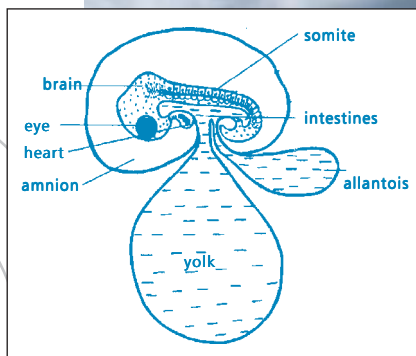


Edition Wissenschaft

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Dr. Hans-Peter Thalau

**Effects of high- and
low-frequency electro-
magnetic fields on
embryonic development**

**An inventory of
teratologic studies**

Edition
Wissenschaft



Forschungsgemeinschaft Funk

Dear readers,

fears and uncertainties regarding possible effects of electromagnetic fields on offspring voiced by the public often are focused on the stage right after egg fertilisation.

Numerous studies have dealt with the effects of electromagnetic fields on embryonic development.

The author of the following study, Dr. Hans-Peter Thalau, from the Institute of Zoology at the University Frankfurt, was commissioned by the Forschungsgemeinschaft Funk e.V. to take an inventory of available teratologic studies. The study is subdivided into three main chapters:

- laboratory studies
- epidemiological studies and
- survey studies

aimed at presenting the current state of knowledge about this scientific area.

The author has added a comprehensive reference index which may be of use to other scientists planning to do in-depth research in this area.

With best regards,

Gerd Friedrich

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Dr. Hans-Peter Thalau

Effects of high- and low-frequency electromagnetic fields on embryonic development

An inventory of teratologic studies

1. Introduction

1.1. About this study

1.1.1. Selection of literature and reference sources

The following study has the intention to present a general survey of to-date published studies on teratologic effects of high- and/or low-frequency electromagnetic fields. Until the nineties of the past century, the number of publications on this issue was relatively small. However, this has changed dramatically over the past ten years following the discussion about possible risks caused by electromagnetic fields. We must point to the fact that not all existing publications dealing with this topic area could be considered in this study which is mainly due to the constantly increasing number of published studies. Moreover, part of the

articles published in scientific journals could not be made available in time. In all, this study encompasses approximately 180 contributions from the years 1975 to 2001; however, the study confines to articles from scientific journals published in German or English. Contributions dealing with studies on biomedical issues related to electromagnetic fields are found in nearly every scientific journal. These journals and the corresponding articles are listed in the reference index attached to this study. Especially recommended are journals such as Bioelectromagnetics, Radiation Research, or Teratology, either exclusively or to a larger extent deal with the topic area investigated by this study and/or with other research fields being associated with potential biological and medical effects of electromagnetic fields.

Summaries of contributions to symposia and/or articles from meet-

ing abstract catalogues were not considered since they mostly contain rather scant information on test design and test performance. Only few exceptions were made, f.e. where sufficient details were included, or where presented results warrant further discussion due to their specific contents (f.e. YOUBICIER-SIMO et al. 1998, ZHAO et al. 1997).

The most important information and reference sources for this study were

1. the archive of the working group around Prof. Dr. Wolfgang Wiltschko (Institute of Zoology at the J.W. Goethe University, Frankfurt/Main) consisting of a huge number of corresponding articles (research foci: magnetic field perception and orientation, neurobiological and teratologic studies on electromagnetic field effects);
2. the library and the electronic journal library, respectively, of the librarian system of the J.W. Goethe

University (www.rz.uni-frankfurt.de);

3. the FEMU database (www.femu.rwth-aachen.de) of Prof. Dr. Silny (TU Aachen);

4. the search engines and databases of "FreeMedline" and of the "National Center for Biotechnology Information" (Entrez PubMed, www.ncbi.nlm.gov). However, since September 2001 (4/16/2002) there is no direct access to Medline and FreeMedline. Therefore, we recommend to call up the URL www.ncbi.nlm.gov;

5. the hompages of the following journals: Bioelectromagnetics (Wiley-Liss, Inc., www.interscience.wiley.com); Radiation Research (Elsevier Academic Press, www.radres.org); Teratology (Wiley-Liss, Inc., www.interscience.wiley.com); Mutation Research (Elsevier Science Pub., www.elsevier.com), and the Journal of Microwave Power (www.impi.org). After we contacted some of the authors whose addresses are listed on these pages, we succeeded (in most cases) to obtain publications directly from them. Current information on congresses, meetings as well as most recent research results can be found on the homepage of the "Bioelectromagnetics Society" (www.bioelectromagnetics.org) included in newsletters and reports from meetings and symposia.

1.1.2 Structure and contents

In addition to making an inventory of to-date published studies, chapter 1 will briefly present the basics of/ the terminology used by teratology,

List of used abbreviations and symbols

A	ampere	kHz	Kilohertz (10^3 Hz)
AC	alternating current	kV	kilovolt (10^3 V)
A/m	ampere/meter	LW	long wave
APAP	N-acetyl-p-aminophenol	m	meter
ARA-C	cytosine arabinosid	MDA	malon-dialdehyde
AVP	arginine vasopressin	mG	milligauss (10^{-3} G)
B	magnetic flux density	MHz	Megahertz (10^6 Hz)
C	Celsius	MNU	methylnitrosourea
c	light speed	M-R	M-cholinergic receptors
Ca	calcium	MRI	magnetic resonance imaging
cAMP	cyclic adenosine-monophosphate	mT	millitesla (10^{-3} T)
CBA/S, CD-1, C57BL/6J	specific mouse lines (stems)	mW	milliwatt (10^{-3} W)
cm	centimeter	MW	medium wave
CNS	central nervous system	n	number of samples of a test series
D	electric flux density	Na	sodium (sodium)
DA	dopamine	NGF	neurite growth factor
DC	direct current	nW	nanowatt (10^{-9} W)
DEB	diepoxybutan	rms, r.m.s.	root mean square
DNA	deoxyribonucleic acid	ODC	ornithine decarboxylase
DOPAC 3.4	dehydroxy-phenyl acetic acid	Oe	oerstedt (1 Oe = 79.5775 A/m)
E	electric field strength	p	level of significance
ELF	extremely low frequency	RF	radio frequency
EMC	electromagnetic compatibility and environment	RNA	ribonucleic acid
EMF	electromagnetic field(s)	S	current density
F1 (F2, F3)	1st (2nd, 3rd) filial generation	s	second
G	gauss (1 G = 100 μ T)	SAR	specific absorption rate
g	gram	SW	short wave
GHz	Gigahertz (109 Hz)	T	tesla
GMS	Global System for Mobile Communication	THz	Terahertz (10^{12} Hz)
Gy	gray	U	voltage
H	magnetic field strength	UHF	ultra-high frequency
h	hour	USW	ultra-short wave
HF	high frequency (English: RF)	UV	ultraviolet light
HVA	homovanilin acid	UWB	ultra-wideband
Hz	Hertz	V	volt
I	current strength	VLF	very low frequency
K	Kalium (potassium)	V/m	volt/meter
kg	kilogram	W	watt
		W/kg	watt/kg
		μ	micro (10^{-6})
		μ g	microgram
		μ l	microliter
		μ s	microsecond
		μ T	microtesla

cytology and by research into non-ionising electromagnetic fields. For a better overview, the investigations dealt with in this study are subdivided into three main categories: laboratory studies (chapter 2), epidemiological studies (chapter 3), and survey studies (chapter 4). Laboratory studies are divided into studies examining low- and high-frequency fields depending on the applied frequency ranges. Additionally, they were divided according to used test animals and/or test models (f.e. chicken embryos, mammals, cell and tissue cultures).

The tables contain the following information: author (when there are more than two authors only the first author is mentioned with the standard addition et al.), year of publication of the study, the examined EMF and the applied frequency range, electric (E in V/m) or magnetic (H in A/m) field strength and/or magnetic flux density B (in T) or current density S (in A/m²). For high-frequency fields, as a rule, power flux density (mW/cm²) and specific absorption rate (SAR in W/kg) are listed. Regrettably, some studies lack sufficient description of exposure conditions. Consequently, in those cases information provided by the tables is incomplete. The magnetic flux density always is given in tesla; where old measurement units like f.e. gauss were used, they were converted into current standard units. Original values are added in brackets.

Further, the tables contain data on the type of the examined organisms

and/or cell cultures, the examined parameters (f.e. embryo mortality, malformation, chromosome breaks, etc.) as well as on observed processes. Data on the sample size are only given in exceptional cases, f.e. where particularly small samples were used (f.e. DELGADO et al. 1982). Detailed information on statistics, sample size as well as on numeric result presentation (when not mentioned in the respective chapter) can be found in the respective publication. A complete list of the studies containing the journals where they have been published, etc. can be found in the attached literature index.

There is a series of studies summarising the results of investigations examining different frequencies. For practical reasons, these results will be separately presented in the corresponding tables on the different frequency ranges. Therefore, the individual studies are listed several times in the tables.

The different chapters try to give an – as far as possible – unbiased summary of the respective state of knowledge. However, single studies were critically evaluated where published results strongly deviated from current knowledge and/or to-be-expected effects, or where it seemed reasonable to suspect that results were falsified by obvious mistakes in test design, test performance or by other artefacts.

1.2. General remarks

Electromagnetic fields are part of the natural environment perceived and used by different organisms. A good example of this are certain electric senses in some fish species, f.e. used in searching for food or for orientation during migration. Numerous bird species, too, are able to use different physical components of the (static) geomagnetic field with remarkable results for orientation. However, since the beginning of the last century technological development is connected with a constantly increased use of electromagnetic fields considerably exceeding the size of natural fields. Therefore, in the past there has often been the question whether and if so, to which extent electromagnetic fields are capable to affect biological systems and, in particular, the human organism. For this reason, in recent years numerous investigations on the issue of interactions between low- and high-frequency electromagnetic fields with organisms have been performed and published. Here, main foci of biological and medical research were, among others, a potential association between electromagnetic fields and different cancerous diseases as well as a possible effect on pineal melatonin synthesis. Since the eighties of the last century, discussion evolved around teratologic effects of low-frequency as well as high-frequency electromagnetic fields (EMF) on embryonic development of vertebrates. Although a large number of scientific studies

has been performed in this topic area, a sufficient and satisfactory explanation of the exact mechanisms possibly affecting embryonic development is still lacking. However, there is a number of investigations describing effects of electromagnetic fields on several enzymes (f.e. ornithine decarboxylase, protein kinase C, cAMP, acetyl-choline-esterase), on RNA and DNA, ion exchange (Ca⁺, K⁺, Na⁺) and cell membrane characteristics (GOODMAN et al. 1995). Such effects of high- or low-frequency EMF at the cellular and/or the molecular level could lead to malformations during the different phases of embryonic development, or even to the developing organisms death.

In 1981 and 1982, DELGADO et al. published two studies indicating a statistically significant increase in malformations in chicken embryos 48 hours after birth if these were incubated in a low-frequency electromagnetic field (100 Hz). Though DELGADO and colleagues were not the first ones to prove effects of electromagnetic fields on embryonic development (among others DIETZEL 1975, JOSHI et al. 1978), these two studies (DELGADO et al. 1981, 1982) stimulated further research along these lines. In the following, research groups mostly from the United States, Canada, Spain, Finland, and Sweden performed and published several teratologic studies. However, published results were highly controversial. Whereas part of the studies could provide evidence for a series of statistically significant

effects (f.e. JUUTILAINEN, 1986, JUUTILAINEN & SAALI 1986, LEAL et al. 1986, CHACON et al. 1990, UBEDA et al. 1994), others could not show any differences between embryos exposed to EMF and sham-exposed controls (f.e. LEAL et al. 1989, Cox et al. 1993, KOCH & KOCH 1991, MARTIN 1992). Various autonomously working research groups formed the so-called „hen-house project“ with the purpose to avoid discrepancies in test design and test performance. Unfortunately, the single studies of the „hen-house project“ neither succeeded in showing consistent results. Thus, also this project failed to elucidate the actual teratogenic potential of the examined EMF.

Apart from low-frequency electromagnetic fields mostly produced by power supply systems, the human organism and its environment due to the expansion of mobile radio networks in the last 8-10 years are also increasingly exposed to high-frequency electromagnetic fields (HF). Whereas thermic effects of high-frequency fields on biological systems are already well-documented, further research on possible non-thermic effects is still needed.

1.3. Electromagnetic fields

The studies dealt with in this paper exclusively performed tests on non-ionising radiation which is subdivided into three categories according to its physical properties:

- low-frequency electromagnetic fields
- high-frequency electromagnetic fields
- optic radiation (infrared; visible light; ultraviolet light; 300 GHz - 3,000 THz)

Electrical engineering presently uses the following units:

In some of the older studies the magnetic flux density is still given in gauss (G); 1 gauss is equivalent to 100 μ T.

In the area of private households electric energy is supplied by alternating voltage; the electric current is characterised by both time-varying strength and direction. The course of technical alternating voltage is sinusoidal. The number of oscillations per second is called frequency and is measured in Hertz (Hz). In Germany, alternating voltage operates on 50 Hz (United States 60 Hz). The effective value of electric voltage is around 230 V in Germany, periodical voltage peaks reach +325 V and/or -325 V. Magnetic alternating fields are produced by moving electric charges. The stronger the current and the smaller the distance from a flowing current, the higher the magnetic field strength. The magnetic flux density (magnetic induction) is proportional to the magnetic field strength.

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	formula	symbol	SI unit
current strength	I		ampere A
voltage	U		volt V
magnetic flux density	B		tesla 1T = 1 Vs/m ²
magnetic field density	H		ampere per meter A/m
electric field strength	E		volt per meter V/m
electric flux density	D		As/m ²

- ultra-short wave (UKW), 30 MHz - 300 MHz
- decimeter waves, 300 MHz - 3 GHz
- centimeter waves, 3 GHz - 30 GHz
- millimeter waves, 30 GHz - 300 GHz.

In contrast to high-frequency fields where electromagnetic waves can detach from their source (antenna) and can propagate through space, low-frequency fields are bound to their source. The field strength decreases with increased distance. It is comparably easy to shield electric fields, whereas shielding from magnetic alternating fields requires large expenditure which often proves unprofitable, too.

Electric and magnetic alternating fields of a frequency of 30 kHz are called low-frequent. To this range belong f.e. the electromagnetic fields of public power networks with a frequency of 50 Hz in Europe. The low-frequency range is divided into the ULF range (ultra-low frequency) of up to 3 Hz, the ELF range (extremely low frequency) of 3 Hz up to 3,000 Hz, and the VLF range (very low frequency) from 3,000 Hz to 30,000 Hz.

In technics and/or biological and medical examinations electric and magnetic fields with different pulsation are used, f.e. unipolar (fig. 1), bipolar (fig. 2), sinusoidal (fig. 1 & 2) and rectangular or sawtooth pulsation.

As already mentioned at the beginning of this chapter, electric fields are tightly connected with magnetic fields. The higher the frequency of an electromagnetic field, the tighter the connection between electric and magnetic field components. High-frequency electromagnetic radiation comprises the radiowave range from 30 kHz up to the microwave range at 300 GHz including 7 orders:

- long wave (LW), 30 kHz - 300 kHz
- medium wave (MW), 300 kHz - 3 MHz
- short wave (SW), 3 MHz - 30 MHz

In high-frequency fields (RF), electromagnetic waves in passage through matter are absorbed and transformed into heat. Penetration depth refers to the distance after which radiation energy has decreased to 37% of its initial value. The term „specific absorption rate“ represents the quantity of radiation energy transformed into heat in proportion to body mass, and is measured in W/kg. Effective radiation power per square unit is measured in Watt per m² (1 W/m² = 0.1 mW/cm²) being equivalent to the product from electric and magnetic field strength.

Among others, the characteristics of a high-frequency electromagnetic

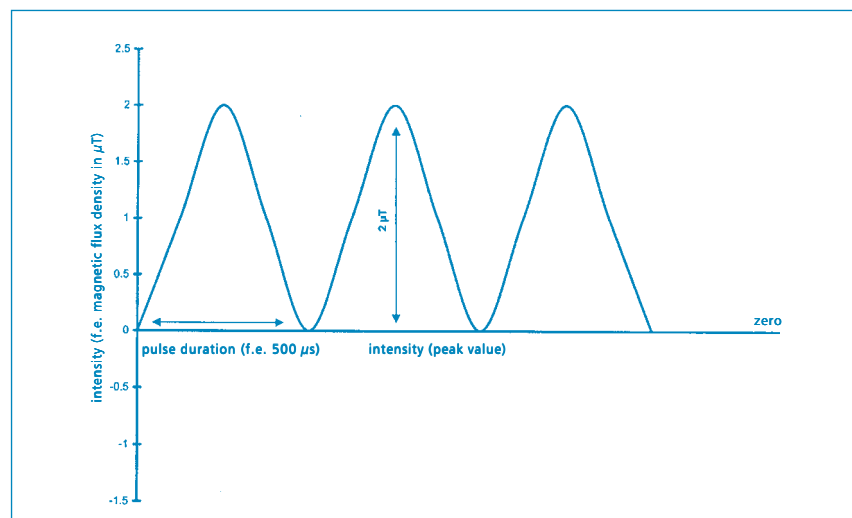


Fig. 1: unipolar sinusoidal magnetic field

field depend on the distance from the radiation source; here, we distinguish between two areas, the near-field and the far-field. In the near-field of a radiation source (antenna) electric (E) and magnetic (H) field strengths are inconsistent and not anymore in phase, that is, they are not perpendicular to each other. As a consequence, when E reaches its maximum at a site in the near-field, $H = 0$ and viceversa.

The far-field range is characterised by a great distance from the radiation source compared to the wavelength of the high-frequent field. Electric and magnetic field strengths are in phase, i.e. they are perpendicular to each other (fig. 3). Both E as well as H alter simultaneously in the same way and are constant. The characteristic value resulting from the relation between H and E is the so-called wave resistance. The individual far-field range for high-frequency fields applied during tests can be calculated by means of the

formula $d = 2D^2/\lambda$ D is the biggest dimension of the antenna and (the wavelength of the applied high-frequency field).

In a vacuum, the propagation velocity of electromagnetic waves is the highest being equivalent – independent of the frequency – to light speed ($c = 299792 \text{ km/s}$). In matter, propagation velocity is the smaller, the more dielectric and magnetic properties of the individual matter deviate from those of the vacuum.

In the early eighties, mobile radio networks having been developed in the different countries were not compatible. In the meantime, with the internationally used GSM system (GSM = Global System for Mobile Communications) a standard has been developed which ensures worldwide use of existing mobile radio networks. For transmission of information, the GSM system applies a carrier frequency of 900 MHz. In

order to reach the great user numbers of mobile radio systems, high-frequency signals (carrier frequency) are digitally coded. This is realised by the so-called pulse modulation (fig. 4) that can simultaneously combine several information transmitting systems. During breaks of one signal the signals of other conversations are transmitted. This method allowed to increase user capacities of predecessor nets (f.e. C-net). Further increases can be achieved by the additional use of amplitude and frequency modulated signals. In the case of the GSM signal, the carrier frequency (f.e. 900 MHz) is pulsed with 217 Hz.

If pulsation of a carrier frequency is achieved by a corresponding temporal increase of its amplitude, we speak of amplitude modulation. If the EMF is applied without pulsation, it is called „continuous wave“ (cw).

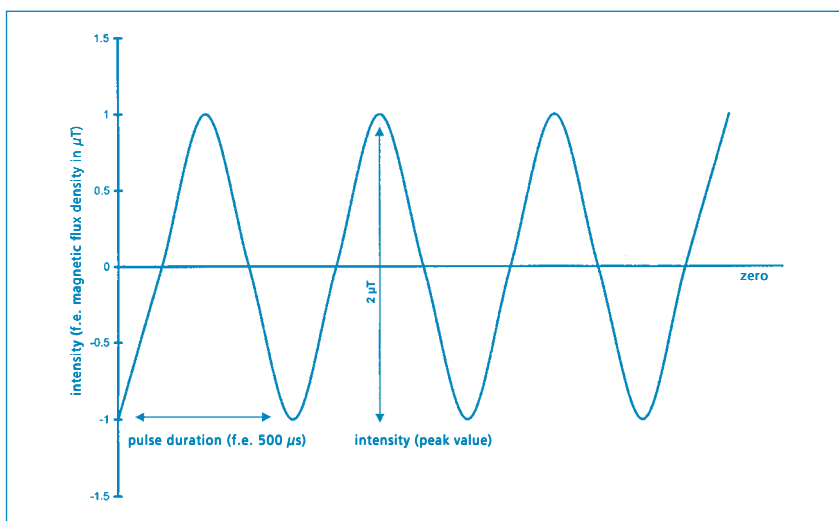


Fig. 2: bipolar sinusoidal magnetic field

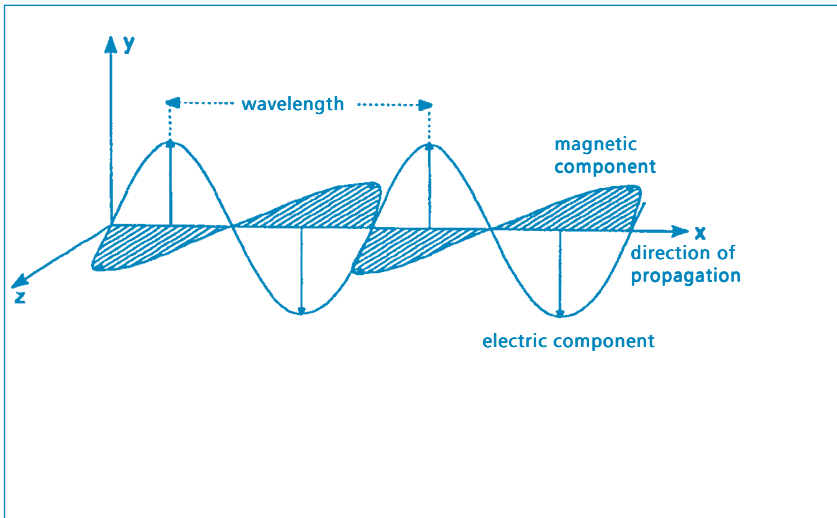


Fig. 3: High-frequency EMF: electric (E) and magnetic (H) field component of a plane wave in the far-field range.

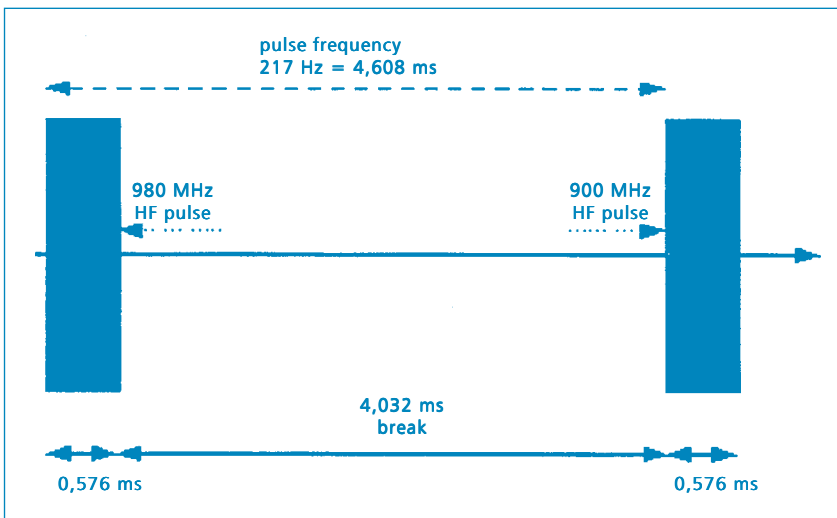


Fig. 4: The signal of a mobile radio base station

1.4. Teratology

1.4.1. Basics

The branch of embryology dealing with the development of congenital malformations (inborn anomalies) is teratology (Greek teratos = monstrum). Assumed causes of congenital malformations are:

1. genetic factors
2. environmental factors.

At the time being, the cause of most congenital malformations is still unknown; however, for some malformations genetic and/or environmental factors are held responsible. It is estimated that in humans approximately 7 % to 10 % of congenital malformations of known origin are exclusively due to environmental factors. Further 10% are exclusively caused by genetic and chromosomal deficiencies. The far bigger percentage, around 80%, results from a combination of genetic and external disorders (SCHUHMACHER et al. 1992, MOORE & PERSAUD 1996). This means that genetically unstable organisms are especially at risk of being damaged by teratogenic environmental parameters.

Known teratogens for humans are certain infectious germs like f.e. the rubeola virus (German measles) or the herpes-simplex virus. Also chemical substances like pharmaceuticals (f.e. thalidomide, cytostatics), artificial hormones (f.e. gestagens, cortisone) or chemicals in the environment (f.e. mercury, herbicides) may damage an embryo and/or fetus or even kill it.

Especially during the phase of the most pronounced cell growth embryos or fetuses are highly at risk from teratogenic effects. However, this crucial growth phase is different in each individual organ and/or tissue depending on the stage of embryo development. Basically, embryonic development is sub-divided into three phases:

During the first phase occurring between egg cell fertilisation and blastogenesis (gastrulation), the so-called blastula period, teratogens potentially may damage all or a huge part of the cells and thus may lead to the embryo's death. Possible as well is that only a small part of the cells is concerned and that the embryo can compensate the damage through its regulatory capacity so there will be no visible malformation. In chickens, blastula and gastrulation already occur during the first few hours after fertilisation, partially even in utero of the mother animal. In humans, this phase occurs during the 1st or 2nd week of pregnancy.

The next phase of development is called embryonic phase. During this stage, the individual organs are formed. In humans, this phase occurs during the 3rd to the 8th week of pregnancy; chicken embryos reach a comparable stage after around 4 days. The embryonic phase is the stage of development where teratogenic factors may have the biggest impact due to the large amount of cell differentiations.

The 3rd and last stage of development is the fetal period where the

growth of the fetus and/or its organs occur. During this stage, as a rule, a decrease of sensitivity of the fetus towards teratogenic influences (LANGMAN 1985) can be observed. Differentiation processes only still occur in few organ systems, like f.e. the cerebellum, the cerebral cortex or parts of the excretion organs. Consequently, there has been evidence for teratogenic effects in rats even in later stages of pregnancy leading to pronounced damages of the cerebral cortex (LANGMAN 1985).

1.4.2. Congenital malformations

Inborn anomalies are called congenital malformations. Partially, they are macroscopically visible; however, in many cases they can only be made evident by microscopic examinations. Disorders occurring during embryonic development can affect metabolism, morphology, heredity and behavior as well as the functional level. In the following, we will in short present a few terms frequently used in embryology:

Anomaly: This term comprises all types of body malformations. From a clinical perspective, anomalies may be sub-divided into four groups (taken from: MOORE & PERSAUD 1996):

Malformations: All morphologically recognisable deficiencies of organs and/or organ parts or of bigger body parts resulting from endogenous development disorders, are called malformations. In this context „endogenous“ means that the developmental potential of a germ is

impaired by chromosomal abnormalities already laid out during fertilisation.

Disruption: The term disruption refers to malformations resulting from exogenously triggered development disorders. Thus, actually all malformations caused by teratogens should be called disruptions, too. Disruptions cannot be passed on, but there are genetic factors potentially being responsible for this type of anomalies.

Deformation: Deformations are anomalies of shape or location (f.e. club-foot) caused by effects of mechanical powers on the germ. In some cases, they can also result from developmental disorders of the central nervous system, like f.e. meningocele, via functional disorders. The term meningocele refers to a serious malformation of the nervous system. It is a cyst containing not only meninges (capsule-like enclosing layer, f.e. dura mater) and liquor (brain and spinal fluid) but also part of the spinal chord (f.e. spinal nerve roots). Meningocele can develop across the whole spinal chord.

Dysplasia: Malformations of cells or tissues being responsible for certain tissue differentiations are called dysplasia.

Apart from congenital malformations, that is, mostly pathogenetic morphological alterations in the embryo, also embryotoxic effects can lead to the death of the embryo and/or fetus in utero without being caused by distinct morphological malformations. Therefore, we should

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distinguish between the terms „teratogenic effect“ (occurrence of congenital malformations) and „embryo mortality“ since a premature death of an embryo and/or fetus during the different stages of development is not necessarily due to congenital malformations. Abortion (spontaneous): Spontaneous abortions quite often occur during the 1st week of pregnancy, that is, during implantation of the blastocyst in the uterus mucous membrane. It is estimated that the actual abortion rate is considerably higher than the often given 15 % since many women think abortion bleeding to be a belated period. The most frequent cause of spontaneous abortions are chromosomal anomalies of the zygote. Further causes are

malformations of the embryo, diseases or detritous environmental influences. During the first 2 to 3 weeks of embryo development teratogens in most cases do not cause malformations but can lead to the death of the blastocyst and thus to spontaneous abortion. Stillbirth: There are many potential causes triggering stillbirth reaching from infectious diseases and illnesses of the mother organism and/or of the embryo via congenital malformations to mechanical problems of the placenta or the umbilical chord. Further causes are insufficient provision of pregnancy, chromosomal damages, multiple pregnancy, drugs, medicines, chemicals, or other environmental parameters (see timetable pregnancy phases, p. 12).

1.5. The chicken embryo as a test model

As in vivo tests in human embryos have to be ruled out for obvious ethical reasons, teratological laboratory tests are performed in animal models with a similar embryonic development. Since the main part of potential teratogens reaches the embryo via the metabolism of the mother animal, most tests, f.e. on pharmacokinetics or effects of chemicals, apply mammals as an animal model (normally dogs, rats, mice). Regarding electromagnetic fields, there is a slightly different situation. We cannot a priori exclude that these because of their physical characteristics have a direct terato-

1 st WEEK preimplantation	2 nd WEEK implantation	EMBRYONIC PHASE 3 rd to 8 th week		FETAL PHASE 9 th to 38 th week (birth)	
zygote morula blastocyst	development of: amniotic cavity germ disc yolk sac (primary) chorion	3 rd week: gastrulation, primitive streaks, chorda dorsalis, neurulation, allantois, somites, colon, blood vessels	4 th to 8 th week: tail, otic placode, eye vesicles, olfactory pits, brain vesicles, extremities, retina (pigment)	maturing and growth of extremities, organs and tissues forming during embryonic phase	
<p>1st to 2nd week</p>		<p>4th week</p>	<p>5th week</p>	<p>20th week</p>	<p>birth</p>
teratogenic influences are compensated or the consequence is ABORTION		serious morphological anomalies in all differentiating extremities, organs and tissues		minor morphological anomalies and functional deficiencies in the CNS, ear, eyes, teeth, palate, genitals	

The different phases of embryo development and their sensitivity towards teratogenic influences

genic effect on the embryo developing in the uterus. For investigating possible teratogenic effects of EMF immediately affecting the embryo, EMC research also to a large extent uses bird embryos, mostly chicken embryos, but also, to a smaller extent, quail embryos as an animal model. Since the neutral observer might have some doubt regarding portability of this animal model to humans, this chapter will deal in more detail with the chicken embryo as an object of teratologic EMC studies.

Because of their common characteristics in embryonic development reptiles, birds and mammals are also termed as "amniotes". At the beginning of the embryonic development in amniotes, embryonic membranes form starting from the rim of the germ disc. Around the embryo a fold develops (amniotic fold) from two egg membranes, the outer being the serosa (= chorion), the inner the amnion. The amnion forms the fluid-filled amniotic cavity enclosing the embryo or fetus. The water stored in the amniotic cavity ensures free movement of the embryo and moreover serves as a shock absorber. A bulge of the embryonic cloaca is the 3rd characteristic egg membrane of amniotes, the allantois. The allantois serves as a deposit for excretions (uric acid) and also as a respiratory organ until the lungs begin to work.

Though processes of early embryonic development in an egg in many aspects equal those of mammals, during the first few days after

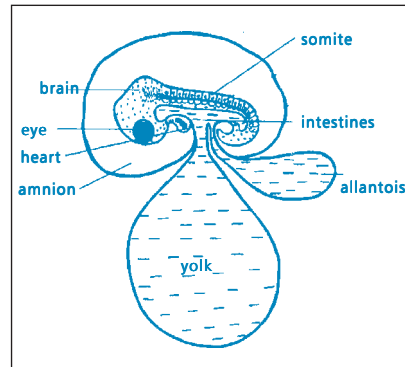


Fig. 5: embryo of an amniote vertebrate (according to ANDERSON BROWN 1988)

fertilisation the development of the embryo in a chicken egg is much faster as f.e. in humans. Only 26 to 29 hours after fertilisation, 4 somites (primary vertebrae) have developed in the chicken embryo, and first signs of blood vessels can be seen (HAMBURGER & HAMILTON 1951). Further, during these stages of development initial differentiations of neuronal tissue are observed (HAMBURGER & HAMILTON 1951). A mouse embryo needs approximately 9.5 days, a human embryo around 20 days to reach a comparable stage of development.

For investigating potential teratogenic effects of certain drugs, medicines or chemicals on the human embryonic development chicken embryos are highly inadequate as a test model. Mainly, this is due to the fact that such substances reach the embryo or the fetus via blood circulation and metabolism of the mother animal having to pass the placenta which acts as a protective barrier.

Still, other factors are important when investigating possible terato-

genic effects of electromagnetic fields. Though secondary teratogenic effects via the mother organism are conceivable, too, it is highly probable that the embryo/fetus also can be directly affected by electromagnetic fields. For studies examining an immediate impact of electromagnetic fields on embryonic development, the chicken embryo has shown to be an adequate test model which is internationally accepted. This has led to a great part of studies on teratogenic effects of electromagnetic fields being performed in chicken embryos. Apart from the possibility to directly examine effects of electromagnetic fields in exposed embryos, the chicken embryo as a test model has several more advantages compared to other animal models described in the following.

In utero, embryos or fetuses (passively) move freely within the applied field caused by the movements of the mother animal inside its holding and/or test cage. This could lead to the examined embryos and/or fetuses being exposed to different field conditions because of inhomogenous field conditions during exposure periods. We cannot exclude that the embryos or fetuses respond to such alterations within an electromagnetic field.

In mammals, different physical conditions are to be expected due to individual differences with respect to body height, fat deposits and other parameters possibly affecting potential effects of electromagnetic fields. Because of these individual differences it is impossible to

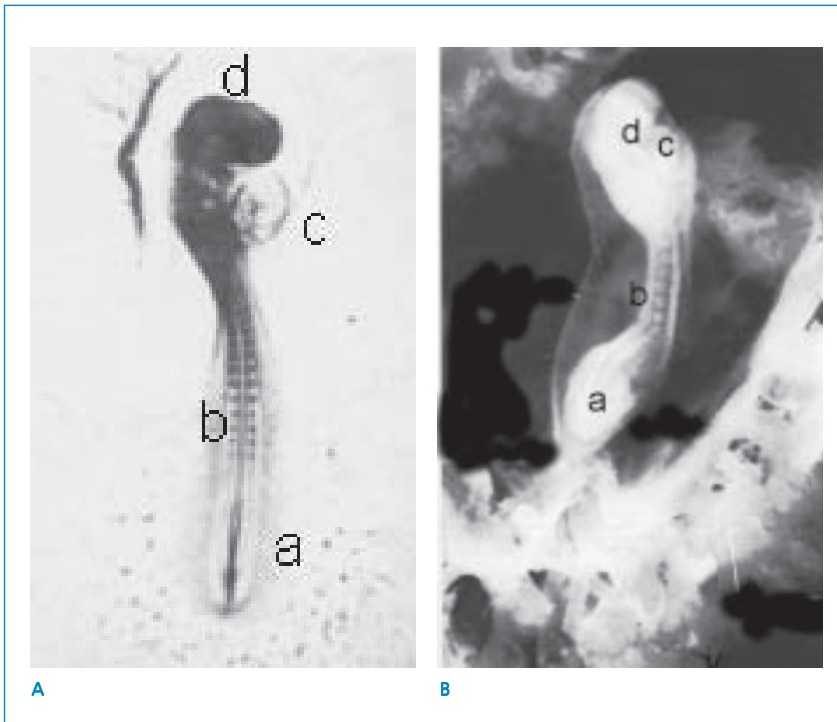


Fig. 6: A: chicken embryo aged around 2 days (taken from HAMBURGER & HAMILTON 1951). B: human embryo on day 24 to 25 (taken from MOORE & PERSAUD 1996). a = tail; b = somites; c = heart; d = head.

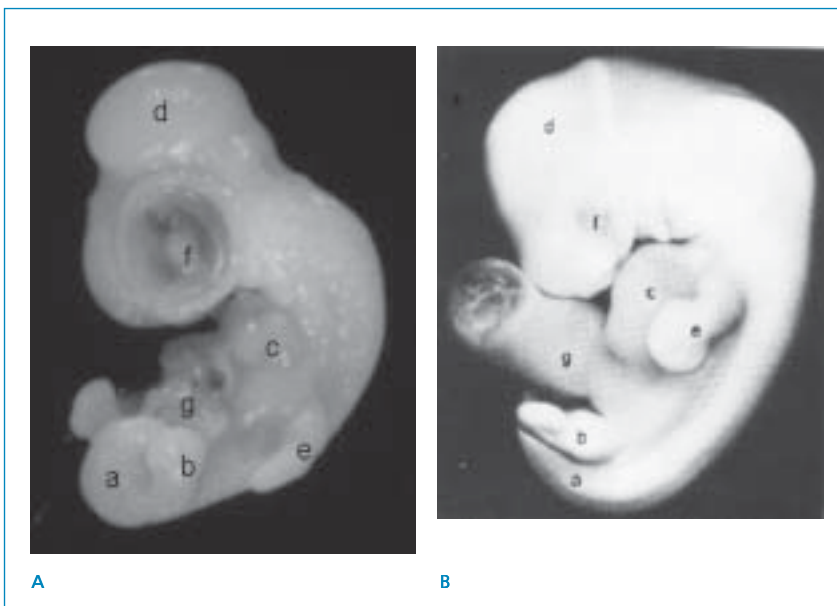


Fig. 7: A: chicken embryo aged 4 to 5 days (photo THALAU). B: human embryo on day 41 (taken from MOORE & PERSAUD 1996). a = tail; b = leg bud; c = heart; d = skull roof; e = arm bud; f = eye; g = umbilicus

precisely determine which field conditions the individual embryos or fetuses were actually exposed to during tests. However, this is of special importance in tests with high-frequency electromagnetic fields since here absorption characteristics of the exposed tissue and/or the whole organism is dependent on the individual physical conditions (f.e. body height, fat or muscle tissue). Therefore, it seems doubtful regarding differences in body height alone to apply results gained from tests with high-frequency fields in rats or mice to the human embryo/fetus. At identical power densities, there certainly are other exposure conditions for human embryos or fetuses in the mother organism than for EMF-exposed rat or mouse embryos/fetuses. We may confidently assume that in humans, due to the thicker tissue layers of gut, body fat and uterus, at least a considerable percentage of the high-frequency field is absorbed and that the embryo or fetus thus is exposed to a substantially smaller power flux density.

Tests in mammals do not allow to reliably determine whether detected teratogenic effects are caused by direct impact of applied EMF on the exposed embryo or fetus, or rather by secondary effects caused by EMF-induced damages of the mother organism. Further parameters which may considerably impair embryonic development in mammals are diseases of the mother animal as well as faulty holding conditions (f.e. feed, temperature, strain caused by holding conditions).

Moreover, tests using high-frequency fields have to consider that chicken eggs (and also those of other bird species) compared to humans at certain frequencies show a distinctly higher absorption capacity in the resonant range. This is the case when the size of the exposed object (egg or embryo) approximately equals one-half of the wavelength. Here also the dielectric properties of the exposed object play a role. Of course, these different physical conditions must be taken into consideration in discussing the portability of results gained from such studies.

1.6. Cytology

Since this survey study will also present a variety of publications examining the effects of electromagnetic fields on the genotype, in the following we will explain some of the most frequently used terms and/or test methods in this area.

– **Mitosis:** An organism develops from the fertilised egg by mitotic cell division. With the exception of certain cell types, like f.e. muscle or nervous cells, cells in the organism normally are between two mitoses, the so-called *interphase*. The **mitosis index** provides the number of mitotic cell divisions per 1,000 cells; a high mitosis index indicates a growing or regenerating tissue. The process of mitotic cell division can be sub-divided into 5 phases. During the first phase, the *prophase*, the interphase ends meaning that the “work cell” transforms into a “division cell”. During this stage, the

cell rounds, the nucleus membrane disappears, and chromosomes become visible. During the *metaphase*, the second chapter, chromosomes become shorter and more compact moving towards the equatorial level of the cell. At the centrosomes, more exactly the kinetochore, the metaphase spindle fibers develop. During the following *anaphase*, the third chapter of mitosis, chromosome halves separately move in the direction of the two cell poles to the centrioles. During *telophase*, the chromosomes are located in the vicinity of the centrioles of both daughter cells, again getting longer and invisible. The nucleus membrane forms, the nucleolus becomes visible, and two new interphase nuclei develop. During *reconstruction phase*, the newly developed cells show their typical shape becoming part of the surrounding tissue. **Kariogenesis** is the movement of chromosomes during mitosis. The term **cytokinesis** refers to the cutting in two of the cell body normally following kariogenesis.

– **Chromosomes:** During the late prophase and/or the metaphase, in the individual chromosomes two chromosome arms are recognisable connected by a centrosome. Within the chromosome arms two spiraling chromatids are visible. The double spiral, the so-called “double helix”, consists of *deoxy nucleic acid*, the DNA. The DNA carries the genetic information of an organism and is the most important component of a chromosome. The chemical structure of the DNA consists of the deoxyri-

bose and the bases adenine, cytosine, guanine, and thymine. At the DNA, the **RNS** – ribonucleic acid – develops transmitting genetic information from the DNA to the functional structures of a cell in the interphase nucleus (protein synthesis). However, the RNS is not a component of chromosomes. The double helix is embedded in low-molecular basic proteins, the so-called *histones*. All components of a cell nucleus being of chromosomal nature are termed as *chromatin*. The chromosome set stemming from one parent is called *haploid*. *Diploid* cell nuclei have two corresponding chromosome sets each stemming from one parent. Correspondingly, *polyploid* cell nuclei are composed of several chromosome sets. As a preparation for fertilisation, in the female- and male-sex cells the chromosome set is cut in two, that is, the cell becomes haploid. This process is termed *meiosis*. During *meiosis*, two division steps occur: the 1st and the 2nd maturing division.

If disorders occur during mitosis and/or meiosis, possible damages can be identified through the numeric determination of alterations at the chromosomes, or with the help of certain test methods.

– **Chromosomal aberrations:** Regarding chromosome alterations we generally distinguish between structural and numeric chromosomal aberrations (chromosomal mutations). Both cases are irreversible. Numeric chromosomal aberrations lead to an alteration in the number of chromosomes of a genome. One

of the causes of this are disorders occurring during meiosis where two paired chromosomes do not separate and thus both reach the same daughter cell instead of being distributed to two different daughter cells. This daughter cell now has one chromosome too much (trisomy), whereas the other lacks one (monosomy). Structural chromosomal aberrations result in chromatid breaks, chromosome breaks, acentric and dicentric chromosomes. Chromosomal aberrations are found in approximately 25 % of all spontaneous abortions. Here, we should bear in mind that this number assumingly is much higher since a huge part of early abortions occur without being noticed.

– **Micronucleus test:** The micronucleus test is a method for (in vivo & in vitro) finding proof of damages of the genome caused by genotoxic or mutagenic agencies. The existence of micronuclei is seen as evidence for chromatid and/or chromosome fragmentation, for damages in the spindle (mitosis), and for the occurrence of numeric chromosomal aberrations. Micronuclei are small nuclei besides the main nuclei which may contain fragments of chromosomes or of the spindle apparatus.

- Sister chromatid exchange test: This test is a short-term experiment for investigating the DNA exchange of two sister chromatids of a replicating chromosome.

2. Laboratory studies

2.1. Low-frequency electromagnetic fields

2.1.1. Studies in chicken and quail embryos (in vivo)

This survey study covers a total of 33 studies (tables 1 to 6) on teratologic effects of low-frequency electromagnetic fields performed in chicken and/or quail embryos during the years 1978 to 1998. Across these studies, 9 different magnetic field types with frequencies in the range of 1 Hz to 10 kHz have been examined (graph 1). Part of the studies applied two or several frequencies during different test series. Thus in graph 1 as well as in our survey tables some studies are listed several times. Four studies examined effects of magnetic resonance tomographs (MRT) and/or computer monitors. Two studies applied a static magnetic field; another one used an electric field of 60 Hz (see graph 1).

Main focus of the treated studies was a possible association between the incidence of different anomalies and the examined EMF. To this end, for the different frequencies a total of 34 tests were performed. Further foci were possible influences of the examined fields on the course of embryonic development (18 tests) and on embryo mortality, respectively (11 tests). Moreover, the following parameters were examined: cellular anomalies in pinealocytes; enzyme activity, cellular growth, fertility, food consumption of

EMF/frequency	number of studies	table
Static field	2	1
1.0 Hz	1	1
10.0 Hz	2	1
16.7 Hz	1	1
30.0 Hz	2	1
50.0 Hz	5	2
60.0 Hz	7	3
100.0 Hz	16	4
1.0 kHz	3	5
10.0 kHz	1	5
Electric field (60 Hz)	1	6
MRT/monitors	4	6

Graph 1: Teratologic studies on effects on low-frequency EMF on chicken and quail embryos. Examined fields and frequencies (electric & magnetic fields)

maternal or paternal animals, gender ratio of hatched young, laying rate (two tests each) as well as protein synthesis, organogenesis, body weight of embryos and/or chicks, hormones and cerebellum development (one test each).

Analysis of to-date available data mainly is made difficult by the fact that for many of the tested frequencies and/or fields (electric fields, MRT, monitors) only one or two studies have been published, in part even done by the same authors. Further difficulties result from the nature of the examined magnetic fields (rectangle, sinus, unipolar, bipolar, vertical or horizontal), the applied magnetic field strengths and/or flux densities as well as the diversity of the examined biological parameters.

For 50, 60 & 100 Hz though there are several studies available which were performed in different laboratories. Thus, in the following we will

deal with the studies investigating these frequencies in detail.

There is a total of 5 teratologic studies examining 50-Hz magnetic fields in chicken and quail embryos in part showing substantial differences with regard to exposure conditions. The same is true for the form (sinus, rectangle) as well as for the magnetic flux density and/or field strength of the examined magnetic fields. There were also considerable differences concerning exposure duration. Detailed data on test conditions can be found in table 2.

In all 5 studies, malformation rate was one of the examined parameters. Two studies (JUUTILAINEN & SAALI 1986, VEICSTEINAS et al. 1996) additionally examined the course of embryonic development, two other dealt with embryo mortality (PAVKOFA et al. 1994, TEROL & PANCHON 1995). One of the studies (VEICSTEINAS et al. 1996) looked into possible effects of the examined

50-Hz magnetic field on organ development, protein synthesis as well as postnatal body weight and other parameters in chicks 90 days of age.

Three studies (COX et al. 1993, PAVKOFA et al. 1994, VEICSTEINAS et al. 1996) did not identify any effects of the applied 50-Hz fields on test parameters. The two other studies (JUUTILAINEN & SAALI 1986, TEROL & PANCHON 1995) showed a statistically significant increase in malformation rate compared to controls, at least for certain magnetic field strengths and/or flux densities. Both studies have been criticised for employing very small samples ($n = 10$ embryos) (TEROL & PANCHON) or for presenting highly unspecific data on the observed effects and/or on statistical evaluation.

A total of 7 available studies deal with 60-Hz magnetic fields and their potential effects on embryonic development of chicken embryos. Regrettably, here the same is true for exposure conditions as for studies covering 50-Hz fields. Nearly all studies present different exposure conditions (f.e. magnetic flux density, exposure duration). Further, different biological parameters were examined (see table 3). KRUEGER et al. (1975), MARTIN (1992), and FARRELL et al. (1997) investigated malformation rate and embryo mortality. While FARRELL et al. (1997) detected a statistically significant increase in malformations in EMF-exposed embryos, the tests done by KRUEGER et al. (1975) and

MARTIN (1992) could not show any effects caused by the examined 60-Hz fields. Specified data on the available studies dealing with possible effects of 60-Hz magnetic fields on chicken embryos are found in table 3.

Most studies covered 100-Hz magnetic fields (table 4). In contrast to studies investigating 50- or 60-Hz fields, exposure conditions were comparable or even more or less identical. This also is true for the examined biological parameters (malformations, embryo mortality, development stage). In 11 studies (DELGADO et al. 1981, 1982, FARRELL et al. 1997, JUUTILAINEN 1986, LEAL et al. 1986, 1989, LITOVITZ et al. 1994, MARTIN 1988, TEROL & PANCHON 1995, UBEDA et al. 1983, 1994), authors report a statistically significant increase in malformation rate for EMF-exposed test groups. In contrast, the remaining 4 studies (KOCH & KOCH 1991, MAFFEO et al. 1984, 1988, MARTUCCI et al. 1984) could not detect any statistically significant difference regarding malformation rate between controls and EMF-exposed embryos.

Due to these discrepancies between research results, at the end of the eighties the so-called "Henhouse Project" was instigated. The results of this project were published in a joint study (BERMAN et al. 1990, table 4). 6 working groups from 4 countries participated in the project aimed at reviewing available results by using identical test design and performance. Single tests were

carried through in the country of the individual working group. But ultimately, when evaluated separately, the tests of the "Henhouse Project" led to results as controversial as those from earlier performed studies. Though 5 of the 6 participating working groups could observe an increase in congenital malformations in EMF-exposed embryos, statistically significant results could be confirmed only in two cases. The remaining 4 working groups could not find any statistically significant difference between sham-exposed controls and EMF-exposed embryos. In summary, data from all 6 working groups showed significant differences of $p > 0.001$ between controls and EMF-exposed embryos (BERMAN et al. 1990). However, from a teratologic point of view, the partially contradictory results from the "Henhouse Project" do not really surprise. Whereas test design, i.e. EMF exposure setup, EMF exposure itself as well as methods for determination were identical, the egg material used in tests was not. All tests examined embryos of the species "white leghorn", but since they took place in 4 different countries, the examined eggs naturally came from different parents populations. Correspondingly, the applied egg material was of different genetic disposition. And since the extent of damaging effects of most teratogens depends on the genetic disposition of the concerned organism and is multifactorial, respectively (see chapter 1.4.1.), the different results of the "Henhouse Project" most probably are due to the genetic

disposition of the embryos having been examined in different laboratories. The same conclusion is ultimately drawn by a study of FARRELL et al. (1997) after reproducing the tests of the "Henhouse Project".

Whatever the examined frequency, 60% of all tests showed statistically significant differences between controls and sham-exposed or EMF-exposed groups with regard to malformation rate as well as to development stage. But despite the fact that the largest part of available studies reports effects on embryonic development, especially malformations, safe conclusions on the teratogenic potential of low-frequency magnetic fields cannot be drawn. The reason for this is that nearly all studies examined embryos during a very early stage of development. In the opinion of some authors (BRENT et al. 1993), we cannot be sure that the observed abnormalities or variations actually are malformations since the teratogenic potential only can be determined in offspring at birth or during hatching. However, studies on this basis giving proof of teratogenic effects of low-frequency fields on embryonic development of chicken and/or quail embryos - with one exception (YUBICIER-SIMO et al. 1997) - are still lacking.

Table 1: Chicken and quail embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields, frequency range: static & 1 to 30 Hz fields) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Joshi et al. 1978	static magnetic field: 0.5 T (5000 Oe). exposure duration: 1 h	chickens	development stage and malformations in embryos aged 24 h	All examined embryos (n = 25) showed malformations of neuronal structures (microcephalia & neuronal tube), of the heart and of somites. The differences compared to controls were statistically significant. In controls (n = 25) only two embryos showed malformations.
Espinar et al. 1997	static magnetic field: 20 mT. test 1: exposure on 6th day of embryonic development over 24 h test 2: constant exposure until 13th or 17th day after breeding.	chickens	development of cerebellum in embryos 13 & 17 days of age	In all tests single layers of the cerebellar cortex in exposed animals were less far developed than in controls. Differences were statistically significant.
Juutilainen & Saali 1986	magnetic fields: 1 Hz; 0.1, 1, 10, 100 A/m. exposure duration: 52 h additional tests covering frequencies in the range of 10 Hz to 100 kHz (see corresponding tables).	chickens	malformations and development stage in embryos 52 h of age	At 0.1 A/m: increase in malformation rate in EMF-exposed embryos (no specified data). The difference compared to controls was statistically significant.
Delgado et al. 1982	magnetic fields (unipolar): 10 Hz; 0.12, 1.2 & 12 μ T exposure duration: 48 h additional tests at 100 & 1000 Hz (see corresponding tables).	chickens	development stage and malformations (somites, heart, blood vessels and neuronal tissue) in embryos 48 h of age	Slight increase in malformation rate in neuronal tissue, blood vessels and heart of the EMF-exposed embryos. Somites showed normal development. Very small samples! At 0.12 μ T n = 3; 1.2 μ T n = 4; 12 μ T n = 5.
Juutilainen & Saali 1986	magnetic fields: 10 Hz; 0.1, 1, 10, 100 A/m exposure duration: 52 h additional tests at frequencies in the range of 1 Hz to 100 kHz (see corresponding tables).	chickens	malformations and development stage in embryos 52 h of age	No statistically verifiable differences between EMF-exposed embryos and controls (details are lacking).
Juutilainen & Saali 1986	magnetic fields: 16.7 Hz; 0.1; 1; 10; 100 A/m exposure duration: 52 h additional tests covering frequencies in the range of 1 Hz to 100 kHz (see corresponding tables).	chickens	malformations and development stage in embryos 52 h of age	At 0.1 & 1.0 A/m: increase in malformation rate in EMF-exposed embryo (details are lacking). The difference compared to controls was statistically significant.
Chacon et al. 1990	magnetic field (bipolar): 30 Hz; 1 μ T pulse duration: 500 ms exposure duration: 48 h	chickens	malformations, embryonic development, embryo mortality in embryos 48 h of age	Embryonic development and malformations: no statistically significant differences between controls and EMF-exposed embryos. The percentage of dead embryos in the EMF-exposed group (16%) showed a statistically significant increase compared to controls (6.8%).
Juutilainen & Saali 1986	magnetic fields: 30 Hz; 0.1, 1, 10 & 100 A/m exposure duration: 52 h additional tests covering frequencies in the range of 1 Hz to 100 kHz (see corresponding tables).	chickens	malformations and development stage in embryos 52 h of age	At 1 & 10 A/m: increase in malformation rate in EMF-exposed embryos (specified data are lacking). Differences between EMF-exposed embryos and controls were statistically significant.

Table 2: Chicken and quail embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields 50 Hz) on embryonic developmentw

Authors	EMF exposure	test animals	examined parameters	result
Cox et al. 1993	Magnetfeld (vertikal), 50 Hz , 10 μ T. EMF-Exposition während d. ersten 52 h.	Hühner	Missbildungen bei 68 h alten Embryonen. Zusätzlich zu den Versuchen: statistische Aufarbeitung der Daten aus verschiedenen anderen veröffentlichten Studien an Hühnerembryonen mit 100 Hz Feldern.	Keine statistisch signifikanten Unterschiede zwischen Kontrollen und EMF-exponierten Embryonen. Kritische Beurteilung der zum Zeitpunkt der Arbeit veröffentlichten Ergebnisse aus anderen Studien. Bisherige Daten werden als nicht sonderlich aussagekräftig ("robust") bezeichnet.
Cox et al. 1993	magnetic field (vertical): 50 Hz, 10 μ T EMF exposure during first 52 h	chickens	malformations in embryos 68 h of age in addition to tests: statistical processing of data from different other published studies in chicken embryos covering 100-Hz fields	No statistically significant differences between controls and EMF-exposed embryos. Critical evaluation of published results from other studies being available when study was done. Available data are classified as not overly conclusive („robust“).
Juutilainen & Saali 1986	magnetic fields: 50 Hz, 0.1, 1, 10 & 100 A/m exposure duration: 52 h additional tests at frequencies in the range of 1 Hz to 100 kHz (see corresponding tables)	chickens	malformations and development stage in embryos 52 h of age	At 10 & 100 A/m: increase in malformation rate in EMF-exposed embryos (no specified data available). The differences compared to controls were statistically significant.
Pavkofa et al. 1994	magnetic fields: 50 Hz, 6 μ T & 10 mT (vertical or horizontal) exposure duration: 8 h/day up to 8th day of breeding further tests in rats (see corresponding tables)	chickens	embryo mortality and malformations (head, brain, beak, body, eyes, extremities) in embryos 9 days of age	No statistically significant difference between controls and EMF-exposed embryos.
Terol & Panchon 1995	magnetic fields (rectangle, bipolar): 50 Hz; 0.2, 1.2, 2.2 & 3.2 μ T exposure duration: 48 h additional tests at 100 Hz (see corresponding table)	quails	malformations and embryo mortality in embryos 48 h of age	Tests at 0.2 to 2.2 μ T: no statistically significant difference between controls and EMF-exposed embryos. At 3.2 μ T, 60% of EMF-exposed embryos showed malformations or died (controls: 20%). Small samples (n = 10) and lack of statistical evaluation of data according to magnetic flux density.
Veicsteinas et al. 1996	magnetic field (sinus): 50 Hz; 200 μ T exposure duration: 2 h/day, during first two days of breeding	chickens	in embryos 48 h of age: malformations and development stage on 7th of breeding: laminin, fibronectin, collagen IV on 7th, 12th & 18th day of breeding: development of brain, liver and heart in chicks 90 days of age: body weight (from date of hatching), morphology, inner organs, CNS	None of the examined parameters gave proof of statistically significant differences between controls and EMF-exposed embryos and/or hatched chicks.

Table 3: Chicken and quail embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields 60 Hz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Bardasano et al. 1986	magnetic fields: 60 Hz (AC, unipolar), 80 μT (800 mG) exposure duration: 6 days (no precise data)	chickens	development stage & cell anomalies in pinealocytes of embryos 6 days of age	Development stage: no statistically significant differences between controls and EMF-exposed animals. Increase in cell anomalies in pinealocytes of EMF-exposed embryos (no details on statistics).
Bardasano & Bujan 1986	magnetic fields: 60 Hz (AC, unipolar); 80 μT (800 mG) exposure duration: 6 days (no precise data)	chickens	cell anomalies in pinealocytes of embryos 6 days of age	Increase in cell anomalies in pinealocytes of EMF-exposed embryos. The differences between controls and EMF-exposed animals were statistically significant.
Farrell et al. 1997	magnetic field (sinus): 60 Hz; 4 μT exposure duration: 48 h additional tests at 100 Hz (see corresponding tables)	chickens	malformations in embryos 48 h of age, embryo mortality	Embryo mortality: no statistically significant difference between controls and EMF-exposed embryos. Malformations: Increase in malformations (head & body) in EMF-exposed embryos (7.1%) compared to controls (2.3%). Differences between controls and EMF-exposed embryos were statistically significant.
Farrell et al. 1998	magnetic field: 60 Hz; 4 μT additional tests 60-Hz field + 4 μT (rms) fields exposure duration: 48 h	chickens	ornithine decarboxylase (ODC) activity in embryos 8 to 26 h of age	Alteration of ODC activity in EMF-exposed embryos during gastrulation and neurulation. In tests applying an additional 4 μT (rms) magnetic field EMF-exposed embryos show a curve of ODC activity similar to that of controls.
Krueger et al. 1975	magnetic field: 60 Hz; B = 140 μT (mean value); B showed variations between 100 and 200 μT exposure duration: 16 weeks (116 days) further tests with electric 60-Hz field, 260 MHz, 915 MHz, 2.435 GHz (see corresponding tables)	chickens	adult animals: fertility, laying rate, food consumption, egg weight chicks: hatching rate, embryo mortality, malformations, gender ratio.	After about 6 weeks the laying rate of EMF-exposed hens decreased to 32% (controls 78-87%). After the field was switched off, the laying rate increased again. None of the other examined parameters showed effects caused by the investigated field. (eggs were removed from cages right after laying)
Martin 1992	magnetic fields: 60 Hz; 3 μT (uni- & bipolar as well as so-called split-pulse) exposure duration: first 48 h of embryonic development	chickens	embryo mortality and malformations in embryos 48 h of age; during one test series, eggs were opened only on 5th day of embryonic development	There was no proof of statistically significant differences between controls and EMF-exposed embryos.
Martin & Moses 1995	magnetic field: 60 Hz; 4 μT additional tests using 60-Hz field + 4 μT (rms) field exposure duration: first 72 h of embryonic development	chickens	enzyme activity (5'-nucleotidase = 5'NT) in embryos 3 and 6 days of age	Tests with 60 Hz (4 μT) without additional 4 μT noise field: Decrease in 5'NT activity in EMF-exposed embryos. The difference between exposed/controls was statistically significant. Tests with 60 Hz (4 μT) and additional 4 μT noise field: No statistically significant difference between EMF-exposed embryos and controls.

Table 4 (continued): Chicken and quail embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields 100 Hz) on the embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Berman et al. 1990	magnetic field (unipolar): 100 Hz; 1 μ T pulse duration: 500 μ s	chickens	malformations and development stage in embryos 48 h of age tests performed by 6 different working groups in Canada, Sweden, Spain and the USA (Henhouse Project)	A total of 5 out of 6 participating working groups could detect an increase in malformations in EMF-exposed embryos. Only in 2 cases significant differences between controls and EMF-exposed embryos were statistically verifiable.
Delgado et al. 1981	magnetic fields: 100 Hz; 1.2 & 12 μ T pulse duration: 500 μ s exposure duration: 48 h	chickens	malformations and development stage (somites, heart, vascular system and neuronal tissue) in embryos 48 h of age	All EMF-exposed embryos (n = 15) showed malformations. All controls (n = 10) were normally developed.
Delgado et al. 1982	magnetic fields (unipolar): 100 Hz; 0.12, 1.2 & 120 μ T exposure duration: 48 h further tests at 10 & 1000 Hz (see corresponding tables)	chickens	malformations and development stage (somites, heart, vascular system and neuronal tissue) in embryos 48 h of age	At all three tested magnetic flux densities, 18 out of 19 EMF-exposed embryos showed malformations of the heart and/or the neuronal tissue and/or the vascular system and/or somites. All controls (n = 10) were normally developed.
Farrell et al. 1997	magnetic field (unipolar): 100 Hz; 1 μ T; 500 μ s exposure duration: the first 2 days of breeding additional test at 60 Hz (see corresponding tables)	chickens	malformations in embryos 48 h of age, embryo mortality total of 4 test series	Embryo mortality: no statistically significant difference between controls and EMF-exposed embryos. Malformations: Increase in malformations (head, body) in EMF-exposed embryos. Three test series showed statistically significant differences between controls and EMF-exposed embryos. The relevance of genetic variability is still under discussion.
Juutilainen 1986	magnetic field (sinus): 100 Hz; 1 A/m different breeding temperatures: 36.3, 37.0, 38.0 & 38.5° C exposure duration: first 2 days of breeding	chickens	malformations in embryos 50 h, 52 h, 55 h, 57 h of age	At a breeding temperature of 36.3 & 37.0° C the number of malformations in EMF-exposed embryos increased. The difference compared to controls was statistically significant. At 38.0 & 38.5° C (breeding temperature), differences between controls and exposed embryos were not statistically significant (caused by an increase in malformation rate of control groups).
Koch & Koch 1991	magnetic fields: 100 Hz; 1 μ T unipolar, bipolar and sinusoidal different periods (100 μ s - 30 ms) exposure duration: no specification, probably 48 and/or 72 h	chickens	malformations and development stage of embryos 48 and 72 h of age	No statistically significant differences between controls and EMF-exposed embryos.

Table 4 (continued): Chicken and quail embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields 100 Hz) on the embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Leal et al. 1986	magnetic fields (bipolar): 100 Hz; 0.4 & 1.0 μT pulse duration: 500 μs exposure duration: 48 h	chickens	malformations in embryos 48 h of age	The authors report a statistically verified significant association between malformation rate in sham-exposed embryos of the control group and natural alterations of the horizontal component of the geomagnetic field. Where the field strength of the natural geomagnetic field grew by about 100 to 150 nT, an increase in malformations was observed.
Leal et al. 1989	magnetic fields (bipolar): 100 Hz; 0.4 & 1.0 μT pulse duration: 500 μs exposure duration: 48 h	chickens	malformations in embryos 48 h of age	5 out of 13 test series could detect an increase in malformation rate in EMF-exposed embryos. The difference compared to controls was statistically significant. In their study, the authors assume an association between alterations of the geomagnetic field (horizontal component) and malformation frequency.
Litovitz et al. 1994	magnetic field (unipolar): 100 Hz; 1 μT pulse duration: 500 μs additional tests with 1 μT (rms) field exposure duration: 48 h	chickens	malformations in embryos 48 h of age	In tests without the 1 μT (rms) „interference field“, in EMF-exposed embryos an increase in malformation rate was observed. The difference between exposed/controls was statistically significant. When an additional 1 μT (rms) field was applied, no statistically significant difference could be detected.
Maffeo et al. 1984	magnetic field (rectangle): 100 Hz; 1.2 & 12 μT pulse duration: 0.5 ms additional tests at 1 kHz (see corresponding tables)	chickens	development stage, malformations (f.e. blood vessels, nervous system, heart, somites, optic vesicles) in embryos 48 h of age	None of the test parameters showed statistically significant effects of the examined 100-Hz field.
Maffeo et al. 1988	magnetic field: 100 Hz; 1 μT pulse duration: 0.5 ms additional positive control with x-rays (15.52 Gy)	chickens	development stage, malformations (f.e. blood vessels, nervous system, heart, somites, optic vesicles) in embryos 48 h of age	None of the test parameters showed statistically significant effects of the examined 100-Hz field.
Martin 1988	magnetic field: 100 Hz; 1 μT exposure duration: the whole first 48 h, the first 24 h and/or the second 24 h of embryonic development	chickens	malformations in embryos 48 h of age	Only tests where embryos were exposed to EMF during the first 24 and/or 48 h, could detect a statistically significant increase in malformations. When the EMF was applied exclusively during the second 24 h of embryonic development, no statistically significant difference between controls and EMF-exposed embryos was determined.
Martucci et al. 1984	magnetic field: 100 Hz; 1.2 μT pulse duration: 0.5 ms exposure duration: 48 h	chickens	malformations in embryos 48 h of age	There was no proof of statistically significant effects of the examined 100-Hz field.
Terol & Panchon 1995	magnetic fields (bipolar): 100 Hz; 0.2, 1.2, 2.2 & 3.2 μT exposure duration: 48 h additional tests at 50 Hz (see corresponding table)	quails	malformations and embryo mortality in embryos 48 h of age	At 0.2 and 3.2 μT , the EMF-exposed groups showed an increased embryo mortality and malformation rate compared to controls. At 1.2 & 2.2 μT no significant differences. Small samples (n = 10) and unprecise statistical evaluation of data.

Table 4: Chicken and quail embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields 100 Hz) on the embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Ubeda et al. 1983	magnetic fields: 100 Hz; 100 μ s; 0.4, 1.0, 10.4, 13.9 & 104 μ T 100 Hz; 2 μ s; 0.4 μ T 100 Hz; 42 μ s; 1 μ T 100 Hz; 42 μ s (signal with peaks); 1 μ T pulse duration: 500 μ s; the rest of the data refer to the time period of increase exposure duration: 48 h	chickens	malformations (somites, nervous system, heart, vascular formation) in embryos 48 h of age	100 Hz, 100 μ s: None of the examined flux densities showed statistically significant differences between controls and EMF-exposed embryos. 100 Hz; 2 μ s; 0.4 μ T: 83% of the EMF-exposed embryos showed malformations (controls 34.7%). 100 Hz; 42 μ s; 1 μ T: 70.8% of the EMF-exposed embryos showed malformations (controls 16.6%). 100 Hz; 42 μ s (signal with peaks): No statistically significant differences between controls and EMF-exposed embryos.
Ubeda et al. 1994	magnetic fields (bipolar): 100 Hz; 1 μ T pulse duration: 500 μ s increase: 2.1 & 85 μ s exposure during the first 48 h of embryonic development	chickens	embryo mortality and malformations (extremities, eyes, skeletal formation) in embryos 48 h of age	100 Hz; 1 μ T; 85 μ s: no statistically significant differences between controls and EMF-exposed embryos. 100 Hz; 1 μ T; 2.1 μ s: malformations in 29.3 % of the EMF-exposed embryos (controls 11.9%).

Table 5: Chicken and quail embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields, frequency range: 1 to 10 kHz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Delgado et al. 1982	magnetic fields (unipolar): 1 kHz; 0.12, 1.2 & 120 μ T exposure duration: 48 h further tests with 10 & 100 Hz (see corresponding tables)	chickens	malformations and development stage (somites, heart, vascular system and neuronal tissue) in embryos 48 h of age	All three examined flux densities showed malformations of the heart and/or neuronal tissue and/or the vascular system and/or the somites in all EMF-exposed embryos (n = 11). Out of controls (n = 10) only three embryos had malformations. Very small sample size, lack of exact statistical data.
Juutilainen & Saali 1985	magnetic fields: 1 kHz; 0.1, 1, 10, 100 A/m exposure duration: 52 h additional tests with frequencies in the range of 1 Hz to 100 kHz (see corresponding tables)	chickens	malformations and development stage in embryos 52 h of age	At 10 & 100 A/m: increase in malformation rate in EMF-exposed embryos (no detailed specifications). Differences compared to controls were statistically significant.
Maffeo et al. 1984	magnetic field (rectangle): 1 kHz; 1.2 & 12 μ T pulse duration: 0.5 ms additional tests at 100 Hz (see corresponding table)	chickens	development stage, malformations (f.e. blood vessels, nervous system, heart, somites, optic vesicles) in embryos 48 h of age	None of the test parameters showed statistically significant effects of the examined 1-kHz field.
Juutilainen & Saali 1986	magnetic fields: 10 kHz; 0.1, 1, 10, 100 A/m exposure duration: 52 h additional tests with frequencies in the range of 1 Hz to 100 kHz (see corresponding tables)	chickens	malformations and development stages in embryos 52 h of age	At 1 & 10 A/m: increase in malformation rate in exposed embryos (no detailed specifications). Differences compared to controls were statistically significant.

Table 6: Chicken and quail embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic resonance tomographs = MRT, monitors) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Krueger et al. 1975	Elektrisches Feld, 60 Hz , 1600 V/m. Expositionsdauer: 16 Wochen (116 Tage). Weitere Versuche mit 60 Hz Magnetfeld, 260 MHz, 915 MHz, 2,435 GHz. S. entsprechende Tabellen.	Hühner	<i>Adulte Tiere</i> : Fertilität, Legerate, Futteraufnahme, Eiengewicht. <i>Küken</i> : Schlüpfrate, Embryonalsterblichkeit, Missbildungen, Geschlechterverhältnis.	Nach ca. 6 Wochen sank die Legerate der EMF-exponierten Hennen auf 51% (Kontrollen 78-87%). Nach ca. 3 weiteren Wochen stieg die Legerate spontan wieder an. Bei allen anderen untersuchten Parametern konnten keine Einflüsse des untersuchten Feldes festgestellt werden. * Die Eier wurden direkt nach dem Legen aus den Käfigen entfernt.
Krueger et al. 1975	electric field: 60 Hz; 1600 V/m exposure duration: 16 weeks (116 days) further tests with 60 Hz magnetic field, 260 MHz, 915 MHz, 2.435 GHz (see corresponding tables)	chickens	adult animals: fertility, laying rate, food consumption, egg weight chicks: hatching rate, embryo mortality, malformations, gender ratio	After about 6 weeks the laying rate of EMF-exposed hens decreased to 51% (controls 78-87%). After further 3 weeks laying rate spontaneously increased again. None of the other test parameters showed effects of the examined field (eggs were removed from the cages right after laying).
Yip et al. 1994a	MRT-field simulation: magnetic field (static): 1.5 T & 64-MHz field (amplitude modulated with 625 Hz) magnetic field: switched between + 60 μ T/cm and - 60 μ T/cm in 1.2 ms exposure (static field = 6 h, 64 MHz field & 60 μ T field = 4 h) after 0-6; 12-18; 24-32 & 36-42 hours of breeding	chickens	malformations, embryo mortality in embryos 53 h and/or 6 days of age	In some tests, both embryo mortality as well as the number of malformations (f.e. somites, body, head) increased in the exposed test group compared to controls. However, differences were not statistically significant.
Yip et al. 1994b	MRT-field simulation: magnetic field (static): 1.5 T & 64-MHz field (amplitude modulated with 625 Hz) magnetic field: switched between + 60 μ T/cm and - 60 μ T/cm in 1.2 ms exposure: (static field = 6 h, 64-MHz field & 60- μ T field = 4 h) 50-53 h and on 3rd day after fertilisation	chickens	cell proliferation and cell movement of motoneurons in embryos 6 and/or 10 days of age	No statistically significant difference between controls and EMF-exposed groups.
Yip et al. 1995	MRT-field simulation: magnetic field (static): 1.5 T & 64-MHz field (amplitude modulated at 625 Hz) magnetic field: switched between + 60 μ T/cm and - 60 μ T/cm in 1.2 ms exposure: (static field = 6 h, 64 MHz field & 60 μ T field = 4h) after 42 h and on 5th day of breeding	chickens	growth of axons in sympathetic nervous system in embryos 6 to 7 days of age	No statistically significant differences between controls and EMF-exposed embryos.
Youbicier-Simo et al. 1997	TV monitor: 50 Hz; 270 nT TV monitor: 15-80 kHz; 4 nT computer monitor (desk top): 15-80 kHz; 13 nT computer monitor (desk top): 50 Hz; 660 nT exposure duration: whole breeding period	chickens	embryo mortality (over whole breeding period), different blood parameters (plasma-melatonin, corticosterone, thyroglobulin antibodies) in hatched chicks	Increase in embryo mortality in EMF-exposed embryos (47-68%). Controls: 15-33%. Decreased melatonin and corticosterone levels as well as thyroglobulin antibodies in EMF-exposed chicks. Differences between controls and EMF-exposed embryos and/or chicks were statistically significant.

2.1.2 Studies in mammalian embryos (in vivo)

The studies on effects of low-frequency fields on the embryonic development of mammals to the main part were performed in rats or mice. One study each investigated electric fields in cattle (ANGELL et al. 1990) and pigs (SIKOV et al. 1987) (table 13). 24 studies describe the results of 32 tests covering magnetic fields in the range of 50-20 kHz (tables 7 to 10), static magnetic fields (table 7), MRT-fields (table 11), and electric fields (20-100 Hz as well as 500 kV, table 12). As was the case with the studies done in chicken and quail embryos, here, too, for most frequencies and/or fields only 1 or 2 papers were published (graph 2). For frequencies which were the subject of more than 3 studies, there were partially considerable differences in test design (f.e. field parameters, dura-

tion and time of exposure), too. Therefore, we abstained from comparing results (graph 2).

The most frequent test parameters were embryo mortality (25 studies), the incidence of malformations (23 studies) and the number of prematurely died fetuses (19 studies). Embryo mortality rate was found via the number of resorbed embryos (blastocytes) determined by means of the resorption scars in the placenta.

Further test parameters were body weight of the fetuses (15 studies), body height and/or head-body-length (8 studies), ossification or skeletal formation (6 studies), gender ratio (4 studies) as well as different blood parameters (2 studies; see graph 3).

18 (55%) of a total of 32 studies could verify at least for one of the

test parameters a statistically significant effect of the examined fields on embryos/fetuses, on young or on the mother animals. At first glance, this seems to be a rather high percentage. However, apart from malformation rate, none of the test parameters showed a distinct accumulation. An increase in embryo mortality of EMF-exposed embryos, for example, could only be observed in 3 (12.0%) of a total of 25 tests. Comparable results were provided by the tests on mortality of EMF-exposed fetuses (graph 3a).

The other parameters examined in embryos and/or fetuses in nearly all tests neither gave proof of effects of the applied EMF (graph 3a). The tests performed in EMF-exposed mother animals showed only weak effects (graph 3b). In young having been exposed to EMF during embryonic development in the uterus a mostly temporary decrease in body weight was observed (MARINO et al. 1976). In one case, after prenatal exposure additionally an increased mortality was detected in young (F1-F3 generation; MARINO et al. 1976). The applied EMF had no effect at all on biological test parameters (f.e. spermatogenesis, fertility, mortality) in the examined male animals (f.e. KOWALCZUK et al. 1995, DAWSON et al. 1998). Similar effects were observed in rats and in mice. Distinct differences between the two animal models cannot be detected.

As was the case in studies performed in chicken embryos, for most frequencies only 1 to 2 studies are available (see graph 2). Thus, it

Magnetic fields/frequency	number of studies	table
static field		2 7
50.0 Hz	7	8
60.0 Hz	2	9
10.0 kHz	1	9
15.6 kHz	1	9
17.8 kHz	1	9
20.0 kHz	6	10
MRT	3	11
Magnetic fields/frequency	number of studies	table
20.0 Hz	1	12
50.0 Hz	1	12
60.0 Hz	5	12
100.0 Hz	1	12
High-voltage (500 kV)	1	12

Graph 2: Teratologic studies on effects of low-frequency EMF on mammalian embryos. Examined fields and frequencies (electric & magnetic fields).

seems reasonable to compare available results only for 50-Hz magnetic fields (7 studies), 20-kHz fields (6 studies) and electric 60-Hz fields (5 studies).

For 50-Hz magnetic fields, there is a total of 7 studies (see table 8) performed between 1985 to 1997. 5 studies used rats, the remaining 2 used mice as test animals. The studies covering 50-Hz magnetic fields could observe only very small

overall effects. One study performed in EMF-exposed rats (HUUSKONEN et al. 1993) could detect a statistically significant increase in minor skeletal anomalies. Interestingly, in these tests the number of implantations and of living fetuses in the EMF-exposed test group was larger than in the control group. In addition, the EMF-exposed mother animals had a larger body and uterus weight than control animals (HUUSKONEN et al. 1993). MEVIS-

SEN et al. (1994), too, report an increase in minor skeletal anomalies (especially of ribs) in EMF-exposed fetuses as well as a higher corpus luteum performance of exposed mother animals. All differences were statistically significant. The remaining 5 studies as well as all other test parameters could give no evidence for effects of the applied 50-Hz fields. However, nearly all studies applied different magnetic flux densities in the range of 10 μ T to 20

Test parameters	studies	effects caused by EMF	no effects
embryo mortality	25	3 (12.0%)	22 (88.0%)
malformations	23	8 (34.8%)	15 (65.2%)
fetus mortality	19	2 (10.5%)	17 (89.5%)
weight of fetuses	15	2 (13.3%)	13 (86.7%)
body size/length	8	1 (12.5%)	7 (87.5%)
ossification/skeletal formation	6	2 (33.3%)	4 (66.7%)
gender ratio	4	0	4
different blood parameters	2	0	2

Graph 3a: Medical and biological parameters examined under the influence of low-frequency fields in mammalian embryos

Test parameters	studies	effects caused by EMF	no effects
<i>corpus luteum</i>	10	1 (10.0%)	9 (90.0%)
number of young/litter	10	0	10
fertility	9	1 (11.1%)	8 (88.9%)
body weight	7	0	7
number of litters/group	5	1 (20.0%)	4 (80.0%)
placenta weight	5	0	5
uterus weight	4	0	4
different blood parameters	4	1 (25.0%)	3 (75.0%)
weight gain during gestation	3	0	3
bone marrow	2	0	2
food consumption	1	0	1
menstrual cycle	1	0	1
mortality	1	0	1
inner organs (weight)	1	0	1
ovulation	1	0	1

Graph 3b: Medical and biological parameters examined under the influence of low-frequency fields in mammals (mother animals)

mT. Though the studies of PAVKOFA et al. (1994) and KOWALCZUK et al. (1995) used an identical magnetic flux density, PAVKOFA et al. (1994) performed tests in rats, whereas KOWALCZUK et al. (1995) examined mice.

A total of 6 studies (table 10) examined potential effects of 20-kHz magnetic fields on the embryonic development of rats (1 study) and mice (5 studies). The study performed in rats showed a statistically significant increase in the number of minor skeletal anomalies in the EMF-exposed group compared to controls (HUUSKONEN et al. 1993). The studies in mice were performed under comparable and/or more or less identical test conditions. So, for instance, magnetic fields had the same form (sawtooth), and also the applied magnetic flux densities were the same: 15, 17, 130 & 200 μT (WILEY et al. 1992, JUUTILAINEN et al. 1997). Nonetheless, available results are heterogeneous: the authors of two studies report a statistically significant increase in the mortality rate of EMF-exposed mouse embryos and/or mouse fetuses (FRÖLEN et al. 1993, SVEDENSTÅL & JOHANSON 1995). The remaining 3 studies could not determine any verifiable effects of the examined 20-kHz fields on the EMF-exposed mouse embryos, fetuses or mother animals (WILEY et al. 1992, JUUTILAINEN et al. 1997, HUUSKONEN et al. 1998). In this case, the different findings are difficult to explain, since apart from the more or less identical test conditions, four studies also applied

mice of the same origin and strain (CBA/S). Only WILEY et al. (1992) used CD-1 mice. In their study from 1997, JUUTILAINEN and colleagues discuss possible factors being responsible for result discrepancies: infections and/or parasites, strong variations of resorption rates in controls, differences between geomagnetic field conditions, the applied spindles as well as applied statistical methods. Still, the question whether, and if so, which one of the possible factors has affected results of the 4 studies, ultimately remains unanswered (JUUTILAINEN et al. 1997, 1998).

Effects of electric 60-Hz fields on the embryonic development of mammals was examined by a total of 5 studies. Three studies used rats, the remaining 2 mice and pigs. 4 out of 5 studies report statistically significant effects of the examined fields on tested embryos, fetuses or maternal/paternal animals. The animals of the F1 and F2 generation from the exposed test groups of MARINO et al. (1976) had a smaller body weight compared to sham-exposed control animals. In addition, the exposed animals of the F1, F2 and F3 generation showed an increased mortality rate between the 8th and 35th day after birth (statistical data are lacking). SIKOV et al. (1984) report alterations of behavioral parameters of rats having been exposed to an electric 60-Hz field during embryonic development and/or from 8th to 25th day of life. However, these effects could only be observed temporarily, namely in the 2nd week of life. A second study of

SIKOV et al. (1987) - this time performed in pigs - showed an increase in litters with congenital malformations (f.e. skeleton, muscles, toes, tail, CNS and eyes), a smaller body weight as well as different skull measures (skull width, interorbital distance) in EMF-exposed test groups. Two studies in rats done by Rommereim et al. (1987, 1990) investigated possible effects of electric 60-Hz fields on embryonic development, ontogenesis and well-being of mother animals. One of the studies demonstrated an increased number of litters with congenital malformations as well as an increased mortality rate of embryos and/or fetuses in the EMF-exposed group compared to controls. Differences were small but still statistically significant. However, the authors do not think that these differences were caused by the applied 60-Hz field, interpreting them instead as a normal biological variation (ROMMEREIM et al. 1987). In their second study (ROMMEREIM et al. 1990), the authors could not prove any effects of the examined fields. Generally, none of the 5 available studies provided evidence for effects of the examined electric 60-Hz fields for most of the used biological parameters.

ZUSMAN et al. (1990) examined the effects of electric 20, 50 & 100 Hz fields in rats. Apart from a temporary decrease of body weight in young, the tests did not show any statistically significant differences between prenatally EMF-exposed animals and controls. A study

performed in cattle exposed to a 500-kV field of a high-voltage line neither could prove effects of the examined field (ANGELL et al. 1990).

In a test series with mice, CHIANG et al. (1995) in addition to the examined EMF (15.6 KHz) applied cytosine arabinosid (ARA-C), a known teratogen. They could show that the 15.6-KHz field not only led to a statistically significant in malformation rate by itself, but - at least in the view of the authors - additionally increased the teratogenic effect of ARA-C (CHIANG et al. 1995, see table 10). Regrettably, this is the only to-date available study applying a potentially teratogenic agency in addition to the electromagnetic field. Thus, consistent results on possible synergistic, antagonistic or potentiating effects of low-frequency EMF in association with potential teratogens are still lacking. In view of the numerous existing teratogenic environmental parameters (building material, chemicals, drugs, etc) this sure is an interesting subject for future tests which in vivo studies should take into consideration.

Table 7: Mammalian embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Mevisen et al. 1994	static magnetic field: 30 mT exposure: constant over the whole duration of embryonic development additional tests at 50 Hz (see corresponding table)	rats	embryos: embryo mortality (resorptions, implantations) fetuses: dead fetuses, skeletal formation and malformations in fetuses 20 days of age mother animals: corpus luteum	young (F1 generation): postnatal development after constant exposure during embryonic development Increase in number of dead and resorbed embryos within EMF-exposed group. Accelerated ossification of the fore extremities (metacarpus). Differences between controls and EMF-exposed embryos/fetuses were statistically significant. The rest of the examined parameters showed no statistically significant differences between controls and exposed animals.
Murakami et al. 1992	static magnetic field: 6.3 T exposure duration: 1 h/day from 7th to 14th day of embryonic development	mice	embryos: mortality (resorptions) fetuses: mortality, malformations (f.e. skeletal formation, exencephalia) and body weight in fetuses 18 days of age mother animals: number of embryos and/ or fetuses, body weight	None of the examined parameters provided evidence for statistically significant differences between controls and EMF-exposed fetuses and/or mother animals.

Table 8: Mammalian embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields 50 Hz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Huuskonen et al. 1993	magnetic field (sinus): 50 Hz; 35.6 μ T exposure duration: first 20 days of embryonic development additional tests with magnetic field (sawtooth): 20 kHz; 15 μ T (see corresponding table)	rats	embryos: embryo mortality (implantations, resorptions) fetuses: dead fetuses, skeletal formation and malformations in fetuses 20 days of age mother animals: body weight, placenta and uterus weight (including fetuses)	Increase in number of minor skeletal anomalies, larger number of implantations and living fetuses in EMF-exposed animals (differences exposed/controls statistically significant). EMF-exposed mother animals: higher body and uterus weight. The differences between exposed and animals of control group were statistically significant.
Juutilainen et al. 1997	magnetic field (sinus): 50 Hz; 13 & 130 μ T (rms) EMF exposure: constant up to 18th day of embryogenesis fetuses. further tests with magnetic field: 20 kHz; 15 μ T (see corresponding table)	mice	embryos: embryo mortality (resorptions, implantations) fetuses: dead fetuses, weight & size of fetuses (18th day of embryonic development), malformations mother animals: fertility, corpus luteum, uterus weight	None of the examined parameters provided evidence for statistically significant differences between controls and EMF-exposed mother animals and/or
Kowalczuk et al. 1994	magnetic field (sinus): 50 Hz; 20 mT EMF-exposure: constant up to 17th day of embryonic development	mice	embryos: embryo mortality fetuses: dead fetuses, malformations (inner organs, skeleton, extremities, cleft palate) in fetuses 17 days of age mother animals: corpus luteum	No statistically significant differences between controls and EMF-exposed animals were found.
Kowalczuk et al. 1995	magnetic field (sinus): 50 Hz; 10 mT EMF exposure: constant, 8 weeks	mice	spermatogenesis in EMF-exposed male mice; indicator: number of pregnant females; living and dead fetuses, corpus luteum in the uterus of mother animals	No statistically significant differences between controls and EMF-exposed animals were found.
Mevissen et al. 1994	magnetic field: 50 Hz; 30 mT EMF exposure: constant over the whole duration of embryonic development additional tests with static 30-mT field (see corresponding table)	rats	embryos: embryo mortality fetuses: dead fetuses, skeletal formation, malformations in fetuses 20 days of age mother animals: corpus luteum	Increase in corpus luteum performance in EMF-exposed mother animals. Increase in minor skeletal anomalies ribs, not described in detail). Differences compared to (especially the controls were statistically significant. The remaining examined parameters did not provide evidence for statistically significant differences between controls and exposed embryos, fetuses and mother animals.
Pavkofa et al. 1994	magnetic fields: 50 Hz; 10 mT vectors: vertical exposure: day 1 to 19 of embryogenesis further tests with chickens (see corresponding table)	rats	embryos: embryo mortality fetuses: dead fetuses, malformations (f.e. head, brain, eyes, extremities, body) in fetuses 19 days of age mother animals: body weight and corpus luteum	None of the examined parameters showed statistically significant differences between controls and EMF-exposed embryos, fetuses and mother animals.
Zecca et al. 1985	magnetic fields: 50 Hz; 58 mT (580 G) exposure: day 6 to 15 of embryogenesis	rats	embryos: embryo mortality fetuses: mortality, malformations (skeletal formation, inner organs, extremities), weight of embryos 20 days of age adult animals: body weight, general well-being, behavior, fecal samples, histological tests in following organs: heart, lungs, liver, pancreas, spleen, bladder, thyroid gland, suprathyroid gland, prostate gland, testes. Various blood parameters: f.e. hemoglobin, leukocytes, glucose, urea, bilirubin, creatinine, cholesterine, lipids, proteins, SGOT, SGPT. Urine samples: ph value, albumen, glucose, blood, ketone, bilirubin.	None of the examined parameters showed statistically significant differences between controls and EMF-exposed fetuses and/or embryos. Impairments caused by the examined 50-Hz field neither could be found in adult animals.

Table 9: Mammalian embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Ryan et al. 1996	magnetic fields: 60 Hz; 2 & 200 μ T & 1 mT (0.02, 2.0 & 10.0 G) exposure duration: 18.5 h/day from 6th to 19th day of embryonic development group with ethyl-thio-uric acid application as a positive control for teratogenicity	rats	embryos: embryo mortality fetuses: mortality, malformations (skeletal formation, head, brain, extremities, inner organs), weight mother animals: food consumption, body weight, mortality rate, weight of inner organs and ovaries, corpus luteum	None of the examined parameters gave proof of statistically significant differences between controls and EMF-exposed animals and/or fetuses.
Ryan et al. 1999	magnetic fields: 60 Hz; 2 & 200 μ T & 1 mT (0.02, 2.0 & 10.0 G) exposure: constant, over the whole duration of embryonic development for 18.5 h/day and/or alternating 1h on/1h off; 1 mT) different exposure periods for F0, F1 and F2 generations	rats up to F2 generation	embryos: embryo mortality fetuses: mortality, body weight, gender ratio mother animal: litter size, fertility young: body weight F1 generation was observed over whole life span	None of the examined parameters showed statistically significant differences between controls and EMF-exposed animals and/or fetuses. This refers to each of the examined generations.
Dawson et al. 1998	magnetic fields: 10 kHz; 0.095, 0.24 & 0.95 mT EMF exposure: test series 1: 20 to 23.5 h/day, constant up to 22th day of embryogenesis; test series 2: male animals, 20 to 23.5 h/day, 45th to 58th day before coupling; test series 3: female animals, 20 to 23.5 h/day, 30 to 72 days before coupling	rats	embryos: embryo mortality (implantations, resorptions) fetuses (22nd day): mortality, gender ratio, weight, malformations, skeletal development, blood parameters (among others leukocytes, monocytes) mother animals: weight increase, number and size of litters, ovulation, menstrual cycle, fertility, blood parameters (among others lymphocytes, albumen, potassium) male animals: weight, fertility, mortality rate, histological and pathological tests (among others sexual organs), blood parameters (see above)	Tests in adult animals showed some minor but statistically significant differences (f.e. blood parameters, number of living fetuses). However, the authors do not think that these were caused by the examined fields interpreting them instead as biological variations. The remaining examined parameters did not show any statistically significant differences between controls and EMF-exposed animals and/or fetuses.
Chiang et al. 1995	magnetic fields (sawtooth): 15.6 kHz; 40 μ T exposure duration: 4 h/day from 6th to 17th day of embryogenesis 1 group only EMF, 1 group EMF + ARA-C (= cytosine arabinosid)	mice	embryos: embryo mortality (resorption) fetuses: prematurely died fetuses, malformations (f.e. cleft lip and cleft palate, brain, extremities), skeletal formation, weight and size in fetuses 18 days of age	In the three test groups (only EMF, EMF + ARA-C, only ARA-C), the number of fetuses with cleft lip and cleft palate showed a statistically significant increase compared to untreated controls. With 49.0% malformation rate within the group EMF + ARA-C was the largest (EMF: 14.9%, ARA-C: 26.1%, controls: 2.6%). The remaining examined parameters showed no teratogenic and/or embryolethal effects of the examined EMF. In the view of the authors, the EMF increases the teratogenic impact of ARA-C.
Stuchly et al. 1988	magnetic field (sawtooth): 17.8 kHz; 5.7; 23 & 66 μ T exposure: 7 h/day, 15 days before coupling, up to 22th day of embryonic development	rats	embryos: embryo mortality (resorptions, implantations) fetuses: mortality, malformations (inner organs, extremities, skeleton), weight mother animals: body weight, weight increase, placenta weight, blood parameters (among others erythrocytes, leukocytes, hematocrite value, hemoglobin), bone marrow samples, number and size of litters	Embryos/fetuses: at 23 μ T & 66 μ T increase in skeletal malformations. The differences between EMF-exposed animals and controls were statistically significant. Neither the remaining test parameters nor an intensity of 5.7 μ T showed any statistically significant differences between controls and EMF-exposed animals Mother animals: at 23 μ T (hemoglobin) & 66 μ T (leukocytes, lymphocytes & erythrocytes) smaller values were observed in the EMF-exposed animals compared to controls. The differences were statistically significant. None of the other parameters did provide evidence for statistically significant differences.

Table 10: Mammalian embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic fields, frequency range: 20 kHz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Frölen et al. 1993	magnetic field (sawtooth): 20 kHz; 15 μ T exposure: test series 1 & 2: 1st to 19th day of embryonic development; test series 3: 2nd to 19th day of embryonic development; test series 4: 5th to 19th day of embryonic development; test series 5: 7th to 19th day of embryonic development	mice (CBA/S)	embryos: embryo mortality (resorptions, implantations) fetuses: number of dead fetuses, malformations, weight and size of fetuses	At EMF exposure on 1st to 19th; 2nd to 19th & 5th to 19th day of pregnancy the number of placental resorptions showed a statistically significant increase in the EMF-exposed groups compared to controls. At EMF-exposure from 1st to 19th day additionally the number of died fetuses showed a statistically significant increase. During tests with EMF exposure from 7th to 19th day the EMF-exposed fetuses were smaller and lighter compared to controls. These differences were statistically significant. The number of malformations provided no evidence for statistically significant differences between EMF-exposed fetuses and controls.
Huuskonen et al. 1993	magnetic field (sawtooth): 20 kHz; 15 μ T (12 A/m) exposure duration: first 20 days of embryonic development additional tests with magnetic field (sinus): 50 Hz; 35.6 μ T (28.3 A/m) (see corresponding table)	rats (Wistar)	embryos: embryo mortality (implantations, resorptions) fetuses: skeletal formation and malformations in fetuses 20 days of age mother animals: body weight, placenta as well as uterus weight (including fetuses)	Increase in number of minor skeletal anomalies in EMF-exposed fetuses. The differences compared to controls were statistically significant. None of the other examined parameters showed statistically significant differences between controls and EMF-exposed fetuses.
Huuskonen et al. 1998	magnetic field (sawtooth): 20 kHz; 15 μ T (150 mG) exposure: constant up to 18th day of embryogenesis	mice (CBA/S)	embryos: embryo mortality (resorptions, implantations) fetuses: malformations and weight in fetuses 18 days of age mother animals: weight, bone marrow & blood samples (erythrocytes, micronuclei), corpus luteum (uterus)	None of the examined parameters gave evidence for statistically significant differences.
Juutilainen et al. 1997	magnetic field (sawtooth): 20 kHz; 13 & 130 μ T (rms) exposure: constant up to 1 for statistically significant differences. 8th day of embryogenesis further tests with magnetic field 50 Hz; 13 & 130 μ T (see corresponding table)	mice (CBA/S)	embryos: embryo mortality (resorptions, implantations) fetuses: dead fetuses, malformations, weight & size of fetuses (18th day of embryonic development) mother animals: fertility, corpus luteum, uterus weight	None of the examined parameters provided evidence for statistically significant differences between controls and EMF-exposed animals and/or fetuses.
Svedenstål & Johanson 1995	magnetic field (sawtooth): 20 kHz; 15 μ T EMF-exposure: group 1: constant, day 1 to 5.5 of embryogenesis; group 2: constant, day 1 to 7 of embryogenesis	mice (CBA/S)	embryos: embryo mortality fetuses: number of prematurely died fetuses, malformations, weight & size of fetuses 19 days of age mother animals: fertility, calcium & progesterone (blood values)	Tests applying EMF-exposure up to day 5.5 showed an increased number of died fetuses in the EMF-exposed group compared to controls. Further, both weight and body size (length) of EMF-exposed fetuses lay below values of controls. The differences were statistically significant. None of the other examined parameters and neither tests applying EMF exposure up to the 7th day of embryonic development showed statistically significant differences between EMF-exposed animals and controls.
Wiley et al. 1992	magnetic fields (sawtooth): 20 kHz; 3.6, 17 & 200 μ T exposure duration: constant from 1st to 18th day of embryonic development	mice (CD-1)	embryos: embryo mortality (implantations, resorptions) fetuses: number of died fetuses, malformations (inner organs, extremities, skeleton), ossification mother animals: uterus weight, body weight, fertility	None of the examined parameters showed statistically significant differences between controls and EMF-exposed animals and/or embryos/fetuses.

Table 12: Mammalian embryos: Studies (in vivo) on effects of low-frequency EMF (electric fields) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Angell et al. 1990	high-voltage line: (+/-) 500 kV exposure over 30 months	cattle	body weight of adult animals, fertility, mortality rate, weight increase in calves	None of the examined parameters showed statistically significant differences between exposed test animals and controls.
Zusman et al. 1990	electric fields: 20 Hz; 0.6 V/m exposure over the whole duration of embryonic development additional tests with 50 & 100 Hz as well as in vitro tests in mouse and rat embryos (see corresponding tables)	rats	number of offspring per litter & body weight of young after 1, 7, 14, 21 & 28 days of prenatal EMF-exposure; number of malformations	Slightly increased postnatal mortality in group of EMF-exposed young. However, a significant difference compared to control animals was not statistically verifiable. On the 1st day after birth the body weight of EMF-exposed rats lay below that of control animals. The difference was statistically significant. In contrast, no statistically significant increase in malformations was shown in EMF-exposed rats.
Zusman et al. 1990	electric fields: 50 Hz; 0.6 V/m EMF exposure over the whole duration of embryonic development; additional tests with 20 & 10 Hz as well as in vitro tests in mouse and rat embryos (see corresponding tables)	rats	number of offspring per litter & body weight of young after 1, 7, 14, 21 & 28 days of prenatal exposure; number of malformations (young)	Slightly increased postnatal mortality in group of EMF-exposed young. However, a significant difference compared to control animals was not statistically verifiable. From the 3rd week of life the body weight of EMF-exposed rats lay below that of control animals. The difference was statistically significant. There was no evidence for a statistically significant increase in malformations in EMF-exposed rats.
Marino et al. 1976	electric fields: 1. test group: horizontal; 60 Hz; 500 V/m; 2. test group: vertical; 60 Hz; 500 V/m exposure duration: constant over three generations	mice up to F3 generation	mortality and body weight of all test animals (all generations)	Both in the vertical and the horizontal field, the EMF-exposed animals of the 1st & 2nd generation (both sexes) had a smaller body weight than controls. The differences were statistically significant. the 8th to 35th day after birth in EMF-exposed animals compared to controls: F1: 10% versus 2%; F2: 58% versus 4%; F3: 35% versus 2% In the vertical field, mortality rate was increased between (statistical specifications are lacking).
Rommereim et al. 1987	electric field: 60 Hz; 100 kV/m exposure: 19 h/day, over the whole duration of tests 2 independent test series were performed	rats up to F1 generation	embryos: embryo mortality (implantations, resorptions) fetuses: number of dead and living fetuses, weight of fetuses, gender ratio, body length (head - body), malformations: among others hydrocephalis, micro- and anophthalmia, extremities, skull, skeletal formation (ossification), inner organs mother animals: fertility, corpus luteum, weight increase, number and size of litters, placenta xweight young: mortality rate, body weight	Embryos/fetuses: Some tests showed a smaller mortality rate in exposed embryos than in controls. In one of the test series differences were statistically significant but could not be repeated. EMF-exposed fetuses were slightly larger and heavier than the fetuses of the control group. Differences were very small but statistically significant. The number of litters where malformations could be detected showed a statistically significant increase in EMF-exposed groups. According to the authors, all these differences are not caused by the examined EMF field; they should be seen as normal variations. None of the other examined parameters showed any statistically significant differences. Mother animals: In female animals of the F1 generation of the EMF-exposed group, less pregnancies were detected compared to control generations (37 versus 47). This difference was statistically significant, however could not be repeated in subsequent experiments. None of the other examined parameters showed statistically significant differences.

Table 12 (continued): Mammalian embryos: Studies (in vivo) on effects of low-frequency EMF (electric fields) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Rommereim et al. 1990	electric fields: 60 Hz; 10, 65 & 130 kV/m (vertical) exposure: 19 h/day; over the whole duration of study	rats up to F1 generation	embryos: embryo mortality (implantations, resorptions) fetuses: number of dead fetuses, weight, gender ratio, body length (head - body), malformations: among others hydrocephalis, micro- or anophthalmia, extremities, skull, bone structure (ossification), inner organs mother animals: fertility, corpus luteum, weight gain, number and size of litters, placenta weight young: mortality rate, body weight	Across all examined electric field strengths, none of the test parameters showed statistically significant differences between controls and EMF-exposed animals and/or fetuses.
Sikov et al. 1984	electric field: 60 Hz; 100 kV/m exposure duration: test 1: constant, 6 days before and during coupling stage as well as from 1st to 20th day of embryonic development test 2: 1st day of embryonic development up to 8th day after birth test 3: 17th day of embryonic development up to 25th after birth	rats	embryos: embryo mortality fetuses: malformations (inner organs, skeletal formation), gender ratio, body size & weight young: behavioral patterns and ontogenesis after pre- and postnatal exposure maternal/paternal animals: fertility, number and size of litters	The first test series showed no statistically significant differences between EMF-exposed animals and controls for the examined parameters. In the second and third test series, some behavioral parameters (f.e. cleanliness, movement, geotropism) gave evidence for statistically significant differences between controls and EMF-exposed animals. These effects, however, were only temporarily observed, namely on 14th day after birth. None of the other examined parameters showed statistically significant differences between controls and EMF-exposed animals.
Sikov et al. 1987	electric field: 60 Hz; 30 kV/m exposure duration: 20 h/day, 7 days/week test 1: 4 months before coupling up to 100th day of gestation test 2: 18 months before coupling up to 100th of gestation test 3: 32 months before coupling up to 100th of gestation	pigs (Hanford miniature) up to F2 generation	embryos: embryo mortality (implantations, resorptions) fetuses: number of prematurely died fetuses, body weight, body length, skull measures, gender ratio, malformations mother animals: fertility, body weight, corpus luteum, general health number and size of litters	Embryos/fetuses: Two tests showed a statistically significant increase in number of litters where malformations could be detected in the EMF-exposed test groups compared to control groups. In addition, during one test smaller body weights and/or skull measures in EMF-exposed fetuses were observed. Differences between exposed/controls were statistically significant. None of the other examined parameters showed statistically significant differences between EMF-exposed animals and controls. Mother animals: None of the other examined parameters showed statistically significant differences between EMF-exposed animals and controls.
Zusman et al. 1990	electric fields: 100 Hz; 0.6 V/m EMF exposure during whole embryonic development additional tests with 20 & 50 Hz as well as in vitro tests in mouse and rat embryos (see corresponding tables)	rats	number of offspring per litter & body weight of young after 1, 7, 14, 21 & 28 days of prenatal EMF exposure number of malformations	Slightly increased postnatal mortality in EMF-exposed young. However, a significant difference was not statistically verifiable. On the 1st day after birth the body weight of EMF-exposed rats lay below that of controls. The difference was statistically significant. There was no statistically significant increase in malformations in EMF-exposed rats.

2.2. High-frequency electromagnetic fields

2.2.1. Tests in chicken and quail embryos (in vivo)

The available 12 studies examined 8 different frequencies (graph 4). Most studies – 4 – deal with the frequency range of 2.45 GHz. The 3 studies for 900 MHz (YOUBICIER-SIMO et al. 1988a, b & c) listed in table 13 are obviously identical (see below). For the other frequencies, there are only one and two studies, respectively.

frequency range	number of studies	table
100 KHz	1	13
260 MHz	1	13
428 MHz	2	13
900 MHz	3	13
915 MHz	1	13
1.25 GHz	1	13
2.43 GHz	1	13
2.45 GHz	4	13

Graph 4: Teratologic studies on effects of high-frequency EMF on chicken and quail embryos. Examined frequencies.

11 of the available studies examined effects of high-frequency fields on embryo mortality. Further test parameters were the incidence of congenital malformations (6 studies), hatching rate, sex ratio (3 studies each), developmental phases (2 studies) as well as duration of embryonic development, water balance, and different blood parameters (all 1 study each). Fertility,

Table 11: Mammalian embryos: Studies (in vivo) on effects of low-frequency EMF (magnetic resonance tomographs) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Tyndall & Sulik 1991	magnetic resonance tomograph magnetic field: 1.5 T; HF field: 64 MHz exposure for 36 min on 7th day of embryonic development	mice (C57BL/6J)	embryos: embryo mortality (implantations, resorptions) fetuses: malformations of eyes (f.e. microphthalmia). The examined mice strain is genetically predisposed to this malformation. Fetuses were examined on 14th day of embryonic development.	In fetuses of the EMF-exposed test groups an increase in malformations of the eyes (15-37%) was determined. Controls: 2-19%. Differences between controls and EMF-exposed fetuses were statistically significant. The examined field had no effect at all on embryo mortality.
Tyndall 1993	magnetic resonance tomograph magnetic field: 1.5 T; HF field: 64 MHz exposure for 36 min on 7th day of embryonic development	mice (C57BL/6J)	embryo mortality (implantations, resorptions), development of skull, size of embryos/fetuses (head - body)	There were statistically significant differences between controls and EMF-exposed embryos and/or fetuses both for skull development and body size of embryos/fetuses. The examined EMF had no effect at all on embryo mortality.
Zimmermann & Hentschel 1987	magnetic resonance tomograph: 3.5T test 1: constant exposure from 1st to 18th day of embryonic development test 2: constant exposure 7 days at time of conception	mice	embryos: mortality, course of embryonic development fetuses: number of died fetuses, malformations (inner organs, f.e. lungs, brain), blood samples mother animals: fertility	When exposed to EMF during contraception, the number of pregnant female mice decreased in the group with EMF exposure compared to controls (statistically significant difference). None of the other examined parameters showed statistically significant differences between controls and EMF-exposed animals and/or embryos/fetuses.

laying rate, and food consumption of the mother animals as well as egg weight were examined by 3 and 4 studies, respectively. One study performed in chicks dealt with body growth, body weight and histological tests on brain ontogenesis with the chicks being exposed to a high-frequency field during embryonic development.

The most thoroughly examined high-frequency range was that of 2.45 GHz (table 13). Two (MCREE et al. 1975, BRAITHWAITE et al. 1991) of a total of four studies could not find any effect of the applied 2.45-GHz fields on test parameters. During a study performed in quails (INOUE et al. 1982), embryos were exposed to a 2.45-GHz field with a power flux density of 5 mW/cm² (SAR 4.03 mW/g) from 1st through 12th day of breeding. On the 12th, 13th, and 14th day of breeding, some of the HF-exposed eggs (11, 9 and 10 exposed, respectively; 11 sham-exposed controls each) were removed from the incubator and opened to histologically determine the developmental status of the cerebellum. The result for HF-exposed embryos was a delayed development of the cerebellum on the 12th to 14th day of breeding. The differences between HF-exposed and sham-exposed groups were verifiably significant. In contrast, hatched chicks eight weeks of age from the same test series showed no difference between HF-exposed and sham-exposed animals. This can be seen as evidence for developmental disturbances found in certain phases of embryonic development in HF-

exposed embryos apparently being compensated during later periods of embryogenesis or ontogenesis. We should also mention that, though the authors discuss whether differences between HF- and sham-exposed embryos observed on 12th to 14th day of breeding are caused by the high-frequency field, they do not answer the question if breeding temperature being decreased for compensation could be responsible for cerebellum retardation (INOUE et al. 1982).

The study of BYMAN et al. (1985) examined quail eggs 30 of which each were exposed two times per day for 30 min to a 2.45-GHz field (cw) and a power flux density of 25 and/or 50 mW/cm² over the 17-days breeding. During EMF exposure, breeding temperature was decreased from about 35.5° C to 21-23° C. At a power flux density of 25 mW/cm² no disturbances in embryonic development could be detected. In contrast, at 50 mW/cm² the hatching rate of HF-exposed embryos (31.6%) decreased compared to that of controls (73.9%). In the view of the authors, the temperature increase caused by the 2.45-GHz field in HF-exposed eggs was responsible for this effect. Postnatal tests in the hatched chicks did not show any disadvantageous effects for either of the used power flux densities.

On the whole, however, we can conclude that detected effects of 2.45-GHz fields are caused by thermal influences. Above all, this suggestion is supported by the

results from tests performed in mammals (see chapter 2.2.2.).

KRUEGER et al. (1975) examined the influence of a 2.435-GHz field (1000 $\mu\text{W}/\text{cm}^2$) on fertility, laying rate, egg weight as well as food consumption of hens. Other test parameters were hatching rate, embryonic mortality, the incidence of malformations and sex ratio of chicks and/or embryos. With the exception of EMF-exposed hens showing a decreasing laying rate during tests, none of the remaining parameters provided evidence for effects resulting from the 2.45-GHz field. A comparable result was shown by tests published by KRUEGER et al. (1975) with 260 and 915 MHz (see table 13). However, validity of results of tests in chicks or embryos is diminished by the fact that the eggs of EMF-exposed hens, due to a special device, rolled out of the test cages thus avoiding high-frequency field radiation (KRUEGER et al. 1975).

In recent years, tests applying a 900-MHz field performed by YOUBICIER-SIMO et al. (1998a, b+c) got quite a lot of attention, especially during scientific symposia. In a total of 3 test series, 60 chicken eggs each were exposed to a 900-MHz field (GSM signal) produced by a mobile phone (Bosch CARTEL SL 2G2) over the whole duration of embryonic development. Compared to sham-exposed controls (60 eggs each), EMF-exposed test groups showed an increase in embryo mortality. During the first test series, 59.3% of the embryos in the EMF-exposed group died prematurely (controls 11.9%);

in the second 57.6% (controls 10.9%), and in the third group 100% compared to 15.8% of controls. Closer inspection of the data for all tests of YOUBICIER-SIMO et al. (1998a, b+c) showed that the main part of HF-exposed embryos died during the third week of breeding, obviously shortly before hatching. The death of embryos and/or chicks occurring at this time suggests faulty breeding conditions (f.e. too high breeding temperatures) rather than teratogenic effects of the examined 900-MHz field, even more so as apparently no congenital malformations were detected in the dead embryos. Other doubts regarding published results have to do with the fact that the authors obviously had a commercial interest in launching a shielding antenna claimed to achieve a considerable decrease in embryo mortality (table 13). Moreover, the fact that the same study with minor changes in test design (breeding temperature), but presented by different authors appeared in at least three different publications casts serious doubt on its scientific value.

As doubtful is the 100%-increase in embryo mortality at exposure to a 1.25-GHz field and at certain power flux densities described by VARGA (1992). Whereas the range of 0.1 to 1.0 mW/cm^2 showed a percentage of dead embryos of 10% to 18%, at a power flux density of 1.5 mW/cm^2 and above embryo mortality in EMF-exposed groups increased to 100% (controls 11.7%). All embryos of the EMF-exposed groups died as early as

in the first 5 days. However, a 100% embryo mortality at power flux densities of 1.5 mW/cm^2 and above as reported by VARGA seems highly unrealistic. This study, too, suggests that the described increase in embryo mortality does not result from the examined high-frequency field, but from faulty breeding. One reason could be a far too low breeding temperature. According to the data given by VARGA (1992), the EMF-exposed eggs were incubated at a temperature of 36.2° C. According to Varga, this temperature was selected to compensate the thermal effect of the 1.25-GHz field assuming a heating of the eggs by 2.1° C at a power flux density of 2.5 mW/cm^2 . However, actual heating of a chicken egg in the area of the embryo is only about 0.5° C (THALAU et al., in prep.). But neither the breeding temperature applied by VARGA in his tests should lead to an embryo mortality of 100%. On the whole, VARGA used the following power flux densities: 0.1; 0.5, 1, 1.5, 2, 2.5 & 3 mW/cm^2 . Each test group as well as the control group consisted of 180 eggs.

In a Japanese study using a 428-MHz field, the authors (SAITO et al. 1991) reported a very high embryo mortality in EMF-exposed embryos (62% versus 15.8% in controls) as well as a breeding time lengthened by up to three days. Additionally, in 89% of the chicks hatched from EMF-exposed eggs a serious malformation of the legs (so-called splay-legs) were detected. In control animals this malformation was not found. Chicken breeders know about

this malformation; in most cases it is caused by too high or too low breeding temperatures (ANDERSON BROWN 1988). Leg malformations as well as the considerably longer breeding duration in EMF-exposed eggs most probably result from a wrong, i.e. too low breeding temperature. Further evidence for this is the fact that many of the chicks died towards the end of breeding when fully developed (SAITO et al. 1991). The delay of embryonic development observed in chicken embryos 48 hs of age during a follow-up study (SAITO & SUZUKI) also should be a result of faulty breeding, not of the examined 428-MHz field. Moreover, the number of examined eggs (50 EMF-exposed, 19 controls) was comparably small.

At first glance, the results of available studies give the impression that the examined high-frequency fields led to considerable development disturbances in exposed embryos. However, with the exception of the studies using 2.45-GHz fields, there is considerable doubt regarding seriosity of most results, especially those of the above presented studies (SAITO et al. 1991, VARGA 1992, YOUBICIER-SIMO et al. 1998a, b+c). Thus, we must conclude that to date there is no evidence at all for an actual teratogenic potential of these fields.

Table 13: Chicken and quail embryos: Studies (in vivo) on effects of high-frequency EMF (frequency range: 100 kHz to 2.45 GHz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Juutilainen & Saali 1986	magnetic fields: 100 kHz ; 0.1, 1, 10, 100 A/m exposure duration: 52 h additional tests with frequencies of 1 Hz to 10 kHz (see corresponding tables)	chickens	malformations and developmental stage in embryos 52 h of age	At 1, 10 & 100 A/m EMF-exposed embryos showed a statistically significant increase in malformations (no precise data).
Krueger et al. 1975	VHF field: 260 MHz ; 125 $\mu\text{W}/\text{cm}^2$ exposure duration: 12 weeks further tests with electric and/or magnetic 60-Hz fields, 915 MHz, 2.435 GHz (see corresponding tables)	chickens	adult animals: fertility, laying rate, food consumption, egg weight embryos and/or chicks: hatching rate, malformations, sex ratio, embryo mortality	Across the different tests, laying rate of EMF-exposed hens sank to 59% (controls 78 to 87%) during 13 th to 16 th week. None of the other test parameters showed influences of the examined field. * Eggs were removed from the cages immediately after laying.
Saito et al. 1991	428 MHz ; 0.05 mW/cm ² to 0.42 mW/cm ² , 5.5 mW/cm ² (very unprecise data) SAR: 3.1 to 47.1 W/kg exposure duration: 21 days (total breeding time)	chickens	malformations, embryo mortality, breeding duration Increase in embryo mortality: EMF-exposed eggs: 62%, controls: 15.8%.	Malformation of legs in 89% of hatched EMF-exposed chicks. Breeding duration was lengthened in EMF-exposed eggs by up to 2 days.
Saito & Suzuki 1995	428 MHz ; 5.5 mW/cm ² exposure duration: the first 48 h of embryogenesis	chickens	embryonic development during the first 48 h (developmental stages, number of somites)	Embryonic development of the EMF-exposed embryos lagged behind that of the control group by about 6 to 16 h.
Youbicier-Simo et al. 1998a	900 MHz (mobile phone, GSM signal)	chickens	embryo mortality, 3 test series	All three test series showed a statistically significant increase of embryo mortality in the EMF-exposed group compared to controls. Test 1: EMF-exposed: 59.3%, control: 11.9% Test 2: EMF-exposed: 57.6%, control: 10.9% Test 3: EMF-exposed: 100%, control: 15.8%
Youbicier-Simo et al. 1998b	900 MHz (mobile phone, GSM signal) with "shielding antenna" exposure duration: 21 days (total breeding time)	chickens	embryo mortality	Mortality rate in EMF-exposed embryos was 57.6% compared to 10.9% in controls. When exposed to a mobile phone equipped with a shielding antenna, the eggs showed an embryo mortality of only 29.3%.
Youbicier-Simo et al. 1998c	900 MHz (mobile phone, GSM signal) with "shielding antenna" exposure duration: 21 days (total breeding time)	chickens	embryo mortality	Mortality rate in EMF-exposed embryos was 61% compared to 11.9% in controls. When exposed to a mobile phone equipped with a shielding antenna, the eggs showed an embryo mortality of only 29.3% (see publication 1998b).
Krueger et al. 1975	915 MHz ; 1000 $\mu\text{W}/\text{cm}^2$ (1 st to 17 th day) 18 th to 25 th day: no field, followed by 200 $\mu\text{W}/\text{cm}^2$ until the end of 12 th week exposure duration: 12 weeks further tests with electric and/or magnetic 60-Hz fields, 260 MHz, 2.435 GHz (see corresponding tables)	chickens	<i>adult animals</i> : fertility, laying rate, food consumption, egg weight <i>embryos and or chicks</i> : hatching rate, malformations, sex ratio, embryo mortality	Over the course of the study the laying rate of EMF-exposed hens varied from 78% to 68% (controls 78% to 87%). None of the remaining test parameters showed influences of the examined field. * The eggs were removed from the cages immediately after laying.
Varga 1992	1.25 GHz ; 0.1 to 3 mW/cm ² exposure duration: 8 h per day up to 5 th day of breeding breeding temperature reduced for compensation	chickens	embryo mortality	At 0.1 to 1 mW/cm ² there was no difference between controls and EMF-exposed embryos. At 1.5 to 3 mW/cm ² all EMF-exposed embryos died (controls 11.7%).

Fortsetzung Table 13: Chicken and quail embryos: Studies (in vivo) on effects of high-frequency EMF (frequency range: 100 kHz to 2.45 GHz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Krueger et al. 1975	2.435 GHz ; 1000 $\mu\text{W}/\text{cm}^2$ exposure duration: 11 weeks further tests with electric and or magnetic 60-Hz fields, 260 MHz, 915 MHz (see corresponding tables)	chickens	adult animals: fertility, laying rate, food consumption, egg weight embryos and/or chicks: hatching rate, malformations, sex ratio, embryo mortality	Over the course of the study the laying rate of EMF-exposed hens varied from 74% to 61% (controls 78% to 87%). None of the other parameters showed influences of the examined field. * The eggs were removed from the cages immediately after laying.
Braithwaite et al. 1991	2.45 GHz (cw); 3.6 mW/cm^2 SAR: 0.8 mW/kg exposure duration : total breeding time (21 days)	chickens	embryo mortality	There was no evidence for effects on embryo mortality. Hatching rate: controls 97.7%, EMF-exposed eggs 82.9%.
Byman et al. 1985	2.45 GHz (cw); 25 & 50 mW/cm^2 SAR: 0.5 W/kg (calculated for 92 mW/cm^2) exposure duration: 2 x 30 min per breeding day, over total breeding time (17 days) breeding temperature during exposure: 21° to 23° C breeding temperature of controls: 37.4° to 37.5° C breeding temperature of sham-exposed animals: about 20° to 24° C	quails	embryo mortality, water balance, egg weight, body growth of chicks	25 mW/cm^2 : no disturbances in hatching rate and/or of growth in chicks hatched from EMF-exposed eggs. 50 mW/cm^2 : decreased hatching rate in EMF-exposed embryos Controls: 73.9%, EMF-exposed animals: 31.6%. The difference was statistically significant.
Inouye et al. 1982	2.45 GHz (cw); 5 mW/cm^2 SAR: 4.03 mW/g exposure duration: constant, from 1 st to 12 th day of breeding (also chicks 8 weeks of age)	quails	embryos (12, 13 & 14 days of age) and chicks (8 weeks) body weight, brain weight, cerebellum (cortex): development of grain layer (stratum granulosum cerebelli), and of the molecular layer (stratum moleculare cerebelli), development of Purkinje cells	In EMF-exposed controls, body weight as well as brain weight were below those of controls. In embryos 12 days of age (body weight; brain) and 14 days of age (brain) differences were statistically significant. In EMF-exposed embryos, the development of different structures of the cerebellum (cortex) lagged behind that of controls (statistical data are lacking). In chicks 8 weeks of age no differences between controls and EMF-exposed chicks could be detected.
McRee et al. 1975	2.45 GHz (cw); 30 mW/cm^2 SAR: 14 mW/g 6 test groups with EMF exposure only on 1 st , 2 nd , 3 rd , 4 th or 5 th day of breeding + 1 group with EMF exposure on all 5 days exposure duration: 4 h per day each breeding temperature during exposure: 24° C	quails	embryo mortality, malformations, different blood parameters (f.e. hemoglobin, leukocytes, lymphocytes, hematocrite value)	No increase of embryo mortality (hatching rate: exposed animals: 67.5%; controls: 64.3%), no increase of malformation rate. No EMF effects on: leukocyte percentage, hemoglobin, hematocrite value, lymphocytes. Differences observed on some test days between controls and EMF-exposed embryos were within known variability.

2.2.2. Studies in mammals (in vivo)

Our survey study could include 26 studies examining 9 different frequencies in the range between 10 MHz and 36.11 GHz (table 5). Two of the studies tested animals in the UWB (ultra-wide band) range from 0.1 to 1.0 GHz (COBB et al. 2000) and/or in the RF and UHF range (88.5 to 950 MHz, MAGRAS & XENOS 1997). In total, 12 of the described 28 studies deal with possible effects of fields of the 2.45-GHz range. 4 publications examined 27.12-MHz fields. For all other frequency ranges, there are only results from one and/or two studies each.

frequency range	number of studies	table
UWB (0,1-1 GHz)	1	15
RF-, UHF-Bereich	1	15
10.00 MHz	2	15
27.12 MHz	4	15
100.0 MHz	1	15
900.0 MHz	1	15
915.0 MHz	2	15
970.0 MHz	1	15
2.45 GHz	12	16
6.00 GHz	2	17
36.11 GHz	1	17

Graph 5: Teratologic studies on effects of high-frequency EMF on mammalian embryos. Examined frequencies.

In addition to embryos, fetuses and mother animals some studies also examined the F1 and/or F2 generation for possible influences of applied high-frequency fields. The tested biological and medical

parameters are listed in graph 6a-6c. Most frequently examined parameters in embryos and/or fetuses (graph 6a) were the incidence of congenital malformations (22 studies), the number of dead embryos and fetuses (20 studies each), and the body weight of fetuses (18 studies). For mother animals being exposed to a high-frequency field during pregnancy, the focus of studies were histological tests in the ovaries, the placenta, the brain as well as a number of other organs (total of 16 studies). Further study foci were fertility (11 studies), weight gain during pregnancy (9 studies) as well as the body weight (7 studies) of mother animals (graph 6b). In young animals, also histological studies (11 studies), body weight (7 studies) as well as different behavioural patterns were the most frequent parameters (graph 6c).

A total of 22 (78.6%) studies (including UWB & RF/UHF range) could detect an influence of the examined field at least on one test parameter. Only 6 (21.4%) studies failed to show statistically significant differences between EMF-exposed test groups and controls (table 15 to 17). However, at closer inspection of single studies this high percentage is highly relative (graph 6a to 6c). In embryos and/or fetuses a total of 102 studies was performed on single biological parameters for all frequency ranges. Here, only 31 (30.4%) of the studies provided evidence for statistically significant differences between EMF-exposed embryos/fetuses and controls.

71 (69.6%) studies showed no influence of the applied fields on test parameters (graph 6a).

The studies in mother animals and/or the subsequent F1 generation show comparable results. Here, only 13 (19.7%) of 66 studies provided evidence for statistically significant differences between exposed animals and controls. For animals of the F1 generation, 16 (29.1%) of a total of 55 studies showed such evidence. Some studies also examined F2-generation animals stemming from exposed parent animals. With one exception, these studies could not detect any distinct effects of the examined fields. Only one study for 6 GHz (JENSH 1997, table 17) showed an increase of resorption numbers in the F2 generation. Additionally, these tests showed a decrease in litter size compared to controls for the group with previous EMF exposure.

The parameter most frequently examined in embryos and/or fetuses was the incidence of congenital malformations. A statistically significant increase in malformation rate was observed in 6 (27.3%) of a total of 22 studies. In 5 of these studies performed in rats, the embryos and/or fetuses were exposed to a 10-MHz field (NELSON et al. 1992, 1994) and/or a 27.12-MHz field (DIETZEL 1975, LARY et al. 1982, 1986, table 15). The sixth study performed in mice (NAWROT et al. 1981, table 16a) examined a 2.45-GHz (cw) field. All six studies showed an increase of the rectal temperature in mother animals

Laboratory studies

Examined parameters	studies	effects caused by EMF	no effects
malformations	22	6 (27.3%)	16 (72.7%)
embryo mortality	20	4 (20.0%)	16 (80.0%)
mortality in fetuses	20	5 (25.0%)	15 (75.0%)
fetus weight	18	9 (50.0%)	9 (50.0%)
sex ratio	5	0	5
ossification/skeletal formation	4	1 (25.0%)	3 (75.0%)
embryonic phases	3	2 (66.7%)	1 (33.3%)
body size/length	3	2 (66.7%)	1 (33.3%)
histological tests:			
eyes, ears	1	0	1
palate, teeth, tongue	1	0	1
brain	1	0	1
number of implantations	2	1 (50.0%)	1 (50.0%)
enzymatic activity	1	0	1
neurochemical tests	1	1	0

Graph 6a: Medical and biological parameters examined in mammalian embryos at exposure to high-frequency fields.

during exposure from normally 38° C to values between 40-43° C. Therefore, we can safely conclude that the increase of congenital malformations found in these studies within the EMF-exposed test group results from thermal effects of the examined high-frequency fields. This is also true for the main part of the other effects described by the publications listed above. Both the increase in embryo mortality found in 4 of 20 studies (DIETZEL 1975, CHAZAN et al. 1983, LARY et al. 1986) as well as the increased number of prematurely died fetuses in 5 of a total of 20 studies (DIETZEL 1975, CHAZAN et al. 1983, LARY et al. 1982, 1986) correlated in most studies with a distinctly increased rectal temperature in the exposed mother animals. This is especially shown by the studies of CHAZAN et al. (1983, table 16a) performed in mice where at a power flux density of 10 mW/cm² no effects of the

applied 2.45-GHz field were found. In contrast, at 40 mW/cm² (rectal temperature about 40° C) there was proof of a significant increase of the mortality rate in exposed embryos and fetuses. In dead fetuses, the authors found bleedings in the area of the abdomen and in the skull – further evidence for a thermal influence of the applied high-frequency field. Only two studies (BROWN-WOODMAN & HADLEY 1988, MAGRAS & XENOS 1997) failed to demonstrate a relation between a thermal effect and the observed mortality increase. However, the validity of one of these studies (MAGRAS & XENOS 1997) is highly doubtful because of the obvious flaws in test design and in result description and presentation.

The studies performed in mother animals as well as in young animals of the F1 generation also show a relation between many of the

described effects and an increased rectal temperature during exposure (f.e. LARY et al. 1986, CHAZAN et al. 1983, BERMAN et al. 1992, JENSH 1997, table 15-17).

Due to the small number of published and accessible studies, a close inspection of available results for most frequency ranges does not make sense. Only for the 2.45-GHz range, there is a total of 12 different studies available, mainly carried out during the eighties of the last century. 7 of these studies were performed in mice (BERMAN et al. 1978, 1982, 1984, CHAZAN et al. 1983, INOUE et al. 1982, NAWROT et al. 1981, 1985, table 16a), 5 in rats (BERMAN & CARTER 1984, BERMAN et al. 1981, INOUE et al. 1983, JENSH et al. 1983, JENSH 1997, table 16b). 10 of these studies examined embryo mortality, the number of died fetuses, and the incidence of congenital malforma-

Examined parameters	studies	effects caused by EMF	no effects
histological tests:			
ovaries, placenta, uterus	6	0	6
	5	1 (20.0%)	4 (80.0%)
	5	1 (20.0%)	4 (80.0%)
fertility	11	1 (9.1%)	10 (90.9%)
weight gain (gestation duration)	9	1 (11.1%)	8 (88.9%)
body weight	7	1 (14.3%)	6 (85.7%)
number of young animals/litter	5	1 (20.0%)	4 (80.0%)
mortality	5	3 (60.0%)	2 (40.0%)
different blood parameters	3	1 (33.3%)	2 (66.6%)
corpus luteum	2	0	2
food consumption	2	0	2
water consumption	2	0	2
number of litters/group	2	1 (50.0%)	1 (50.0%)
neurochemical tests	1	1	0
behavior (in general)	1	1	0

Graph 6b: Medical and biological parameters examined in mammals (mother animals) at exposure to high-frequency fields

Examined parameters	studies	effects caused by EMF	no effects
histological tests			
brain	7	2 (28.6%)	5 (71.4%)
inner organs	3	1 (33.3%)	2 (66.6%)
ovaries, testes, etc	2	0	2
body weight	7	4 (57.1%)	3 (42.9%)
different behavioral parameters	6	2 (33.3%)	4 (66.7%)
different blood parameters	4	0	4
fertility	4	1 (25.0%)	3 (75.0%)
ontogenesis (in general)	4	0	4
psycho-physical tests	4	2 (50.0%)	2 (50.0%)
sex ratio	2	0	2
weight gain	2	0	2
neurochemical tests	2	2	0
infection susceptibility	1	1	0
immunological tests	1	0	1
skeletal formation (ossification)	1	0	1
malformations	1	0	1
mortality	1	0	1
stress symptoms	1	1	0
toxicological tests	1	0	1
urine samples	1	0	1

Graph 6c: Medical and biological parameters examined in mammals (young animals of the F1-F2 generation, prenatally exposed) at exposure to high-frequency fields

tions. Further test parameters were f.e. the body weight of fetuses, skeletal formation (ossification), and histological tests (table 16a+b). Two studies examined only young animals of the F1 generation as well as their mothers (INOUE et al. 1983, BERMAN et al. 1984). Whereas only 2 of the studies performed in rats could find a statistically significant difference between EMF-exposed embryos, fetuses, mother or young animals for at least one test parameter, 6 of 7 studies performed in mice succeeded in doing so. The authors describe the following effects observed in mice at exposure to a 2.45-GHz field: an increase in embryo mortality and/or the number of died fetuses (CHAZAN et al. 1983), a smaller body weight of fetuses (BERMAN et al. 1978, BERMAN et al. 1982, NAWROT et al. 1981), a smaller number of implantations (NAWROT et al. 1981), an increased number of congenital malformations (NAWROT et al. 1981), less pregnancies (NAWROT et al. 1981), smaller body weight of young animals of the F1 generation (BERMAN et al. 1982, BERMAN et al. 1984), a special susceptibility to infections (CHAZAN et al. 1983), smaller brain weight (BERMAN et al. 1984). Effects determined in rats were: smaller body weight, delayed ossification (BERMAN & CARTER 1984), a smaller body weight in the F1 generation, and smaller weights of liver and brain in mother animals (JENSH 1997). In nearly all cases, the authors explain the described effects as being caused by thermal influences of the examined fields (f.e. BERMAN et al. 1981).

Looking closely at results of all available studies – independent of the tested frequency range – we find a total of 25.4% of the studies in rats and 29.8% of the studies performed in mice providing evidence for statistically significant differences between EMF exposed groups (embryos, fetuses, mother animals, young animals) and controls. In spite of that, we cannot necessarily assume a general increased susceptibility of mice to teratologic effects caused by high-frequency fields on the basis of to-date available data.

In summary, to date there is scarcely conclusive data on non-thermal effects of high-frequency fields on embryonic development and ontogenesis of mammals. Nearly all described disturbances in embryogenesis and ontogenesis with high probability are caused by thermal effects, independent of the examined frequency range.

Table 14: Mammalian embryos: Studies (in vivo) on effects of high-frequency EMF (frequency range: 10 MHz to 1 GHz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Nelson et al. 1991	10 MHz (cw); SAR: 6.6 W/kg Due to the applied 10-MHz field the rectal temperature of exposed mother animals increased from 38° C (normal) to 42° C over 30 min. Total exposure duration was 60 min. During an additional test series, EMF-exposed mother animals were injected with 150 mg/kg 2-metoxo-ethanol. EMF exposure as well as the application of 2-metoxo-ethanol took place on the 13 th day of pregnancy.	rats	<i>embryos</i> : mortality <i>fetuses</i> : sex ratio, weight, malformations (skeleton, organs) Fetuses were examined on 20 th day of embryonic development. <i>mother animals</i> : fertility, mortality, food and water consumption, weight gain	In the EMF exposed group (without 2-metoxo-ethanol), 30% of the fetuses of 56% of the litters were malformed. When 2-metoxo-ethanol was applied without exposure to the 10-MHz field, 14% of the fetuses of 56% of the litters were malformed. When the 10-MHz field was applied in combination with injections of 150 mg 2-metoxo-ethanol, malformations could be detected in 76% of the fetuses from all exposed litters. In controls, no malformations could be found. For all other test parameters and for the examined mother animals as well no effects of the examined 10-MHz field (with or without 2-metoxo-ethanol) could be observed.
Nelson et al. 1994	10 MHz (cw); SAR: 5.3 to 6.6 W/kg Caused by the applied field there was an increase of rectal temperature in exposed mother animals from 38° C for 10, 20 or 30 min to 42° C. Exposure duration of the different test series was 30, 40, 50 or 60 min. During further tests EMF exposed mother animals additionally were treated with 2-metoxo-ethanol (75, 100, 125 or 150 mg/kg). Treatment and/or EMF exposure of mother animals was performed on 9 th and/or 13 th day of pregnancy.	rats	<i>embryos</i> : mortality <i>fetuses</i> : sex ratio, weight, malformations (skeleton, organs) Fetuses were examined on 20 th day of embryonic development. <i>mother animals</i> : fertility, mortality, general behavior, weight gain <i>Fetuses</i> : Independent of the application of 2-metoxo-ethanol, EMF exposure (30 min at 42° C) on 9 th day of embryonic development led to an increase in malformation rate (fore/hind extremities, tail).	Additionally, EMF-exposed fetuses had smaller body weight than controls. When the 10-MHz field was applied on the 13 th day of embryonic development (together with 2-metoxo-ethanol), an increase in malformations of fore and hind extremities could be detected. Moreover, the weight of treated fetuses was smaller than that of controls. All differences between controls and EMF exposed fetuses were statistically significant. <i>Mother animals</i> : 20% of EMF-exposed animals with a rectal temperature increased to 42° C for 30 min died 1 to 2 days after exposure. In addition, short-time effects as f.e. lethargy could be observed.
Brown-Woodman & Hadley 1988	27.12 MHz ; pulse rate/SAR/exposure duration: 10 Hz/2.8 W/kg/60 min 20 Hz/4.2 W/kg/45 min 30 Hz/5.6 W/kg/30 min 15 Hz/no data/60 min 26 Hz/no data/45 min 35 Hz/no data/30 min EMF exposure on 9 th day of pregnancy	rats	<i>embryos</i> : mortality <i>fetuses</i> : weight, malformations Fetuses were delivered and examined on 20 th day of embryonic development. <i>mother animals</i> : fertility	At a pulse rate of 10 Hz and an exposure duration of 60 min the EMF-exposed group showed an increased percentage of died (resorbed) embryos (20.4%) compared to controls (7.4%; no statistical data available). None of the other examined parameters showed an influence of the examined 27.12-MHz field.

Table 14 (continued)

Authors	EMF exposure	test animals	examined parameters	result
Dietzel 1975	27.12 MHz (cw) three test groups (55, 70 & 100 W) duration of EMF exposure: 5 and 10 min At 55 W (5 min) a rectal temperature of 39° C was measured (normal = 38° C), at 75 W (10 min) the temperature was 40.5° C, and at 100 W (10 min) 42° C. The animals were exposed to the EMF between the 1 st and the 16 th day of embryonic development. (Note: very unprecise EMF exposure parameters!)	rats	<i>embryos</i> : resorptions, implantations <i>fetuses</i> (20 days of age): malformations, mortality	Embryos (blastocytes): In the EMF exposed groups the number of embryos having died before or after implantation was increased compared to controls. <i>Fetuses</i> : An increase in mortality rate could be observed in EMF-exposed groups. In addition, malformation rate was increased compared to controls. Controls: 0.26%; 55 W: 0.27%; 70 W: 12.4%; 100 W: 46.1%. Data on statistical processing of results are lacking. The author explains observed effects by the decreased DNA synthesis rate.
Lary et al. 1982	27.12 MHz (electric field: 300 V/m, magnetic field; 55 A/m); SAR: 11-12.5 W/kg 8 test groups: exposure on 1 st , 3 rd , 5 th , 7 th , 9 th , 11 th , 13 th or 15 th day of embryonic development over 20 to 40 min until a rectal temperature of 43° C was reached	rats	<i>embryos</i> : implantations, resorptions <i>fetuses</i> : mortality, malformations, weight, sex ratio, body size <i>mother animals</i> : corpus luteum, mortality	EMF exposure on the 1 st , 3 rd or 5 th day of embryonic development had no effect on fetus and/or embryo mortality (before implantation). When the 27.12-MHz was applied on 7 th (29%) or on 9 th day (49%) of embryonic development, the increase in the number of died EMF-exposed fetuses (29 & 49%) was statistically significant compared to controls (12 & 6%) and sham-exposed fetuses (22 & 16%). EMF exposure on 11 th , 13 th or 15 th day did not lead to a statistically significant increase in mortality rate. Both body size (EMF on 1 st to 15 th day) as well as weight (EMF on 7 th to 15 th day) were below values of controls and/or sham-exposed animals (statistically significant). All test series showed a statistically significant increase of malformation rate (extremities, skeletal formation, inner organs, etc) in EMF-exposed embryos and/or fetuses compared to controls and sham-exposed animals. Here, malformation rate in EMF-exposed animals rose to 87%-94% (controls 0 to 24%) depending on the day of EMF application. 26 (11%) of EMF-exposed mother animals died during or shortly after EMF exposure. There was no loss of animals in controls and/or the sham-exposed group.
Lary et al. 1986	27.12 MHz ; SAR: 10.8 (±0.3) W/kg magnetic field: 55 A/m, electric field: 300 V/m exposure on 9 th day of embryonic development over 10 to 40 min (depending on the intended rectal temperature) In mother animals, the following values of rectal temperature were measured: 41° C, 41.5° C, 42° C, 42.5° C and 43° C. Normal are 38° C.	rats	<i>embryos</i> : resorptions, implantations <i>fetuses</i> : (20 th day of embryonic development) mortality, malformations <i>mother animals</i> : mortality	At a rectal temperature of 41° C and above there was an increase in mortality rate (embryos/fetuses) and in the number of malformations. At 43° C a number of mother animals died. Results were comparable to those of the study of Lary et al 1982 (see above).

Table 14 (continued)

Authors	EMF exposure	test animals	examined parameters	result
Smialowicz et al. 1981	100 MHz (cw); power flux density: 46 mW/cm ² ; SAR: 2.8 mW/g (± 1.5) exposure: 4 h per day, from 6 th day of embryonic development Mother animals as well as their offspring were exposed up to the 97 th day after birth of the F1 generation.	rats	weight gain of mother animals during gestation different tests on postnatal development of young animals (opening of eyes, muscle reflexes, locomotor activity) on 35 th and 84 th day different blood parameters: f.e. lymphocytes, erythrocytes, leukocytes, hematocrite value, hemoglobin in F1 generation rats 22 and 42 days of age different immunologic and toxicologic tests (mitosis, mutagenicity, antibodies) neurochemical tests in rats 22, 40 and 97 days of age (striatum, cerebellum, hippocampus, cortex, hypothalamus, medulla, mesencephalon)	In rats 22 days (striatum, medulla) and 40 days (mesencephalon) of age (prenatal EMF exposure) acetyl-choline-sterase activity temporarily was smaller than that of controls (no effect on 97 th day). The difference was statistically significant. The exposed young animals opened their eyes earlier than controls. None of the other test parameters provided evidence for statistically significant differences between EMF-exposed animals and controls.
Bornhausen & Scheingraber 2000	900 MHz (217 Hz); power flux density: 0.1 mW/cm ² SAR: 17.5 to 75 mW/kg duration of exposure: 1 st to 20 th day of embryonic development	rats	behavioral tests in rats after prenatal EMF-exposure 2 behavioral tests in Skinner box: 1. differential reinforcement of high rate (DRH) = this test requires a high lever activation rate of test animals 2. differential reinforcement of low rate (DRL) = test demands a low lever activation rate both test procedures reward the animals by giving them food in addition to behavioral tests, the following parameters were examined: number of young animals per litter, development of body weights in young and old animals	None of the test parameters showed an influence of the examined 900-MHz field.
Jensh et al. 1982	915 MHz ; power flux density: 10 mW/cm ² SAR: 3.57 W/kg exposure: 6 h per day, 1 st to 21 st day of embryonic development	rats	embryos: embryo mortality (resorptions, implantations) fetuses: number of died fetuses, malformations, weight (22 th day of embryonic development) mother animals: histological tests in brain, liver, kidneys, placenta, ovaries, body weight	None of the test parameters showed statistically significant differences between controls and EMF-exposed embryos, fetuses and mother animals.
Jensh 1997	915 MHz (cw); power flux density: 10, 20 or 30 mW/cm ² exposure: 6 h per day, 1 st to 21 st day of pregnancy additional tests using 2.45 & 6 GHz (see corresponding tables)	rats	<i>embryos</i> : embryo mortality (resorptions, implantations) <i>fetuses</i> : number of died fetuses, malformations, weight (22 th day of embryonic development) <i>F1 generation</i> : ontogenesis, behavior, fertility, histological tests in brain, liver, kidneys, ovaries and testes on 100 th day <i>psycho-physical tests</i> : among others negative geotaxis, reflexes, swimming, locomotor activity, blood parameter (see below) <i>F2 generation</i> : teratologic tests (f.e. weight, size of litters, malformations) <i>mother animals</i> : histological tests in brain, liver, kidneys, placenta, ovaries, on body weight, fertility; blood parameters: leukocytes, erythrocytes, lymphocytes, monocytes, hemoglobin, hematocrite value	The body weight of the EMF-exposed F1 generation lay above that of controls (statistically significant). Further, statistically significant differences could be observed in some behavioral tests (reflexes). None of the other test parameters showed statistically significant differences between EMF-exposed fetuses and/or young animals and controls. To the main part, this study is a review of earlier studies performed by the author.

Table 14 (continued)

Authors	EMF exposure	test animals	examined parameters	result
Berman et al. 1992	970 MHz ; SAR values: 0.07, 2.4 & 4.8 W/kg exposure: 22 h per day, 1 st to 19 th day of embryonic development	rats	<i>embryos/fetuses</i> : embryo mortality (implantations, resorptions), number of dead and living fetuses, weight of fetuses, skeletal formation (ossification of sternum), malformations <i>mother animals</i> : body weight, fertility, number and size of litters, corpus luteum, weight gain	SAR 4.8 W/kg: The EMF-exposed mother animals showed a smaller weight gain during tests than controls over the same period. The weight of EMF-exposed fetuses was 12% below that of controls. Both differences were statistically significant. None of the other test parameters provided evidence for statistically significant differences. Tests with 0.07 & 2.4 W/kg could not demonstrate any statistically significant differences. The differences observed at 4.8 W/kg are explained by hyperthermia caused by EMF.
Magras & Xenos 1997	different frequencies in the RF and the UHF range (88.5 to 950 MHz) power flux densities from 168 to 1053 nW/cm ² SAR value: 1.935 mW/kg constant exposure over the whole duration of test	mice	<i>embryos</i> : mortality <i>fetuses</i> : mortality, malformations, body size, body weight, skeletal formation (ossification) 2 test groups <i>mother animals</i> : number of litters & young animals	In the EMF-exposed test groups the number of litters as well as that of living fetuses and young animals were smaller than in control. None of the other parameters provided evidence for effects caused by EMF. Note: data presentation is flawed; statistical data lack altogether.
Cobb et al. 2000	UWB (ultra wideband), 0.1 to 1 GHz SAR: 45 mW/kg (calculated for whole body) absorption rate per pulse: 0.45 mJ/kg electric field: 55 kV/m peak pulse duration: 300 ps pulse duration: 1.8 ns pulse rate: 1000 pps duration of exposure: 2 min, from 3 rd to 18 th day of embryonic development, and in one group additionally from 1 st to 10 th day after birth positive control with application of lead acetate (2 g/l, from 3 rd to 18 th day after birth)	rats	<i>mother animals</i> : body weight, water consumption, fertility, number of young animals, mortality <i>F1 generation</i> : course of juvenile development, histological tests in hippocampus, different behavioural tests (locomotorial activity, 'Morris Water-Maze'-Test, food consumption), body weight at birth, weight gain, fertility of male animals, malformations in F2 generation, ultrasound noise (as a consequence of strain), sex ratio In UWB-exposed animals of the F1 generation the following statistically significant differences compared to sham-exposed controls could be detected:	The UWB-exposed animals produced more (stress-related) ultrasound noise, and had a bigger (medial-lateral) hippocampus than controls. Moreover, in UWB-exposed males (F1 generation) a smaller coupling rate was observed. None of the other test parameters showed statistically significant differences between controls and UWB-exposed animals.

Table 15a: Mammalian embryos (mice): Studies (in vivo) on effects of high-frequency EMF (2.45 GHz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Berman et al. 1978	2.45 GHz (cw); power flux density: 3.4, 13.6 & 14 mW/cm ² SAR value: 2.1, 8.1, 8.3 & 22.2 W/kg duration of exposure: 100 min per day, 1 st to 17 th day of embryonic development test with 28 mW/cm ² from 6 th to 15 th day of embryonic development	mice	<i>embryos</i> : mortality <i>fetuses</i> : mortality, malformations, weight (on 18 th day of embryonic development)	At exposure with a SAR of 22 W/kg the body weight of EMF-exposed fetuses was smaller than that of controls. The difference was statistically significant. None of the other tests could find statistically significant differences between controls and EMF-exposed embryos and/or fetuses. In total (all data taken together), there was a statistically significant increase in the number of malformations in the head (craniochisis) of exposed fetuses.
Berman et al. 1982	2.45 GHz (cw); power flux density: 28 mW/cm ² duration of exposure: 100 min per day, from 6 th to 17 th day of embryonic development	mice	<i>embryos</i> : mortality <i>fetuses</i> : mortality, malformations, weight, skeletal formation (ossification) <i>F1 generation</i> : body weight of young animals 7 days of age, mortality	Both EMF-exposed fetuses (on 18 th day of embryonic development) as well as (prenatally) EMF-exposed F1 generation showed a smaller body weight compared to controls. The differences were statistically significant. None of the other test parameters provided evidence for statistically significant differences.
Berman et al. 1984	2.45 GHz (cw); power flux density: 28 mW/cm ² SAR: 16.5 W/kg duration of exposure: 100 min per day, from 6 th to 15 th day of embryonic development	mice	young animals (1, 5, 10, 12, 15 & 17 days of age) after prenatal exposure: body weight, urine, brain and bone development	In young animals 1 day of age of the EMF-exposed group, body weight was statistically significant below that of sham-exposed controls. The brains of (prenatally) EMF-exposed young animals 10, 12 and 17 days of age had a smaller weight compared to controls. The differences were statistically significant. None of the other test parameters provided evidence for statistically significant differences.
Chazan et al. 1983	2.45 GHz (cw); power flux density: 10 & 40 mW/cm ² SAR: 4 to 5 and/or 16 to 18 W/kg duration of exposure: 2 h per day, from 1 st to 7 th , 8 th to 18 th and/or 1 st to 18 th day of embryonic development	mice	<i>embryos</i> : embryo mortality (implantations, resorptions) <i>fetuses</i> : mortality, malformations <i>F1 generation</i> : resistance towards infections	At exposure to a power flux density of 40 mW/cm ² (rectal temperature of mother animals increased by about 2° C) an increase in embryo and fetal mortality was determined. In EMF-exposed fetuses, bleedings in the abdomen as well as in the skull were observed. After prenatal EMF exposure, the young animals of the F1 generation were more susceptible to viral or bacteria infections. All differences compared to controls were statistically significant. Tests using 10 mW/cm ² could not show any statistically significant differences between EMF-exposed animals and controls.
Inouye et al. 1982	2.45 GHz (cw); power flux density: 9 & 19 mW/cm ² SAR: 11.7 & 24.7 W/kg exposure over 3 h on 2 nd or 3 rd day of embryonic development additional tests with heat strain (holding of mother animals at 38° C)	mice	embryo mortality, embryonic stages and malformations in embryos 4 days of age	No verified statistically significant effects of the examined 2.45-GHz fields (9 & 19 mW/cm ²) could be proved.

Table 15a (continued)

Authors	EMF exposure	test animals	examined parameters	result
Nawrot et al. 1981	2.45 GHz (cw); power flux density: 5, 21 and 30 mW/cm ² SAR: 6.7, 28.14 or 40.2 W/kg duration of exposure: at 5 mW/cm ² : 8 h per day from 1 st to 15 th day of embryonic development at 21 & 30 mW/cm ² : 8 h per day from 1 st to 6 th or 6 th to 15 th day of embryonic development At 21 and/or 30 mW/cm ² the rectal temperature of exposed animals increased by 1 and/or 2.3° C.	mice	<i>embryos</i> : number of implantations, mortality (resorptions) <i>fetuses</i> (18 days of age): number of living and/or dead fetuses, sex, weight, malformations <i>mother animals</i> : weight gain during pregnancy	At exposure to a power flux density of 30 mW/cm ² on the 1 st to 6 th day of embryonic development, the number of implantations in the EMF-exposed group showed a statistically significant decrease compared to controls. Additionally, EMF-exposed fetuses were (statistically significant) lighter than controls. EMF exposure from 6 th to 15 th day of embryonic development (30 mW/cm ²) led in the EMF-exposed group to a statistically significant increase of malformations (mainly cleft palate). None of the other test parameters could prove verifiable statistically significant effects of the examined 2.45-GHz fields.
Nawrot et al. 1985	2.45 GHz (cw); power flux density: 30 mW/cm ² SAR: 40.2 W/kg duration of exposure: 8 h per day from 1 st to 6 th and/or 6 th to 15 th day of embryonic development	mice	<i>embryos</i> : number of implantations, mortality (resorptions) <i>fetuses</i> (18 days of age): number of living and dead fetuses, sex, weight, malformations (skeletal formation, inner organs), cholinesterase activity in the brain, histological tests in the brain, the tongue, teeth, eyes, ears and palate <i>mother animals</i> : weight gain during pregnancy, number of pregnancies	In female animals being exposed to the 2.45-GHz field during the first 6 days, a smaller percentage of pregnancies could be found compared to control group animals. The difference was statistically significant. None of the other tests provided evidence for verifiable statistically significant effects of the examined 2.45-GHz field.

Table 15b: Mammalian embryos (rats): Studies (in vivo) on effects of high-frequency EMF (2.45 GHz) on the embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Berman & Carter 1984	2.45 GHz (cw); power flux density: 40 mW/cm ² SAR value: 2 & 4 W/kg duration of exposure: 100 min per day, 6 th to 15 th day of embryonic development	rats	<i>fetuses</i> : number of living or dead fetuses, malformations, skeletal formation (ossification), weight <i>mother animals</i> : fertility	The fetuses within the EMF-exposed group were 9% lighter than those of the control group. In EMF-exposed fetuses, ossification in the sternum was less developed compared to controls. Both differences were statistically significant. Caused by the applied 2.45-GHz field during exposure the temperature in the colon of the animals increased by 2° C to about 40° C. Observed alterations are explained by a thermal effect of the examined 2.45-GHz field.
Berman et al. 1981	2.45 GHz (cw); power flux density : 28 mW/cm ² SAR: 4.2 W/kg duration of exposure: 100 min per day from 6 th to 15 th day of embryonic development	rats	<i>fetuses</i> : mortality, malformations (extremities, innards, skeleton), body weight <i>mother animals</i> : pregnancy rate	None of the test parameters could provide evidence for a statistically significant difference between EMF-exposed fetuses and controls.
Inouye et al. 1983	2.45 GHz (cw); power flux density: 10.34 mW/cm ² SAR (mother animals): 1.76 W/kg brain SAR: Animals 2 days of age: 13.95 W/kg 15 days: 19.18 W/kg 20 days: 10.05 W/kg 30 days: 9.72 W/kg 40 days: 9.52 W/kg duration of exposure: 3 h per day from 4 th to 21 th day of embryonic development as well as from 2 nd to 40 th day of life (postnatal)	rats	<i>young animals</i> (postnatal): brain: weight and size, histological tests in the cerebellum; malformations, body weight, sex ratio <i>mother animals</i> : number of pregnancies, number of young animals per litter	There was no evidence for verifiable statistically significant effects of the examined 2.45-GHz field.
Jensh et al. 1983	2.45 GHz (cw); power flux density: 20 mW/cm ² SAR: 2 to 4 W/kg exposure: 6 h per day over the whole duration of embryonic development The mother animals were sacrificed on the day of birth and examined like the fetuses.	rats	<i>embryos</i> : embryo mortality (resorptions, implantations) <i>fetuses</i> : mortality, weight, malformations <i>mother animals</i> : weight gain during pregnancy, weight of liver, brain, kidneys and ovaries	None of the other test parameters provided evidence for statistically significant differences between controls and EMF-exposed embryos/fetuses and/or mother animals.
Jensh 1997	2.45 GHz (cw); power flux density: 10, 20, 30 mW/cm ² exposure: 6 h per day, 1 st to 21 st day of embryonic development further tests with 915 MHz & 6 GHz (see corresponding tables)	rats	<i>embryos</i> : embryo mortality (resorptions, implantations) <i>fetuses</i> : number of dead fetuses, malformations, weight (22 nd day of embryonic development) <i>F1 generation</i> : ontogenesis, behavior, fertility, histological tests in brain, liver, kidneys, ovaries and/or testes on 100 th day Psycho-physical tests: among others, negative geotaxis, reflexes, swimming, locomotorial activity, blood parameters (see below), weight <i>F2 generation</i> : teratologic tests (f.e. weight, litter size, malformations) <i>mother animals</i> : histological tests in brain, liver, kidneys, placenta, ovaries, body weight, fertility, blood parameters: leukocytes, erythrocytes, lymphocytes, monocytes, hemoglobin, hematocrite value	In EMF-exposed mother animals, the weight of the liver was increased compared to that of control animals. The difference was statistically significant. None of the other test parameters could show statistically significant differences between EMF-exposed fetuses and/or young animals and controls. To the main part, the study is a review of earlier tests performed by the author.

Table 16: Mammalian embryos: Studies (in vivo) on effects of high-frequency EMF (frequency range: 6 to 40 GHz) on embryonic development

Authors	EMF exposure	test animals	examined parameters	result
Jensh 1984	6 GHz (cw); power flux density: 35 mW/cm ² SAR: 7 W/kg exposure: 8 h per day, 1 st to 22 nd day of embryonic development	rats	<i>embryos</i> : embryo mortality (implantations, resorptions) <i>fetuses</i> : number of dead fetuses, malformations, weight and developmental stage <i>mother animals</i> : body weight, weight of different organs (brain, liver, kidneys, ovaries), blood samples (hematocrite, hemoglobin, leukocytes, monocytes)	<i>Fetuses</i> : Delayed growth in EMF-exposed fetuses. The difference compared to controls was statistically significant. <i>Mother animals</i> : The number of monocytes was smaller in EMF-exposed animals compared to controls. The difference was statistically significant. None of the other test parameters provided evidence for statistically significant differences between controls and EMF-exposed fetuses and/or mother animals.
Jensh 1997	6 GHz (cw); power flux density: 10, 20 and 30 mW/cm ² exposure: 6 h per day, 1 st to 21 st day of embryonic development additional tests with 915 MHz & 2.45 GHz (see corresponding tables)	rats	<i>embryos</i> : embryo mortality (resorptions, implantations) <i>fetuses</i> : number of died fetuses, malformations, weight (22 nd day of embryonic development), developmental stages <i>F1 generation</i> : ontogenesis, behavior, fertility, histological tests in brain, liver, kidneys, ovaries and/or testes on 100 th day psycho-physical tests: among others, negative geotaxis, reflexes, swimming, locomotor activity, blood parameters (see below) <i>F2 generation</i> : teratologic tests (f.e. weight, litter size, malformations) <i>mother animals</i> : histological tests in brain, liver, kidneys, placenta, ovaries, body weight, fertility, blood parameters; leukocytes, erythrocytes, lymphocytes, monocytes, hemoglobin, hematocrite value	<i>Fetuses</i> : Delayed growth in EMF-exposed fetuses. The difference compared to controls was statistically significant. <i>F1 generation</i> : Statistically significant differences in some of the psycho-physical tests as well as in weight proportions of some organs between EMF-exposed animals and controls. <i>Mother animals</i> : The number of monocytes was smaller in EMF-exposed animals than in controls. None of the other test parameters provided evidence for difference was statistically significant. In addition, weight proportions of brain, liver and kidneys statistically significant differences were found compared to non-exposed animals. statistically significant differences between controls and EMF-exposed fetuses and/or mother animals. performed by the author. To the main part, this study summarises earlier studies
Zhao et al. 1997	36.11 GHz (cw); power flux density: 10 mW/cm ² exposure: 2 h per day from 6 th to 15 th day of embryonic development	mice	<i>fetuses</i> : body size (birth), birth weight <i>F1 generation</i> : development of body weight, different behavioural patterns and/or reflexes <i>mother animals</i> : weight gain during pregnancy, body weight, weight of placenta <i>fetuses/F1 generation/mother animals</i> : different neurochemical tests (postnatal) in the brain: number of M-choline receptors (M-R), concentration of arginine vasopressin (AVP), and somatostatin (SS) in the hypothalamus and hypophysis, DOPAC (3,4-dihydroxy-phenyl-acetic-acid), dopamine (DA), HVA (homovanilin-acid)	<i>Fetuses</i> : On the day of birth, body size and body weight of EMF-exposed fetuses lay below those of controls. <i>F1 generation</i> : During the first eight weeks of life, the body weight of prenatally EMF-exposed young animals was below that of controls. Additionally, disturbances in behavioural patterns could be observed. <i>Mother animals</i> : Both body weight gain during gestation as well as body weight at the time of birth were smaller in EMF-exposed mother animals compared to control group. <i>Neurochemical tests</i> : The concentration of AVP (hypophysis of fetuses; hypothalamus of F1 generation) and DOPAC (brain of F1 generation) decreased in EMF-exposed animals compared to controls. In contrast, the concentration of SS (hypophysis and hypothalamus of fetuses and F1 generation), M-R (hippocampus of F1 generation) & HVA (brain of mother animals) was increased compared to controls. This study originally was an abstract written for a congress; more precise data and/or statistics are not available.

2.3. Vertebrates and invertebrates: Embryonic development (in vitro) and tissue growth at exposure to electromagnetic fields

2.3.1. Magnetic fields

The studies presented in this chapter deal with the effects of electromagnetic fields on very early embryonic stages. The time course of the first two cell division phases after fertilisation was examined, as well as embryonic development up to morula or blastula stage. Further test parameters were fertility (sperm), malformations, embryonic anomalies (detection of reporter genes) as well as histone synthesis. Test animals were sea urchin embryos, fruitflies, zebrafish embryos, mouse embryos, and planaries.

The 8 studies included in this survey looked at a total of 18 studies using

magnetic fields in the range of 25 Hz to 6 kHz as well as static fields (graph 7).

For most frequencies, only one study was performed each (graph 7). An exception were 60-Hz magnetic fields for which there are results from 6 studies. Three of these studies (ZIMMERMANN et al. 1990, CAMERON et al. 1993, LEVIN & ERNST 1995), were conducted in eggs of the sea urchin *strongylocentrotus purpuratus*. One study (CAMERON et al. 1993) cultivated mouse embryos over 48 hours at exposure to a 60-Hz magnetic field. The two remaining studies examined the influence of different 60-Hz magnetic fields on tissue growth in planaries (*dugesia tigrina*).

Sea urchin embryos as well as mouse embryos exposed to the 60-Hz fields showed a delay in early embryonic stages (morula, blastula) as well as in cell division rate (ZIMMERMANN et al. 1990, CAMERON et al. 1993, LEVIN & ERNST 1995, table 17).

Additionally, one test demonstrated a decrease in histone synthesis of exposed embryos (CAMERON et al. 1993).

The two studies performed in planaries (JENROW et al. 1995, 1996) as well provided evidence for statistically significant differences between controls and EMF-exposed animals. Here, regenerating capability of planaries served as a biological parameter. After incisions were made in the head area, the animals were exposed to different 60-Hz magnetic fields. At exposure to some of the examined fields (1, 10 & 78.4 μ T, ac field), the regeneration process was prolonged compared to controls. In addition, anomalies and/or malformation incidence was heightened (JENROW et al. 1996).

All other examined low-frequency magnetic fields as well showed disturbances in the embryonic development of the exposed embryos. However, most tests were part of a comprehensive study done by LEVIN & ERNST (1995). In this study, EMF-exposure led to an alteration of the time course of embryonic development for all examined frequencies (25, 60, 100, 150, 240, 360, 420, 600 & 6000 Hz) and in a static field. In their study from 1997, the same authors reported a statistically significant increase in morphological anomalies in sea urchin eggs in a static 30-mT magnetic field. Moreover, embryo mortality was increased in exposed eggs by 64% compared to 18% in controls (LEVIN & ERNST 1997). Effects

Magnetic fields/frequency	number of studies	table
static field	2	17
25.0 Hz	1	17
50.0 Hz	2	17
60.0 Hz	6	17
100.0 Hz	1	17
150.0 Hz	1	17
240.0 Hz	1	17
360.0 Hz	1	17
420.0 Hz	1	17
600.0 Hz	1	17
6.0 kHz	1	17

Graph 7: Teratologic studies (in vitro) on effects of low-frequency EMF on vertebrates and invertebrates. Examined fields and frequencies (magnetic fields).

of the examined EMF on sperm fertility could not be found.

Two recent studies dealt with the influence of a 50-Hz magnetic field on the embryonic development of fruitflies (*drosophila melanogaster*, MICHEL & GUTZEIT 2000) and zebrafish, respectively (*danio rerio*, SKAULI et al. 2000). During tests performed in *drosophila melanogaster*, the examined 50-Hz magnetic field (100 μ T), in combination with heat strain, led to a statistically significant increase in anomaly incidence as well as to a delay in embryonic development. Anomalies were detected using lacZ reporter genes (MICHEL & GUTZEIT 2000). In zebrafish, 54 hours after fertilisation there were less hatchlings compared to controls, when the 50-Hz field (1 mT) was applied 48 hours after fertilisation. However, when the number of hatchlings was examined 48, 72, 78 or 96 hours after fertilisation, no statistically significant differences between controls and exposed animals could be found. This was also the case when the EMF was switched on already two hours after fertilisation.

2.3.2. Electric fields

ZUSMAN et al. (1990, table 18) examined the influence of electric fields on the course of embryonic development of rats and mice in vitro. To this end, mouse embryos (blastocytes) and/or rat embryos 10.5 days of age were held in a culture medium for testing embryonic development in different electric fields (0.6 V/m). The following frequencies were applied: 1 (only

mice), 20, 50 & 70 Hz (only rats). In addition, ZUSMAN et al. examined the incidence rate of malformations as well as effects on DNA and proteins (no exact data available). With the exception of tests using 1-Hz fields (no statistically significant differences), the authors describe a series of statistically significant differences between controls and exposed embryos for all remaining test fields. At 20 Hz, after 72 hours 60%, and at 50 Hz, 51% of the EMF-exposed blastocytes (mice) were not developed. In controls this applied only to 23%. In EMF-exposed rat embryos, all test series showed a decrease in body length, the number of somites, and of the yolk sack diameter compared to controls. During tests with 20 Hz, 58% of the exposed rat embryos had an underdeveloped blood vascular system, at 50 Hz 63%, and at 70 Hz 70%. In controls, 20% of the embryos showed an underdeveloped blood vascular system. While in controls no malformations were found, 22% (50 Hz) and/or 30% (70 Hz) of rat embryos were malformed (f.e. missing optic vesicles, exencephalia, missing vesicles in the telencephalon, heart hypertrophy, missing buds of the fore extremities).

2.3.3. High-frequency fields

Two studies (table 19) examined the embryonic development of sea urchin embryos at exposure to high-frequency fields. LEVIN & ERNST (1995) looked at time course and duration of the first two cell division phases in sea urchin eggs which

were examined over the whole duration of experiments in a 60- and/or a 600-kHz field (2.5 mT). Additionally, fertility of the EMF-exposed sperm was examined; here, no effects could be found. These results basically agree with those described by the authors with regard to tests using low-frequency magnetic fields in the range of 60 Hz to 6 kHz (see chapter 2.3.1., table 17) in the same study (LEVIN & ERNST 1995). Koldayev & SHCHEPIN (1997) fertilised sea urchin eggs priorly having been exposed to a 450-MHz field (100, 200 & 300 mW/cm²) over 5 to 20 min using normal non-exposed sperms. Depending on exposure duration as well as on the examined power flux density, the number of fertilised eggs (zygotes) showed a 1.2- to 2.6-fold decrease compared to controls (both gametes were non-exposed). In addition, 2 to 11 times as many anomalies of the zygote membrane were evident than in controls when one of the gametes was exposed to a 450-MHz field before fertilisation. In a second test series, instead of oocytes, sperms were exposed to a high-frequency field (at identical power flux densities) over 5 to 20 min. Whereas tests at 100 mW/cm² could not detect any differences between controls and EMF-exposed zygotes, the remaining tests with 200 and/or 300 mW/cm² led to a 1.1- to 1.6-fold decrease in the number of fertilised eggs and, on the other side, to a 1.3- to 7.3-fold increase in zygote shell anomalies. Additional tests using EMF-exposed zygotes showed that not only the course of subsequent embryonic development

(pluteus larva, blastomere, blastula, gastrula, prisma) but lipid metabolism and the quota of free amino acids as well decreased compared to controls (f.e. methionine by 58-66%, valine by 21-23%; KOLDAYEV & SHCHEPIN 1997). However, though this study depicts a number of interesting effects, the presentation of results and, foremost, the statistical processing, are highly unsatisfactory.

Nearly all studies presented in this chapter examined very early stages of embryonic development. In humans, damages caused by teratogenic effects during these phases are fully repaired thus mostly preventing congenital malformations. If damages are too severe, though, the embryo will die and will be resorbed if implantation already occurred. In spite of that, results gained from such studies possibly allow to draw important conclusions on potential interactions between the developing human organism and electromagnetic fields if portability is ensured.

Table 17: Vertebrates and evertebrates: Cell growth and embryonic development (in vitro) at exposure to low-frequency EMF (magnetic fields).

Authors	EMF exposure	test animals	examined parameters	result
Levin & Ernst 1995	static magnetic field: 2.5 & 4 mT exposure: over the whole duration of experiment (no exact data) further tests with 60 Hz (1.7 to 8.8 mT), with 25, 100, 150, 240, 360, and 420 Hz (4 mT); 240 Hz (6.5 mT), and 0.6, 6, 60 & 600 kHz (2.5 mT) (see corresponding tables)	sea urchin <i>strongylocentrotus purpuratus</i> (embryos after egg cell fertilisation, and sperm cells)	time course and duration of the first two cell division phases, fertility (sperm)	In EMF-exposed embryos, the first two cell division phases occurred earlier. More exact data and a statistical analysis are lacking. The examined field had no influence on the fertility of tested sperm cells.
Levin & Ernst 1997	static magnetic field: 30 mT exposure duration: sperm: 1 h eggs (prior to fertilisation): 6, 15, 30 and/or 45 min eggs (after fertilisation): 3.5 & 26 h (only course of embryonic development) as well as over 48 to 94 h (morphological anomalies)	sea urchin, <i>strongylocentrotus purpuratus</i> and <i>lytechinus pictus</i> (fertilised egg cells, sperm)	embryonic development, hatching rate after 26 h (after fertilisation), fertility (sperm), morphological anomalies	The static magnetic field (30 mT) led to following effects: Statistically significant increase in morphological anomalies (exogastrulation). Delay in embryonic development after exposure of eggs both before and after fertilisation (statistical data are lacking). If eggs were exposed to the magnetic field after fertilisation over 26 h, hatching rate in the exposed group decreased (36%) compared to controls (82%). The difference was statistically significant. Exposure of sperm showed no effect at all.
Levin & Ernst 1995	magnetic field: 25 Hz , 4 mT exposure: over the whole duration of experiment (no exact data) further tests with 60 Hz (1.7 to 8.8 mT), with 0, 100, 150, 240, 360, and 420 Hz (4 mT); 240 Hz (6.5 mT), as well as with 0.6, 6, 60 & 600 kHz (2.5 mT) (see corresponding tables)	sea urchin <i>strongylocentrotus purpuratus</i> (embryos after egg cell fertilisation and sperm cells)	time course and duration of the first two cell division phases, fertility (sperm)	In EMF-exposed embryos, the first two cell division phases occurred earlier. Detailed data and a statistical analysis of data are lacking. The examined field had no effect on fertility of tested sperm cells.

Table 17 (continued)

Authors	EMF exposure	test animals	examined parameters	result
Michel & Gutzeit 2000	magnetic field: 50 Hz ; 100 μ T exposure duration: 30 min In addition to EMF exposure, the eggs were exposed to increased temperatures (normal = 25° C) of 34 to 35° C and/or 36 to 37° C (heat strain)	<i>drosophila melanogaster</i> used stems: en-lacZ, ftz-lacZ, slp-lacZ	course of embryonic development, embryo anomalies, detection of anomalies using lacZ reporter gene and corresponding coloring The eggs were exposed to the EMF and/or heat strain for 2 h 30 min to 3 h; 3 h to 3 h 30 min and/or 3 h 30 min to 4 h after the beginning of embryonic development.	The examined 50-Hz field in combination with heat strain (increased environmental temperature) showed a synergetic effect. Compared to controls and/or eggs exposed to heat strain, eggs with EMF exposure in combination with an increased environmental temperature showed a statistically significant increase in anomalies as well as delayed embryonic development.
Skauli et al. 2000	magnetic field: 50 Hz ; 1000 μ T onset of exposure: 2 h and/or 48 h after fertilisation; end of exposure: 96 h after fertilisation additional tests with simultaneous application of 5 μ M progesterone (48 h after fertilisation) and/or 0.1 mM natrium cyanide (78 h after fertilisation) By applying 5 μ M progesterone hatching was postponed "backwards". 0.1 mM natrium cyanide led to immediate hatching of fish.	fertilised eggs (zebrafish, <i>danio rerio</i>)	embryo mortality, malformations, time of hatching The number of hatchlings was determined 48, 54, 72, 78, and 96 h after egg fertilisation.	When EMF-exposure onset was performed 48 h after fertilisation, after 54 h less young fish (statistically significant) had hatched from exposed eggs than from sham-exposed eggs. For all other measurement times as well as during tests with EMF exposure onset as early as 2 h after fertilisation, no statistically significant differences could be found compared to controls. Embryo mortality and the number of malformations were not affected by the examined field. Neither a synergetic nor a potentiating effect could be found when simultaneously applying progesterone or natrium cyanide.
Cameron et al. 1993	magnetic fields: 60 Hz ; 50 μ T (500 mG) exposure duration: 10, 16 & 22 h after fertilisation further tests in mice (see below) To the main part, this study is a summary of earlier papers.	sea urchin (embryos) <i>strongylocentrotus purpuratus</i>	development stages (morula, blastula), histone synthesis	After EMF-exposure over 16 and/or 22 h, in the EMF-exposed group only 2% of the embryos reached the blastula stage (40% of the sham-exposed embryos). Both after 10 h and after 16 h EMF-exposure EMF-exposed sea urchin embryos provided no and/or only very small evidence for histone synthesis.
Cameron et al. 1993	magnetic field: 60 Hz ; 10 & 50 μ T (100 & 500 mG) exposure duration: 48-64 h further tests in sea urchins (see above) To the main part, this study is a summary of earlier papers.	mouse embryos (2-cell stage in culture)	development stages (morula, blastula), histone synthesis	Both at 10 as well as at 50 μ T a delayed embryonic development was found in EMF-exposed mouse embryos. All differences between controls and EMF-exposed embryos were statistically significant.
Levin & Ernst 1995	magnetic fields: 60 Hz ; 1.7, 3.4, 4.8 & 8.8 mT, as well as two other field strengths (incomplete data, partially given only in diagrams) exposure duration: for about 4.5 to 5 h (exact data are lacking) after fertilisation further tests with 4 mT: only time course of first and second cell division phase further experiments with 0, 25, 100, 150, 240, 360, and 420 Hz (4 mT); 240 Hz (6.5 mT), and 0, 0.6, 60 & 600 kHz (2.5 mT) (see corresponding tables)	sea urchin <i>strongylocentrotus purpuratus</i> (embryos after egg cell fertilisation and sperm cells)	cell division rate, fertility (sperm), time course and duration of the first two cell division phases	At 3.4 mT and above, there was a delay in cell division rate of EMF-exposed embryos. The length of this delay increased with applied field strength values. During tests with 4 mT, the EMF-exposed cell cultures of the first two cell divisions occurred earlier than in controls. Overall embryonic development was faster in EMF-exposed embryos than in controls. Detailed data as well as statistical data are lacking. There was no influence of the examined fields on fertility of tested sperm cells.

Table 17 (continued)

Authors	EMF exposure	test animals	examined parameters	result
Jenrow & Ernst 1995	Magnetic fields: 60 Hz ; 10 & 51.1 μT (ac); 51.1 & 78.4 μT (dc) EMF-exposure: 23 h per day over the whole duration of experiments duration of study: 12 months	planaries (<i>dugesia tigrina</i>)	tissue growth (regeneration) following a lesion in the head area	When planaries were tested in a 60-Hz field with 78.4 μT (dc) and 10 μT (ac) – their longitudinal axis parallel to the field –, the regeneration process was prolonged (statistically significant). Tests where planaries could move freely within the magnetic field as well as using fields with 51.1 μT (dc) and 51.1 μT (ac), could not detect any statistically significant differences compared to controls.
Jenrow et al. 1996	magnetic fields: 60 Hz , 1, 10 μT ; 40 & 78.4 μT (ac) ; 51.1 & 78.4 μT (dc) exposure duration: 23 h per day for 12 days duration of study: 18 months	planaries (<i>dugesia tigrina</i>)	tissue growth (regeneration) following a lesion in the head area	At different intensities (1, 10 & 78.4 μT ac), an increase of anomalies in tissue growth of EMF-exposed planaries could be detected. Differences compared to controls were statistically significant. When the longitudinal axis of the planaries was parallel to the applied magnetic field, the number of anomalies was considerably higher than in tests where planaries could move freely within the magnetic fields. The differences were statistically significant.
Zimmermann et al. 1990	magnetic fields: 60 Hz , 0.1 mT exposure duration: 23 h onset of exposure 2 to 4 min after fertilisation	sea urchin (eggs) <i>strongylocentrotus purpuratus</i>	early stages of embryonic development (blastula, gastrula)	During a time period of 2 to 18 h after fertilisation, no statistically significant difference between EMF-exposed eggs and controls could be found. After 23 h controls had reached medium gastrula stage, while EMF-eggs only had reached the early gastrula stage. This difference was statistically significant.
Levin & Ernst 1995	magnetic fields: 100, 150, 240, 360 & 420 Hz ; 4 mT and 6.5 mT (only at 240 Hz) exposure: over the whole duration of tests (no detailed data) further tests with 60 Hz (1.7 to 8.8 mT), with 0, 25 & 60 Hz (4 mT), as well as with 0.6, 6, 60 & 600 kHz (2.5 mT)	sea urchin <i>strongylocentrotus purpuratus</i> (embryos beginning with egg cell fertilisation, sperm cells)	time course and duration of the first two cell division phases, fertility (sperm)	In EMF-exposed embryos, the first two cell division phases occurred earlier. Exact data as well as a statistical analysis of data are lacking. The examined field had no effect on the fertility of tested sperm cells.
Levin & Ernst 1995	magnetic field: 600 Hz & 6 kHz ; 2.5 mT exposure: over the whole duration of tests (no precise data available) further tests with 60 Hz (1.7 to 8.8 mT), with 0, 25, 100, 150, 240, 360 and 420 Hz (4 mT); 240 Hz (6.5 mT), and 0, 0.6 & 60 Hz (see corresponding tables)	sea urchin <i>strongylocentrotus purpuratus</i> (embryos beginning with egg cell fertilisation)	time course and duration of the first two cell division phases, fertility (sperm), and sperm cells	The first two cell division phases occurred later in EMF-exposed embryos. Exact data as well as a statistical analysis of data are lacking. Fertility of the tested sperm cells was not affected by the examined field.

Table 18: Embryonic development (in vitro) at exposure to electric fields

Authors	EMF exposure	test animals	examined parameters	result
Zusman et al. 1990	1, 20 & 50 Hz ; 0.6 V/m exposure duration: 72 h additional in vivo studies in rats & mice (see corresponding tables)	mouse embryos (blastocytes), 3.5 days of age over 72 h in culture medium	course of embryonic development detection after 24 & 72 h	In tests with 1 Hz no embryotoxic effects could be detected. However, after 72 h EMF-exposed embryos had reached a higher development stage than controls (statistically significant). In tests using 20 and/or 50 Hz, EMF-exposed embryos had reached a higher development stage as early as after 24 h. In addition, the number of dead blastocytes showed a statistically significant increase compared to controls.
Zusman et al. 1990	20, 50 & 70 Hz ; 0.6 V/m exposure duration: 48 h additional in vivo studies in rats & mice (see corresponding tables)	rat embryos, 10.5 days of age over 48 h in a culture medium	development stage, growth, malformations, proteins & DNA	EMF-exposed embryos showed a smaller yolk sac (perimeter) compared to controls for all examined field strengths. Moreover, EMF-exposed embryos were smaller and showed a smaller number of somites. The blood vascular system was underdeveloped in all EMF-exposed embryos. In tests with 70 Hz also the number of embryos with malformations (missing fore extremities, dorsal distortion) were increased compared to controls. All differences were statistically significant. None of the remaining tests and/or examined parameters provided evidence for statistically significant differences.

Table 19: Effects of high-frequency EMF on embryonic development (in vitro)

Authors	EMF exposure	test animals	examined parameters	result
Levin & Ernst 1995	magnetic field: 60 & 600 kHz ; 2.5 mT exposure duration: whole test (no precise data) further tests with 60 Hz (1.7 to 8.8 mT), with 0, 25, 100, 150, 240, 360 and 420 Hz (4 mT); 240 Hz (6.5 mT) and 0, 0.6 & 6 kHz (2.5 mT) (see corresponding tables)	sea urchin <i>strongylocentrotus purpuratus</i> (embryos beginning with egg cell fertilisation and sperm cells)	time course and duration of the first two cell division phases, fertility (sperm)	In EMF-exposed embryos, the first two cell division phases were delayed. More precise data and a statistical analysis of data are lacking. The examined field had no influence on fertility of the examined sperm cells.
Koldayev & Shchepin 1997	450 MHz ; 100, 200 & 300 mW/cm ² exposure duration: 1 to 20 min	zygotes, sperm & oocytes (eggs) of the sea urchin <i>strongylocentrotus intermedius</i>	EMF-exposed sperm + non-exposed eggs as well as EMF-exposed eggs + non-exposed sperm: anomalies, fertility embryos: various development stages (blastomere, blastula, gastrula, prisma, pluteus larvae)	concentration of alanine, arginine, glutamine, methionine, phenyl-alanine, serine, valine, and lipid metabolism in cell membranes (via malondialdehyde = MDA concentration) During both test series (EMF-exposed sperm + non-exposed eggs as well as non-exposed eggs + EMF-exposed eggs), for all three examined power flux densities a decrease in the number of fertilised eggs could be detected. Simultaneously, the number of eggs with anomalies increased (no precise data on statistics). The level of free aminosoureas in EMF embryos showed a statistically significant decrease compared to controls. MDA concentration was increased in EMF-exposed embryos (statistical data are lacking).

2.4. Genetic and cytotoxic effects of electromagnetic fields

In the following chapter, we will present a selection of publications examining the influence of high- and low-frequency fields on the genome and/or on cytotoxic effects. Such studies can provide evidence for possible interaction mechanisms between EMF and biological systems both from an oncological as well as from a teratologic perspective. This is the reason why a selection of studies using low-frequency as well as high-frequency fields was included in this literature survey.

2.4.1. Genetic and cytotoxic effects of low-frequency EMF

In total, the tables (20-23) contain 16 publications examining cyto- and/or genotoxic effects of magnetic fields in the range from 50 Hz to 6 kHz (graph 8) in 18 test series. Four studies (table 23) dealt with cells and/or cell cultures being exposed to electrical fields.

Most studies – a total of 9 – refer to magnetic fields with a frequency of 50 Hz (table 20). However, since test conditions considerably varied regarding applied generators and/or spindles, the applied magnetic flux densities and also the cells & cell cultures, available results are difficult to compare. In 5 of these studies, human lymphocytes were cultivated in a 50-Hz magnetic field over 24 to 72 h each examining the following parameters: sister chromatid exchange, chromosome aberrations, micronucleus formation, mitosis index, cell proliferation.

In their tests conducted in human lymphocytes, SCARFI et al. (1994, 1999) could not detect any influence of the tested 50-Hz magnetic field on micronucleus formation and/or the occurrence of chromosome aberrations. However, tests performed for the study published in 1994 showed a statistically significant increase in the mitosis index of EMF-exposed lymphocytes compared to controls. This parameter was not examined by the 1999 study of SCARFI et al. (table 20), though.

Effects of the examined 50-Hz magnetic fields on the number of chromosome aberrations as well as on sister chromatid exchange neither were found by the studies of MAES et al. (2000). In addition to the 50-Hz field, some of the test series applied x-rays (1 Gy/min) and/or 0.1 µg/ml of the teratogen mitomycin C. However, there was no evidence for a synergetic, potentiating or antagonistic (protective) effect of the 50-Hz field in these tests (MAES et al. 2000).

In the tests of ROSENTHAL & OBE (1989), the examined 50-Hz magnetic field (exposure over 48 and/or 72 h) neither led to an alteration in the number of chromosome aberrations nor of sister chromatid exchanges. On the other side, these tests showed a statistically significant increase in cell proliferation rates at exposure to EMF compared to non-exposed controls.

In contrast to the above listed studies, the tests performed by KHALIL & QASSEM (1991) not only showed a decrease in mitosis index, but also an increase in chromosome aberrations in EMF-exposed lymphocytes (24, 48 & 72 hours, see table 20). When test cultures were exposed to the 50-Hz field (1 mT) over 72 hours, an additional decrease of cell proliferation rate as well as an increase in sister chromatid exchange was detected.

In their 1998 published study, SIMKÓ et al. tested 50-Hz magnetic fields with a magnetic flux density of 1 mT, applied either vertically or

magnetic fields/frequency	number of studies	table
50,0 Hz	9	20
60,0 Hz	4	21
100.0 Hz	1	22
600.0 Hz	1	22
6.0 kHz	1	22
22p/4.8 ms	1	22
therapeutical device	1	22
electric fields/frequency	number of studies	table
1.0 Hz	1	23
50.0 Hz	2	23
therapeutical device	1	23

Graph 8: Cytologic and toxicologic studies on low-frequency EMF.

horizontally (see table 20). Fields were produced using a Helmholtz spindle and/or a Merritt spindle. The aim of the study was to examine whether differently produced fields have different effects on micronucleus formation in cells from human amnion fluid. Exposure duration was 24, 48 & 72 h. During tests using a Helmholtz spindle in a horizontal field a statistically significant increase in micronucleus formation could be found regardless of EMF exposure duration. In contrast, in the vertical field there was no evidence for statistically significant differences between controls and exposed cells. When the magnetic field was produced by a Merritt spindle, the number of micronuclei showed a statistically significant increase only in cells being exposed over 72 h to a vertical field. All other tests showed no effect of the examined magnetic fields on micronucleus formation. In some tests, in addition to the tested 50-Hz field, different doses (0.3 to 2.5 mM) of N-acetyl-p-aminophenol (APAP, inhibits DNA repair) were administered. These tests showed no synergistic, antagonistic or potentiating effects of the 50-Hz field (SIMKÓ et al. 1998).

A further study of SIMKÓ et al. (1999) determined a statistically significant increase in micronuclei in cells taken from human amnion fluid after 24-, 48- and/or 72-h exposure to a horizontal 50-Hz magnetic field (1 mT, Helmholtz spindle) compared to controls. In additional tests performed during this study, also the impact of a 6- and/or a 12-days exposure on cell growth was exam-

ined. However, no statistically significant differences between controls and EMF-exposed cells could be found here. There was neither evidence for differences in test series additionally applying crocidolite asbestos ($1\mu\text{g}/\text{cm}^3$; SIMKÓ et al. 1999, table 20).

In a 1994 published study performed in cells from the human amnion fluid at exposure to a 50-Hz magnetic field (at $30\mu\text{T}$), NORDENSON et al. detected an increase in chromosome aberrations. In contrast, at a magnetic flux density of $300\mu\text{T}$, the differences between exposed cells and controls were not statistically significant. Exposure duration in these tests was 3 days. Tests where human sperm cells were exposed to a 50-Hz magnetic field (20 mT) over 2 hours, showed no evidence for EMF-affected chromosome aberrations (TATENÓ et al. 1998).

The tests with 60-Hz magnetic fields provided no evidence for toxic or teratogenic effects. The four presented publications examined baker's yeast (mutations & mitosis, AGER & RADUL 1992), human lymphocytes (sister chromatid exchange, different cell phases, chromosomal breaks, COHEN et al. 1986), bacteria (salmonella typhimurium, mutation rate, MORANDI et al. 1996) as well as embryonic cells and/or embryos of fruit flies (microtubules, ganglia, malformations, NGUYEN et al. 1995).

Studies on the influence of 100-Hz, 600-Hz, and 6-kHz fields (JUUTI-

LAINEN & LIMATAINEN 1986, MORANDI et al. 1996) neither could show verifiable effects on the mutation rate of salmonella typhimurium (table 22). JACOBSON-KRAM et al. (1997) examined possible effects of magnetic fields produced by a therapeutical device for bone growth stimulation in salmonella typhimurium and escherichia coli (mutation rate), cell cultures (ovaries) of hamsters (chromosome aberrations), embryonic cells of mice (cytotoxic effects), and liver cells of rats (DNA synthesis). These tests neither could find effects of the examined magnetic fields on test parameters (table 22). In a study of GREENEBAUM et al. (1996), the growth of neurites from the spinal ganglion of chicken embryos at exposure to a magnetic field ($22\mu\text{s}$, 4 mT, 22 pulses/4.8 ms) was examined. In additional tests the examined cell cultures were treated with 50 and/or 100 ng/ml NGF (7S NGF, neurite growth factor). Whereas the magnetic field alone showed no effect on neurite growth, a simultaneous application of 7S NGF led to an increased asymmetrical neurite growth (not at treatment with 7S NGF alone).

With the exception of some tests at 50 Hz, the examined magnetic fields had no effect on mutation rate, the incidence of chromosome aberrations and other cytologic and genetic parameters, regardless of frequency, form, intensity, exposure duration, and used generator (spindle). However, it is possible that in some cases there could be synergistic or even potentiating

effects in connection with toxic or teratogenic agents.

The studies on different electric fields listed in table 23 which were performed in human lymphocytes, bacteria, and different cell cultures (hamsters, mice, rats) neither could determine verifiable effects (VALIUS et al. 1993, JACOBSON-KRAM et al. 1997). This also applies to test series where additionally teratogenic or mutagenic agents (mitomycin C, UV radiation) were administered (CHAHAL et al. 1993, SCARFI et al. 1993).

Table 20: Toxicologic studies (genome, cell growth) at exposure to low-frequency EMF (magnetic fields, 50 Hz)

Authors	EMF exposure	test animals	examined parameters	result
Khalil & Qassem 191	50-Hz fields; 1 mT exposure duration: 24, 48 & 72 h	lymphocytes (human)	chromosome aberrations, cell proliferation, mitosis index, sister chromatid exchange test	In all three test series, EMF exposure led to a decrease of mitosis rate and to an increase of cells with chromosome aberrations (in both cases differences compared to controls were statistically significant). At exposure over a time period of 72 h, an additional increase in sister chromatid exchange and a decreased cell proliferation rate were observed. Both differences were statistically significant.
Maes et al. 2000	50-Hz fields; 62.8, 80, 88.4, 504, 1061, 1750 & 2500 μ T EMF exposure over the whole duration of cultivation (exact data are lacking) additional tests with simultaneous application of mitomycin C (0.1 μ g/ml) or x-rays (1 Gy/min)	lymphocytes (human)	chromosome aberrations, sister chromatid exchange test	No genotoxic effects of the examined 50-Hz fields could be found. A combined treatment of samples with 50 Hz and x-rays or mitomycin C could not give proof of any synergetic, potentiating or antagonistic effects.
Nordenson et al. 1994	50-Hz fields (sinus); 20 & 300 μ T (15 s on/15 s off and/or 2 s on/20 s off) exposure duration: 3 days	amnion cells (human)	chromosome aberrations	During tests with 30 μ T, in EMF-exposed cell cultures a statistically significant increase in chromosome aberrations (EMF = 4%; controls = 2%) could be observed. In contrast, during tests with 300 μ T there was no evidence for statistically significant differences between EMF-exposed cells and controls.

Table 20 (continued)

Authors	EMF exposure	test animals	examined parameters	result
Rosenthal & Obe 1989	50-Hz field; 5 mT exposure duration: 48 and/or 72 h additional tests with 0.1, 0.5, 2.5, 5 & 7.5 mT with simultaneous application of DEB (diepoxybutane, C ₄ H ₆ O ₂), trenimone (2, 3, 5-triethylamine-1,4-benzoquinone, applied in chemotherapy), and MNU (methylNitrosourea, C ₂ H ₅ N ₃ O ₂)	lymphocytes (human)	sister chromatid exchange test, chromosome aberrations, cell proliferation rate	EMF exposure over 48 and/or 72 h led to an increase in cell proliferation rate in exposed cell cultures. EMF exposure with simultaneous application of MNU, DEB or trenimon resulted in an increased sister chromatid exchange in the EMF-exposed cell cultures. The differences from controls were statistically significant. None of the other test parameters provided evidence for statistically significant differences.
Scarfi et al. 1994	50-Hz fields (sinus); 2.5 mT (exact data are lacking, instead earlier studies conducted by the authors are referred to) exposure duration: 72 h	lymphocytes (human)	micronucleus test, mitosis index, chromosome aberrations	Proof of genotoxic effects of the examined magnetic fields was not found. In contrast, mitosis index in EMF-exposed cell cultures showed a statistically significant increase compared to controls (contrary to the abstract where no alterations are mentioned).
Scarfi et al. 1999	50-Hz fields (sinus); 0.05, 0.25, 0.5, 0.75 & 1 mT exposure duration: 72 h	lymphocytes (human)	micronucleus test, cell proliferation rate	There was no evidence for genotoxic effects of the examined magnetic fields.
Simkó et al. 1998	50-Hz fields; 1 mT Merritt spindle; vertical Merritt spindle; horizontal Helmholtz spindle; vertical Helmholtz spindle; horizontal exposure duration: 24, 48 & 72 h each additional tests with simultaneous application of 0.3 to 2.5 mM APAP (N-acetyl-p-aminophenol, inhibits DNA repair)	cells from amnion fluid (human)	micronucleus test	<i>Helmholtz spindle</i> : When cell cultures were exposed to a horizontal field (50 Hz, 1 mT) over 24, 48 or 72 h, a statistically significant increase in micronucleus formation could be detected. In contrast, in a vertical field no statistically significant differences between EMF-exposed cell cultures and controls were shown. <i>Merritt spindle</i> : During these tests, statistically significant differences between controls and EMF-exposed cell cultures could only be observed at 72-h exposure in a vertical 50-Hz field. An increase in effects of applied APAP caused by the 50-Hz field could not be detected.
Simkó et al. 1999	50-Hz fields; 1 mT horizontal, Helmholtz spindle exposure duration: 24, 48 & 72 h, as well as 6 & 12 days (only cell growth) additional application of asbestos fibers (crocidolit asbestos, 1 µg/cm ²)	cells from amnion fluid (human)	micronucleus test, cell growth	EMF-exposure over 6 & 12 days had no effect on cell growth. At EMF exposure over 24, 48 & 72 h there was no statistically significant increase in micronucleus formation of EMF-exposed cells compared to controls. A synergetic effect between the 50-Hz field and asbestos fibers could not be detected.
Tateno et al. 1998	50-Hz fields; 20 mT exposure duration: 2 h	sperm cells (human)	chromosome aberrations	There was no evidence for EMF-induced chromosome aberrations. additional control tests with gamma rays

Table 21: Toxicologic studies (genome, cell growth) at exposure to low-frequency EMF (magnetic fields 60 Hz)

Authors	EMF exposure	test animals	examined parameters	result
Ager & Radul 1992	60-Hz magnetic fields; 1 mT + UV light (254 nm) dose: 0, 12, 25 & 50 J/m ² exposure duration: 3 days; during the first 3 h, the EMF was switched off and on every 15 min (baker's yeast)	<i>saccharomyces cerevisiae</i>	mutations, mitosis	There was no proof of verifiable statistically significant effects of the examined fields.
Cohen et al. 1986	60-Hz fields (sinus); EF: 30 μ A/cm ² ; MF: 100 & 200 μ T (1 & 2 G)	lymphocytes (human)	sister chromatid exchange test, chromosomal breaks, cell phases	There was no proof of verifiable statistically significant effects of the examined fields.
Morandi et al. 1996	Magnetic fields: 60 Hz ; 0.3 mT (300 V/in) exposure duration: 48 h The electric and the magnetic field were applied separately and simultaneously. further tests with 600 Hz & 6 kHz (see corresponding tables)	salmonella typhimurium different stems: TA97a, TA98, TA100 & TA102	mutation rate	None of the different test series could provide evidence for statistically significant differences between controls and EMF-exposed cell cultures.
Nguyen et al. 1995	magnetic fields: 60 Hz ; 10 & 100 μ T exposure duration: 16 to 18 h (cell cultures), 24 h (embryos, gastrula stage) and/or 10 days (up to imago) additional tests (cultures) with cadmium sulfate, hydroxy-urea, retinol acid	embryonic cell cultures as well as embryos (beginning with gastrula stage) of <i>drosophila melanogaster</i>	<i>cell cultures</i> : development of microtubules and ganglia <i>embryos</i> : malformations	There was no proof of teratogenic effects of the examined fields. An influence of the examined EMF on effects of simultaneously applied teratogenic substances could not be detected.

Table 22: Toxicologic studies (genome, cell growth) at exposure to low-frequency EMF (magnetic fields)

Juutilainen & Limatainen 1986	magnetic fields: 100 Hz ; 0.1, 1, 10 and 100 A/m test series with cultures on agar (petri dishes) exposure duration: 48 h test series with cultures in fluid culture medium (in bottles) exposure duration: 6.5 h additional tests with application of natrium acid and/or 1,2-diamino-4-nitro-benzyl	<i>salmonella typhimurium</i> stems: TA98, TA100	mutation rate	There was no evidence for mutagenic effects of the examined 100-Hz fields. This applies also to the tests with simultaneous application of chemical mutagens (natrium acids & 1,2-diamino-4-nitro-benzyl).
Morandi et al. 1996	magnetic field: 600 Hz & 6 kHz ; 0.3 mT (300 V/in) exposure duration: 48 h Electric and magnetic field were administered either separately or simultaneously. further tests with 60 Hz (see corresponding table)	<i>salmonella typhimurium</i> different stems: TA97a, TA98, TA100 & TA102	mutation rate	None of the different test series could provide evidence for statistically significant differences between controls and EMF-exposed cell cultures.
Greenebaum et al. 1996	magnetic field: 220 µs; 4 mT ; 22 pulses/4.8 ms, every 15 and/or 25 s additional tests with simultaneous application of NGF (neurite growth factor) exposure duration: 18 h	neurites (chickens)	growth of neurites (spinal ganglion) isolated from chicken embryos	The simultaneous application of EMF + NGF led to both an increased as well as an asymmetrical neurite growth. EMF exposure without NGF had no effect on neurite growth.
Jacobson-Kram et al. 1997	therapeutical device for bone growth stimulation magnetic fields: 9 & 90 T/s exposure duration: 24 h electric fields: 3 & 30 mV/cm (see corresponding tables)	cell cultures of: <i>salmonella typhimurium</i> , <i>escherischia coli</i> ; hamsters & mice (cell cultures of ovary and/or embryonic cells); rats (liver cells)	mutagenicity (<i>salmonella</i> & <i>e.coli</i>), chromosome aberrations (hamsters), cytotoxic effects (mice), DNA synthesis (liver cells of rats)	None of the test parameters gave proof of an influence of the examined fields.

Table 23: Toxicologic studies (genome, cell growth) at exposure to low-frequency EMF (electric fields)

Authors	EMF exposure	test animals	examined parameters	result
Jacobson-Kram et al. 1997	therapeutical device for bone growth stimulation electric fields: 3 & 30 mV/cm exposure duration: 24 h magnetic fields: 9 & 90 T/s (see corresponding tables)	cell cultures of: <i>salmonella typhimurium</i> , <i>escherischia coli</i> ; hamsters & mice (cell cultures of ovary and/or embryonic cells); rats (liver cells)	mutagenicity (<i>salmonella</i> & <i>e.coli</i>), chromosome aberrations (hamsters), cytotoxic effects (mice), DNA synthesis (liver cells of rats)	None of the test parameters gave proof of an influence of the examined fields.
Chahal et al. 1993	electric fields: 1 Hz ; 1 & 3kV/m exposure duration: 1 h (3 kV/m) and/or 16 h (1 kV/m) additional tests with simultaneous application of UV or mitomycin C	<i>escherischia coli</i> 3 K12 stems: AB1157, AB1157 umuC ⁺ , AB1157 umuC ¹ uvrB, TK702 umuC, TK702 umuC uvrB ⁺ , TK 501 umuC uvrB	mutation rate, UV sensitivity, DNA repair mechanisms	Verifiable statistically significant effects of the applied electric fields on test parameters could not be detected.
Scarfi et al. 1993	electric fields: 50 Hz (ac, sinus); 0.5, 2.5 & 10 kV/m exposure duration: 72 h additional tests with simultaneous application of mitomycin C	lymphocytes (human)	micronucleus test	None of the performed test series could confirm genotoxic effects of the examined electric effects.
Valjus et al. 1993	electric fields: 50 Hz Examined were power electricians having worked over a time period of about 10 years at exposure to high-voltage power lines of 110 to 400 kV. The reference group consisted of the staff of a phone corporation.	blood samples (lymphocytes), humans	chromosome aberrations, sister chromatid exchange test, micronucleus test	There was no proof of a relation between chromosome aberrations, micronucleus formation or sister chromatid exchange and long-term exposure. The increased number of chromatid breaks detected during tests in the group of power electricians probably is connected with intense smoking.

frequency-range	number of studies	table
900 MHz	2	24
935 MHz	1	24
954 MHz	2	24
2.45 GHz	6	24
7.70 GHz	2	24
9.40 GHz	1	24

Graph 9: Cytologic and toxicologic studies performed in high-frequency EMF.

For the range from 900 to 954 MHz, 4 out of 5 included studies were performed in human lymphocytes (MAES et al. 1995, 1996, 1997, 2001) and one in baker's yeast (GOS et al. 2000). Parameters examined in these studies were: mutations and recombination (baker's yeast, *saccharomyces cerevisiae*), chromosome aberrations, sister chromatid exchange, and cell kinetics (lymphocytes). In none of these studies the examined high-frequency field showed statistically verifiable effects on test parameters. With the exception of one study (MAES et al. 1996), neither synergetic effects of the examined fields could be detected when mutagens (mitomycin C, methyl-methansulfonate) were applied simultaneously. Only in the

2.4.2. Genetic and cytotoxic effects of high-frequency EMF
In this chapter, table 24 lists a total of 14 studies examining high-frequency EMF for possible cytotoxic and/or genotoxic effects. In these studies, frequencies in the range from 900 to 954 MHz, 2.45 and 7.7 GHz were tested (graph 9).

study of MAES et al. (1996) the examined 954-MHz field (GSM signal) led to an increase in effects of the mitomycin C administered during tests.

In mice (sperm) tested in a 2.45-GHz field (cw; 1, 100 & 400 mW/cm²), BEECHEY et al. (1986) found no influence on the number of chromosome aberrations or spermatogenesis. Only on the 12th to 13th day after exposure, some tests could show a temporary increase in the number of sperms. In contrast to this, MANIKOWSKA CZERSKA et al. (1985) observed an increase in chromosomal anomalies in sperm cells of mice having been exposed to a 2.45-GHz field (cw, 0.05 to 20 mW/cm²) over 2 weeks (6 days/week) at 10 & 20 mW/cm².

Two studies in rats (cells from the area of the hippocampus) having been exposed to a 2.45-GHz field (2 mW/cm², cw & pulsed: 2 μ s, 500 pps) over 2 hours showed a statistically significant increase in DNA damages (double and single strand breaks) 4 hours after exposure (LAI & SINGH 1995, 1996).

No evidence was provided for effects on sister chromatid exchange and/or the number of chromosome aberrations by studies exposing human lymphocytes over 20 min to a field of 2.45 GHz (cw, SAR: 4 to 200 W/kg). This also applied to the test series with a considerable hyperthermic effect (LLOYD et al. 1986). In contrast, a study of MAES et al. (1993) performed in human lymphocytes (2.45 GHz, pulsed with 50 Hz,

SAR: 75.5 W/kg), too, detected a statistically significant increase both in the number of chromosome aberrations as well as in micronucleus formation compared to controls. There was no influence of exposure on cell kinetics or sister chromatid exchange. In these tests, exposure duration was 30 or 120 min. The authors explain observed effects by a thermic effect of the examined fields (MAES et al. 1993).

In two studies, GARAJ VRHOVAC et al. (1991 & 1992) investigated the number of chromosome aberrations as well as micronucleus formation in V79 cells (fibroblasts, lungs) of hamsters and/or human lymphocytes at exposure to a 7.7-GHz field (cw; table 24). The applied power flux densities were 0.5 and 10 mW/cm² (lymphocytes), and 30 mW/cm² (V79 cells and lymphocytes). Tests with a power flux density of 0.5 mW/cm² could provide no evidence for effects of the examined 7.7-GHz field. During the tests with 10 mW/cm² (lymphocytes) and 30 mW/cm² (V79 cells, lymphocytes) both the number of chromosome aberrations as well as of micronuclei showed a statistically significant increase compared to controls (GARAJ VRHOVAC et al. 1991, 1992). In these tests, a temperature increase of 1° C was measured at the surface of the examined cell cultures during EMF exposure. However, the authors do not answer the question whether the observed effects are caused by hyperthermia of exposed cells.

An increase of chromosomal anomalies was seen in tests exposing sperm

cells of mice to a 9.4-GHz field (0.1 to 10 mW/cm², pulsed with 1 kHz). Beginning with a power flux density of 0.5 mW/cm², in these tests both the number of translocations (metaphase) as well as the number of metaphases with univalent chromosome pairs showed a statistically significant increase compared to controls (MANIKOWSKA et al. 1979).

In summary, we may conclude that none of the available studies using high-frequency fields provided evidence for a special relevance of modulation and/or pulsation. Available results also suggest that the effects observed in some of the studies probably may be explained by thermic effects of the tested fields (see VERSCHAEVE & MAES 1998).

Table 24: Toxicologic studies (genome, cell growth) at exposure to high-frequency EMF

Authors	EMF exposure	test animals	examined parameters	result
Gos et al. 2000	900 MHz (GSM, pulse modulated) SAR: 0.13 and/or 1.3 W/kg exposure duration: 1 h (0.13 W/kg) or 36 h (1.3 W/kg) additional tests with simultaneous application of methyl-methansulfonate (0.01 %)	cultures of baker's yeast, <i>saccharomyces cerevisiae</i>	mutation, recombination in resting and/or active (growing) yeast cells	No statistically significant differences between the EMF-exposed cell cultures and controls could be detected. A synergetic effect between the 900-MHz field and simultaneously applied methyl-methansulfonate could not be found.
Maes et al. 2001	900 MHz (cw; GSM, 'pseudo-random') initial power: 0, 2, 8, 15, 25 & 50 W SAR: 0.4, 2, 3.5, 5.5 & 10 W/kg exposure duration: 2 h additional tests with mitomycin C (0.1 µg/ml) and/or x-rays (1 Gy)	lymphocytes (human)	chromosome aberrations, sister chromatid exchange test	No influence of the tested 900-MHz fields on test parameters could be found. A combined treatment of the examined samples with 900 MHz and mitomycin C or x-rays provided no evidence for synergetic, potentiating or antagonistic effects of EMF exposure.
Maes et al. 1997	935.2 MHz (GSM); SAR: 0.4 W/kg exposure duration: 2 h additional tests with simultaneously applied mitomycin C (a mutagene)	lymphocytes (human)	chromosome aberrations, sister chromatid exchange test	No effects of the applied 953.2-MHz field on the examined samples (lymphocytes) could be detected. When samples were simultaneously treated with mitomycin C, synergetic effects neither could be verified.
Maes et al. 1995	954 MHz (GSM, base station antenna) electric field: 49 V/m; initial power: 15 W; SAR: 1.5 W/kg exposure duration: 2 h In an additional pilot study, blood samples of 6 participants working around transmission facilities were tested for chromosome aberrations. Different frequencies from the mobile radio range were examined (among others, 450 & 900 MHz; exact data are lacking).	lymphocytes (human)	chromosome aberrations in vitro tests with cell cultures as well as in vivo tests with 6 mobile radio workers	There was no evidence for statistically significant differences between the EMF-exposed blood samples and/or cell cultures.
Maes et al. 1996	954 MHz (GSM, base station); electric field: 49 V/m; initial power: 15 W SAR: 1.5 W/kg exposure duration: 2 h additional tests with simultaneous application of mitomycin C	lymphocytes (human)	sister chromatid exchange test, cell kinetics (metaphase stages, cell proliferation)	The examined 954-MHz field had a synergetic effect on the mutagenic impact of the simultaneously applied mitomycin C. The difference compared to the samples with mitomycin C and without EMF was statistically significant. When only the 954-MHz field was applied, no influence on cell kinetics and/or increase in the sister chromatid exchange could be proved. A synergetic effect of the EMF with simultaneously applied mitomycin C on cell kinetics was not found.
Beechey et al. 1986	2.45 GHz (cw); 1, 100 & 400 mW/cm ² exposure duration: 30 min/day, 6 days per week over a total of 14 days	sperm (mice)	sperm cells (chromosome aberrations) 2-3, 12-13, 30 & 41 days after EMF exposure	12-13 days after exposure EMF-exposed mice showed a slight, but statistically significant increase in the number of sperm cells. The remaining test days showed no statistically significant differences between controls and EMF-exposed mice. The incidence of chromosome aberrations was not affected by the examined 2.45-GHz fields.

Table 24 (contin.): Toxicologic studies (genome, cell growth) at exposure to high-frequency EMF (frequency range: 60 kHz to 8 GHz)

Authors	EMF exposure	test animals	examined parameters	result
Lai & Singh 1995	2.45 GHz (cw and/or pulsed: 2 μ s; 500 pps) SAR: 0.6 and/or 1.2 W/kg (whole body); 1 (only at pulsed field) and/or 2 mW/cm ² exposure duration: 2 h	brain cells (rats)	DNA damages (single strand breaks) tests took place immediately and/or 4 h after EMF exposure	Pulsed field: brain cells (hippocampus & remaining brain, no data on other areas) examined immediately after exposure showed no statistically significant differences from controls. When the cells were examined 4 h after exposure, an increase in DNA damages was detected. Differences from controls were statistically significant. If cells were exposed to a unpulsed 2.45-GHz field, an increase in DNA damages was found immediately after exposure as well as 4 h later. Differences from controls were statistically significant.
Lai & Singh 1996	2.45 GHz (cw and/or pulsed: 2 μ s; 500 pps) SAR: 1.2 W/kg (whole body); 2 mW/cm ² exposure duration: 2 h	brain cells (rats)	DNA damages (single and double strand breaks) tests performed 4 h after EMF exposure	Both in the pulsed as well as in the unpulsed 2.45-GHz field, the examined brain cells of rats showed an increase of DNA damages (double and single strand breaks). The differences compared to controls were statistically significant.
Lloyd et al. 1986	2.45 GHz (cw); 0, 4, 40, 100 & 200 W/kg exposure duration: 20 min	lymphocytes (human)	chromosome aberrations, sister chromatid exchange test	Despite a hyperthermic effect there were no effects of the applied 2.45-GHz fields on the examined blood samples (lymphocytes).
Maes et al. 1993	2.45 GHz (modulated with 50 Hz); SAR: 75.5 W/kg exposure duration: 30 & 120 min	lymphocytes (human)	chromosome aberrations, sister chromatid exchange test, cell kinetics, micronucleus test	In the EMF-exposed lymphocytes a statistically significant increase of chromosome aberrations as well as an increase in micronucleus formation was found. The authors do not exclude a thermic effect. Sister chromatid exchange and cell kinetics were not affected by the examined 2.45-GHz field.
Manikowska Czerska et al. 1985	2.45 GHz (cw); SAR: 0.05, 0.5, 10 & 20 mW/g exposure duration: 6 days/week over a time period of 2 weeks	sperm cells (mice)	spermatogenesis, chromosomal damages (translocation)	At 10 & 20 mW/cm ² , an increase of chromosomal anomalies (translocation) was detected in the sperms of the EMF-exposed mice.
Garaj Vrhovac et al. 1991	7.7 GHz (cw); 30 mW/cm ² exposure duration: 15, 30 & 60 min	V79 cells (fibroblasts, lungs, hamsters)	chromosome aberrations (chromatid breaks, chromosomal breaks, rings; acentric and dicentric chromosomes), micronucleus test	After 15-min exposure the number of chromosome aberrations and of micronuclei showed a statistically significant increase compared to controls.
Garaj Vrhovac et al. 1992	7.7 GHz (cw); 0.5, 10, 30 mW/cm ² exposure duration: at 0.5 & 10 mW/cm ² over 30 min each; at 30 mW/cm ² over 10, 30 & 60 min	blood samples (lymphocytes, human)	chromosome aberrations (chromatid breaks, chromosomal breaks, rings; acentric and dicentric chromosomes), micronucleus test	At 0.5 mW/cm ² no statistically significant differences between controls and EMF-exposed cells were found. At 10 mW/cm ² and in tests with 30 mW/cm ² , the increase in the number of micronuclei and of chromosome aberrations in EMF-exposed cells was statistically significantly.
Manikowska et al. 1979	9.4 GHz (pulsed: 1000 Hz); 0.1, 0.5, 1 & 10 mW/cm ² exposure duration: 1 per day (over 2 weeks, 5 days/week)	sperm (mice)	chromosome aberrations	All tests showed statistically significant differences between controls and exposed sperm cells (number of translocations during metaphase, number of metaphases with univalent chromosomes).

3. Epidemiologic studies

Since teratologic studies in many cases cannot be performed in the human organisms for ethical considerations, as a rule in vivo studies are carried out in selected animals models. Knowledge gained from such laboratory studies, even when appropriately scientifically verified, only allow indirect and, in some cases, not always accurate conclusions regarding possible health risks for the human organism. Instead, so-called epidemiologic studies are performed in participant groups selected according to certain criteria.

Until now published worldwide conducted epidemiologic studies have examined possible effects of following sources producing low- and high-frequency electromagnetic fields:

low-frequency EMF:

- high-voltage lines and electric installations for domestic power supply
- television and computer monitors
- heating cables and electric blankets

high-frequency EMF:

- physiotherapeutical devices
- microwaves
- short waves.

In planning and performing epidemiologic studies some basic rules should be heeded. Participant groups have to be selected according to criteria that are relevant to reach the study's goals (age, history:

for example, known hereditary diseases, predamages, etc). Further, epidemiologic studies on teratologic issues have to consider that the occurrence of congenital malformations as well as embryo mortality in many cases are connected with existing latent genetic alterations. Moreover, the embryo's sensitivity towards teratogenic influences changes during pregnancy (see chapter 1.4.). Also, abortions in an early development phase very often are not identified as such. Thus, evaluation of epidemiologic data from this crucial stage of embryonic development often is made nearly impossible.

In studies of small statistical sample size, group size at least must be sufficient to obtain statistically verifiable results. As can be seen when looking at the number of examined test persons, some studies did not meet this criterion.

When selecting corresponding control groups it is essential to ensure as far as possible that test persons are not exposed to electromagnetic fields. However, considering worldwide coverage of power supply facilities as well as of broadcasting, television and telephone networks, this concept seems unrealistic.

Thus, epidemiologic studies in general show a lack of „authentic“ controls casting considerable doubt on available results. Another weak point are exposure conditions – both of the test group as well as of control groups – not being mea-

sured sufficiently or measured at all in some cases. Also, in some cases, flawed test designs caused by insufficient embryologic/teratologic knowledge as well as by bias and subjective assessment both of test persons and of scientific staff, make scientific evaluation of available data more difficult. To-date available data do not provide evidence for an increased risk for pregnant women, though.

This survey study will not deal in detail with the results listed by the tables 25 to 28. The main reason for this is that exact exposure and test conditions in some cases were not available or at least incomplete. Furthermore, it is questionable whether results obtained from certain groups are generally portable or applicable, since social, medical, pathological and biological parameters as well as environmental conditions for the various groups and population stratas of current society differ hugely.

In summary, the results of to-date performed epidemiologic studies provide no evidence for an increased risk for pregnant women caused by monitors, electric installations and/or other sources of low-frequency electromagnetic fields. The by far biggest part of the studies showed no relation between embryo mortality, malformations and other disturbances in embryonic development and low-frequent fields. But the question whether this is applicable to the whole population, or whether at least certain risk groups are excluded, is not answered by available

data. That such risk groups could possibly exist is shown by the results of the study performed by LI et al. (1995) where in offspring of women with a certain diagnosed reproductive disorder a relation between EMF exposure and congenital malformations of the urogenital system was demonstrated.

Until now, final conclusions on possible risks caused by mobile radio facilities and mobile phones related to reproductive disorders cannot be drawn for lack of data.

Table 25: Epidemiologic studies (monitors)

authors	title	type of EMF exposure	study result
al Ansary & Babay 1994	Risk factors for spontaneous abortion: a preliminary study on Saudi women.	monitors	no connection between abortion rate and EMF exposure
Bracken et al. 1995	Exposure to electromagnetic fields during pregnancy with emphasis on electrically heated beds: association with birthweight and intrauterine growth retardation.	monitors, electric blankets, electrically heated waterbeds	no connection between EMF exposure and embryonic development/birth weight
Brandt & Nielsen 1990	Congenital malformations among children of women working with video display terminals.	monitors	no connection between congenital malformations and the examined fields
Brandt & Nielsen 1992	Fecundity and the use of video display	monitors, terminals	A statistically significant connection between the EMF and fecundity could be found only when test persons were exposed longer than 21 hours per week.
Bryant & Love 1989	Video display terminal use and spontaneous abortion.	monitors	no connection between abortion rate and EMF exposure
Kurppa et al. 1985	Birth defects and exposure to video display terminals during pregnancy. A Finnish case-referent study.	monitors	no connection between congenital malformations and EMF exposure
Li et al. 1995	Electric blanket use during pregnancy in relation to the risk of congenital urinary tract anomalies among women with a history of subfertility.	monitors, electric blankets, electrically heated waterbeds	no connection between congenital malformations of the urogenital system and EMF exposure in healthy women increased risk in women with fertility disorders
Lindbohm et al. 1992	Magnetic fields of video display terminals and spontaneous abortion.	monitors	slight increase of spontaneous abortions at higher intensities (>0.9 mT)
Nielsen & Brandt 1992	Fetal growth, preterm birth and infant mortality in relation to work with video display terminals during pregnancy.	monitors	no connection between EMF and embryonic development, preterm birth as well as infant mortality
Nurminen & Kurppa 1988	Office employment, work with video display terminals, and course of pregnancy. Reference mothers' experience from a Finnish case-referent study of birth defects	monitors	no connection between course of pregnancy and EMF exposure
Parazzini et al. 1993	Video display terminal use during pregnancy and reproductive outcome- a meta-analysis.	monitors	no connection between EMF exposure and abortion rate, birth weight or congenital malformations
Pastore et al. 1997	Risk of stillborn from occupational and residential exposures.	monitors	no connection between stillbirth and EMF exposure
Roman et al. 1992	Spontaneous abortion and work with visual display units.	monitors	no connection between abortion rate and EMF exposure
Schnorr et al. 1991	Video display terminals and the risk of spontaneous abortion.	monitors	no connection between abortion rate and EMF exposure
Tikkanen & Heinonen 1990	Occupational risk factors for congenital heart disease.	monitors	slightly increased risk of congenital heart diseases at EMF exposure
Tikkanen et al. 1990	Cardiovascular malformations and maternal exposure to video display terminals pregnancy.	monitors	no connection between EMF exposure and cardiovascular malformations
Windham et al. 1990	Use of video display terminals during pregnancy and the risk of spontaneous abortion, low birthweight, or intrauterine growth retardation.	monitors	During the first 12 weeks of pregnancy abortion rate was slightly increased in EMF-exposed test persons. Further there was a slight increase in prenatal growth disturbances

Epidemiologic studies

Table 26: Epidemiologic studies (electric blankets, heated waterbeds & heating cables)

authors	title	type of EMF exposure	study result
Belanger et al. 1998	Spontaneous abortion and exposure to electric blankets and heated water beds.	electric blankets, electrically heated waterbeds	no connection between abortion rate and EMF exposure
Bracken et al. 1995	Exposure to electromagnetic fields during pregnancy with emphasis on electrically heated beds: association with birthweight and intrauterine growth retardation.	electric blankets, electrically heated waterbeds, monitor	no connection between EMF exposure and embryonic development/birth weight
Dlugosz et al. 1992	Congenital defects and electric bed heating in New York State: a register-based case-control study.	electric blankets	A connection between the occurrence of cleft palates, malformations of the neural ear and the use of electric blankets could not be found.
Li et al. 1995	Electric blanket use during pregnancy in relation to the risk of congenital urinary tract anomalies among women with a history of subfertility.	electric blankets, electrically heated waterbeds, monitors	no connection between congenital malformations of the urogenital system and EMF exposure in healthy women increased risk in women with subfertility
Shaw et al. 1999	Maternal preconception use of electric bed-heating devices and risk for neural tube defects and orofacial clefts.	electric blankets, electrically heated beds	slight increase in congenital malformations (f.e. cleft palates) very small risk according to the authors
Wertheimer & Leeper 1989	Fetal loss associated with two seasonal Sources of electromagnetic field exposure.	electric heating cables, electrically heated waterbeds (60 Hz; 1 μ T; 10 to 50 V/m)	Abortion rate correlated with seasonal use of heating blanket cables and electrically heated beds.

Table 27: Epidemiologic studies (high-voltage power lines)

authors	title	type of EMF exposure	study result
Martin et al. 1986	Epidemiologic study of Holstein dairy cow performance and reproduction near a high-voltage direct-current powerline.	high-voltage power lines	no connection between EMF exposure and reproductive disorders
Robert 1993	Birth defects and high voltage power lines: an exploratory study based on registry data.	high-voltage power lines (225 & 400 kV)	statistically significant decrease in malformations in children being born near high-voltage power lines
Robert et al. 1996	Case-control study on maternal residential proximity to high voltage power lines and congenital anomalies in France.	high-voltage power lines (225 & 400 kV)	no connection between residential proximity to high-voltage power lines and congenital malformations

Table 28: Epidemiologic studies (short-wave and microwave physiotherapeutical devices)

authors	title	type of EMF exposure	study result
Gubéran et al. 1994	Gender ratio of offspring and exposure to shortwave radiation among female physiotherapists.	short-wave physiotherapeutical devices	no connection between gender ratio of offspring and EMF exposure
Källén et al. 1982	Delivery outcome among physiotherapists in Sweden: Is non-ionizing radiation a fetal hazard?	Short waves, microwaves, ultrasound, x-rays	slight increase in malformations and embryo mortality at exposure to short waves for all other exposure types: no connection between malformations, embryo mortality, birth weight and duration of pregnancy
Larsen 1991	Congenital malformations and exposure to high-frequency electromagnetic radiation among Danish physio-therapists.	short- and microwave physiotherapeutical devices	no connection between congenital malformations and EMF exposure
Ouellet Hellstrom & Stewart 1993	Miscarriages among female physical therapists who report using radio- and microwave-frequency electromagnetic radiation.	short- and microwave physiotherapeutical devices	<i>microwaves</i> : slight increase in miscarriages <i>short waves</i> : no connection between EMF and miscarriages

4 Review articles

Only three of the survey studies presented in this chapter deal with teratologic studies examining high-frequency electromagnetic fields (O'CONNOR 1999; ROBERT 1999; VERSCHAEVE & MAES 1998). The study of ROBERT (1999), too, mainly deals with studies applying low-frequency fields. The remaining studies listed in table 29 exclusively deal with low-frequency EMF, in part having been performed in the early nineties.

The to-date most comprehensive study probably is the survey study performed by BRENT et al. 1993 including about 100 teratologic studies dealing with low-frequency electromagnetic fields. Besides, the study of BRENT and colleagues deals with the physics of low-frequency electromagnetic fields and provides a knowledgeable introduction into teratology. The single studies are listed in tables according to laboratory and epidemiologic studies. Apart from data on the examined electromagnetic fields, these tables contain information about the tested animal model, the number of participants and/or test animals as well as a short commentary of the authors. Though the evaluation of the study object as a whole, as well as of single issues not always seems to be done without bias, the study of BRENT et al. (1993) is a very knowledgeable and excellently written survey on studies published until 1992/93 on possible teratologic effects of low-frequency electromagnetic fields. More or less identical is

a survey study published in 1999, this time BRENT being the only author (BRENT 1999). This investigation exclusively deals with laboratory studies (in vivo & in vitro). Regrettably, this newer survey includes only very few recent studies (after 1993). Further, the conclusions drawn by the authors on the basis of the reviewed material are basically the same as those presented in his 1993 published study (BRENT et al. 1993). All in all, BRENT's perspective on the studies presented by him and his colleagues is very critical. This concerns not only results described in the studies, but also the often flawed test design.

Much less comprehensive is a survey study published in 1991 by JUUTILAINEN. Besides a short introduction into low-frequency electromagnetic fields, mostly in vivo tests performed in chick and mammal embryos as well as epidemiologic studies, to the main part dealing with possible health risks caused by monitors and visual displays, are discussed and analysed. Though results of studies performed in chick embryos are seen as evidence for the assumption that there could be possible adverse effects of low-frequency EMF on embryonic development, the authors emphasize that biological factors and environmental parameters to date are not sufficiently understood. Less clear, according to JUUTILAINEN, are the results of studies in mammals. In his opinion, results mainly suggest that embryo mortality is increased in EMF-exposed embryos, whereas congenital malformations are observed less

often (JUUTILAINEN 1991). Moreover, according to the author, tests in mice more often led to teratogenic effects than tests in rats. On the whole, JUUTILAINEN is convinced that low-frequency EMF do cause only comparably slight disturbances in the embryonic development of mammals. In JUUTILAINEN's view, results from epidemiologic studies presented in his survey all in all do not provide clear evidence for possible pregnancy risks for EMF-exposed women.

The same author – JUUTILAINEN – also participated in the review published in 1998 by HUUSKONEN et al. This survey presents epidemiologic studies as well as laboratory studies with low-frequency magnetic fields. For laboratory studies, the focus here is on studies in mammals; studies performed in chicks play a minor role. The studies are both reviewed as well as listed in tables. According to the authors, the examined low-frequency EMF on the whole pose a very small risk for embryonic development. There would be a slightly increased risk only for very early embryonic stages (resorptions, early abortions). Thus, according to the authors, future projects should confine to early stages of embryonic development, postnatal effects (after prenatal exposure), as well as on the interaction between electromagnetic fields and known teratogenic agents (HUUSKONEN et al. 1998).

In his review published in 1990, BERMAN nearly exclusively deals with the until then published studies

conducted in chick embryos at exposure to low-frequency electromagnetic fields. The included studies are discussed according to exposure conditions and statistical methods. Seen as responsible for the partially heterogenous results are the often different exposure conditions, environmental parameters, and statistical methods. The overall evaluation of results of the presented studies is similar to that of JUUTILAINEN (1991). However, BERMAN avoids drawing possible conclusions on portability of observed effects pointing to the still unresolved question of interaction mechanisms in humans.

In their literature survey, CHERNOFF et al. (1992) present about 100 investigations – epidemiologic studies as well as laboratory studies done in different animal models using electric and magnetic fields. The single studies are summarised in the corresponding chapters according to the examined fields and used animal models. Results are very critically discussed. Due to the heterogenous results as well as the morphological differences between birds and mammals, the authors classify studies performed in chick and/or quail embryos as „difficult to interpret“. Neither do studies in mammals provide clear evidence for

possible teratogenic effects of low-frequency electromagnetic fields, since results often were not replicated. According to the authors, this applies also to epidemiologic investigations presented in the survey study (CHERNOFF et al. 1992).

The survey study of ROBERT published in 1999, exclusively deals with the results of more than 50 epidemiologic studies on possible risks of low- and high-frequency electromagnetic fields for human embryonic development. Validity of to-date available epidemiologic studies is seen as low. Due to the lack of

Table 29: Survey studies

authors	title	type of EMF exposure	test animals/models
Berman 1990	The developmental effects of pulsed magnetic fields on animal embryos.	low-frequency fields	chicks, mammals
Brent et al. 1993	Reproductive and teratologic effects of electromagnetic fields.	low-frequency fields	cell cultures, single-cell organisms, insects, fish, amphibians, chicks, mammals, epidemiologic studies
Brent 1999	Reproductive and teratologic effects of low-frequency electromagnetic fields: A review of in vivo and in vitro studies using animal models.	low-frequency fields	among others, chicks, mammals
Chernoff et al. 1992	A review of the literature on potential reproductive and developmental toxicity of electric and magnetic fields.	low-frequency fields	birds (chicks & quails), mammals, epidemiologic studies
Huuskonen et al. 1998	Teratogenic and reproductive effects of low-frequency magnetic fields.	low-frequency fields	birds (chicks & quails), mammals, epidemiologic studies
Juutilainen 1991	Effects of low-frequency magnetic fields on embryonic development and pregnancy.	low-frequency fields	chicks, mammals (rats, mice), epidemiologic studies
O'Connor 1999	Intrauterine effects in animals exposed to radiofrequency and microwave fields.	high-frequency fields	among others, insects, quails, mice, rats
Robert 1999	Intrauterine effects of electromagnetic (low-frequency, mid-frequency RF and microwave): Review of epidemiologic studies.	low- and high-frequency fields	epidemiologic studies
Verschaeve & Maes 1998	Genetic, carcinogenic and teratogenic effects of radiofrequency fields.	high-frequency fields	different in vitro and in vivo studies in hamsters, mice, humans, rats on genetic, oncologic and teratologic issues

sufficient data, no assessment refers to high-frequency fields. In summary, potential risks caused by electromagnetic fields for human embryonic development are seen as very small.

The survey study published by VERSCHAEVE & MAES (1997) analyses studies examining high-frequency fields in connection with genetics, oncology and teratology.

Beside numerous studies on genetic and cytologic issues, a total of about 25 teratologic studies performed in mammalian embryos are listed. The chapter dealing with teratologic in vivo studies is very short: there is no comprehensive analysis of the listed studies. From the available studies, the authors conclude that effects caused by high-frequency fields exclusively result from thermic effects of the examined fields (VERSCHAEVE & MAES 1997). The by far bigger part of the survey study of VERSCHAEVE & MAES deals with toxicologic studies (genetics), studies on fertility of HF-exposed animals, and studies on oncologic issues.

In her 1999 published review, O'CONNOR analyses teratologic studies on high-frequency fields performed in insects, quails, rats and mice. The effects observed in some of these studies on the body weight of HF-exposed embryos are seen as clinically irrelevant. Potential risks caused by high-frequency fields are seen as relatively small; potentially occurring disturbances are explained by thermic effects caused by too

high power flux densities (O'CONNOR 1999).

5. EMF-induced pregnancy risks?

On the whole, to-date available results suggest that non-ionising electromagnetic fields in the non-thermal range have a comparably low teratogenic potential with regard to humans. Though some studies in mammals could in fact detect teratogenic effects of the examined low-frequency fields, they were not replicable or confined to certain breeding lines (f.e. CBA/S mice; f.e. SVEDENSTAL & JOHANSON 1995; TYNDALL 1993). In the studies performed in chick and/or quail embryos nearly exclusively the first 2 to 3 days of embryonic development were examined. Studies testing embryos up to hatching are lacking. Thus, we cannot safely assume that disturbances in embryonic development detected by some tests necessarily will occur in hatched chicks, too.

Teratogenic and embryo-lethal effects showed by some studies examining high-frequency fields in mammals and chicks and/or quails probably were caused by thermic effects of the examined EMF. The question to which degree currently existing mobile radio networks (base stations, antennas, mobile phones) are a risk for human embryonic development (in animals for cattle, game, breeding birds), cannot be answered yet. Though this issue has been the focus of public interest and discussion for some years now, there are very few (900 MHz, D-net) or no studies at all (1.8 GHz, E-net, wireless phones) available on the

frequencies applied by mobile radio. At least, the few studies performed with fields in the 900-MHz range in mammals (rats) suggest that here, too, no or only slight effects on embryonic development are expected (f.e. BORNHAUSEN & SCHEIN-GRÄBER 2000; JENSH 1997). Flawed or downright unreliable studies suggest an embryo mortality of up to 100% (f.e. YOUBICIER-SIMO et al. 1998; VARGA 1992) at exposure to high-frequency fields (f.e. 900 MHz, 1.25 GHz). Regrettably, these studies still are not scientifically disproved by valid investigations. To-date available data from a series of cell biological studies could not provide evidence for genotoxic and/or cytotoxic effects of the examined fields in the 900-MHz range (f.e. MAES et al. 2001; GOS et al. 2000). Also mutagenic and/or toxic effects observed by some studies (f.e. at 2.45 GHz) most certainly are caused by thermal effects of the tested EMF (MAES et al. 1993). However, here, too, studies on fields in the 1.8-GHz range are lacking.

A very interesting perspective is presented by studies simultaneously applying electromagnetic fields and teratogenic, mutagenic or toxic agents to find out about potential synergetic, antagonistic (protective) or potentiating effects. While there are numerous cytologic studies (f.e. EMF + mitomycin C) on this issue, in vivo studies are very few. However, for example the studies of CHIANG et al. 1995 (chapter 2.1.2., table 9) or NELSON et al. 1991 (chapter 2.2.2., table 14) do show that there could be interactions between EMF

and other factors and/or agents where the examined electromagnetic fields together with simultaneous applications of teratogenic agents lead to a distinctive increase in malformations. Due to the to-date still insufficient data, it is necessary to perform further studies above all looking at other parameters (f.e. strain, diseases) or nutrition and smoking habits (f.e. nicotine, alcohol) in relation with electromagnetic fields.

As already described in chapter 1.4., the by far biggest part of to-date known teratogens lead to anomalies, malformations or even to the death of the embryo and/or the fetus only in connection with pre-existing genetic defects. Apart from exogenous factors (holding and test conditions), this genetic predisposition probably is one of the causes for the contradictory results of many studies (f.e. „henhouse project“, chapter 2.1.1.). Therefore, it is necessary to perform further studies in special breeding-lines. The studies of TYNDALL & SULIK (1991) and TYNDALL (1993) performed in C57BL/6J mice with a genetic predisposition for malformations of the eyes do confirm that there actually is a connection between genetic predisposition and teratogenic effects of electromagnetic fields. Both studies showed a statistically significant increase in the number of this type of anomaly in EMF-exposed animals (chapter 2.1.2., table 11).

Despite the huge number of published studies, the issue of the actual

teratogenic potential of electromagnetic fields cannot be satisfactorily resolved yet. Due to the many unresolved issues, there still is considerable need for research. Above all, this need arises from the current media coverage where features on higher malformation incidence and increased mortality of animals held in the vicinity of transmission facilities help to increase uncertainties and fears of the public.

6. References

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