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SPECIAL ARTICLE

The Sensitivity of Children to Electromagnetic Fields

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ABSTRACT. In today's world, technologic developments bring social and economic benefits to large sections of society; however, the health consequences of these developments can be difficult to predict and manage. With rapid advances in electromagnetic field (EMF) technologies and communications, children are increasingly exposed to EMFs at earlier and earlier ages. Consistent epidemiologic evidence of an association between childhood leukemia and exposure to extremely low frequency (ELF) magnetic fields has led to their classification by the International Agency for Research on Cancer as a "possible human carcinogen." Concerns about the potential vulnerability of children to radio frequency (RF) fields have been raised because of the potentially greater susceptibility of their developing nervous systems; in addition, their brain tissue is more conductive, RF penetration is greater relative to head size, and they will have a longer lifetime of exposure than adults. To evaluate information relevant to children's sensitivity to both ELF and RF EMFs and to identify research needs, the World Health Organization held an expert workshop in Istanbul, Turkey, in June 2004. This article is based on discussions from the workshop and provides background information on the development of the embryo, fetus, and child, with particular attention to the developing brain; an outline of childhood susceptibility to environmental toxicants and childhood diseases implicated in EMF studies; and a review of childhood exposure to EMFs. It also includes an assessment of the potential susceptibility of children to EMFs and concludes with a recommendation for additional research and the development of precautionary policies in the face of scientific uncertainty. *Pediatrics* **2005;116:e303–e313. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-2541;** ***children, environmental risk, policies, sensitive periods, mobile phones, electromagnetic fields, power lines.***

ABBREVIATIONS. ELF, extremely low frequency; IARC, International Agency for Research on Cancer; RF, radio frequency; EMF, electromagnetic field; WHO, World Health Organization; CNS, central nervous system; ALL, acute lymphoblastic leukemia; AML, acute myeloblastic leukemia; SAR, specific absorption rate.

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Children in both industrialized and developing countries are exposed to a large variety of environmental agents including indoor and outdoor air pollution, water and food contaminants, chemicals (eg, pesticides, lead, mercury), and physical agents such as ultraviolet radiation and excessive noise. Changes in exposure to these agents are being linked to real or perceived increases in the incidence of certain childhood diseases, such as asthma, leukemia, and brain cancer, and in some behavioral and learning disabilities. Environmental exposures can be particularly harmful to children because of their special vulnerability during periods of development before and after birth.

Exposure to electric and magnetic fields from 0 to 300 GHz has been increasing greatly as countries increase their capacity to generate and distribute electricity and take advantage of the many new technologies, such as telecommunications, to improve lifestyle and work efficiency (Fig 1). Evidence of an association between childhood leukemia and exposure to extremely low frequency (ELF) magnetic fields has led to their classification by the International Agency for Research on Cancer (IARC) as a "possible human carcinogen"[1] based on consistent epidemiologic data and lack of support by laboratory studies in animals and cells. The reason why the results of the childhood leukemia studies are consistent is still being investigated, but one possibility is that children may be more sensitive to radiation in some or all parts of the electromagnetic spectrum.

Concerns about the potential vulnerability of children to radio frequency (RF) fields from mobile telephony were first raised by an expert group in the United Kingdom[2] on the grounds that children have a longer lifetime of exposure than adults, and from a physiologic point of view, they have a developing nervous system, their brain tissue is more conductive than that of adults because it has a higher water content and ion concentration, and they have greater absorption of RF energy in the tissues of the head at mobile telephone frequencies. This topic was discussed further at a European Cooperation in the Field of Scientific and Technical Research (COST) 281 workshop,[3] in a report of the Health Council of the Netherlands,[4] and in a recent report from the United Kingdom's National Radiological Protection Board.[5]

To evaluate the available information relevant to children's sensitivity to electromagnetic fields (EMFs) and to identify research needs, the World Health Organization (WHO) held an expert workshop in Istanbul, Turkey, in June 2004. This article is based on discussions and recommendations from the workshop and provides background information on

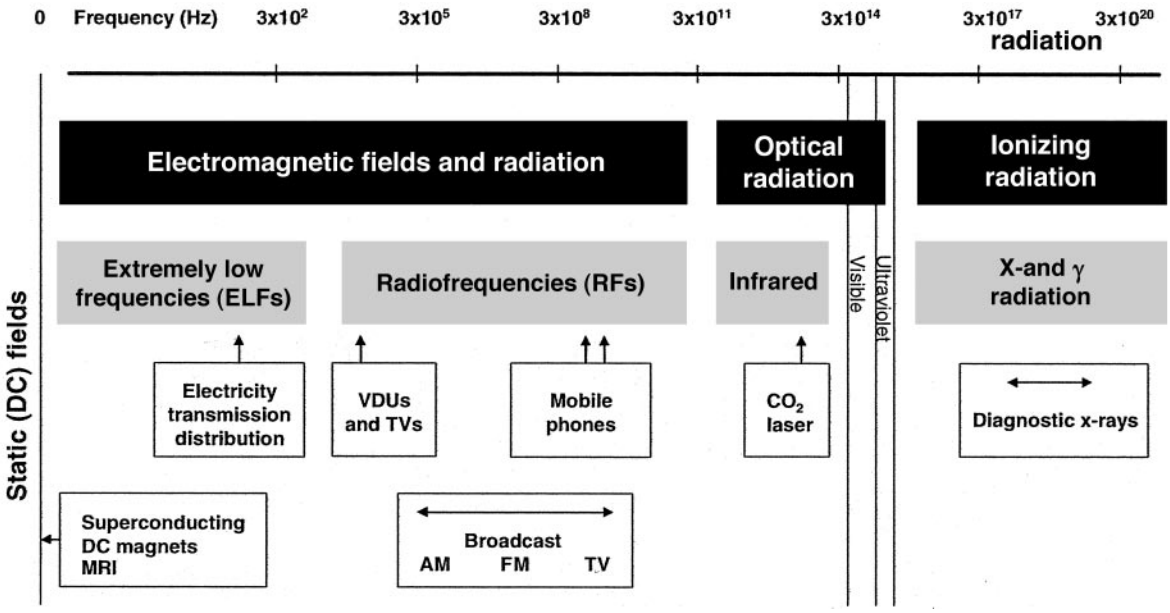

Fig 1. Electromagnetic spectrum. VDUs indicates video display units.

the development of the embryo, fetus, and child, with particular attention to the developing brain; an outline of childhood susceptibility to environmental toxicants, childhood diseases implicated in EMF studies, and exposure to ELF and RF fields, with a focus on children. After a brief presentation of the EMF science most pertinent to effects on children and a review of several proposed mechanisms, the potential sensitivity of children to EMFs is discussed. Finally, recommendations are outlined on the protection of children through the development of precautionary approaches in the face of scientific uncertainty.

FROM EMBRYO TO ADOLESCENCE

Embryo, Fetal, and Childhood Development

Development proceeds from conception to adulthood through a number of different stages in which the developmental processes are markedly different, and their susceptibility to environmental teratogens varies. The prenatal period of development is divided roughly into 3 periods: the preimplantation period, extending from fertilization to the settling of the embryo into the uterine wall; a period of organogenesis, characterized by the formation of the main body structures; and the fetal period, during which growth of the structures already formed takes place. Additional developmental changes take place after birth. Postnatal changes are characterized by slower growth and maturation of existing organ systems, notably the central nervous system (CNS), the hemopoietic and immune systems, the endocrine and reproductive systems, and the skeletal system. The completion of sexual development at the end of the second or the beginning of the third decade of human life marks the completion of this period of growth and maturation. Essentially, however, the nature of the toxicant and the timing and magnitude of exposure determine the risk of any adverse effects in terms of both severity and occurrence. Vulnerability can vary quite rapidly during the prenatal period, whereas slower changes occur postnatally.[6]

During the first 2 weeks of embryonic development (known as the "all-or-none period"), the embryo is very sensitive to the lethal effects of toxic agents and much less sensitive to the induction of malformation. Many of the cells are still omnipotential stem cells, and if the embryo survives a toxic exposure it can recuperate without an increased risk of birth defects or growth retardation. During the next 6 to 8 weeks of development, major organogenic events occur and toxic agents with teratogenic potential can cause major malformations of the visceral organs, the CNS, the face, and the limbs. From the 8th to the 15th week, neuron proliferation, differentiation, and migration in the CNS are particularly vulnerable.[7] Genitourinary and other malformations, gonad cell depletion, and neurodevelopmental problems may occur if the thresholds for these effects are exceeded. During the late fetal period, effects on growth of the fetus and susceptible organs such as the CNS diminish, but vulnerability to deleterious effects remains high compared with adults.

Development continues after birth, but now this process largely entails the maturation of existing organ systems, although growth is still occurring. Neurobiologists long believed that neurogenesis in the human ends during the first months of postnatal life, but recent rodent and primate studies demonstrate that there is lifelong neuron production in some parts of the CNS.[8] However, with some particular exceptions, most adult neurons are already produced by birth. The number of connections (synapses) between neurons in the human brain peaks at ~2 years and decreases by 40% to the adult number during adolescence[8] as experience is acquired and "redundant" connections lost. This reflects the balance between the formation of new synapses (synaptogenesis) and synapse elimination, a "pruning" back of excess synapses between neurons, which are key

processes in the development of the postnatal "hard-wiring" of the brain. Another important neurologic event that occurs postnatally is myelination, which facilitates the transmission of information within the CNS and occurs most rapidly from birth to 24 months but may also continue into the second decade. Unfortunately, the susceptibility of these processes to environmental agents has not been studied extensively and thus is not well understood. However, because developmental processes are vulnerable to disruption by agents that may not be toxic to mature systems, it is reasonable to expect that the later stages of brain development present special risks.[8]

Other threshold effects that can result from postnatal exposures include interference with fertility and endocrine function, alterations in sexual maturation, and interference with the development of the immune system. Endocrine disrupters, exogenous substances that mimic the action of hormones (particularly steroids), may alter the function of the developing endocrine system and have adverse effects on the reproductive organs, liver, kidney, adrenal glands, CNS, immune system, cardiovascular system, and bones.[9]

Exposure to toxic agents with mutagenic and carcinogenic potential, such as ionizing radiation, cancer chemotherapeutic drugs, and some chemicals, poses theoretical, stochastic risks for the induction or progression of cancer during embryonic and childhood development. However, although many agents have been alleged to be responsible for cancer and genetic disease, such effects will only result from agents that have either mutagenic properties or the ability to produce more subtle effects on carcinogenic processes, such as the stimulation of excessive cell proliferation or an influence on cell-to-cell communication, apoptosis, or DNA repair.

Children's Susceptibility to Environmental Exposures

Several aspects of exposure and susceptibility warrant a focus on children. In some exposure scenarios, children may receive higher doses than adults, resulting from higher intake and accumulation or differences in behavior. Greater susceptibility to some toxicants and physical agents has been demonstrated in children. Because the period from embryonic life to adolescence is characterized by growth and development, deleterious effects can occur at lower levels and be more severe or lead to effects that do not occur in adults; on the other hand, children can be more resilient because of better recuperative capacities.

Toxic exposures in utero have produced effects that are quite surprising, given the period or level of exposure. Cassidy et al[10] reported that exposure to the persistent organochlorine chlordane in utero at quite low levels causes significant long-term alterations in sexual behavior. These effects were evident at levels of exposure very similar to those experienced in homes in the United States when chlordane and heptachlor were universally applied as termiticides. Both of these chemicals produced marked changes in sexually dimorphic functions in rats; females exposed in utero developed masculine behaviors, and males showed exaggerated male mating behaviors. These observations suggest that these chemicals masculinized by mimicking steroid hormones or by changing hormone levels.

Of perhaps more specific interest are toxic exposures that affect the nervous system of the fetus, infant, and child. Because development of the nervous system is very specific in pattern and timing, exposure to various agents at critical periods of development can cause long-lasting or permanent injury. For instance, exposure to ethanol or methylmercury has been shown to affect neuronal proliferation in rodents and in other experimental models. Some agents such as ethanol, lead, methylmercury, and some pesticides seem to affect synaptogenesis. Each of the multiple processes of neural development has been shown to be affected by specific toxic agents, often at low doses but at critical periods of development.

The timing of exposure might be critical as well: for ionizing radiation, excess risk for leukemias and brain and thyroid cancer is higher for exposures that occur in childhood; the risk of breast cancer was highest for Japanese women exposed to ionizing radiation from the atomic bomb during puberty, although the risk also increased in women who were <10 years old (an age at which girls have little or no breast tissue) at the time of the explosion.[11] Similarly, sunburns in childhood seem to be particularly potent in increasing the risk of skin cancer later in life.[12] Exposure in childhood may also increase the risk of disease later in life simply because the duration of exposure can be much longer if it starts early. There is evidence, for instance, that the younger a person is when starting smoking, the higher the risk of lung cancer.[13]

Childhood Diseases Relevant to EMF Exposure

Some diseases are limited to the embryo, child, or adolescent; other diseases that occur in children and adults manifest themselves differently in children. Of particular relevance to EMF exposure are childhood leukemia and brain cancer. There is consistent evidence from epidemiologic studies of a risk of childhood leukemia associated with exposure to environmentally high levels of ELF magnetic fields. There is no explanation for this effect from laboratory studies. An increased risk of brain cancer has been investigated in relation to ELF exposures and has been raised particularly in the context of mobile-phone use and the absorption of RF signals by the brain, although there is no convincing evidence suggesting an increased risk. To put potential EMF effects in perspective and determine how EMFs might be involved in the development of these diseases, we provide a brief overview of rates and risk factors for them.

Childhood Leukemia

Leukemias are the most common cancer to affect children, accounting for 25% to 35% of all childhood malignancies. The biological heterogeneity of childhood leukemia is well documented; the major mor-

phologic types are acute lymphoblastic leukemia (ALL) and acute myeloblastic leukemia (AML).

The rate of leukemia for children <15 years old has been estimated to be ~4 per 100 000 per year in the developed world and 2.5 per 100 000 per year in the developing world.[14] In developed countries, the incidence of leukemia rises rapidly after birth, peaking at ~3 years of age before declining and then rising steadily again throughout life. Thus, unlike many cancers, it has a short latency and a peak incidence early in life[15] that has resulted in many etiologic hypotheses, most notably those involving exposure to infections.[16]

Subtypes of AML and ALL are frequently characterized by genetic alterations, including changes in chromosome number (hyperdiploidy or hypodiploidy) and chromosomal translocations that may involve chimeric or fusion genes.[17,18] These genes include *MLL*, *TEL*, and *AML1*, all of which can fuse with many other genes and, in the case of *TEL* and *AML1*, with each other. There is strong evidence that this rearrangement may originate in utero, supported by data obtained from studies of identical twins or children with concordant ALL. Screening of newborn blood samples suggests that ~1% have the *TEL-AML1* gene fusion, 100 times the proportion of children that will develop ALL with a *TEL-AML1* gene fusion before the age of 15 years. This implies that the conversion of the preleukemic clone to overt disease is low and that development of childhood ALL is a multistep process requiring at least 1 prenatal event in combination with additional prenatal and/or postnatal events. Although the "first hit," the initiating in utero event, is believed to be common, the "second hit," possibly occurring postnatally, is rare and therefore acts as the rate-determining step in development of the disease.

As with most other cancers, the mechanism by which leukemia arises is likely to involve gene-environment interactions, the environmental exposures being derived from both endogenous and exogenous sources. Accordingly, it is important to identify exposures that either cause DNA damage and induce chromosome breaks that are repaired inadequately or act as promoters and/or progressers, ultimately leading to the overt expression of the disease. Exposures acting before birth and early in life have long been thought to be important determinants of leukemia; it is unfortunate that the evidence regarding the majority of suggested exposures is limited and often contradictory. Ionizing radiation given at large doses is one of the few known risk factors for leukemia.

Brain Cancer

CNS tumors account for ~20% of all malignancies in children <15 years old[19] but account for <2% of cancers in adults. CNS cancers in children occur in tissues of mesodermal or embryonic origin, but in adults they occur in epithelial tissues. Another difference between childhood and adult tumors is that adult tumors tend to occur in the cerebral hemispheres, whereas the majority of pediatric tumors are brainstem gliomas.

The international incidence rates of childhood CNS tumors (0–14 years) vary between developed and developing nations, with the higher rates observed in most Westernized countries reaching 3 per 100 000 per year compared with 1 to 2 per 100 000 in other parts of the world.[19] Over recent decades, steady rises in the incidence of childhood CNS tumors have been observed in several populations of the United Kingdom, the United States, Japan, and Australia. The debate continues over whether these increases are "real" or an artifact of improved diagnostic practice and case finding by cancer registries.

The causes of CNS cancers are largely unknown, although up to 5% may be explained by genetic predisposition, associated with disorders such as neurofibromatosis type I.[20,21] Having a parent or sibling with a CNS tumor also increases the risk. The identification of environmental risk factors for CNS tumors has generally been inconsistent.[20,21] Again, ionizing radiation given in therapeutic doses is one of the few known risk factors for CNS tumors.

CHILDREN'S EXPOSURE TO RF AND ELF FIELDS

In evaluating the potential role of environmental exposures in the development of childhood diseases, it is important to consider not only the fact that childhood exposures can be different from exposures during adulthood but also the fact that they can be highly age dependent. Exposures of interest during the preconception and gestation periods include residential and parental exposures to ELF and RF fields, including mothers' exposure from use of domestic appliances and mobile phones. Infants and toddlers are exposed mostly at home or at day care facilities. Among preteens, exposure sources expand to include mobile-phone use and sources at school, with an increased use of mobile phones in adolescence. Here we focus on 2 major exposure scenarios: residential ELF and RF exposures and exposure from mobile phones.

Residential Exposure

Everyone is exposed to ELF electric and magnetic fields at home.[22] High-voltage power lines are a major source of exposure for children who live near them; however, only ~ 1% of children live in close proximity to high-voltage lines. For most children, exposure to low-level fields from primary and secondary distribution wiring is continuous; short-duration and intermittent exposure to higher fields results from proximity to domestic appliances. ELF exposure also occurs at school, during transport, and even during mobile-phone use. Typical average magnetic fields in homes seem to be ~0.05 to 0.1 μT. Generally, magnetic fields in homes vary from country to country; geometric-mean fields are ~35 nT in the United Kingdom and 70 nT in the United States. This difference results from the supply voltage used in the United States (110 V) being approximately half that used in the United Kingdom (220 V), leading to approximately twice the electric current and magnetic field exposure. The fraction of homes with average fields above certain thresholds likewise varies; for example, 1% to 2% of homes in the United Kingdom and 10% in the United States have fields of >0.2

μT. Exposure to appliances has been estimated to be 30% of total exposure. Maximum fields experienced are typically in the tens of microtesla. There is evidence that younger children use appliances less (and spend less time outside the home), so their personal exposure is closer to and correlates better with the fields in the home.

RF fields are produced by radio and television broadcasts, mobile phones and base stations, and other communications infrastructure. Radio and television signals are broadcast to a large area from comparatively few sites. Mobile-phone base stations cover a smaller area and produce much lower emissions but are now much more common than radio and television stations (tens of thousands in many countries). Because of the width and angle of the RF signal beam and perturbation by the earth and building materials, there is little correlation between field strength and distance to the source. Typical power densities outdoors would be 0.01 to 1 $mW \cdot m^{-2}$ but could be orders of magnitude higher (ie, $\geq$100 $mW \cdot m^{-2}$). Depending on where the measurements are taken, base stations can be the largest individual source of RF fields, but other sources such as radio or television transmitters can result in comparable or greater exposures. Indoor levels are often lower by orders of magnitude, because buildings screen fields. A European median indoor power density of 0.005 $mW \cdot m^{-2}$ has been reported.

Background environmental levels are the primary source of RF exposure for very young children. Potential sources of residential RF exposure to children are wireless in-house communications (eg, wireless monitors used in children's cribs, cordless phones, Wi-Fi) and mobile-phone use by someone in close proximity to a child, creating passive exposure. Because children <5 years of age usually spend most of their time at home, residential exposure can be a sufficient predictor of individual exposure.[22,23] RF exposure may be estimated more easily for children than for adults, because the variety of exposure sources is smaller. When they reach adulthood, today's children will have a much higher cumulative exposure to RF fields than today's adults.

At present, population exposure to RF fields has been much less characterized than ELF fields, partly because of technical challenges (lack of adequate measuring equipment), the rapid evolution of mobile-phone technology (frequency, coding schemes), and new patterns of use (duration of calls, short-message services). However, the main reason ELF fields are better understood than RF fields is that they have been studied more.

Mobile-Phone Use

Modern children will experience a longer period of exposure to RF fields from mobile-phone use than adults, because they started using mobile phones at an early age and are likely to continue using them. Data from a multinational case-control study of potential causes of adult brain cancer show that both the prevalence of regular mobile-phone users and daily use are highest in the younger age groups (eg, 19% of younger subjects made calls for >30 minutes a day, compared with 10% of older subjects).[24,25] Moreover, several recent trends (such as increased popularity, reduced price, and advertising to children) have led to increased mobile-phone use among children.[26] A steep increase in mobile-phone ownership among children has been reported in several public-opinion surveys.[27] For example, in Australia >90% of 6- to 9-year-olds reported sometimes using their parents' mobile phones, and in Germany approximately one third of 9- to 10-year-olds reported owning a mobile phone. Clearly, mobile phones are the dominant source of RF exposure for teens and preteens.

HEALTH-RISK ASSESSMENT

The workshop addressed the potential sensitivity of children at all stages of development from conception through to sexual maturity. The nature of any adverse health effect that ensues from exposure to an environmental toxicant depends not only on the timing and magnitude of the exposure but also on the mechanisms by which the toxicant interacts with the developing tissue or organ. As a consequence, it is not possible to generalize about the possible health effects that might ensue from exposure to an agent posing unknown risks to health by drawing parallels with other toxic agents unless they have very similar mechanisms of interaction. Instead, it is necessary to examine the experimental and epidemiologic evidence by formulating and testing hypotheses on the basis of an examination of the known and possible interaction mechanisms.

Health Risks to Children From ELF Fields

Exposure to ELF EMFs induces electric fields and currents within the body; guidance on exposure is based on avoiding the risks to health that result from the interaction of the induced fields and currents with electrically excitable nerve tissue, particular that of the CNS (see, for example, refs [28] and [29]). Present guidance on occupational exposure is based on a basic restriction on induced current density in the CNS of 10 $mA \cdot m^{-2}$, which approximates an electric field in CNS tissue of ~100 $mV \cdot m^{-1}$. Guidance on public exposure incorporates an additional safety factor, reducing the basic restriction to 2 $mA \cdot m^{-2}$ (20 $mV \cdot m^{-1}$). The basic restrictions are linked to external field strengths (reference levels) through dosimetric calculation, which is based on realistic anatomic human models and measurements of the dielectric properties of human tissue. For general public exposure, the corresponding reference levels for power-frequency electric and magnetic fields are of the order of 5 kV/m and 100 μT, respectively.

Dosimetric calculations have not been conducted extensively for children and have not been undertaken for pregnant women and their unborn children. In general, adults exposed to ELF electric or magnetic fields have higher internal electric-field strengths and current densities than children because of size and shape differences. However, the distributions are different, and in children some tissues have higher field strengths and current densities for the same external field. Furthermore, children have sig-

nificantly higher internal field strengths and current densities from contact currents than do adults. Dose computations using anatomically correct models of children[30] reveal that modest, imperceptible current into the hand (10 μA) produces ~50 mV · m^{-1} averaged across the lower-arm marrow of a small child and approximately ≥130 mV · m^{-1} in 5% of that tissue. During pregnancy, the magnitude and distribution of induced electric fields and currents in the mother will be different because of changes in body shape and will not have been assessed in the embryo or fetus. These factors, along with differences in dielectric properties, need to be taken into account in assessing health risks to children from ELF EMFs.

The guidance cited above was based on a consideration of laboratory evidence, including evidence from volunteer studies of magnetic phosphenes, and more recently on evidence from voltage-gated ion channel and neural-network behavior.[29] Neurobehavioral studies in volunteers and in animals, mostly in adults, have not reported robust responses to ELF exposure[31]; overall, any changes seen have been subtle, transient, and reversible. Workshop participants thought that there is no reason to suppose a greater sensitivity of CNS neural networks and ion channels to induced electric fields in children or in the embryo or fetus. Reduced myelination seen in childhood and early adolescence was not thought likely to increase sensitivity either. It is not clear what the impact would be of an overabundance of synaptic connections seen in infants and early childhood, but any increased sensitivity was considered to be covered by the more restrictive guidance on public exposure.

The evidence that induced electric fields might affect development of the nervous system and other tissue was discussed at the workshop in some detail. Evidence was presented that endogenous direct-current electric fields of 10 to 100 V · m^{-1} played a role in prenatal development. There is little evidence regarding susceptibility to ELF electric fields, although it was thought that there is no reason to suppose greater sensitivity. It was noted that the direct-current electric fields were several orders of magnitude above present guidance values. However, the possible influence of such fields on synaptogenesis and/or synapse elimination is not known.

Results from several independent research groups suggest that exposure to ELF magnetic fields at microtesla levels may disturb early development of bird embryos. However, replication attempts have been unsuccessful in some laboratories. Results from experiments with other nonmammalian experimental models (fish, sea urchins, and insects) have also suggested subtle effects on developmental stability.[32] In mammals, prenatal exposure to ELF magnetic or electric fields does not result in strong adverse effects on development. Some effects of magnetic (or combined electric and magnetic) fields on postnatal development have been reported, but evaluation of the consistency of the findings is difficult because of the varying methods and approaches used in different studies.

Numerous epidemiologic studies of various pregnancy outcomes in relation to EMFs are available in the scientific literature. They include studies investigating the use of video display terminals, electric blankets, or heated waterbeds, as well as studies of parental occupational exposure. Most studies have found no effects, but these studies have been limited in exposure assessment and lacked the power to examine high exposure levels. Two studies have included personal measurements of ELF exposure and reported effects on spontaneous abortion in relation to maximum measured magnetic fields.[33,34] The possibility of exposure assessment bias in these studies has been discussed, and results need to be confirmed in additional studies before firm conclusions can be drawn.

The potential cancer risks to children of exposure to ELF EMF, estimated from residential proximity to power sources and from measured fields, have been investigated in relation to in utero and postnatal time periods and to paternal exposure. No consistent associations have been observed for childhood CNS tumors.[35] One recent study[36] found an increased risk of childhood leukemia with high maternal occupational exposure during pregnancy.

An increased risk of childhood leukemia has been found to be consistently associated with exposure to environmental levels of power-frequency magnetic fields at levels very much below present guidance. Initial studies used a surrogate for magnetic fields (known as wire codes) that was based on distance and thickness of power lines near the residence.[37] As instruments became available, the focus shifted to measured or calculated magnetic fields. Results of dozens of increasingly sophisticated studies and the 2 pooled analyses have reported a doubling of risk for children exposed to magnetic fields >0.3 to 0.4 μT compared with children exposed to fields <0.1 μT.[38,39] Although a number of factors, including socioeconomic status, have been evaluated as confounders, substantial confounding has not been identified. However, because of limited knowledge of the etiology of childhood leukemia, it is difficult to exclude the possibility of some yet-to-be-identified confounder or of confounding by a combination of factors. Nevertheless, substantial confounding of the observed association, it seems to us, is unlikely. Although these results are also not likely to be a result of chance, bias cannot be ruled out.[40] An epidemiologically detectable risk of leukemia for children, but not for adults, might result from either better exposure assessment for children or from greater susceptibility in children.

At present there is no experimental evidence that supports the view that this relationship is causal; however, few animal studies have been conducted using animal models of the predominant form of childhood leukemia, and most carcinogenesis bioassays begin when animals are sexually mature. In addition, there is no biophysical explanation for biologically significant interactions at these low field values, so if the association is causal, then there is currently no scientific explanation. Two hypotheses for such effects were discussed at the workshop.

One hypothesis discussed at the workshop proposed that the association of power-frequency mag-

netic fields with childhood leukemia may result from the flow of electric current through the bone marrow of children after contact with water fixtures or a water stream in which a small voltage difference exists as a result of the grounding of the residential electrical system to the water pipe.[41] Calculation shows that potentially significant electric fields (more than ~100 $mV \cdot m^{-1}$) may be induced in the bone marrow in these circumstances; this lends biological plausibility to the proposed mechanism. The effect of such weak electric fields in inducing effects in hematopoietic tissue that might increase the risk of ALL, possibly by affecting preleukemic clones (see above), has not been investigated.

A second hypothesis suggested that exposure to power-frequency magnetic fields increases the risk of childhood leukemia through disruption of the nocturnal production of melatonin in the pineal gland.[42] Although the International Commission on Non-ionizing Radiation Protection[43] concluded that there is no convincing evidence of an effect, subtle effects on melatonin physiology are not easily excluded, and such studies have not been conducted specifically on children.

Recommendations were made for additional research regarding the association between exposure to power-frequency magnetic fields and childhood leukemia; it is clear that this issue is unresolved. Although such scientific uncertainty remains, the WHO recommends the adoption of precautionary measures for the protection of children (see below).

Health Risks to Children From RF Fields

Exposure to RF radiation induces heating in body tissues and imposes a heat load on the whole body; guidance on exposure is based on avoiding the risks to health that result from localized rises in tissue temperature and from the physiologic stress engendered by excessive whole-body heat loads.[28,29] Present guidance on occupational exposure is based on restricting the RF-induced whole-body specific absorption rate (SAR) to $<0.4\ W \cdot kg^{-1}$, a heat load sufficiently small that its contribution to other possible heat loads, generated from hard physical work and/or imposed by high ambient temperatures, can be neglected. Basic restrictions on localized SARs, averaged over any 10 g of contiguous tissue, are 10 $W \cdot kg^{-1}$ in the head and trunk and 20 $W \cdot kg^{-1}$ in the limbs.[28] These are intended to restrict local tissue temperature rises to acceptable levels. Guidance on public exposure incorporates an additional safety factor of 5, reducing the basic restrictions to 0.08 $W \cdot kg^{-1}$ to the whole body and 2 $W \cdot kg^{-1}$ to the head. Temperatures are derived from dosimetric calculation and thermal modeling; SARs are also related to external field values via dosimetric calculation. The corresponding reference levels, which for RF fields are power densities, are frequency dependent and are of the order of 10 $W \cdot m^{-2}$ at 1800 MHz for general public exposure.

Dosimetric calculation has for more than a decade allowed for differences in body size between children and adults, and these differences have been factored into guidance. Despite large differences in the size, shape, and tissue distribution of heads, the SAR values and exposure variations for child models are similar to those for adults, although somewhat higher. In addition, the relative depth of penetration is larger for children, a logical consequence of smaller head diameter. Dielectric studies encompassing several tissue types, including brain, obtained from newborn to fully grown rats, mice, and rabbits exposed to RF EMF in the frequency ranges of 130 MHz to 10 GHz and 300 kHz to 300 MHz report large, age-related variations in the permittivity and conductivity of brain tissue and even larger variations for skin and skull tissue.[44–46] Thus, there is a need for dosimetric modeling of the distribution of SAR and temperature in children and also a requirement for appropriate age-related values for the dielectric properties of tissue.

In addition, the distribution of SAR and temperature should be addressed in pregnancy, taking into account the fact that the circulation of blood in the fetus is separate from maternal blood flow. The heat produced by fetal metabolism is dissipated to the mother mostly at the placenta, but this is less efficient than expected and the temperature of the fetus is usually ~0.5°C above that of the mother.[47]

The difference between the ability of children and that of adults to dissipate whole-body heat loads is small. During exercise in thermally neutral or warm environments, children thermoregulate as effectively as adults. When ambient temperatures exceed body temperature, however, children are more liable to have a higher rate of heat absorption compared with adults. Also, although neither children nor adults replace fluid loss sufficiently during exercise in the heat, dehydration may have a more detrimental effect on children because of their greater reliance on elevated skin blood flow to dissipate heat.

Hyperthermia during pregnancy can cause embryonic death, abortion, growth retardation, and developmental defects; animal studies indicate that the development of the CNS is especially susceptible.[47] In humans, epidemiologic studies suggest that an elevation of maternal body temperature by 2°C for at least 24 hours during fever can cause a range of developmental defects, although a causal relationship has not been established. In addition, young infants aged 2 to 3 months are even more vulnerable than neonates because of their higher metabolic rate, better tissue insulation, and slightly lower surface area/mass ratio. However, serious health effects are associated only with greatly elevated body temperatures (>40°C), and such temperature rises are well above the maximum allowable for public RF exposure.

Many different nonthermal mechanisms for RF interaction with tissue have been considered in recent studies.[48–50] These are not particular to children, but if any were confirmed at levels below current guidance, then questions might also be raised about potential childhood susceptibility. Possible RF electric-field interactions[51] include (1) changes in the conformation of proteins, including ATPases associated with ion channels, resulting in functional changes in the proteins, (2) changes in the binding of

ligands such as Ca^{2+} to cell receptor proteins, also resulting in changed receptor function, (3) absorption of RF energy by the vibrational states of biological components such as microtubules, (4) enhanced attraction between cells (the pearl-chain effect), and (5) demodulation of a modulated RF signal, producing ELF electric fields. Generally, it was considered that such interactions are unlikely to be biologically significant at RF levels below guidance values.

In addition, there is evidence concerning RF interactions with magnetite affecting nearby ion channel function by exerting a torque. Possible RF magnetic field effects include (1) interaction with magnetite particles in biological tissue and (2) radical pair interactions, potentially increasing free-radical concentrations, thereby leading to an increased risk of oxidative damage. Although these interaction mechanisms are also considered unlikely to be of biological significance at RF levels below guidance values, given the link between free radicals and disease, RF effects on free-radical concentrations via radical-pair interactions are considered worth exploring.

For infant, childhood, and adolescent exposure, the maturation of the CNS has been raised as potentially susceptible. In this context, the major changes to the CNS during this period comprise a maturation of the hard-wiring (namely, increased myelination), facilitating the transmission of information, which occurs rapidly over the first 2 years but extends into the second decade of life, and remodeling of the synaptic connections between neurons[8] after the first 2 years and into adolescence, mostly by synapse elimination as redundant connections are lost. With regard to synaptogenesis, spontaneous and stimulus-evoked electrical activity in the CNS is believed to play a crucial role in local competition between growing nerve axons and the distribution of their synaptic boutons on target cells.[52] Whether RF fields could affect these processes is not known. Neurobehavioral studies in volunteers and in animals, mostly adults, have not reported robust responses to RF exposure, particularly that associated with mobile phones.[31]

Numerous studies have evaluated developmental effects of RF fields on mammals, birds, and other nonmammalian species.[53,54] These studies have shown clearly that RF fields are teratogenic at exposure levels that are high enough to cause significant increases in temperature. There is no consistent evidence of effects at nonthermal exposure levels, although only a few studies have evaluated possible effects on postnatal development using sensitive end points such as behavioral effects.

Several studies of maternal occupational RF exposure, primarily to physiotherapists, have reported an increased risk of congenital malformations. However, no specific type of malformation has been consistently reported, and there is a potential for recall bias in these studies. Exposure to the fetus from a mobile phone kept in a pocket, handbag, or belt by the hip when a pregnant woman is using hands-free equipment has been mentioned. Thus far, no studies are available on pregnancy outcomes related to mobile telephony.

All the studies have reported negative results for carcinogenicity in normal animals at SARs compatible with mobile telephony,[55] although controversy still exists about the carcinogenic effects of RF radiation in a transgenic mouse model.[56] Two studies in particular reported the lack of an effect of perinatal RF exposure, continuing for 24 months, on spontaneous and chemically induced brain tumors in rats.[57,58]

Several ecological studies[59–66] have examined cancer risk, including risk of childhood leukemia, among populations living in proximity to radio and television broadcast towers. Often driven by a previously identified cluster, these analyses are based simply on distance from the source and often include an extremely small number of cases. Such studies have been uninformative. More rigorous investigations might be feasible with development of new instruments capable of capturing personal RF exposure.

Few relevant epidemiologic or laboratory studies have addressed the possible effects of RF exposure on children. Because of widespread use of mobile phones among children and adolescents and relatively high exposures to the brain, investigation of the potential effects of RF fields on the development of childhood brain tumors is warranted. The importance of longer lifetime exposure has been emphasized by a recent study[67] in which acoustic neuroma occurred only after 10-year use of mobile phones. The type of mobile-phone use among children (eg, text messaging), their potential biological vulnerability, and longer lifetime exposure make extrapolation from adult studies problematic. Such scientific uncertainty can be addressed through both the application of precautionary policies and through additional research.

DEVELOPING POLICY FOR CHILDREN AND PREGNANT WOMEN

In today's world, technologic developments bring both social and economic benefits to large sections of society; however, the health consequences of these developments can be difficult to predict and manage. Nevertheless, even if the effects are small, a widespread exposure can have large public health consequences. When risks are complex, an established cause-effect relationship is absent, or the scientific findings are not robustly quantifiable, the need for timely preventive action makes a precautionary approach an essential part of policy making. Many societies believe that this is particularly true regarding children (including the unborn child): they represent the future of the society, have the potential for longer exposure than adults, and yet are less able to manage their own risk.

International guidance on occupational and public exposure to EMFs, described above, is based on avoiding risks to health that are well understood and for which there is good scientific evidence. However, with regard to childhood exposure to EMFs (and exposure during pregnancy), several factors argue for the adoption of precautionary measures, including the possibility that EMFs might affect children;

the dread with which some of the diseases raised in this context, such as leukemia and brain cancer, are perceived; the involuntary nature of some of the exposure; its extensiveness; and its likely rapid growth in the future.

The WHO International EMF Project (www.who.int/emf) is finalizing a practical framework for guiding policy options in areas of scientific uncertainty that is based on the application of precaution.[68] In general terms, the draft WHO precautionary framework aims to develop a set of public health policy options that can be applied according to the degree of scientific uncertainty and the anticipated severity of the harm that might ensue from exposure, taking into account the size of the affected population and the cost of exposure reduction. These measures should not be seen as undermining science-based guidance on exposure; rather, they represent additional steps with application that may vary from country to country depending on social and economic considerations.

Precautionary measures may also be adopted at an individual level, depending on the degree of concern felt by the exposed person. In giving advice to their patients, physicians should weigh the strength of scientific evidence for the risk, if any, of an adverse outcome, the benefits of the technology, and the feasibility of reducing exposure, as well as the overall health of the patient, which includes freedom from worry and anxiety.

For ELF (power-frequency) fields, there is some evidence that exposure to environmental magnetic fields that are relatively high but well below guidance levels is associated with an increase in the risk of childhood leukemia, a very rare disease (even if the risk is doubled, it remains small at ~5–8 per 100 000 children per year). Although the evidence is regarded as insufficient to justify more restrictive limits on exposure, the possibility that exposure to ELF magnetic fields increases risk cannot be discounted. For the physician faced with questions from, for example, a couple planning a family and concerned about this issue, or from someone pregnant and occupationally exposed to relatively high ELF magnetic fields, standardized advice is not possible. Instead, physicians could inform their patients of possible risk and advise them to weigh all the advantages and disadvantages of the options available to them (of which EMF reduction is but one consideration). Some simple options include reducing exposure by minimizing the use of certain electrical appliances or changing work practices to increase distance from the source of exposure. People living near overhead power lines should be advised that such proximity is just an indicator of exposure and that homes far away from power lines can have similar or higher fields.

Regarding the long-term health effects of mobile-phone use, the paucity of data, particularly for children, suggests that low-cost precautionary measures are appropriate, especially because some of the exposures are close to guideline limits. Physicians could advise parents that their children's RF exposure can be reduced by restricting the length of calls or by using hands-free devices to keep mobile phones away from the head and body. On the other hand, exposure levels from mobile-phone base stations are extremely low, and therefore precautionary measures do not need to be recommended.

RESEARCH RECOMMENDATIONS

In addition to reviewing the available evidence summarized in this article, workshop participants developed a research agenda that identifies high-priority studies needed to fully assess the potential vulnerability of children to ELF and RF fields and outlines the rationale for these studies (see www.who.int/peh-emf/research/rf03/en for more details). Additional laboratory and epidemiologic studies relating to childhood leukemia and ELF magnetic field exposure were strongly recommended. In addition, because of widespread use of mobile phones and relatively high exposures to the brain among children and adolescents, investigation of the potential effects of RF fields on cognition and the development of childhood brain tumors was considered particularly urgent. Laboratory studies using children are, of course, subject to appropriate ethical design and approval.

APPENDIX: GLOSSARY

Absorption: dissipation of the energy of a radio wave (ie, conversion of its energy into another form, such as heat) into the surrounding medium.

Basic restriction: restriction on exposure to time-varying electric, magnetic, and electromagnetic fields that are based directly on established health effects. Depending on the frequency of the field, the physical quantities used to specify these restrictions are current density (J), SAR, and power density (S). Only power density in air, outside the body, can be readily measured in exposed individuals.

Contact current: current flowing through a person in contact with 2 surfaces that are at different potentials.

Current density: a vector of which the integral over a given surface is equal to the current flowing through the surface; the mean density in a linear conductor is equal to the current divided by the cross-sectional area of the conductor; expressed in ampere per square meter (A/m^2).

Dosimetry: measurement or determination by calculation of the internal electric-field strength or induced current density, or of the specific absorption (SA) or SAR distribution in humans or animals exposed to EMF.

Electric field or electric-field strength (E): the force (**E**) on a stationary unit positive charge at a point in an electric field; measured in volts per meter (V/m).

Electric and magnetic fields or electromagnetic fields (EMFs): the combination of time-varying electric and magnetic fields.

Extremely low frequency (ELF) EMFs: EMFs at frequencies of >0 Hz and <300 Hz.

Field strength: the magnitude of the electric or magnetic field, normally the root-mean-square value.

Frequency: the number of sinusoidal cycles completed by electromagnetic waves in 1 second; usually expressed in units of hertz (Hz).

Induced current: current induced in a human body exposed to EMF.

Magnetic field or magnetic field strength (H): an axial vector quantity, **H**, which, together with magnetic induction, specifies a magnetic field at any point in space; expressed in units of ampere per meter (A/m^2).

Magnetic flux density (B): a vector field quantity, **B**, that results in a force that acts on a moving charge or charges; expressed in tesla (T) or gauss (G).

Nonionizing radiation: includes all radiation and fields of the electromagnetic spectrum that do not normally have sufficient energy to produce ionization in matter; characterized by energy per photon less than ~12 eV, wavelengths >100 nm, and frequencies <3 $\times$ 10^{14} Hz.

Power density: the rate of electromagnetic energy flow crossing a unit area normal to the direction of wave propagation; expressed in watts per square meter ($W \cdot m^{-2}$).

Power frequency: the frequency at which alternating-current electricity is generated. For electric utilities, the power frequency is 60 Hz in North America, Brazil, and parts of Japan. Electric power is 50 Hz in much of the rest of the world. Isolated alternating-current electrical systems may have other power frequencies, eg, 440 Hz in commercial airliners and 16⅔ Hz in some railway systems.

Radiation (electromagnetic): the emission or transfer of energy through space in the form of electromagnetic waves.

Radio frequency (RF): any frequency at which electromagnetic radiation is useful for telecommunication. In this article, RF refers to the frequency range of 10 MHz to 300 GHz.

Reference level: EMF exposure level provided for practical exposure-assessment purposes to determine if basic restrictions are likely to be exceeded. Some reference levels are derived from relevant basic restrictions using measurement and/or computational techniques, and some address perception and adverse indirect effects of exposure to EMF.

Specific absorption: the energy absorbed per unit mass of biological tissue, expressed in joules per kilogram (J/kg); specific absorption is the time integral of the SAR.

Specific absorption rate (SAR): the rate at which energy is absorbed in body tissues; expressed in watts per kilogram (W/kg); SAR is the dosimetric measure that has been widely adopted at frequencies above ~100 kHz.

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