

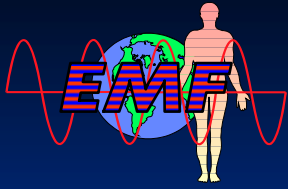
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Istanbul, June 2004



WORKSHOP REPORTS: WEAK ELECTRIC FIELD AND THERMAL EFFECTS

Richard Saunders

Radiation and Environmental Health
World Health Organization
Geneva, Switzerland



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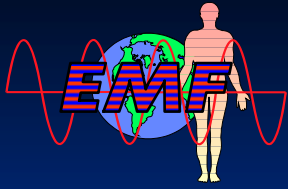


Weak ELF Electric Field Effects in the Body. NRPB, Chilton, 24-25 March 2003

Radiation Protection Dosimetry,
Vol. 106(4), 2003

Adverse Temperature Levels in Humans. WHO, Geneva, 21-22 March 2002

International Journal of Hyperthermia,
Vol. 19(3), 2003



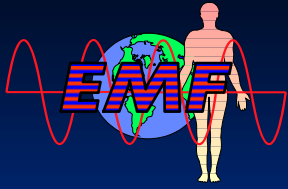
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Developmental Effects of Induced Electric Fields or Heat

One paper in each workshop addressed the sensitivity of developing animals to:

- Perturbation of the endogenous electric fields that occur in the embryo/fetus, as might result from ELF exposure
- Increased maternal body temperature, and/or embryo/fetal temperature, as might result from during RF exposure



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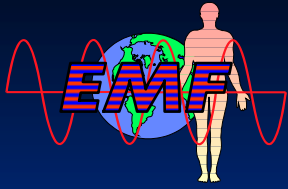


Endogenous Electric Fields in Embryos During Development, Regeneration and Wound Healing

Richard Nuccitelli

Essential points are:

- Electrical signaling ubiquitous in cellular and organ functions
- Transepithelial electric potentials (TEPs), which result from the asymmetric distribution of ion channels, have a role in normal development
- The paper examined the effect of perturbing these electric fields on the developmental process



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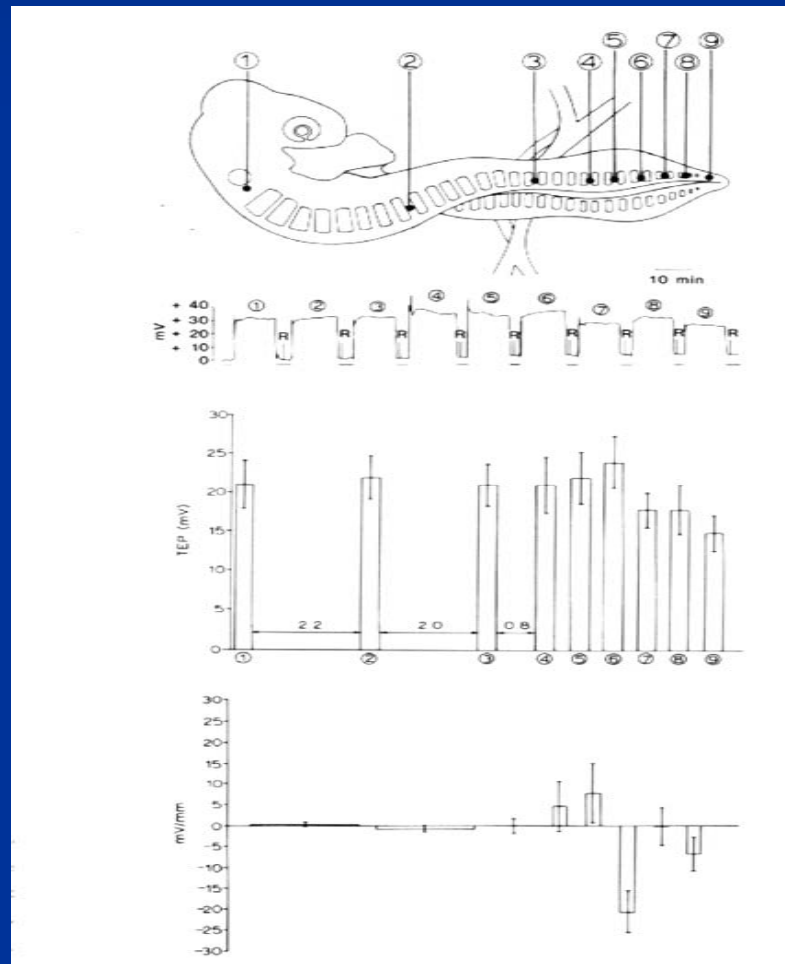
Transepithelial Potentials (TEPs) In Chick Embryos

Chick Embryo

Voltage

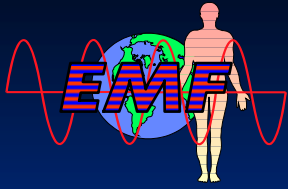
Transepithelial
potential

Potential
gradient



Hotary and Robinson,
Dev. Biol. 140:149
(1990)

Steep voltage gradient
observed between
positions 6 and 7



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Experimental Modification of TEPs

Chick Embryos:

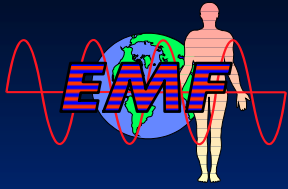
- Normal transepithelial DC potentials of $5 - 20 \text{ mV mm}^{-1}$
- Perturbation by 'conductive shunt' results in abnormalities in the tail region

Hotary and Robinson, 1990

Amphibian (Axolotl) embryo:

- Normal transepithelial DC potentials of $10 - 20 \text{ mV mm}^{-1}$
- Developmental abnormalities induced by applied DC field of $25-75 \text{ mV mm}^{-1}$

Metcalf *et al*, 1994



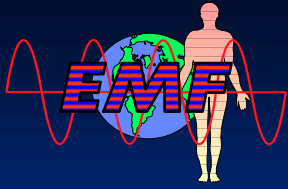
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Endogenous Electric Fields and Development

Weak Electric Fields Workshop Conclusions:

- Endogenous DC electric potentials of $\sim 10\text{-}20 \text{ mV mm}^{-1}$ play a role in normal development
- Significant field perturbations can result in developmental abnormalities
- The effects of AC (ELF) electric fields have not been extensively investigated
- However, thresholds likely to be significantly above current guidance levels



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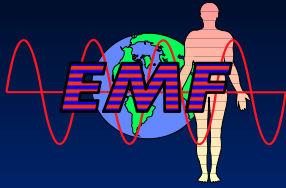


Effects of Heat on Embryos and Fetuses

Edwards MJ, Saunders RD and Shiota K

Essential points are:

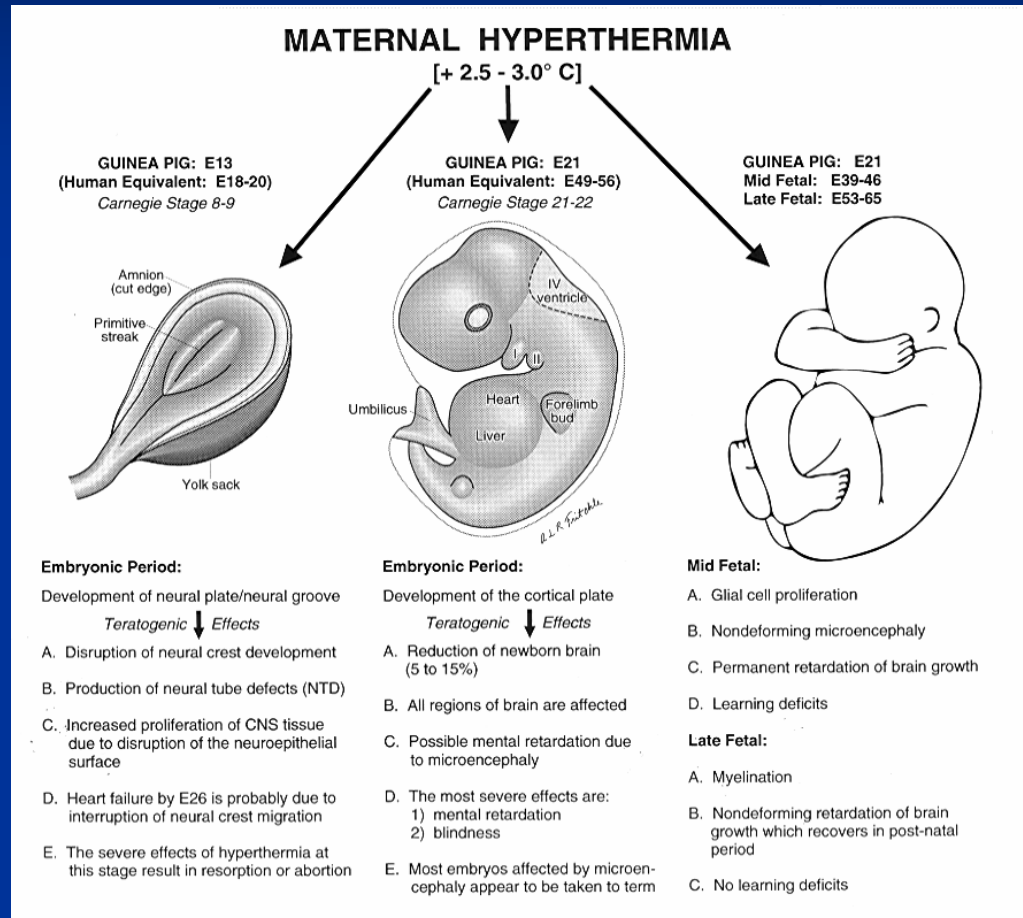
- Pathogenic mechanisms of heat include proliferating cell death and disturbed cell migration
- Thresholds are tissue and developmental-stage specific
- The paper examined the known effects of heat on embryo and fetal development

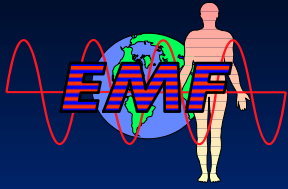


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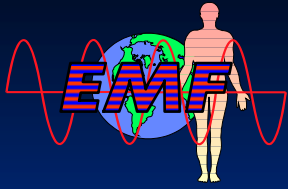


The Central Nervous System

Particularly vulnerable because:

- Limited number and restricted physical location of cohorts of proliferating cells.
- Extreme precision required for complex neuronal architecture.

Kimler, 1998



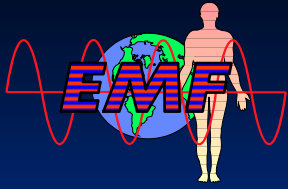
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Neurulation

The neural plate closes to form the neural tube, which gives rise to the brain and spinal cord

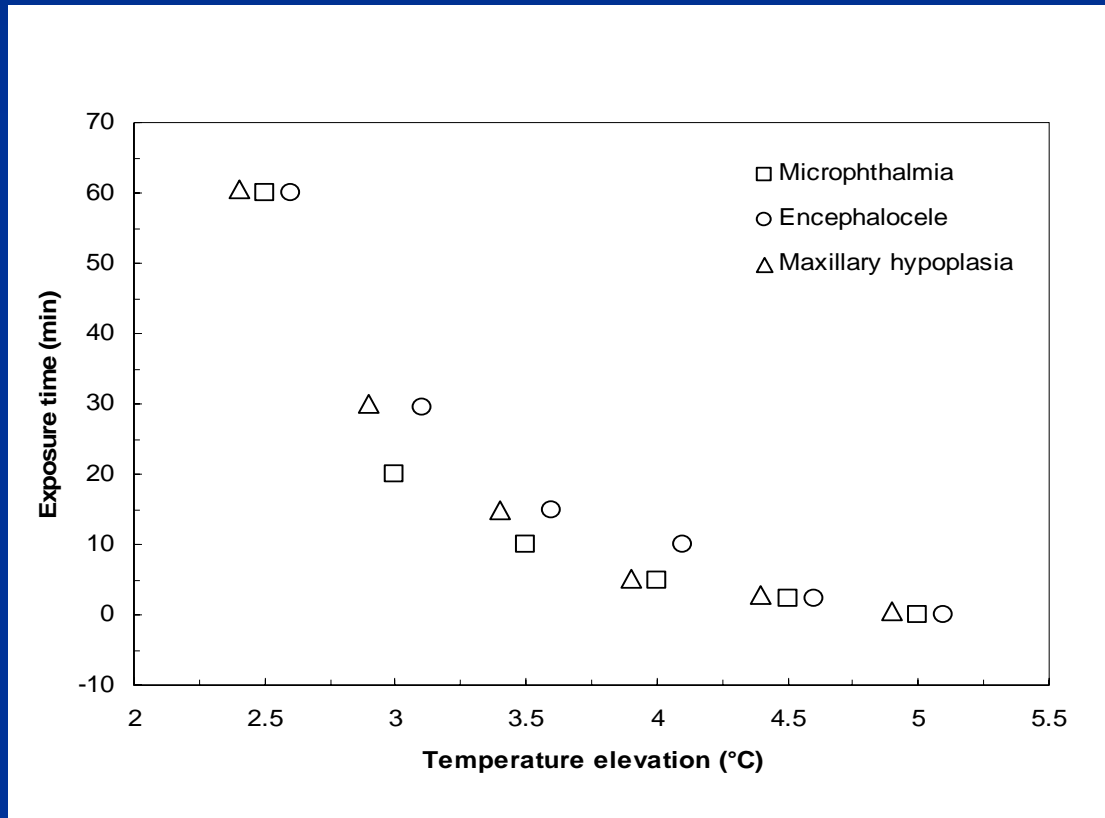
- Elevated maternal temperatures induce cranio-facial abnormalities such as neural tube defects (NTDs) in animals; similar effects seen humans



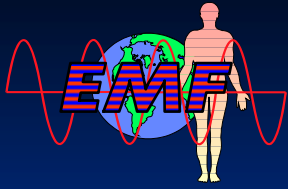
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Cranio-Facial Defects Induced During Neurulation



Germain *et al*, 1985



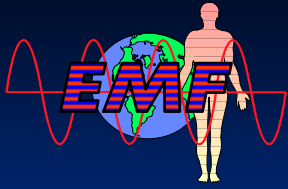
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Early Neurogenesis

Beginning of the formation of the cortex

- The most sensitive endpoint in animals studies is the induction of microencephaly (small head size)
- Thresholds are around a **peak** rise in maternal body temperature of 2.0– 2.5°C during a 1 h heat exposure



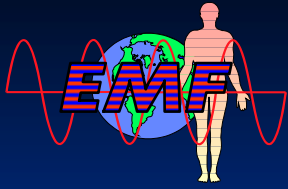
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Corticogenesis

Corticogenesis is a potentially more vulnerable period of brain development, but is under-explored in this context:

- Neuronal progenitor cells migrate **mm-cm** along a 'scaffolding' of radial glial cells.
- Synaptic connections are formed as they pass through other cortical cell layers



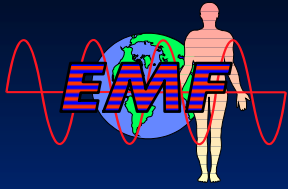
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Corticogenesis

Experimentally:

- Decreased cortical cell proliferation and migration, reduced cortex thickness after $\sim 4.5^{\circ}\text{C}$ elevation for 6-7 minutes (Hinoue *et al*, 2001)
- Reduced multiple T-maze and shuttle-box performance after similar exposure once or twice per day (Shiota and Kayamura, 1989)



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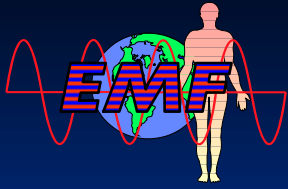


Human Studies

Studies based on the effects of fever, or less frequently on exposure to hot tubs, saunas or heavy work in the heat, resulting in maternal temperatures $> 38.9^{\circ}\text{C}$; > 24 h

Increased frequency NTDs: (eg Shiota *et al*, 1982; Milunsky *et al*, 1992; Chambers *et al*, 1998).

Mental deficiency present in (all) 28 cases following fever: (Pleet *et al*, 1981)



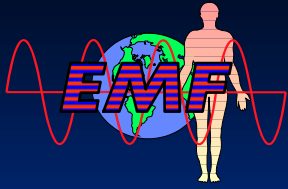
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Raised Maternal Temperature and Development

Conclusions:

- Raised maternal temperature is known to be teratogenic in animals and may well be in humans
- The central nervous system is the most sensitive organ
- There are some experimental uncertainties to resolve
- However, thresholds likely to be significantly above current guidance levels



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OVERALL CONCLUSIONS

Generally, conventional developmental biology and teratology studies indicate that:

- Thresholds for perturbing effects of induced e-fields or heat likely to be well above guidance values
- Despite experimental uncertainties