Outcome in women with tetanus after induced abortions

Country	Year	Age	Gravidity	Outcome
Bangladesh	1982	18	Primipara	Died
	1988	28?	Multipara	Died
	1991	32?	Multipara	Died
	1994	36	Multipara	Died
Nigeria	1986	19	Primipara	Survived
	1988	24	Multipara	Died
Pakistan	1989	19	Primipara	Died

who are at high risk of developing maternal tetanus. This is because women (especially teenagers) with unwanted pregnancies often do not attend for antenatal care and may resort to unsafe abortion.

On the basis of our personal experience we support the authors' proposal to include adolescent girls as a target for vaccination for tetanus toxoid. This strategy would substantially reduce the rates of maternal mortality in young women from maternal tetanus secondary to induced abortion.

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Nestlé obeys Indian label laws

EDITOR,—It is disappointing that a professional journal like the *BMJ* should print stories in an obviously slanted way, and the inaccuracies of Claire Lockwood's news report¹ need to be corrected.

The Indian court case is a direct result of a conflict between two laws which will have to be determined by the government or by the courts. One law requires the labels to contain the statement, "Breast milk is best for your baby," while the other requires "Mother's milk is best for your baby." It is clearly right that the law should be observed, and either is equally acceptable to Nestlé. The issue is of no significance to the health of infants, which is presumably everyone's prime concern.

Similarly, your reporter misrepresents the issue of language. The Indian government determines the language of the labels and these laws are adhered to by Nestlé. Although this is not a legal obligation, almost all Nestlé labels for products dealing with infant feeding are printed in both English and Hindi, and they include pictorial instructions for those who cannot read. Some other infant formula products in India have until recently had labels in English only, and we are aware of no court action against these manufacturers. The language "problem" is not about instructions or warnings, as your readers may expect, but only concerns the one phrase about which there remains doubt within the law—which Nestlé prints in both English and Hindi.

Lockwood does not identify the "potentially misleading instructions" mentioned. There are none.

Nestlé adheres fully to the WHO International

Code and to Indian law. We fully investigate all allegations and guarantee swift response and action if required. It is noteworthy that none of the complaints against Nestlé are made by the Indian government or regulatory bodies of the health and paediatric services. Nestlé's reputation in this field is the highest in India. It is sad that the *BMJ* does not pursue balanced reporting on this as in other matters.

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1 Lockwood C. Nestlé appears in court in India. *BMJ* 1995;311:348. (5 August.)

Non-Hodgkin's lymphoma and skin cancer

Ultraviolet light is unlikely explanation for association

EDITOR,—Johanna Adami and colleagues provide data showing a greatly increased risk of melanoma and squamous cell skin cancer after non-Hodgkin's lymphoma and chronic lymphocytic leukaemia.¹ They also show a smaller but significantly increased risk for the reverse (non-Hodgkin's lymphoma and chronic lymphocytic leukaemia after skin cancer). They conclude that "this supports the hypothesis of a role for ultraviolet light in the increasing incidence of non-Hodgkin's lymphoma." We believe that this inference lacks justification, particularly since the relative risk of non-Hodgkin's lymphoma and chronic lymphocytic leukaemia associated with ultraviolet light would have to be of similar magnitude to that of melanoma to explain the substantial increase in the incidence of non-Hodgkin's lymphoma and chronic lymphocytic leukaemia (even after correction for changes in diagnosis).²

Geographical correlations of rates of melanoma (*International Classification of Diseases, Ninth Revision* (ICD-9) code 172) and non-Hodgkin's lymphoma and chronic lymphocytic leukaemia (ICD-9 codes 200, 202) in white populations do not support the role of ultraviolet light (table). The most likely explanation for the increased risk of skin cancer after non-Hodgkin's lymphoma and chronic lymphocytic leukaemia is immunodeficiency from non-Hodgkin's lymphoma and chronic lymphocytic leukaemia themselves and from the immunosuppressive treatments given. It is well documented that recipients of renal transplants are at greatly increased risk of squamous cell skin cancer and, to a lesser extent, malignant melanoma.³

We do not have an explanation for the smaller increased risk of non-Hodgkin's lymphoma and

chronic lymphocytic leukaemia after squamous cell skin cancer other than the possibility that both cancers were caused by immunodeficiency predating the squamous cell skin cancer. The risk of non-Hodgkin's lymphoma and chronic lymphocytic leukaemia after melanoma was only marginally significant ($P=0.05$ for ICD-9 codes 200, 202, and 204.0 combined).

We believe that simpler explanations for the association between these cancers, such as that skin cancers are caused by immunosuppression, are more plausible than the claim that ultraviolet light could be responsible for the rapid increase in rates of non-Hodgkin's lymphoma and chronic lymphocytic leukaemia.

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Pathogenesis is multifactorial

EDITOR,—Johanna Adami and colleagues present evidence of an association between lymphoma and skin cancer, interpreting their findings as evidence of the role of immunosuppression induced by ultraviolet light in the pathogenesis of non-Hodgkin's lymphoma and leukaemia.¹ There are, however, several reasons for believing that this conclusion may not be valid. According to the authors' line of reasoning, the incidence of lymphoma in countries where people are exposed to high doses of ultraviolet radiation should be considerably higher than that in countries with more temperate climates. Such a difference has never been reported. In contrast, the incidence of skin cancer in sunny countries is strictly related to exposure to ultraviolet radiation—for example, the incidence of malignant melanoma is 20.5/100 000 person years in Hawaii compared with 8.8 in Detroit.²

Melanin in people with dark skin serves as a filter for ultraviolet radiation, and thus local and systemic effects of such radiation are much less pronounced in these people. This difference is shown by the incidence of skin cancer: the

Age standardised incidences* of malignant melanoma and non-Hodgkin's lymphoma from selected cancer registries.³ Figures are per 100 000

Registry	Male		Female	
	Melanoma (ICD-9 code 172)	Non-Hodgkin's lymphoma and chronic lymphocytic leukaemia (ICD-9 codes 200, 202)	Melanoma (ICD-9 code 172)	Non-Hodgkin's lymphoma and chronic lymphocytic leukaemia (ICD-9 codes 200, 202)
Australia (New South Wales)	25.9	10.2	23.8	7.6
Hawaii (white)	22.2	11.3	14.9	8.1
New Zealand (non-Maori)	18.6	8.6	23.0	5.9
Australia (Victoria)	16.4	11.9	18.0	8.0
Los Angeles (white)	14.6	13.0	11.6	8.1
Ontario	9.0	12.5	8.9	8.8
Detroit (white)	9.0	13.9	7.2	9.6
Denmark	7.7	8.0	9.8	5.6
England and Wales	3.0	7.1	5.0	4.8
Quebec	3.0	12.5	3.2	9.6

*World standard population.

incidence of both melanoma and non-melanoma skin cancer in people with pigmented skin is several times lower than that in people with less pigmented skin.² How do the authors explain an apparent lack of association of lymphoma and leukaemia with skin colour?

The authors' reasoning is based on two assumptions: that the incidence of skin cancer can be used as a marker of exposure to ultraviolet radiation and that immunosuppression has a dominant role in the pathogenesis of cancer induced by ultraviolet radiation. Both assumptions may be false. Although ultraviolet radiation has an unequivocal role in the development of skin cancer, the pathogenesis of skin neoplasms is multifactorial. This is shown by the fact that exposure to the sun increases the relative risk of melanoma by only a factor of two to five, which is not impressive in comparison with the 85-1269 times higher risk in people with two family members with melanoma.³ Moreover, recent evidence suggests that, in the pathogenesis of skin cancer, mechanisms other than immunosuppression are relevant, such as mutagenesis and suppression of apoptosis induced by ultraviolet radiation. Factors other than exposure to ultraviolet radiation—for example, genetic predisposition—probably better explain the association between skin cancer and the occurrence of lymphoma and leukaemia.

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Association may be iatrogenic

EDITOR.—Johanna Adami and colleagues postulate that exposure to ultraviolet light causes immunosuppression and, thereby, non-Hodgkin's lymphoma.¹ To support their hypothesis they report that patients with non-Hodgkin's lymphoma had a relative risk of 5.5 of developing squamous cell skin cancer. Conversely, patients with squamous cell skin cancer had a twofold excess risk of developing non-Hodgkin's lymphoma or the closely related chronic lymphocytic leukaemia. The relation between ultraviolet light and non-Hodgkin's lymphoma was therefore examined only indirectly.

Patients with non-Hodgkin's lymphoma are often treated with drugs, notably alkylating agents, that are inherently mutagenic. Although Adami and colleagues highlight the immunosuppressive effects of these agents, they do not mention their mutagenicity. In support of the importance of the latter mechanism of action, the authors show that patients with non-Hodgkin's lymphoma have an increased general risk of malignancy of 1.2 times normal (95% confidence interval 1.1 to 1.3), a finding referred to as "close to the expected" in their abstract. Indeed, this figure can be expected to rise with time as the latent period after chemotherapy for myeloid and lymphoid malignancies is shorter than that for most of the common solid tumours.²

It has been a puzzle for many years that immunocompromised transplant recipients are predisposed to develop only two types of malignancy, skin cancer and non-Hodgkin's lymphoma. Most of the cases of non-Hodgkin's lymphoma are caused by uncontrolled proliferation of lymphocytes infected with Epstein-Barr virus. Furthermore, lesions of non-Hodgkin's lymphoma

in patients immunocompromised by HIV infection have been shown to contain the newly described herpesvirus-like agent that has been postulated to cause Kaposi's sarcoma.³ This agent has now been reported in non-Kaposi's sarcoma skin lesions, notably squamous cell carcinoma, in transplant recipients.⁴

I find Adami and colleagues' explanation of their findings implausible. Alternative explanations are, firstly, the mutagenicity of agents used to treat non-Hodgkin's lymphoma and, secondly, infection with an agent that predisposes to malignant transformation in both skin and lymphoid cells.

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American data refute ultraviolet hypothesis

EDITOR.—Johanna Adami and colleagues suggest that an association between non-Hodgkin's lymphoma and skin cancer supports the hypothesis that exposure to ultraviolet light may be causally related to the development of non-Hodgkin's lymphoma.¹ Such an association would, however, be expected in a cohort of survivors of immunosuppressive treatment for cancer since it is well known that immunosuppression increases the risk of non-Hodgkin's lymphoma, squamous cell carcinoma of the skin, and malignant melanoma.^{2,3} In the absence of information on exposure the relation cannot, therefore, be attributed to ultraviolet light.

Furthermore, there is no strong evidence that the incidence of non-Hodgkin's lymphoma is increased in people living in places where exposure to solar ultraviolet light is likely to be high. Published data on the incidence of cancer⁴ and measures of exposure to solar ultraviolet light at six locations in the United States (Seattle, Detroit, Iowa, Utah, Atlanta, and New Mexico)⁵ suggest that the incidence of non-Hodgkin's lymphoma declines, rather than increases, with increasing exposure, both in men (regression coefficient -0.044; 95% confidence interval -0.030 to -0.058) and in women (-0.022; 0.003 to -0.047) (figure). Taken at face value, these data do not support the hypothesis that exposure to ultraviolet light increases the risk of non-Hodgkin's lymphoma. The analyses must, however, be viewed with caution because they take no account

Incidence of non-Hodgkin's lymphoma at six centres in United States related to exposure to solar ultraviolet light

of possible confounding factors, such as socio-economic status.

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Author's reply

EDITOR.—Peter Sasieni and Veronique Bataille argue that the relative risk after exposure to ultraviolet light should be of the same magnitude for subsequent non-Hodgkin's lymphoma and malignant melanoma for a causal association between ultraviolet light and non-Hodgkin's lymphoma to be plausible and for ultraviolet light to explain part of the increase in the incidence of non-Hodgkin's lymphoma. This argument is problematic, because the size of the relative risks cannot be interpreted in such a simplistic way. Theoretically, if ultraviolet light has a directly causal role in the pathogenesis of malignant melanoma (that is, no other components are needed to generate malignant melanoma or, alternatively, the component causes are ubiquitous) whereas it is only one of several component causes of non-Hodgkin's lymphoma, the relative risks for the two malignancies need not be identical. The relative risk for non-Hodgkin's lymphoma would depend on the prevalence of the other component causes.

Furthermore, if non-Hodgkin's lymphoma has important causes other than ultraviolet light, the incidence of non-Hodgkin's lymphoma would correlate only poorly with measures of the intensity of the ultraviolet light. This could explain why the incidences of malignant melanoma and non-Hodgkin's lymphoma show little covariation in different geographical areas, as discussed by Sasieni and Bataille and by Robert Gniadecki. Unlike Gniadecki, however, we believe that there is good evidence that coloured people have lower incidences of non-Hodgkin's lymphoma than white people.¹ This is compatible with the hypothesis that ultraviolet light has an impact on the incidence of non-Hodgkin's lymphoma, a theory that is further supported by the observation of an increased risk of non-Hodgkin's lymphoma in people with outdoor occupations.²

Mark Vickers adds the mutagenic action of alkylating agents to the possible explanations of the high risk of skin cancer in patients with non-Hodgkin's lymphoma. Such iatrogenic mutagenicity might contribute to the much stronger associations observed between initial systemic malignancies and subsequent skin cancers but is unlikely to contribute to the reverse sequence. Sasieni and Bataille suggest that immunodeficiency predating the squamous cell skin cancer could explain this finding. Malignancies that antedate the squamous cell skin cancer or the immunosuppressive mutagenic treatment of such antedating malignancies could explain part of this association. However, in a large scale analysis of cancers after basal cell carcinoma, which may be equally useful as a proxy for exposure to ultraviolet light, the subsequent risk of non-Hodgkin's lymphoma remained virtually unchanged whether