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Review

SYSTEMIC EFFECTS OF RADIOFREQUENCY ELECTROMAGNETIC FIELDS (REVIEW). SPLEEN, EXCRETORY SYSTEM, SKIN, BONE SYSTEM

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Currently, isolated publications appear to report the results of experimental and monitoring studies that provide solid evidence of the spleen, excretory system, skin and skeletal system being sensitive to effects produced by radio frequency electromagnetic fields (RF EMF) in a wide frequency range (from 900 MHz to 2.45 GHz). Since health and normal functioning of these organs and systems are the most important conditions for vital activity of the body, systematization of the available data determines the relevance of this review.

Analysis of the available results obtained by experimental studies has showed that numerous histopathological changes are registered in the spleen (for example, in the white pulp), excretory system (in the kidneys as degeneration of glomeruli and vessels, vacuolization of tubules, fibrosis, etc.; in the bladder as cell apoptosis, etc.), and skeletal system (decreased bone density) upon repeated exposure to RF EMF of various frequency ranges.

A special place belongs to studies with their focus on RF EMF effects in the 5G range on the skin, which is currently a new critical organ of its impact. The studies have reported acceleration of skin aging, pigmentation disorders, mitochondrial stress in fibroblasts and keratinocytes.

Negative changes in the spleen were recorded in studies that applied electrophotonic visualization during short-term exposure to RF EMF on adolescents.

Epidemiological studies indicate that the duration of conversations using a cell phone increases the risk of kidney disease and decreased bone density, detected in active mobile communication users, especially when they carry a gadget in trouser pockets.

The obtained results are relevant and have practical significance for children and adolescents who are currently active users of cellular communications.

Summarizing the available data on the negative impact of RF EMF not only on the nervous system, but also on other systems of the body, we can state its systemic effects.

In this regard, as noted in a number of foreign studies, there is a need to revise the previously adopted FCC and ICNIRP limits for the impact of RF EMF on the human body. The expert society should concentrate its future efforts on developing updated safe RF EMF limits and probable future revision of sanitary rules and norms in accordance with new identified health risks primarily for children and adolescents as a population group, which is the most susceptible to any environmental exposure.

We believe that guidelines should be developed for implementing relevant culture for safe use of up-to-date gadgets for children and adolescents including predominant use of wire-based hands-free kits (not Bluetooth), speakerphones, as well as messengers used for subsequent exchange of text and multimedia messages, and not carrying a gadget 'on oneself' (in shirt or trousers pockets).This will allow a significant reduction in negative effects produced by RF EMF, in particular, by mobile phones / smartphones, on the growing generations' health.

Keywords: *radio frequency electromagnetic fields, 5G, cellular communications, spleen, excretory system, skin, skeletal system, young animals, children, adolescents.*

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Currently, isolated publications appear to report the results of experimental and monitoring studies that provide solid evidence of the spleen, excretory system, skin and skeletal system being sensitive to effects produced by radio frequency electromagnetic fields (RF EMF) in a wide frequency range (from 900 MHz to 2.45 GHz).

Long-term effects of RF EMF on the ***spleen*** were investigated using two-month old female C57BL/6 mice [1], adult albino mice [2], and young Wistar rats [3]; also, subtle energy levels were identified by the electrophotonic imaging technique in 61 healthy adolescents (22 boys and 39 girls) aged 17.40 ± 0.24 who studied in educational organization in Bangalore [4].

Experimental research established that exposure to 900 MHz radiation (2 h/day for 1, 2 or 4 weeks to an SAR of 1 or 2 W/kg) with expected effects on lymphocytes in the spleen of female C57BL/6 mice did not lead to any substantial changes in the T- or B-lymphocyte count. The authors believe that clinically relevant effect on the immune system is unlikely to occur upon the given duration of RF RMF exposure [1]. Enlarged white pulp with increased sinusoidal spaces was established in spleen sections upon exposure to Nokia 1112 radiation (850/1900 Mhz) (1 h/day, 10 days) when compared to the control group. Some white pulp of tissue sections appeared to be fused upon exposure 12h/day for 10 days. This disorganization was due to hyperplasia of the lymphoid tissue [2].

Enlarged sinusoids and disappearing central vacuoles in white pulp were found by P. Chauhan et al. in an experiment on young albino Wistar rats upon exposure to 2.45 GHz (2 h/day, 35 days; power density was 0.2 mW/cm^2; SAR, 0.14 W/kg) [3].

A statistically significant decline in subtle energy levels in the spleen was detected by the electrophotonic imaging technique after a short RF EF exposure on adolescents [4].

In addition to the established adverse effects produced by RF EMF of various frequencies on the spleen as a part of the immune system, as shown above, histopathological changes have been detected in the excretory system, namely, the ***kidneys***.

A study on effects produced by RF EMF (1800 MHz) from telecommunication masts (1.40 W/cm^2 at 24-m distance, 5 weeks) established histopathological changes in the liver, heart, testicles as well as kidneys of young rats: hyperchromatic nuclei, gradual loss and degeneration of flattened squamous epithelial cells lining the wide Bowman space, and glomerule degeneration with concomitant areas [5].

As revealed by literature analysis, RF EMF effects on the ***kidneys*** of experimental animals and humans have been examined in a wide frequency range, between 900 MHz and 2.45 GHz.

Exposure to 900 MHz was found to induce the following changes in ***experimental animals'*** kidneys: interstitial inflammation, hemorrhage and stagnation in glomeruli and vessels (1, 2 and 4 h/day, 30 days, 12-week old Sprague Dawley rats) [6]; dilatation and vacuolization in the distal and proximal tubules, degeneration in glomeruli and an increase in cells tending to apoptosis were observed in kidney tissue (1 h/day in postnatal days 22–59 inclusively) [7]; the mean volume of the cortex, medulla, proximal and distal tubules increased significantly in the EMR groups compared to the control ($p < 0.01$) (60 min/day for a period of 21 days, animals aged 11–12 weeks) [8]; the authors reported hemorrhage in glomeruli, vacuolization and irregularity in the proximal and distal tubular epithelium, diffuse glomerular degeneration and edema, occasional degeneration in Bowman capsules, hemorrhage in the medullary region, disturbed nucleus location and morphology, and tubular edema in the cortex (1 h/day on the 35–59th day after birth) [9].

However, a study by A.L. Monfared et al. did not report any morphometric, ultrastructural or light microscopic changes in the kidneys upon exposure to 915 MHz (4 h/day for 60 days, mice aged 8–9 weeks) [10].

B. Al-Glaib et al., using Nokia 1112 (850–1900 MHz) for 10 days, compared histopathological changes in the kidneys of albino mice (aged 10–12 weeks) under two daily exposure modes, 1 h/day and 12 h/day accordingly. Upon 1-hour exposure, the authors established mononuclear leukocytic infiltration

between the kidney tubules in addition to enlargement of some tubules; some glomeruli were atrophied and some kidney tubules vacuolated. Upon a longer exposure (12 h/day), the kidney sections were found to have areas with some stagnated glomeruli, some vacuolated kidney tubules and some inflammatory areas between the kidney tubules [2].

Histopathological changes were compared in a study by R. Bedir et al. (2100 MHz, 6 and 12 h/day, 30 days, Sprague Dawley rats aged 4–5 months); as a result, the authors revealed more enlarged Bowman capsules and kidney tubules, loss of the brush border in proximal tubules, vacuolization in the tubule epithelium and glomerule structures as well as fibrosis in inter-tubular areas in the daily 6-hour exposure group. Similar results were obtained for the 12-hour exposure group; however, they were more pronounced than in the 6-hour exposure group [11].

Shrunk glomeruli (mostly atrophied) and abnormal kidney tubules (cytoplasmic vacuolization with pyknotic nuclei was established in epithelial cells) were reported by P. Chauhan et al. upon exposure to 2.45 GHz (2 h/day for a period of 35 days; power density was 0.2 mW/cm^2; SAR, 0.14 W/kg) [3].

RF EMF effects were studied not only on kidney tissues but also on the bladder. In this respect, two studies conducted in 2010 and 2014 by N. Gurbuz et al. should be mentioned; both studies involved assessing micronuclei accumulation in the bladder cells. However, neither study identified any changes either upon exposure to 1800 MHz (20 min/day, 5 days a week for a month) [12], or upon exposure to 1800 MHz (30 min/day, 6 days a week for a month), or upon a similar exposure to 2100 MHz for one month and 2 months.

However, later S. Türedi et al. revealed degeneration in the transitional epithelium and stromal irregularity and an increase in cells tending to apoptosis in the bladder tissue upon exposure to 900 Mhz (1 h/day on postnatal days 22–59 inclusively) [7].

Therefore, experimental studies have established various adverse impacts on the kidney and bladder tissue upon exposure to RF EMF of various frequencies.

In addition to experimental research, effects on adolescents (aged 17.40 ± 0.24 years, both sexes) produced by a short-term RF EMF exposure (15 minutes) was examined using the electrophotonic imaging technique; the study revealed a decline in subtle energy levels in the right kidney [4].

We believe epidemiological studies by Y. Zhang et al. to be quite interesting; the authors analyzed progression of chronic kidney disease (CKD) depending on how actively patients (aged 37–73 years) used a mobile phone. MP use for longer than 30 min/day was found to increase a risk of new developing CKD [13].

Both experimental results and data reported by H. Bhargav et al. and Y. Zhang et al. are likely to indicate, among other things, that carrying a mobile phone / smartphone in back pockets can have a negative effect on the excretory system functioning.

Skin is known to be the largest organ in the body. It performs multiple functions such as protecting organs and tissues from mechanical damage, effects of ultraviolet radiation, malignant bacteria and adverse chemicals; participating in thermal regulation; being an organ that provides tactile, pain and temperature sensitivity; maintaining extraction of urea and mineral salts with sweat; and many others. Many researchers believe skin to be the primary target upon EMF exposure. This is especially relevant nowadays since skin is really becoming the primary target organ due to implementation of new telecommunication technologies (5G) [14, 15].

In this respect, some attention should be paid to ***in vitro*** studies by K. Kim et al., J.H. Kim et al., L. Patrignoni et al. and F. Havas et al. [16–19]**.**

K. Kim et al. investigated the effects of EMFs with long-term evolution (LTE, 1.762 GHz) and 5G (28 GHz) bandwidth on skin pigmentation in vitro. Murine and human melanoma cells (B16F10 and MNT-1) were exposed to either LTE or 5G for 4 h per day, which the authors considered the upper bound

of average smartphone use time. It was shown that neither LTE nor 5G exposure induced significant effects on cell viability or pigmentation. The authors concluded that exposure to LTE and 5G EMFs may not affect melanin synthesis or skin pigmentation under normal smartphone use condition [16].

J.H. Kim et al. used HaCaT human keratinocytes in their study with its aim to examine exposure to 1760 MHz RF-EMF (4.0 W/kg specific absorption rate for 2 h/day during 4 days). The study reported an increase in production of reactive oxygen species (ROS), which can ultimately lead to skin cells ageing. However, the authors did not establish any impairment in cell growth or viability [17].

Guided by an assumption that subsequent exposure to 5G signal could alter the capacity of UV-B to damage skin cells, L. Patrignoni et al. evaluated the impact of 5G-modulated 3.5 GHz radiofrequency (RF) EMF (SAR is 0.25, 1 and 4 W/kg for 24 hours) on mitochondrial stress in human fibroblasts and keratinocytes. The authors found a statistically significant reduction in mitochondrial ROS concentration in fibroblasts exposed to 5G signal at 1 W/kg, which statistically significantly enhanced the effects of UV-B radiation specifically in keratinocytes at 0.25 and 1 W/kg. Still, no effect was found on cell viability, mitochondrial membrane potential or apoptosis in any cell types, both separately and after UV-B exposure [18].

F. Havas et al. examined effects of a short-term (1-hour) exposure to 6GHz on primary normal human epidermal keratinocytes. Clear effects on keratinocyte function were observed: increased key inflammatory cytokine IL1-α; reduced collagenase inhibitor TIMP1; increased wound healing/differentiation facilitator ANGPLT4; and increased SA100A9, involved in immune recruitment during injury. In addition, the authors established that the effects per all four markers became less pronounced upon a longer exposure, which can be explained by adaptation. Nevertheless, the authors believe their findings to allow concluding that 5G-ratiation can have an effect on skin appearance inducing premature ageing and / or early or too marked signs of ageing (wrinkles or pigment disorders) [19].

In addition to the foregoing effects produced by 5G on skin cells, it is worth noting that multiple sudoriferous glands can also be affected by RF EMF. In particular, S.R. Tripathi et al. and N. Betzalel, using optical coherent tomography, shoed in their study that the ends of the sweat ducts had a helical structure and could be considered a helical antenna able to increase the skin specific absorption rate in extremely high frequency band [20, 21].

In our opinion, all the foregoing findings give evidence of skin being a new critical organ under exposure to 5G. This circumstance should be taken into account when new telecommunication technologies (not only 5G but also 6G) are being widely implemented.

By now, it has been shown that stimulation with an impulse electromagnetic field is a promising, non-invasive and safe physiotherapeutic strategy to accelerate ***bone*** recovery [22], but not a radio frequency band is used in this case.

However, several researchers conducted experiments to investigate RF EMF effects on bone tissue in a wide frequency range between 900 MHZ and 2.45 GHz, including bone tissue recovery after fractures. Their findings are rather ambiguous.

Thus, in 2011, A. Aslan et al. reported that exposure to 900 MHz (30 min/day, 5 days a week for 4 and 8 weeks; average power intensity was 1.04 mW/cm^2 and SAR = 0.008 W/kg) led to a decline in bone density in rats, both in the lumbar spine and in the shaft of femur. However, the authors concluded that this exposure did not have any substantial influence on rat bone tissue since the difference from the control was ‘not statistically significant’ [23].

Later, the same authors’ team made an effort to investigate use of radiofrequency band to treat fractures in young rats upon exposure to 900 MHz (30 min/day, 5 days a week for 8 weeks) [24], and 1800 MHz (30 min/day for 5 days) [25]. In the first case, negative results were obtained per x-ray, histological and manual biomechanical indicators together with an

established decline in mineralization. In the second case, no changes were found against the control.

Nevertheless, M. Durgun et al. exposed mature rabbits with mandibular fracture to 2100 MHz (3 h/day, 28 days); histopathological studies revealed better fracture healing in the experimental group against the control with a simultaneous increase in bone strength [26].

At the same time, it should be noted that most studies report negative RF EMF effects on bone tissue.

Thus, exposure to RF EMF 900 and 1800 MHz (30 min/day, 28 days) reduced bone density in rats [27]. Similar results were obtained upon the same exposure and its duration by E. Cicek et al. [28].

Significant morphological and biomechanics alterations on mechanical properties in the rat cortical femur were found by A. Akar et al. upon RF EMF exposure (about 12 V/m, 0.079 W/kg) in 2.45 GHz (2 h/day, 21 day) [29].

A study by H. Bektas et al. reported a declining value of the Young's modulus (it is a mechanical property of solid materials that measures the tensile or compressive stiffness when the force is applied lengthwise or under elastic strain) and other bone tissue properties upon exposure to RF EMF (900, 1800 and 2100 MHz; 2 h/day, 5 days a week for a month) [30].

Still, a study by T. Atay et al. involved exposure to 1800 MHz (30 min/day, 5 days a week for 4 weeks with the power equal to 1 ± 04 mW/cm^2). At the end, bone mineral density (BMD) of all rats was measured by scanning with Dual Energy X-ray Absorptiometry. Although a small increase in lumbar BMD and a decrease in BMD of the femur was determined in the group affected by 1800 MHz EMF, a significant difference was not found ($p > 0.05$) [31].

Ambiguous results were obtained by K. Sieroń-Stołtny et al. The authors concluded that concluded that electromagnetic field generated by Nokia 5110 (900 MHz; 22 h/day for 28 days; SAR = 0.69 W/kg) did not have a direct impact on macrometric parameters of bones; however, it altered the processes of bone mineralization and the intensity of bone turnover processes and thus influenced the mechanical strength of bones [32].

Negative changes in bone tissue were detected not only in experimental research.

Using Dual Energy X-ray Absorptiometry, several authors established negative change in bone tissue in active mobile phone users.

In particular, M. Cidem et al. investigated forearm mineral bone density in male and female mobile phone users aged 20–35 years. The user group included 86 men and 97 women; the control one, 14 men and 66 women. Mineral bone density was found to be significantly lower in mobile phone users. Binary logistic regression analysis indicated that a risk for osteopenia was found to be higher in females than and in MP users than MP non-users [33].

Earlier, T. Atay et al. and F.D. Saraví et al. investigated bone mineral density of the human iliac bone wings in male mobile users who wore their phones close to this area. In the first case, (150 men aged 21–57 years) revealed a decrease in bone mineral density of the human iliac bone wings but there was no statistically significant difference from the control [34]. In the second case, the authors assessed differences in bone mineralization in the right and left hip of healthy male adult volunteers who were either nonusers of mobile phones ($n = 24$) or users who carried the phone close to the right hip, for at least 1 year ($n = 24$). The authors found that mobile phone users, but not non-users, had lower BMD at the right trochanter ($P = 0.027$) and lower BMC at the right trochanter ($P = 0.014$) and right total hip ($P = 0.039$). The authors believed that these findings could also be relevant for children (especially if they carry their mobile phones ‘on themselves’ in trousers pockets – *the authors’ note*) since they are more sensitive to environmental exposures, RF EMF included [35].

Summing up all available data on adverse effects produced by RF EMF not only on the nervous system but also on other sys-

tems in the body, we can consider these effects systemic.

Conclusion. At present, it seems quite necessary to revise limits of RF EMF effects on the human body, previously fixed FCC and ICNIRP [36], including children and adolescents [37], as shown in Figure.

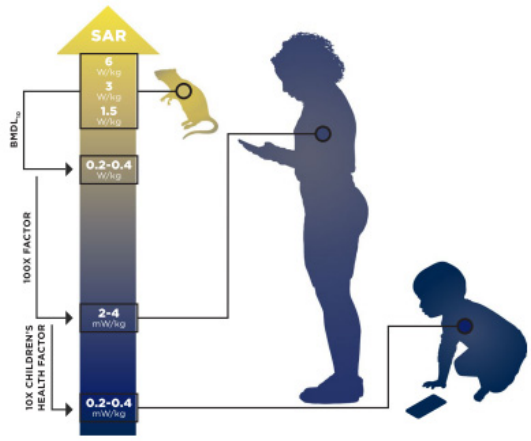

Figure. Health-based exposure limits established in [37]

SAR of 0.2–0.4 W/kg for all sites was selected as a point of departure to calculate recommended health-based exposure limits. Applying two ten-fold safety factors for interspecies and intraspecies variability (100X overall), whole-body SAR limit of 2 to 4 mW/kg was derived for adults. Use of an additional ten-fold children's health safety factor points to a whole-body SAR limit of 0.2–0.4 mW/kg for young children [cited per 37].

Based on all the above stated and in conformity with the representative international research works (included those by the International Commission on the Biological Effects of Electromagnetic Fields), The expert society should concentrate its future efforts on developing updated safe RF EMF limits and probable future revision of sanitary rules and norms in accordance with new identified health risks primarily for children and adolescents as a population group, which is the most susceptible to any environmental exposure.

At present, children and adolescents tend to use up-do-date gadgets uncontrollably. We believe that guidelines should be developed for implementing relevant culture for safe use of up-to-date gadgets for children and adolescents including predominant use of *wire-based hands-free kits* (not Bluetooth), speakerphones, as well as messengers used for subsequent exchange of text and multimedia messages, and not carrying a gadget ‘on oneself’ (in shirt or trousers pockets). This will allow a significant reduction in negative effects produced by RF EMF, in particular, by mobile phones / smartphones, on the rising generation’s health.

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