Melatonin and Health Benefits

This article is separated into 5 sections, each of which can be individually downloaded. It is a 'work in progress' incorporating new information whenever time permits.

Section 4

Melatonin suppressors

1. Introduction; Age-related biological changes and increased life span; Alcohol-induced damage; asthma; autism; behaviour; bladder; blood-brain barrier; blood flow; blood pressure; brain damage; burns; cancer; cardiovascular support; Central Nervous System (CNS) injuries and diseases; chemical; dementia

2. Depression, bipolar disorder and mood control; diabetes, diabetic retinopathy; DNA damage; drug dependency; drug interaction; eye problems; fibromyalgia; headaches; head injury; height; immune system effects; infertility; inflammatory conditions; Irritable Bowel Syndrome (IBS) and other gastric problems; kidneys; learning and memory; light at night; light pollution; liver damage; lung injury; malaria; menopause; metabolic disorders; mitochondrial dysfunction; mouth diseases; nerve damage; neurocognitive functions; Neurodegenerative diseases, such as Huntington's disease; neurodevelopmental disorders; nitric oxide interaction; obesity

3. Operation trauma; ovarian disease; pain relief; pancreatitis; Parkinson's disease; plants; pregnancy and reproduction; radiation side effects; schizophrenia; sciatic nerve injury; scoliosis; skin effects; sleep, sleep apnoea; spinal cord injury; stress; stroke; testicular protection; thyroid; toxin protection; treatment side effect reduction; vaccinations; ventilator-induced lung injury; Wi-Fi

4. Melatonin suppressors: Alcohol; age; baby crying; cancer; chemicals; diet; weight; electromagnetic fields (EMFs), powerfrequency radiation; occupational radar exposure; radiofrequency radiation; light; light at night (LAN); light wavelength, smartphone; fracture risk;

5. References – 467 references

4. Melatonin suppressors

The involvement of melatonin in so many bodily processes means that any disruption in its function is of critical importance. Erren & Reiter (2008) have proposed that "*the final common cause of many cases of cancer may be what has been termed chronodisruption (CD), relevant disturbance of the temporal organization or order of physiology, endocrinology, metabolism and behaviour, with melatonin as a key time messenger and keeper being a marker of CD.*"

Alcohol

Alcohol consumption was found to reduce urinary levels of melatonin in women, with 4 or more drinks reducing the levels by 17% (Stevens 2000). This may result in an increase in circulating oestrogen, which could affect breast cancer risk.

Age

It has been suggested that melatonin production reduces with age, but Richard Stevens, one of the foremost researchers into melatonin, considers this belief to be wrong. Diminished melatonin concentrations have been measured in spleen, liver, and heart during aging. The loss of the potent anti-oxidant capabilities may contribute to onset of aging (Sánchez-Hidalgo 2009).

Baby crying

Babies born with low levels of vitamin B12 can have undeveloped nervous systems, causing low levels of melatonin, which results in their crying for much longer periods.

Cancer

Night work was found to increase the risk at several sites (including lung, colon, bladder, prostate, rectal, pancreatic cancers and non-Hodgkin's lymphoma) among men. The mechanism suggested was due to melatonin suppression (Parent 2012). Bhatti (2012) commented that the findings not only address the need for shift-work studies that evaluate cancers other than breast and prostate cancer but also support the increasing concern that the negative effects of shift work may be applicable to risk of many cancers via the direct oncostatic properties of melatonin.

Uninterrupted darkness, at night, enables optimum melatonin production, and is a previously unappreciated endogenous mechanism of cancer prevention (Blask 2009).

Chemicals

Melatonin levels were decreased in PCB-exposed rats, which improved with supplementation (Venkataraman 2008).

Diet

High-fat diets significantly decrease nocturnal pineal melatonin synthesis (Cano 2009). Intake of red meat, but not poultry (including turkey), nor fish consumption has been associated with the lowering of melatonin concentrations, which may affect cancer risk (Schernhammer 2009).

Weight

A higher body mass index is related to lower circulating concentrations of melatonin (Schernhammer 2009).

Electromagnetic fields (EMFs)

Powerfrequency radiation

Electronic equipment repairers, exposed to ELF-EMF had low levels of serum melatonin. They are at risk of oxidative stress and sleep insufficiency. El-Helaly & Abu-Hashem (2010) recommend antioxidant supplementation, such as melatonin, should be taken to ameliorate these effects. Zwirska-Korczala (2004) also reported that ELF magnetic fields significantly reduced the antioxidative actions of melatonin. Erdem Koç (2016) reported that melatonin can protect the cell against neuronal damage in the hippocampus induced by 900 MHz EMF.

Studies in human populations, though not in wild kestrels (Dell'Omo 2009) have shown that magnetic fields, such as those from powerlines and other powerfrequency, are capable of disrupting the night-time production of the important hormone melatonin in the pineal gland, especially polarised fields, in combination with the earth's geomagnetic field disturbances (Burch 1999, 2000), and in exposed workers (Burch 1998, 1999).

Halgamuge (2013) found that exposure to weak EMFs via melatonin disruption could adversely affect human health. Women working at least four hours per day, five days a week, in front of a video screen experienced a 54% reduction in 6-sulfatoxymelatonin in their night-time urine production (Santini 2003).

Corona ions emitted by powerlines produce highly variable disturbances in the atmospheric electric field down wind. It is hypothesised (Henshaw 2008) that these random disturbances can result in the disruption of nocturnal melatonin synthesis and related circadian rhythms leading to an increased risk of a number of adverse effects.

Dr Yves Primault, Honorary Professor at the University of Milan suggested that exposure to magnetic field levels of more than 0.1 microtesla can stop, or reduce (Davis 2006) overnight production of melatonin. The batteries from a mobile phone will exceed this level at the user's head. Girgert (2010) found that EMFs significantly disrupted the antioestrogenic effect of melatonin in breast cancer cells.

Radar

A study by Singh (2015) showed that EMF significantly changed plasma melatonin and serotonin concentration in radar workers exposed to 8-18 GHz.

Radiofrequency radiation

A study by the Citizens Initiative Kempten West (in Germany) found that a mobile phone transmitter affected levels of melatonin and serotonin. 'Before' and 'after' blood samples were taken from residents near a newly installed mobile phone mast. The participants had removed other RF sources such as DECT phones and wLANs from their homes. Measured microwave fields showed a several fold increase in RF exposure after the mast was activated. 84% of participants reacted with a massive decrease in serotonin level. Nearby residents nearly all experienced increases in depressive mood disturbances, lethargy and listlessness, appetite

disturbances, inner agitation and reduced quality of life. There was also a fairly steep nightly melatonin decrease for 56% of the group. More than half the group reported sleep disturbances. Some genetic variations (on SLC6A4 and BDNF genes) make people more likely to suffer from depression as a result of environmental stressors, yet other changes in the same gene appear to be protective. Many complained of waking between 2 and 4 a.m. and had difficulty getting back to sleep again. Sleep disturbance is increasingly being seen as a cancer promoting risk factor. They also found a displacement in time of melatonin excretion, when getting up rather than earlier in the morning. This results in feeling very tired on getting up, and consequent tiredness, irritability, loss of concentration during the day.

Clark (2007) found that postmenopausal women may be a sensitive subgroup of the population, whose melatonin excretion increases when they live near radio & TV transmitters.

A study by Burch (2002) concluded that the prolonged use of mobile phones may lead to reduced melatonin production, and elevated magnetic field exposure could make it worse. Wood (2006) found that melatonin onset time was delayed by mobile phone handset emission exposure.

Circadian rhythms were disturbed after exposure to RF, with the effect being more pronounced on melatonin than testosterone (Qin 2012). The authors suggest that regulation of testosterone is controlled by melatonin which is more sensitive to RF exposure.

A significant decrease in the level of pineal melatonin was recorded in a group of rats exposed to 2.45GHz microwave radiation for 2 hours a day. A significant increase in creatine kinase, caspase 3, and calcium ion concentration was observed in the whole brain of the group of rats. The study (Kesari 2012) concludes that a reduction in melatonin or an increase in caspase 3, creatine kinase ans calcium ion may cause significant damage in the brain due to chronic microwave exposure.

Light

Green light was found to enhance positive clock genes expression, leading to melatonin synthesis, whereas red light enhanced negative genes expression, suppressing melatonin synthesis (Jiang 2016). Dim light reduced melatonin levels less than bright light after an evening meal (Albreiki 2017).

Light at Night (LAN)

Until recent times, humans in temperate climates were exposed to up to 18 hours of darkness in the winter. In the modern world, artificial lighting reduces this to typically eight hours or less per day all year round. Even low light levels inhibit melatonin production to some extent, but over-illumination can create significant reduction in melatonin production.

Circadian rhythms are endogenous and will continue indefinitely in the absence of light signals. Light just serves to synchronise them to the true day/night cycle. Their function is to enable the body to anticipate its needs throughout the day night cycle. It's not just sleep that is affected; almost all of our metabolism is regulated in this way so that it makes the best use of limited resources. If the amplitude of these rhythms were to be reduced (e.g. by electromagnetic radiation) it would not perform any of these functions at maximum efficiency. One of the casualties would be the production of melatonin (which would be reduced – Reiter 2007, Korkmaz 2009), and we would also become tired more easily during the day and our immune systems would be less efficient at night. Reiter says that a potential negative consequence of chronodisruption and nocturnal melatonin inhibition is cancer initiation and growth. The frequency of breast, prostate, endometrial and colorectal cancers has increased in individuals

whose circadian rhythms have been disrupted. In addition to cancer, there may be other diseases that result from the chronic suppression of melatonin by light at night.

There have been suggestions that light in the evening and at night time, at the red end of the spectrum, is less likely to disrupt melatonin production during the following hours of sleep. Stevens (2006, Schernhammer 2004, 2005 Srinivasan 2008) also suggest that light (especially blue light Figueiro 2009) at night reduces melatonin production. However, short-wavelength 'blue' light in the *morning* helps entrain the circadian system, and the removal can delay dim light melatonin onset in adolescents (Rea & Figueiro 2010). This finding is relevant to lighting practice in schools.

A Russian article (Panchenko 2008) found that constant lighting increased tumour growth, whereas light deprivation slowed down growth. Hanifin (2006) found that bright red light also suppresses melatonin, so care has to be taken with the intensity of any light chosen.

Long-term, night shiftwork has been identified as a potential carcinogenic risk factor, possibly because increased light at night exposure during shiftwork reduces melatonin production. Grundy (2009) found that 2 nights of rotating shift work may not change the timing of melatonin production. Bright fluorescent lighting @ 3000K and 5000K were found to supress melatonin, but 2300K or dim light appeared to have no effect (Kozaki 2008). This could easily be implemented in work environments to decrease breast cancer risk. Kloog (2011) found a positive association between bedroom light intensity and breast cancer risk.

However, in addition to LAN, in humans, sleep is normally timed to occur during the biological night, when body temperature is low and melatonin is synthesized. Desynchrony of sleep-wake timing and other circadian rhythms, such as occurs in shift work and jet lag, are associated with disruption of rhythmicity in physiology and endocrinology. Mistimed sleep affects molecular processes at the core of circadian rhythm generation (Archer 2014). Signs of desynchronization in terms of suppressed amplitude of melatonin and phase delay of salivary cortisol were consequences of the increasing number of consecutive night shifts among police officers at work. Lack of synchronization has been suggested as a possible mechanism linking night work to disease (Jensen 2016).

Wideman & Murphy (2009) found that rats exposed to light all the time had decreased melatonin levels and changed metabolism, circadian rhythms and behaviour, compared with rats on 12 hr light/ 12 hr dark and those exposed to dark conditions all the time.

Hill (2011) reported that studies in both rats and humans indicated that LAN induced circadian disruption of the nocturnal melatonin signal activates human breast cancer growth, metabolism, and signalling, providing the strongest mechanistic support for epidemiological studies demonstrating the elevated breast cancer risk in night shift workers and other individuals increasingly exposed to LAN. Kloog (2008) had found a strong positive association between LAN intensity and breast cancer, but not lung cancer.

It was felt that increased light exposure of different types (e.g. fluorescent) may be responsible (Blask 2005), at least in part, for the incidence of breast cancer, especially as blind women have a lower incidence. Pukkala (2006) also found that breast cancer risk in females decreased according to the amount of visual impairment. There was a similar but less consistent trend for prostate cancer in males. Keshet-Sitton (2017) suggests an outdoor light threshold of approximately 16 lux as the minimal intensity to affect melatonin levels and breast cancer morbidity.

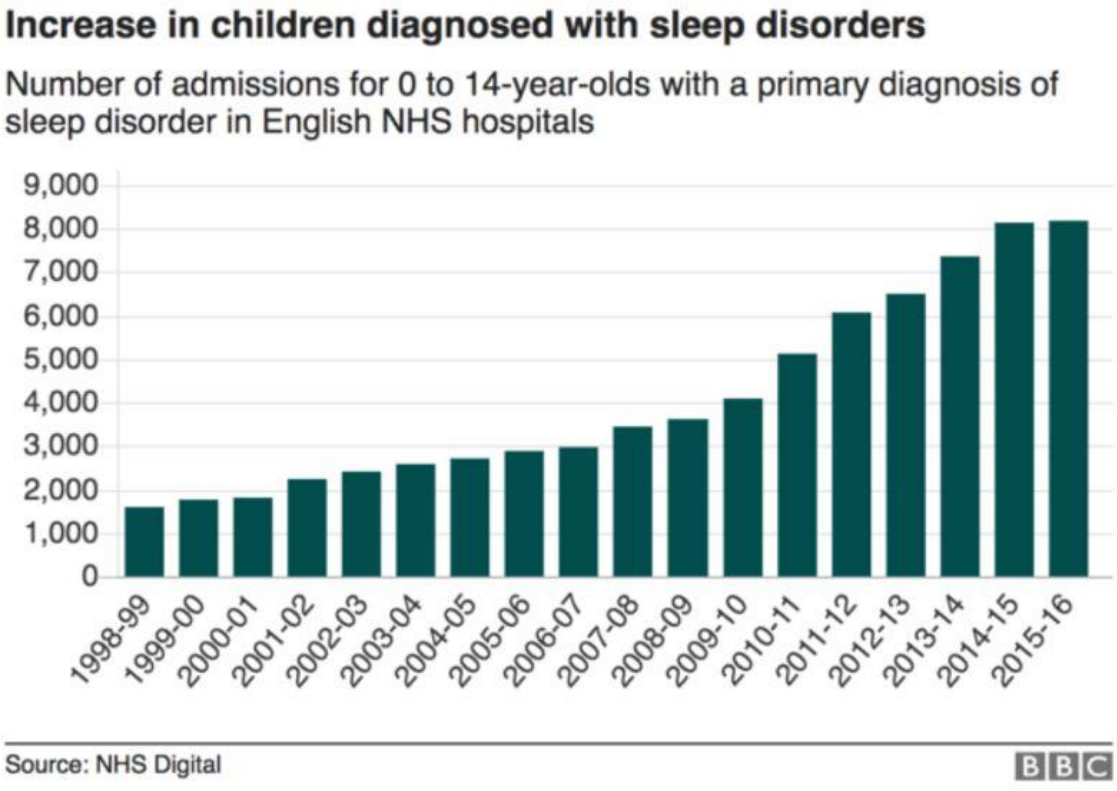
Investigations by Brainard (2001) suggested that a single retinaldehyde based photopigment may be primarily responsible for melatonin suppression.

The diseases of civilisation, obesity, insulin resistance and arterial hypertension are a direct result of chronic metabolic disturbance due to light pollution and its effect on melatonin (Russian authors 2012).

In June 2016, the American Medical Association (AMA) recognised the detrimental effects of poorly-designed, high-intensity LED lighting, and encouraged communities to minimise and control blue-rich environmental lighting by using the lowest emission of blue light possible to reduce glare. The AMA also recommended that all LED lighting should be properly shielded to minimise glare and detrimental human health and environmental effects, and consideration should be given to utilise the ability of LED lighting to be dimmed for off-peak time periods. As a side effect (!?) this should also reduce the night-time exposure to light at the blue end of the spectrum which reduces melatonin production. Perhaps this is included in minimising 'detrimental human health' referred to.

Light wavelength

460 nm monochromatic light causes twice the amount of melatonin suppression compared to 555 nm monochromatic light, and the effect is dependent on the duration of exposure in addition to the wavelength. This demonstrates that the peak of sensitivity of the human circadian pacemaker to light is blue-shifted (Lockley 2003). Chellappa (2012) suggests that humans homozygous for the PER3 5/5 allele are particularly sensitive to blue-enriched light, as indexed by the suppression of endogenous melatonin and waking theta activity. Light sensitivity in humans may be modulated by a clock gene polymorphism implicated in the sleep-wake regulation. Blue light emitted by smartphones and tablets is known to reduce the natural production of melatonin, and negatively affect sleep (Heo 2017, BBC 2017).



Fracture risk

Experimental evidence suggests that light at night (including nightshift work) acts through endocrine disruption likely mediated by melatonin. Osteoporotic fractures are highly sensitive to sex steroids. Feskanich (2009) found that 20+ years of nightshift work was associated with a significantly increased risk of wrist and hip fractures. The risk was strongest for women with a lower body mass index and those who had never used hormone replacement therapy.