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Effect of maintenance chemotherapy in childhood on numbers of melanocytic naevi

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Abstract

***Objective*—(*a*) To determine whether children given chemotherapy for haematological malignancy have significantly more melanocytic naevi than age matched children in the local population; (*b*) to establish whether any observed variation in naevus counts from normal is seen at the start of maintenance chemotherapy.**

***Design*—Follow up of 29 consecutive children starting maintenance chemotherapy, with parental interview and count of all melanocytic naevi ≥2 mm on the child's skin. Assessment repeated three years later after completion of maintenance chemotherapy. Other dermatological problems identified at either visit were also recorded.**

***Setting*—Royal Hospital for Sick Children, Glasgow.**

***Results*—At the start of maintenance chemotherapy all children had total body counts of melanocytic naevi within the normal range established for age matched children in the local population. Three years later total body naevus counts were significantly increased, the median increase being 66 naevi per child (95% confidence interval 57 to 94). The only other problem noted in these children was relatively poor regrowth of scalp hair.**

***Conclusion*—Children on maintenance chemotherapy for haematological malignancies develop an excessive number of melanocytic naevi. Excessive numbers of melanocytic naevi are the most important risk factor for melanoma in the general population. These children should have periodic skin examinations at their follow up visits, and both child and parent should be educated about clinical features of early melanoma.**

Introduction

While modern chemotherapy and radiotherapy regimens for childhood haematological malignancies are becoming increasingly successful in inducing long term remissions sequelae of such regimens are slowly being elucidated. Hughes *et al*[1] and de Wit *et al*[2] have reported a larger number of melanocytic naevi in children who have undergone chemotherapy for haematological malignancies compared with children who have not received chemotherapy. As the design of their studies was retrospective, however, it was not possible to determine whether the high naevi counts were present before chemotherapy and possibly associated with a phenotype also predisposed to develop haematological malignancy.

We decided to answer this question with a prospective study, counting naevi in children over a three year period at the start of and after maintenance chemotherapy, in order to quantify any changes in counts of melanocytic naevi. Other dermatological problems identified at the start or completion of chemotherapy were also recorded.

Patients and methods

In 1988, 29 children were enrolled in the study. All were undergoing treatment for a childhood haematological malignancy. The majority of children (n=25) had acute common type lymphoblastic leukaemia. Of the remaining four children, two had acute T cell lymphoblastic leukaemia, one acute myeloid leukaemia, and one Hodgkin's disease. The child with Hodgkin's disease and one with T cell leukaemia had a marrow transplant. The majority of the children were receiving the United Kingdom acute lymphoblastic leukaemia trial (UKALL 10) chemotherapy regimen, which consists of an initial induction course with vincristine, prednisolone, daunorubicin, and asparaginase. Intrathecal methotrexate is also given. After induction cranial irradiation is given. Maintenance therapy is continued for two years with monthly courses of vincristine and prednisolone, weekly methotrexate, and daily mercaptopurine.

The children's naevi were not counted at the time of diagnosis while they were undergoing induction chemotherapy for several reasons. Full skin examination is difficult when children are acutely unwell and less mobile than usual owing to illness and peripheral and central lines. In addition, we thought it inappropriate to ask parents to allow their children to participate in this study at such a sensitive time. They were therefore first assessed at the start of maintenance chemotherapy.

Parents were asked about specific dermatological problems encountered, including episodes of severe sunburn and any family history of multiple naevi or of malignant melanoma. The children were examined by looking specifically at hair growth, nails, and skin. A count of all melanocytic naevi ≥2 mm on the entire body surface was undertaken.

The children were reviewed three years later by using the same questionnaire and total body naevi recounted. At that time exposure to natural ultraviolet light was assessed by asking about holidays taken in the United Kingdom and abroad. Seven of the children were not assessed at the three year follow up. Three had died, three were geographically inaccessible, and one parent declined.

Naevus counts before and after chemotherapy were compared with numbers of naevi previously recorded in healthy children in the same age range, from the same geographical area. These children had their naevi counted either while attending for a routine school medical examination or while attending the outpatient department for minor ocular problems or viral warts.[3]

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Statistical analysis—A Wilcoxon signed ranks test and calculation of the corresponding 95% confidence interval for the median were carried out on the differences of the naevi counts before and after maintenance chemotherapy.

Results

The 22 children reassessed at three years comprised 19 with acute common type lymphoblastic leukaemia, two with T cell leukaemia, and one with Hodgkin's disease. All subjects were white. Of the 22 children, 11 were female and 11 male. The age range at diagnosis was 1 to 14 years, the peak incidence occurring at 3 to 5 years of age.

TABLE I—*Absolute counts of melanocytic naevi ≥2 mm before and after maintenance chemotherapy*

Before	After
Girls aged 0-9 years	
4	50
6	107
2	38
8	74
0	66
11	88
1	30
0	NR
1	38
4	52
Boys aged 0-9 years	
8	194
5	70
10	58
0	NR
0	44
3	88
3	NR
4	78
0	47
Girls aged 10-14 years	
34	90
4	NR
12	98
14	NR
Boys aged 10-14 years	
22	124
19	198
30	NR
18	104
27	199
1	NR

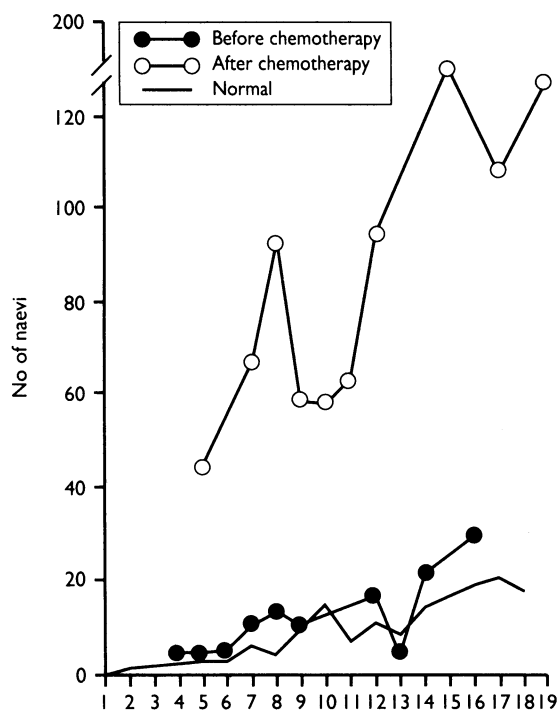
NR=Not reassessed (lost to follow up etc).

NAEVUS COUNTS

At the first assessment the number of naevi ≥2 mm on the 29 children ranged from zero to 34 (median 4) (table I). These figures were within the range for those previously reported for normal age matched children of the west of Scotland.[3] The number of naevi counted on these same children three years later was significantly greater than would be expected in a normal age matched population, with a range of 30 to 199 (median 76). The increase in naevus counts was significantly greater than that experienced by healthy children in the same geographical area over three years (figure).

There was a highly significant increase in numbers of melanocytic naevi, the mean increase being 66 naevi per child (95% confidence interval 57 to 94; $p<0{\cdot}0001$). Tables I and II show the increase in naevi on each individual child and the pooled figures for the two age ranges (0-9 and 10-14 years).

Some of the naevi were located on unusual sites, such as on the palms and soles and in finger webs and toe webs. Eight of the 22 patients (36%) were found to have naevi on acral sites. All the naevi were, however, clinically banal. Specifically, none was greater than 5 mm diameter and none had irregular pigmentation or an irregular edge or inflammation—all characteristics of clinically atypical or pathologically dysplastic naevi. None of the children had a history of severe sunburn or excessive sun exposure, and none of the patients reviewed had been abroad on holiday during the three year interval. Few had even left the west of Scotland since diagnosis as their parents were concerned about their ongoing care should problems arise.



Mean naevus counts of children before and after maintenance chemotherapy compared with healthy children of same age in same geographical area. Note interrupted vertical scale

TABLE II—*Melanocytic naevi ≥2 mm before and after maintenance chemotherapy in girls and boys aged 0-9 and ≥10 years*

	Median (mean) No of naevi			
	Girls		Boys	
	0-9 Years	≥10 Years	0-9 Years	≥10 Years
Before	3 (4)	13 (16)	3 (4)	21 (20)
After	52 (60)	94 (94)	70 (83)	161 (156)
Normal*	0 (3)	16 (23)	2 (2)	10 (18)

*Naevus counts >2 mm for children in same age range previously published.[1]

TABLE III—*Dermatological problems observed during and after maintenance chemotherapy*

	No
Infective:	
Hand warts	7 (including two patients with transplants)
Plantar verrucae	3
Molluscum contagiosum	1
Non-infective:	
Juvenile plantar dermatosis	2
Eczema (not atopic)	1
Atopic eczema	1
Keratosis pilaris	1
Polymorphic light eruption (? related to treatment)	1
Juvenile spring eruption	1

OTHER DERMATOLOGICAL PROBLEMS

Many of the children had alopecia when first assessed due to the induction chemotherapy that they had received. Three years later hair growth had taken place, but many parents noticed that the hair was thin and lifeless with a low sheen and little body. Objectively, there seemed to be a difference in quality and quantity of hair growth in these children compared with their siblings.

No problems were encountered with nails, but a number of minor dermatological problems were noted (table III), none of which was thought to be serious by the children's parents. All of these had responded or were responding to treatment. Ten of the children had viral warts, but none had large numbers of such lesions.

Discussion

This group of 22 children seemed to have few longstanding dermatological problems associated with their chemotherapy, apart from the development of high numbers of benign melanocytic naevi. At the time of beginning maintenance chemotherapy their naevus counts were within the normal range, and it would therefore seem to have been the chemotherapy or the immunosuppression associated with it that was the stimulus to the development of large numbers of melanocytic naevi.

The ideal study design would have been to follow the naevus counts on healthy siblings in the same age range over the same period, but ethical considerations and extreme parental anxiety in two pilot families approached obliged us to modify the design. The highly significant difference in numbers of naevi on the chemotherapy treated children before and after therapy compared with what would be expected in the local population over three years is reasonable evidence that our conclusions are valid.

The biology of benign naevi is not well understood. Racial and genetic factors are known to be important. Naevi increase in number during childhood, reaching

maximum numbers in early adulthood and decline thereafter. Gallagher *et al* studied 913 schoolchildren in western Canada and reported that large numbers of naevi in children aged 6 and over are found in fair skinned children who have a history of burning sunburn.[4] The children in our study did not have a history of severe sunburn.

The significance of such high naevus counts in these children is not yet established. Studies from the west of Scotland,[5] Scandinavia,[6] and the west coast of America[7] have all established that large numbers of banal naevi are the strongest risk factors for subsequent development of malignant melanoma. In the west of Scotland the three next most important risk factors, in descending order of importance, are a freckling tendency, clinically atypical naevi (greater than 5 mm and with an irregular edge, irregular pigment, or inflammation), and a history of episodes of severe blistering sunburn.[8]

It is important to emphasise that not all melanomas develop on these pre-existing naevi but that it is speculated that factors which give rise to melanoma are also risk factors for naevi.

Though we know that children treated in childhood for malignancies with chemotherapy are at risk of developing second malignancies, malignant melanoma is not at present recognised as such a second malignancy. Long term follow up of these children already occurs, and it is recommended that they should have periodic skin examinations. In addition, advice should be given to both parents and children on the clinical appearance of early melanoma and on avoiding excessive sun exposure and in particular frank sunburn.

We are grateful to Dr Brenda Gibson, of the Royal Hospital for Sick Children, Glasgow, for allowing us to study these children.

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Female streetworking prostitution and HIV infection in Glasgow

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Abstract

***Objectives*—To identify the extent of HIV infection and injecting drug use among female streetworking prostitutes in Glasgow; to estimate the size of the female streetworking prostitute population in the city; and to estimate the number of HIV positive women working as prostitutes on the streets in Glasgow.**

***Design*—Observation and interviewing of female prostitutes over seven months in red light district; analysis of saliva samples for presence of antibodies to HIV; capture-recapture approach to estimating the size of the female streetworking prostitute population.**

***Setting*—Glasgow.**

***Subjects*—206 female streetworking prostitutes.**

***Main outcome measures*—Number of women with antibodies to HIV, self reported use of injecting drugs, history of contact with 206 women.**

***Results*—Saliva samples were requested from 197 women; 159 (81%) provided samples. Four (2·5%, 95% confidence interval 0·7%-6·3%) of the samples were positive for HIV, all of which had been provided by women who injected drugs. Of the 206 streetworking women contacted 147 (71%) were injecting drug users. About 1150 women are estimated to work on the streets in Glasgow over a 12 month period.**

***Conclusions*—HIV is not as widespread among female prostitutes as many reports in the tabloid press suggest. A greater proportion of female streetworking prostitutes in Glasgow are injecting drugs than has been reported for other British cities.**

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Introduction

Female prostitutes have often been presented as a major source of HIV infection. This image derives in large part from the situation in certain countries in sub-Saharan Africa, where prostitution has undoubtedly played a key role in the heterosexual transmission of HIV infection.[1] There are obvious dangers in extrapolating from what may be happening in one area to what may be happening in another, especially when the areas in question are different in virtually every respect. HIV seroprevalence studies of female prostitutes in Europe and North America, for example, have rarely identified a prevalence of HIV in excess of 5%.[2] This figure has tended to be higher when the women surveyed were prostitutes and injecting drugs.[3]

We report on the prevalence of HIV infection among a sample of female streetworking prostitutes in Glasgow and on the extent of injecting drug use among such women. We also estimate the size of the female streetworking prostitute population in Glasgow and the total number of HIV positive female prostitutes working on the streets in the city.

Methods

From January 1991 to September 1991 the main authors of this paper (NM and MB) carried out fieldwork on 53 nights (a total of more than 156 hours) in Glasgow's main red light area. This work was organised in accordance with strict time sampling procedures covering every day of the week and the times of day prostitute women were observed working (approximately 8 pm to 2 am). By spreading the data collection over seven months we sought to reduce any bias associated with seasonal variations in working.

Fieldwork for this study entailed the researchers repeatedly walking around the entire set of streets comprising the red light area in the city and approaching as many women as possible during each two hour fieldwork period. We were consistently able to contact about 90% of all women seen working during each fieldwork period. Although all of these women spend a