

COMMENTARY

The New, Old World of Functional Medicine: Part 1

An Interview With Mark Hyman, MD

Hansa Bhargava, MD | October 12, 2016

Editor's note: This is the first part of a three-part interview with [Mark Hyman, MD](#), director of the Center for Functional Medicine at Cleveland Clinic. It has been edited for clarity.

Hansa Bhargava, MD: I am Dr Hansa Bhargava, medical editor for Medscape and WebMD. Today we are privileged to have Dr Mark Hyman joining us. In addition to his role at Cleveland Clinic, Dr Hyman is a renowned author of several books and a *New York Times* best-selling author. Dr Hyman, thank you for being here.

Mark Hyman, MD: Thanks for having me.

Dr Bhargava: Can you tell us a little bit about yourself? Our readers will want to know what led you to your current path.

Dr Hyman: It's pretty exciting here at Cleveland Clinic, being at the center of one of the best healthcare institutions in the world, bringing functional medicine to scale, doing the research, and addressing the science in a rigorous way. I came to it through a very different path.

I was a family doctor. I worked in a small town in Idaho doing rural medicine, C-sections, and running the emergency room (ER). I was the old-time country family doctor for many years. Then I became an ER doctor in Massachusetts in the inner city for a couple of years. Afterwards, I got a job at Canyon Ranch in Lenox as the medical director, focused on lifestyle and wellness, which is where my heart has always been.

Right after I started at Canyon Ranch, I became quite ill. I had chronic fatigue syndrome. My whole system broke down: My muscle enzymes were elevated with creatine phosphokinase levels over 600. I had a positive anti-nuclear antibody, a low white blood cell count, elevated liver function tests, and severe cognitive dysfunction. I had myalgia, weakness, rashes, sores on my tongue, and severe diarrhea for years. My whole system just collapsed. I went from physician to physician, to Harvard and Columbia, and more. But I got no answers other than to take antidepressants or sleeping pills.

I began to search for other ways to understand what was happening. I knew it wasn't in my head. I finally discovered that after living in China for a year I had gotten mercury poisoning.

I learned through this process that there was a whole new field of thinking that had a systems-biology view of medicine. It addressed the root causes of disease—not just symptoms but also etiology. It's medicine by cause, not just symptoms. It's medicine by understanding mechanisms, not just geography, or where the symptom or pathology exists. It was a whole new operating system for understanding how to diagnose and treat chronic disease.

So I started practicing functional medicine at Canyon Ranch and healing myself. I started seeing extraordinary results with patients and myself. I joined the faculty and eventually became the chairman of the board of the [Institute for Functional Medicine](#), which trains physicians and other healthcare providers in functional medicine, a powerful systems-based model that takes our observations of the root causes of disease and our biological networks, and integrates them into a framework for clinical application.

One example is the microbiome. All of a sudden, the microbiome is big medical news. We have been addressing the gut, the gut flora, and the microbiome for decades in functional medicine. It is a central focus of functional medicine—how to restore normal gut function and balance the microbiome. How can we explain, given our current reductionist diagnostic

framework, that depression, autism, autoimmune diseases, heart disease, obesity, type 2 diabetes, cancer, and many other illnesses are all connected to your gut flora? It doesn't make sense given our current paradigm. At Cleveland Clinic, Stanley Hazen, MD, PhD, is doing research examining how the microbiome plays a role in regulating certain metabolites that may lead to heart disease.

These observations force us to rethink our diagnostic paradigm and question our current view. When you go to the rheumatologist, they do not ask about your gut flora; and when you go to the cardiologist, they do not ask about your gut flora. In functional medicine, it's exactly what we do. We look at the root causes. It's a new view of the body as a system, a biological network.

Functional and Western Medicine: A Case Study Comparison

Dr Bhargava: That is very interesting. The Institute for Functional Medicine defines this model as a systems-oriented approach that encompasses genetics, environment, and lifestyle. Can you explain that a little bit more to the traditional doctor?

Dr Hyman: I went to medical school like everybody else. In the second year of medical school, we had a course on systems. The cardiovascular system, gastrointestinal system, neurologic system, and so on. We separated and organized the body into these discrete systems. But that is not actually how the body is organized.

Why is it that all of a sudden we're learning that cardiac disease is not a plumbing problem but an immune or an endocrine problem?

Rather, the body is organized through biological networks that are all dynamically interacting. For example, how is inflammation linked to dementia, cancer, heart disease, and obesity, as well as autoimmune, inflammatory, and allergic disorders? How does that work? Why is it that all of a sudden we're learning that cardiac disease is not a plumbing problem but an immune or an endocrine problem? How do we explain that?

We have to begin to think upstream. As medicine evolves, we're now realizing that the body isn't actually what we thought it was. It's a dynamic, complex, adaptive ecosystem that responds to inputs from the environment. These influence gene expression and create your phenotype.

Most of us are still stuck in the siloed version of medicine. Nobody's communicating with each other across specialties to see these connections and understand how to work the dynamic complex adaptive system that is the human body.

I'll give you an example of how we would approach a patient with psoriatic arthritis differently. It's an autoimmune disease. With conventional medicine, these patients would need an immune suppressant, right? A woman who I saw was on ustekinumab (Stelara®), which costs approximately \$30,000-\$70,000 a year.^[1] She also had a host of comorbidities, including migraines, depression, prediabetes, reflux, and irritable bowel syndrome (IBS). She had itching everywhere: anal itching, vaginal itching, dandruff. We would say that these are all comorbidities. She needs to see the psychiatrist for depression, the gastroenterologist for her reflux and IBS, the neurologist for migraines, the rheumatologist for her autoimmune disease, and the dermatologist for her skin conditions. And she was. She was getting the best possible care, the best standard of care. But no one asked, "How are these connected?"

In functional medicine, we don't believe in comorbidities. We believe that there are fundamental root causes that can explain a lot of discrete phenomena.

In functional medicine, we don't believe in comorbidities. We believe that there are fundamental root causes that can explain a lot of discrete phenomena that aren't necessarily immediately obvious but are linked together. John Muir [is [alleged](#) to have] said that when you pull on something in the universe, you can see that it's connected to everything else.

Understanding those networks and connections is what functional medicine is about.

This woman had an autoimmune disease. We know that there are multiple causes. It could be a disturbance of the microbiome. It could be changes in intestinal permeability that lead to uptake of inflammatory peptides such as lipopolysaccharides (LPS) from the gut flora. She might have developed food sensitivities. She might have had an infection like Lyme disease, or she could have had toxic exposure. We look at the root causes, which are typically toxins, allergens, microbes, stress, or poor diet. I did that analysis on her. She was having postprandial bloating, a lot of yeast infections, and terrible digestive issues. All of those things could be linked to a disturbed gut microbiome. So I started there. She had psoriatic arthritis, but I started in her gut.

I put her on an elimination diet and got her off of common triggers such as gluten and dairy to reduce inflammation. I put her on a low-sugar and -starch or –glycemic load diet to prevent small bowel intestinal overgrowth and yeast overgrowth. I gave her the antibiotic rifaximin (Xifaxan®), which is used for small intestine bacterial overgrowth. I gave her an antifungal, fluconazole (Diflucan®), for yeast infections. I gave her digestive enzymes, probiotics, fish oil, and vitamin D.

She came back 2 months later and all of her symptoms were gone. Her psoriatic arthritis was gone and she was off the Stelara and all of her other medications. She had no more reflux, IBS, migraines, or depression. She lost 20 pounds. She had no more itching. All of her symptoms got better, not by treating each disease separately but by treating the system. That is an example of how functional medicine would work. It's not siloed in all of these specialties, with all of these doctors for different illnesses. We ask, "How is everything connected?"

We use a methodology that allows you to assess the patient and then filter the data into buckets of these biological networks. We call it the matrix, which is the system of thinking through and sorting the data that you see through history and physical examination. We look at all of the predisposing factors, genetics, and triggering factors. We look at lifestyle factors and how they influence the biological networks that drive disease.

Dr Bhargava: That was very interesting. I look forward to continuing our conversation. Thank you for being here, Dr Hyman.

Dr Hyman: Thank you.

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Cite this article: The New, Old World of Functional Medicine: Part 1. *Medscape*. Oct 12, 2016.

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COMMENTARY

The New, Old World of Functional Medicine With Dr Hyman: Part 2

Hansa Bhargava, MD | October 12, 2016

Editor's note: *This is the second part of a three-part interview with [Mark Hyman, MD](#), director of the Center for Functional Medicine at Cleveland Clinic. (The first part may be found [here](#).) It has been edited for clarity.*

Hansa Bhargava, MD: Hi. I'm Dr Hansa Bhargava, a medical editor for Medscape and WebMD. I am joined again today by Dr Mark Hyman to continue our conversation on functional medicine.

A lot of physicians may feel that you might miss something big with functional medicine. Let me be the devil's advocate. If you go through a review of systems with your patients, will that ensure that we don't miss anything like an occult fracture, an occult bacteremia, or an occult cancer? How do you make sure that you encompass traditional medicine as well?

Mark Hyman, MD: Functional medicine is not throwing out what we all learned in medical school. We still go through a traditional history, physical assessment, and traditional diagnostics, whether they are imaging or laboratory tests. They are all part of it. But in conventional thinking, the end stop is the differential diagnosis, which we all learned in medical school. That's usually the end of our thinking. Once we've made the differential diagnosis and we have the diagnosis, we know what to do. We pick up the *Washington Manual of Medical Therapeutics* for residents. We have the standard of care. It's not that complicated. Once you make the diagnosis, you know what the treatment is, right?

In functional medicine, the diagnosis is the place where we *start* to think. It's not the end of our thinking. In traditional medicine, it's the naming and blaming game. We name the disease and blame the name for the problem, and then we tame it with a drug. Let's take depression, for example. Someone comes in, and they're hopeless and helpless. They're sad. They have no interest in life. They have no appetite. They're not sleeping. They have thoughts of suicide. You say, "I know what's wrong with you. You have depression." Depression isn't the cause of those symptoms. It's the name of those symptoms. Then, we ask, "What's the cause of those symptoms?"

Well, there may be dozens of causes of depression, right? It could be psychosocial trauma, early life experiences, or Hashimoto thyroiditis, an autoimmune disease that leads to low thyroid function and is caused by eating gluten, which creates an autoimmune thyroid disease. The depression could be because you have been taking a proton-pump inhibitor for 10 years and you have vitamin B₁₂ deficiency, or because you live in the Northeast and you have vitamin D deficiency, or because you have taken antibiotics that altered your gut flora, or because you love sushi and you're eating sushi all the time and you have mercury poisoning, or maybe you hate fish and have omega-3 fatty acid deficiency, or maybe you're insulin resistant and love cinnamon buns and have prediabetes. All of those can cause depression. So it's a methodology for sorting through the root causes and the things that are driving it and then addressing those.

Dr Bhargava: You're saying that you take the traditional approach, but you're adding on a whole number of other diagnostics as well to find the underlying causes for the diagnosis.

Dr Hyman: Absolutely. I'm a trained family doctor, and I do all of the traditional diagnostics. I can make the regular diagnoses, but I don't stop there. I don't say, "Okay, you've got psoriatic arthritis. The treatment is a biologic drug or methotrexate." I ask what's going on. I had a patient the other day who had rheumatoid arthritis for a year. She was on intensive immunosuppressive therapy. It turned out that she had babesiosis and Lyme disease that nobody had ever thought of. I just go through an algorithm of what the root causes are. And then I ask what the missing ingredients are. It's not just asking what the triggers for disease are, but also: What is the biological terrain? Louis Pasteur came up with the germ theory. The germ was seen as the cause of disease. And then at the same time, Claude Bernard had a competing theory, which was that it's the biological terrain.

We know that if you inject rhinoviruses into people's noses, not everybody is going to get a cold. It's going to be stratified based on their level of stress, which suppresses the immune system. We know this in medicine. So the question is: What is your biological terrain and how do you enhance it? In a way, functional medicine is the science of creating health. It removes the impediments to health and provides the ingredients to health. The body has a natural healing capacity. It's very powerful. We think of food, nutrients, the right balance of hormones, light, air, water, sleep, exercise, restoration, and even meaning, purpose, connection, and love as ingredients for a healthy human. We try to support the removal of the impediments to health and provide the ingredients for health.

Dr Bhargava: So, you're adding areas to the history and physical that we don't normally do as physicians. You're not ignoring traditional medicine but actually adding other areas that are just as important. How does that compare with integrative medicine?

Dr Hyman: Integrative medicine is an advance that happened a couple of decades ago. It grew out of a holistic health movement during which we discovered alternative therapies such as acupuncture, homeopathy, energy medicine, chiropractic care, and osteopathic care. There were various modalities in mind-body medicine that were being ignored but that had the capacity to support health. So, Andy Weil and a group of innovative doctors decided to integrate these modalities into conventional medicine and began to develop integrative medicine centers. However, the doctors were just learning about these alternative therapies and then recommending them. It became more of a triage and referral system. I'm not trained as an acupuncturist, and I'm not a homeopath. I don't know anything about many of these modalities, but I'm a Western biomedically trained doctor. What I wanted to know was how to actually work with my patients and help them.

I would say that functional medicine is the map. It's the map of what the root causes are. Which biological systems are out of balance? How do we work with those? And then, with the modalities, if someone needs surgery, they get surgery. I use medications all the time. I will use lifestyle change when it's most appropriate. If someone comes in with diabetes, the treatment isn't metformin or glipizide or insulin. The treatment is changing what they eat. You can eat cinnamon buns all day and take more and more insulin, but we know from the ACCORD study^[1] that there's a higher risk for mortality and heart attacks in those who had more rigorous insulin therapy and more aggressive control of their blood sugar. It matters how you get there. We put people on aggressive dietary interventions, and we see people getting off 30, 40, or 50 U of insulin in a week. It's unheard of because most physicians don't know how to apply food as medicine.

It's as if you have a headache and I give you 2 mg of aspirin. Is it going to work? No, it's not going to work. You need two 325-mg aspirins to get rid of your headache because it's dose-dependent. It's the intensity of the intervention that matters.

Dr Bhargava: That was very interesting. I look forward to continuing our conversation. Thank you for being here, Dr Hyman.

Dr Hyman: Thank you.

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1. ACCORD Study Group, Gerstein HC, Miller ME, et al. Long-term effects of intensive glucose lowering on cardiovascular outcomes. *N Engl J Med*. 2011;364:818-828. [Abstract](#)

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Cite this article: The New, Old World of Functional Medicine With Dr Hyman: Part 2. *Medscape*. Oct 12, 2016.

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COMMENTARY

The New, Old World of Functional Medicine With Dr Hyman: Part 3

Hansa Bhargava, MD | October 12, 2016

Editor's Note:

This is the final part of a three-part interview with [Mark Hyman, MD](#), director of the Center for Functional Medicine at Cleveland Clinic. (Click to access [part 1](#) and [part 2](#).) It has been edited for clarity.

Integrative Therapies

Hansa Bhargava, MD: I am Dr Hansa Bhargava, a medical editor for Medscape and WebMD. I am joined again today by Dr Mark Hyman to continue our conversation on functional medicine.

How do you feel about all these integrative therapies? Do you have any thoughts on acupuncture, yoga, and meditation?

Dr Hyman: Yes, of course. I was a yoga teacher, trained before I was a doctor. I studied Chinese in medical school and learned about Chinese traditional healing systems. I've had much acupuncture in my life. In fact, it cured me of chronic pain that I had from back surgery. I do use other alternative modalities all the time as an adjunct to support my health.

But, when you use other modalities, how do you use them? When do you use the modalities? What is the diagnostic map? If you have migraines and you go to a group of integrative medicine doctors, one might say that you have a dosha imbalance, that maybe your vata/pitta is out of balance. An acupuncturist might say that your kidney chi is not right. The psychologist is going to say that maybe you're stressed and you should get therapy. The biofeedback person will say you need biofeedback. The herbalist is going to tell you to take feverfew.

In functional medicine, we don't do that. We ask, "Why are you having a migraine? What's the cause of your migraine?" If the cause of your migraine is that you're eating gluten, all these modalities are not going to help. We have a simple rule: If you're standing on a tack, it takes a lot of aspirin to feel better. You need to take out the tack. If you're standing on two tacks, taking one out isn't going to make you 50% better. You need to get rid of all the causes.

It's very important for us to understand that we have the capacity to think through this new model in a powerful way to really improve many chronic diseases. That's what we're focused on here at Cleveland Clinic.

Dr Bhargava: Now I'm going to take the lens of the skeptics. You have probably seen their websites.

Dr Hyman: I've seen them all. Have you looked at their credentials? They're usually shills for pharma. I'm saying things that are not popular.

Dr Bhargava: But when people have been trained in the traditional medical pathway, they may have questions. A lot of what you're saying makes sense and hopefully will help them to understand. If you have to say one thing about why functional medicine is important, what would you say?

Dr Hyman: We have been seeing increasing failure of our conventional approaches to dealing with the burden of chronic disease. One in 2 Americans has chronic disease.^[1] We are seeing increasing costs. I think we're at \$3.3 billion for our national healthcare bill. The annual cost per capita has now exceeded \$10,000 in America. We are not winning this battle. There are increasing numbers of people with autoimmune disease, allergic disorders, diabetes, and cancer. Even with heart disease, although the death rate is going down because of better treatments, the incidence is going up. We saw a [400% increase](#) in diabetes in the past 30 years across the globe.

These conditions are not getting better, and what we're doing is not working. We're good at ameliorating symptoms and managing disease, but our system is really broken. That's why [Toby Cosgrove, MD](#), president and chief executive officer at the Cleveland Clinic, invited the [Institute for Functional Medicine](#) to partner with the Clinic to start the [Center for Functional Medicine](#).

Dr Cosgrove and the Cleveland Clinic are investing a lot in this effort. He sees that the future is around root cause analysis and systems biology. There are initiatives around precision medicine, personalized medicine. This is exactly what functional medicine is. It's understanding that we're talking about an n of 1. We need to be able to think differently about disease.

Precision Medicine

Dr Bhargava: Precision medicine is another area that I wanted to ask you about. President Obama created the [Precision Medicine Initiative](#), and WebMD has released a report on precision medicine called [Path to a Breakthrough](#). How is functional medicine different from precision medicine? How is Cleveland Clinic integrating all of this into their system? Will they be doing research in this area?

Dr Hyman: The first question is, what is precision medicine and how does this apply clinically? Functional medicine is the original precision medicine. It's personalized medicine that focuses on the individual and understands that your genes and the influence of the environment on those genes play a huge role in your health. But it's not actually autosomal dominant genetics; it's about gene expression.

We have millions of single-nucleotide polymorphisms (SNPs). I had my whole genome sequenced with Craig Venter. I have 20,000 genes but 5.7 million SNPs, which is a lot of SNPs. There is a huge variation in the population. SNPs affect all the different functions in the body. One third of our entire DNA codes for enzymes, which are basically catalysts. Those catalysts require coenzymes, which are vitamins and minerals. So, we have this huge variation in our needs as individuals for different nutrients and different diets.

I think the concept of precision medicine is fantastic. It is in alignment with functional medicine. In fact, functional medicine is the first application of precision medicine.

I get concerned about this getting coopted by pharma as being about pharmacogenomics. Precision medicine is how we match the drugs to the person. We know that if you have a 2C19 polymorphism, then maybe you should be adjusting your warfarin differently. Fertility doctors will check methylated SNPs, *MTHFR*. If you have a methylated SNP, you might need methylated folate or a higher dose. These are more personalized drug therapies as opposed to a holistic systems approach.

I think we have to be careful with it. It's really looking at more of a [Leroy Hood model in systems biology](#), what he calls P4 medicine: personalized, preventive, predictive, and participatory. That's essentially what we do in functional medicine.

Dr Bhargava: Will Cleveland Clinic be putting research dollars into looking at functional medicine? One of the questions that doctors will have is whether there is research and evidence.

Dr Hyman: Absolutely.

What Does Functional Medicine Cost?

Dr Bhargava: I want to make sure that we have enough time to talk about cost.

Dr Hyman: Part of the reason I decided to come to Cleveland Clinic was because of Toby Cosgrove. I asked, "Toby, what would you say if I could empty out half of your hospitals, if I could cut your bypasses and angioplasties in half?" I thought he was going to say that I was nuts. But he said that that's exactly what we need to be doing. And then, he wouldn't stop

calling me after that.

I said to him that we need to do research to show that this model works. So now, Cleveland Clinic is spending millions of dollars of its own money to fund the research. We're not even going to the National Institutes of Health (NIH) or others, because it's very difficult to get money for these types of systems approaches. What we're looking at is reversing diabetes and getting people off insulin. We're looking at patients with treatment-resistant asthma. We're looking at inflammatory bowel disease. We're looking at doing research around autoimmune disease, and even reversing early dementia. We're being aggressive in our approach to doing randomized trials.

We're also doing something else, something that I think everybody should do, which is to look at outcomes and cost. In the healthcare system, we're not very good at doing this. It's one of the things that we implemented here when we started the Center for Functional Medicine. Every patient fills out an NIH-validated patient outcome test, which is called the [Patient-Reported Outcomes Measurement Information System \(PROMIS®\)](#). It's a free online tool. Any healthcare organization can use it, and there are many different versions of it. We test everybody at every visit. We've seen a 28% improvement in outcomes *[Editor's note: unpublished data]* over every other area in healthcare, on the basis of our own work at the Center for Functional Medicine.

We're also looking at the total cost of care. We want to know visits, prescriptions, and hospitalizations. We've seen dramatic changes in our costs in our employee health plan. We're measuring cost, and we're measuring outcomes. We're looking at value, because at the end of the day, it's about value-based care. We can do all the randomized controlled trials we want, but at the end of the day, there will be skeptics. The payers will start to realize that if they pay for this, we'll see dramatic improvements.

Dr Bhargava: In terms of the cost to the person, do you think that payers will be covering this at some point? Because innovative medicine costs hundreds of dollars.

Dr Hyman: Here's the challenge: We're in a no-man's land between the medicine we have and what we're going to have, and between the reimbursement model that we have and the reimbursement model we're going to have. Right now, we're in fee-for-service. We are going to be moving to accountable care organizations and more capitated per member per month payments, which is changing the landscape.

Here at Cleveland Clinic, we're moving toward population health, which means being accountable for the health of populations. It's not just waiting until they get into the hospital and getting a check for that. We're actually going to be reimbursed on the basis of how much value we create in the healthcare system. We are very focused on that. We started programs with population health to do decentralized care, working with people in groups. We're working with our employee health group.

Things are going to shift. The answer is that we're in a tough situation right now. We are now covered by insurance. People can come see us here, and they're covered by their insurance for their labs. But, it's still cost-intensive.

One patient whom I referred to in part 1 of our discussion saved \$30,000-\$50,000 per year on medication when she was able to discontinue Stelara® (ustekinumab). Who gets the value from that? The insurance company. The people who created the value don't get the value. So, we need to create a shared-savings model. We need to redistribute the economics. I think there are a lot of challenges, but this is all happening within healthcare right now.

The Secret to Good Health

Dr Bhargava: That's wonderful to hear. I just have one more quick question. We know that you were very involved with President Clinton's care. What is the secret to his good health?

Dr Hyman: Eating real food. No more McDonald's. He was the McDonald's President. You know, I used to watch those *Saturday Night Live* skits. Just eating real food.

Dr Bhargava: All Americans need to eat more real food.

Board Certification Coming Soon?

Dr Bhargava: Do you see board certification happening in this specialty at some point?

Dr Hyman: Yes. We are now building training at Cleveland Clinic. We've implemented a nutrition curriculum in the medical school. We have an 18-month certification program at the Institute for Functional Medicine. We're going to be putting that online so that physicians can get trained. Finally, we're looking towards building a fellowship program here at Cleveland Clinic, as well as residencies down the road.

Dr Bhargava: Thank you very much, Dr Hyman. It sounds like it's a great new specialty. We look forward to seeing certification in it. We also look forward to seeing payers help patients to actually afford it. Thank you so much for being here.

Dr Hyman: One additional comment. Functional medicine is not a specialty. It's a way of thinking, and it applies to every area of medicine. For example, I was talking to the chair of orthopedics here yesterday, who is interested in how we can improve the health of patients going into surgery and after surgery. We have people going into surgery who have osteoarthritis. Can we deal with them through other modalities that will help to reduce the cost of care? It really applies to every area of medicine. It's an overarching model of thinking about disease that applies to every disease.

Dr Bhargava: If it can help the chronic diseases in this nation, we'll all be very happy. Thank you, Dr Hyman.

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