

Heart TALK

Heart-healthy and Stroke-free Living with Dr. Amy L. Doneen, DNP, ARNP

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Thoughts
from
Dr. Amy

Navigating the Complexity of High-Density Lipoprotein (HDL)



A correlation between high-density lipoprotein (HDL) cholesterol levels and the risk of dementia has become a focal point for research and a topic of casual conversation due to widespread interest and recent publications in mainstream media. A study titled: *Association of plasma high-density lipoprotein cholesterol level with risk of incident dementia: a cohort study of healthy older adults* has garnered public attention. This prompts a deeper exploration into the multifaceted nature of HDL and its intricate and complicated relationship with long-term cognitive health.

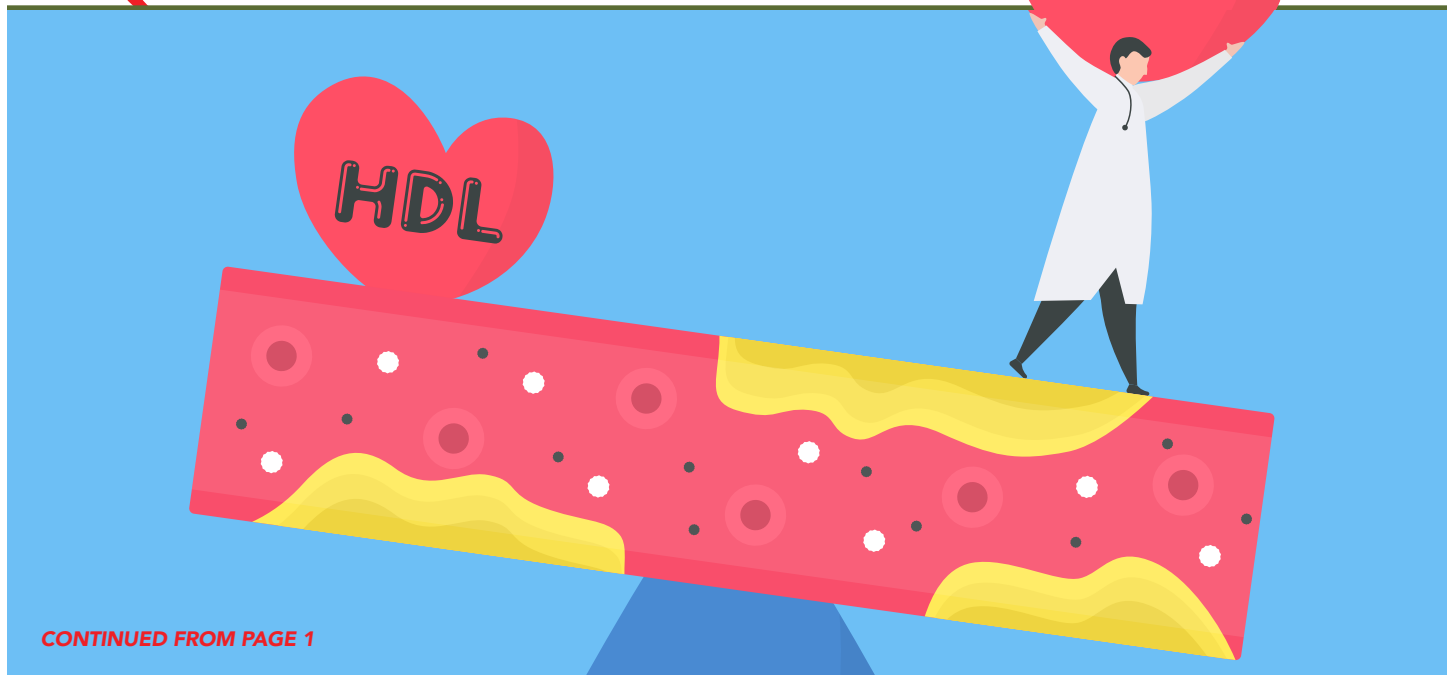
While HDL is often heralded as the “good cholesterol” and LDL the “bad,” we are the first to recognize that this over-simplification misrepresents the nuanced and complex nature of what we know about HDL.

REVISITING THE ASPREE TRIAL

The ASPREE (Aspirin in Reducing Events in the Elderly) trial focused primarily on healthy older adults with no known cardiovascular disease, dementia, or other significant comorbidities. The researchers observed an association with baseline HDL levels above 80mg/dL and a 27% increased risk of dementia in participants over age 75 years of age followed for 6.3 years. Similarly, those with low levels of HDL (<40) also show an associated risk of dementia. This effect was significant after adjusting for age, sex, daily exercise, education, alcohol consumption, weight change over time, non-HDL-C and APOE genotype.

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It is vital to note that findings of this study are not universally applicable, as the dynamics of HDL and its implications differ across diverse populations (ie: people with plaque in their arteries may have high HDL cholesterol as the result of excellent treatment). It is essential to consider additional evidence and viewpoints for a more comprehensive perspective.

SUPPORTING STUDIES: COPENHAGEN INSIGHTS

The Copenhagen General Population Study and the Copenhagen City Heart Study, as elucidated by Kjeldsen et al. (2022), lends support to the notion of an association between very high baseline levels of plasma HDL cholesterol and dementia risk. However, a genetic randomization showed that genetically elevated HDL is **not** associated with Alzheimer's disease. The takeaway from this data is that HDL cholesterol can and should be considered as one of many biomarkers to further personalize an individual's risk for all forms of dementia.

CONTRADICTIONARY NARRATIVES: EXAMINING THE DISSENT

Studies by Sáiz-Vazquez et al. (2020), Zhong et al. (2020), Wan et al. (2019), Button et al. (2019), and W. et al. (2015) introduce a layer of complexity by challenging the presumed straightforward relationship between HDL cholesterol and dementia risk. These meta-analyses and retrospective cohort studies pres-

ent alternative viewpoints, prompting a reassessment of our understanding and emphasizing the need for cautious interpretation of results.

In these studies, results showed no difference in HDL-C serum levels between patients with Alzheimer's Disease and those without; additionally, Button et al. suggests high HDL-C levels are associated with reduced dementia risk and is instead protective against cerebrovascular dysfunction.

Iwagami et al. (2021) examined the relationship between HDL cholesterol and risk of dementia over two decades, utilizing a retrospective cohort study. The study aimed to examine the association between baseline total cholesterol, LDL, HDL and triglycerides and incident dementia diagnosis. Results showed no consistent associations for HDL and triglycerides in relationship to incident dementia.

THE COMPLEXITY OF HDL: UNANSWERED QUESTIONS

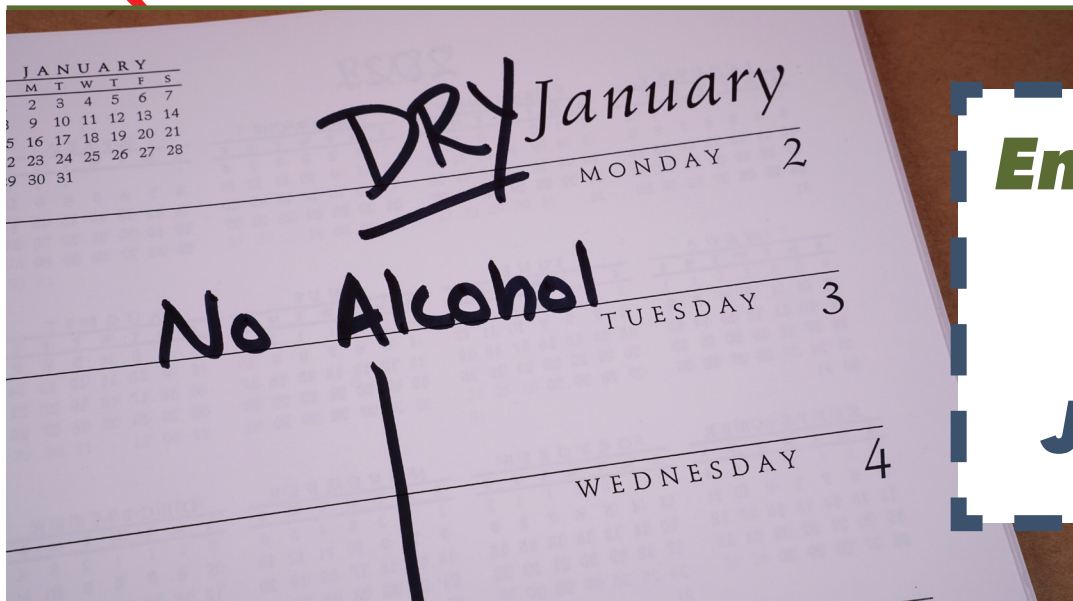
Biomarkers utilized within the Bale-Doneen Method such as haptoglobin lend complexity to this issue, as we know that haptoglobin 2-2 individuals often have elevated HDL due to oxidation of free hemoglobin. In this case, HDL elevation is a byproduct of oxidative stress, which we recognize as the root cause of disease. We also know that the studies linking elevated HDL to dementia risk did not explore the effects of sleep apnea or dental pathogens, which have both demonstrated a strong relationship with dementia.

BOTTOM LINE: High-density lipoproteins are complex, and we are far from having the clinical tools to understand their functionality. HDL is known to be protective in many ways, but we also know that HDL particles can lose their protective functions and even gain adverse functions in the presence of chronic disease or infections, such as autoimmune conditions, diabetes and chronic kidney disease. When HDL dysfunction is present, HDL has the potential to do more harm than good.

A NUANCED CONCLUSION

The recent publication linking WZHDH levels to an increased risk for dementia serves as a catalyst for a more nuanced examination of this complicated relationship. HDL has emerged as an extremely complex player with multifaceted functions, demanding a more comprehensive understanding of its implications for cognitive health.

The existence of contradictory evidence calls for continued work to understand HDL's many complexities and functions. The ongoing evolution of research in this field will certainly shed more light on this nuanced issue, hopefully guiding us toward a more holistic comprehension of HDL's role in both health and disease. For now, a conversation with your provider about your HDL level in the context of your overall health, duration of treatment, genetics and potential for risk is an excellent place to start.



Embracing Dry or Damp January

As we ring in the New Year, the traditional talk of “Dry January” starts popping up in the media and casual conversation. The concept of abstaining from alcohol for a period, often after a season of over-indulgence, has become a popular resolution over the past few years. Beyond its popularity, the decision to mindfully abstain holds scientifically backed benefits that extend beyond the month of sobriety. This month, we thought it timely to discuss the risks and benefits of alcohol consumption, and to encourage mindfulness around whatever amount of alcohol you choose to consume.

If you are reading this, you likely have an interest in heart health and probably know something about your own genetic make-up. The relationship between alcohol consumption and heart health has long been debated. Over the years, studies have demonstrated moderate intake (one drink daily for women, two for men) may have potential cardiovascular benefits, including lowered inflammation and raising of HDL. However, this association can be a double-edged sword, as the line between moderate and excessive alcohol consumption is quite thin. The latter poses significant health risks, including an increased risk for hypertension, atherosclerosis, diabetes, fatty liver disease, stroke and brain disease.

While the conversation surrounding alcohol intake and heart health remains controversial, the detrimental effects of alcohol on the brain are well understood and widely acknowledged. There is no reputable research supporting the intake

of alcohol for brain health or cognitive function, but this detrimental effect may be more pronounced in some individuals than others.

The Apolipoprotein E (ApoE) gene plays a vital role in lipid metabolism and has different variants, including ApoE2, ApoE3, and ApoE4. The ApoE4 allele is associated with an increased risk of developing Alzheimer’s Disease. At the same time, studies suggest that individuals carrying at least one copy of the ApoE4 gene may be more susceptible to the harmful effects of alcohol on cognitive function and brain health.

Individuals with the ApoE4 gene variant who consume alcohol, even the “heart healthy” moderate amount, seem to experience amplified negative effects on brain structure and function as compared to those without this genotype. Once again, this highlights the importance of a personalized approach to medicine and to our health-related lifestyle choices.

Beyond the long-term health benefits and risks associated with alcohol intake, whether moderate or excessive, partaking in a “Dry January” ritual provides individuals the opportunity to reassess their relationship with alcohol. This is a time to reflect on the impact of alcohol on your general well-being and to experience the possible immediate benefits of abstaining, such as improved sleep, mental clarity, improvement in triglycerides and other metabolic markers.

The debate regarding the effects of alcohol specifically on heart health will continue to rage on, but the well-documented adverse impact on brain health

is widely acknowledged. While the ApoE genotype and personalization of dietary recommendations adds another layer of complexity, taking a beat to step back from alcohol consumption and examine its impact on our everyday lives can be a helpful and worthwhile undertaking.

“Dry January” serves as an annual reminder for the potential benefits of reducing or eliminating alcohol intake. Ultimately, embracing a healthier lifestyle, making informed choices about alcohol intake and considering individual genetic factors are crucial steps toward maintaining overall optimal health. Must we all abstain from alcohol completely? Probably not. Should we all take the opportunity to assess our relationship to alcohol and the way it affects our bodies and mind? Probably so.

This month, we encourage you to consider what it might look like to take a step back from whatever alcohol consumption looks like for you. Take a moment to examine any hold it may have on your life, and make some mindful decisions about how, why and when you choose to partake in alcohol consumption in the future. And if taking a complete break from drinking for a month sounds daunting, too restrictive, or just plain unrealistic, consider what it may look like to abstain for one week each month. This would result in three full months of sobriety annually — but in chunks of time that may be more realistic to your life.

In this newsletter you will find a few ideas for fun “mocktails” to try if you do decide to take a break from alcohol consumption. We hope you find them so be as festive and delicious as we do!



PAJGE-LEDFORD/UNSPLASH

Grapefruit Thyme Sparkler

Makes 1 full mocktail with enough honey thyme syrup for 4

Looking for a non-boring way to spice up your Friday night without the hangover or sugar bomb of traditional cocktails or mocktails? Look no further than this deliciously simple grapefruit and thyme fizz.

INGREDIENTS

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|-------------------|------------------------|
| 1 cup water | ½ cup grapefruit juice |
| ¼ cup honey | ⅓ cup soda water |
| ½ cup fresh thyme | |

DIRECTIONS:

1. In a small saucepan, combine water and honey over medium heat. Stir until well combined and barely simmering.
2. Add the fresh thyme and continue to simmer on low for 8-10 minutes.
3. Remove from heat and allow syrup to cool completely, about 30-60 minutes.
4. Run syrup through a strainer to remove thyme debris
5. Add 1 T honey thyme syrup and ½ cup grapefruit juice to a glass and fill to the brim with ice. Top with bubbly soda water and stir to combine.
6. Enjoy!

Soda Water & Bitters

Serves 1

This no-frills mocktail matches the appearance of a whiskey cocktail such as an Old Fashioned without the sugar or booze. Try different flavors of bitters to switch up the taste profile!

INGREDIENTS

- 4 oz soda water
- 3-4 dashes bitters to taste (Angostura or orange bitters are excellent!)
- 1 wedge of orange or lemon
- Ice for serving

DIRECTIONS:

1. Fill glass with ice then pour soda water to fill glass. Top with bitters and a squeeze of orange or lemon wedge.
2. Serve immediately and enjoy!