oil, but for electronic stuff or something along those lines. You see what I'm saying?

**Heather** 02:24

Yeah, I think there's a reason you didn't go into this line for advertising.

**Bret** 02:27

Yes, that's that's possible. Yeah, I would have been atrocious at it. To say the least. Yes, yes.

**Heather** 02:33

Yes. Although I mean, I so we wanted to start out and I don't like pivoting this way. But you do come up with pithy sayings like your algorithms, no good here. And we are willing to have them available on things like hoodies and shirts and such so anyone who's interested can go wherever whatever that site is, it is called a store dot Darkhorse podcast.org Yes, to get such things if you're so interested,

**Bret** 03:00

at least one person on Twitter thought that your confirmation bias is not my problem was also a slogan worthy of a shirt. I don't know if it's worth it for one person, but it's possible that they speak for a multitude

**Heather** 03:14

your convert your confirmation bias is not my problem. I also see an interest in first against the wall club, the first

**Bret** 03:20

against the wall club. Of course, that could be a beautiful shirt. Yeah, yep. Yes, and I don't know how we ended up on this we actually created an intro screen. Actually, Zack created it though I'm going to take credit on all of our behalf. The he created an interest stream that is supposed to free us from talking about things like merchandise by saying it in text without us having to Sully ourselves by saying it out loud. Except the

**Heather** 03:46

many more than half of the people who encounter this podcast only in audio form don't see that

**Bret** 03:51

well, but they could infer it. You see what I'm saying? They could read. They could listen between the lines I say yeah, so actually here I just accidentally have this on the desk here. This came for us.

**Heather** 04:04

And I was watching the YouTube viewers aren't you? I am over Yes.

**Bret** 04:08

So for those of you listening on audio only versions what I have here is a dark horse coffee mug. And I was skeptical at first when I tried it works great holds coffee. Yeah, I mean your joke but the thing is there are 1000s of ways an object like this can fail and there's only a few it can work and this one threads the needle. It works great.

**Heather** 04:31

You're speaking to a ceramicist. So yeah, I'm quite aware of how many ways a mug can fail Yeah, they

**Bret** 04:36

usually Yeah, they can fail a lot of ways a lot of them when they're still before they're, they're dried.

**Heather** 04:42

Yeah, you want to get them up to the the cone that both the clay body and the Glazer derived for totally devised for created for

**Bret** 04:50

I did also I invented a new drink using this. Oh boy. No, I did what you do.

**Heather** 04:58

It looks very dry.

**Bret** 05:00

It's not here now. In fact, I'm it's not here in part because I don't want us to get d monetized. Right?

**Heather** 05:06

What kind of drink? Is it? What does it in fact have mRNA? And

**Bret** 05:10

we'll get there. No, what you do is you take you take the glass, you put it on a flat surface and you load it with about an ounce of I use rum. I think it would work with tequila probably would work with vodka. I don't know if it would work with scotch or whiskey because I'm allergic to wheat and therefore I don't touch those things. It might. So anyway, on a flat surface, you put a an ounce of, of rum in there. It's a super innovative so far. Then you drink it, and it's called, oh, a Portland mug shot. All right, okay. Yeah, but

**Heather** 05:52

that could have been worse. You know, actually, I used to give you points. I used to get some points. Yes, yes. Yes. negative points. That's

**Bret** 06:01

the thing is it's wonderful. When one's wife will actually award points for a good joke. That's a great thing. But when the scale goes negative, it can go wrong.

**Heather** 06:09

Mighty quickly, so quickly. So I'll give you seven points for that one.

**Bret** 06:13

That's not bad experience. That's pretty good. All right, one mug shot. A Portland mug shot. Yep. I feel that was worth it. All right.

**Heather** 06:21

So today, we want to talk a bit about vaccines. We feel compelled to talk about vaccines. I can't say that I actually want to talk about vaccines, but we compel we feel compelled to talk a bit about vaccines. You had some things to say about journalism and the media. We wanted to talk a little bit about some observations about traffic. And if we have time, a little bit about sexy flies.

**Bret** 06:48

Totally. I'm very much looking forward to that part of the conversation because I I'm finding it hard to imagine the sexy fly. Oh, you're not talking about Spanish flies? Are you? No, no. Alright, then I can't figure out what that would be in reference to. So I'm excellent suspense, like the rest of you. Terrific. All right. So yes, I will just say that I, this may be a me thing. But I feel that I am being driven slowly crazy by the conversation surrounding vaccines, generally, Coronavirus, vaccines, specifically, the ongoing pandemic and where we are and might be and all of those things. And as those who have been around for the last couple of live streams now, I also feel a certain amount of Jeopardy around discussing these things. Because there is this absolutely oppressive, authoritarian, nanny voice that belongs to the tech platforms where they somehow believe that they are in a position to know what is true and who may voice what kind of skepticism when one cannot look up these things. There's no phone number, you can call and ask, is it permissible to discuss this, even though I don't believe that they should be in a position to say it is or it isn't? I'd at least like to know whether or not we are putting the channel in danger by doing so. But I don't I increasingly just don't think we have a choice. I think you we are in a position to discuss it responsibly. And it must be done in spite of the fact that there are risks in that discussion. They're not they do not justify censoring such discussions.

**Heather** 08:23

Yeah. Let me just as one piece of evidence that there are risks here that the dominant narrative sounds a particular way. It's sort of one of scolding and tutting and how could you be so dumb as to believe these things? Here, Zachary is thing from BBC News called reality check from second of December, called vaccine rumors debunked. microchips altered DNA and more. And we have we've talked about things like this in different contexts where some, some batshit conspiracy hypothesis like the lizard people are among us, right? is mixed in with things that are not mainstream, but that should be plausibly considered, right? So we have here, for instance, in this in this list, the fear that a vaccine will somehow change your DNA. injecting RNA into a person doesn't do anything to the DNA of a human cell says Professor Ahmed of Oxford University. That's true. We don't this as as far as we know, an mRNA vaccine has no access to a DNA as far as we know. Yes, l gates and microchip claims this does seem absurd, and it seemed absurd from the beginning. fetal tissue claims I have no idea. I there's no reason there's no reason given what kind of vaccine This is for them ever to have engaged any fetal tissue at all. And then just the last one on this list, I think recovery rate claims Well, we actually don't know how to assess recovery rate, unless all we're looking at is death versus not death. And this is something that we talked about a lot in the first, whatever it was 16 1718 episodes of this livestream.

**Bret** 10:19

Yes. And as we, you know, of the many things that we have said that I think constitute a better model than the one publicly being discussed. In some cases, the public model has caught up and in some many places it hasn't. But the right way to think of it is how much life does being sick with the Coronavirus rob you up, right? And the answer is very likely to be a substantial number of years, which means even if you appear to have recovered, what we know about the tissue damage that comes with this thing, suggests that that you didn't die is not evidence that you got away with it. It is evidence that there you had a buffer. So anyway, people should be very much aware of that. All right,

**Heather** 11:09

and we have this because it would play through my computer, I'm not going to show it because it won't, you won't guys won't be able to hear it. But when the UK approved for the first time ever, as a as a health as a major health agency and mRNA vaccine, whatever this was last week, I guess what the regulator in chief said was, quote, The benefits far outweigh any risk. And this is this is what you would say, if you were heading up an agency that had just decided to to go forward with this, but there is no way that anyone can plausibly say that at this point, because we cannot know right? We cannot know what all the risks are, I would

**Bret** 11:51

never utter a statement like you might say, if you wanted to say that statement in a way that it was perfectly defensible, you might say the benefits outweigh any known harm. Right? By putting it in the context of risk, they are saying something insane and indefensible.

**Heather** 12:10

Yeah, and actually, I thought we might wrap up with this. But maybe before you launch into what you're going to launch into, it occurred to me that there are at least four questions that we should be asking about, about any treatment really, but in this case, it's about a vaccine, how safe is it? Quite aside from how effective it is? how effective is it quite aside from how safe it is? What are the risks from contracting COVID-19? Not just the death rates by age, etc, but the long term health effects? And for this third question, we cannot know all of those answers, nor can we even nor for that first question, can we know all of the long term safety answers, but given those first two questions, safety, not efficacy, efficacy, not safety, and also the actual risks from the disease that you would be being vaccinated against? Given the answers to those, those first three questions? How do we then generate an answer to shouldn't individual take the vaccine? Should whole populations take the vaccine? Under what circumstances? Should it be allowed to be a personal choice? and under what circumstances should it be a top down move by a government that says actually, in order to participate in school, for instance, you're gonna need to take this vaccine because we know we have we have diseases like that, for which those those decisions have been made.

**Bret** 13:27

Yeah, I love that list. That matrix is a is an excellent one for discussing. And I would just point out that one thing that is very clear, if you look at that matrix, is that, wow, do we not know a lot about the harm of COVID-19. But boy, do we know a hell of a lot more about COVID-19 than we know about these vaccines. And the reason is because we have had exposure to the consequences of COVID-19 for a longer period of time than this vaccine has been administered to human beings. So we see something more of you know, a time series what develops six months out, for example. And the other thing is a much larger population has been exposed. So to the extent to the disease, then to the vaccine, right? There are tail risks and things were in a much better position to see them and to understand what they look like. And so in some sense, you are in a decent position to calibrate you have any any individual all together collectively are in a much better position to calibrate how we feel the risks associated with COVID-19 stackup than we are with respect to the vaccine. Right. And that is a key thing because at the same time that you know vastly more about this disease, you don't know nearly enough, right? We don't know whether or not people who have recovered from COVID-19 have plausible in my opinion have been robbed on average of 10 years of youth. Right That is to say they are 10 years closer to death off things being equal, they are their tissues, it could be particular tissues, or it could be very general that there has been destruction. And so they have been advanced in their senescence profile. And I would say, this is something that we should be asking for every disease, right? The model that we typically walk around with, where you get the flu, and you get over it, and you think, well, the cost was, you know, a week or a week and then some, some lagging symptoms or something like that. The answer is no, you were you were robbed of things you don't know about, because that's the nature of tissue damage, we can say the same thing for broken limbs. I mean, I think people Intuit this with respect to joint damage, if you physically damaged a joint, you know that there's only so many times you can put it back together. But you know, the same goes for a broken wrist, right, you're extending some of your lifetime capacity to repair, to repair that damage. And the chances that you're the fact that you've advanced the age of your wrist bones a little bit is going to be critical is very, very low. But But nonetheless, that's the model we should be using for anything that does damage to the body. And

**Heather** 16:06

this is a place where, you know, we will tend to argue that an engineering approach to the world is far too simple when you're talking about complex systems like like, evolved ones, like biological systems, and that it's, like I said, reductionist. But here, even an engineering approach a body as machine approach, which is often far too simple to actually get you where you need to go, can work. If you think of, you know, a long bone as akin to like a rod of steel. Well, you bend it and you bend it and you bend it, and obviously you're not, you know, you're not, you don't have tensile strength and a long bone. Once it pretty much shatters. But it's not going to continue to retain all of its strength, you know, I just feel it's not

**Bret** 16:50

the way a rod of steel is somewhat calm. Yes, that

**Heather** 16:54

is that is what I'm in fact, what you have is strength, very much strength in in one direction and not not ensuring direction, right. But, but even with something like steel, with prolonged stress, it becomes weakened.

**Bret** 17:13

Yes, and there are all sorts of, you know, I don't know how we ended up in metallurgy territory. But there are all sorts of interesting facts about, you know, two tubes of steel that look alike, can have very different properties based on things like their internal shaping. And so the writing of bones has an impact and the fact that you've repaired the damage and don't get quite the same shape back as implications. There are also weird things like tempering steel with heat that causes you know, a realignment of the molecules that you can't see in the macroscopic structure, but nonetheless, can greatly enhance strength, you can also decorate it with heat,

**Heather** 17:54

the analog there and bones is going to be used the way you make bones more anti fragile as you use them. And we don't understand all of the mechanisms by which that makes them stronger, some of them are likely to be that it reforms the inner margins of the bones, there are going to be many other mechanisms, mechanisms, we just don't know yet. But what we do know for sure, is use it and it will become more not just robust, but more stronger in the face of stress.

**Bret** 18:20

It's literally anti fragile, and apologies to Nassim Taleb, if he has used that example, which is highly likely,

**Heather** 18:27

I'm sure, yeah, I'm sure that's

**Bret** 18:28

given the nature of the model and his mindset. But in any case, in this case, you can actually say, Well, okay, bones are anti fragile, that's interesting. But of course, they're anti fragile, because, you know, if you were going to design, you know, we we, as designers tend to think in terms of what does that part look like, and then you send it to the factory, and they make it, whereas a part where the factory is internal to the part and can reshape it based on what it turns out happens in the field, right? If you're using it, and you're stressing it, then the point is, oh, maybe it's not strong enough. Anytime you get anywhere near the breaking threshold, you're telling the body actually a little more resource should be spent here. It'll be worth it. And so you know, stressing systems causes them to be made more robust.

**Heather** 19:10

So I we did, we did jump between the the simple the engineering model and the more complex biological model where you know, the simple stuff is, is going to be less likely to be anti fragile. So you put an extreme stress on a bone, and it's simply going to break and if you do that multiple times it will become weaker. So this this anti fragility model has of course, bounce. Yep.

**Bret** 19:35

Okay. Well, interestingly, I think the way you set this up makes good sense because the current predicament with the vaccines and there are two of them that are rapidly moving towards widespread distribution shows us both the strength of the engineering approach and the weakness of the engineering approach in the context of a complex system. So in some sense, the engineering approach caused us to be able to generate and I say us, I mean humanity to generate vaccines in less than a year, which is a very rapid production production schedule. And you know, there is no way you should regard this as anything other than a spectacular achievement no matter what else may be true of these vaccines, the ability to get a vaccine that actually does create substantial immunity, and it looks really good. In this case, after two, two vaccinations, it looks like 90% successful or close to it in both cases. So that's an amazing achievement. The question is, what else does it do? And I want to point to three things that I believe are worrisome in this case, and that mean that your normal model, your normal model for how to feel about vaccine safety may be good, or it may be cruddy or probably it's somewhere in between. But this doesn't belong in the same category. And unfortunately, because we use these heuristics, and because there is this voice out there, that for many different reasons, some of them purely financial, and some of them policy in policy based, there's this voice that sort of wants you to default into standard vaccine brain. And it's not appropriate here.

**Heather** 21:25

So a few episodes ago, maybe in the q&a, we raised this just briefly, and I reported that I had had a conversation with a with a mutual acquaintance, who had asked me, you know, what, what do I do? What do I know? And I at that point, it was just just beginning to emerge. And I did not know that they were mRNA vaccines. And what I said to her, and when I said on air that I had said to her was, it might not be effective, but it's unlikely to be any more dangerous than any other vaccine. And I think I think that is not true. And and I don't know, I think I think we can't know if that is true. How about that it is possible that the safety is even greater than other vaccines. But because exactly this technology, this is the first time that it's ever been approved for use in humans. And because one of the benefits of an mRNA vaccine is that it doesn't require the virus itself to develop it. And so it can be developed and distributed extremely rapidly. So it's no accident that we are seeing to mRNA vaccines as opposed to more traditional and gender protein based vaccines is precisely because it is one of the key features of an mRNA vaccine. And the fact is that there are just there are a couple of things about what this is doing that are so novel, they aren't inherently dangerous, but they are inherently novel. Now we inherently hold on and we inherently don't know what happens down that novel road.

**Bret** 23:01

Okay, so I want to I want to level us all up here. Okay. These vaccines, and if you frickin toss us off YouTube for speaking, literal, careful truth and explaining it, then we'll go Greg guns on this because we have to stop playing the stupid game. Okay. These vaccines are dangerous, that does not mean they are harmful. Okay. And the distinction is this. We do not know what the consequences of these vaccines will be on a body long term, it may be that the consequence is not serious harm, or that serious harm comes to a very tiny fraction of people. And it's well worth it in the context of as you point out, the harm that we know comes from this virus. But the way to think about this is Russian roulette. is Russian Roulette dangerous. Yes, it's fucking dangerous, right? But it only harms something like 18% of the people who play around, right? So the thing is, it has no harm to most people who experience right. And the point is, the risk that comes from pulling the trigger in Russian Roulette is not the same thing as the harm of the bullet that either is or isn't in the chamber. And so the distinction

**Heather** 24:25

is an important one. But that's a dangerous analogy, because there is no benefit to playing Russian roulette.

**Bret** 24:30

Well, I would agree. But my point is simply about when we say that something is safe. What does that mean? And when we say that something is safe, what it means is that we know it doesn't do harm, it doesn't mean that we have not yet identified a harm, right? So all I'm saying is that the nature of the complex system that we are interfering with is such that there are many possible consequences that we are not in a position to rule out yet and because Have that I believe we have an obligation to talk to people about what the consideration is. And as you point out, you know, as we both pointed out, the harm of COVID-19 is very, very serious. Even if the number, the percentage of people who die from it while they're sick is low, right? So it is not as if the fact that there are big risks that come along with this vaccine is indicative of something. And in fact, I think it's a little hard to say, but you know, just eyeballing the technique that they have used here, in many ways, it is fairly low likelihood of interfering with the immune system in a disastrous way, because, as you point out, there's no virus involved. They're basically a pseudo virus, they've created a coat of liquid coat, and they've got a segment of RNA. And

**Heather** 25:55

there's there's literally no infectious agent and right vaccine unlike traditional vaccines, which can themselves be infectious, infective, I'm not actually sure which of those are the right words here, an mRNA vaccine is not itself an infectious agent,

**Bret** 26:09

right? So in some sense, what's good about this vaccine is that you are taking the so we should describe a little bit about how it works. So you've got mRNA, the M is a lowercase M. And that means messenger, there are different kinds of RNA that do different kinds of things. mRNA is the standard molecule that takes information from the DNA in your nucleus of your cells transported into the cytoplasm of your cells, the part outside the nucleus. And in the cytoplasm, there are all of these RNA machines called ribosomes, that take mRNA, specifically, and they translate them into proteins, which do all kinds of things. So in this case, just as just as coronaviruses do, we are taking a messenger RNA and injecting it directly into or injecting it indirectly into the cytoplasm of these cells. Well,

**Heather** 26:58

this big asterisk here, yeah, which we'll get back to you tell this part of the story, and then I'll get back to it. So

**Bret** 27:03

you've got a, basically a lipid fatty layer that protects the mRNA. And this lipid fatty layer joins a cell and that mRNA finds itself in the cytoplasm of the cell. And the ribosomes discovering this mRNA do exactly what they would do with an mRNA that was transcribed from the nuclear DNA, which is that they translated into protein. So those proteins are the spike protein of the Coronavirus. In the absence of the other components of it, those spike proteins are then found on the surface of the cell that has produced them, which makes them visible to the immune system. So that visibility to the immune system, I'll talk a little bit more about how immune systems work in a second to get is kind of crucial to understand this. But the very fact of a protein that is unfamiliar, showing up on the surface of familiar cells, alerts the immune system that there is something to be identified, and then the immune system does its incredible job, which is to learn the structure of this foreign protein so that it can recognize it instantaneously. And then the point is, if you get COVID, what happens is that spike protein shows up in the virus and any cells that it has infected, and your immune system doesn't need to learn it because it already knows it. Right? That's the hope. So what are you gonna say you had a caveat.

**Heather** 28:29

The caveat is, you get a vaccine in which the injection does not go directly into the 100,000 cells, I have no idea if that's even the order of magnitude. That's correct. But you know, it doesn't go directly into any cells, it just goes into your bloodstream. Yeah. And then somehow, this mRNA has to get into the cells. And mRNA is, is very, very fragile. Right? It actually, and this is one of the downsides of these vaccines is in it decays so rapidly, it has to be kept in incredibly low temperatures. And somehow it has to be warmed up sufficiently that you don't get killed by injection of a super cold substance into your, into your vein. But it has to be it has to have been warm for such a short period of time that the mRNA didn't decay. So then it goes into your bloodstream. And somehow it has to get into your cells before it decay is because what is going on in the intercellular space, that is the space between the cells. In the intercellular space, you have a whole lot of ribonuclease aces rnases is how it looks when it's spelled out or when it's written usually. And what ribonuclease is do Ace that that ASE ending is the ending that means it's an enzyme that goes after the thing that it's named for. And what ribo nucleases do, which are intercellular spaces filled with ribonuclease is, is it destroys RNA. Okay, so how do you get an RNA vaccine that you've just injected into your bloodstream into the cells before the rival nucleuses that are in your bloodstream? Destroy them? Well, one of the things that you do is you code A bunch of these mRNA vaccine particles with this lipid nanoparticle, which is of course yet another synthetic thing that you're now putting into your into your body. And we don't know what the long term effects are. One thing that I do not know the answer to, but that I am skeptical that we should be certain that it's safe is if there is such a huge book, if there are so many ribonuclease aces in the intercellular space of mammalian cells. Why do we think that putting RNA into the intercellular space of mammalian cells is inherently safe? Right, whatever the selection has revealed to us by what it is left behind, that it is really important for the intracellular space of mammals to not have active RNA in it.

**Bret** 30:47

So it and there are various possible answers that would be positive to this question. It's possible that mRNA is free, for example, that are inside of cells for adaptive reasons, are lost to the intracellular space when cells die, and that there's some hazard in that in other words, they might put the hazard well, right. But the point is, if the hazard comes from the fact that there's lots of mRNA, in cells, it gets dumped into this interstitial space with some regularity, and there's a garbage patrol that cleans it up, because you don't want random messages translated where they shouldn't be, right? If that's the case, then a vaccine that dumps a small amount of mRNA into the system, and that mRNA is able to get into the cells may not have an important implication

**Heather** 31:35

big if there though, right? So and in fact, I believe if, if I read this correctly, that these vaccines actually have a combination of the naked mRNA and the lipid nanoparticle coated RNA, the idea being that one, one of the other of those things is going to work for some cells and, and it's going to get into enough of them and you're gonna end up getting, you know, production into protein and then immune response. But there is going to be some naked mRNA from the vaccine in the intracellular space that the ribonuclease will presumably act on. But again, I just I don't know. I cannot be 100% confident here,

**Bret** 32:15

right? Nobody can, maybe that they're experts in what this is who would be able to take a pretty good guess on what the net effect is. But again, the real

**Heather** 32:24

well, except that this is so new. Well, this is so new. And in fact, the here's I just put up my screen for just a second. This is a 2016 paper from a journal called therapeutic delivery. So again, it's a peer reviewed paper in the medical research literature called mRNA vaccine delivery using nipple lipid nanoparticles, in which it describes what what are the liver nanoparticles doing in the last sentence of the abstract here indeed, lipo nanoparticles can be synthesized with relative ease in a scalable manner, protect the mRNA against degradation, facilitate and assemble escape can be targeted to the desired cell type by surface decoration with ligands. And as needed can be co delivered with adjuvants. So ligand is just like a molecule with a metal ion in the middle. And that's not quite a sufficient definition. And then an adjuvant. It turns out, I had to look this one up is just something that increases the efficacy of the of the vaccine. And so it's kind of vague about what the mechanism might be. There's lots of different kinds of mechanisms.

**Bret** 33:29

Yeah. Did you encounter in looking at the mechanisms here? How specific is this nanoparticle code in targeting particular cells? And if so, what's what cells are they targeting?

**Heather** 33:41

What's the lipid nanoparticle? Is that is being used is wait for it. proprietary. Whoa, yeah. So we don't know.

**Bret** 33:50

Hey, look at that. Yeah. Okay. So what we've got is a technology that in principle is extremely promising, and for which there is some reason to imagine that the risks that are being taken are smaller than other mechanisms, like inactivated viruses. Okay,

**Heather** 34:09

well, and we just don't have the time to get a vaccine using an activated virus virus.

**Bret** 34:14

Right? So what we've got is an unproven technology that on paper sounds like it should be quite safe. But the problem is on paper is not the same thing as it being safe in a complex system, especially especially when you're interfacing with the adaptive immunity of the host. And that's the thing is, adaptive immunity is the most amazing process. I so I took immuno biology as an undergraduate, it was taught in the medical school at Penn, and it was something I there was no reason for me to take it. It just sounded really cool. Right? And I did not have the prereqs but I took it and it was among the most stunning courses I ever encountered. The description of what the means system is profoundly altered my understanding of creatures it under changed my understanding of evolution and it still pays dividends to this day. But the point is this system is the most marvelous, you know, if you think the AI is marvelous, check out the immune system, right? It's even more marvelous. And what it accomplishes is spectacular, but the delicateness with which it has to be balanced in order to do what it does well without over achieving and killing you is, that is not a small feat. And so anytime you're interfacing with that system, you're running a whole host of risks that don't necessarily come from the small intervention you made. It comes from what the immune system which has never seen that intervention before will do with it, right? Because in some sense, the key of the immune system is that it understands anything that isn't you as a hostile agent. And the thing is, that tendency can result in annoyances, like seasonal allergies, right? We have a subset of our our B cell immunity that is antibody based immunity, that reacts to things like pollen, as if they weren't pathogenic, which they're not and so that, you know, overwhelming mucus and all that's a histamine reaction that occurs because your body has misunderstood itself is under attack by a pathogen, right? That's annoying.

**Heather** 36:29

It's under attack by pollen,

**Bret** 36:30

right? It's under attack by pollen. But likewise, you can die of a bee sting, right? A bee sting isn't the pathogen either. And your immune reaction to it can kill you, right? And if lactic shock, for example, it can kill you. So the system when you introduce something,

**Heather** 36:44

yes, actually, just, maybe you said this, but the distinction between pathogen and toxin is critical here. Yeah, right. Like, our bodies should respond to toxins, by taking them apart as quickly as possible, and clearing them in some clearing them in some way. If you simply take, try to take apart a pathogen, we'll say, a toxin will not tend to be self replicating and a pathogen will be so excuse me, a pathogen that you simply that the body simply tries to take apart. Unless it gets absolutely every single single instantiation of it, it will not be it will not be a job that is well done. And you have no protection against future encounters with that pathogen, right. And so the body's response to pathogen versus toxin ought to be very different. It generally is. But the body is sometimes confused when it runs into toxins, like whatever the molecule is, and in beasting, right? Or even things that aren't toxins, but are definitely not self like pollen, and treats it like pathogen and basically it's shunted into I'm gonna respond to this as it's as if it's an immune threat as if it's a pathogenic threat, right?

**Bret** 37:55

So, you know, the, the thing is, these things contain a toxin, right? They don't contain very much of it. And it's not enough to hurt you on its own, but your own overreaction can

**Heather** 38:05

kill it, and it's not self replicating and it's not pathogenic.

**Bret** 38:07

Right, right. Right. So anyway, the point is, wow, is this an amazing system, and it's keeping you alive, right? If your immune system fails, boy, do you have a whole host of problems that you don't even know exist, which is one of the things you know, we discovered with AIDS and other immunodeficiency syndromes, right is all of the things that are being fended off routinely, right. So, without getting terribly deep, I want to just describe a little bit of the immune system so that people can understand how this vaccine technology could potentially interact with it badly. Although, again, I think the technology itself on paper looks very promising and less likely to cause this kind of harm than many other technologies, which we have managed the risk for, including traditional vaccines, including

**Heather** 38:56

traditional vaccines. So you are arguing let me just put that in a, in a soundbite, you are arguing that the mRNA vaccine has the potential to actually be safer with regard to auto immune response than a traditional vaccine?

**Bret** 39:10

Well, autoimmune response is one thing. But let's just say, and we should say this carefully, it could be that we ultimately discover that mRNA vaccines are the key to managing risks that come along with vaccines of other kinds, and that this is a better technology, that doesn't mean that these current vaccines are there, right? It could be that we discover something here that then lets us go to the next generation of these things, which might be vastly safer. So anyway,

**Heather** 39:39

or at the very least, very low on the adaptive slope.

**Bret** 39:42

This is this is so early, and so let's just list the three things that make this instance of vaccine one that you should file separately from other instances of vaccine and I don't think that what we do with other vaccines is is very nuanced. I think we very frequently Miss The way to talk about those things so that we could actually understand the hazards. But okay, so the first thing that makes this of a separate type is the novelty of the technology, which we've talked about here. Anytime you are going to inject something into your body that's based on some sophisticated nano interaction, and the technology is new, you're taking a massive risk. Nobody knows what the consequences of it are. Safety testing is, in fact, our only way to assess that, and it hasn't been going on very long, which has to do with the second thing that puts us at so you got a new technology, you've got rapid development, right? The fact that

**Heather** 40:42

we have got just the technology, but if this instantiation of this technology, right,

**Bret** 40:46

so we have gone from zero to 60 and 2.2 seconds, right? We've got viable vaccines, which is amazing, whether they're good or not, it's amazing that we've gotten this far. Right. So novel technology, rapid development. And the third thing is that there is an expectation of wide scale, rapid deployment of these things. In other words, there's some limit to how many of these things can be produced. But people want to get this stuff into people as quickly as possible to doses what's expected to be necessary to get the full level of immunity. And they want it to go out to everybody. And, frankly, they want to prioritize certain communities and you know, get our frontline health workers vaccinated, all this stuff. And the point is, all three of those things are independent reasons to be concerned. And all three of those things compound each other, right. So anyway, that's where we are, we're in a situation where there's a whole lot we don't know, and, to the extent, and this is actually a general bias in medicine, and all of its auxiliary fields, there's a general bias to measure short term harm. And when something does not do short term harm, to declare it safe, when in fact, in many of these cases, there's no way to assess the long term harm until a long period of time has passed. And you know, you can appreciate the dilemma. If you have a pharmaceutical, for example, that does some kind of good, you don't want to wait 60 years, you know, to give it to people and see what happens to them in old age, if they've taken it before you deploy it. So you're inherently taking the risk that it has a long term consequence that you don't know. But it is wrong to say that it's safe. If you don't know what the long term consequences are, you can say it is safe in the short term, that's the most you can say.

**Heather** 42:36

And one of the reasons that that is so dangerous is that once you have a number, once you have an estimation of safety, something that has been quantified, it's very easy to glom on to that and imagine that that reflects reality that that was not just measured correctly, but that the thing that you measured was the correct thing to measure in the first place. And that second category is actually in some ways a bigger issue, it's really easy also to focus on Oh, the data were bad, because because the measuring is bad. We had researcher error we had, you know, whatever machine failure, but did you In fact, measure the right thing in the first place? And this is part of what you're talking about that, you know, it's it's very much harder to actually take the time and you know, we're talking about research on which people's careers depend. Yeah. And you cannot build a career based on a 50 years in the future, we might have a result. So for for people who are interested in pursuing this question of why applying metrics and sort of, you know, pseudo numerator in newborn thinking to things that would appear to be numerator is such a problem I recommend so highly the short, but incredibly powerful book the tyranny of metrics by Jerry molar. So that's just a little shout out for that, because he does a terrific job of describing exactly some of these problems. Excellent.

**Bret** 44:02

So yes, we are obsessed with short term risk. And we tend, once we have established numbers, which may be erroneous for other reasons, we tend to assume that we know how safe something is. So it's very common for a doctor, you know, if a doctor prescribes a drug to you, and you say, you know, how safe is acid, totally safe drug that's only been out for five years. You don't know that? I can't know that. And to the extent that they will have some answer, it may be Well, I mean, there's the deeply inside baseball thing. But we do in order to figure out the long term risks and we don't want to spend a lot of time at it. Because we give large doses to animals that live a short life and assume that the long term effects would show up quickly in them, which is a garbage assumption. And the mice themselves are compromised as people who have paid attention to the Tila mirror mouse discussion will be well aware. So anyway, the

**Heather** 44:57

basic assumption used on garbage model organisms Yeah, it might be garbage all the way down.

**Bret** 45:02

Yeah, it's a lot of garbage. And the idea that we're at the point that we discover a long term consequence that we don't like, Who could have known like, you wouldn't have known the specifics, but you could have known you were taking this risk. And that's, that's the point. Okay, so let me quickly talk about the immune system so that we can talk about the risk here. The key thing to understand is, the immune system is built around a, an ability to recognize almost any large organic molecule, and to recognize whether it effectively to recognize all large organic molecules that you yourself Do not make. So early in development, there is a period of time in which so you have a diversity of cells, B and T cells and their progenitors that recognize molecules, that fraction that is triggered by molecules you yourself are making are eliminated from the population. So what is left over is that fraction of this large population of cells, hundreds of billions of cells that do different things and recognize different molecules, right, the fraction that doesn't react to you is leftover, right? And it just hangs out in a kind of dormant circulates. And anytime a molecule is introduced to you that you yourself Do not make it is very strongly likely to react at least somewhat with some fraction of this population, a tiny subset of this large population of cells, and then that cell that has been triggered by a molecule that you don't make, and the fact that the cell is triggered tells you it's not a molecule you make, right? That cell then produces a whole bunch of descendant cells that have a slightly different formula. This is called clonal selection. So you yourself are an organism that might live 8590 years carrying the same genome and making the same molecules but you have a subset of cells that evolves on the scale of hours to days, that gets better and better at identifying a target and antigen based on this clonal selection right? It's an amazing fact how

**Heather** 47:08

old is this? When did they mean when this form the immune system evolved? We know when did it evolve? Yeah, I fought i'm i'm sure we know. But do you know I'm

**Bret** 47:16

about to take a huge risk with my reputation and say that I think I think it goes back to our common ancestor with salamanders.

**Heather** 47:27

You think it's tetrapods? Yes. Okay. Not vertebrates. So that was so that if that is true, you were saying that your salmon don't have this kind of immune response. But any of the the descendants of the first vertebrates that came onto the land do

**Bret** 47:44

yes now this worries me because that seems like it can't possibly true be true because what do you do with a very long lived animal some sharks are incredibly long lived large body and how did they avoid being parasitized? Do they have a progenitor of this clonal selection phenomenon? Have I misunderstood it is it vertebrates that have it but any long lived large bodied organism is very likely to encounter pathogens that invade it and adaptive immunity would be a key way to go as

**Heather** 48:12

well there obviously there are different ways to do it. There are long lived organisms like redwood trees, they have anything they have it easy because they've got things like segregation of the germline, and they don't have a segregation I mean, they they sorry, it the lack of segregated germline, but they also because they effectively have total potency in in their cells they can they can just drop pieces of themselves they are not modular they can

**Bret** 48:37

kill them off so you know, there's no part of a redwood tree that you couldn't turn off if it got infected so you can have a big you know, wound that just goes dead kills itself off to protect the rest of the tree. You can't do that if your liver goes dead you're cooked so

**Heather** 48:55

and no vertebrate. There There are there are a few vertebrates actually a few salamanders that can lose a limb and grow one back but I don't think it's actually understood to be in response to infection. I think it's if if damaged, if I don't think we've ever seen it as a response to infection, it's just if damaged, you end up with a new hand the

**Bret** 49:17

only time I've seen it it was in response to having put two species of salamanders in the same aquarium that didn't get along as well as I was hoping

**Heather** 49:27

you can tell the story I don't know.

**Bret** 49:30

Yeah, I put North when you're a kid at this point. No is this I'm I guess I'm a professor at evergreen. Oh my god. So I took Northwest

**Heather** 49:42

salamander I guess these are m best.

**Bret** 49:45

Am I and Teresa granulosa the rough skin new

**Heather** 49:49

Okay, so pretty distantly related to from two different families of Salomon. Totally

**Bret** 49:53

different from the same pond. So I sort of thought Oh, this would be cool. That will they'll get along well enough and the The Teresa

**Heather** 50:00

went after the investment I didn't wait after limbs

**Bret** 50:03

off of all of them. I'm trying to remember it was multiple limbs. I may have separated them at some point. But But in any case, yes, the the the, the Northwest, the Northwest salamander lost its limbs to the, to the rough skin new rough skin nuke being the most toxic pound for pound creature on earth, or at least arguably so yeah. And then the limb started to regenerate which you saw the budding half house absolutely amazing. Stunning.

**Heather** 50:33

You know, we were married and had kids at this point. I remember the story somehow you kept the suit. You didn't want to tell knowed Yeah,

**Bret** 50:39

I really yeah. You just don't a lot of a lot has happened. Yes, somehow you probably you know, still remember the theme to the Brady Bunch, though you I'm sure you've never watched it. Or maybe you watched an episode but you don't remember this because it's been crowded out by I don't know. COVID or evergreen or not. Okay, back to the story. Yeah. You got to just wait, yeah.

**Heather** 51:03

tariqa newts. Also salamanders cannot regrow their limbs. So this ability to regrow limbs is actually limited. I think that it's for a very small group of tetrapods. And so anyway, most the vast majority of even vertebrates cannot do that.

**Bret** 51:20

So anyway, some question, I'll be curious to know whether sharks have adaptive immunity, and I've misunderstood or something. But anyway, I think it goes back at least to salamanders, if I remember correctly. But anyway, you've got this adaptive immunity system, it's predicated on the ability to distinguish self from non self, the way it does that is it has a population of cells that only responds to non self. And that thing, waits for any molecule it doesn't recognize, and then it mounts a response to it. And so vaccines, the way they work is you dump something into the system that carries molecules that you yourself Do not make something that has been rendered harmless or nearly harmless. The immune system sees it regards it as a pathogen learns the formula. And then when you get sick with the actual thing, the immune system is primed to react and react so quickly that you don't detect sickness, right? Same reason that you don't get sick twice from a lot of things. You don't get sick after the vaccine because you've been pseudo sick with molecules that it's like a wanted poster in the in the post office that alerts you to somebody dangerous, so you know, right away, they don't have to harm you for you to discover that they're the enemy, right? Okay. So the way this, you're looking for a prop? Well, I don't know if it's worth the image. But just since these terms are so frequently used. I think I have this backwards, I do. I can't drop that out. You got this, this is an antibody shape. And it is actually the shape of a number of other things to receptors on the surface of T cells. But this is a basic antibody, right? It's y shaped, and it's got this is called a heavy chain. It's heavy, because it's long. This is a light chain, it's like because it's short. And then there are always two light chains, two light chains and two heavy chains, and they have this y shape. And then up at the tip here, you have a variable region. So all of this stuff is basically standard toolkit, right, that's the frame of the bike that just holds the parts together, the rubber meets the road here at the variable regions. And these variable regions are highly variable, and each cell produces a specific antibody. And when that cell is triggered to produce more cells like it, there's variation between them in these variable regions. And these regions, just kind of stick to anything that they have the right formula for

**Heather** 53:58

just a point of order, since you use the analogy that if anyone else would use it, I would just accept it. But you saying the most of this is like the frame of the bike that just holds the parts together? Yeah, you have actually designed and built your own bike, not just bought a frame and put parts on it. You have actually done the you know, the bracing and the TIG welding, TIG welding? No, I do I do brace just just the bracing. So you know that actually all frames of bikes aren't the same. And you said that as if so is Do you really mean this is like frame of a bike and they're all a little bit different, but it doesn't really matter because the real functional stuff is at the sides or is that actually not

**Bret** 54:39

I said it because the purpose of a frame is to hold the parts on frame itself doesn't do anything. What it does is it holds the parts in the right orientation and distance

**Heather** 54:48

apart a little bit. It also holds the rider in the right orientation. Sure,

**Bret** 54:52

but I mean you know the seat, you're not really touching the frame as you ride. So anyway, the point really is this is a structural thing and you know that As well as a bunch of different kinds of antibodies in the tails do different things and whatever. But the basic point is from the point of view of recognizing hostile entities, it's this variable region up at the tip of the antibodies and the T cells. So B cells make antibodies. B cells also have receptors that look like antibodies on their surface, which is how they know whether or not they've been triggered and make more of themselves. T cells don't make any freeflowing antibodies. But they do have receptors like this on their surface. And they do things with their various different kinds of T cells. But anyway, there's the specific immunity, the adaptive immunity, this evolving army of cells that adapts to the particular pathogen that is responsible for you being so free of pathogens, right. It's really good at finding cells that are infected and killing them, finding free flowing pathogens and killing them. And you know, as long as it's good at recognizing the difference between self and non self and not overreacting, then this all just happens passively in the background. And occasionally, you get sick enough with something that it takes you two weeks to get the formula. But by and large, you're not sick, right? The problem is, if you think about it, imagine a pathogen gets into your system, right? It doesn't look like you molecularly. So the system reacts to it, right? And it starts killing it off. Well, there's variation in these pathogens, too. They're evolving, right? Those that are most easily recognized by the immune system are most vulnerable, right? Those that look least like that, or at least recognizable, are least vulnerable. And so there's selection for those that are not easily found by the immune system, right? So there's selection inside your body, and you're trying to adapt quickly enough to spot the thing. And it's adapting. Hey, it's a hemiptera isn't. It is adapting to escape the immune system, right? Now the problem is that because this system reacts to anything that looks not like you, but it doesn't react to things that look like you, there's selection for pathogens to look like you, right? molecularly, right. So that's the game that we are interfering with your and hopefully we are interfering in a way in which the pathogen is too far from looking like you. And the vaccine doesn't disrupt the self non self recognition system in a massive way. But the number of things that can go wrong with this as many So you mentioned autoimmune disorders. I think it's one of the things that ought to be on our list, right? What our list of what hazards here, what might show up if we did have 10 2030 years of data on what happens to people who get this vaccine.

**Heather** 57:47

And I mean, already I've seen I can't pull it up. I don't remember where but news reports suggesting that people with a lot of allergies should use caution and considered not taking these vaccines, which strikes me as exactly squarely on target if what you're talking about right.

**Bret** 58:04

So what we get from that is, we know that this is having an unpredictable effect based on individual variation in immunity, right? And we don't

**Heather** 58:15

like the type of immune response the strength and speed of immune response within your body,

**Bret** 58:21

right. And we don't know why. Because typically, you know, a lot of vaccines can cause an anaphylactic reaction in people who are sensitive to them. But typically, it has to do with something like the eggs that they were grown in have a lot of proteins. And for some reason your immune system sees one of these proteins as much more dangerous than it actually is. And maps are an immune response that can then jeopardize your life, right? So we don't know why something as simple as this is triggering NF lactic shock or the potential for it. But the fact that in some people that's happening says, Oh, this is having an unpredictable effect with some immune systems, right? What other unpredictable effects might it have with some immune systems? We don't know yet because it ain't been around long enough for us to even just detect all of these patterns. And then we have another indication of a kind of harm which showed up this week and this one, it's interesting because you can see how the narrative is being shaped around it, which is that can you show the Bell's Palsy? The there's a PDF I sent you. Yeah. Okay, can you scroll down? I can only read on that screen. Scroll down to where I highlighted. Keep going. There it is. Okay. that paragraph. Okay, so what this says I won't put you through all of it. But safety data from approximately 38,000 participants who were more than 16 years old randomized one to one that means 20,000, little less than 20,000 got the actual vaccine, the others got a placebo with two months follow up after the second dose suggest a favorable safety profile. And then they go through what the reaction is that they saw where it's a very standard list for the most part. They saw some fatigue, some headaches, muscle pain, some chills, some joint pain, fever, none of that is all that surprise, severe

**Heather** 1:00:42

adverse reactions occurred in zero to 4.6% of participants, which is a weird number. Why is that a range? Why at a rate, why is that

**Bret** 1:00:50

at all? Why is that a range, okay. But then, the highlighted section says, among non serious unsolicited adverse events, there was a numerical imbalance of four cases of Bell's Palsy in the vaccine group compared to no cases in the placebo groups placebo group, though the four cases in the vaccine group do not represent a frequency above that expected in the general population. So this news got out people didn't know what to make of it. But now the fact is, we can actually interpret what they've said here pretty clearly. So can you show the, the diagram of Bell's Palsy that I sent you the cartoon? Okay, so Bell's Palsy involves some facial symptoms, in which one side of the face droops, the forehead is d wrinkled by by the Bell's palsy, it is the result of something going on with a facial nerve, and its cause is still unknown. So you've got four cases in this group. Now, Bell's Palsy a isn't a permanent condition, in general, it clears up. B, there is some frequency of it. I think it's something like one in 10,000 people is expected to encounter it, to have it as a symptom in any given year, on average, so these groups, the test group and the control group, in this case, we're 20,000 people, but for much less than a year. And so what they've said is actually this, Bell's Palsy might just be the background, Bell's Palsy that you would expect, but conspicuously the four cases that they've got showed up in the treatment group, not the control group. Now, the point is, this is all so small,

**Heather** 1:02:45

I want to see bigger numbers before I know what to make it as exactly

**Bret** 1:02:47

it is this could easily be a case where there's a surprising amount of Bell's palsy and their short period of time, it just accidentally shows up in your treatment group. And it has nothing to do with it. That could easily be the case with numbers. The small. On the other hand, the pattern is conspicuous, right? They've got a short to me, but

**Heather** 1:03:06

I mean this this is what statistics is for. Exactly. I've never done it. That's the first time I've seen I don't even know what exactly what document we were looking at. But those would be easy statistics to do. Even I know what statistics to do on that if I had the background right for the population and their date. Well, but we

**Bret** 1:03:23

know what it is that they concluded if we assume that they did the math, right. We know what they conclude

**Heather** 1:03:28

we know what they said. But they didn't show any statistics, which means that they made a conclusion based on Yeah, yeah, it looks fine. No, no, I suppose. No,

**Bret** 1:03:37

I don't think that's right. I think I did the stats. And what they came up with is that this is a pattern but it's not statistically significant. Right. So can you show me

**Heather** 1:03:46

what I would hope if I were reviewing that paper before? You know, if I were a peer reviewer of that paper, I would have said, this claim is unsubstantiated. Show me you know, show me the test you used and

**Bret** 1:03:58

so that was not a peer reviewed paper. Right? That was you know, internal FDA document evaluating the risk and you know, they have to be able to do this they got to be able to get people into a room and say what have we seen? What do we think chances are that it means anything? Okay, so they do all that there's nothing wrong with them having done that, and there's nothing wrong with them saying this is not a statistically significant trend. But by Can you show the Snopes debunk

**Heather** 1:04:25

is Snopes debunking the FDA here?

**Bret** 1:04:27

No, Snopes is debunking. Can you put that on? Snopes is debunking the widely circulated claims of Bell's Palsy likely being caused by this vaccine? Can you scroll up?

**Heather** 1:04:45

That's scrolling down. Okay.

**Bret** 1:04:49

We will talk about whether that's scrolling on for scrolling down. Oh, so this, I'm unclear on that if I misread something, but anyway, it says had more than 20,000 patients who took Pfizer's trial vaccine for COVID-19 for developed Bell's palsy.

**Heather** 1:05:10

So it's true that four out of more than 20,000 patients, although I don't get how they get more than 20,000, but anyway, for more than 20,000 patients developed it, but we don't know if the vaccine caused it. That's that looks right. Yep. I get get if assuming that this is based on an FDA paper that you just showed, which you haven't seen exactly what everyone watching has seen,

**Bret** 1:05:32

in this case, it's right. And I am not sure whether something changed about this. That's a live link, or whether I just read it when I first looked at it, can you show the other URL

**Bret** 1:05:50

sees no causal relationship? Right? So CDC will monitor for Bell's Palsy among Pfizer vaccine recipients, but sees no causal relationship now. This is something that has to be understood as a scientist would evaluate what we've got is a clear trend for to zero between the treatment group and

**Heather** 1:06:15

I would be real careful, I wouldn't call that a clear trend.

**Bret** 1:06:17

Well, it is it is it is statistically not significant because samples

**Heather** 1:06:23

disparity in the incidence of Bell's Palsy between the vaccine and the placebo group. trend suggests something that we that we just don't have enough information to say, Yeah,

**Bret** 1:06:36

I agree with you better way to say it is a discrepancy, or a disparity between the two is significant enough, informally speaking, to monitor it, it is not significant enough to infer a causal relationship, because the sample sizes are small and sample sizes were larger, that is to say, more people and longer time, then we would either this pattern to the extent that there is a pattern would disappear, because it's actually the result of sampling error. Or it would be reinforced if it is causal. But this is the reason that you need large datasets, and we don't have it. And part of that is because we just don't have a lot of time. So this is reflective of we are rapidly racing to deploy this vaccine, which means that this is all happening,

**Heather** 1:07:25

we hope for for good reason for excellent, right? I mean, not, not only are there long term health effects from getting COVID-19 among those who survive, not all of them, but among many of those who survive. But globally, the economy is tanking. Yep, oh, well, businesses are just this, this is unimaginable, and how huge number of sectors of not just the US. But the world economies recover from this is frankly impossible to imagine. And every week that this goes on, it becomes harder and harder to dig ourselves out of the hole. Yes,

**Bret** 1:07:59

this is a disaster at many different levels. And what I want to see us do is have a proper adult conversation about the fact that we have much greater than normal risk for a vaccine because we have much less information on the consequences of this vaccine. And we have a bigger crisis, both at the level of society grinding to a halt, and not knowing how to deal with the, with distributing the arbitrary costs of the pandemic, fairly, or whatever it has to do. And we have a virus that does a tremendous amount of bodily damage to people circulating in an uncontrolled way. So there's lots of reasons that you might take, and in fact, should be willing to take more than the average level of risk. But pretending that that doesn't exist here is in my opinion, unconscionable. Right. And so the last thing I want to say, is, we are constantly caught in this bind. You and I have talked about it on the podcast several times before between the public health level analysis, and the individual health level analysis. And the lying in order to make the public health level analysis turn into the individual level analysis is the problem. Yeah. So to make this clear, for people who don't know what we're talking about, imagine for a second that you had, let's take COVID out of the scenario. Let's imagine that you had a deadly disease and a vaccine that created high levels of immunity to it with substantial risk or maybe even substantial harm, let's say, you know, one in 10,000 people at a crippling reaction. And you wanted to deploy this because the harm of the disease outweighed that one in 10,000 people who was crippled but you were going to cripple somebody who might have well not gotten the disease or been okay with it. So you're doing serious harm, but you've got to account for in that case. Imagine the analysis The last person on earth to get the vaccine imagine you could magically produce the vaccine and produce enough doses, and you get it to everybody. The last person on earth to take that vaccine has no reason to take the risk, right? Because everybody else is vaccinated, the circulating levels of the disease will be low, and there's no reason for them to take the risk. Okay. You can then back that analysis off the second the last person has the same analysis. And then there's some point,

**Heather** 1:10:28

it's not the same with every every person before that has a bit more reason Yes, there are taken inclusion

**Bret** 1:10:34

for the second to last person would be the same, but the calculation would be very slightly different.

**Heather** 1:10:39

No, I would say that the conclusion is very slightly different in the calculation, the calculation itself is the same, but the result of the calculation is slightly different. And therefore the conclusion is slightly different. Which is to say, if you are the last person on earth, not vaccinated, there is no reason for you to take it. If you are now one of two people who are not vaccinated, and you're next, there is some reason to take it, but it's miniscule. And

**Bret** 1:11:01

when I say conclusion, I just mean up or down, right? I'm taking or not taking it, they both reach the same conclusion if they're rationally deducing. So how

**Heather** 1:11:10

many people do you go back right before you start to get into territory that looks like well, individuals, and here's like individuals might well be wanting to make different decisions than the government's who are looking out for their entire populations would make for them. So

**Bret** 1:11:30

if everybody's doing the calculation for their individual well being you've got a category based on how late they are in the sequence in which it's clear that it's not worth the risk, you've got a category in which reasonable people could disagree. And then you've got a category in which the risks of the disease outweigh the risks of the vaccination substantially enough that every reasonable person should go with it. So then you get people jockeying for position. Now, the point that I want to make is a we've got a problem with anti vaxxers, because some fraction of anti vaxxers are enough. So that category of people who doesn't want to take the vaccine, right,

**Heather** 1:12:09

so when you say anti vaxxer, you're talking about anti anti COVID-19 vaxxers are just the whole the bigger I

**Bret** 1:12:14

wouldn't call those anti vaxxers. Yeah, say that there's an anti vaxxers out there and some fraction of it are effectively free riders, right? So what we've just described as a free rider problem in which people who are late in the sequence get the benefit of everybody else's being vaccinated without paying the cost of their own risk. It's a very rational decision to make. It's unfair, but it's rational from the point of view of the individual. And so part of what we get the Vax the anti vaxxers versus the vaccine triumphalist is about a triumphalist are trying to sell the idea that these things are safe in there. For anybody who talks about safety as a crazy person. There's no reason to pay any attention to anybody in the anti Vax group, right? That thing is really a cryptic free rider versus collective action. Question like so many things are right, the collective action problem might have a an analysis that says everybody takes their share of the risk, and we all get the benefit of the immunity and nobody gets an exemption unless there's a medical reason for it. So

**Heather** 1:13:15

just to be clear, you're saying that this is actually what the two camps are, even though the cover story and indeed, the conscious belief of many people in both camps does not match? Well, its conclusion,

**Bret** 1:13:25

I don't want to say that this is what that debate is, because I think there's a very, there's a variety of ways that people find themselves in these.

**Heather** 1:13:33

That's my point that regardless of what your cover story is, regardless of who you talk to in the way you talk about it, that it is effectively sort of this is this is a public health analysis. versus a we have to we have to stamp out the free riders, right?

**Bret** 1:13:50

So it's, yeah, it's it's a free rider problem in disguise. And the other thing, the bitter pill of this analysis is, if you are going to wag your finger at safety skeptics of vaccines, right, then what you have to do is rig the system, the safety system, so that it is biased in the direction of caution, right, and a safety system in which you've got for profit companies that have partially or completely captured the safety mechanism, right? That is not a safe system. And so what in effect we have done is we have fueled the free riders, however they come to us and whatever arguments they deploy, because in fact, they have a better point with respect to safety than they ought to. And that comes in two forms. One, safety isn't nearly as good as we claim it is, it could be better and we have not made it better in part because of financial considerations which should, you know, we should neutralize we should use our governmental apparatus to neutralize the perverse incentives for the companies that are making these things. So that the Things are as safe as possible. And then when we effectively dictate that people have to take the risk for our collective well being, we've minimized the risk, right? That would be the responsible thing to do. But the other reason that they have more of a point than they should, is that we are not honest about the costs and benefits because we basically treat people like children. And we basically pretend that these things are safe, and that anybody who believes otherwise is, you know, effectively claiming that there are lizard people. We fuel that movement. Right? Right. So yes, anyway, I think that's pretty much where we needed to go here, right? You've got a complex system. We're intervening in with it in ways that could create autoimmunity. We don't know that it does, we know that this having at least, you know, one effect and maybe two effects that we didn't expect, you know, possibly Bell's palsy. And it seems like an electic reactions that we didn't see coming. And hopefully, and

**Heather** 1:16:03

these are the known short term effects from groups of from a group of 20,000 people known very short term, and so at a tiny fraction of the number of people who will ultimately be vaccinated with these vaccines.

**Bret** 1:16:16

Right, exactly. And so I guess the last thing to say is, were we going to be adult about this and have a proper conversation, there would be at least the question of is there some scheme that distributes our collective risk better than simply rushing every doctor, nurse and other person who works on the front lines into this program? In other words, do you want to hold half those people back or a quarter of them? You know why? I'm not saying that I expect anything to happen to everybody who's vaccinated here. I don't in fact, I think this technology is really promising. But I wouldn't want to take the risk with all of them that seems really only afford

**Heather** 1:16:58

to have deeply compromised our entire healthcare force three years down the road right now we cannot right.

**Bret** 1:17:04

So anyway, what is the scheme in which you hedge the risk of this with some sort of contingency backup plan that doesn't completely up end us? If it turns out there's something going on here? We don't see coming? Right. That's really the question.

**Heather** 1:17:18

Yeah. Well, okay, that's our that's our will we get canceled conversation for today. Yeah. I think we've been at it for a very long time already. So we should save the discussion of journalism and my observations about how people drive and what I think it means about their politics for next time. But I do want to say just a couple words about sexy flies. finished with that. All right, do that I'm sitting down. Alright, so the journal animal behavior this month, Summer 2020, published an article that found that male flies are differently attractive to female flies is a Drosophila melanogaster. standard model organism that mostly in genetics, that is not so far as I know, nearly so compromises those mice, but, but who knows.

**Bret** 1:18:06

Okay, so when I took population genetics in Santa Cruz, I was very lucky to take population genetics with one of the world's great population geneticists, Bill rice, and he, he worked on flies and he was the genesis still, of course, it's a great organism and we know a lot about it. And anyway, it's it's it's been a standby. But anyway, he joked that for the population geneticist going out into nature to get study organisms involved going over to the trash cans, collecting the flies that were that were flying around the banana peels or whatever been thrown in there. I thought that was funny.

**Heather** 1:18:43

Yeah. And these are, these are fruit flies. They're not, they're not like course flies or black flies. It's their

**Bret** 1:18:49

shoe flies.

**Heather** 1:18:51

Right. Okay, so we know from from previous research, that female Drosophila female flies strongly prefer males who have longer bigger wings to males who have more rounded wings. And we are also finding that wing shape is affected by diet. And so it's not simply, some males have the the Leos for longer and bigger wings, and those are the alpha males as the studly males and some wings have rounder wings and too bad for them. Nope. It's affected by diet. And

**Bret** 1:19:31

presumably better diets result in the sexier wings.

**Heather** 1:19:34

Well, what makes it better? So the so the diet so they have these five strains of flies, and they actually this is I think it was like 15 years. So they've got five, five strains of flies on five different diets for a long time is very long time and flight time because they have such short generation times. Yeah. So they've got a standard, just off the diet of cornmeal, and then they fed some apple, some banana, some carrot, and some tomato. So we've got these five different strains of flies, apples, carrots, carrots, and tomato and cornmeal. So five different flies. You have any idea? What do you think was the sexiest

**Bret** 1:20:15

tomato? Yeah. Did I nail it? You didn't know. Yeah.

**Heather** 1:20:19

And I have really nothing to say about why that might be and you just got you know you well the 20% there I have

**Bret** 1:20:24

a sense that tomato is chemically quite a bit more diverse than anything else on that list.

**Heather** 1:20:31

Why? What is what is that about?

**Bret** 1:20:33

Well, a it's a nice shade, and so it's bound to have some fancy Apple IDs in it.

**Heather** 1:20:40

So let's let's just go there for a moment. So cornmeal probably okay, all five of these are going to have been strongly humans selected by agriculture, apple, banana, carrot, tomato, cornmeal. All right. Corn, and I know the least about what we've done to carrots, but corn, banana, and Apple, we have certainly selected strongly to take out all the secondary metabolites that would at least for humans, cause any distress and I don't know if that if we would share the metabolic pathways with flies that would would cause them to stress. But those are certainly the easiest to digest of those five, five plants. For us, carrots I just know less about but that's interesting. You say tomato is a knightshayes like potatoes like eggplant, and nightshades we have not managed to select out of nightshades some of the toxicity Yeah, and you were saying that effectively almost almost like the tiny kernel of truth and homeopathy that you write the loop a little bit of, of toxicity can potentially create

**Bret** 1:21:50

Yeah, I want to be careful with that tiny truth of course, in homeopathy, that tiny drop may be exactly equal to zero, right but

**Heather** 1:21:59

but but some some tiny little insult can actually create create a stress that can then create a kind of anti fragility perhaps that can that can make

**Bret** 1:22:09

us stronger? Yeah, I don't actually know what I'm responding to. Yes, on the one hand, you might expect that the tomato would be

**Heather** 1:22:15

you might expect to be extreme and couldn't predict you might have like a two tailed hypothesis like it's going to either be the best or the worst flies, but I'm not

**Bret** 1:22:22

sure which Yeah, or it selects against the Yeah, I could see it going a lot of ways I'd love to know more about exactly what happened but it's also possible there's just a greater diversity of molecules in tomatoes than anything else on that list. And that results in what I'm inferring is that if in effect the wing shape is revealing to the females that a male is very well fed, which according to the hypothesis I deployed in my dissertation, would suggest that all of the things that her offspring might get from that male if he's only getting genes all of those things are spelled properly spelled well and coordinate well with each other right so any male who does really well in finding food is likely not to be heavily compromised in any heritable way and so

**Heather** 1:23:14

well if there's if if it were at that level you might expect positive assertive meeting for diet I don't actually think the article says what the females are raised on but they should have raised the females also on each of these five diets and then you know given carrot females to you know tomato males and

**Bret** 1:23:32

but no i the rest I agree with you that that would be an interesting question and that there are other systems that I think work like that but in this case of a female was just assessing how nutritious a diet a male had managed to find for himself. She's evaluating how his wings look because only on a really good diet to the wings end up taking their full beautiful form. Listen to be talking about flights this way.

**Heather** 1:23:56

Flies who eat tomatoes or sexiest Breton

**Bret** 1:23:58

sexiest, sexiest doesn't make them sexy. I didn't say that. Okay, but So in any case, it might be that she's just evaluating how good was his diet because a male in the wild a male whose diet was excellent is probably really well constructed in every way she should care about, which wouldn't require her to be on the same diet.

**Heather** 1:24:18

True. Yeah, right. But But if it's if she is assessing local pneus, for instance, right, right. Then you would expect positive assertive meeting for diet because that's a really good indicator of how local you are. Did you eat the same thing I did. Then you probably had access to the same stuff. Sure. Yeah. And you know, otherwise, maybe we get Zena phobic flies and make choice. Yep. That's pretty much it. We don't know for sure the tomato diet created the sexy wings, but those males who ate tomatoes, were the sexiest

**Bret** 1:24:47

awesome, yeah. All right. I will keep that in mind. Yeah, it's also possible that I was inferring it was the tomato because just anecdotally, tomatoes are more likely to have flies around them, and that I've somehow subconsciously picked up that fact. But I don't know that that's true. I would say bananas are very common.

**Heather** 1:25:03

Yeah, I mean, I think tomatoes will decay on your counter more quickly than a banana or an apple well, and most people would keep their cornmeal, you know, in a sealed content, we would keep our cornfield in a sealed container and our carrots in the refrigerator, etc. And don't tend to let fruit. We have occasionally let tomatoes get to that spot, get to that stage, and very rarely let any of the rest of these things get to that stage where they remain. They were not by the flies. No, no. All right. Are we there? There? Were there. All right. So I guess we have where's the end of this? We have the usual end of end of stream announcements then. Right? If I can find the end of my notes here. All right. Yes, you can go to store Darkhorse podcast.org. As you see on the screen there, if you're interested in Dark Horse merchandise, you can email the Dark Horse dot moderator@gmail.com. moderator for any logistical questions like how do I pose a question? When is the private q&a? The answer to that we will tell you right now is in about 15 minutes. For now, we only have it here on YouTube. I'm beginning to hear from people who say, since since we began doing this, people have been saying why don't you make the q&a part of the podcast? Like why don't you also upload that and I think it's just so much more casual that it would it feels like it would gum up the podcast that we don't want to do that. But there are some people who are saying, I really don't want to be on YouTube at this point. I don't want to I don't want to participate in the YouTube universe at all. Is there any other place you could put up your q&a? We don't have anything that we're working on in that regard. But we are hearing the concerns as we also have the concerns for being completely dependent on the big tech tech platforms. You can join either via Patreon to get access at mine to the private q&a every month

**Bret** 1:26:56

to Yes, and actually I do need to make an announcement. Oh, yeah, I forgot. Yes, there wasn't. It's my error. But there's a flaw in the way Patreon is structured that resulted in some of the people who are supposed to get an invite for the coalition of the reasonable discussion not having gotten the invite. And so I'm going to do a makeup conversation for anybody who didn't get the invite, or anybody who did get the invite, but wasn't able to make it to that discussion. So that the timing will be announced. But if you didn't get your invite, or you weren't able to make it, please let us know at support at Brett Weinstein dotnet Brett has one T

**Heather** 1:27:42

is a second one and Weinstein.

**Bret** 1:27:44

Brett has one t Weinstein has the backup T. Right. And so anyway, yes, if you want to participate in the makeup conversation, or I suppose if you are signing up late, I can pay on Friday and for that one, but anyway, contact us at that address and let us know and we'll set up a time. I think

**Heather** 1:28:08

if you're signing up late and you get access to your grandchild.

**Bret** 1:28:14

Okay, I'm gonna have to meditate on that.

**Heather** 1:28:17

So lots of good stuff going on those Patreon is including access to the discord server where there are apparently a whole lot of other conversations going on. And we're going to take a 15 minute break and then come back to answer your questions picking up a few from last episode, a number of your super chat questions from this hour and then picking up super chat questions that you begin to ask next hour in the order that they come in. We look forward to seeing you then.

**Bret** 1:28:44

Yes. And if you will not be there for the q&a. Continue to have an excellent Hanukkah and keep your immune system targeted on nonself. Alright, we'll see in 15