

Atopic dermatitis and cancer risk

H. Wang and T.L. Diepgen

Department of Clinical Social Medicine, Occupational and Environmental Dermatology, University of Heidelberg, Thibaut Str. 3, 69115 Heidelberg, Germany

Summary

Correspondence

T.L. Diepgen.

E-mail: thomas_diepgen@med.uni-heidelberg.de

Accepted for publication

4 September 2005

Key words

atopic dermatitis, eczema, epidemiology, malignancy

Conflicts of interest

None declared.

Background Epidemiological studies have provided growing evidence of a link between atopy and cancer risk.

Objectives To review the evidence from case-control studies and cohort studies on a possible association between atopic dermatitis (AD) and cancer risk, with particular attention to the case definition of AD.

Methods Studies with quantitative data on the association between AD (eczematous disease) and cancer risk were obtained from MEDLINE in combination with a review of cited references.

Results In 23 publications, AD was implicated in the risk of haematological [childhood leukaemia ($n = 3$), adult leukaemia ($n = 3$), non-Hodgkin lymphoma (NHL; $n = 4$) and different haematological cancers ($n = 1$)], pancreatic ($n = 5$), skin ($n = 2$) and brain malignancies ($n = 5$). The overall picture of the results of these studies shows that a history of AD may be associated with a decreased risk of pancreatic cancer, brain tumour and childhood leukaemia, although in most instances the findings were not statistically significant. No consistent associations were observed for skin cancer or NHL. The definition of AD had varying quality, and was imprecise in the majority of publications.

Conclusions The findings of the epidemiological studies tend to support a lower risk of cancer among persons with a history of AD. Although a more careful definition of AD is needed, these epidemiological studies could provide an estimate of the background cancer risk in patients with AD when the long-term effects of treatments for AD are assessed.

Over the past decades, several studies have looked into a possible association between the atopic state and other diseases such as certain autoimmune diseases [for example, the inverse association between atopic dermatitis (AD) and insulin-dependent diabetes mellitus] or specific cancers.^{1,2} These studies are based on the concept of atopic diseases as a hyper-reactive state of the immune system. Theoretically, this hyper-reactive state might be accompanied by an enhanced immune surveillance, which in turn may decrease the chance of proliferation of aberrant cells. On the other hand, it can also be argued that a (sub)chronic state of inflammation in certain tissues makes it likely that atopy is responsible for the positive associations observed with cancer risk. These considerations might, in theory, be supported by epidemiological observations, demonstrating either a protective role of atopy for certain types of cancer, or acting as a risk factor for other cancer types. Papers published before 1985 tend to support a decreased risk of cancer.³ Results from the epidemiological data since 1985 are more complex, indicating that the association might depend on both the specific allergic condition and the particular organ site under consideration.

In AD, which is mostly a disease of childhood, the hyper-reactivity of the skin is evident, whereby the extrinsic type of AD is often accompanied by high serum levels of IgE. With a focus on AD as a clinically defined disease, we reviewed the currently available evidence for a possible relationship between AD and cancer. Our aim was to examine the associations, expressed as relative risks (RRs) or odds ratios (ORs), between AD and specific cancer sites reported since 1985, with special attention to the terminologies that were used to define AD in these publications.

Materials and methods

By a thorough literature search (a combination of electronic searching of MEDLINE and checking cited references) from 1985 to December 2004, we identified all publications dealing with atopy or atopic diseases (including asthma, hay fever, allergies, eczema/dermatitis, urticaria/hives and immunity-related diseases) in relation to cancer.² These publications were screened on whether they contained original data or described original databases on cancer risk, and whether their

analysis presented data on an eczematous disease which was likely to represent AD; we excluded papers in which the skin atopy was defined as rash/hives due to allergies. In addition, all the literature references in all the papers that were retrieved were checked to see whether they referred to any publication with information on AD or eczematous diseases.

We subsequently grouped the publications according to cancer site; if more than one cancer site was studied, the relevant information was allocated to the respective site or type of malignancy. In addition to the type of study and the risk estimate, we tabulated the number of cases that were in a particular study, and we summarized the terminology that was used for identifying the subjects with AD. The risk estimates were given as OR or RR, with the 95% confidence interval (CI).

Results

A total of 23 publications was found in which AD (or eczema) was studied as risk factor for haematological, pancreatic, skin and brain malignancies. In Tables 1–4 the results are summarized according to these cancer sites. Almost all studies were case–control studies, and only two studies had a cohort design.

Haematological malignancies

We identified 11 case–control studies on haematological malignancies: three studies on childhood leukaemia, three studies on adult leukaemia, four studies on non-Hodgkin lymphoma (NHL) and one study on different haematological cancers (Table 1).

A population-based case–control study on 1842 cases, identified throughout the U.S.A. between 1989 and 1993, reported that a history of eczema had a significant protective effect against acute lymphoblastic leukaemia (ALL) among children (OR 0.7, 95% CI 0.5–0.9).⁴ The protective effect of AD in the development of childhood leukaemia was pronounced in a German case–control study which used a convincing diagnosis of AD;⁵ it found a statistically significant reduction of 50% in the risk of ALL and a (statistically not significant) 20% reduction in the risk of acute myeloid leukaemia (AML) in children with a history of physician-diagnosed AD (called neurodermatitis in German). These findings have been refuted by a more recent study among 180 cases of childhood ALL, which showed no significant differences between cases and controls for a history of physician-diagnosed eczema (OR 1.1, 95% CI 0.6–2.0).⁶

Three studies have looked at adult leukaemia, with varying results. A lower, not statistically significant risk of chronic lymphocytic leukaemia in adults with a history of eczema was observed in a population-based case–control study in the U.S.A. (OR 0.7, 95% CI 0.3–1.5).⁷ In a study in Shanghai, China, cases with ALL were more often (not statistically significant) reporting ever having had a history of physician-diagnosed eczema (OR 1.7, 95% CI 0.7–4.5), but this was reversed for cases with AML and chronic myeloid leukaemia.⁸

Another case–control study in the U.S.A. did not find any increased risk of AML, although there was a statistically non-significant risk of 1.7 of ALL for a history of eczema.⁹

The results from four case–control studies in NHL did not agree consistently about the effect of eczema on the NHL risk; increased and decreased risks have been noted. A population-based case–control study in the U.S.A. suggested that people with a history of eczema tended to have a significantly lower risk of NHL (OR 0.6, 95% CI 0.4–1.0).¹⁰ The findings from this study were confirmed in a recently published study in France (OR 0.5, 95% CI 0.3–0.7).¹¹ On the other hand, there was a suggestion of a positive association, although it was not significant, with eczema in another U.S.-based study.¹² A study in the U.K., using hospital records for the confirmation of AD, was supportive of a significantly increased risk of NHL.¹³ The results from an Italian study on different haematolymphopoietic malignancies (lymphomas, myelomas and leukaemia) in relation to AD were varying; when the different haematolymphopoietic cancers were combined, there was no association.¹⁴

Pancreatic cancer

Out of five case–control studies of eczema and pancreatic cancer risk conducted in the years 1985–2004, an inverse association was demonstrated in four, of which two were statistically significant (Table 2).

A U.S.-based study of 490 pancreatic cancer cases observed a statistically significant OR of 0.2 (95% CI 0.1–0.5) for persons who had a history of eczema.¹⁵ The significant protective effect of eczema on pancreatic cancer was further confirmed in a more recent case–control study carried out in the San Francisco Bay Area between 1994 and 2001 (OR 0.6, 95% CI 0.4–1.0).¹⁶ A study in the Netherlands¹⁷ showed that a history of physician-diagnosed eczema conferred a slight, statistically nonsignificant reduction in the risk of pancreatic cancer, which agreed with the findings of a Canadian study (OR 0.7, 95% CI 0.3–1.5).¹⁸ However, there was no association between physician-diagnosed eczema and risk of pancreatic cancer in a study carried out in three areas in the U.S.A. (OR 1.1, 95% CI 0.7–1.9).¹⁹

Brain tumours

The inverse association between eczema and the risk of brain tumours was observed consistently in the four case–control studies as well as in one cohort study (Table 3). All these five studies were suggestive of a protective effect on glioma, although in only two of these five studies were the findings statistically significant. In a combined analysis of a large multicentre study on brain tumours, having a history of physician-diagnosed eczema decreased the risk of meningioma by 30% (OR 0.7, 95% CI 0.4–1.1), and resulted in an even more pronounced, statistically significant, decreased risk of glioma (OR 0.6, 95% CI 0.5–0.9).²⁰ This multicentre study included earlier published data from two centres in Australia.^{21,22} The data

Table 1 Studies of association between atopic dermatitis and haematological malignancies

Study	Type of cancer	Types of study	No. of cases	Risk estimate (OR/RR, with 95% CI)	Terminology used for (skin) atopy
Wen <i>et al.</i> (2000), U.S.A. ⁴	Childhood leukaemia	Case-control, population based	1842	ALL: 0.7 (0.5-0.9)	Eczema (allergic, in the context of hay fever, asthma; unknown physician-diagnosed or self-assessment)
Schuz <i>et al.</i> (2003), Germany ⁵	Childhood leukaemia	Case-control, population based	1294	ALL: 0.5 (0.3-0.7) AML: 0.8 (0.4-1.7)	Physician-diagnosed neurodermatitis in children
Spector <i>et al.</i> (2004), U.S.A. ⁶	Childhood leukaemia	Case-control, population based	180	ALL: 1.1 (0.6-2.0)	Physician-diagnosed eczema (allergic)
Linet <i>et al.</i> (1986), U.S.A. ⁷	Adult leukaemia	Case-control, hospital based	342	0.7 (0.3-1.5)	Eczema (allergic, in the context of hay fever, asthma; unknown physician-diagnosed or self-assessment)
Zheng <i>et al.</i> (1993), China ⁸	Adult leukaemia	Case-control, population based	486	ALL: 1.7 (0.7-4.5) AML: 0.6 (0.3-1.5) CML: 0.5 (0.1-2.2)	Physician-diagnosed eczema (allergic, in the context of hay fever, asthma)
Cooper <i>et al.</i> (1996), U.S.A. ⁹	Adult leukaemia	Case-control, population based	624	AML: 1.1 (0.6-2.0)	Eczema (any type; unknown physician-diagnosed or self-assessment)
Bernstein and Ronald (1992), U.S.A. ¹⁰	NHL	Case-control, population based	124	ALL: 1.7 (0.7-4.2) 0.6 (0.4-1.0)	Eczema (any type; unknown physician-diagnosed or self-assessment)
Fabbro-Peray <i>et al.</i> (2001), France ¹¹	NHL	Case-control, population based	445	0.5 (0.3-0.7)	Eczema (any type; unknown physician-diagnosed or self-assessment)
Doody <i>et al.</i> (1992), U.S.A. ¹²	NHL	Case-control, population based	100	1.9 (0.6-5.8)	Eczema (allergic, in the context of hay fever, asthma; unknown physician-diagnosed or self-assessment)
Cartwright <i>et al.</i> (1988), U.K. ¹³	NHL	Case-control, hospital based	437	1.6 (1.1-2.4)	Confirmed eczema dermatitis (hospital records)
Vineis <i>et al.</i> (2000), Italy ¹⁴	Haematopoietic	Case-control, population based	1388	NHL: 1.2 (0.9-1.6) HD: 0.7 (0.4-1.3) MM: 0.6 (0.3-1.3) LL: 1.2 (0.7-2.1) ML: 0.9 (0.6-1.3) Combined: 1.0 (0.8-1.3)	Physician-diagnosed eczema (any type)

OR, odds ratio; RR, relative risk; CI, confidence interval; ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; NHL, non-Hodgkin lymphoma; HD, Hodgkin disease; MM, multiple myeloma; LL, lymphocytic leukaemia; ML, myeloid leukaemia.

Table 2 Studies on association between atopic dermatitis and pancreatic cancer

Study	Types of study	No. of cases	Risk estimate (OR/RR, with 95% CI)	Terminology used for (skin) atopy
Mack et al. (1986), U.S.A. ¹⁵	Case-control, population based	490	0.2 (0.1–0.5)	Eczema (any type; unknown physician-diagnosed or self-assessment)
Holly et al. (2003), U.S.A. ¹⁶	Case-control, population based	532	0.6 (0.4–1.0)	Self-assessment eczema (allergic)
Bueno de Mesquita et al. (1992), Netherlands ¹⁷	Case-control, population based	176	0.8 (0.4–1.3)	Physician-diagnosed eczema (allergic, in the context of asthma, hay fever)
Jain et al. (1991), Canada ¹⁸	Case-control, population based	249	0.7 (0.3–1.5)	Eczema (allergic in the context of asthma, hay fever; unknown physician-diagnosed or self-assessment)
Silverman et al. (1999), U.S.A. ¹⁹	Case-control, population based	484	1.1 (0.7–1.9)	Physician-diagnosed eczema (allergic, in the context of hay fever, asthma)

OR, odds ratio; RR, relative risk; CI, confidence interval.

Table 3 Studies on association between atopic dermatitis and brain tumours

Study	Types of study	Subtype	No. of cases	Risk estimate (OR/RR, with 95% CI)	Terminology used for (skin) atopy
Schlehofer et al. (1999), Germany ²⁰	Case-control, population based	Glioma	1178	0.6 (0.5–0.9)	Physician-diagnosed eczema (allergic)
		Meningioma	331	0.7 (0.4–1.1)	
Ryan et al. (1992), Australia ²¹	Case-control, population based	Glioma	110	0.2 (0.1–0.9)	Physician-diagnosed eczema (allergic)
		Meningioma	60	0.6 (0.2–1.7)	
Cicuttini et al. (1997), Australia ²²	Case-control, population based	Glioma	416	0.9 (0.5–1.4)	Physician-diagnosed eczema (allergic, in the context of hay fever, asthma)
Brenner et al. (2002), U.S.A. ²³	Case-control, hospital based	Glioma	489	0.8 (0.5–1.3)	Physician-diagnosed eczema (allergic, in the context of hay fever, asthma)
		Meningioma	197	0.8 (0.4–1.5)	
		Ac Neur	96	0.9 (0.3–2.5)	
Schwartzbaum et al. (2003), Sweden ²⁴	Cohort	Glioma	37	0.5 (0.2–1.5)	Eczema after infancy (unknown physician-diagnosed or self-assessment)
		Meningioma	41	0.7 (0.3–1.7)	

OR, odds ratio; RR, relative risk; CI, confidence interval; Ac Neur, acoustic neuroma.

Table 4 Studies on association between atopic dermatitis (AD) and skin cancer

Study	Type of cancer	Types of study	No. of cases	Risk estimate (OR/RR, with 95% CI)	Terminology used for (skin) atopy
Milan et al. (2003), Finland ²⁵	Skin (BCC)	Cohort	333	M: 1.1 (0.5–2.6) F: 1.8 (0.8–3.9)	Atopic eczema
Ming et al. (2004), U.S.A. ²⁶	Skin (NMSC)	Case–control, population based	1533	0.8 (0.6–1.0) 0.9 (0.7–1.3) 0.9 (0.7–1.1) 1.0 (0.8–1.3)	UKDX History of AD History of eczema History of dermatitis

OR, odds ratio; RR, relative risk; CI, confidence interval; BCC, basal cell carcinoma; NMSC, nonmelanoma skin cancer; UKDX, U.K. Working Party diagnostic criteria.

from the centre in Adelaide, Australia, gave risk estimates for glioma and meningioma of, respectively, 0.2 (95% CI 0.1–0.9) and 0.6 (95% CI 0.2–1.7).²¹ The study from the centre in Melbourne pointed towards a slight statistically nonsignificant decreased risk of glioma associated with a history of physician-diagnosed eczema.²² The more recent U.S.A.-based study gave a similar, nonsignificantly decreased risk estimate for glioma, meningioma and acoustic neuroma.²³ The prospective study, carried out in Sweden and based on 37 glioma cases and 41 meningioma cases, also detected a slight, nonsignificantly inverse association with eczema after infancy.²⁴

Skin cancer

Surprisingly little information was available on the relationship between AD and skin cancer (Table 4). The Finish Adult Twin Cohort study showed that females with a history of AD tended to be more likely to develop a basal cell carcinoma (BCC), although it was statistically nonsignificant (OR 1.8, 95% CI 0.8–3.9); this tendency was not present among males (OR 1.1, 95% CI 0.5–2.6).²⁵ In another study, which looked specifically at the association between AD and risk of nonmelanoma skin cancer, several possible definitions for the diagnosis of AD were evaluated: the U.K. Working Party diagnostic criteria (UKDX) for AD, and the patients' self-reported history of AD, eczema, and chronic dermatitis. After adjustment for age, gender and other confounders, only AD based on the UKDX had a significantly protective effect.²⁶ In addition, we identified a hospital-based case–control study on melanoma and atopy (not shown in the table), which did not present a risk estimate (OR), but reported three subjects with pure eczema among 331 melanoma cases, vs. 11 with eczema (seven pure eczema, three with eczema and rhinitis, and one with eczema and rhinitis and asthma) among 380 controls.²⁷

Discussion

The findings of the epidemiological studies on the association of AD with cancer tend to support a lower risk of cancer among people with AD, especially for ALL and glioma, according to well-performed, large epidemiological studies.

The reduced risk for ALL was statistically significant in two large population-based case–control studies,^{4,5} whereas only one small case–control study indicated no association.⁶ For glioma, a statistically significantly reduced risk was found in two of three population-based case–control studies,^{20–22} whereas according to a hospital-based case–control study the risk did not differ.²³ These data support the immune surveillance hypothesis that AD might be protective against cancer because an enhanced immune system can detect and destroy malignant mutant cells. It can also be argued that the genetic and/or environmental factors that cause AD may also be protective against ALL and glioma.

In almost all studies, however, AD was assessed in the context of atopy in general: only one study focused specifically on AD as primary risk factor.²⁶ That study was prompted by concern about the unknown long-term effects of the new topical immunomodulators in the context of an unknown skin cancer risk by AD and/or its classical topical treatments (e.g. tar, steroids). Although skin cancer would be an obvious focus of attention in AD, only two studies reported, respectively, on BCC and on nonmelanoma skin cancer risk; both were inconclusive.^{25,26} An adjusted risk estimate was not calculated in a study on melanoma in a pre-1985 study; the RR for melanoma associated with eczema was 1.1 and with dermatitis was 0.6,²⁸ while the association of a relatively low number of naevi with AD has also been documented.²⁹

Another major issue is the definition of AD. Only in one study²⁶ were well-defined and validated diagnostic criteria for AD used: the UKDX for AD. Most of the studies were questionnaire based, using imprecise terminology. In many instances the term 'eczema' was used, whereby the alleged AD could be diluted with other skin conditions such as urticaria, nonspecific rashes, drug rashes, or even contact dermatitis. This was quite obvious in one of the studies on pancreatic cancer;³⁰ contact dermatitis in the context of allergic disease was also used in a study on oesophagus cancer by the same group.³¹ Although some studies looked at skin-prick reactivity or radioallergosorbent tests, this was always in the context of atopy in general, and was not used to define the extrinsic subtype of AD. Moreover, the duration of AD and, perhaps more importantly, the severity of the skin symptoms have not been taken into account.

Theoretically, it is possible that a protective effect of AD is counteracted by the therapies that have been applied; this could be immune suppression by corticosteroids or carcinogenicity by the old coal tar preparations. Most studies did not collect information about treatment of AD. Other methodological issues should also be considered in the interpretation of the studies, including the differences in study design, the small numbers of subjects, the recall and/or selection bias, and the lack of adjustment for confounding factors.

Further research should focus on a more carefully defined and documented case definition of AD, as well as its duration and intensity. With the development of new immunomodulating treatments, there is a need to know the background cancer risk in AD when the long-term effects of such novel treatments are evaluated.

References

- Olesen AB, Juul S, Birkebaek N, Thestrup-Pedersen K. Association between atopic dermatitis and insulin-dependent diabetes mellitus: a case-control study. *Lancet* 2001; **357**:1749-52.
- Wang H, Diepgen TL. Is atopy a protective or a risk factor for cancer? A review of epidemiological studies. *Allergy* 2005; **60**: 1098-111.
- Vena JE, Bona JR, Byers TE et al. Allergy-related diseases and cancer: an inverse association. *Am J Epidemiol* 1985; **122**:66-74.
- Wen W, Shu XO, Linet MS et al. Allergic disorders and the risk of childhood acute lymphoblastic leukemia (United States). *Cancer Causes Control* 2000; **11**:303-7.
- Schuz J, Morgan G, Bohler E et al. Atopic disease and childhood acute lymphoblastic leukemia. *Int J Cancer* 2003; **105**:255-60.
- Spector L, Groves F, DeStefano F et al. Medically recorded allergies and the risk of childhood acute lymphoblastic leukaemia. *Eur J Cancer* 2004; **40**:579-84.
- Linet MS, McCaffrey LD, Humphrey RL et al. Chronic lymphocytic leukemia and acquired disorders affecting the immune system: a case-control study. *J Natl Cancer Inst* 1986; **77**:371-8.
- Zheng W, Linet MS, Shu XO et al. Prior medical conditions and the risk of adult leukemia in Shanghai, People's Republic of China. *Cancer Causes Control* 1993; **4**:361-8.
- Cooper GS, Kamel F, Sandler DP et al. Risk of adult acute leukemia in relation to prior immune-related conditions. *Cancer Epidemiol Biomarkers Prev* 1996; **5**:867-72.
- Bernstein L, Ronald RK. Prior medication use and health history as risk factors for non-Hodgkin's lymphoma: preliminary results from a case-control study in Los Angeles County. *Cancer Res* 1992; **52**:S5510-15.
- Fabbro-Peray P, Daures JP, Rossi JF. Environmental risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Languedoc-Roussillon, France. *Cancer Causes Control* 2001; **12**:201-12.
- Doody MM, Linet MS, Glass AG et al. Leukemia, lymphoma, and multiple myeloma following selected medical conditions. *Cancer Causes Control* 1992; **3**:449-56.
- Cartwright RA, McKinney PA, O'Brien C et al. Non-Hodgkin's lymphoma: case control epidemiological study in Yorkshire. *Leuk Res* 1988; **12**:81-8.
- Vineis P, Crosignani P, Sacerdote C et al. Haematopoietic cancer and medical history: a multicentre case control study. *J Epidemiol Community Health* 2000; **54**:431-6.
- Mack TM, Yu MC, Hanisch R et al. Pancreas cancer and smoking, beverage consumption, and past medical history. *J Natl Cancer Inst* 1986; **76**:49-60.
- Holly EA, Eberle CA, Bracci PM. Prior history of allergies and pancreatic cancer in the San Francisco Bay area. *Am J Epidemiol* 2003; **158**:432-41.
- Bueno de Mesquita HB, Maisonneuve P, Moerman CJ et al. Aspects of medical history and exocrine carcinoma of the pancreas: a population-based case-control study in the Netherlands. *Int J Cancer* 1992; **52**:17-23.
- Jain M, Howe GR, St Louis P et al. Coffee and alcohol as determinants of risk of pancreas cancer: a case-control study from Toronto. *Int J Cancer* 1991; **47**:384-9.
- Silverman DT, Schiffman M, Everhart J et al. Diabetes mellitus, other medical conditions and familial history of cancer as risk factors for pancreatic cancer. *Br J Cancer* 1999; **80**:1830-7.
- Schlehofer B, Blettner M, Preston-Martin S et al. Role of medical history in brain tumour development. Results from the international adult brain tumour study. *Int J Cancer* 1999; **82**:155-60.
- Ryan P, Lee MW, North B et al. Risk factors for tumors of the brain and meninges: results from the Adelaide Adult Brain Tumor Study. *Int J Cancer* 1992; **51**:20-7.
- Cicuttini FM, Hurley SF, Forbes A et al. Association of adult glioma with medical conditions, family and reproductive history. *Int J Cancer* 1997; **71**:203-7.
- Brenner AV, Linet MS, Fine HA et al. History of allergies and autoimmune diseases and risk of brain tumors in adults. *Int J Cancer* 2002; **99**: 252-9.
- Schwartzbaum J, Jonsson F, Ahlbom A et al. Cohort studies of association between self-reported allergic conditions, immune-related diagnoses and glioma and meningioma risk. *Int J Cancer* 2003; **106**:423-8.
- Milan T, Verkasalo PK, Kaprio J, Koskenvuo M. Lifestyle differences in twin pairs discordant for basal cell carcinoma of the skin. *Br J Dermatol* 2003; **149**:115-23.
- Ming ME, Levy R, Hoffstad O et al. The lack of a relationship between atopic dermatitis and nonmelanoma skin cancers. *J Am Acad Dermatol* 2004; **50**:357-62.
- Kölmel KF, Compagnone D. Melanom und Atopie. *Dtsch Med Wochenschr* 1988; **113**:169-71.
- Beral V, Evans S, Shaw H, Milton G. Cutaneous factors related to the risk of malignant melanoma. *Br J Dermatol* 1983; **109**:165-72.
- Synnerstad I, Nilsson L, Fredrikson M, Rosdahl I. Fewer melanocytic nevi found in children with active atopic dermatitis than in children without dermatitis. *Arch Dermatol* 2004; **140**:1471-5.
- Dai Q, Zheng W, Ji BT et al. Prior immunity-related medical conditions and pancreatic-cancer risk in Shanghai. *Int J Cancer* 1995; **63**:337-40.
- Dai Q, Zheng W, Ji BT et al. Prior immunity-related medical conditions and oesophageal cancer risk: a population-based case-control study in Shanghai. *Eur J Cancer Prev* 1997; **6**:152-7.