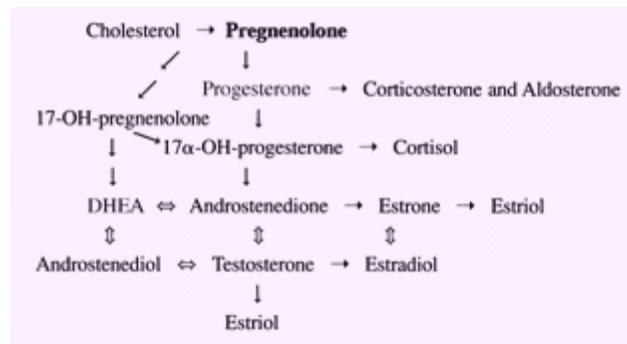


# Pregnenolone Review

## Pregnenolone - The Basics

**Pregnenolone is a steroid precursor** hormone produced principally in the adrenal glands, but also in the liver, skin, brain, testicles, ovaries, and retina of the eyes. Steroids are a large family of structurally similar biochemicals that have sex-determining, anti-inflammatory, and growth-regulatory roles. Indeed, pregnenolone is the grand precursor from which almost all of the other steroid hormones are made; including DHEA, progesterone, testosterone, the estrogens, and cortisol (See Figure 1). Life extension physician and author, Ray Sahelian, MD, refers to pregnenolone as the "grandmother" of all the steroid hormones. Despite its powerful metabolites, pregnenolone is acknowledged to be without significant side effects, with minimal or no anabolic, estrogenic or androgenic activity.



**Figure 1. The progesterone and DHEA hormone synthesis pathways.**

Pregnenolone also operates as a powerful neurosteroid in the brain, modulating the transmission of messages from neuron to neuron and strongly influencing learning and memory processes.<sup>1,2</sup>

As with DHEA, pregnenolone levels naturally peak during youth and begin a long, slow decline with age. By the age of 75 our bodies produce 60% less pregnenolone than the levels produced in our mid-thirties.<sup>3</sup> For this reason pregnenolone is one of the biomarkers of aging. Like counting the rings of a tree, by measuring the level of pregnenolone at any given point of a person's life, it is often possible to make an educated guess as to his or her age.

Some other hormones that decline with age are DHEA, estrogen, testosterone, and growth hormone.<sup>4</sup> These are considered biomarkers of aging as well. Since pregnenolone provides the initial raw material from which all the other steroid hormones are made, some of our other hormones will decline in a parallel fashion. While our youth-giving hormones are diminishing, loss of quality of life progressively settles in. We slowly begin to experience physical and mental decline; loss of energy, memory loss, visual and hearing impairment, arthritis, cardiovascular disease, and sexual decline, just to name a few. Supplementing small amounts of these neurohormones may slow these age-related processes, improving one's quality of life by rejuvenating the body to more youthful functioning.

The best known example of hormone replacement therapy is estrogen replacement for menopausal women to prevent heart disease, osteoporosis, vaginal discomfort and many other

conditions of menopause. More recent studies have shown that replacing growth hormone in elderly individuals can also produce age-reversing changes, including increased lean muscle mass, reduced fat, stronger bones, and thicker skin.

### **Pregnenolone - A Little History**

Research on pregnenolone, as well as usage of pregnenolone, dates back as far as the 1930's. Human studies were conducted in the 1940's on factory workers to test the effect of pregnenolone on anti-fatigability<sup>5,6,7</sup> and autoimmune disorders,<sup>8</sup> including rheumatoid arthritis. The results were successful and improvements were noted. Even though pregnenolone was proving to be not only effective, but safe as well, it was discarded when Merck's newly introduced pharmaceutical agent, cortisone, was announced to be a cure-all for rheumatoid arthritis in 1949.<sup>9</sup>

### **Pregnenolone - Is It Safer Than Prescription Steroids?**

Soon after cortisone and cortisol came into use, the synthetic steroid hormones dexamethasone, and later prednisone, were introduced. Remember that these steroids are hundreds of times more powerful than **pregnenolone** (or DHEA for that matter). Because they could be patented, it was more politically and economically advantageous for pharmaceutical companies to promote these drugs rather than pregnenolone. Additionally, these steroids were very fast acting compared to pregnenolone. Users and doctors preferred the quick fix. However, these steroidal compounds proved to have (and still do have) serious downsides, including compromising the immune system and inducing osteoporosis, among other serious complications.

Even though cortisone and cortisol are stress hormones which are natural to the body, they have historically been and continue to be administered in pharmacological doses rather than at physiological amounts natural to the body. The pharmacological levels at which cortisone and cortisol are generally administered give them a risk profile not unlike that of the synthetic hormones.

### **Pregnenolone - Powerful Intelligence and Memory Enhancer**

Scientists have been studying the impact of hormones on learning and memory for many years. Dr Eugene Roberts has been a leading figure in neurochemistry for more than half a century. He has been a primary figure in reviving interest in pregnenolone and DHEA as therapeutic agents. Regarding pregnenolone, Dr Roberts has said, "Of all the things that have been tested anywhere in the brain, this is by far the most potent."<sup>10</sup>

Although many substances have been found to help maintain healthy cognitive function, pregnenolone seems to have extraordinary activity in this regard.<sup>11</sup> Various studies have found that pregnenolone supports motivation, the ability to acquire knowledge, and long-term memory.<sup>12</sup> One study found pregnenolone to be one hundred times more effective for memory support than other memory-promoting steroids.<sup>13</sup> Other studies have revealed pregnenolone's ability to maintain learning function even when used in exceptionally small amounts.<sup>14</sup>

One of the most remarkable properties of pregnenolone is its apparent ability to support certain aspects of memory when taken "after the fact."<sup>15</sup> This has been found to be true for DHEA also, but to a lesser degree. Thus, the use of pregnenolone may help recall of information encountered prior to ingestion. You may wake up in the morning, decide that you really want to embed information previously absorbed, and take some pregnenolone.

### **Pregnenolone - Feel Happier and Get More Done**

A research group of industrial psychologists conducted studies in the 1940's to test pregnenolone on students and workers for the ability to enhance job performance.<sup>5-8</sup> They found that the students/workers had a markedly improved ability to learn and remember difficult tasks. It is also amazing that pregnenolone not only enhanced job performance of the students/workers; but they additionally experienced heightened feelings of well-being. In the words of Dr William Regelson, renowned oncologist, researcher and leading figure of the "superhormone" revolution puts it this way, "... this superhormone [pregnenolone] has the ability to make us not only smarter but happier."<sup>16</sup>

The same research group performed a study on factory workers to see if pregnenolone could improve their work productivity. Productivity increased most notably in the workers whose situations were considered the most stressful; for example, the workers who got paid per piece and whose living depended on their productivity. Improvement was noted, but less so, in workers who got paid a fixed wage regardless of their productivity levels. Not only did pregnenolone improve productivity for both groups, but the workers reported enhanced mood.

### **Pregnenolone - May be More Appropriate for Depression**

The insidious disappearance of well-being is a common experience for many of us as we age. The onset of depression and energy loss is so universal for older and elderly people that it is written off as part of the normal aging process and left unattended. This is particularly unfortunate since there is something that can be done.

We know that neurohormones affect neurotransmitters and can have profound effects on mental function. Many scientists and physicians believe depression in older people may be due to deficiency in the hormones that were once circulating at youthful concentrations. Restoring youthful levels of pregnenolone and possibly other neurohormones may prevent or even reverse age-related depression.

Dr Ray Sahelian states, "When older individuals find they are experiencing declining mental abilities, and doctors prescribe pharmaceutical agents for them, usually antidepressants, they're not addressing the primary problem. The primary problem is the deficiency of the neurosteroids. When the replacement of these neurosteroids is done appropriately, I think there can be amazing benefits."<sup>17</sup>

In addition to a steady stream of anecdotal reports, there have been other experiments indicating pregnenolone's association with elevated mood, increased energy, and alleviated or improved depression. If further studies solidify pregnenolone's role, as well as the role of other

neurosteroids, with regard to depression and other possible mood dysfunctions, it will further the natural hormone replacement revolution within the life extension arena and possibly bring about a total reformation in psychiatric medicine.

### **Pregnenolone - For a Lot More**

Historically, pregnenolone has been used successfully for the treatment of rheumatoid arthritis as far back as the 1940's. This is an autoimmune disease which is more likely to occur with advancing age. It is characterized by painful joints and fatigue, among other symptoms. Studies were conducted to determine the effects of pregnenolone on other autoimmune disorders such as lupus and ankylosing spondylitis. While results with osteoarthritis were not apparent, probably because inflammation is not as severe, Dr Roberts suggests that even here pregnenolone might be effective because of its ability to increase production of endogenous cortisone.<sup>3</sup>

It is believed by some physicians and scientists that pregnenolone may have use in various other areas, including high cholesterol, diabetes, heart disease, PMS, and immune dysfunction. Additionally, studies on the horizon will determine whether pregnenolone has the ability to help reverse paralysis for spinal cord injuries and more.

As previously mentioned, despite successful results, research on pregnenolone halted in the 1950's when cortisone became available as an immediate cure all. Because pregnenolone, unlike cortisone, couldn't be patented, pharmaceutical companies had no financial incentive to pursue the research.

It is unfortunate that pharmaceutical companies are governed by a financial system which imposes the requirement that for a molecule to be profitable it must be patentable. If there were half as many studies done on pregnenolone as the patented drugs, pregnenolone's therapeutic potential would be expected to be far reaching.

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