



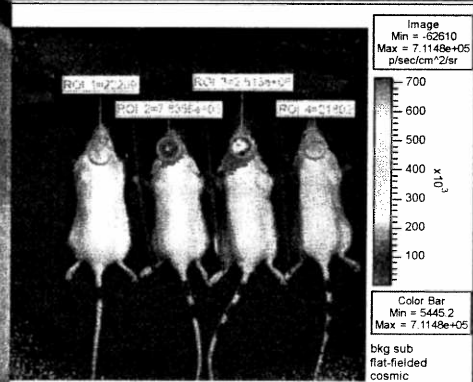
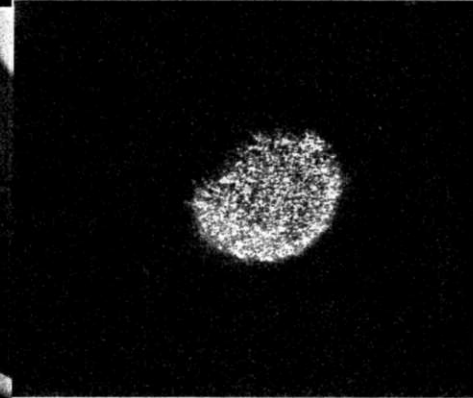
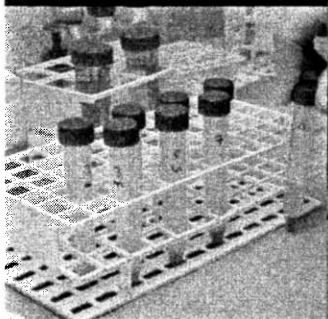
UZ
LEUVEN

KINDERGENEESKUNDE



An academic reflection On non-ionising irradiation

Stefaan Van Gool, M.D., Ph.D.
Kliniekhoofd kinderhemato-oncologie UZL
Buitengewoon Hoogleraar KUL
Fundamenteel Klinisch Navorser FWO-V



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Effects on biological systems

- Molecular level
- Cellular level
- Animal experiments
- Experiments on humans
- Case/control studies
- Epidemiologic research
- Meta-analysis
- Opinion, Discussion forum

Effect



Disease

Genetic damage in mobile phone users: some preliminary findings

Gursatej Gandhi, Anita

Department of Human Genetics, Guru Nanak Dev University, Amritsar 143 005.

BACKGROUND : The impact of microwave (MW)/radio frequency radiation (RFR) on important biological parameters is probably more than a simply thermal one. Exposure to radio frequency (RF) signals generated by the use of cellular telephones have increased dramatically and reported to affect physiological, neurological, cognitive and behavioural changes and to induce, initiate and promote carcinogenesis. Genotoxicity of RFR has also been reported in various test systems after *in vitro* and/or *in vivo* exposure but none in mobile phone users.

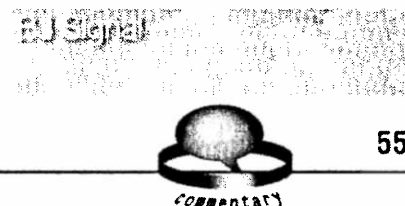
AIMS : In the present study, DNA and chromosomal damage investigations were carried out on the peripheral blood lymphocytes of individuals using mobile phones, being exposed to MW frequency ranging from 800 to 2000 MHz.

METHODS : DNA damage was assessed using the single cell gel electrophoresis assay and aneugenic and clastogenic damage by the *in vivo* capillary blood micronucleus test (MNT) in a total of 24 mobile phone users.

RESULTS : Mean comet tail length ($26.76 \pm 0.054 \mu\text{m}$; 39.75% of cells damaged) in mobile phone users was highly significant from that in the control group. The *in vivo* capillary blood MNT also revealed highly significant (0.25) frequency of micronucleated (MNd) cells.

CONCLUSIONS : These results highlight a correlation between mobile phone use (exposure to RFR) and genetic damage and require interim public health actions in the wake of widespread use of mobile telephony.

Key words: DNA damage; micronuclei; microwaves.



Mechanism of short-term ERK activation by electromagnetic fields at mobile phone frequencies

Joseph FRIEDMAN*, Sarah KRAUS*, Yirmi HAUPTMAN†, Yoni SCHIFF† and Rony SEGER*¹

*Department of Biological Regulation, The Weizmann Institute of Science, Rehovot 76100, Israel, and †Gal Safe Ltd, Rishon Lezion, Israel 75153

The exposure to non-thermal microwave electromagnetic fields generated by mobile phones affects the expression of many proteins. This effect on transcription and protein stability can be mediated by the MAPK (mitogen-activated protein kinase) cascades, which serve as central signalling pathways and govern essentially all stimulated cellular processes. Indeed, long-term exposure of cells to mobile phone irradiation results in the activation of p38 as well as the ERK (extracellular-signal-regulated kinase) MAPKs. In the present study, we have studied the immediate effect of irradiation on the MAPK cascades, and found that ERKs, but not stress-related MAPKs, are rapidly activated in response to various frequencies and intensities. Using signalling inhibitors, we delineated the mechanism that is involved in this activation. We found that the first step is mediated in the plasma membrane by NADH oxidase, which rapidly generates

ROS (reactive oxygen species). These ROS then directly stimulate MMPs (matrix metalloproteinases) and allow them to cleave and release Hb-EGF [heparin-binding EGF (epidermal growth factor)]. This secreted factor activates the EGF receptor, which in turn further activates the ERK cascade. Thus this study demonstrates for the first time a detailed molecular mechanism by which electromagnetic irradiation from mobile phones induces the activation of the ERK cascade and thereby induces transcription and other cellular processes.

Key words: extracellular-signal-regulated kinase (ERK), heparin-binding epidermal growth factor (Hb-EGF), matrix metalloproteinase (MMP), mobile phone irradiation, NADH oxidase, reactive oxygen species (ROS).

The effect of pulsed electromagnetic fields on the physiologic behaviour of a human astrocytoma cell line

Carlo Aldinucci ^a, Mitri Palmi ^b, Gianpietro Sgaragli ^b, Alberto Benocci ^b,
Antonella Meini ^b, Federica Pessina ^b, Gian Paolo Pessina ^{a,*}

^a *Institute of General Physiology and Nutritional Science, University of Siena, via A. Moro, 53100 Siena, Italy*

^b *Institute of Pharmacological Sciences, University of Siena, via E.S. Piccolomini 170, 53100 Siena, Italy*

Received 13 July 2000; received in revised form 4 October 2000; accepted 10 October 2000

Abstract

We evaluated the effects of 50 Hz pulsed electromagnetic fields (EMFs) with a peak magnetic field of 3 mT on human astrocytoma cells. Our results clearly demonstrate that, after the cells were exposed to EMFs for 24 h, the basal $[Ca^{2+}]_i$ levels increased significantly from 124 ± 51 nM to 200 ± 79 nM. Pretreatment of the cells with 1.2 μ M substance P increased the $[Ca^{2+}]_i$ to 555 ± 278 nM, while EMF exposure caused a significant drop in $[Ca^{2+}]_i$ to 327 ± 146 nM. The overall effect of EMFs probably depends on the prevailing Ca^{2+} conditions of the cells. After exposure, the proliferative responses of both normal and substance P-pretreated cells increased slightly from 1.03 to 1.07 and 1.04 to 1.06, respectively. U-373 MG cells spontaneously released about 10 pg/ml of interleukin-6 which was significantly increased after the addition of substance P. Moreover, immediately after EMF exposure and 24 h thereafter, the interleukin-6 levels were more elevated (about 40%) than in controls. On the whole, our data suggest that, by changing the properties of cell membranes, EMFs can influence Ca^{2+} transport processes and hence Ca^{2+} homeostasis. The increased levels of interleukin-6 after 24 h of EMF exposure may confirm the complex connection between Ca^{2+} levels, substance P and the cytokine network. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Intracellular calcium; Cell proliferation; Substance P; Caffeine; Cytokine; Interleukin-6

Blood-brain barrier permeability in rats exposed to electromagnetic fields used in wireless communication

Bertil R.R. Persson *, Leif G. Salford and Arne Brun

Lund University, S-221 85 Lund, Sweden

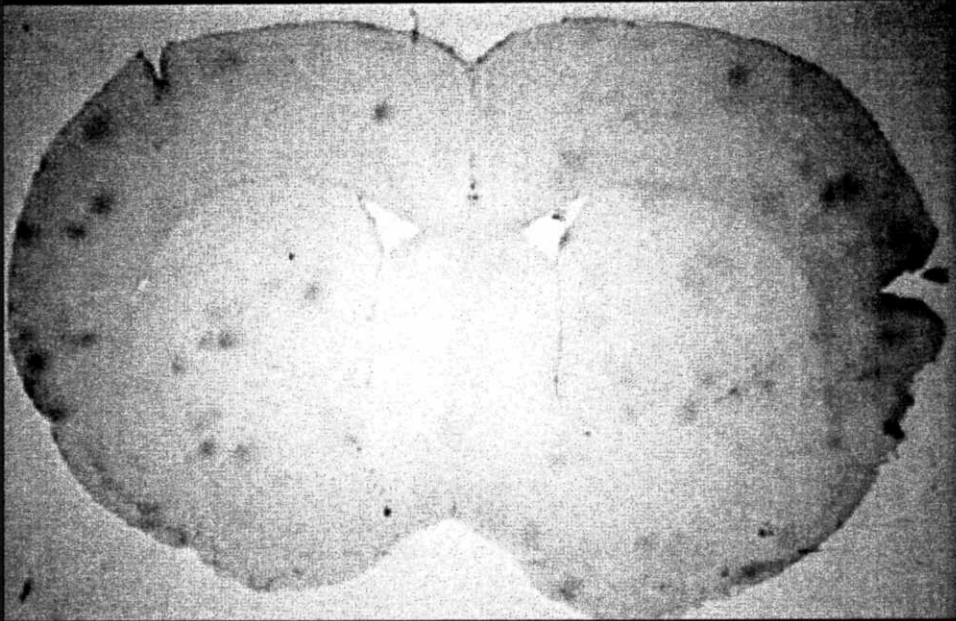
Biological effects of *radio frequency* electromagnetic fields (EMF) on the blood-brain barrier (BBB) have been studied in Fischer 344 rats of both sexes. The rats were not anaesthetised during the exposure. All animals were sacrificed by perfusion-fixation of the brains under chloralhydrate anaesthesia after the exposure. The brains were perfused with saline for 3–4 minutes, and thereafter perfusion fixed with 4% formaldehyde for 5–6 minutes. Whole coronal sections of the brains were dehydrated and embedded in paraffin and sectioned at 5 μm . Albumin and fibrinogen were demonstrated immunohistochemically and classified as normal versus pathological leakage. In the present investigation we exposed male and female Fischer 344 rats in a Transverse Electromagnetic Transmission line chamber to microwaves of 915 MHz as continuous wave (CW) and pulse-modulated with different pulse power and at various time intervals. The CW-pulse power varied from 0.001 W to 10 W and the exposure time from 2 min to 960 min. In each experiment we exposed 4–6 rats with 2–4 controls randomly placed in excited and non-excited TEM-cells respectively. We have in total investigated 630 exposed rats at various modulation frequencies and 372 controls. The frequency of pathological rats is significantly increased ($p < 0.0001$) from 62/372 (ratio: 0.17 ± 0.02) for control rats to 244/630 (ratio: 0.39 ± 0.03) in all exposed rats. Grouping the exposed animals according to the level of specific absorbed energy (J/kg) give significant difference in all levels above 1.5 J/kg. The exposure was 915 MHz microwaves either pulse modulated (PW) at 217 Hz with 0.57 ms pulse width, at 50 Hz with 6.6 ms pulse width or continuous wave (CW). The frequency of pathological rats (0.17) among controls in the various groups is not significantly different. The frequency of pathological rats was 170/481 (0.35 ± 0.03) among rats exposed to pulse modulated (PW) and 74/149 (0.50 ± 0.07) among rats exposed to continuous wave exposure (CW). These results are both highly significantly different to their corresponding controls ($p < 0.0001$) and the frequency of pathological rats after exposure to pulsed radiation (PW) is significantly less ($p < 0.002$) than after exposure to continuous radiation (CW).

Sham exposed rat brain



Normal occurrence of albumin in the meninges

Exposed rat brain, albumin leakage around capillaries



Mobile Phone Emissions and Human Brain Excitability

Florinda Ferreri, MD,^{1,2} Giuseppe Curcio, PhD,^{1,3} Patrizio Pasqualetti, PhD,² Luigi De Gennaro, PhD,³
Rita Fini, Tech,^{1,2} and Paolo Maria Rossini, MD, PhD^{1,2,4}

Objective: To test—via Transcranial Magnetic Stimulation (TMS)—the excitability of each brain hemisphere after ‘real’ or ‘sham’ exposure to the electromagnetic field (EMF) generated by a mobile phone operating in the Global System for Mobile Communication (GSM).

Methods: Fifteen male volunteers attended two experimental sessions, one week apart, in a cross-over, double-blind paradigm. In one session the signal was turned ON (EMF-on, real exposure), in the other it was turned OFF (EMF-off, sham exposure), for 45 minutes. Motor Evoked Potentials (MEPs) were recorded using a paired-pulse paradigm (testing intracortical excitability with 1 to 17 ms interstimulus intervals), both before and at different times after exposure to the EMF. Short Intracortical Inhibition (SICI) and Facilitation (ICF) curves were evaluated both on the exposed and non-exposed hemispheres. Tympanic temperature was collected during each session.

Results: The intracortical excitability curve becomes significantly modified during *real* exposure, with SICI being reduced and ICF enhanced in the *acutely* exposed brain hemisphere as compared to the contralateral, non-exposed hemisphere or to sham exposure. Tympanic temperature showed no significant main effect or interactions.

Interpretation: These results demonstrate that GSM-EMFs modify brain excitability. Possible implications and applications are discussed.

Ann Neurol 2006;60:188–196

Mobile phone affects cerebral blood flow in humans

Sargo Aalto^{1,2}, Christian Haarala^{3,4}, Anna Brück¹, Hannu Sipilä¹, Heikki Hämäläinen^{3,4} and Juha O Rinne¹

Turku PET Centre, University of Turku, Turku, Finland; ²Department of Psychology, Åbo Akademi University, Åbo, Finland; ³Centre for Cognitive Neuroscience, University of Turku, Turku, Finland; ⁴Department of Psychology, University of Turku, Turku, Finland

Mobile phones create a radio-frequency electromagnetic field (EMF) around them when in use, the effects of which on brain physiology in humans are not well known. We studied the effects of a commercial mobile phone on regional cerebral blood flow (rCBF) in healthy humans using positron emission tomography (PET) imaging. Positron emission tomography data was acquired using a double-blind, counterbalanced study design with 12 male subjects performing a computer-controlled verbal working memory task (letter 1-back). Explorative and objective voxel-based statistical analysis revealed that a mobile phone in operation induces a local decrease in rCBF beneath the antenna in the inferior temporal cortex and an increase more distantly in the prefrontal cortex. Our results provide the first evidence, suggesting that the EMF emitted by a commercial mobile phone affects rCBF in humans. These results are consistent with the postulation that EMF induces changes in neuronal activity.

Journal of Cerebral Blood Flow & Metabolism (2006) 26, 885–890. doi:10.1038/sj.jcbfm.9600279; published online 22 February 2006

Paternal Occupational Exposure to Electro-Magnetic Fields as a Risk Factor for Cancer in Children and Young Adults: A Case-Control Study From the North of England

Mark S. Pearce, PhD,^{1*} Donna M. Hammal, MSc,¹ M. Tefvik Dorak, PhD,¹
Richard J.Q. McNally, PhD,^{1,2} and Louise Parker, PhD¹

Background. Numerous studies have implied that paternal occupational exposures, in particular electromagnetic fields (EMF) and ionizing radiation, may be involved in the etiology of childhood cancers. We investigated whether an association exists between paternal occupations at birth involving such exposures and cancer risk in offspring, using data from the Northern Region Young Persons' Malignant Disease Registry (NRYPMR). **Procedure.** Cases ($n = 4,723$) were matched, on sex and year of birth, to controls from two independent sources: (i) all other patients from the NRYPMR with a different cancer, (ii) 100 cancer-free individuals per case from the Cumbrian Births Database. An occupational exposure matrix was used to assign individuals to exposure groups. **Results.** There was an increased risk of leukemia among the offspring of men employed in occupations likely to be associated with EMF or radiation exposures

(OR 1.31, 95% CI 1.02–1.69), particularly in males aged less than 6 years (OR 1.81, 95% CI 1.19–2.75). No significant association was seen in females. Increased risks were also seen for chondrosarcoma (OR 8.7, 95% CI 1.55–49.4) and renal carcinoma (OR 6.75, 95% CI 1.73–26.0). These associations were consistent between control groups and remained after adjustment for socio-economic status. **Conclusions.** This large case-control study identified a significantly increased risk of leukemia among the offspring of men likely to have been occupationally exposed to EMF, with differing associations between males and females. Increased risks of chondrosarcoma and renal carcinoma were also seen, although based on smaller numbers. Further detailed investigations in this area are required to understand this association. *Pediatr Blood Cancer*
© 2006 Wiley-Liss, Inc.

Key words: cancer; electro-magnetic fields; epidemiology; paternal exposures; radiation

Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study

Ashok Agarwal, Ph.D., H.C.L.D.,^a Fnu Deepinder, M.D.,^a Rakesh K. Sharma, Ph.D.,^a
Geetha Ranga, Ph.D.,^b and Jianbo Li, Ph.D.^c

^a Reproductive Research Center, Glickman Urological Institute and Department of Obstetrics-Gynecology, Cleveland Clinic Foundation, Cleveland, Ohio; ^b Karthekeya Medical Research and Diagnostic Center, Mumbai, India; and ^c Department of Quantitative Health, Cleveland Clinic Foundation, Cleveland, Ohio

Objective: To investigate the effect of cell phone use on various markers of semen quality.

Design: Observational study.

Setting: Infertility clinic.

Patient(s): Three hundred sixty-one men undergoing infertility evaluation were divided into four groups according to their active cell phone use: group A: no use; group B: <2 h/day; group C: 2–4 h/day; and group D: >4 h/day.

Intervention(s): None.

Main Outcome Measure(s): Sperm parameters (volume, liquefaction time, pH, viscosity, sperm count, motility, viability, and morphology).

Result(s): The comparisons of mean sperm count, motility, viability, and normal morphology among four different cell phone user groups were statistically significant. Mean sperm motility, viability, and normal morphology were significantly different in cell phone user groups within two sperm count groups. The laboratory values of the above four sperm parameters decreased in all four cell phone user groups as the duration of daily exposure to cell phones increased.

Conclusion(s): Use of cell phones decrease the semen quality in men by decreasing the sperm count, motility, viability, and normal morphology. The decrease in sperm parameters was dependent on the duration of daily exposure to cell phones and independent of the initial semen quality. (Fertil Steril® 2008;89:124–8. ©2008 by American Society for Reproductive Medicine.)

Key Words: Cell phone, electromagnetic radiations, sperm parameters, male infertility



Original article

Biological effects from electromagnetic field exposure and public exposure standards[☆]

Lennart Hardell^{a,*}, Cindy Sage^b

^a *Department of Oncology, University Hospital, SE-701 85 Örebro, Sweden*

^b *Sage Associates, Santa Barbara, CA, USA*

Received 6 December 2007; accepted 12 December 2007

Q1

Abstract

During recent years there has been increasing public concern on potential health risks from power-frequency fields (extremely low frequency electromagnetic fields; ELF) and from radiofrequency/microwave radiation emissions (RF) from wireless communications. Non-thermal biological effects have not been considered for regulation of microwave exposure, although numerous scientific reports indicate such effects. The BioInitiative Report is based on an international research and public policy initiative to give an overview of what is known of biological effects that occur at low-intensity electromagnetic fields (EMFs) exposure. Health endpoints reported to be associated with ELF and/or RF include childhood leukaemia, brain tumours, genotoxic effects, neurological effects and neurodegenerative diseases, immune system deregulation, allergic and inflammatory responses, breast cancer, miscarriage and some cardiovascular effects. The BioInitiative Report concluded that a reasonable suspicion of risk exists based on clear evidence of bioeffects at environmentally relevant levels, which, with prolonged exposures may reasonably be presumed to result in health impacts. Regarding ELF a new lower public safety limit for habitable space adjacent to all new or upgraded power lines and for all other new constructions should be applied. A new lower limit should also be used for existing habitable space for children and/or women who are pregnant. A precautionary limit should be adopted for outdoor, cumulative RF exposure and for cumulative indoor RF fields with considerably lower limits than existing guidelines, see the BioInitiative Report. The current guidelines for the US and European microwave exposure from mobile phones, for the brain are 1.6 W/Kg and 2 W/Kg, respectively. Since use of mobile phones is associated with an increased risk for brain tumour after 10 years, a new biologically based guideline is warranted. Other health impacts associated with exposure to electromagnetic fields not summarized here may be found in the BioInitiative Report at www.bioinitiative.org.

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Keywords: Electromagnetic fields (EMFs); Extremely low frequency electromagnetic fields (ELF); Radiofrequency fields (RF); Carcinogenesis; Public health; Standard setting

06 January 2012

Occup Environ Med 2011;68:631-640

Interphone study

The OR increased with increasing Total Cumulative Specific Energy 7+ years before diagnosis ($p=0.01$; OR 1.91; 95% CI 1.05-3.47)

44 glioma and 135 meningioma in the most exposed area compared to elsewhere: increase ORs for tumors in the most exposed part of the brain in those with 10+ years of mobile phone use (OR 2.8; 95% CI 1.13-6.94)

Risk of brain tumours in relation to estimated RF dose from mobile phones: results from five Interphone countries

E Cardis,¹ B K Armstrong,² J D Bowman,³ G G Giles,^{4,5} M Hours,⁶ D Krewski,⁷ M McBride,⁸ M E Parent,⁹ S Sadetzki,^{10,11} A Woodward,¹² J Brown,² A Chetrit,¹⁰ J Figuerola,¹ C Hoffmann,^{11,13} A Jarus-Hakak,¹⁰ L Montestrucq,⁶ L Nadon,⁹ L Richardson,¹⁴ R Villegas,¹ M Vrijheid¹

ORIGINAL ARTICLE

Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations

H-P Hutter, H Moshhammer, P Wallner, M Kundi

Occup Environ Med 2006;**63**:307–313. doi: 10.1136/oem.2005.020784

See end of article for
authors' affiliations

Correspondence to:
Dr H-P Hutter, Institute of
Environmental Health,
Medical University of
Vienna, Kinderspitalgasse
15, A-1095 Vienna,
Austria; hans-peter.
hutter@univie.ac.at

Accepted
11 November 2005

Background: The erection of mobile telephone base stations in inhabited areas has raised concerns about possible health effects caused by emitted microwaves.

Methods: In a cross-sectional study of randomly selected inhabitants living in urban and rural areas for more than one year near to 10 selected base stations, 365 subjects were investigated. Several cognitive tests were performed, and wellbeing and sleep quality were assessed. Field strength of high-frequency electromagnetic fields (HF-EMF) was measured in the bedrooms of 336 households.

Results: Total HF-EMF and exposure related to mobile telecommunication were far below recommended levels (max. 4.1 mW/m²). Distance from antennae was 24–600 m in the rural area and 20–250 m in the urban area. Average power density was slightly higher in the rural area (0.05 mW/m²) than in the urban area (0.02 mW/m²). Despite the influence of confounding variables, including fear of adverse effects from exposure to HF-EMF from the base station, there was a significant relation of some symptoms to measured power density; this was highest for headaches. Perceptual speed increased, while accuracy decreased insignificantly with increasing exposure levels. There was no significant effect on sleep quality.

Conclusion: Despite very low exposure to HF-EMF, effects on wellbeing and performance cannot be ruled out, as shown by recently obtained experimental results; however, mechanisms of action at these low levels are unknown.

Effects on biological systems

- Molecular level
- Cellular level
- Animal experiments
- Experiments on humans
- Case/control studies
- Epidemiologic research
- Meta-analysis
- Opinion, Discussion forum

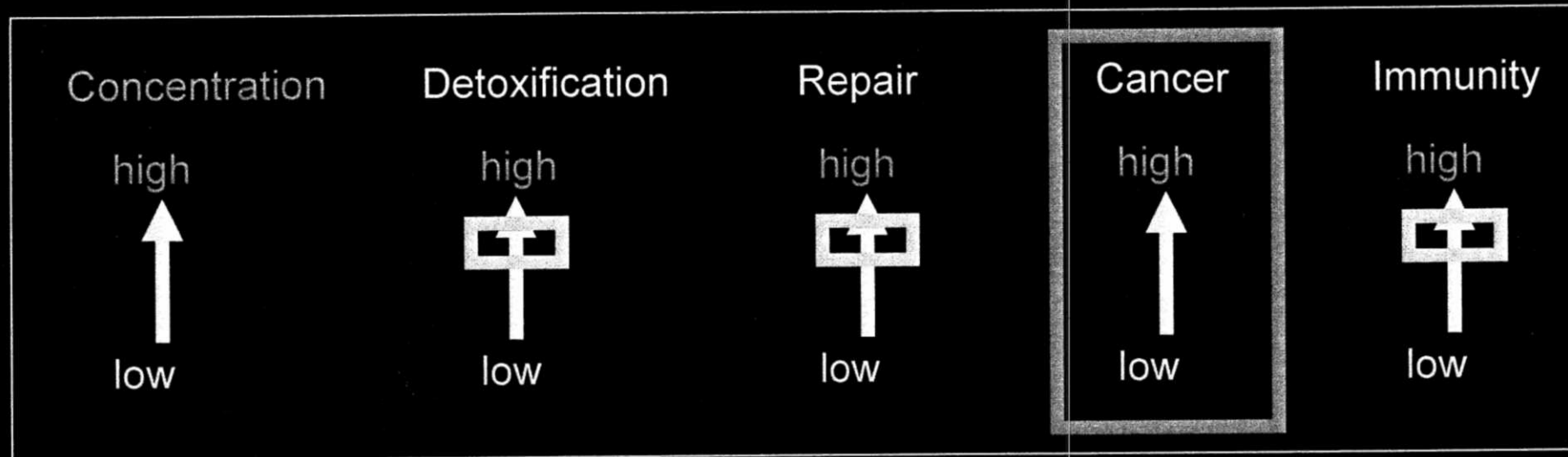
•Signal transduction
•Free radicals
•Calcium
•Membrane
•DNA, RNA

Effect



Disease

- polygenetic system; monogenetic subgroups
- Multifactorial
- The variable = continu – discrete
- Different thresholds
- Cumulative effects
- Effects over time



Etiologic heterogeneity + polygenetic system -> health issue 1
 monogenetic subgroups -> health issue 2
 health issue 3
 health issue x

To be measured with accurate instruments



CONCLUSION IARC

		EVIDENCE IN EXPERIMENTAL ANIMALS			
		Sufficient	Limited	Inadequate	ESLC
Evidence In Humans	Sufficient	Group 2A	Group 1		
	Limited	Group 2B	Group 2B		
	Inadequate			Group 3	
	ESLC		Group 3		Group 4

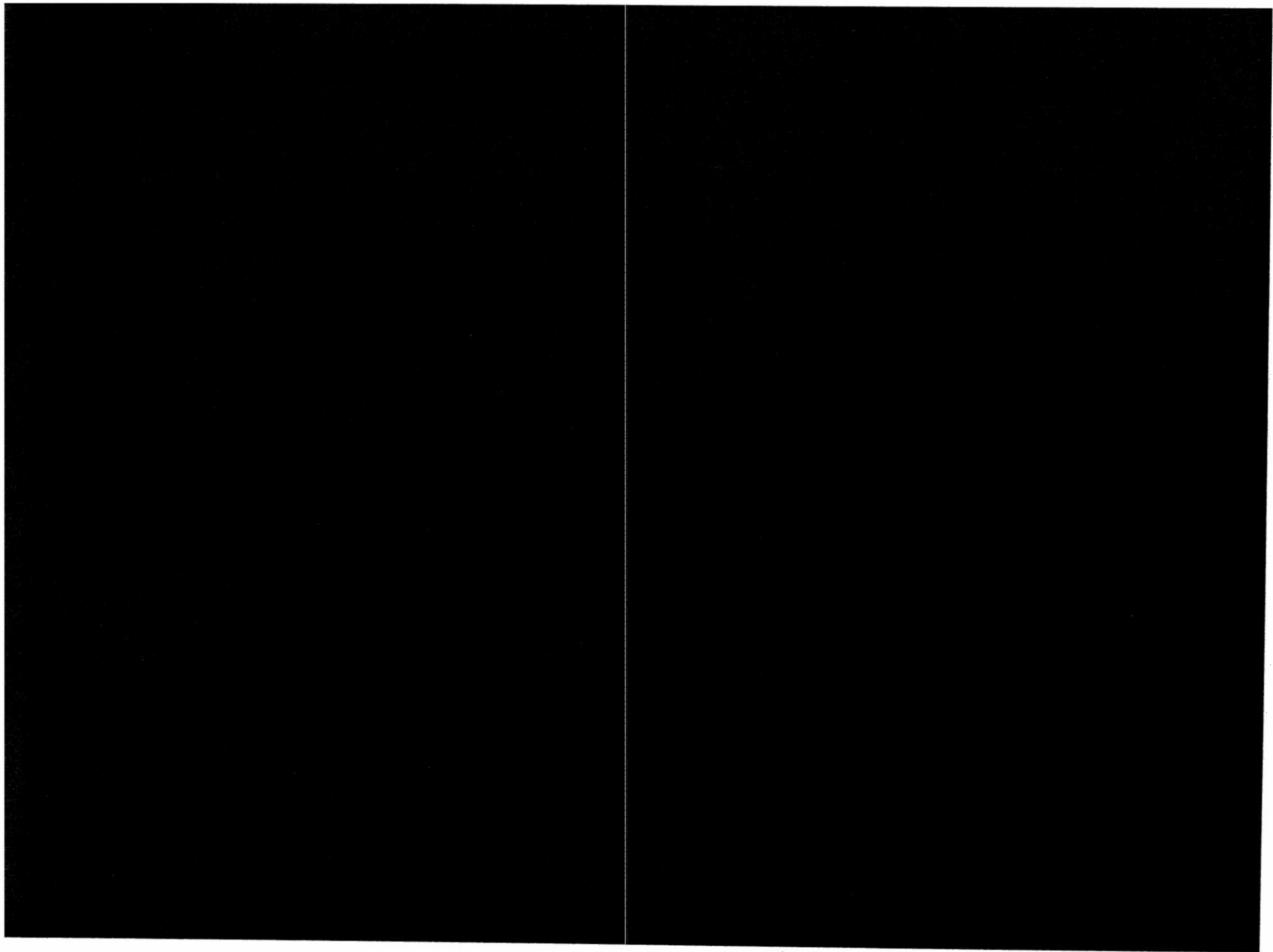
Mechanistic data can be pivotable when the human data are not conclusive

Uncertainties in the calculations

Karakteristieken onzekerheid	Categorieën
Locatie: de locatie in het rekenmodel waar de onzekerheid tot uitdrukking komt	Context: de grenzen van het rekenmodel, gebaseerd op keuzen betreffende systeemgrenzen en -definities
	Model structuur: de structuur en vorm van de relaties binnen de modelvariabelen die het systeem beschrijven
	Parameters: constanten in functies die de relaties in het rekenmodel bepalen
	Input data: input data sets in het rekenmodel
Aard: de onderliggende oorzaak van de onzekerheid	Epistemisch: onzekerheid door onvolledige kennis
	Ontisch: onzekerheid door de intrinsieke eigenschappen van het systeem
Range: een kwantitatieve schatting van de onzekerheid	Statistisch: mogelijke uitkomsten gerelateerd aan waarschijnlijkheden
	Scenario: een set van mogelijke uitkomsten (paden)
Onwetendheid: onzekere uitkomsten, onzekere waarschijnlijkheden – het is bekend dat er onzekerheden zijn, maar er kan geen schatting gegeven worden van de grootte ervan	
Methodologische onbetrouwbaarheid: onzekerheid betreffende de methodologische kwaliteit binnen de input data van de rekenketen, en de berekeningen binnen de rekenketen	
Waarde-diversiteit tussen onderzoekers: Mogelijke waardegeladenheid van aannames die (tot op zekere hoogte) arbitraire beslissingen bij onderzoekers met zich meebrengen	

Tabel 1.1: Typologie van onzekerheid. Bron: Knol *et al.* 2009, aangepast

1.1 Onzekerheidstypologie: uitwerking per locatie



Recommendation / Reflection

- Precautionary Principle
 - ALARA
 - PRUDENT AVOIDANCE
- Sustainability of innovative technology
- Standards are influenced by Needs
- Community problem
 - Trend: reversible; controllable ?
 - Jouth as victim
 - Addiction
 - Individuals at the end of the spectrum with hypersensitivity : *do we take care of them ?*
- Welfare *versus* MILIEU *versus* ECONOMICS

