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Estrogen and Dementia: Challenging Conventional Wisdom

Analysis by Dr. Joseph Mercola | July 29, 2024

STORY AT-A-GLANCE

- A new study in JAMA Neurology challenges the long-held belief that estrogen protects against dementia in women. The research found that pure estrogen receptor antagonists and aromatase inhibitors were associated with a lower risk of dementia across women's lifespans
- This study contradicts previous research suggesting estrogen's protective effects on the brain, particularly in post-menopausal women
- The findings imply that other substances with anti-estrogenic effects, such as progesterone and certain vitamins, might also protect against dementia
- The medical establishment's response to this study has been mixed, with some attempts to misrepresent or downplay its implications
- Natural anti-estrogenic approaches, including diet, exercise, and progesterone supplementation, may offer potential strategies for reducing dementia risk

For decades, mainstream medicine has promoted the idea that estrogen is protective for the brain, particularly in post-menopausal women. The conventional wisdom has been that the increased risk of dementia in older women is due to the "deficiency" of estrogen that occurs during menopause. However, a groundbreaking new study published in JAMA Neurology challenges this long-held belief, providing compelling evidence that blocking estrogen may lower the risk of dementia.[1]

Research Causing a Paradigm Shift

This recent study is perhaps the most damaging piece of evidence I've encountered in the last five years that contradicts the claim that estrogen protects the brain. The research, published in one of the most prestigious medical journals, found that using pure estrogen receptor antagonists or aromatase inhibitors was associated with a lower risk of developing dementia across the entire expected female lifespan.

What makes this study particularly significant is its use of "pure" anti-estrogen drugs. Previous studies showing protective effects against dementia often used selective estrogen receptor modulators (SERMs) like clomiphene, tamoxifen, or raloxifene. These drugs have anti-estrogenic effects in some tissues but are potent estrogens in others.

This dual nature allowed the medical establishment to explain away the protective effects as actually confirming the "benefit" of estrogen for the brain, since SERMs can be estrogenic in brain tissue.

However, the current study leaves no room for such interpretations. It examined the effects of pure estrogen receptor antagonists like Faslodex (fulvestrant) and its nonsteroidal analog Elacestrant, as well as aromatase inhibitors like letrozole. These drugs are highly selective blockers of estrogen receptors with no other known major effects.

The fact that aromatase inhibitors, which reduce the body's production of estrogen, also showed protective effects against dementia further solidifies the case against estrogen as a protective factor for brain health.

Rethinking Estrogen's Role

These findings suggest that other substances with anti-estrogenic effects might also have protective effects against dementia. This includes:

1. Progesterone
2. Fat-soluble vitamins (A, D, E, K)

3. Aspirin
4. DHT (dihydrotestosterone)
5. Flavones and flavanones (apigenin, naringenin, chrysin, quercetin, luteolin)

The study's results were particularly pronounced in patients under 75 years of age, indicating that anti-estrogenic interventions might be most effective when started earlier in life.

The Medical Establishment's Response

It will be interesting to see how the medical establishment responds to this study. Given its publication in JAMA, a highly respected journal, it will be difficult to dismiss outright. However, we're already seeing some concerning trends in how the information is being presented and interpreted.

Nefarious Tactics in Reporting

1. **Progesterone misrepresentation —** Some popular press articles reporting on this study have attempted to implicate progesterone as a co-culprit with estrogen. They mention that the anti-estrogenic drugs in the study are used to treat breast cancers caused by "estrogen and progesterone."

   This misrepresentation could lead the public to believe that progesterone increases the risk of dementia or cancer, when in fact, the opposite is true. The drugs mentioned in the study target exclusively estrogen and estrogen-positive cancers, not progesterone-positive cancers. Moreover, progesterone itself acts as both an estrogen receptor antagonist and an aromatase inhibitor, potentially offering protection against dementia based on the study's findings.

2. **Misleading terminology —** The study itself uses the term "hormone modulating therapy" (HMT) to describe the anti-estrogenic treatments. This vague terminology avoids stating that the therapy is purely estrogen-blocking in nature, unlike SERM

drugs which have mixed effects. It also fails to clarify that the therapy targets solely estrogen, not progesterone.

These tactics appear to be attempts to twist the science to serve pharmaceutical interests and avoid stating the obvious conclusion based on the study's findings: that estrogen may be a cause of dementia and Alzheimer's, while anti-estrogenic therapy (including natural options like progesterone) may be protective and possibly even therapeutic for existing dementias.

A Critical Examination of the Estrogen Hypothesis

For years, the medical community has operated under the assumption that estrogen is beneficial for brain health, particularly in post-menopausal women. This belief has led to widespread use of hormone replacement therapy (HRT) and other estrogen-boosting interventions. However, this new study forces us to critically examine this hypothesis.

The idea that estrogen deficiency causes cognitive decline in older women has been based largely on observational studies and the timing of when women typically experience increased rates of dementia (post-menopause). However, correlation does not imply causation, and there are many other factors that change as women age that could contribute to cognitive decline.

Moreover, previous clinical trials of hormone replacement therapy have yielded mixed results regarding cognitive function and dementia risk. The Women's Health Initiative Memory Study,[2] for instance, found that combined estrogen-progestin therapy actually increased the risk of dementia in postmenopausal women.

The current study provides strong evidence that blocking estrogen or reducing its production may be protective against dementia. This suggests that estrogen might actually be harmful to brain health, rather than protective. If this is the case, it would explain why rates of dementia increase after menopause — not because of estrogen deficiency, but because of the cumulative effects of lifelong estrogen exposure.

Natural Anti-Estrogenic Approaches

If blocking estrogen indeed proves protective against dementia, it opens up a range of potential preventive strategies beyond pharmaceutical interventions. Many natural compounds and lifestyle factors can have anti-estrogenic effects:

1. **Cruciferous vegetables —** Compounds in broccoli, cauliflower, and Brussels sprouts can help metabolize estrogen.
2. **Green tea —** Contains compounds that may inhibit aromatase, the enzyme that produces estrogen.
3. **Exercise —** Regular physical activity can help balance hormones and may have anti-estrogenic effects.
4. **Sleep —** Proper sleep hygiene is crucial for hormonal balance, including estrogen regulation.
5. **Stress management —** Chronic stress can disrupt hormone balance. Techniques like meditation, yoga, or deep breathing can help.
6. **Vitamin D —** This fat-soluble vitamin has been shown to have anti-estrogenic effects.
7. **Progesterone —** As mentioned earlier, natural progesterone can act as an estrogen antagonist.

The Role of Progesterone

It's worth delving deeper into the role of progesterone, given its potential importance in light of this study's findings. Progesterone is often overlooked in discussions about hormones and brain health, with most of the focus being on estrogen. However, progesterone has several properties that make it potentially neuroprotective:

1. **Estrogen receptor antagonist —** Progesterone can block the effects of estrogen in certain tissues.
2. **Aromatase inhibitor —** It can reduce the production of estrogen in the body.
3. **Neuroprotective effects —** Independent of its effects on estrogen, progesterone has been shown to have direct neuroprotective properties in animal studies.
4. **Anti-inflammatory —** Progesterone can reduce inflammation in the brain, which is thought to play a role in the development of dementia.

Given these properties, and the findings of the current study, it's possible that progesterone supplementation could be a natural way to potentially reduce dementia risk. However, more research is needed to confirm this hypothesis.

How to Use Progesterone

Before you consider using progesterone it is important to understand that it is not a magic bullet, and that you get the most benefit by implementing a Bioenergetic diet approach that allows you to effectively burn glucose as your primary fuel without backing up electrons in your mitochondria that reduces your energy production. My new book, "Cellular Health: The Unified Theory of All Disease for Ultimate Longevity and Joy" comes out very soon and covers this process in great detail.

Once you have dialed in your diet, an effective strategy that can help counteract estrogen excess is to take transmucosal progesterone (i.e., applied to your gums, not oral or transdermal), which is a natural estrogen antagonist. Progesterone is one of only four hormones I believe many adults can benefit from. (The other three are thyroid hormone T3, DHEA and pregnenolone.)

I do not recommend transdermal progesterone, as your skin expresses high levels of 5-alpha reductase enzyme, which causes a significant portion of the progesterone you're taking to be irreversibly converted primarily into allopregnanolone and cannot be converted back into progesterone.

Ideal Way to Administer Progesterone

Please note that when progesterone is used transmucosally on your gums as I advise, the FDA believes that somehow converts it into a drug and prohibits any company from advising that on its label. This is why companies like Health Natura promote their progesterone products as topical only.

However, please understand that it is perfectly legal for any physician to recommend an off-label indication for a drug to their patient. In this case progesterone is a natural hormone and not a drug and is very safe even in high doses. This is unlike synthetic progesterone called progestins that are used by drug companies, but frequently, and incorrectly, referred.

Dr. Ray Peat has done the seminal work in progesterone and probably was the world's greatest expert on progesterone. He wrote his Ph.D. on estrogen in 1982 and spent most of his professional career documenting the need to counteract the dangers of excess estrogen with low LA diets and transmucosal progesterone supplementation.

He determined that most solvents do not dissolve progesterone well and discovered that vitamin E is the best solvent to optimally provide progesterone in your tissue. Vitamin E also protects you against damage from LA. You just need to be very careful about which vitamin E you use as most supplemental vitamin E on the market is worse than worthless and will cause you harm not benefit.

It is imperative to avoid using any synthetic vitamin E (alpha tocopherol acetate — the acetate indicates that it's synthetic). Natural vitamin E will be labeled "d alpha tocopherol." This is the pure D isomer, which is what your body can use. There are also other vitamin E isomers, and you want the complete spectrum of tocopherols and tocotrienols, specifically the beta, gamma, and delta types, in the effective D isomer.

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You can purchase pharmaceutical grade bioidentical progesterone as Progesterone Powder, Bioidentical Micronized Powder, 10 Grams for about $40 on many online stores like Amazon. That is nearly a year's supply, depending on the dose you choose.

However, you will need to purchase some small stainless steel measuring spoons as you will need a 1/64 tsp which is 25 mg and a 1/32 tsp which is 50 mg. A normal dose is typically 25 to 50 mg and is taken 30 minutes before bed, as it has an anti-cortisol function and will increase GABA levels for a good night's sleep.

Unfortunately, this vendor frequently runs out of product, and if that's the case, then you can use **Simply Progesterone by Health Natura**. It's premixed with vitamin E and MCT oil. Again, while Health Natura states that its product is for "topical use only," I recommend applying it transmucosally, by rubbing it on your gums.

If you are a menstruating woman, you should take the progesterone during the luteal phase or the last half of your cycle, which can be determined by starting 10 days after the first day of your period and stopping the progesterone when your period starts.

If you are a male or non-menstruating woman you can take the progesterone every day for four to six months and then cycle off for one week. The best time of day to take progesterone is 30 minutes before bed as it has an anti-cortisol function and will increase GABA levels for a good night's sleep.

This is what I have personally doing for over a year with very good results. I am a physician so do not have any problems doing this. If you aren't a physician you should consult one before using this therapy, as transmucosal progesterone therapy requires a doctor's prescription.

Implications for Current Medical Practices

If the findings of this study are corroborated by further research, it could have significant implications for current medical practices:

1. **Hormone replacement therapy —** The use of estrogen-based HRT for menopausal symptoms and osteoporosis prevention may need to be reconsidered, especially in women with a family history of dementia.

2. **Breast cancer treatment —** The potential cognitive benefits of anti-estrogen therapies used in breast cancer treatment could be an additional factor to consider when weighing treatment options.

3. **Preventive strategies —** Healthcare providers may need to start considering anti-estrogenic approaches as part of dementia prevention strategies, particularly in high-risk individuals.

4. **Research focus —** This study may shift the focus of dementia research towards investigating the potential harmful effects of estrogen on the brain, rather than its presumed protective effects.

Challenges and Controversies

Despite the strength of this study's findings, it's likely to face significant pushback from certain sectors of the medical community. The estrogen hypothesis has been deeply ingrained in medical thinking for decades, and paradigm shifts often face resistance.

Moreover, there are powerful financial interests at stake. The hormone replacement therapy industry is worth billions of dollars globally. A shift away from estrogen-based therapies could have significant economic implications.

There's also the challenge of reconciling these findings with other known effects of estrogen. For instance, estrogen is known to have protective effects against osteoporosis. How do we balance the potential cognitive risks with other health considerations? These challenges underscore the need for more research in this area.

So, while this study provides compelling evidence, it's just one piece of the puzzle. We need large-scale, long-term studies to fully understand the relationship between estrogen, anti-estrogen therapies, and cognitive health.

A Call for Open-Minded Inquiry

The findings of this study challenge long-held beliefs about estrogen and brain health. They suggest that our understanding of hormones and cognitive function may be more complex than previously thought.

As a medical professional and health advocate, I believe it's crucial that we approach these findings with an open mind. We must be willing to question our assumptions and follow the evidence where it leads, even if it contradicts established beliefs.

For individuals concerned about cognitive health, these findings offer new avenues to explore. While it's too early to make definitive recommendations based on this single study, it may be worth discussing anti-estrogenic strategies with your healthcare provider, especially if you have a family history of dementia.

Remember, hormonal balance is complex and individualized. What works for one person may not work for another. Always consult with a qualified healthcare professional before making significant changes to your health regimen.

As we move forward, it's my hope that this study will stimulate further research into the relationship between hormones and brain health. By continuing to ask questions and challenge our assumptions, we can work towards a better understanding of how to prevent and treat devastating conditions like dementia and Alzheimer's disease.

In the meantime, focusing on overall brain health through a balanced diet, regular exercise, stress management, and cognitive stimulation remains a prudent approach for everyone. As we await further developments in this exciting area of research, these lifestyle factors continue to be our best defense against cognitive decline.