

Cellular Aging and The Care of Older Patients

Insights from the GSA Publication, [What's Hot: Cellular Nutrition and Its Influence on Age-Associated Cellular Decline](#)

GSA Momentum Discussion, a podcast from The Gerontological Society of America

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Welcome to the Gerontological Society of America Momentum Discussion podcast series, where researchers, educators, and practitioners stimulate dialogue on trends with great momentum to advance gerontology. The content of the podcast today was developed by GSA, and this program has received a grant from Nestle Health Sciences.

Dr. Fielding:

Welcome to the podcast. I'm Roger Fielding, and I'm the Associate Director of the Jean Mayer, USDA Human Nutrition Research Center on Aging. And I'm also the Lead Scientist of the Nutrition, Exercise Physiology, and Sarcopenia Team here at the Human Nutrition Research Center on Aging. I'm excited to be your host for a series of podcasts that are based on the GSA What's Hot publication, Cellular Nutrition and Its Influence on Age-Associated Cellular Decline.

Researchers have identified several molecular pathways at a cellular level, including defects in mitochondrial function, which appear to influence both aging and age-related chronic disease. These cellular changes associated with aging are cumulatively referred to as age-associated cellular decline or AACD. Identifying AACD risk factors and intervening with cellular nutrients early in the aging process, before major mobility disabilities and disease-driven limitations emerge, could help improve overall healthy aging.

Today we will explore how to apply what is currently known about AACD to the care of patients and older adults in clinical practice. To discuss this with me, I'm so pleased to introduce Dr. Nathan LeBrasseur, who is a Professor and Co-chair of Research in the Department of Physical Medicine and Rehabilitation. Nathan is also the Scientific Director of the Office of Translation to Practice, the Co-Director of the Paul F. Glenn Center for Biology of Aging Research, and plays a leadership role in the Robert and Arlene Kogod Center on Aging at the Mayo Clinic in Rochester, Minnesota. Welcome Nathan.

Dr. LeBrasseur:

Thanks, Roger. Great to be here and take part in this exciting discussion.

Dr. Fielding:

We're so glad you could join us.

To start, what types of questions do you hear from older folks that relate to age-associated cellular decline and people's desire to preserve their health and well-being as they age?

Dr. LeBrasseur:

That's a great question. I think there are a couple of elements to unpack there. One is older adults are often interested in what can impact their trajectory of aging. Most people realize that some 70-year-olds and 80-year-olds are incredibly active and physically fit, very robust, resilient to age-related diseases and geriatric syndromes. They seem to have lower susceptibility to challenges such as COVID while their peers may have multimorbidity and several conditions associated with advanced age. And the question is what distinguishes these individuals?

Dr. LeBrasseur:

There's a large public interest now in the distinction between chronological age—what we can learn from our driver's license or our birth certificate—and our biological age, which is a much more complicated question and highly related to the topic of interest, which is age-associated cellular decline.

Dr. Fielding:

So, where does age-associated cellular decline fit in your conversations with people about healthy aging? I think you've started to talk about this, but what is it that you tell them about this process?

Dr. LeBrasseur:

I think there is a tendency for us to think about aging only in the context of individuals over the age of 65, 70, or 80. But the truth is that age-associated decline probably starts before conception, or if not, at the time of conception. So, we think of aging as a lifelong process, and throughout the life course, several things can determine our health and function.

When we think about aging, we specifically think about different forms of damage that our cells accumulate over time and our ability to repair that damage. So, when we think about age-related diseases, we now link them to the accumulation of this damage over time. And it's a story about what determines our trajectory. You know, is it just genes? Is it the environment? Is it behaviors? Is it nutritional activities? Is it sleep habits? The answer is really "yes" to all of those things, but we're quite interested in getting a better understanding of what influences the rate of damage accumulation.

Dr. Fielding:

Yeah. I think we'll get to some of those interventions in a minute, but I want to ask a very specific question. What I want to know about this is, when I go to see my doctor, is there a test I can ask the doctor to do?

Dr. LeBrasseur:

Well, that's a great question. You know, at a cellular level we're getting there, and we can kind of dig into that a lot more. But as you know, simple parameters of physical health and function, cardiac health and function, metabolic health and function, and immune health and function are highly reflective, I think, of our biological age.

On the physical side, your team has profound expertise in measuring things like strength and physical function, mobility, and gait speed. On the metabolic side, it might be a glucose tolerance test or insulin sensitivity. On the cardiac side, we typically all get EKGs when we go into the clinic, but more sophisticated measures may tell us more about our cardiac health and function and pulmonary function. So, there are several different tests and measures on the physiological side that can show us the manifestations of this biological age.

Dr. Fielding:

That's excellent. So, in one of the previous podcasts, we talked a little bit about diet and sort of things like extremes of diet, like caloric restriction. Is it true that just like your mother told you, if you eat more fruits and vegetables or adopt healthy eating patterns - is that going to improve some of these markers of aging?

Dr. LeBrasseur:

I think there are a couple of elements there. We know for sure that nutrient excess is pouring fuel on the aging fire if you will. Nutrient excess and obesity accelerate the biology of aging without question. We also know that healthy nutrition patterns have a profound preventative effect on the accumulation of age-related damage. And we're learning a lot more about how to not only leverage that knowledge for the prevention of aging-related diseases and geriatric syndromes, but how can we apply that in later life to delay that progression or even reverse it.

Dr. Fielding

That's good stuff. Are there any specific nutrients that I should start thinking about taking, or we're not there yet?

Dr. LeBrasseur:

I don't think we're there yet. I do think that we're learning a lot about different parameters of what is in the diet, and the timing of the diet. There's a lot of interest now in different dietary interventions ranging from the time of day that we eat and how long we should fast after that. And I do think we're gaining insights into how those nutritional patterns may optimize the regeneration and rejuvenation of damaged tissues and organs and cells. You know, there are benefits. I guess this is where I'm not sure if I could say anything about how to answer those about specific nutrients.

Dr. Fielding:

That's okay. You can say we're not there yet. So, I think this is remarkably important when you think about the idea that maybe 60-plus percent of older adults are either overweight or obese. This point you have mentioned about over-nutrition. I think, from a public health standpoint, it's not a small problem.

Dr. LeBrasseur:

That's right. We often use this phrase of what concerns us, clinically, as a healthcare institution is that we are witnessing population aging collide with the epidemic of obesity.

Dr. Fielding:

And it is scary to think about the number of overweight and obese youth, what their trajectory of aging is going to be, and how that is going to impact both healthcare and the population. So, more to learn about that. So, something near and dear to both of our hearts, what about exercise in all this? Good, bad?

Dr. LeBrasseur:

Yeah. We're really in this era now that we've developed a reasonable understanding of this age-associated cellular decline. Now that we've been able to somewhat define it in its different features, the big question and the question that has the potential to transform human health is: Can we intervene and use the interventions that are available to us today?

Dr. LeBrasseur:

I may not be able to prescribe a specific medication or nutrient, but we know that exercise has profound effects on this underlying biology. And it's quite remarkable. Exercise can protect against damage to our DNA, or the instruction manuals in our cells.

Dr. LeBrasseur:

It can promote the turnover of old and damaged proteins by activating garbage disposal within our cells, something that we refer to as autophagy. It can improve mitochondrial health and function, which is quite remarkable and critical to the health and function of cells. The beauty of this is that this is not just effective in our youth or middle age, but it's even very effective in later life. And there's more and more data to support that concept.

Dr. Fielding:

That's great stuff. And I think it's something that we want to learn more about. But, in your work, haven't you begun to understand how exercise influences some of these biological signatures of aging?

Dr. LeBrasseur:

Yes, we have, and that's been encouraging. We've been able to look, really under the hood within a cell, and see how exercise can both promote repair and prevent damage, and that's encouraging. And the question is, who do we choose then in later life to administer these interventions? How do we determine the responsiveness of individuals to these interventions?

In preclinical models, such as mice rats, or other organisms, it's easy to collect different tissues and examine them at a molecular level. But what we're excited about now for human application is the development of biomarkers. These are circulating factors that are easily accessible and reflect the extent to which you've experienced this age-associated cellular decline.

So, features such as senescence or mitochondrial dysfunction or impaired protein turnover - our ability to simply take a blood draw, a urine sample, or saliva, and examine the extent to which your system has undergone aging is very informative. And, we're excited to see how this may help guide interventions such as nutrient interventions or exercise to improve the health and function of older adults.

Dr. Fielding:

Along with that, you know, we all see these advertisements for things like spas that are offering NAD infusions and other things. And then also a plethora of over-the-counter aging tests that companies are promoting. But, what do you tell older people about those sorts of things if they ask you about them specifically?

Dr. LeBrasseur:

I think on the positive side, we have to recognize that we now have the world's attention. We have the attention of not just academics and medical centers, but certainly the commercial private sector. I think is a good thing because they bring resources to the game and, I think, will help us move the science forward.

Having said that, we are at such an early stage in this that we need to be patient and humble and do clinical trials in a methodical and informative way that tells us how effective some of these interventions may be. And things like NAD supplements rapalogs or metformin.

Dr. LeBrasseur:

There's a lot of promise out there, but I think we need to be cautious to make sure that we do not harm. I think the other part of this is that the answer to some of these questions about "Are some of these supplements effective?" is not 20 years away, but it's more in the more immediate future that I think we will have a good grasp on if they are beneficial for the health and function of older adults.

Dr. Fielding:

The science is evolving, but it's not that long ago that you think people just sort of thought that it was normal for people, as they got older, to have a decline in their cognitive function. That was just thought of as a normally accepted consequence of aging. I think now we acknowledge that that is not always the case and this can be a serious condition or disease. And I think the same is true with people slowing down as they age. We acknowledge that it's something that potentially can be intervenable. So, I think this point about really trying to increase awareness and understanding what the evidence base is for therapies to treat these conditions of aging is going to be important.

Dr. LeBrasseur:

Yes. And I think that we shouldn't trivialize that. You know, we've gone from thinking about aging as being this rigid construct that is not malleable to this new radical idea that we can intervene in the fundamental biology of aging. And, for a long time, people have been cautious to endorse that approach because they feel it's immoral or that there's some type of inappropriateness to intervening there. But, when you step back and recognize that aging is by far the greatest risk factor for the overwhelming majority of chronic diseases ranging from cancer to Alzheimer's disease, to cardiovascular disease, no one pauses to say that we should target those conditions, right? So, I'm excited about this change in the premise that we can perhaps do something about the underlying biology.

Dr. Fielding:

In the United States, we spend millions of dollars on drugs that extend the lifespan of some diseases by months. You know, when we have this opportunity to think about not only extending lifespan but extending health span and quality of life by years, I think we do a society a great service when we think about those things.

Dr. LeBrasseur:

Yes. Without question, we're talking about the health and well-being of, and function of, individuals and our loved ones. But then also the profound impact on society and the cost of care. The ability to compress morbidity into the very final months or days of life would be remarkable.

Dr. Fielding:

Well, this has been great. Thank you, Nathan, for a terrific discussion today. This podcast is one of three on the topic of cellular nutrition and its influence on age-associated cellular decline. The other two podcasts focus on mitochondria and aging with Anthony Molina and nutrition and cellular aging with Dr. Sai Das. For more in-depth information on the topic, please refer to the GSA What's Hot publication, Cellular Nutrition and Its Influence on Age-Associated Cellular Decline. Thank you and have a great day.