

Vitamin D in Children and Adults

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Guest

Michael Holick, PhD, MD

- International expert on vitamin D metabolism, bone health, and skin and collagen matters
 - As a graduate student he was the first to identify the major circulating form of vitamin D as 25-hydroxyvitamin D3 and the active form as 1,25-dihydroxyvitamin D3.
 - He has been a professor of medicine, physiology, biophysics, and molecular medicine.
 - He has been a chief of endocrinology (diabetes and metabolism section), director of the General Clinical Research Center, and founder of a bone health clinic.
- Recognized physician, author, and scientist
 - Thompson Reuters recognized him as one of the most influential physician scientists in internal medicine in the world.
 - He has published more than 600 peer-reviewed articles including one of the most cited reviews in the New England Journal of Medicine: Vitamin D Deficiency.
 - He is a Fellow of the American Society for Nutrition and a Diplomate of the American Board of Internal Medicine.

Host

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- She has extensive expertise with leadership development and executive coaching and a background in content development, visual performance, speaking, and podcast hosting.

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- She is a nurse planner for Colibri Group and a certified legal nurse consultant. She is a quality-focused, results-driven nursing education professional. As a continuing education leader with nurse executive experience in developing interprofessional educational programs, she supports healthcare workers with educational activities to help increase communication within the healthcare team.

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Transcript

Episode 1 – Vitamin D and Your Health from Birth until Death

SOUNDBITE OF MUSIC

LEANA MCGUIRE, HOST: Hello and thank you for taking time to join us on this podcast. I'm Leana McGuire, your host with Colibri Healthcare. Today, we will be discussing vitamin D. We probably all know how vitamin D and calcium are good for strong, healthy bones. We've heard of the connection between osteoporosis and fractures from falls based on deficiencies in vitamin D and calcium intake.

But there are so many other important functions that vitamin D plays as a part of our overall health. We'll cover all of that and more, including the intake of vitamin D and safe or safer ways to increase vitamin D when it's needed. In addition, we'll discuss how some consider vitamin D to be a hormone. Is it a vitamin? Is it a hormone? We also want to chat about sources of vitamin D, how to increase our intake if we have inadequate levels and vitamin D in the laboratory. Are there things we should know about Vitamin D testing or interpretation of lab results? Oh, and what about this question? What's the difference between vitamin D2 and vitamin D3? Well, we're super fortunate to have a pioneer here with us who can bring us up to speed.

I'm joined by an international expert on vitamin D metabolism, bone health, and skin and collagen matters, Dr. Michael Holick. Welcome, Dr. Holick.

DR. MICHAEL HOLICK, GUEST: Thank you. It's a pleasure to be here.

MCGUIRE: Dr. Holick is a dedicated and accomplished physician and researcher. He has been a professor of medicine, physiology, biophysics, and molecular medicine. He has also been a chief of endocrinology, diabetes and metabolism, director of the General Clinical Research Center, and founder of a bone health clinic.

As a graduate student, he was the first to identify the major circulating form of vitamin D as 25-hydroxyvitamin D3 and the active form as 1,25-Dihydroxyvitamin D3. It's a mouthful. Dr. Holick has been involved with learning and educating about vitamin D, cancer research, psoriasis, bone disease, calcium metabolism, and much more for 50 years.

He was recognized by Thomson Reuters as one of the most influential physician scientists in internal medicine in the world. He has published more than 600 peer reviewed articles, including one of the most cited reviews in the New England Journal of Medicine: Vitamin D Deficiency.

Dr. Holick, is there anything else you'd like to share with us about yourself with regard to your life's mission that has evolved around vitamin D? Like, how did you become *the* vitamin D guy, for example?

HOLICK: It's a very good question that I'm often asked, is, "How did I get involved in vitamin D in the first place?" And it turns out that I was a lowly graduate student at the University of Wisconsin. And in typical fashion, you know, students really want to work in the hottest topics. And back then, um, in/at the end of the 1960s, DNA was discovered, ... and lots of activity.

So, I was interested in working in the field of DNA, but there were many other postdoctoral fellows and others in the laboratories. And so, they didn't need a simple-minded graduate student. And so, they sent me over to Dr. DeLuca, and they told me, they said that you're going to be working in vitamin D. And I said, I have no interest in working in vitamin D!

It's a boring subject, right? It's found in cod liver oil. It prevents rickets in children. And so, why do I want to work in this? But it turned out that I made basically a sow's ear into a golden purse. And little would I know that we began to recognize that if you do animal studies and give vitamin D deficient rats vitamin D, it took 24 hours to work on regulating and increasing intestinal absorption of calcium.

And so, the thinking was either A) vitamin D is a dumb vitamin hormone or B) is that maybe it needed to be activated. And so, it was shown in pigs that if you gave huge amounts of vitamin D that they had in their blood, 25-hydroxyvitamin D₃. The problem with that issue was that they got massive amounts of vitamin D.

So how do we know that, just simply a toxic product? And so, I was given as my master's project is human blood, about 100 mls of human blood from patients that were getting high doses of vitamin D, because they had a disorder called hypoparathyroidism. And back then, that was the way to treat this disorder.

And so, I was given the blood and was told, follow the directions that was done for the pigs and that you should be able to be successful maybe in a year or two in getting a master's degree. Well, I started immediately and realized two months into it that there was a contaminant in human blood that was not in pig blood, and that no matter what type of separation technique you used, you could not separate it.

And so, on Thanksgiving morning um in 1969, um I realized that I needed to do something else. And I found on the shelf a product that I had worked with as an undergraduate student and ... and made a formulation with it. I put my material on, and 2 hours later, I had purified, and we identified the major circulating form of vitamin D in human blood as 25-hydroxyvitamin D.

MCGUIRE: Wow.

HOLICK: We now recognize that it's what is used by doctors to measure your vitamin D status. It's used worldwide. I helped develop some of the first assays for it. But then the real question was you give 25-hydroxyvitamin D now to vitamin D deficient rats. And now it takes about 6 to 8 hours to work. And so, the question is, does it really need to get even activated more?

We knew that the 25-hydroxylation occurred in the liver. And it was also curious at the time that patients with kidney disease had bone disease and that if you gave them vitamin D, it didn't work. And so, there was always a strange misunderstanding of how vitamin D and kidney disease interacted. Well, it turns out that the kidneys activate vitamin D.

And so now the hunt was on to identify it. And so, again, using my new separation techniques, um, I was fortunate enough to be the first in the world, um, as a graduate student to identify the active form of vitamin D

known as 1,25-Dihydroxyvitamin D3. And then I decided that I knew all along that I wanted to get my PhD first and then get my M.D. degree.

And, um and so now I'm applying to medical school. And at the same time, we realized that kidney failure patients have bone disease. So, what if you gave the active form 1,25-D to them? Could you improve their lives? And so my roommate and I spent actually two years, um, and worked on the first chemical synthesis of 1,25-Dihydroxyvitamin D3.

It was given to doctors around the world to treat bone disease in children and in adults, um, called X-linked hypophosphatemic rickets as well as vitamin D dependent rickets. We gave it to adults with renal failure, children with renal failure that had improvement, significant improvement in their bone disease. It's one of the first treatments of choice for helping to prevent bone disease in kidney failure patients.

And also, it was given to, ah, rare genetic disorders called vitamin D dependent rickets type 1. All very effective. So that was my first introduction into translational medicine and got me really excited about Vitamin D!

MCGUIRE: Yeah, it's no longer boring at that point!

HOLICK: Exactly! And so, then I, after graduating from University of Wisconsin, both my medical degree and my PhD degree, I went to Massachusetts General Hospital, and I was a resident. And at the same time, I set up my laboratory, a vitamin D laboratory, because I realized something. That vitamin D, the major source for humans, has always been sun exposure, but nobody has ever asked the question, how do you make vitamin D in your skin and what are the regulators?

So, for example, does skin pigmentation, time of day, season, latitude, um and sunscreen use have any effect? And so, over the next decade, I started doing all those studies and answering those questions. And, then another interesting observation occurred, which was we realized that not only does your skin make vitamin D, but also your skin cells have a receptor for vitamin D.

And we wondered why. And so, I then um started growing human skin cells in culture and asked the question, if you added the active vitamin D that I had chemically synthesized, what would happen to those cells? And, it turns out that it inhibited their proliferation and induced differentiation. Well, that's nice observation, but the real question was, is there any practical value?

And so, I put my M.D. hat back on and asked, "Is there a hyperproliferative skin disorder?" Right? ... that is nonmalignant, um that has minimum treatment opportunities. And, it turns out to be psoriasis. And so back in the mid-1980s, I introduced a concept of using activated vitamin D topically to treat psoriasis. We published some of the earliest papers on this.

So as a result, vitamin D has been kind of part of my life, and it's continued to grow in leaps and bounds ever since.

MCGUIRE: Okay. That's really fascinating, really is. Tell us more about being busy over the years, treating patients, researching, and being a subject matter expert.

HOLICK: So, I started um my basic research career like I said, in Dr. DeLuca's lab in 1969. I got my master's degree six months later, got my PhD degree a year later, and then became a full-time postdoc and a full-time medical student. And, and then continued after medical school at Massachusetts General Hospital, my residency. And, then because of my expertise in vitamin D and metabolic bone disease, I set up a pediatric and adult metabolic bone clinic as part of my activity at Massachusetts General Hospital.

I continue that activity, then went off to Tufts and at New England Medical Center, continued that activity. And, then I was recruited by Boston City Hospital, which was considered one of the world's best hospitals to set up and be chief of endocrinology, nutrition, diabetes. ... set up a metabolic bone clinic for pediatrics and adult patients and also to be director of the General Clinical Research Center.

And, I basically have been involved in helping infants, children, and adults with metabolic bone disease of various causes for more than 40 years.

MCGUIRE: Wow! It sounds like you have a lot to share in helping us understand this topic. We are definitely grateful for the opportunity to chat with you, so thank you again. It feels like most people know that vitamin D is part of a healthy diet and that a deficiency of vitamin D can have negative effects on our bones and overall health.

But, I also think most people don't know what their vitamin D level is. I think many assume all is okay in the vitamin D department, but is it? Do you find that many people are aware of their vitamin D status? And, is it true that you can get adequate amounts from dietary sources?

HOLICK: Yeah, so herein lies the problem, which is, I always ask my students in my clinic and also my patients, where do you think you're getting vitamin D from in your diet? And, it turns out that there are only really three or four major dietary sources. The first is oily fish like wild caught salmon, mackerel, herring. We did a study and showed that farmed salmon have very little vitamin D, so that if you're gonna buy your salmon and you want to get your vitamin D, it's in wild caught fish.

We found that there's about 500 to 1000 units in about 3.5 ounces of, of salmon, a typical meal, cod liver oil, which is not a favorite, right?, for both children and adults. Mushrooms exposed to sunlight. Right? Those are the three major natural sources. That is it! Right?

MCGUIRE: Wow!

HOLICK: Dairy products are fortified with vitamin D as is now orange juice, because we actually did the study and showed that you could put vitamin D in orange juice, and it's bioavailable. There's only a hundred units in a glass. And so, and it's known that the Institute of Medicine had recommended that children over one year of age and all adults need 600 units of vitamin D a day. Well, you can't get that from your dairy or drinking orange juice unless you're going to be drinking six glasses every day.

MCGUIRE: Right.

HOLICK: And, and we'll talk about a little bit more later on that we think for maximum vitamin D benefit, you need much, much more vitamin D as recommended by the Endocrine Society Practice Guidelines on vitamin D.

MCGUIRE: Wow. And, what about the continuum from in utero through adulthood?

HOLICK: Right. And so, I often give talks about vitamin D is necessary from birth until death. And so good examples are during pregnancy. Preeclampsia is one of the most serious complications. And we had published many years ago with a group in Pittsburgh um that um ... higher your 25-hydroxyvitamin D level during pregnancy, lower was your risk of developing preeclampsia, um up to 60% reduced risk by another study, showing that improvement of vitamin D status plays a major role.

They've also shown that premature births are markedly reduced if blood levels of 25-hydroxyvitamin D are in the range of about 40 nanograms per mL. And we also know that in utero, if the fetus is vitamin D sufficient,

after birth, that infant is less likely to have wheezing disorders and asthma and reduces risk for dental caries. So, that's just the beginning of the story, right?

We also know that a study was done in Finland where they showed that if you give infants, first year of life 2000 units of vitamin D a day, it reduced their risk 31 years later of developing type 1 diabetes, right?, which is an autoimmune disorder.

MCGUIRE: Amazing.

HOLICK: We also know a study, many studies have shown if you were born above Atlanta, Georgia, and for the first ten years of your life, you live there, you have 100% increased risk of developing multiple sclerosis for the rest of your life no matter where you live. And so, we think that during childhood, vitamin D is very important for reducing risk for autoimmune disorders and possibly even cardiovascular disease and other chronic illnesses later in life.

We did a study with Dr. Dong in Georgia where he gave teenage black children that were 14 years of age, they were all vitamin D deficient. They had a 25-hydroxyvitamin D of around 11 nanograms per mL. We think that to be sufficient you need to be at least 30. And, he gave these children for three months, 2000 units of vitamin D a day or 400 units of vitamin D a day.

And, then he looked at blood flow using ultrasound to get a sense of the stiffness of the blood vessels. And, he showed that those teenagers that were on 400 units a day raised their blood level to about 24, had no effect on their blood vessel stiffness. But those teenage, teenagers that were on 2000 units a day, right?, they had their blood level on average, 34 nanograms per mL.

And, they had significant relaxation in their arterial system, suggesting that that is kind of the precursor for developing hypertension and heart disease later in life. So, reducing that activity on your blood vessels can have a significant health benefit.

MCGUIRE: That is fascinating! How do you think nurses and physicians could work better together to help spread awareness of the importance of vitamin D or to treat vitamin D insufficiencies?

HOLICK: So, I think physicians, you know, are often overwhelmed, and they're focusing on a patient with diabetes or thyroid disease or osteoporosis. Right? But they may not be thinking about some of the benefits of vitamin D in many chronic illnesses. So, for example, a cardiologist probably wouldn't be thinking about their patient's vitamin D status. But the nurse, you know, being aware of this association could very well make the recommendation both to the patient, right?, for the intake that, you know, you may want to think about having your vitamin D status determined, or maybe, you know, your cardiologist will recommend that as well and want to order it for you.

MCGUIRE: Excellent. Now, there was a large-scale in-depth survey/research, which I believe is some of the most recent national data of that level from the National Health and Nutrition Examination Surveys or NHANES. In the early 2000s, approximately 25% were deemed at risk of vitamin D inadequacy and approximately 8% at risk for deficiency. With a little bit of online searching, it seems many more recent studies are based around vitamin D and effects on illness or disease, rather than studies to estimate national averages for vitamin D status. Do you know of any more recent research that discusses the levels of vitamin D in the U.S.?

HOLICK: So, the CDC had also published a similar type of observation where they found that about 33% of both children and adults are at risk of vitamin D deficiency, worldwide, I think it's well documented, and we've published reviews on this. On average, 40% are vitamin D deficient, and 60% are deficient or insufficient.

MCGUIRE: Hmm. Goodness sakes!

HOLICK: And, the reason is simple. Right? I mean, we said there is no vitamin D in your diet.

MCGUIRE: Right.

HOLICK: Right. And so, as a result, it's mainly from sun exposure. And the problem, of course, with that is, A) we're all busy. And, B) you only make vitamin D from about 10 a.m. until 3 p.m., and C) is everybody's been warned, "Always wear sun protection before you go outside."

MCGUIRE: Sure.

HOLICK: And, so as a result, vitamin D deficiency is incredibly common, because there really isn't very much vitamin D available in your diet.

MCGUIRE: Right.

HOLICK: Mother Nature had always designed us to be as hunter gatherers, right?, exposed to sunlight every day, and make your vitamin D.

MCGUIRE: Right. Mm hmm. Good point. Do you find most people who you've interacted with as a physician have adequate levels of vitamin D?

HOLICK: I mean, studies have been done in physicians and they show that most are vitamin D deficient, and a very interesting study done in Australia, in Australian dermatologists, at the end of the summer, 87% were found to be vitamin D deficient.

MCGUIRE: Really? Oh, dear. Isn't that interesting? Okay. Can you give us an introduction to vitamin D? It's about more than just our bones. So, what does vitamin D do for us, and how, primarily, how is it a vitamin and a hormone? That's the big question.

HOLICK: Right. So by definition, vitamin D is a hormone. Right? It's not a vitamin. And, the reason is a hormone means that it's made in your body. Right? And, then it travels someplace to have a biologic effect. Well, vitamin D is made in your skin from sun exposure. So automatically it's a hormone, because it gets into your blood and then it goes to your liver to get activated to 25-hydroxyvitamin D and then to your kidneys to 1,25-Dihydroxyvitamin D.

So, the fact that they have to get activated into additional organs before they can go to the target tissue, by definition is a hormone. It's not a vitamin. A vitamin means that it's something you can't make. Right? ... that you have to have coming in from dietary sources.

MCGUIRE: Right. Okay!

HOLICK: And now, why is vitamin D playing an overall role in health? And so, we knew, right, that the major function of vitamin D is to maintain your blood calcium in a normal range. And, the reason for that is that calcium plays a critical role in most metabolic activities, cardiovascular function, and brain function. And so, when you are vitamin D deficient, right?, and you're not getting enough calcium from your diet into your bloodstream. Then you wind up stealing it out of your bones.

MCGUIRE: Ahh.

HOLICK: So, we knew that the receptor for active vitamin D, right?, is in your intestine, in your bones, and then another place is in your kidneys, because your kidneys can regulate how much calcium is lost into the urine, for

example. But then in the, in the 1980s, we and many other investigators began to realize that colon, breast, brain, um muscle, um all ... and your immune cells all have a vitamin D receptor. MCGUIRE: Hmm.

So then, the obvious question is, "Why is it there?" Mother Nature would not have it there if it wasn't having a biologic response. And so, many investigators, including our own, showed that if you culture colon cancer cells or if you culture prostate cancer cells, incubate them with active vitamin D, if they had a receptor, it helped them decrease their malignant growth pattern and, and, and help to make them more normal.

A study done on preleukemic cells showed that if you incubated with active vitamin D, if they had a receptor, that they in fact became normal. This was a study done by Dr. Suda back in 1979. And so, we then started asking other questions, like your immune cells. So interesting that you have what are called T lymphocytes which make cytokines and B lymphocytes which make antibodies.

And so, we had done a study with Dr. Crane's group many years ago, and others have done similar studies. And we asked the question, why is the vitamin D receptor there? It turns out that an inactivated T lymphocyte has no vitamin D receptor, and only when it's activated, then the cell needs something, and it develops a vitamin D receptor.

And then when you add 1,25-D to these immune cells, they have amazing effects on cytokine production in regulating cytokines, which we think is now playing a role in COVID, which we can talk about a little bit later on. B Lymphocytes, also resting B Lymphocytes, have no receptor. You activate them, and they do. And, guess what? 1,25-Dihydroxyvitamin D modulates immunoglobulin synthesis.

Why is that important? We think, because, we think that it may help reduce the development of autoimmune disorders by regulating ... downregulating the production of autoimmune antibodies.

MCGUIRE: Wow! That is really interesting! I'm amazed by all the magic that vitamin D performs! I really am. This is really interesting! We're going to talk about sources of vitamin D in a few minutes. But, before we get to that, let's talk about vitamin D as a fat-soluble vitamin. I know in nursing school we were taught how A, D, E, and K were fat-soluble, so people needed to be careful that they didn't get too much of these in case the levels got too high.

However, it seems nowadays that it's not that easy with a normal lifestyle and standard dietary intake to overdose on vitamin D (without supplementing or otherwise taking in vitamin D). Have you met people who have had levels that were too high or is that rare?

HOLICK: Well, let's put it into perspective. So, I'm sure that you were taught, probably certainly I was taught, that of all the fat-soluble vitamins, certainly vitamin A is one of the most toxic that you have to be extremely careful about. But, the second one on the list is vitamin D. And so, pediatricians, in particular, have been very concerned about giving too much vitamin D to infants and worrying about toxicity.

And what does toxicity mean? It means that your blood calcium and your blood phosphate level are elevated. That means that it basically starts to mineralize um and develop kidney stones cause ... what's called nephrocalcinosis in your kidneys, decrease in kidney function, and ultimately it will cause calcification of your blood vessels, ultimately leading to death.

But, we now recognize that vitamin D is one of the least toxic, fat-soluble vitamins, and that you really need to be taking literally hundreds of thousands of units a day for at least a year before you have to worry about.

And, I'll give you an example. I had a lawyer call me up, and he was very concerned, because back in the 1990s, I had been already recommending, others have as well, that if you improve your vitamin D intake to about 2000 units a day, reduced risk of prostate cancer. And so, he went to his local drugstore. There wasn't any.

So, nobody had any interest in vitamin D supplements. So, he went on the Internet, and he bought a product, made out of Canada. And, he took two teaspoons a day, because each teaspoon was said to have a thousand units in it. And he did it for more than a year, and he became severely intoxicated. And so, I told him that, you know, this doesn't make any sense. And, that ... send the material up, and we'll do an analysis of the product. The company forgot to dilute it.

MCGUIRE: Oh, no!

HOLICK: He was taking a million units a day for more than a year.

MCGUIRE: Oh, my goodness!

HOLICK: So, I became his doctor. I made recommendations where I told him, you have to lower your calcium. You have to wear sunscreen all the time, because he lives in Florida, and no vitamin D in dairy or anything else. And, we published him, New England Journal of Medicine, and showed that his calcium quickly came down with good hydration and that even though his 25-hydroxyvitamin D was over 500,

MCGUIRE: Wow.

HOLICK: ... even a year later at 300, right?, he had no sequelae, no complications from this. Right? The Endocrine Society practice guidelines states that you have to have a blood level of over 150 nanograms per mL before you have to worry about toxicity. Vitamin D intoxication is one of the most rarest medical conditions caused by either inadvertent intake because the product wasn't properly made or intentional intake.

MCGUIRE: Wow. Amazing!

HOLICK: So, as you can see, a lot to talk about ... vitamin D.

MCGUIRE: I'm, I'm amazed. I'm not even kidding! I just want to eat wild caught salmon in the sun this afternoon. That's really my, that's my goal for the day. I'm not even kidding!

HOLICK: Yeah, but wait. Wait until you ask me about sunlight, and then I'll give you a better insight.

MCGUIRE: Then I'll change my mind? Okay?

HOLICK: No. Maybe yes. Maybe you don't, it depends upon where you're, where you live.

SOUNDBITE OF MUSIC

MCGUIRE: Well, it's time to conclude part one of this podcast. Again, thank you for joining us. Please return for part two as we continue discussing vitamin D and health and explore sunshine and some laboratory-related questions. A sincere thank you to Dr. Michael Holick for chatting today. This is Leana McGuire for Elite Learning by Colibri Healthcare.

SOUNDBITE OF MUSIC

Episode 2 – Vitamin D2, Vitamin D3, Sunshine, the Laboratory, and Me!

SOUNDBITE OF MUSIC

MCGUIRE: Hello and welcome back for part two of our series on vitamin D. I'm Leana McGuire, your host for this Elite Learning podcast by Colibri Healthcare. And, back with me is Dr. Michael Holick. Thank you again, Dr. Holick, for taking the time to continue this discussion.

HOLICK: My pleasure.

MCGUIRE: We're so glad to have you. Now let's dive into sources of vitamin D, including making vitamin D from sunshine. Also, ... questions about vitamin D level testing. Dr. Holick, tell us about vitamin D and the sun. I know you have a good way of explaining the benefits, risks, and nuances. So, you have the mic. Is it as simple as going outside and getting some vitamin D?

HOLICK: Well, first of all, um let me just talk just a little bit about vitamin D2 and vitamin D3.

MCGUIRE: Please.

HOLICK: So, vitamin D2 comes from yeast. It's the precursor, ergosterol. This was made back in the 1930s and was used for fortification of food in Europe and the United States um for decades. Vitamin D3 is what you make in your skin, um it's found in cod liver oil, found in oily fish like salmon.

MCGUIRE: Got it. Okay.

HOLICK: From, from my experience, vitamin D2 is as effective as vitamin D3 in maintaining vitamin D status.

MCGUIRE: Okay.

HOLICK: So, talking about the sun.

MCGUIRE: Yes, yes.

HOLICK: And so, as I had mentioned in part one, time of day, season, latitude, degree, skin pigmentation, all play a role. And, I'll give you some insight. So, for example, you would think that if you're in Texas at 8:00 in the morning on a sunny summer day, right?, that you go out, do your jogging, make your vitamin D, and less damaging to your skin. That's usually what the recommendation is from dermatologists. Go out in the early morning and late afternoon. It turns out you cannot make any vitamin D before about 9/10:00 in the morning, even if you live at the equator. And, it abruptly stops at around 3 to 4:00 in the afternoon.

And the reason is that it's the same for living here in Boston in the wintertime. You cannot make any vitamin D in your skin from about the end of October until around middle of April. And the reason is, it's the zenith angle of the sun. And if it's more oblique, it has to go through more ozone. And, the vitamin D-producing rays are absorbed by the ozone layer. And so, as a result, morning sunlight is just like winter sunlight. And so, it's really important to know when you're going out.

Skin pigmentation: It's well documented that people of color need much more exposure, because the melanin is like a natural sunscreen, and it's absorbing the vitamin D-producing rays, reducing vitamin D production. We did a study in black adults with very dark skin and showed compared to a white adult like myself, they would need to be outside 5 to 10 times longer to make the same amount of vitamin D.

MCGUIRE: Interesting.

HOLICK: What about sunscreen use? Right? A sunscreen with an SPF of 30, by definition is supposed to be absorbing about 97.5% of your ultraviolet B radiation. Ultraviolet B radiation is responsible for making vitamin

D. And so, therefore, if you put on the sunscreen properly, it will reduce your ability to make vitamin D in your skin by 97.5%.

MCGUIRE: Goodness.

HOLICK: And we did a study in farmers many years ago and showed farmers who wore sunscreen all the time because of worry about skin cancer, they had a history. They were vitamin D deficient. So. Yeah. Because they were wearing sunscreen all the time. And so, time of day, season, latitude degree, and skin pigmentation all play a role.

Sorry, so just one of the questions that I'm often asked is, "How much can you make?" So, we did another study on healthy adults, and we put them in a tanning bed which has UVB radiation for making vitamin D and in a bathing suit and expose them to what's called one minimal erythemal dose. And, we compared that to giving an oral dose of vitamin D. One whole body exposure in a bathing suit, right?, will produce about 15000 to 20000 units of vitamin D. So, your skin has a huge capacity to make vitamin D.

MCGUIRE: Wow! So how do we find the balance between intake of vitamin D and mitigating risk from sunshine exposure with regard to unhealthy rays? Can you talk about UVA and UVB rays for us?

HOLICK: Sure, well, UVA rays make no vitamin D, and UVA rays, even though they have less energy, they actually penetrate more deeply into your skin, because your, your DNA and RNA and other properties in your skin don't absorb it. So, it goes deep down and as a result, it affects your immune system and may increase risk for melanoma. UVB: Excessive exposure increases risk for nonmelanoma skin cancer.

But, it's been shown that occupational sun exposure reduces risk of melanoma, right?, the most serious kind of skin cancer. And so, I think, you know, the listeners should be aware of this. And so, how do you balance all this? So, like I said, there's 100 units in a glass of milk or orange juice fortified with vitamin D. Right? You need, in my opinion, based on the Endocrine Society practice guidelines on vitamin D, I chaired that committee, and those members were all experts in vitamin D, we recommended 400 to 1000 units in infants, 600 to 1000 units in children. And, I think teenagers should be treated like adults, which is 1500 to 2000 units a day. If you're obese, vitamin D gets diluted in your body fat. You need 2 to 3 times more vitamin D.

So bottom line is, we did a study many years ago from the National Health Survey you talked about. We showed even, even to try to get to 600 units a day, no child or adult is able to get enough vitamin D from dietary sources. The problem is that you're not a hunter gatherer any longer.

MCGUIRE: Right?

HOLICK: And so, just exposing your face, which we don't recommend, because it's the most sun exposed. So, I always tell my patients, wear sun protection, either a hat or sunscreen. Right? But arms, legs, abdomen and back is okay. And, what you want is to be out there for an amount of time that would, that would be about 25 to 50% of the time that it would cause you to have a mild pinkness to your skin 24 hours later known as an MED (minimal erythema dose).

So, you can't get enough from sun exposure unless you're a lifeguard or if you're a hunter gatherer.

MCGUIRE: Right?

HOLICK: And so, a study was done. A study was done in Maasai herders, and they showed, right?, that they're out all the time. Right? And Hadza bushmen as well, that their blood levels on average are about 40 to 60 nanograms per mL.

And here's a just another point, right, which is human breast milk contains essentially no vitamin D. So, if you are breastfeeding your infant, there absolutely needs 400 units a day, as recommended by the American Academy of Pediatrics. But the real question should be, it doesn't make any sense. Why would Mother Nature not have adequate vitamin D in human breast milk?

Well, it turns out a study was done by Bruce Hollis and Carol Wagner, and they showed if you give lactating women 6400 units a day, they put enough vitamin D in their milk to satisfy their infant's requirement. So, that's why we're beginning to realize that we need a lot more vitamin D. And, I think the hunter gatherers, like I said, they're 40 nanogram per ml, you would need to take about 4000 to 5000 units a day.

MCGUIRE: Wow. Now what about rays of sun being filtered through a car window or a window at work or even at home?

HOLICK: So, a study was done back in the 1930s, and they showed, yeah, that, um that you can't make any vitamin D when you're exposed to sunlight through glass.

MCGUIRE: Okay.

HOLICK: The glass absorbs all UVB.

MCGUIRE: I'm also curious about how geographic location plays a role in this topic. I know someone who traveled to a location closer to the equator and received the worst sunburn of their life. It wasn't a really bad sunburn, because they used sunscreen, but it was definitely the worst for them.

HOLICK: You know, so there's that concept out there, which is really incorrect. And, that is that if you are out there for a very long time, you can make lots of vitamin D. Mother Nature designed us so that we could make enough as a hunter gatherer. So, you never want to get a sunburn, and um and as a result, if we showed, we published this to show that excessive exposure to sunlight actually destroys the vitamin D that you're making.

And so, it doesn't benefit. In terms of latitude, like I said, if you live near the equator, right?, if you live below about Atlanta, Georgia, you can make vitamin D in your skin year-round. Right? But so, for example, in Florida, in the wintertime, you probably make about 10 to 20% of what you would make in the summertime.

Okay. But if you live above Atlanta, Georgia, basically you could not make any significant vitamin D from about like say end of October until the next April. And the higher you go, the longer that period. So, for example, we did a study in Edmonton, Canada. So, it's six months of the year. They basically could not make any vitamin D when they're out exposed to sunlight.

MCGUIRE: Interesting. So, our bodies can make vitamin D from exposure to sunshine in the ways you explained. Other sources include diet supplementation and what else? Is there anything else?

HOLICK: Right. So, my recommendation has always been for my patients and even for myself and my family, you have to take a supplement. It's the only way to guarantee sufficiency. And, we don't recommend, the Endocrine Society does not recommend, and I don't recommend to my patients that they should be getting their blood levels tested. Right? If they're getting an adequate amount of vitamin D, unless they have a malabsorption problem or a hypersensitivity to vitamin D, if you take the amount of vitamin D recommended by the Endocrine Society, you should be vitamin D sufficient. And so, it's only those that are not, um that have other issues that you should be measuring their blood level.

MCGUIRE: Okay. And, is there a recommended dosage from research or reputable organizations about intake?

HOLICK: So, like I said, the Institute of Medicine, they did a population model study. Right? And, they reported that children, well infants, 400 units a day, children and adults, 600 units a day. But like I said, the Endocrine Society Practice guidelines, our recommendations were for health professionals ... how to treat and prevent vitamin D deficiency. And reviewing all the literature, we concluded that infants 400 to 1000 units a day and so that you don't have to worry about just 400, but up to a thousand units is perfectly safe. Children, 600 to 1000 units a day, and then adults 1500 to 2000 units a day. And, obese people need 2 to 3 times more.

MCGUIRE: We've discussed a lot of really interesting information so far, all of which helps us understand more about the complexity of vitamin D intake. Now, let's specifically talk about testing. If a healthcare provider orders a vitamin D level, most are familiar with serum testing, taking a blood sample and sending it for analysis. Are there other ways to test for vitamin D levels? I'm just curious.

HOLICK: No. And, make sure that if you're going to get your doctor to measure your vitamin D status, right, you're not measuring your vitamin D level, because you don't measure vitamin D. Vitamin D status and 25-hydroxyvitamin D, you don't ever want to order 1,25-Dihydroxyvitamin D, because it's normal or elevated when you're vitamin D deficient. And, there's a reason for that.

MCGUIRE: Oh, okay. Are there interpretation details that are helpful to be aware of? For example, are there things that you can interfere with an accurate, trusted result other than things like improper lab technique or a bad or clotted blood sample?

HOLICK: Um, the gold standard assay is what's called liquid chromatography tandem mass spectroscopy. It's extremely reliable. There are also more quick assays that are antibody-related, and they can be problematic um and not always as accurate as you would like them to be. So liquid chromatography tandem mass spectroscopy, which is readily available in the United States, would be a good choice.

MCGUIRE: Okay. I think many are used to hearing about vitamin D in terms of international units. Can you tell us about the unit of measurement of international units? And when we see something with micrograms?

HOLICK: Right. So, 25 nanograms is equal to one international unit.

MCGUIRE: Okay.

HOLICK: So, 400 units is ten micrograms.

MCGUIRE: Got it. Okay. Wow, we've discussed effects of vitamin D, sources in intake, and lab factors related to vitamin D. What are other health benefits related to vitamin D, Dr. Holick?

HOLICK: Well, just to give you kind of a rundown, as we talked about preeclampsia, premature births, asthma, wheezing disorders, dental caries in infants, decreased risk for autoimmune disorders, but also decreased risk for cardiovascular disease, including heart attack and stroke. Also, there's good evidence reduces risk for depression and neurocognitive dysfunction, including Alzheimer's disease. And also, good evidence that it helps to reduce risk of infection.

MCGUIRE: Wow. That's amazing! Okay. And what about its relationship to COVID? Is there any information about vitamin D and COVID?

HOLICK: So we did a study back in 2020 as soon as this pandemic was initiated and working with a reference laboratory, and we collected 191,000 blood samples of COVID positive patients and demonstrated that if you are vitamin D sufficient, you had a 54% reduced risk of acquiring this infection.

MCGUIRE: Amazing.

HOLICK: Right? And, then we went on to do another study in Iran and then also in our own hospital and showed if you're vitamin D sufficient when you walk into the hospital ... reduces risk of having complications from COVID and also reduces risk of morbidity and mortality by more than 54%. Many other studies have, have shown very similar observations. So, we think that improvement in vitamin D status is very important in this era of the COVID pandemic.

MCGUIRE: I've heard another physician say something about if you're going to have to fight COVID, why fight COVID with a low vitamin D level? So that's, that is interesting. That's exactly what I expected you to say. So, make sure you have a normal level before you face the infection. Correct? Be strong before you get sick. What do you think about that line or thought?

HOLICK: Well, I mean, we didn't talk very much about bone health, but it turns out that vitamin D deficiency not only can precipitate and exacerbate osteoporosis, which are basically holes in your bones, which does not cause bone pain, but it can also cause another disorder known as osteomalacia, which causes aches and pains in your bones and muscles. And, even physicians have come to me thanking me for my New England Journal review that they read, realizing in the wintertime when they were feeling fatigued, depressed, they had aches and pains in their bones and muscles.

They just thought that they were being overworked. Right? And, it was just the weather. No, they were vitamin D deficient. And they had osteomalacia, which causes aches and pains in your bones and muscles. And so, improvement in your vitamin D status can definitely have additional health benefits.

MCGUIRE: So, there's really no downside unless it gets too high.

HOLICK: Exactly. And, that's usually the conclusion of my presentations. There is no downside to increasing your vitamin D intake, right?, unless you have like we talked about a hypersensitivity to vitamin D, then you need to talk to your doctor. But otherwise, if you take the amount recommended by the Endocrine Society Practice guidelines, right?, infants 400 to 1000 units, children 600 to 1000 units, teenagers and adults 1500 to 2000 units a day. And, if you're obese, 2 to 3 times more. I personally take 6000 units of vitamin D a day, and my blood level is 72 nanograms per mL.

MCGUIRE: Wow. All right. I hope when everyone's paying attention to that, who's listening? Yes. This is this is really, really important stuff. This has really been a fascinating, fascinating interview with you, Dr. Holick. I'm amazed, and what a journey from being assigned vitamin D to literally changed your life and ultimately the lives of a lot of people. So it's, it's really fascinating.

Wow. So, we've discussed the effects of vitamin D, sources and intake, and lab factors related to vitamin D. Before we wrap up, let's talk about teamwork and healthcare around vitamin D. We know there's been an advantageous trend at the intersection of healthcare, education, and healthcare treatment. That is the move toward interprofessional education, where we increase communication and teamwork between healthcare team members.

There is the concept of discussing information within our disciplines, like physicians conferring with other physicians and nurses discussing information with other nurses, etc. But interprofessional approaches would pertain to multiple members of a healthcare team, even the patient, communicating with each other, learning from each other, and trying to provide team care. So providers, nurses, therapists, registered dietitian nutritionists, etc. are all talking to provide quality care. That being said, what do you see as barriers to patients who are unaware of the importance of vitamin D or how to make sure they don't forget about this component of health?

HOLICK: Yeah, it's extremely important, and I give a lot of presentations not only to doctors, but also healthcare professionals, including nurses. ... um and um to reiterate the importance of vitamin D for your health. And, when I point out to them is that I'm not really just teaching them about vitamin D for their patients, but I'm teaching them for their own health benefit and the families' health benefit. And, that then kind of provides the opportunity for them to now think, well, if I can benefit, you know, my patients can benefit. And, then I think that it's much more a topic that they are now thinking about when doing patient care, because I've already convinced them that improving your vitamin D intake and status will improve your health and the health of your family members.

MCGUIRE: How do you think healthcare teams, whether a hospital provider's office, clinical public health offering, etc., can communicate with each other to better address or address at all lower deficient vitamin D levels in patients or clients?

HOLICK: Yeah. Um so, what you want to do is, you know, when they're having an intake, you know, they may be seeing a PA, right?, or a nurse practitioner or a nurse. Right? So, they probably should ask, you know, what is your dietary intake or are you taking a vitamin D supplement? Because, like I said, you can't get enough from your diet. We already know that. And so, if you're not taking a supplement, you're likely to be vitamin D deficient or insufficient. And, then the recommendation is, if you are concerned, is to measure your vitamin D status, which is 25-hydroxyvitamin D.

MCGUIRE: Status versus level.

HOLICK: Correct, because it's very confusing, because people think you're measuring your vitamin D level. You're not.

MCGUIRE: Right?

HOLICK: Even though vitamin D is in your bloodstream, even though vitamin D is made in your skin, you're not measuring it. You're measuring what is made by your liver, which is the major circulating form, 25-hydroxyvitamin D.

MCGUIRE: Got it. Okay. Can you give us a case scenario that illustrates how a healthcare team could have minimal communication and miss the signs and symptoms of low D levels in a patient?

HOLICK: I mean, that's pretty straightforward, because so as we had talked about. Cardiologists seeing a patient because of angina, the last thing they're probably thinking about is their vitamin D status.

MCGUIRE: Sure.

HOLICK: But it would be, you know, the, the intake person, the PA or nurse that if realizing that vitamin D is so important, reduces risk of cardiovascular disease and stroke, that would make the recommendation that, you know, maybe the vitamin D status should be evaluated or at least recommend that, you know, you may want to think about taking the supplement and following the guidelines of the Endocrine Society practice guidelines.

MCGUIRE: Fantastic. Well, you have had a fascinating career, my friend. Uh to be assigned vitamin D and how it affected your own life and the lives of so many. It's just, it's a fascinating journey. And, I could honestly, could talk all day about this with you. I'm amazed by it!

SOUNDBITE OF MUSIC

MCGUIRE: It seems vitamin D has become more popular as far as getting attention in various research, media, journals, and magazines, etc. It was great to be able to tackle this topic today and learn from a notable physician in this area. Another sincere thank you to you, Dr. Holick, for joining us.

HOLICK: It's been my pleasure. I hope that you have a delightful day.

MCGUIRE: Thank you, thank you again for listening. This is Leana McGuire for Elite Learning by Colibri Healthcare.

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