

Childhood Brain Tumours: Epidemiology and Risk factors

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Sensitivity of Children to EMF exposures
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- Descriptive epidemiology of childhood Central Nervous System (CNS) tumours
- Identify differences between cancers and CNS tumours in adults and children
- Risk factors
- Considerations for studying children and mobile phone use

Childhood CNS tumours: basic facts 1

- Second most common childhood malignancy approximately 20% of all childhood cancers
- Most common solid tumour
- Incidence rate 3.9 per 100,000 pyrs in 0-19 yr olds (CBTRUS 2003/4, includes both malignant and benign)
- New cases/yr in US 2,330 under 15 years

Childhood CNS tumours: Basic facts 2

- Male excess M:F ratio 1.2:1
- Ethnic origin white populations may be at higher risk than non-white
- Geography incidence in Africa 11 /million
Japan, US, Europe 20-30 /million
- Social class higher risk possibly associated with higher social class

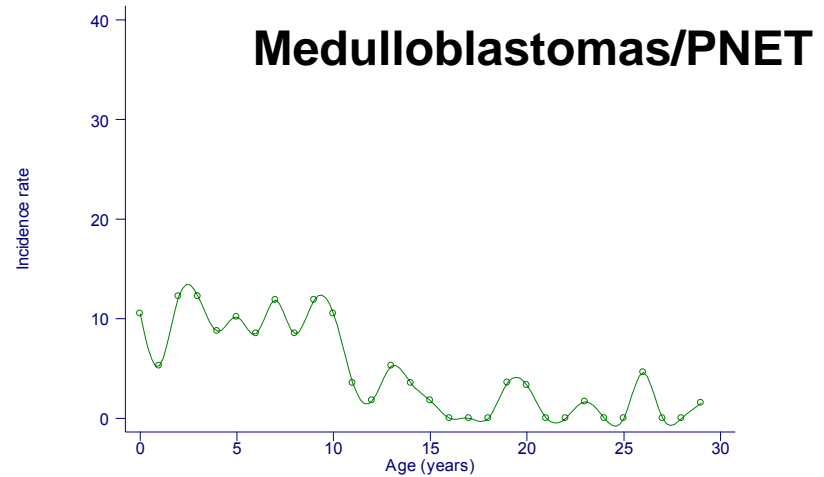
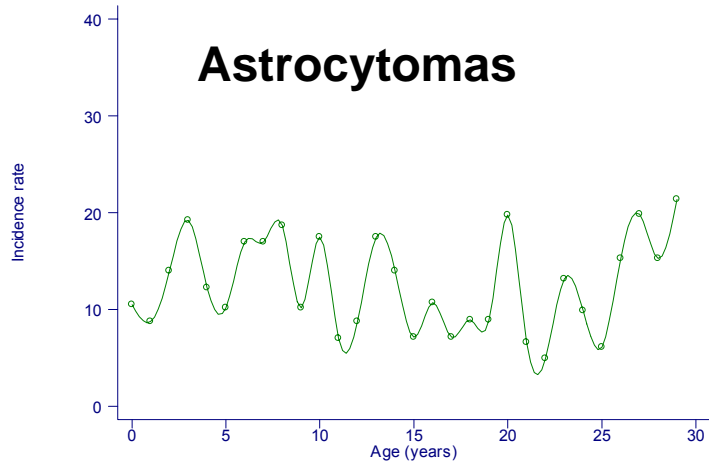
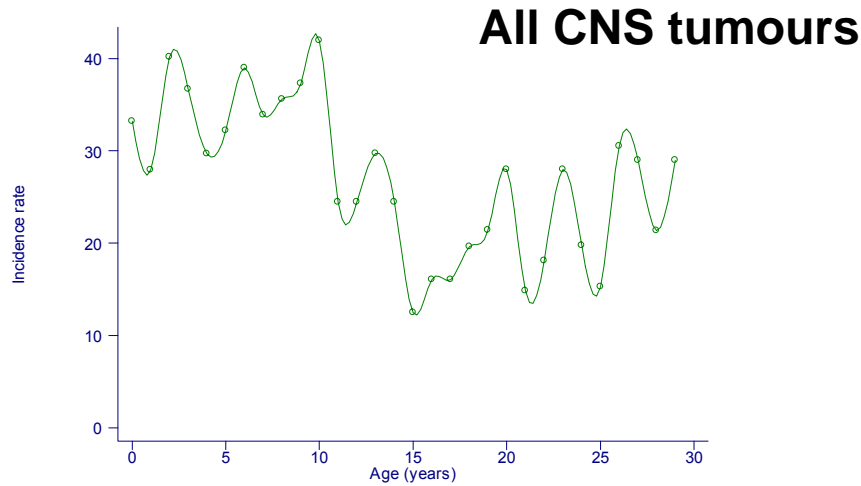
Classification of childhood CNS tumours

International Classification of Childhood Cancers (ICCC) Kramarova IARC no 29. 1996

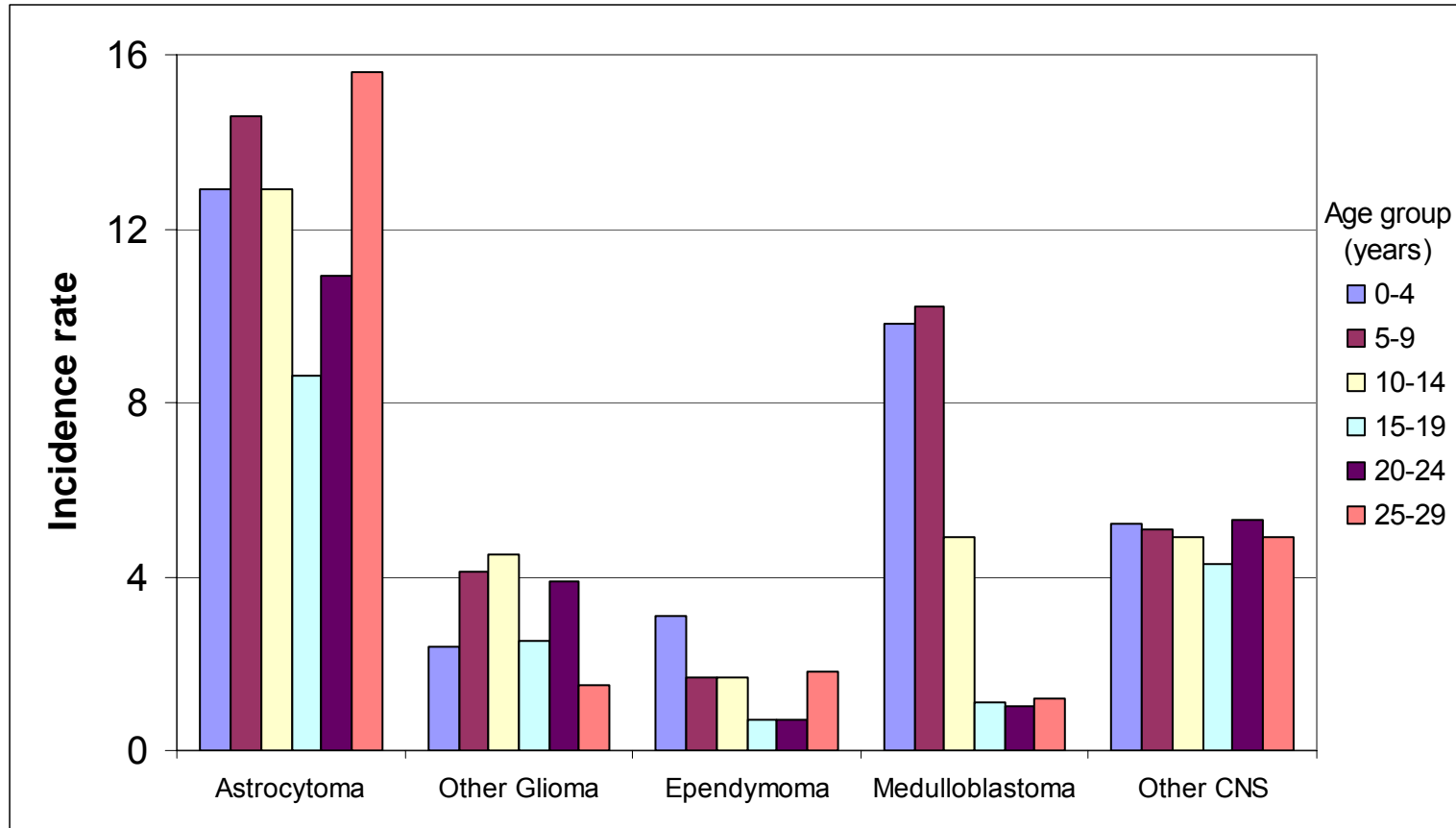
Group III CNS and miscellaneous intracranial neoplasms

Distinct histological subtypes	%
a Ependymomas	10
b Astrocytomas	40-50
c Primitive Neuroectodermal Tumours (PNET) (medulloblastomas)	25
d Other gliomas	10
ef Other specified and unspecified CNS	8-13

Age specific incidence rates for CNS tumours (0-29 years) in Yorkshire 1990-2001



Incidence rates (per million pyrs) for CNS tumours (0-29 years) 1990-2001 in Yorkshire



Time trends in childhood CNS tumours

- Is the incidence rising??
- Evidence suggests approximate 2-3% rise from 1970s
- Increases vary by age, sex, tumour type and ethnic group
- Debate continues over whether increases result from improved detection and registration

Cancers in adults and children: differences

1. Occur in tissues with different foetal origins

Adults: carcinomas which develop in **epithelial** or 'covering' tissues

Children: **embryonal** origin – mesodermal (non-epithelial) tissues

2. Different disease classification scheme

Adults: classified by **topography** i.e. anatomical site not histological subtype e.g. lung

Children: classified by **morphology** i.e. histological picture e.g. germ cell tumour

CNS tumours show differences between adults and children

1. Different tumour types predominate

Adults: fewer Primitive Neuroectodermal Tumours (PNET) (medulloblastoma)

Children: fewer meningiomas (tumours of brain 'covering', the meninges)

2. Astrocytomas/gliomas different histologies

Adults: gliomas (44% of all CNS tumours)

Children: juvenile pilocytic astrocytomas (19%)

CNS tumours show differences between adults and children

3. Proportion of all cancers

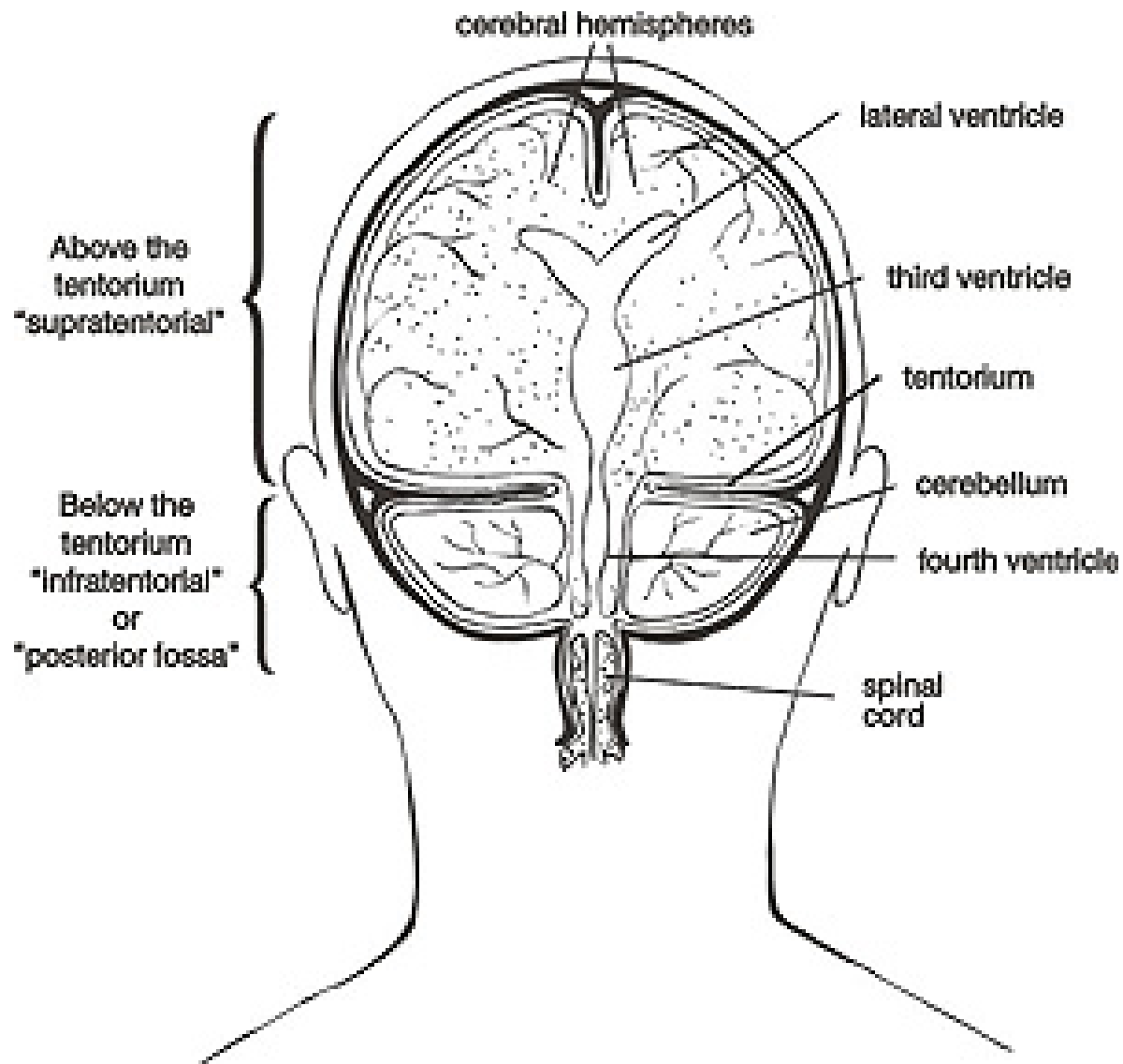
Adults: less than 2% of all cancers

Children: 20% of all cancers under 15 years

4. Vary by anatomical site

Adults: more **above** tentorium

Children: more commonly **below** tentorium

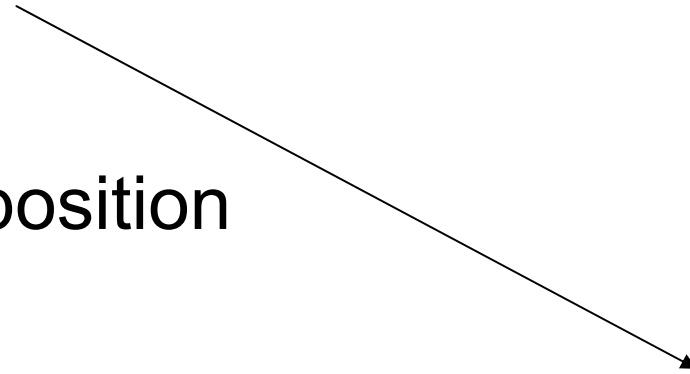


Risk factors for childhood CNS tumours

Causes largely unknown



Genetic predisposition



Environmental influences

Genetic predisposition

Genetic syndromes	e.g neurofibromatosis
Familial cancers	inconsistent evidence (?parent/sib)
Second primary tumours	little evidence following untreated tumours

Genetic predisposition

Predisposing genes	NF1, NF2, TP53
Polymorphisms	oxidation, detoxification, DNA repair, immune functioning yet to be studied in large samples
Estimates	5% childhood CNS tumours

Environmental risk factors: considerations

Time window of exposure

Preconception – mothers/fathers

In-utero – mothers

Postnatal – child (mothers/fathers)

Type of study

Biases

Confounding

Exposure estimates

Measured

Reported

Environmental risk factors

- Ionising radiation
- Chemicals
- Immune factors
- ELF - EMF

Ionising radiation

Preconception No consistent association apparent but studies limited which identify CNS tumours

In-utero For abdominal Xrays early studies in 1970s showed raised risks but no associations more recently

Postnatal **Increased risk with high therapeutic doses e.g. following radiotherapy for a first cancer, tinea capitis treatment**

Little evidence for other X ray exposures
Inconsistent evidence for dental Xrays

Chemicals: 1

- N-nitroso compounds are mutagenic and transplacental neurocarcinogens in animal models.
- Human exposure from diet, drugs, beer, smoking.....
- Raised risk for maternal cured meat consumption during pregnancy consistent association
- Protective effect of vitamin consumption during pregnancy

Chemicals: 2

- No associations with maternal smoking
- N nitroso hypothesis not consistently supported
- Extensive list of other associations observed but results are inconsistent

e.g. some paternal occupations
residential pesticides

Immune factors: 1

- Viruses induce brain tumours in animal models; little support for this occurring in humans.
- Atopic diseases, markers of immune dysfunction are 'protective' for adult gliomas; not been investigated in children.

Immune factors: 2

- Clustering, seasonality of diagnosis, population mixing indicate an infectious aetiology (UK studies)
- Further investigations may be fruitful

ELF EMF (30-300Hz, 50/60 Hz)

NRPB 2004

.....overall evidence for adverse effects of EMFs on health at levels of exposure experienced by the general public is weak. The least weak evidence is for the exposure of children to power frequency magnetic fields and childhood leukaemia.

- Residential exposure
- Excess risk above $0.4\mu\text{T}$ / $0.3\mu\text{T}$ (pooled analyses)

ELF EMF (50/60 Hz)

- Childhood CNS tumours: fewer studies
- Generally combine all subtypes
- Early studies in the Nordic countries and USA found some positive associations
- More recent investigations have not confirmed earlier findings

ELF EMF (50/60 Hz)

Recent studies showing no associations

UK Children's Cancer Study (1999)	household measurements CNS cases n=387
UK Children's Cancer Study (2000)	proximity to power lines CNS cases n=614
German study (Schuz et al 2001)	household measurements CNS cases n=62

Overall size/power lower than leukaemia BUT
Numbers of cases highly exposed ($\geq 0.4\mu\text{T}$) similar

ELF EMF (30-300Hz, 50/60 Hz)

NRPB 2004

.....overall EVIDENCE for excess cancer risks
(including CNS tumours) in children and adults
as a result of exposure to ELF EMF is
INADEQUATE

Extension of evidence base required

?pooled analysis

Mobile phone use and child health

Currently no published studies on children

Adult studies

- On balance mobile phone use currently does not indicate increased risk for CNS tumours
- Acoustic neuromas, rare benign tumour of acoustic nerve. No evidence from 'small studies' of any increased risk

Mobile phone use and child CNS tumours

Considerations for the future: 1

- Clear definition of disease: Biological diversity
- Age of exposure: latency for tumour development unclear
- Could exposure in childhood increase risks in later life?
- Rarely occur in the population: study size an issue

Mobile phone use and child CNS tumours

Considerations for the future: 2

Time period of exposure: preconception, in-utero,
POSTNATAL

Type of study: case control, cohort studies
population studies

- Case control retrospective studies of children extended to young adults to capture any effect
- Biases in control group
- Unmeasured confounding

Mobile phone use and child CNS tumours

Considerations for the future: 3

Cohort studies: very large base populations required
could look at other health outcomes

Incidence studies: correlate patterns of use in children with changing patterns of CNS cancers
e.g CNS tumours or acoustic neuromas
appearing at younger ages

- Timescale extensive
- Registration of CNS tumours not universally of high quality or timely

Mobile phone use and child CNS tumours

Considerations for the future: 4

Exposure estimates: informed by current studies
e.g INTERPHONE study

INTERPHONE Study

- Large international case control study (13 countries)
- Focussing on relating reported phone use to good exposure estimates
- Power output related to frequency of use, make and model of phone, location of use (urban/rural)

Future studies will need to be
carefully planned!