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What about the Effect of EMFs on Melatonin and Breast Cancer?

A Set of Frequently Asked Questions Specifically about Melatonin

Critique by

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This document is written in response to a section posted on the HPA website: "What about the Effect of EMFs on Melatonin and Breast Cancer? A Set of Frequently Asked Questions Specifically about Melatonin". This document may be viewed at:
http://www.hpa.org.uk/radiation/faq/emf/emfsupp3.htm

The set of frequently asked questions (FAQs) and responses, appears to have been written as a follow-up to the recent AGNIR Melatonin Report for which a detailed critique has already been written. This critique may be accessed at:
http://www.electric-fields.bris.ac.uk/CritAGNIR.htm

While there is some merit in the responses given to the FAQs, in many cases the serious errors and misrepresentations in the AGNIR Report are simply repeated, indeed further factually incorrect information is given.

This critique will provide comments on specific items in the FAQs document.

1. Under: "**Why did the HPA request the AGNIR to produce a report on power frequency electromagnetic fields, melatonin and the risk of breast cancer?**", it is stated: "*The report considers the relevant scientific evidence for the melatonin hypothesis in detail"*.

Given that much relevant evidence is not considered at all, this begs the question as to what the AGNIR would regard as "relevant evidence".

For example, On the 27th April 2005 I was invited to give oral evidence to the AGNIR Melatonin Sub-committee. This evidence summarised the findings described in an invited paper at the World Health Organisation meeting on EMF and Child Health, held in Istanbul in

June 2004. The paper was written jointly with Professor Russ Reiter of the University of Texas Medical Center and was subsequently published in peer-reviewed form by Henshaw & Reiter in *Bioelectromagnetics* in 2005 (Supp **7**, S86-S97). Whereas human volunteer experiments have provided equivocal evidence of melatonin disruption following acute exposure to laboratory-controlled magnetic fields, 12 studies, comprising (i) studies in volunteers exposed to magnetic fields for several days and (ii) populations exposed to neighbourhood fields have, taken together, found a consistent pattern of melatonin suppression/disruption. The effect is particularly evident when magnetic field switching and/or electric fields are present.

The Henshaw & Reiter peer-reviewed paper is not cited in the Report, despite the fact that it was the subject of invited evidence to the AGNIR. It should be pointed out that the AGNIR Report was not sent for blind peer-review prior to publication, had it been so this omission along with a number of serious errors and misunderstandings would surely have been picked up by the referees.

2. Under: "**What effects does melatonin have?**", it is stated: "*Melatonin can also act as an antioxidant, helping to prevent free radicals (produced as a part of normal metabolic processes) from causing damage to DNA and which could lead to malignancy*."

This appears to be a welcome U-turn on the claim in the AGNIR Melatonin Report in section 3.8.6, page 67, paragraph 2, lines 7 - 10 which states: "*Its* [melatonin's] *role as a free radical scavenger at physiological concentrations and hence in vivo is less convincing, as there are many other cellular candidates such as glutathione, vitamin A, or vitamin E that are found in much higher natural concentrations than melatonin, and therefore potentially play a greater role in cellular defence*."

It is indeed well known that melatonin acts in a different way to glutathione, vitamin A and vitamin E, in particular it enters cells and can be present on DNA at concentrations considerably higher than in blood. Its concentration in some tissues and organs is orders of magnitude higher than in blood, and the multiple actions of melatonin, some of which are receptor mediated, make it a broad-spectrum and ubiquitously acting antioxidant. These features of melatonin are discussed more fully in a 2003 editorial in the Journal of Pineal Research (vol. 34, 79-80): *What constitutes a physiological concentration of melatonin?*

3. Under: "**Can exposure to EMFs affect melatonin**?" There are two statements:

"The report concludes that the exposure of humans to EMFs at levels likely to be found at work or at home does not appear to be associated with changes in melatonin."

and

"The results of epidemiological studies are more difficult to interpret, and although many studies have found some changes, no consistent effects have been observed."

This begs the question as to what the AGNIR means by "*does not appear to be associated*". If we look at public exposure, i.e. general populations chronically exposed to neighbourhood electric and magnetic fields, then we could adopt a criterion in studies that we take most note

of those that are deemed to be statistically significant, $p<0.05$, or a probability of 1 in 20 (or better) that the result occurs by chance. If we then carry out 20 studies, then purely by chance we would expect to find one which is statistically significant. The AGNIR state that many studies have found some changes in melatonin with EMF exposure. Does this mean that this result could easily have been obtained by chance because large numbers of studies have been carried out where no discernable effect was seen? Perhaps the AGNIR would like to clarify matters here.

As stated under (1) above, Henshaw & Reiter 2005 found that populations exposed to neighbourhood fields have, taken together, found a consistent pattern of melatonin suppression/disruption. The effect is particularly evident when magnetic field switching and/or electric fields are present. In other words, how does the AGNIR justify the comment "*does not appear to be associated*", when the data gives every appearance of an association? To whom does it '*not appear'* to and for what reason?

The AGNIR claim that no consistent effects have been observed, but the invited evidence given to them on 27th April 2005 specifically pointed out that it was neighbourhood magnetic fields, together with the effects of switching and/or the additional effect of electric fields which appeared to be particularly evident in being associated with melatonin disruption in those so exposed.

4. Under: "**Does melatonin affect the risk of breast cancer?**" There is the statement that the AGNIR "*...concludes that melatonin can reduce the growth and development of cancers in some types of cancer cells and in animals, although it is not clear that this occurs in humans*."

Since publication of the AGNIR Report, an important mechanistic study has been published by Blask *et al* (*Cancer Res*. 2005; 65: (23) 1-11) in which blood containing the normal nocturnal physiological concentration in melatonin was taken from women during the night and given to nude rats (genetically modified rats having a suppressed immune system) which had MCF-7 human breast tumours transplanted into them. The blood effectively arrested the growth of these tumours. The effect was not found with blood taken at night but with the light switched on so that nocturnal melatonin had been suppressed. As a check of the efficacy of melatonin *per se*, rats were separately fed with melatonin at the same physiological nocturnal concentration level as that in the blood taken from women at night during darkness. Again, the growth of the human tumours was arrested. This study is the closest one is likely to get to the human situation and confirms the effectiveness of normal physiological concentrations of nocturnal melatonin in preventing the growth of human breast tumours. This study received wide publicity in the United States. It is a pity that the HPA did not draw attention to this study in their FAQ document.

5. Under: "**Does exposure to EMFs affect the risk of breast cancer?**", it is stated: "*Similarly, there was no convincing evidence that EMFs had a direct effect on breast cancer cells or on the growth and development of tumours in animals.*"

This begs the question on what constitutes "*convincing evidence*". Convincing to whom? The statement appears to contradict the findings in the peer-reviewed literature. For example, a peer-reviewed study by Ishido *et al.* (2001) showed that 1.2 μT magnetic fields inhibit the

action of melatonin at normal physiological concentrations, between 10^{-9} and 10^{-11} molar, in preventing the growth of MCF-7 breast cancer cells *in vitro*. At the time this was the fifth laboratory to make this finding. It has also been reported that 1.2 μT magnetic fields inhibit the action of Tamoxifen in preventing the growth of breast cancer cells.

The term "*convincing evidence*" needs to be defined. There is also the issue of misrepresentation, why doesn't the FAQ document discuss to the above findings?

The statement mentions *direct effects*, but what about *indirect effects*? The AGNIR Report concerns melatonin, which has an indirect effect in regulating cancer risk but virtue of its multiple actions, some of which are receptor mediated, make it a broad-spectrum and ubiquitously acting antioxidant.

6. Under: "**What do more recent studies show?**", it is stated: "*However, of the few recent studies that have addressed the effects of EMFs, none appear to provide any data that challenge the conclusions of the report*".

To my knowledge, only one peer-reviewed study has been published on melatonin disruption by EMFs since publication of the AGNIR Melatonin Report. This is the study by Davis *et al* (*Annals of Epidemiology*, **16**, 622-631, 2006) in which 115 women volunteers were non-acutely exposed to a magnetic field source of 0.8 μT during the night. Compared with no exposure, a statistically significant reduction in nocturnal melatonin was found. The conclusion of the AGNIR Report that EMFs do not appear to affect melatonin is in any case the opposite of what appears to be the case. In the light of the further evidence by Davis *et al.* 2006 could the HPA now describe in detail how they justify these further comments?

7. Under: "**Should I try and reduce my exposure to EMFs, especially at night**?" The statement: "*The report on power frequency electromagnetic fields, melatonin and the risk of breast cancer concluded that there was no compelling evidence to indicate that typical exposure to EMFs, especially at night, could have a substantial effect on melatonin …*".

What does the term "*compelling evidence*" mean? Does it mean there is evidence but a value judgement has been made that it is not compelling? Compelling to whom? This would appear to be simply a subjective judgement. What does the term "*could have a substantial effect on melatonin*" mean? Does this mean that there is evidence that EMF does have an effect on melatonin but that a value judgement has been made that the effect is not substantial? Henshaw & Reiter (2005) tabulate studies of melatonin disruption with magnetic fields as low as 0.2 μT. In several cases reductions of up to 40% are seen with very low field exposures. What is meant by *typical* exposures? The findings summarised in Henshaw & Reiter 2005, refer to field levels that are found in the neighbourhood to which populations are exposed. This means they are well within the range of what would normally be called '*typical*'.

8. Under: "**Should I turn off the lights in the bedroom at night?**" A number of statements are made:

(i) "*Although the report on power frequency electromagnetic fields, melatonin and the risk of breast cancer found that there was some evidence suggesting that working shifts at night might increase the risk of breast cancer in women, there was no evidence that this was caused by changes in melatonin brought about by exposure to light.*"

What does the term "*no evidence*" mean in this sentence? For example, does it mean that extensive studies have been carried out but that negative or null results have been found? If so, can the AGNIR please provide the details. Alternatively, is it the case that the relevant studies simply haven't been done? Or, is the statement meant in a very specific sense, that the particular studies on light at night and breast cancer did not carry evidence about melatonin in the same subjects. If that is what was meant, it should be stated clearly. Otherwise it gives a false impression that there is no scientific evidence in the literature at large which might support the involvement of melatonin in such an association.

A major peer-reviewed prospective study by Schernhammer & Hankinson (*Journal of the National Cancer Institute*, Vol. 97 (14), 1084-1087, July 2005), published within the period looked at by the AGNIR Melatonin Committee (August 2005), reported an association between nocturnal melatonin levels and the risk of breast cancer. Those with the highest nocturnal melatonin levels had significantly lower risk of breast cancer (OR = 0.59, 95% CI = 0.36 – 0.97). A further paper by Schernhammer *et al*. (*Epidemiology*, Vol. 17 (1), 108-111, 2006), published after August 2005, reports increased risk of breast cancer in nightshift workers (RR = 1.79, 95% CI = 1.06 – 3.01), further adding to the existing body of evidence that nightshift workers have increased breast cancer risk. Given the long established fact of melatonin suppression by light-at-night and given the recent paper by Blask *et al.* 2005, why does the HPA consider that there is *no evidenc*e that increased breast cancer risk in nightshift workers is brought about by changes in melatonin?

The HPA should be asked to provide a detailed justification of their comments.

(ii) "*Although brief exposures to bright light at night can produce a reduction in melatonin levels circulating in the blood, these changes are likely to* [be] *transient, and will quickly recover.*"

What is the basis for this statement?

At the CHILDREN with LEUKAEMIA Scientific Conference in September 2004, Professor Russ Reiter of the University of Texas Medical Centre gave an invited talk on melatonin. Concerning disruption by light-at-night, Professor Reiter showed data demonstrating that a short exposure to light prior to the peak in normal nocturnal melatonin production, which occurs between midnight and 1am, results in immediate quenching of nocturnal melatonin levels, but which recovers after about 3 hours. In other words, while recovery takes place there is a significant reduction in the total amount of melatonin produced during the night-time period. However, a short exposure to light after the peak in nocturnal melatonin, for example at about 3am, quenches the whole of the further production of melatonin during the remainder of the night. These data are clearly at variance with the HPA statement.

Professor Reiter's talk may be accessed at:
http://www.leukaemiaconference.org/programme/speakers/day3-reiter-pres.pdf
scroll through to slide 9.

(iii) "*Therefore sleeping in darkness may not be necessary*."

I have concerns regarding this statement, especially following the recent announcement of an 80% rise in breast cancer cases since the 1970s in the UK. In the US the question has been debated as to whether the public should be advised to reduce their exposure to light-at-night or indeed whether people should be advised to take melatonin supplements. The latter in particular is clearly an ethical question as is the question as to whether to vaccinate young girls against cervical cancer – the latter being a positive suggestion in the UK.

In the light of public concerns at the very substantial rise in breast cancer, for the HPA to apparently suggest that it is not necessary to reduce exposure to light-at-night seems somewhat strange. The public could at least be given the facts so that they can make up their minds.