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#### **Definition**

Magnetic fields are generated by the movement of any electrical charge. A continuous electric current passing through a conductor creates a static magnetic field, while an electric current changing in time creates a variable magnetic field, which radiates electromagnetic waves spreading around the surrounding space at light speed. These electromagnetic fields enter the living tissue but are known as non-ionizing radiation since they are weak and unable to break molecular bonds. Metals such as iron, zinc, manganese, and cobalt are sensitive to electromagnetic fields that may exert their effects on proteins and cellular components containing these metallic elements.

# **Characteristics**

Few environmental issues are as contentious as the question of whether exposure to electromagnetic fields affects biological systems. Considering the exponentially increasing widespread use of electromagnetic radiation-generating applications such as radio, television, wireless devices, and cell phones, the continuing change in the frequencies used, the health hazard implications of any connection between electromagnetic fields, and the cancer risk have raised a growing interest in the potential biological effects of electromagnetic fields on the mammalian cell growth, viability, and response to genotoxic injury. This topic is still a subject of repeated argument, and caution in the interpretation of the effects of static and variable magnetic fields on cellular behavior and individuals' health needs to be claimed. A measurable magnetic field is created even by the residential electric current. It is noteworthy that we are pervaded by the Earth's static magnetic field that is hundreds of times greater than the low-frequency electromagnetic fields created by current within homes.

#### **Epidemiological and Clinical Evidence**

The first connection between human disease and electromagnetic fields was suggested by the observation of a higher incidence of cancer in children (childhood cancer) living near power distribution lines. Afterward, major power lines have been held responsible for the occurrence of different cancer varieties. Results of different studies of a possible link between exposure to electromagnetic fields and childhood cancer, namely, leukemia, have been rather inconsistent. One large study found no association between electromagnetic field exposure and an increased

risk of childhood leukemia, in contrast to previous reports showing that the exposure to electromagnetic fields resulted in nearly a 20 % increase in the risk of leukemia. This case-control investigation (case-control association study) did not find a significant link between the risk of childhood leukemia and the actual measurement of magnetic fields in children's current and former homes, including homes their mothers lived in during pregnancy of the affected subjects. Electromagnetic field exposure has also been associated with the risk of breast cancer, mainly in men. Epidemiological studies have shown that in industrialized countries, where the electromagnetic field-generating devices are in use on a large scale, breast cancer risk is higher. It has been suggested that electromagnetic field exposure might promote breast neoplasm through inhibition of melatonin release. Different occupational epidemiological studies have shown an increased incidence of breast neoplasm in women employed in occupations with high electromagnetic field exposure as well as in male electrical workers. However, other investigations, not producing any significant correlation, failed to confirm these suggestive data from occupational studies. In a large Swedish cohort study, an  $\sim 10$  % increase in the risk of cancer was documented in people in the medium- and highexposure levels. Several types of cancer, including skin, digestive, respiratory, reproductive, and urinary organs, were linked with occupational magnetic field exposure, suggesting an involvement of the endocrine and immune systems. Discrepancies in epidemiological studies dealing with this matter have involved different estimates of electromagnetic field exposure, measurement, and characteristics; the statistical analysis performed with data obtained in such epidemiological reports is another Achilles heel, and considerable biases can create misleading conclusions. Higher exposure has been associated with an increase in the cancer risk even though care needs to be taken in drawing any conclusion, because no dose-response relation has been documented so far. New technologies have been introduced on a large scale only in more recent years, and the possible short lag

period between exposure and disease manifestation needs to be considered when examining the available data. Children are increasingly heavy users of communication sources (mobile phones), and they are likely to accumulate many years of exposure during their lives. They should be thoroughly monitored in the study population to detect possible effects involving long induction periods or effects from long-term exposure.

### **Experimental Evidence**

In case of high-frequency magnetic fields, biological effects and health risks are related to the thermal effect associated with sources emitting fields high enough to cause a significant temperature rise in living tissue. Carcinogenesis is a multistep process of accumulating mutations and promoting events. It has been proposed that electromagnetic field exposure might enhance the effects of other carcinogens, provided that both exposures are chronic. The potential for genotoxicity of electromagnetic fields has been investigated, and several negative studies in several exposure categories have presented sound and independent, reproducible data. Using in vivo animal models of carcinogenesis, the assessment of the potential carcinogenic activity of electromagnetic fields has yielded negative results in different studies, while using the rat mammary carcinoma model results seem to be conflicting. According to available data, it is unlikely that long-term exposure to electromagnetic fields is carcinogenic per se in animal models. However, a promoting effect in the development of cancer under certain exposure conditions cannot be ruled out. Since exposure conditions vary widely in the different models thus far proposed, independent replication of experimental results is absolutely crucial. Exposure to electromagnetic field, alone or in combination with ionizing radiation, appears to induce an insult at the cellular level, to inhibit DNA synthesis and the growth of human tumor cell lines in vitro. However, controversies still exist about the possibility that electromagnetic fields may influence tumor promotion. Different in vitro studies have failed to demonstrate any detectable effect of electromagnetic fields on the

rate of DNA synthesis and cultured cell growth. Moreover, exposure of cultured mammalian cells to electromagnetic fields has not resulted in the production of detectable DNA lesions and has not affected intracellular ATP levels, suggesting that electromagnetic fields are not genotoxic and cytotoxic. On the other hand, investigating the genotoxic potential of electromagnetic fields using in vitro experiments, statistically significant and suggestive positive results have been reported. Following electromagnetic field exposure, enzymatic activity induction, DNA mutation in human and nonhuman cells, and DNA strand breaks in rat brain cells have been demonstrated. The static magnetic field has been shown to induce a remodeling and differentiation of human neuronal cells in the absence of any alteration of DNA, thus ruling out a direct effect of the magnetic field on DNA stability. Investigating the effects of a static magnetic field on the ability to proliferate of human breast cancer cells in vitro, it has been observed that magnetic field exposure only temporarily slows down cellular growth, which then eventually fully recovers. The reduced cell growth caused by the magnetic field could be explained by a temporary effect on some cellular metabolic events leading to the reduced DNA synthesis. Alternatively, it could be ascribed to a transient cellular differentiation, since induction of differentiated phenotype often correlates with decreased cell proliferation. These results are consistent with the observation that magnetic field induces time-dependent developmental effects on the process of differentiation of the chick cerebellar cortex. Human skin fibroblasts exposed to electromagnetic fields, generated by mobile phones, show alterations in cell morphology and increased expression of mitogenic signal transduction genes (MAP kinase kinase 3 [MAP kinase], G2/mitoticspecific cyclin G1 [cyclin G-associated kinase]), cell growth inhibitors (transforming growth factor beta [transforming growth factor]), and genes controlling apoptosis (bax) [apoptosis signaling]; a significant increase in DNA synthesis and intracellular mitogenic second messenger formation [signal transduction] matches the high expression of MAP kinase family genes. A recent report (Blank and Goodman 2011) proposes the interesting interpretation of DNA as an antenna able to respond to electromagnetic fields in different frequency ranges. The authors found that electromagnetic field interactions with DNA were similar over a range of non-ionizing frequencies, from extremely low to radio frequencies, and concluded that DNA shows the functional characteristic of a fractal antenna, since it is endowed with two structural characteristics of fractal antennas, i.e., electronic conduction and selfsymmetry. This concept of DNA as an antenna opens fascinating perspective that goes far beyond the field of oncology. In fact, if an antenna is capable of receiving signals, i.e., to interact with electromagnetic fields, it is conceivable that it is also capable of sending signals. The existence, nature, and meaning of such hypothetical signals transmitted by DNA are not yet even imagined, but we feel confident that this field of research will see important developments in the future. In fact, endogenous electromagnetic fields are continuously generated by electrically active cells within a body, and the intensity of such electromagnetic fields is enough to alter gene expression. For example, it was demonstrated that the myoelectrical activity of the gut induces the expression of heat-shock protection mechanisms in the cells of gut epithelium as well as in gastrointestinal microorganisms thus de facto altering the delicate balance of the gut microbiome (Laubitz et al. 2006). Considering that the human microbiome is involved in the development and function of all other organs and systems and most notably the immune system (Palm et al. 2015), we hypothesize that the alteration of the microbiome may be one of the mechanisms through which electromagnetic fields, both endogenous and exogenous, exert their biological effects. Thus, the effects of electromagnetic fields on the human microbiome open a new perspective in assessing the risks for health and in preventing them. So far, most of the research was concentrated on assessing the effects of electromagnetic fields on those areas of the body that were exposed to their energies. In other words, all the effects of electromagnetic fields on human health were ascribed to their interaction with the

human cells of our bodies. However, since we have learned that electromagnetic fields, even of minimal intensity such as the endogenous electromagnetic fields, modify microbiome, their effects might be much more complex and far ranging. In fact, microbes and the microbiome may amplify or mitigate carcinogenesis, responsiveness to cancer therapeutics, and cancer-associated complication (Garrett 2015), and, therefore, electromagnetic fields modifying the microbiome may interfere with all such cancer-related responses. It is foreseeable that the development of functional foods containing probiotics for the prevention and treatment of cancer will have to take into account the effects of endogenous as well as exogenous electromagnetic fields on the human microbiome.

#### **Clinical Relevance**

Although some studies have given no consistent or convincing evidence for a causal relation between electromagnetic fields and cancer, other reports suggest that the exposure to electromagnetic fields brings about a weak increase in the risk estimates of neoplasm. In general, many of the earlier studies lack statistical power and show methodological deficiencies. In recent years, however, larger studies and meta-analyses epidemiological describing an association between exposure to different types of electromagnetic fields and various types of cancer were conducted with the goal of overcoming these shortcomings and providing precautionary public health protection strategies. In fact, ever increasing use of wireless devices and cell phones prompted researchers to further investigate the association between commonly encountered electromagnetic fields and most common tumors. For example, a recent review on the association between childhood leukemia and frequency magnetic fields concluded that still there is no clear indication of harm at the field levels analyzed and that if the risk is real, its impact is likely to be small. This notwithstanding, according to the authors, "a precautionary approach suggests that low-cost intervention to reduce exposure is appropriate." Another recent review analyzed various adverse health outcomes

associated with cell phone use, describing the epidemiology of tumors such as of glioma, acoustic neuroma, meningioma, testicular and salivary gland tumors, malignant melanoma of the eye, intratemporal facial nerve tumor, breast cancer, and non-Hodgkin lymphoma. In this review, the authors conclude that a precautionary principle should be used and invite health authorities to revise current standard of exposure to microwave during mobile phone use. We are sure that this field will be the object of many more investigations, and therefore this entry will be continuously updated. At this point in time, however, on the basis of available evidence, we too are convinced that a precautionary principle should be used, in particular, considering that millions people use cell phones, with children among the heaviest users. Until further evidence is collected, we believe that the safety recommendations put forward by Dubey et al. (2010) should be taken into consideration.

#### **Cross-References**

- ► Adaptive Immunity
- ► Genomic Instability
- ► Gut Microbiota
- ► Mutation Rate

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