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CC/05/7

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Expert opinion on trends in Childhood Cancer Incidence

1. At the last meeting, Members discussed an overview paper on childhood cancer which identified 4 types of childhood cancer which appeared to be increasing in incidence: acute lymphocytic leukaemia (ALL); germ cell tumours (GCT), CNS tumours and neuroblastomas (NBT). On this basis, it was proposed that these cancer types should be considered further, with a view to determining whether they have chemical aetiologies.
2. Members noted that, although the data presented suggested an increasing trend, part or all of this might be accounted for by better data acquisition or improved diagnostic techniques. It was suggested that independent experts be contacted for views on this issue, in particular (i) whether there was an increase in CNS tumour incidence and (ii) for a definitive statement on whether childhood ALL was increasing in the UK.
3. The following groups/individuals were contacted:
 - UK Childhood Cancer Research Group, University of Oxford (UKCCRG) (Dr Mike Murphy)
 - Newcastle Childhood Cancer Group (Professor Alan Craft and Dr Louise Parker)
 - Dr Colin Smith, Paediatric Neuropathologist, Western General Hospital, Edinburgh
4. The views of these groups/individuals are given in Annex 1 and summarised below.
5. **ALL.** The majority view was that there was an increase in ALL incidence and that this is, at least in part, real. The UKCCRG data show an upward trend of 0.7% per year between 1974 and 1998. The Newcastle group commented that this was probably due to the change in the pattern of antigenic exposure *in utero* and in early life in relation to immunological competence and that chemical pollution probably does not play a significant part.
6. **CNS tumours.** The majority view is that there is an upward trend in the incidence of childhood CNS tumours (mainly due to an increase in astrocytoma, which shows an upward trend of 2.2% per year between 1974 to 1998) but that it is not clear whether the upward trend is real or due to better diagnosis.
7. **Germ cell tumours.** The UKCCRG data indicate that there has been an increase since 1974-78 (when the register began) but this mainly occurred before

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1984-88. Professor Craft agreed that these were definitely increasing in incidence and that the incidence is real. However, Dr Parker considered that there was no increase in the under 14s.

8. Neuroblastomas.

The UKCCRG indicates an upward trend of 1.4% per year between 1974 and 1998. Professor Stott agreed that there is an increase but thought that this was probably largely in benign tumours, under 1 year of age, and due to better diagnosis.

9. Members will wish to note the data and opinions received on trends in childhood cancer incidence. Do Members have any comments?

Secretariat
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Annex 1 to CC/05/7

1. From Dr Mike Murphy, UKCCRG:

“Our most recent publications containing material and comment relating to these questions are the Cancer Research UK Cancer Stats Monograph Chapter 9 (2004), the ACCIS publication (Lancet 11/12/04, about European-wide trends) and a poster/oral presentation at the SIOP conference in Norway, September 2004 (attached).

As you will see in the NRCT there is a significant upward trend (average annual change about +1.1% in Britain during 1974-98) in the incidence of childhood CNS tumours, which is mainly due to an increase in astrocytoma. We don't know the extent to which this is attributable to increased risk, better diagnosis, earlier diagnosis or improved registration. The subject is controversial. As your report points out data from the USA were found to be consistent with an increase from a lower to a higher constant rate around the time MRI scanning became widely available. The trends found in the Manchester Children's Tumour Registry were not thought to be attributable entirely to improved diagnosis and registration (McNally *et al*, Cancer 2001;92(7):1967-76) again as you note in your report.

There is a similar significant upward trend in the incidence of childhood ALL (average annual change about +0.7% in Britain during 1974-98). We can't exclude some (important) contribution from improved quality and completeness of registration, but we believe that there has been a real increase also. The balance presently is indeterminate.

We are investigating these questions, and plan to analyse formally the possible contribution to apparent increases in incidence of many childhood cancers, of improved registration across the entire period covered by NRCT (1962 to present). This is likely to form the core of a member of CCRG's intended DPhil thesis.

Occasionally, on a localised basis, cases of childhood cancer of which we were unaware at the time, are brought to our attention. We have checked the completeness of registration of the NRCT, using the variety of different methods which may be relevant, at a number of points in time when the opportunities presented themselves. The assumptions underlying the use of these methods are usually quite strong, but a high degree of completeness has been consistently indicated. The most recent completed example of this point-in-time approach was against the roster of cases independently assembled for the UK Childhood Cancer (case-control) Study, conducted across England, Wales and Scotland again suggesting a high degree of completeness of the NRCT against this source.

These comparative results using different methods are reassuring about NRCT registration efficiency at a point-in-time, but because on each occasion the factors influencing registration might be affecting both the NRCT data and the method of comparison (i.e. a lack of independence), we cannot, at present, assert that trends in registration faithfully represent trends in incidence.

2. From Dr Colin Smith, Edinburgh (by phone):

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It is not difficult to do a trend analysis on cancer rates, most centres have data on this. The commonest childhood cancers he sees are medulloblastomas. In his view these are no more common now than 10 years ago – if anything, he sees less. Overall, he did not think that childhood CNS tumours were increasing in incidence.

3. **Professor Alan Craft, Newcastle**

My immediate response is ALL is increasing but this is almost certainly due to increasing cleanliness and sophistication of society. There is a direct correlation between a countries level of economic development and its rate of ALL.

There is a biological explanation for this around immune modulation and chemical pollution probaly does not play a significant part.

CNS tumours are on the increase. There is dispute about whether this is real or due to better diagnostic methods and picking up indolent tumours at an early stage by MRI etc. Probably is a true increase, cause unknown.

Germ Cell tumours. Probably a real increase as there is with adult testicular tumours. Thoughts around exposure to phytoestrogens/oestrogens in the environment

Neuroblastoma. There is an increase but probably largely in the benign variety, under 1 year of age, and due to better diagnosis.

4. **Dr Louise Parker, Newcastle**

I agree with Alan. The world wide increase in childhood leukaemia is likely due to a change in the pattern of antigenic exposure in utero and in early life in relation to immunological competence (part of the 'hygiene hypothesis' which also takes in asthma, eczema and ulcerative colitis in children).

The cause of the increase in brain tumours -also widespread - is as Alan says, unknown, though there is some (albeit somewhat tentative) evidence that infection may be playing a role in this too.

Germ cell tumours are certainly on the increase - not in the under 14's but certainly in the over 15's. This is a birth cohort phenomenon which has been going on since at least in people born since the 1930s, though there is some evidence of a plateauing of this in the US. I have just had a student finish an Mphil on this in the Northern Region - and have another grad student assembling data on hypospadias and cryptorchidism - which may be linked conditions (testicular dysgenesis syndrome).

There have been anecdotal reports of 'clusters' of neuroblastomas and possibly some bone sarcomas in the context of (?implausible -so-far?) environmental exposures - but these are necessarily very hard to look at since these conditions are so rare.