Could a prenatal virus infection promote the initial genetic lesion in the development of Acute Lymphoblastic Leukaemia in children ?

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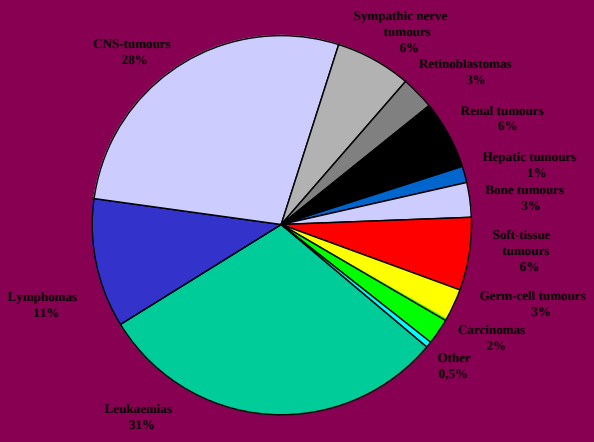
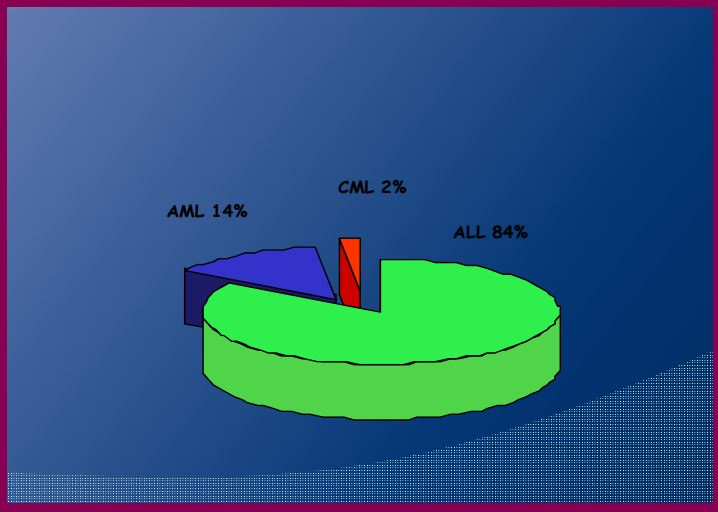
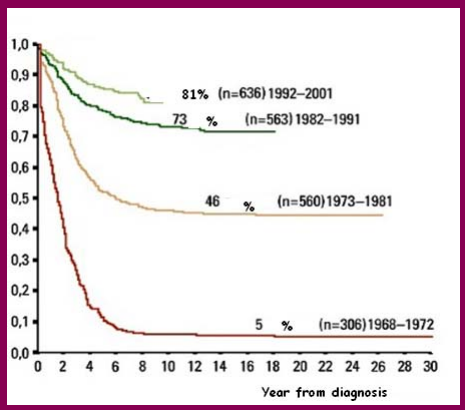
Incidence of childhood cancer



Childhood leukaemia



5-year survival



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……..better survival

- **Correct diagnosis**
- More intensive treatment

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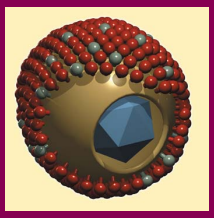
Leukaemic clones

- High hyperdiploidy
- **TEL/AML fusion**

- **IGH or TCR clonotypic rearrangements**

- Philadelphia chromosome positive ALLs
- Hypodiploidy
- **MLL-rearranged ALLs**

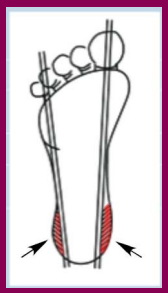
Virus infection in utero

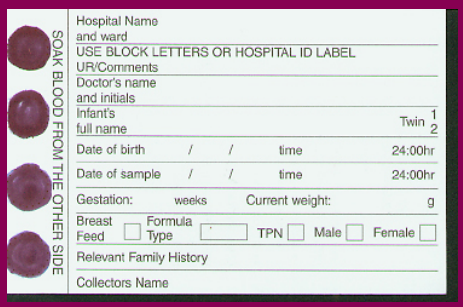


- Primary infection
- Reactivation

- Cross placenta
- "Limited" oncogen potential
- Induce genomic instability
- Specific effect on B-lymphocytes
- Asymtomatic primar inf.
- Not causing severe fetal abnormalities

Guthrie cards preserve a sample of nucleated cell DNA near birth





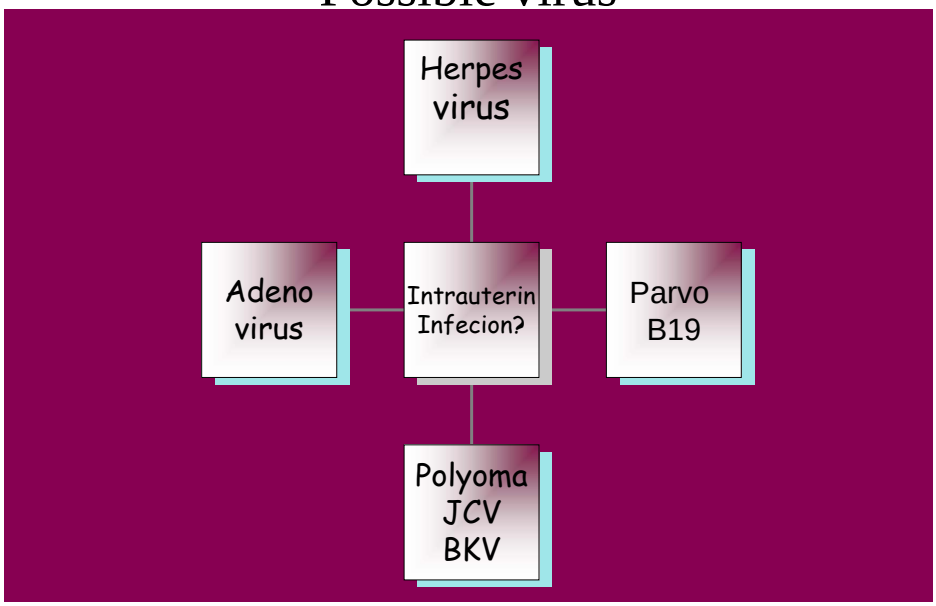
Material and patients

- Pilot study
- 417 Guhtrie cards from children with ALL 1992-2006
- 834 controls (2 cards from the patient)
- Clinical data from NOPHO registry

Methods

- Four spots, 3 mm in diameter were punched out from each Guthrie card=12uL blood
  → 4 spot contains approximately 12 uL blood, and at least 180.000 leukocytes and app. 120.000 lymphocytes
- DNA was extracted using "Minimal Essential Medium" [MEM] method
- TaqMan real-time PCR with primers and probe for human albumin

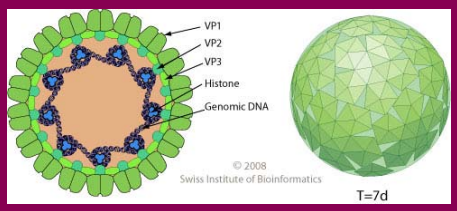
Possible virus



Five human Polyomaviruses

- **BKV 1971**
- **JCV 1971**
- KIPyV 2007
- WUPyV 2007
- MCPyV 2008

- Double-stranded DNA



Considerations of a possible viral aetiologi

- Clusters of childhood ALL
- ALL varies worldvide
- Potential tumour viruses
- 15-20% of the world wode cancer burden is caused by a virus
- Leukemia in cats are caused by a feline virus

Acknowledgements

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Thank you for your attention!