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

Pregnenolone itself has a stimulatory action on brain function and 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

Pregnenolone CRT™ is provided through a proprietary controlled release technology (CRT). Controlled release technology (developed for pharmaceutical delivery) is also known as steady-state or zero-order release, allowing for a very slow 10-12 hour continuous release of pregnenolone into the body in a very uniform manner. This helps to eliminate the spikes and surges found in other pregnenolone delivery systems. This technology is designed to deliver measurable amounts of an ingredient to the body at a prescribed rate in a therapeutic window for an extended period of time, ideally allowing for a convenient once-daily dosing, a feature particularly critical in hormone precursor therapy. An example of the therapeutic window (see illustration below) helps explain this. When an immediate release product is taken, an ingredient may have a burst or spike effect and exceed the body’s ability to absorb the entire given ingredient, in some cases causing unwanted side effects. As the dosing period lapses, too little of the ingredient may remain, falling below the minimum level deemed necessary to maintain therapeutic value. An effective controlled delivery product is designed to release the ideal amount of the ingredient to maintain a steady state in the body over an extended period of time, allowing for optimal absorption.

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

- Aging: the average daily production of pregnenolone is around 15mg in a young adult. However, by the age of 75 pregnenolone production may be only 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 general 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. 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.
- Stimulates the layout of new brain connections (improved neurogenesis or neuroplasticity).
- 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. Significant amounts of pregnenolone have been found in the myelin sheaths of sciatric nerves, which suggest a role in nerve health. Depression and social phobia patients have been found to have significantly lower levels of blood/cerebral spinal fluid pregnenolone than normal subjects.

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. A number of studies in the 1950's have shown that supplementation with 30-600mg/day of pregnenolone (oral or intra muscular injection) for more than a month, have brought about alleviation of autoimmune symptoms. Unfortunately, no studies have been done since then, so no conclusions can be drawn on the popularity of corticoesteroid 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.

Menstrual Migraines: Since these are associated with low progesterone levels, pregnenolone supplementation may help indirectly by improving progesterone levels, commonly low in women.

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: 30-100mg/day. For autoimmune disease: 200-500mg/day (oral or intra muscular injection) for more than a month.

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, etc.). It is not recommended 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. 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.

References: