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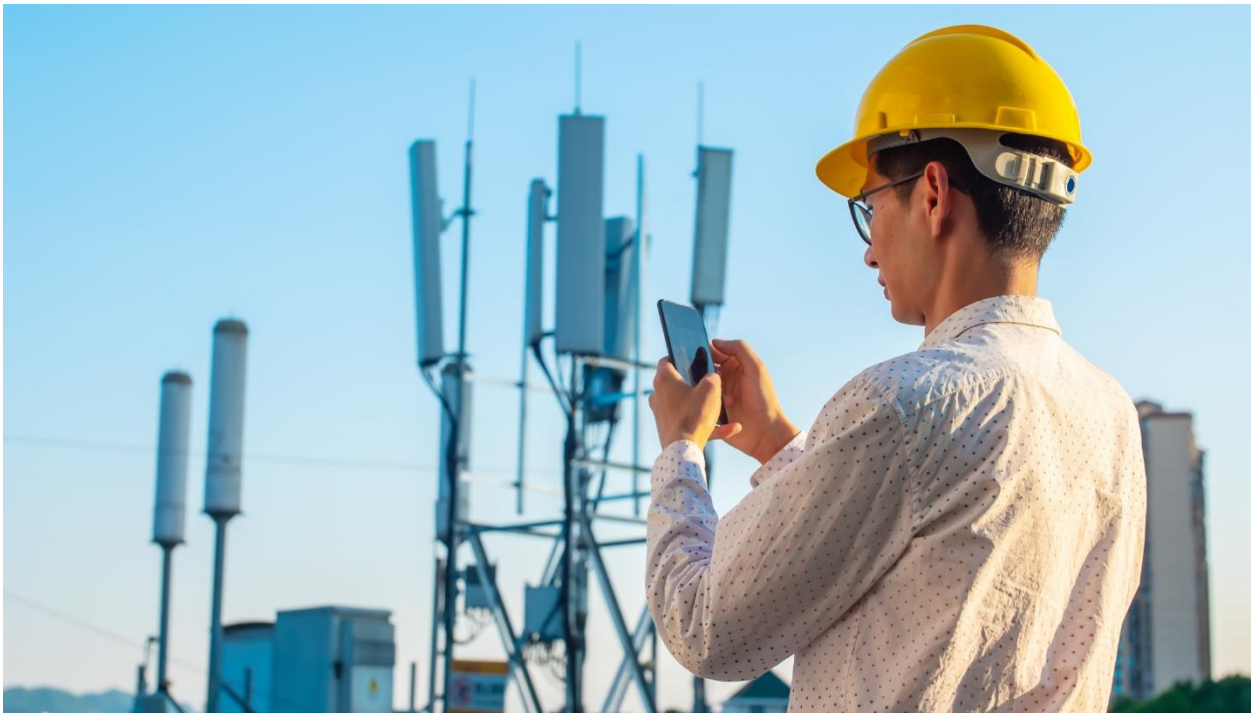
Health Effects of Radiofrequency Electromagnetic Fields, Including 5G



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Key Findings

- Radiofrequency (RF) electromagnetic fields (EMF) are a type of non-ionizing radiation with several technological applications. For decades, RF has been used for purposes such as telecommunication signals and microwave heating.
- Health Canada's guidelines, referred to as Safety Code 6, set recommended human exposure limits to RF. Safety Code 6, which is based on peer-reviewed scientific literature, is intended to protect all members of the public from potential adverse effects to RF exposure.
- At the present time, there is no consistent evidence for adverse human health effects from RF exposures below Canadian limits (Safety Code 6). There is a clear dose-response for acute health effects from RF exposures approximately 50 times greater than Safety Code 6, which is not expected to occur in the community setting.

- With proposed 5G technology and the expanded use of wireless technology, exposures to RF may increase, but are expected to remain under Safety Code 6 limits. Similarly to RF, there is no consistent evidence for adverse human health effects from 5G technology. Further research is needed to clarify some findings which at this time do not consistently support clinical effects.

Introduction

Radiofrequency (RF) energy produces electromagnetic fields (EMFs) which is a type of non-ionizing radiation. The RF range (3kHz-300GHz) of the electromagnetic (EM) spectrum is used for telecommunications. The roll out of 5G (5th Generation) mobile technology uses more frequencies within the RF range, and will likely increase the number of transmitting sources. Transmitting sources emit radiofrequency to which the public may be exposed. RF exposure limits are recommended by Health Canada under Safety Code 6 to protect against possible adverse health effects from RF exposure. The purpose of this report is to provide a summary of the available literature based on recent reviews on the health effects of RF, with special attention to new frequencies that may be used in 5G technologies. This is not a detailed review of individual studies, but rather intended to be a broad overview of relevant summaries to provide key findings from the available literature.

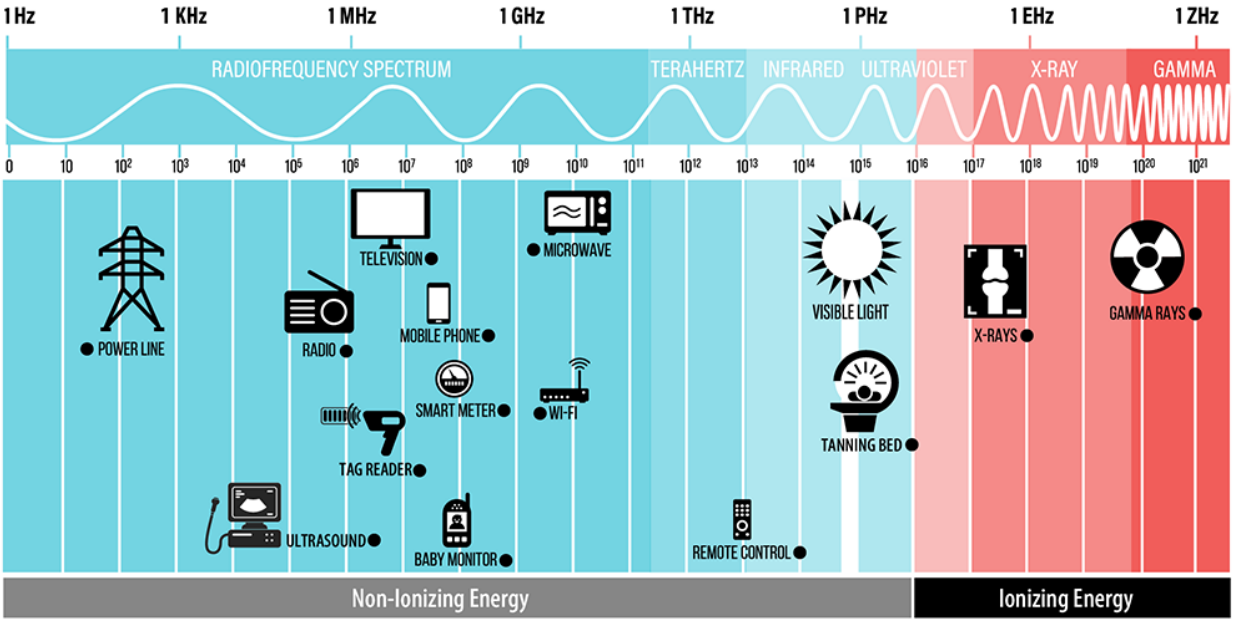
Background

The term radiation refers to energy that travels via waves or particles; the amount of energy present is in part determined by the frequency of the wave, with hertz (Hz, or number of waves per second) as the basic unit of measurement. The range of frequencies is referred to as the electromagnetic (EM) radiation spectrum, which is subdivided into categories (see Figure 1). Lower frequencies (longer wavelengths) are broadly categorized as non-ionizing. As the frequency increases, the radiation becomes ionizing, meaning there is sufficient energy to dislodge electrons from atoms. Exposure to ionizing energy increases the risk of deoxyribonucleic acid (DNA) damage, associated with an increased risk for the development of cancer. Examples of ionizing radiation sources are those that occur naturally (radon from soil and rock) or from anthropogenic sources (such as x-rays or nuclear fallout).

Non-ionizing radiation covers a broad spectrum of energy frequencies, which includes RF. RF is part of the EM spectrum and spans 3 kHz to 300 GHz. RF is both naturally-occurring and generated from human activities, and has been used in many applications for communications globally for decades. Examples include television and radio broadcast, Wi-Fi, cellphones, cordless telephones, smart meters, and satellite communication. Microwave ovens also use RF to heat objects.

Though existing and planned telecommunications networks (including 5G) operate within the EM spectrum, more higher-frequency bands will come into use with the roll out of 5G technology, which will enable increased mobile data capacity, decreased latency, and the “internet of things”, which refers to devices that autonomously use data (e.g., autonomous vehicles). 5G will make greater use of RF frequencies from 6000 MHz (6GHz) to around 30 GHz, and possibly higher, within what has been referred to as the “millimetre band” or “millimetre wave” (MMB or MMW) range (which extends to 300 GHz).[1,2] All these applications normally emit RF energy at levels that are in compliance with regulations and are below those that are expected to cause health effects.

Figure 1: Radiation frequency spectrum



Source: Government of Canada. Radiofrequency energy and safety [Internet]. Ottawa, ON: Government of Canada; 2019 [modified 2020 May 13; cited 2022 Aug 16]. What is radiofrequency (RF) energy? Reproduction is a copy of the version available from: https://ised-isde.canada.ca/site/spectrum-management-telecommunications/en/safety-and-compliance/facts-about-towers/radiofrequency-energy-and-safety#s1. Used with permission.

Potential exposure to RF (and other forms of radiation) is inversely proportional to distance from source (significant decrease in exposure with increased distance from source). Numerous other variables are also relevant, including the emitting power of the source, the presence and density of objects in the pathway, and the direction of emission. Therefore the mere presence of RF energy does not necessarily imply significant exposure is occurring.

Though RF cannot dislodge an electron, it can still cause atomic-level vibration, which is how in the higher frequencies (above 100 KHz) it can heat objects. This is harnessed in technologies such as the microwave oven.[1] This effect has been observed into the millimeter band as well.[3] At lower frequencies (below 10 MHz), high exposures (e.g. greater than 50 times the Safety Code 6 limit) can result in nerve stimulation (causing a tingling sensation).[1] This ability to cause heating or nerve stimulation occurs predictably at appropriate frequencies with sufficient amplitude (strength). These health effects serve as a basis for setting exposure limits, with a safety factor applied.

Regulation of RF-EMF Exposure

In Canada, recommended human exposure limits are set by Health Canada in Safety Code 6 (SC6). Most recently updated in 2015, the limits are comparable to similar regulations or recommendations in other countries, such as the United States (US).[1,4] Innovation, Science and Economic Development Canada (ISED) regulates wireless devices and their associated infrastructure under the Radiocommunication Act and requires compliance with the limits set out in Safety Code 6. SC6 applies a weight-of-evidence approach in assessing the peer reviewed scientific literature to establish lowest adverse effect levels (LOAELs) and generally applies a safety factor of 10 (sets the limit 10 times lower than the LOAEL) for

limits in “controlled environments” (occupational/non-public settings), and a factor of 50 for “uncontrolled environments” (for the general public) for whole body exposure.[1,4,5] In comparison, the International Commission on Non-Ionizing Radiation Protection's (ICNIRP) guidelines provide slightly higher allowable limits than SC6.[1]

RF exposure limits change based on the frequency. For lower frequencies (below 10 MHz), field strength limits are used to protect against nerve stimulation.[4] Specific Absorption Rate (SAR), which is power absorbed (Watts or W) per unit mass (kg), are used for frequencies between 100 kHz and 6 GHz to protect against tissue heating, given as a whole-body average, or as a localized measurement.[4] Limits for SARs are based upon laboratory-observed effects of tissue heating in non-human primates and other animals, which occurs above 4 W/kg of whole body exposure.[4] Given the very low penetration of tissue from EMFs in the MMW range, the metric of exposure for frequencies >6 GHz is the incident power density (W/m^2).[4]

The dose of energy received by the body is used to estimate the health effects of RF. This is dependent on the part of the body exposed, because of the thermoregulatory differences between tissues. Broadly speaking, the health effects can generally be categorized into acute or chronic health effects, as well as system-based effects (e.g., cardiac, ocular, reproductive).

Methods

This report is based on an overview of the most recent published reviews, supplemented by a review of primary literature published after the last review available.

The most recent available regulations and reviews included reviews from the World Health Organization, the International Agency for Research on Cancer (IARC), various governments, commissions (including the Royal Society of Canada 2014 Expert Panel), health agencies (British Columbia Centre for Disease Control and Institut National de Santé Publique du Québec), as well as other groups (the BioInitiatives Working Group from 2012). These were reviewed, and references from these publications also considered for inclusion.

The online repository of EMF-related research, emf-portal.org, was searched for relevant titles.

A scoping literature review for new publications was then carried out using MEDLINE, Scopus and Inspec. Search terms combined ("emf" or "rf" or "radiofrequency" or "electromagnetic field" or "radio waves" or “5g” or "wi-fi") and (“health” or "health effects" or "adverse health effects" or “illness” or “disease”), limited to human, English reviews and meta-analyses from 2010 to the time of writing (December 2020). This search yielded 672 results, of which 38 were relevant. An additional MEDLINE search for EMF and carcinogenicity was performed, using search terms "electromagnetic fields" or "EMF" or radiofrequency or RF or "non-ionizing radiation" AND cancer.mp. or exp Neoplasms, limited to English language and humans, from and 2013 –Current, and meta-analysis or "systematic review" which yielded 162 citations, of which 7 were relevant.

In addition, the Public Health Ontario (PHO) Library Services performed an additional more comprehensive MEDLINE search, which yielded two more relevant articles. Library Services also performed a second grey literature search, identifying 81 articles, of which 15 were deemed relevant for inclusion. A Google scholar search was also performed using search terms including “5G,” “millimetre wave,” “EMF,” “Electromagnetic fields,” and “health effects,” and relevant articles were reviewed from

the first 5 pages of results. The PHO library search methodology is available upon request from library@oahpp.ca.

Title review identified reviews and key large studies, for which abstracts were then reviewed for relevance. Articles were then selected for review if they had been published in peer-reviewed journals and were published after 2010. Reference lists of selected articles were also hand searched for relevant articles and reports.

Results

Health Effects of RF Exposure

Research on the health effects of RF-EMFs remains an ongoing focus of scientific enquiry.[6] Broadly, studies examine either RF exposure, such as estimated doses of RFs based on various scenarios (usually experimental studies in a laboratory setting), or the effects of RF exposure (experimental or observational studies).

Exposure Research

Exposure research studies consider RF power density (W/m^2), frequency and duration of exposure, and distance from the source in relation to health effects.[7] Many recent studies focus on cellphone-related RFs given the significant development and expansion of this form of telecommunications over recent decades.

With the upcoming incorporation of 5G frequencies, the question of how much individual exposure to RFs may change has been of interest. A systematic literature review conducted in Europe compiled EMF measurement data in everyday microenvironments including homes, schools, and offices from 2005-2013 to estimate typical doses to the public.[8] They found that typical exposures were well below regulatory or recommended limits, and the highest exposures were due to uplink transmission (observed on commuter trains).[8] Uplink refers to EMFs emitted from a mobile phone during normal use, rather than toward the phone from transmitting arrays. An updated systematic review was performed which included measurements to 2018, using similar methodology. The authors found that in spite of increased wireless technology use since 2012, mean levels in typical microenvironments remained well below regulatory or recommended limits and had not increased from previous measurements. This was attributed to increased efficiency in both devices and data transmission.[9] No similar study looking at Canadian exposures was identified.

A recent review by the Institute of Electrical and Electronics Engineers (IEEE) discusses the potential changes to public exposure to EMFs with 5G. They note that net exposure to EMFs for the general public may be partially lowered due to a more “targeted” approach (“beamforming”), which targets signals to a specific user while communicating with their device, and does not emit EMFs when not in use.[10]

For most of the population, there are numerous and ubiquitous exposure sources to EMFs (e.g., power lines, radio signals, visible light, the earth’s magnetic field, electric appliances) but current day lifestyles mean cellphones, which must meet RF regulatory or recommended limits, are a potentially important source of RF exposure. As noted in the above studies, for those who use cellphones, the source of highest exposure to cellphone associated EMF comes from uplink transmission.[10]

Outcomes Research

The terms used to describe effects from an exposure vary and reflect the many types of studies. Biological effect is generally meant to describe any change, positive or negative, on a tissue or cell (such as can be observed in a petri dish in a lab). Human health effect (or simply "health effects," for the purpose of this discussion), in contrast, is any change, positive or negative, observed in a person. Though both are useful to better understand exposure and effect relationships, consistency of evidence across the full spectrum of biological to human health studies is needed to make inferences about real world exposures. While acute health effects from high dose exposures (such as heating or tingling from exposures many times higher than regulatory or recommended limits) have been well described, studies exploring possible chronic human health effects from RF exposure show varying results. Though some laboratory studies demonstrate varying degrees of biological effects from EMF exposure, the relevance to human health is less clear.

Based on the available scientific literature, the consensus among various international committees and expert panels, including the World Health Organization (WHO), Health Canada, and provincial agencies is that the established adverse health effects associated with RF exposure are tissue heating and peripheral nerve stimulation with high-dose exposures (e.g., greater than 50 times higher than the limit for the general public).[10-14,15,5,16,17] Health Canada, the WHO, the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), the International Commission on Non-Ionizing Radiation Protection (ICNIRP), and the United States Federal Drug Administration have all stated that typical community exposures to EMFs (such as from cellphone use or from cellphone towers, and including 5G frequencies) are not expected to cause adverse health effects, noting the evidence is most robust for frequencies currently in use.[12,18-21]

One exception to this opinion is the BioInitiative Working Group's 2007 and updated 2012 (and 2014/17) paper from a group of researchers from universities and public and private institutions.[22] This non-peer reviewed report, which does not include a clear methodology for their analysis makes different conclusions from other scientific panels, stating that "bioeffects can reasonably be presumed to result in adverse health effects if the exposures are prolonged or chronic," and on this basis a significantly lower regulatory or recommended limit should be set (e.g. compared to Safety Code 6 and other similar limits).[22] Some have noted that the Bioinitiative Working Group's reports neither account for methodological issues in some of the cited studies nor include most of the relevant *in vivo* cancer studies.[23, 24]

An overview of studies on potential adverse health effects by body system and RF exposure can be found in Appendix A. It is based upon the most recent comprehensive weight-of-evidence reviews from the Royal Society of Canada Expert Panel (RSC) in 2014, the SCENIHR 2015 review, as well as a 2018 review on 5G (which does not employ a weight of evidence approach) by Di Ciaula.[23, 13, 25] Weight-of-evidence reviews employ a systematic approach which accounts for the type and quality of the evidence in synthesizing heterogeneous studies on a given topic.[26] Relevant primary literature published since 2015 is cited as well.

ACUTE HEALTH EFFECTS ASSOCIATED WITH RF EXPOSURE

Well known acute health effects from RF exposure relate to the potential tissue heating properties (at higher frequencies between 100 kHz and 300 GHz) and nerve-stimulating effects (at lower frequencies between 3 kHz and 10 MHz).[1] These effects have been measured and replicated in experimental studies. RF exposure of sufficient intensity and duration in the frequency range of 3 kHz-10 MHz alters the resting membrane potentials of nervous tissues causing depolarization and subsequent sensory effects.[4]

Tissue heating has also been well-characterized in experimental studies of both non-human primates and in human volunteers under a variety of exposure scenarios.[4] With exposures to RF in frequencies between 100 kHz and 300 GHz, sufficient intensity and duration will heat tissues in a tissue-specific manner (with approximately 1 degree Celsius temperature change in the body considered a relevant threshold).[4] These thresholds form the basis for recommended limits in SC6.[4,5]

CHRONIC HEALTH EFFECTS ASSOCIATED WITH RF EXPOSURE

Although there is likely widespread exposure to RF in the population, the observational nature of epidemiologic research on its long term health effects makes causal associations difficult to establish when no obvious outcome (e.g., increased incidence of certain cancers) has been observed. Health outcomes that have been studied include carcinogenicity and electromagnetic hypersensitivity (EHS) as well as ocular, cardiac, reproductive, neurological, and developmental effects. Overall, the literature is broadest regarding carcinogenicity, with large reviews completed on human carcinogenic effects incorporating a range of literature (mechanistic, animal, human studies). This section will focus on carcinogenicity and EHS. Effects on specific systems for which the research is more limited are summarized in Appendix A; however the evidence does not consistently support the clinical relevance of the findings.

CARCINOGENICITY

Evidence on the potential for EMF exposure to cause cancer remains unclear despite a wide range of studies including mechanistic, animal, and observational human studies. The International Agency for Research on Cancer (IARC) designated RF as Group 2B (Possibly Carcinogenic to Humans) in the 2011 Monograph based on observational human studies from the 1990s examining cellphone use and possible increased risk of certain cancers (gliomas, acoustic neuromas, and temporal lobe tumours).[27,28] However validation studies have since noted potential sources of bias, similar studies have not observed an increased risk, and ongoing brain tumour incidence trends have not significantly changed in the last 2 decades, which argues against a clear causal association.[23,29,30] The RSC report also did not find an association with cancer from occupational cohort studies which generally involve higher exposures than the general public.[23] Since the RSC report:

- Several recent systematic reviews and meta-analyses on cellphone use and cancer have not found statistically significant associations, though in one of these reports an increased risk of cancer in the highest exposure subgroup was noted and studies by one research group (Hardell and colleagues) were the ones consistently finding associations with cancer.[28,31-33] One systematic review on cellphone use and parotid gland tumours did find a positive association, but the authors caution interpretation due to the limited number and retrospective design of the studies used.[34]

- A recent large-scale animal study conducted over 2 years by the US National Toxicology Program (NTP) exposed rats and mice to RFs from 2G/3G technology frequencies (mice at 1900 MHz, rats at 900 MHz), and observed a mildly increased incidence of a rare cancer (malignant schwannoma of the heart) in male rats.[35,36] The relevance to humans remains unclear given the doses administered in the experiment were much higher (75 times) than Safety Code 6 limits, and the exposed study animals lived longer than the non-exposed.[35,36] This study was included in a recent US FDA report on RF and cancer spanning 2008 to 2018 which concluded that "there is no quantifiable causal link between RFR [radiofrequency radiation] exposure and tumor formation."[37] The ICNIRP also reviewed these findings and concluded similarly to the FDA.[38]

More detail on EMFs and cancer can be found in Appendix A.

ELECTROMAGNETIC HYPERSENSITIVITY

In communities worldwide, a proportion of individuals (2-13%) report physical symptoms attributed to RF exposure at levels below regulatory or recommended standards, though the criteria for this vary widely.[23] This has been labelled as electromagnetic hypersensitivity (EMS or EHS), electrosensitivity, and by the WHO 2004 Workshop report, "Idiopathic Environmental Intolerance with attribution to EMF" (IEI-EMF).[39] Reported symptoms attributed to EMFs include neurocognitive disturbances (dizziness, fatigue, headaches, tinnitus, sleep problems, concentration problems), sweating, pain in the muscles and joints, eye burning, ear, nose and throat issues, and gastrointestinal issues.[40] Because these symptoms are not specific to EHS and may be experienced in other syndromes and diseases, they are also described in the literature as "medically unexplained physical symptoms" (MUPS).[41] Proposed criteria to identify EHS include self-reported sensitivity to EMFs, physical symptoms that occur within a relatively brief timeframe after exposure (<24 h) that are attributed to EMFs, and the absence of a diagnosis that may otherwise explain the symptoms.[42] A specific frequency range has not been attributed to symptoms, and frequencies from 50 Hz to 300 GHz have been implicated, which include proposed frequencies in 5G technology.[43]

The RSC report reviewed studies correlating symptoms to measurable EMFs in controlled settings, including double-blinded provocation studies, the majority of which have demonstrated no reproducible symptoms with measured exposure to EMFs.[23] The RSC concludes, "…research in the past ten years does not provide firm evidence for the hypotheses that people with IEI-EMF can perceive RF energy at levels below the limits in SC6 or that there is a causal link between exposure to RF energy and their symptoms," consistent with the comprehensive 2004 report from the WHO.[23,39]

Studies on 5G/MMW and Therapeutic Applications

Given that 5G technology is anticipated to make greater use of higher frequencies in the RF range, particularly >25 GHz and into the MMW range, as well as an anticipated increased density of transmitters in order to propagate these frequencies, studies focusing on these frequencies were appraised to ascertain if any specific health risks from exposure have been identified. Because MMW does not penetrate deeply into tissue, the main concerns are based on skin and ocular effects.[44]

Di Ciaula reviewed research on MMW effects from *in vitro* and animal studies, many of which discuss potential medical applications for MMW at much higher intensities than SC6 limits such as skin heating modalities to treat skin cancers.[25,45] In a variety of in vitro and animal studies where experimental exposure doses were higher than SC6, other potential effects on gene expression, cell membrane permeability, and nervous tissue were also discussed but the generalizability to human health is unclear.[46-51] Cited studies of EMF and neural tissue generally did not observe any effect at exposure levels below SC6 limits.[52-56] The author also notes some conflicting evidence for ocular damage in animal studies.[25] The relevance of these findings to human health effects are not discussed.[25]

A recent review of *in vivo* and *in vitro* studies on 5G frequencies (6-100 GHz) characterized 94 relevant publications based on study type, biological material and endpoint, exposure metrics, and quality criteria.[57] The review found that though most studies observed some effect, there was no consistent dose-response (i.e., power density or duration and magnitude of effect) or replicative studies to confirm the findings.[57] Most studies concluded that "non-thermal" effects were measured, however few were noted to have actually measured or controlled temperature in a validated manner to determine if

heating may have occurred and confounded the results.[57] The authors conclude that at this time there is insufficient information to conclude if human health effects are expected from 5G frequency EMF exposure, and call for more research.[57] Similar findings were summarized in a recent systematic review and meta-analysis of 107 experimental studies which focused on the biological effects of RF fields above 6 GHz, at levels below the ICNIRP occupational limits.[58] The review included 31 epidemiologic studies of occupational exposure to radar (which can potentially include frequencies used in 5G, up to 300GHz), with some reporting follow up post-exposure up to 40 years, and which did not identify an increased risk of adverse health outcomes, including cancer.[58]

Another way to assess the evidence on RF and health effects is to look at medical studies that demonstrate any physiologic change in humans at intensities below SC6, such as medical therapies. For instance, pulsed EMF has been studied as potential treatment for a variety of diagnoses. Although the frequency range used is typically below the RF range (e.g., 5-300Hz) some overlap with the RF range is seen in a few studies.[59] A systematic review from 2012 identified 11 trials that attempted to assess the efficacy of whole-body pulsed EMF for various diseases, and found that due to small sample sizes (12-71 subjects), inconsistent results, and lack of independent confirmation of positive effects, there is insufficient evidence that whole-body pulsed EMF has any therapeutic effect.[59] Other systematic reviews found that pulsed EMF or other modalities that variably include frequencies in and out of the RF range, and some which use intensities above SC6, had uncertain or no efficacy for treatment of knee osteoarthritis, adhesive capsulitis, neck pain, or rotator cuff disease.[60-66]

Discussion

While the evidence on acute health effects such as nerve stimulation and tissue heating is clear and measurable, studies on chronic effects are inconclusive. At this time, there is no consistent evidence that typical exposure to RFs in the community will lead to adverse human health effects. The clinical relevance of observed biological effects in animal or tissue models remains unclear. These experimental studies provide hypotheses for further study, but the World Health Organization also notes that a "'biological effect' does not equal 'health hazard.'"[67] While research continues, individuals who still seek to reduce personal exposures could consider some strategies provided by the British Columbia Centre for Disease Control and Health Canada.[68, 18]

Conclusion

With the expanded use of wireless technology, exposures to RF may increase, but are expected to remain under regulatory or recommended limits. With exposures to RF below SC6 recommendations, frequencies currently in use and those proposed for 5G technology have not been shown to have adverse human health effects in the literature. Studies examining biological effects of new/expanded RF bands to be used, such as MMW or 5G, have so far not demonstrated a clear human health risk under typical or expected exposure conditions for the general public. Further research is needed to clarify the clinical relevance of some findings.

Appendix A: Summary of Evidence by Body System

Carcinogenicity

The International Agency for Research on Cancer (IARC) designated RF as Group 2B (Possibly Carcinogenic to Humans) in the 2011 Monograph based upon several epidemiologic studies based on cellphone use rather than environmental RF sources such as cellular network antennas or FM radio towers.[27] The RSC review provides an overview of IARC's approach and update of the evidence for this designation.[23] The basis of the IARC assessment was the large INTERPHONE epidemiologic studies as well as case-control studies from Hardell and colleagues, which all used self-reported cellphone use (generally from late 1990s and early 2000s) for the estimate of exposure.[28] These case-control studies (which were each based upon cases with N≈1000-3000) found an increased risk of gliomas, acoustic neuromas, and temporal lobe tumours in users with highest self-reported cellphone use, but validation studies suggested that these findings were subject to potential systematic errors and biases which could alter the strength of association.[23] A large Danish cohort study (N=420,095) did not find an association, though similar methodological flaws were noted.[29] The IARC working group also considered ecological findings that there has been no concomitant increase in overall cancer rates with increased cellphone use, though they acknowledge that conclusions cannot be drawn using such methodology.[23] Overall there were dissenting opinions within the IARC working group on whether the 2B designation was justified (e.g., "inadequate" as opposed to "possibly"), and some organizations view the relationship between RF exposure and cancer in humans as inconclusive.[69,13,17]

Occupational cohort studies can be useful in determining the carcinogenicity of a given exposure since these groups tend to have higher exposures than the general public which are more frequently objectively measured and quantified. This can serve as a basis for estimating risk to non-occupationally exposed groups. In the case of RF, such an association was not found in the 8 cohort studies reviewed.[23]

Since the RSC report, a few relevant studies have been published:

- A systematic review and meta-analysis from 2020 looking at cellular phone use and cancer (any type) incorporated 46 case-control studies primarily from 1996-2005 (N=66,075), and calculated a meta-OR of 0.99, suggesting no increased risk for cancer associated with (some versus none) cellphone use.[31] "Use" was not consistently defined, nor did it clearly mention technological advances such as "hands-free" technology. However, in the subgroup analysis, a statistically significant increased risk for cancer was observed in the highest exposure group with an OR of 1.6 (CI 1.12 to 2.30).[31] There was significant variability between studies, and in a subgroup analysis by research group, studies from Hardell and colleagues was the only subgroup consistently finding positive associations.[31] There was some overlap between this group of researchers and the others, in terms of study data and cohorts used.[31]

- A meta-analysis from 2019 of various epidemiologic studies evaluating cellphone use and brain/salivary gland tumor risk found that given the recent, sudden and widespread use of cellphones, the robust cancer registry data in many countries, and with the relatively small number of competing environmental risk factors for brain tumors, the epidemiological evidence for brain and salivary gland tumors from RF exposure via cellphone use is weak.[32] Meta-RRs calculated for various tumors (glioma, meningioma, neuroma, pituitary tumors, and salivary tumors) did not yield statistically significant increased risks, ranging between 0.74-1.19.[32]

However, the authors recognize that more rare or long-latency cancer subtypes may not have been identified.[32]

- A 2018 meta-analysis looking at ever cellphone use and risk of glioma did not find a statistically significant association in the ten studies evaluated.[33]

- A systematic review from 2017 looking at cellphone use and parotid gland tumors identified three studies appropriate for meta-analysis.[34] The study calculated an OR of 1.28 (95% confidence interval: 1.09–1.51) for reported highest use (in fixed effects models only), with two of three studies finding a positive association. The authors caution interpretation of a conclusive relationship given the limited number of studies, the conflicting findings, and the exposure assessment based upon questionnaires.[34]

The US National Toxicology Program (NTP) recently completed animal studies exposing rats and mice to RFs from 2G/3G technology frequencies (mice at 1900 MHz, rats at 900 MHz) and modulations (Global System for Mobiles, or GSM, and Code Division Multiple Access, or CDMA) at increasing intensities (0-10 W/kg) daily for 28 days or two years.[35,36] In the mice, at both durations, there were no differences in outcomes (including cancer) seen between the various exposure groups.[35] In the rats, the NTP concluded that there was "some evidence" (along the spectrum of "clear", "some", "equivocal" or "no" evidence) of malignant schwannoma of the heart in male rats.[36] The increased incidence of cardiac schwannomas occurred in the highest exposure group of male rats at 6 W/kg, equivalent to 75 times the whole body SAR limit (0.08 W/kg) in SC6.[4,36] However, in both the rat and mouse studies, the non-exposed groups had a statistically significant *decrease* in life span compared to exposed groups, in spite of the presence of carcinogenicity in the exposed rat groups.[35,36]

Carcinogenic findings were also seen in a separate study by Falcioni et al., with increased incidence of cardiac schwannoma in male rats after a lifetime of exposure to 1835 MHz GSM-modulated base station signals at whole-body SARs of 0.001, 0.03 or 0.1 W/kg for 19 hours per day.[70] Note that the doses in this study were significantly lower than the NTP study, which makes drawing overall conclusions difficult.

The US FDA released a report in 2020 that evaluated the literature from 2008-2018 on radiofrequency radiation and cancer, which included the US NTP animal studies discussed above, as well as *in vivo* and epidemiologic studies, and concluded that "there is no quantifiable causal link between RFR [radiofrequency radiation] exposure and tumor formation."[37] The ICNIRP also reviewed these findings and concluded similarly to the FDA.[38]

Ocular Effects

Experimental studies from the 1960s and 70s suggested the possibility of cataract formation and other lens effects from RF exposure. However, a significant number of more recent dosimetric studies have not been able to replicate these earlier findings and have not demonstrated adverse ocular effects at exposures at or below the SC6 limits at frequencies up to 5.8 GHz.[23] Comprehensive reviews by both the IEEE[3] and ICNIRP[11] are consistent with the RSC conclusions that the overall evidence does not suggest that RF exposures below SC6 will cause adverse ocular effects.[23] The RSC notes that the effects of RF on visual acuity have not been studied and may be an important area of focus given the high vascularity and presence of stem cells in the retina.[23]

Since this review a few experimental studies focusing on MMW frequencies have been conducted, which are consistent with the above. One study on rabbits found exposures of 10 mW/cm^2 (100 W/m^2) at 95, 75, and 40 GHz did not cause any ocular effects; at higher intensities there was corneal damage,

opacity and edema documented.[71] Note that this level is ten times the SC6 limit of 10 W/m^2 for those frequencies.[4,71] Another study looking at effects of chronic exposure to 60 GHz RF at the SC6 limit of 10 W/m^2 did not find adverse responses to human lens and corneal epithelial cells.[72]

Cardiac Effects

The effects of RF on cardiac function, including heart rate variability, ECG, and blood pressure changes have been studied, and there have been no consistent findings that a causal relationship exists.[24] Any findings that have been seen were associated with exposures well above SC6, and were generally related to thermoregulatory responses rather than direct cardiac effects.[23] The one exception noted by the RSC was a 2013 study that found marked increases in heart rate when a cordless phone base station was moved close to subjects.[73] This study was discordant with the other nine papers reviewed, and the RSC noted methodological flaws and potential for confounding in the study's methodology.[23] The RSC concluded that there remains no conclusive evidence for adverse cardiac effects from RF exposures below SC6.[24]

Since the RSC review, an additional eight experimental human volunteer studies that examined this issue were identified. Four studies measured an effect, and four did not. Of the four that measured an effect, two small studies (N=46, and N=50) observed small changes to the R-R interval on EKGs during brief exposure to RF below SC6.[74,75] The third and fourth studies measured changes in heart rate variability (HRV) when exposed to cellphone RF. One, an experimental study, observed a change when breathing was paced in a non-physiologic manner (1:1 inhalation to exhalation, versus the normal 1:2 ratio of relaxed breathing), making the findings difficult to interpret.[76] The other was an observational study using cellphone billing records as the exposure metric, and noted a decrease in HRV parameters in the highest exposure group.[77] Multiple confounding factors were present that could affect the observations, including M:F ratio (not disclosed), a significant age difference between the experimental and control groups, and a higher BMI in the exposure group.[76-78]

For the negative studies, similar methodologies were carried out, though physiologic measurements were generally less extensive. These experimental studies measured HRV or cardiovascular physiologic parameters in volunteers during various EMF exposures analogous to typical environmental exposures, and observed no difference between exposure and control groups.[79-82] Overall, these additional findings do not suggest a change to the RSC conclusion.

Reproductive Effects

The effect of RF on reproductive outcomes have been studied, with particular focus on testicular function or sperm morphology; the RSC noted that confounding from concomitant heat exposure was often not accounted for and dosimetry poorly quantified.[23] Reviews on female reproductive effects, including adverse pregnancy outcomes, were similarly affected.[23] Overall, multiple reviews have concluded that evidence for RF energy effect on male and female reproduction remain weak and inconsistent.[23] A review by the United Kingdom's Advisory Group on Non-Ionizing Radiation (AGNIR) concludes that in spite of this, negative impacts of low-dose RF exposures on the male reproductive system cannot be ruled out; the RSC similarly calls for further research in this area.[14,23]

Since the RSC review, one other review was found that included two small animal studies not cited in their review.[83] However, the review methodology is not specified and does not appear to use a systematic or weight-of-evidence approach.[83] One of the included studies was a small study of male rats exposed to WiFi transmitters at 2.45 GHz that found changes in cellular-level sperm parameters in the

higher exposure group compared to the low exposure and control groups (9 rats in each group).[84] The second study was of pregnant female mice (N=15) exposed daily to EMF at 50 Hz.[85] The female offspring in the experimental group had oocyte abnormalities compared to the control group.[85] The 50 Hz frequency used is Extremely Low Frequency (ELF), outside the RF spectrum and is not used in 5G technology or any civilian-use telecommunications; thus, it cannot be generalized to this discussion and relevance to human health is unclear.[86]

Neurological Effects

Aside from nerve stimulation known to be related to RF exposure, other neurologic effects have been studied. The RSC reviewed studies that document neurophysiological effects from RF exposure, some of which demonstrate EEG changes in subjects when exposed to RF.[23] They noted that experimental exposure doses varied widely, with some meant to simulate "typical" community doses (e.g., below SC6).[23] Sleep EEG changes seem to have the most reproducibility between studies (particularly those conducted by Niels Kuster and Peter Achermann laboratories), though none document consistent clinically relevant health effects of these findings (e.g., decreased sleep, cognitive changes).[23] A few studies documented small changes in blood-brain-barrier permeability with RF exposure, but this was dependent on doses above SC6 where heating occurred, and is therefore of limited relevance in the community settings.[87] Overall the RSC concludes that there are currently no consistent neurologic effects from expected RF exposures below SC6 defined levels, but that further research is needed to clarify these findings.[23] The SCENIHR report notes that RF studies using EEG as a biomarker of effect suggest the potential for brain activity alteration, though the findings are subtle, and the physiological mechanisms and clinical relevance are unclear.[13]

Developmental Effects

The RSC identified two key reviews on developmental effects of RF from van Rongen et al (2009) and Feychting (2011), both of which found methodological limitations such as confounding and selection bias, preventing a conclusive link between EMF exposure and neurobehavioral or developmental effects in children.[23] They conclude that the current evidence does not suggest that pre- or post-natal exposure to RF below SC6 limits has any neurocognitive sequelae, but echo the WHO's assertion that this should be a priority area of research.[23] The SCENIHR review notes that though there is evidence for teratogenicity in RF exposures that can cause core temperature elevations >1°C in animal studies, there is no consistent evidence for adverse developmental outcomes with exposures below this intensity (i.e., below SC6 defined levels).[13] The SCENIHR report concludes that the evidence for the development of neurobehavioural disorders in children from maternal cellphone use in pregnancy remains weak.[13]

A recent review of 4 large pregnancy cohort studies comprising a study group totalling 55,507 pregnant women and their children, grouped individuals according to self-reported cellphone use (none, low, intermediate, and high) and observed subsequent pregnancy duration, fetal growth, and birth weight.[88] The study found no increased risk of adverse fetal growth outcomes or birth weight, but did identify a small but statistically significant increased risk (HR = 1.04, 95% CI 1.01, 1.07) for birth at lower gestational age with reported intermediate (but not high) cellphone use.[88] A hypothesis for why the highest exposure group did not have a similar risk was not provided.[88]

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Summary of Revisions

Revision Date	Description of Changes	Page number
August 2023	Clarified language relating to Safety Code 6 and how it is used to inform regulation, but is not a regulation itself.	1-8

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