

Note to HPA-DG 3-3-08

Please find attached a courtesy copy of a new paper Aggregating Disparate Epidemiological Evidence. It looks at the evidence associating ELF EMF with adult leukaemia and adult brain cancer as considered by IARC and California DHS in 2002, raises questions about methodology and makes recommendations for future reviews.

Last year's paper by Lowenthal et al., which I think the DG has seen, reinforces the view about adult leukaemia, and is only mentioned in a Post Script in our paper.

While our approach is deliberately simple, it is entirely valid within its stated limitations. It does not use all the available information but does indicate the numerical strength of evidence in aggregate. Indeed it tends to understate that strength because of its simplicity.

It is interesting that the evidence for association of residential exposure with childhood leukaemia, before selection for pooling, had a relatively weak meta-analytic summary with OR = 1.3. Ahlbom et al.'s study of selected more homogeneous results then led to the pooled OR of 2.0 for TWA exposures above 0.4 μ T. Although there were about twice as many studies of adult leukaemia, with comparably strong aggregate features to those of childhood leukaemia, there has not so far been a focused pooled analysis, as far as I know.

Another outcome where a meta-analysis has now been published is Alzheimer's Disease (AD). The paper by Garcia et al 2008 is also attached, since this should be central to the subject and to precautionary considerations. This meta-analysis of 14 studies derives overall OR or RR around 2.0, despite moderate to high heterogeneity.

Back in 2002 the review bodies IARC and CDHS had only 5 or 6 studies to consider. As IARC's primary consideration is carcinogenicity (and of an agent rather than for a specific outcome), neurodegenerative diseases are considered only briefly under section 4 ("other data relevant to the evaluation of carcinogenicity ...") of the IARC methodology. On page 269 the epidemiology is dismissed without argument and with deference to ICNIRP, and AD isn't mentioned either in animal evidence or in the summative assessment. CDHS assesses AD with an average degree of certainty around 25%, less than half that for childhood leukaemia.

WHO EHC 2007 considers AD evidence "Inadequate", mentioning inconsistency and weaker evidence in higher quality studies of morbidity rather than mortality. Garcia et al. address that form of heterogeneity. WHO recommends the association should be further investigated, with priority "High". After an extensive discussion of the epidemiology, WHO conclude there is only "very limited evidence" of association when evaluated across all studies. Garcia et al. cover the studies cited by WHO plus Noonan 2002 and Harmanzi 2003 which WHO missed (except for Noonan on Parkinson's disease). Garcia et al. take us forward from WHO EHC 2007.

WHO acknowledges the possibility of partly common pathogenic mechanisms for neurodegenerative diseases, so there is an argument that evidence for association with ALS and with AD is mutually reinforcing. The idea of aggregation and significance of evidence essentially relates to underlying hypotheses, which brings us back to our

paper on aggregation, but I'll not pursue that further here. Compound hypothesis structure is something which review bodies should be on top of, yet they are not.

The broad hypothesis, that environmental ELF-EMF exposure and/or proximity to powerlines may be harmful to public health, gains support from the combination of all the above, with evidence relating to both child and adult leukaemia, and that relating to neurodegenerative diseases, needing to be taken into consideration in aggregate rather than fragmented and dismissed.

The broader philosophy of assessing evidence with regard to precaution in a context of multi-causality is nicely addressed in my third attachment, a paper by David Gee: *Basic & Clinical Pharmacology & Toxicology*, **102**, 257–266, 2008.

All of these attachments and this commentary are offered as worth the attention of DG and indeed of HPA.

With thanks for your forbearance,
- Mike