

# Pregnenolone

## Neurological And Hormonal Benefits

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### Potential benefits shown in research:

#### Brain Function

- neuroprotective<sup>1</sup>
- improves memory and learning<sup>4</sup>
- may reduce age related cognitive decline<sup>2</sup>
- low levels correlate with depression and social phobia<sup>6,13</sup>
- may alleviate symptoms of Alzheimer's<sup>4,12</sup>

#### Nervous System

- may support recovery from spinal injury<sup>8</sup>

#### Skin Quality

- may support skin hydration and collagen<sup>10</sup>

#### Adrenal Exhaustion

When cortisol is too low:

- may reduce fatigue
- may improve exercise endurance<sup>7</sup>

#### Autoimmune Conditions

- May improve symptoms<sup>14,15</sup>

#### Menstrual Migraines<sup>19</sup>

**P**regnenolone is a hormone, which is normally manufactured in the body from cholesterol inside the mitochondria of many different types of cells such as brain, retina, myelin sheaths, adrenal gland, liver, skin, thymus and testes or ovaries. Pregnenolone can be converted into numerous other hormones as needed such as DHEA, progesterone, estrogens, testosterone, cortisol and aldosterone.

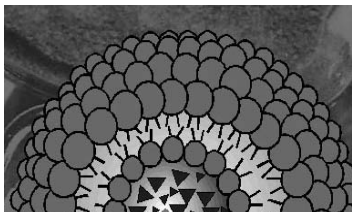
Pregnenolone itself has a stimulatory action on brain function but exerts many other effects through the many different hormones it converts into. Typical pregnenolone supplements, which are encapsulated powder, are absorbed like any other fat soluble substance, with the aid of bile and digestive enzymes, into the lymphatic circulation, and then to the liver before they are delivered to the blood circulation.

### Unique Effective Delivery

DFH Pregnenolone is provided through a liposomal delivery system (see details in fig 1) in a liquid that can be absorbed both sublingually (when held under the tongue) and through the digestive tract (when swallowed).

If the liposomal liquid is held under the tongue, the pregnenolone is absorbed through the oral mucosa, and can go directly into the blood circulation. This makes it more readily available to be taken up by various tissues before going through liver metabolism. If the liposomal liquid is swallowed, pregnenolone absorption goes through the regular fat absorption pathway: ⇒ Lymphatics ⇒ liver ⇒ blood circulation. The advantage presented by the liposomal delivery in this case is that there is no need for pregnenolone emulsification by bile and incorporation in a micelle as usually necessary for any fat to be absorbed, because the pregnenolone molecule is already incorporated into a phospholipid structure.

Fig. 1 - Liposome structure



The liposomes are microscopic "fatty" spheres composed of a bilayer of various phospholipids that enclose the bioactive molecules, in this case pregnenolone. This enables easier penetration through cell membranes, oral mucosa or GI tract.

### Possible causes of suboptimal synthesis of pregnenolone in the body may be the following:

- Aging: the average daily production of pregnenolone is around 15mg in a young adult. However, by the age of 75 the pregnenolone production may be as low as 60% compared to age 30.
- Hypothyroidism
- Cholesterol lowering therapy such as statin drugs
- Lifestyle factors such as: malnutrition, malabsorption, excessive exercise, vegetarian diets, sleep deprivation
- Corticosteroid treatment (such as cortisone)

Pregnenolone deficiency can be assessed partially from measuring circulating pregnenolone sulfate or as salivary pregnenolone, but this may not entirely reflect potential deficiencies at the intracellular level.

**Brain Function:** Pregnenolone is also considered to be a neurosteroid because it is synthesized locally by the brain cells. It crosses the blood-brain barrier, so pregnenolone from the circulation can be taken up by the brain cells when necessary. Supplementation with pregnenolone in animals and humans has shown improvements in memory or cognition and it increased mental performance under stressful conditions.<sup>18</sup> These effects are believed to be due to the following mechanisms:

- Improves the release of the neurotransmitter acetylcholine, which may also have an application for alleviating symptoms of Alzheimer's<sup>4,12</sup>
- Stimulates the layout of new brain connections (improved neurogenesis or neuroplasticity)<sup>1</sup>
- Has an excitatory effect due to its affinity for two types of brain receptors:
  - Activates NMDA receptors
  - Occupies the GABA receptor sites, thus reducing the inhibitory effects of GABA or Gabanergic drugs. GABA activity is known to increase with aging, so pregnenolone may compensate for age-related increase in neuronal inhibition.

The local conversion of pregnenolone to estrogens inside the brain is believed to have a neuroprotective effect.<sup>1</sup> Significant amounts of pregnenolone have been found in the myelin sheaths of sciatic nerves, which suggest a role in nerve health.<sup>11</sup> Depression and social phobia patients have been found to have significantly lower levels of blood/cerebral spinal fluid of pregnenolone than normal subjects.<sup>6, 13</sup>

**Autoimmune Disease:** Patients with various types of autoimmune conditions such as rheumatoid arthritis, lupus, and scleroderma were found in many studies to have significantly lower blood levels of pregnenolone, DHEA, androgens and cortisol, and even lower with cortisone therapy.<sup>15</sup> A number of studies in the 1950's have shown that supplementation with 50-600mg/day of pregnenolone (oral or intra-muscular injection) for more than a month, have brought about alleviation of their symptoms.<sup>14, 17</sup> Unfortunately, no studies have been done since then because of the popularity of corticosteroid therapy.

**Skin Health:** Studies with topical pregnenolone have shown improved skin hydration. It is conceivable that oral pregnenolone would have a similar effect since the skin tissue is very active in processing steroid hormones.<sup>16</sup>

**Menstrual Migraines:** Since these are associated with low progesterone levels, pregnenolone supplementation probably helps indirectly by improving progesterone levels commonly low in women.<sup>19</sup>

**Dosage:** Due to its stimulatory effect pregnenolone should be administered mostly during the first part of the day in order to best mimic its normal circadian production rhythm and because its excitatory action may interfere with sleep. For brain function stimulation and the correction of pregnenolone deficiency: 50-100mg/day. For autoimmune disease: 200-500mg/day oral or intra-muscular injection, under close health care supervision

***Supplementation with pregnenolone should be monitored by a health care practitioner for baseline and subsequent levels of pregnenolone, testosterone, DHT, estradiol, estrone, progesterone, aldosterone and cortisol at any age for males and females due to the wide range of biochemical individuality in pregnenolone metabolism.***

**Who Should Not Take Pregnenolone:** Due to its many possible hormonal metabolites, it is not recommended during pregnancy, lactation and hormonal sensitive cancers (breast, prostate, adrenal). Not for patients with epilepsy (history of seizures) or meningioma (non-cancerous brain tumour). Pregnenolone reduces the effectiveness of any drug that stimulates the GABA receptors such as benzodiazepines. It may also negate the effect of supplementation with GABA.

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