Science of the Total Environment 454–455 (2013) 393–400

Contents lists available at SciVerse ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

Reaction of the immune system to low-level RF/MW exposures

Stanislaw Szmigielski *

Military Institute of Hygiene and Epidemiology, Warsaw, Poland

A R T I C L E I N F O

Article history:
Received 15 June 2012
Received in revised form 6 March 2013
Accepted 11 March 2013
Available online 9 April 2013

Keywords:
Radiofrequency/microwave (RF/MW) radiations
Low-level radiation
Immune reactions
Cancer risks

A B S T R A C T

Radiofrequency (RF) and microwave (MW) radiation have been used in the modern world for many years. The rapidly increasing use of cellular phones in recent years has seen increased interest in relation to the possible health effects of exposure to RF/MW radiation. In 2011 a group of international experts organized by the IARC (International Agency for Research on Cancer in Lyon) concluded that RF/MW radiations should be listed as a possible carcinogen (group 2B) for humans. The incomplete knowledge of RF/MW-related cancer risks has initiated searches for biological indicators sensitive enough to measure the “weak biological influence” of RF/MWs. One of the main candidates is the immune system, which is able to react in a measurable way to discrete environmental stimuli.

In this review, the impacts of weak RF/MW fields, including cell phone radiation, on various immune functions, both *in vitro* and *in vivo*, are discussed. The bulk of available evidence clearly indicates that various shifts in the number and/or activity of immunocompetent cells are possible, however the results are inconsistent. For example, a number of lymphocyte functions have been found to be enhanced and weakened within single experiments based on exposure to similar intensities of MW radiation.

Certain premises exist which indicate that, in general, short-term exposure to weak MW radiation may temporarily stimulate certain humoral or cellular immune functions, while prolonged irradiation inhibits the same functions.

Contents

1. Introduction

Radiofrequency (RF) and microwave (MW) radiation, which are part of the electromagnetic spectrum at frequencies of 0.1–300,000 MHz, have been used in the modern world for many years, particularly in the areas of radio-communication and radio-location. The rapidly increasing use of cellular phones, called recent attention to the possible health risks of RF/MW exposures. In 2011 a group of international experts organized by the IARC (International Agency for Research on Cancer in Lyon) concluded that RF/MW radiations should be listed as a possible carcinogen (group 2B) for humans (Baan et al., 2011).

The absorption of large amounts of RF/MW energy results in the development of thermal effects, with the main determinants being specific absorption rate (SAR) and power flux density. Many other physical parameters of exposure have been reported to be important for non-thermal biological effects, which are induced by MWs at intensities well below any detectable limit. Reports of non-thermal effects started appearing in the 1970s and have been frequently reviewed (Adey, 1999; Blackman, 1992; Belyaev et al., 2000; Betskii et al., 2000; Banik et al., 2003; de Gannes et al., 2009; Grigoriev et al., 2003, 2010; Grigoriev, 2004; Lai, 2005; Jauchem, 2008; Pakhomov et al., 1998). Some studies have reported stress response in exposed cultured cells (Kwee et al., 2001; Leszczynski et al., 2002; Blank and Goodman, 2004, 2009; Czyż et al., 2004). In other studies, no effects of non-thermal microwaves were observed (Meltz, 2003).

After 30 years of research into this area, there is still insufficient information on the specific biological influence of non-thermal intensity of RF/MW radiation (Jauchem, 2008). According to WHO Environmental

* Tel.: +48 603920360.
E-mail address: szmigielski@wihe.waw.pl.

0048-9697/$ – see front matter © 2013 Published by Elsevier B.V.
http://dx.doi.org/10.1016/j.scitotenv.2013.03.034

Health Criteria (1993) nonthermal intensities of MWs are presently recognized as a “weak factor of biological influence”. This imprecise description has initiated searches for biological detectors sensitive enough to measure the “weak biological influence” of MWs. One of the main candidates is the immune system, which is able to react in a measurable way to discrete environmental stimuli. As an important part of the homeostatic neuro-endocrine network of many organisms, the immune system is crucial for protection against various pathogens as well as for the maintenance of immune tolerance towards the organism itself. The role of the immune system in development of cancer cells, as well as in modification of course of neoplastic diseases is well established (for review, see Deschaux and Kahn, 1995; Abès and Teillaud, 2011; Sun et al., 2010, 2011). These different reactions of the immune system can be investigated using *in vitro* or *in vivo* tests to evaluate the possible influences of external stimuli (*e.g.* drugs or physicochemical factors). Unfortunately, available data on the influence of MWs on the immune system are fragmentary, report on changes of few immune functions, mainly phagocytosis, lymphocyte proliferation, or antibody production, and are frequently controversial or not confirmed by the results of repeated experiments (Black, and Heynick, 2003). Some authors (for review, see Stavrulakis, 2003), report immunosuppressive or immunostimulatory phenomena in animals with long-term exposure to low-level MW fields.

Recently, Jauchem (2008) reviewed the effects of RF/MW radiation on the immune system and concluded that although both positive and negative findings were reported in some studies, in a majority of instances no significant health effects were found. However, most studies had some methodological limitations. Some changes in immunoglobulin levels and in peripheral blood lymphocytes were reported in different studies of radar and radio/television-transmission workers (Moszczyński et al., 1999).

Due to variations in results and difficulties in comparing presumably exposed subjects with controls, however, it is difficult to propose a unifying hypothesis of the immune system effects. Although subjective symptoms may be produced in some sensitive individuals exposed to RF/MWs, there were no straightforward differences in such symptoms between exposed and control subjects in most epidemiological and laboratory studies. Consistently, strong associations were not found for RF/MW exposure and adverse health effects. The majority of changes relating to each of the diseases or conditions were small and not significant (Tuschl et al., 1999).

Even the epidemiological investigations of workers exposed to MW radiation did not confirm the existence of measurable shift in the immune status of investigated populations, despite some observations on abnormalities in single immune parameters in several individuals (*e.g.* changed number of blood lymphocytes, lowered level of serum immunoglobulins or weaker response of lymphocytes to mitogens) (Johansson, 2009). In the available literature no reports exist on the complex assessment of immune phenomena under RF/MW influence, all investigations were aimed to evaluate only selected, fragmentary reactions of the system or selected types of immune cells.

Some changes in immunoglobulin levels and in peripheral blood lymphocytes were reported in different studies of radar and radio/television-transmission workers. Due to variations in results and difficulties in comparing presumably exposed subjects with controls, however, it is difficult to propose a unifying hypothesis of the immune-system effects (Jauchem, 2008).

Moszczyński et al. (1999) assessed the concentrations of immunoglobulins and T lymphocyte subsets during occupational exposures to MW radiation. In workers of retransmission TV center and center of satellite communications an increased IgG and IgA concentration and decreased count of lymphocytes and T8 cells were found. However, in radar operators IgM concentration was elevated and a decrease in the total T8 cell count was observed. The different behaviors of examined immunological parameters indicate that the effect of MW radiation on the immune system depends on character of an exposure. Disorders in the concentrations of immunoglobulins and in the T8 cell count did not cause any clinical consequences. Consistently, strong associations were not found for RF/MW exposure and adverse health effects.

At the present state of knowledge it is, therefore, not possible to conclude about the specific immunotropic potencies of MW radiation, as the assessment of the immunotropic potency requires a general insight into the whole complex immune network, taking in advance the determination of immune status of the host or the investigated cellular population prior to the MW exposure.

The final effect of exposure of biological material to MW radiation depends on the physical properties of applied electromagnetic field on the one side, and on the functional state of exposed living target on the other. The RF/MWs used in different experiments may differ in countless dosimetric elements, including wavelength and frequency, pulse modulation, intensity of RF/MW field influencing the degree of specific absorption rate (SAR) and duration of the exposure. The functional characteristics of biological material, *e.g.* blood mononuclear cells mainly used for *in vitro* studies, are even more complex. The RF/MW exposure may affect the cell at different levels of its structure: the surface receptors changing their distribution and conformation, the cellular membrane changing its rigidity and permeability, mitochondrial metabolic activity, transcription and translation processes or several of these elements at different intensities.

2. Immunotropic effects of RF/MW exposure in *in vitro* studies

The mononuclear cells isolated from peripheral blood mononuclear cell (PBMC) remain in their most stable and inert metabolic state, the G0 phase of cell cycle, in which the cell represents low sensitivity to external influence. When the cells cultured *in vitro* enter more active phases of cell cycle (Gl, S, G2, M), its sensitivity to influence of RF/MW radiation may change significantly. *E.g.*, exposure of cells to RF/MWs during the culture, although methodically much more difficult, may deliver better insight into the potential immunotropic effects of the exposure.

One of the best methods of evaluation of immunotropic influences of RF/MWs administered *in vitro* is the system of microcultures of PBMC, representing *in vitro* the abilities of the immune system *in vivo*. The advantages of the method are accessibility of human cells, donor safety, and wide repertoire of immune tests which can be performed (Stankiewicz et al., 2006, 2010).

PBMC, both human and animal, was also frequently used in search of genotoxic effects of RF/MW radiation, changes in DNA/RNA molecules or efficiency of DNA repair mechanisms under influence of different protocols of RF/MW exposures.

Here, immunotropic effects reported in PBMC exposed *in vitro* prior to or during culture will be discussed.

In one of the early studies Cleary et al. (1990) studied human peripheral blood exposed or sham-exposed *in vitro* for 2 h to 27 or 2450 MHz RF radiation under isothermal conditions (37 ± 0.2 °C). Immediately after exposure, PBMC was separated from blood by Ficoll density-gradient centrifugation and cultured for 3 days at 37 °C with or without mitogenic stimulation by PHA (phytohemagglutinin). Lymphocyte proliferation was assayed at the end of the culture period by 6 h of pulse-labeling with ^{3}H-thymidine (^{3}H-TdR). Exposure to radiation at either frequency at specific absorption rates (SARs) below 50 W/kg resulted in a dose-dependent, statistically significant increase of ^{3}H-TdR uptake in PHA-activated or unstimulated lymphocytes. Exposure at 50 W/kg or higher suppressed ^{3}H-TdR uptake relative to that of sham-exposed cells. There were no detectable effects of RF radiation on lymphocyte morphology or viability.

A couple of years later Cleary et al. (1996) published another paper on the effects of RF/MW exposure on cytolytic T lymphocytes. To obtain insight regarding interaction mechanisms, they investigated the effects of RF radiation on interleukin 2 (IL-2)-dependent