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Cardiovascular disease: Time to identify emerging environmental risk factors

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Vernon et al.[1] recently reported a significant increase in the proportion of first-time ST elevation myocardial infarction (STEMI) patients without standard modifiable cardiovascular risk factors (hypercholesterolaemia, hypertension, diabetes and smoking). While the authors correctly highlighted the need for discovering new mechanisms of coronary heart disease based on theirs and other complementing data, we would like to draw the attention of researchers in cardiovascular disease (CVD) to emerging environmental risk factors, focusing here on microwave radiofrequency electromagnetic radiation (RF-EMR).

Human exposure to RF-EMR has exponentially increased over the past three decades due to rapid and widespread deployment of wireless communication and surveillance infrastructure and the use of personal wireless devices. Public exposures have increased from extremely low natural radiofrequency levels[2] below 10^{-15} W/m^2, to above 10^{-2} W/m^2 now.[3,4] RF-EMR is an environmental pollutant with cytotoxic effects.[5,6]

Despite the European Academy for Environmental Medicine (EUROPAEM)[7] and the American Academy of Environmental Medicine (AAEM)[8] publishing evidence linking RF-EMR to adverse health effects and calling for exposure reduction, there is widespread ignorance about the scientific evidence of radiofrequency-induced biological/health effects within the medical fraternity. This appears to be largely due to the controversial approach by the International EMF Project at the World Health Organization (WHO),[4] which has ignored the calls by a large group of international electromagnetic field (EMF) scientists[9] for improved exposure regulation.

The WHO's International Agency for Research on Cancer (IARC) appointed an expert panel to examine the evidence related to cancer in 2011 which classified RF-EMR as a group 2B possible carcinogen.[10] The new scientific evidence that has emerged since then, particularly epidemiological evidence linking mobile/cordless phone use to brain tumours[11,12] and experimental evidence of genotoxicity and carcinogenicity[6,13] warrants an update to this classification.[14] However, no such evaluation of CVD risk has been carried out. Furthermore, there are serious shortcomings in the few panel reports that have so far evaluated biological/health effects.[15]

In our latest review, 242 RF-EMR studies that investigated experimental endpoints related to oxidative stress (OS)[16] were identified. A staggering 216 (89%) of them found significant effects related to OS, similar to a previous review.[17] These are being further analysed following presentation at the recent Australasian Radiation Protection Society conference.[18] Mostly in-vivo animal studies and in-vitro studies have demonstrated increased markers of endogenous OS and/or affected antioxidant levels in different tissue/cell types upon exposure to RF-EMR. Some studies have further demonstrated amelioration of RF-induced OS upon treatment with various antioxidants. Limited human studies at this stage complement these studies demonstrating OS and/or reduced antioxidant status upon acute radiofrequency exposure under experimental settings,[19] in mobile phone users[20] and residents near mobile phone base stations.[21] Renowned physical scientists have recently presented experimental evidence and a theoretical explanation on how low-intensity RF-EMR can generate OS.[22]

OS is known to be implicated in CVD[23,24] and therefore RF-EMR, a new ubiquitous environmental exposure, may contribute to CVD by maintaining chronic OS, and thereby causing oxidative damage to cellular constituents and altering signal transduction pathways.

Acute RF-EMR exposure has been shown to increase blood pressure under experimental conditions,[25] while chronic exposure has been found to be associated with an increased CVD risk[26] as well as alteration in the diurnal rhythms of blood pressure

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and heart rate[27] in studies investigating clinical, anthropometric, behavioural, environmental and socio-economic parameters.

Research on biological/health effects of RF-EMR started mostly within the military due to RF use in radar,[28] with former Soviet Bloc countries conducting the most. A US Army medical intelligence document[29] reporting on Soviet research stated:

> Comparison of a group of engineers and administrative officials who were exposed to microwaves for a period of years and an unexposed control group revealed a significantly higher incidence of coronary disease, hypertension, and disturbances of lipid metabolism among the exposed individuals. Hereditary predisposition to heart disease was approximately the same for both groups, but overt disorders developed much more frequently in the previously exposed group. It was concluded that microwaves may act as a nonspecific factor which, under certain conditions, interferes with adaptation to unfavorable influences. Exposure may, therefore, promote an earlier onset of cardiovascular disease in susceptible individuals.

However, despite substantial evidence of biological effects and some evidence of adverse health effects even back in the 1970s, the west did not stringently control public exposure as did the Soviet Bloc countries, and conflicts of interest are apparent in same military report:

> If the more advanced nations of the West are more stringent in the enforcement of stringent exposure standards, there could be unfavorable effects on industrial output and military functions.

This divergent approach to recognition of radiofrequency-induced health effects and exposure regulation still continues today between the USA and Russia and their allies.

Early epidemiological evidence from chronically exposed populations near radiofrequency transmitters (radio/TV/radar towers) before RF-EMR emitters became common everyday gadgets is extremely valuable. Now everyone is exposed and, therefore, it is very difficult to obtain reliable epidemiological data. However, there is still great variation in the level of exposure which can be assessed only by individual measurement in controlled studies. A 1994 US Air Force report[30] gives important insights on early epidemiological evidence:

> In response to earlier Soviet reports, the World Health Organization (WHO) decided to conduct a comprehensive study on the biological effects of exposure to RF/MW radiation. In 1976, M. Zaret published the results of the study (reference found in [8]). The WHO investigation focused on the population of North Karelia, a remote area of Finland that borders the Soviet Union. This region was selected because of its close proximity to a then Soviet early warning radar station. North Karelia is geographically located in the path of intercontinental ballistic missiles that would originate from the midwest United States. To detect these missiles, the Soviets constructed a number of high power tropospheric scattering radar units adjacent to nearby Lake Ladoga. The operation of these units exposes the residents of North Karelia to large doses of ground and scatter radiation. The WHO investigation found evidence linking exposure of RF/MW radiation to cardiovascular disease and cancer. The North Karelian population suffered from an unusually high number of heart attacks and cases of cancer. In addition, it was found that the affliction rate of these diseases was much higher among residents living closest to the radar site.

Although the success of the North Karelia project lifestyle intervention programme that reduced the CVD mortality is well known,[31] how many are aware of this reported CVD risk identified by the WHO related to chronic RF-EMR exposure? While a PubMed search with 'North Karelia' and 'cardiovascular' picked up 191 publications, 'North Karelia' and 'radar/radiofrequency/radiation' picked up none (on 2 September 2017). We therefore assume that this WHO/military knowledge about RF-EMR risk in CVD was not passed on to the scientific community for investigation. The success of the North Karelia project by increasing the consumption of fruit and vegetables, i.e. antioxidant therapy, supports our hypothesis that chronic exposure to RF-EMR causes CVD via redox mechanisms of OS which can be countered, albeit not fully, with increased dietary intake of antioxidants. However, what about measures to reduce exposure? While regular use of/being close to personal wireless devices such as phones, computers and WiFi routers as well as living close to wireless infrastructure such as mobile phone base stations can greatly increase one's exposure, the common habit of carrying a connected mobile phone in a shirt pocket is of particular concern regarding radiofrequency exposure to the heart.

As for recovery from STEMI, restoration of myocardial perfusion can be compromised by changes of endothelial integrity, platelet aggregation, neutrophil infiltration and inflammation after an acute thrombotic coronary occlusion. At a cellular level, these processes are controlled by redox mechanisms/signalling pathways and therefore, actively reducing exposure to

RF-EMR warrants consideration as part of post-STEMI patient management. Indeed, we require high quality clinical studies to investigate if such an approach is effective.

Radiofrequency exposure may also contribute to standard modifiable cardiovascular risk factors. The risk of hypertension, hypercholesterolaemia and truncal obesity was significantly higher in the occupationally radiofrequency-exposed radio/TV station operators (mean age 47.9 years) compared to their occupationally unexposed colleagues in a study by researchers at the Bulgarian National Centre of Public Health Protection.[26] This was despite a lower incidence of smoking in the radiofrequency-exposed group. Similar to several other studies, these researchers also found increased excretion rates of stress hormones: cortisol, adrenaline and noradrenaline in the radiofrequency-exposed.[32] It is very concerning that the occupational RF-EMR exposure levels of this group of radio and TV station workers are now common in the general public due to widespread wireless technologies, with little investigation of the health consequences.

Apart from an OS-mediated chronic effect in coronary heart disease, there may be chronic and acute effects involving OS/other mechanisms on cardiac electrophysiology. Dysregulation of the autonomic control of the cardiovascular system in healthy men (under 50 years) occupationally exposed to RF-EMR has been reported[27,33] compared to their unexposed colleagues, as well as altered heart rate variability under acute experimental exposure to cordless and mobile phones.[34,35] There is also evidence for immediate responses of voltage-gated ion channels, particularly Ca^{2+} channels (VGCC) upon radiofrequency exposure.[36] The downstream effects of VGCC disruption may involve alteration of important functions of Ca^{2+}/calmodulin-dependent enzymes (such as nitric oxide synthase and protein kinase II), influencing the pathophysiology of CVD.[37] Chronic disturbance of ion channels directly/via OS by persistent RF-EMR exposure may lead to pathologies of the heart muscle similar to primary electrical diseases (i.e. channelopathies). While the manufacturers of pacemakers have developed shielding to prevent electromagnetic interference from RF-EMR over the years, we note that the natural cardiac electrical network remains susceptible to interference by common RF-EMR emitters.

Although a few western countries have recently taken steps to reduce public exposure to RF-EMR, particularly of children, such as discouraging the use of wireless devices by children and banning/restricting WiFi in schools,[38,39] there is largely inaction at this stage. Intriguingly, a professor in public health at the University of California recently went to court and accessed the cell phone safety 'fact sheet' (on health risks with instructions to reduce exposure) prepared by the Californian Department of Public Health.[40] It is reported that this document, originally prepared in 2009 and revised 27 times up to 2014, was abandoned due to influences from vested interests. Meanwhile in France, a physician took legal action to access data from government testing of mobile phones[41] revealing that most phones would not even pass the entirely thermally based (tissue heating) current exposure standards if held directly against the body, such as in a garment pocket.

It is clearly time to investigate the potential role of RF-EMR exposure from common wireless device use on CVD. Noting that existing research findings are influenced by the funding source,[42] fresh directives are necessary for objective high quality research to expand current primary and secondary prevention strategies.[43]

Author contribution

PB drafted the manuscript, PB and SW jointly conducted the review of studies on OS and both agreed on the final version of this research communication.

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