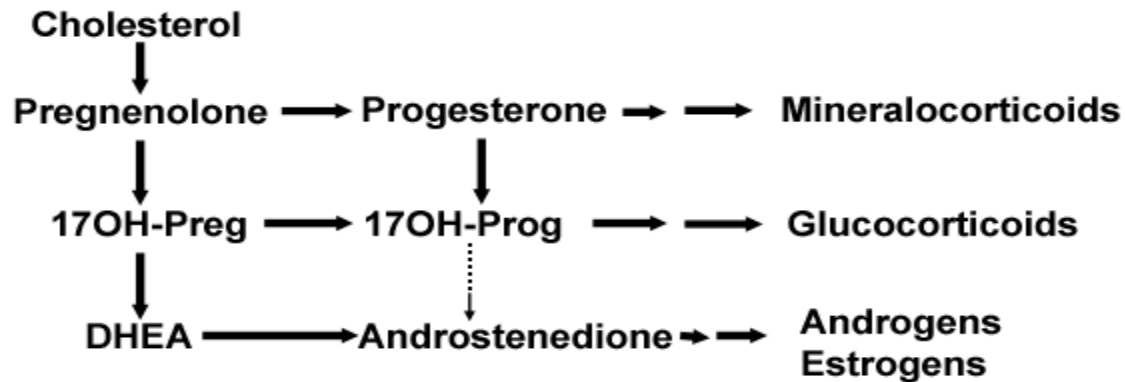


Pregnenolone: "Mother of all steroid hormones"



Background

- Pregnenolone is a precursor to DHEA, progesterone, estrogen, testosterone, and cortisol. As with most hormones, progesterone levels decrease with age. Pregnenolone levels can be decreased 65% at age 75 compared to age 35.^{1,2}
- Pregnenolone was first explored in the 1940's as a therapeutic agent in the treatment of a number of conditions, including rheumatoid arthritis. Once cortisone's effect on arthritis and pain was discovered, pregnenolone research was shelved until the 1990's due to its connection with the popularity of DHEA. Pregnenolone is available over the counter. OTC products may not have the potency described on the label.^{1,2}

Benefits

- *Brain:* increased intelligence, learning ability, alertness, memory, and the feeling of well-being. May help reduce the emotional symptoms of PMS. Study conducted by National Institute of Mental Health found that individuals with depression had a lower-than-normal level of pregnenolone in the fluid that bathes the brain. Another study showed that schizophrenics have decreased pregnenolone concentrations.
- *Adrenal:* anti-stress hormone.
- *Immunity:* help with pain and fatigue in rheumatoid arthritis
- Enhances the benefits of DHEA among patients who are unable to take the needed level of DHEA to be effective because of side effects.
- *Nicotine dependence:* A study by Duke University showed that pregnenolone levels were positively correlated with cotinine concentration, a metabolite of nicotine, leading to a potential new treatment for smoking cessation.

Functions

- Regulates the balance between excitation and inhibition in the nervous system.
- Increases resistance to stress
- Improves energy both physically and mentally
- Enhances nerve transmission and memory
- Reduces pain and inflammation
- Blocks the production of acid-forming compounds

RESEARCH

Mechanism of Action

- Classified as an excitatory neurosteroid that positively modulates N-methyl-D-aspartate (NMDA) receptors.³
- Negatively modulates GABA_A receptors.⁴

- Acts presynaptically to enhance glutamate neurotransmission.^{5,6}
- Pregnenolone sulfate acts through a Gi/o-protein coupled sigma-1 like receptor to enhance short-term synaptic facilitation onto adult rat hippocampal CA1 neurons.^{7,8}

Memory Enhancer

- Various animal studies have demonstrated pregnenolone's effectiveness in improving learning and memory.
 - Low levels of pregnenolone in rat hippocampus are associated with cognitive performance deficits that can be improved with intrahippocampal injections of pregnenolone sulfate. Since there was no correlation found between levels of pregnenolone and changes in other brain areas such as the cortex or amygdala, it is suggested that the hippocampus is primarily where pregnenolone plays its role in memory enhancement.⁹
 - A study performed at the Universite de Lille in France infused pregnenolone sulfate into rat brains. The study concluded that not only did pregnenolone improve recognition memory of a familiar environment, but also enhanced acetylcholine release by more than 50%.¹⁰
 - Another French study found that intracerebral infusions of pregnenolone reversed memory deficits but also found that it dramatically increased neurogenesis (the creation of new brain cells).¹¹
 - Attenuates amyloid peptide induced amnesia in mice.⁸
 - Significant negative correlation between beta-amyloid peptides and pregnenolone sulfate in the brains of patients with Alzheimer's Disease.¹²

Fatigue and Endurance

- Pregnenolone concentrations are much higher in the brain than in blood plasma, therefore it is not surprising that it has a number of mental benefits.¹³
- Several studies have demonstrated that oral administration of pregnenolone reduces fatigue while increasing endurance.¹⁴
 - Five college students trained at a constant pace on a machine that produced exhaustion. At different times, they were given oral pregnenolone, and oral adrenal cortical hormone, or progesterone. Only the pregnenolone group had a significant influence on their scores during a three-hour run.
 - A study of aviators found that pregnenolone improved their functioning and perception of their work. Fourteen subjects took 50mg of pregnenolone daily and performed tests with an automatic scoring device that operated like the joystick for a video game. Researchers concluded that the improvements the aviators experienced during the two weeks of administration had a cumulative effect that continued for several days afterward.
 - Pregnenolone 25-75mg was given daily to 8 leather cutters, 12 lathe operators, and 77 optical workers. There was little benefit compared to placebo when the workers were not "under pressure," but productivity rose when the level of work-related stress was higher. Subjects revealed that they tired less and were better able to cope with the demands of their jobs.
- Larger, more controlled studies are necessary to conclude pregnenolone's overall effect on fatigue and endurance.

Depression

- Patients with generalized social phobia or generalized anxiety disorder have low plasma pregnenolone sulfate levels.^{15,16}
- Women being treated for anxiety-depressive disorder with fluoxetine have elevated pregnenolone sulfate levels.¹⁷

Rheumatoid Arthritis

- Pregnenolone has been shown to relieve symptoms associated with rheumatoid arthritis. However, the dosage used in these studies was 500mg daily, significantly higher than the dose used for cognitive function.
- A comparative study of cortisone and pregnenolone found that improvements lasted longer after the study ended when pregnenolone was administered.¹⁴

Nicotine Dependence

- New research shows that pregnenolone levels are positively related to any nicotine in the body, potentially due to upregulation of the HPA axis.

- The elevated pregnenolone can lead to increases in other steroid hormones and has been associated with an elevated mood.
- This finding may lead to a novel approach for smoking cessation by using pregnenolone to lessen the negative affect associated with nicotine withdrawal.¹⁹

Dosage

- Available as 50mg and 100mg capsules, 5-10mg/drop sublingual drops
- Dosing: 50-100mg once a day at breakfast. Absorption is better if the meal contains fat.

Blood levels

- Important to obtain a baseline blood level before initiating therapy
- After 3 months, draw a level six hours after dose
- Life Extension suggests that serum pregnenolone levels approximately 180ng/dl for men and 200 ng/dl for women may be optimal.

Interactions

- May decrease effectiveness of benzodiazepines¹⁸

Side effects

- Edginess, acne, headaches, drowsiness, heart palpitations
- Contraindicated in patients with seizure disorders

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