

Lifestyle effect on total IgE

Lifestyles have a cumulative impact on controlling total IgE levels

T. SHIRAKAWA, & K. MORIMOTO

Department of Hygiene and Preventive Medicine, School of Medicine, Osaka University, Japan

Recent studies have demonstrated an increasing number of cases of allergy in economically developed societies. Many of these allergic reactions are mediated by IgE antibodies whose levels are under genetic control. However, this large increase of allergy prevalence cannot be explained by genetic mutations; comprehensive lifestyles may also play roles in determining total IgE levels. Total IgE levels were determined from serum samples taken from 706 hard metal workers who responded to a questionnaire including 17 items related to physical and mental health practices. Five factors tending to normalize IgE upward and three tending to normalize IgE downward when we keep good lifestyles were extracted using MANOVA analysis. We therefore constructed a Health Practice Index in Allergic reactions (HPIA); eight physical and mental health practices were significantly ($P < 0.05$) associated with cumulative elevations or suppressions of total IgE levels when sex, age and environmental factors were controlled for. Multivariate analyses demonstrated a dramatic synergism (Relative Risk > 2.0 , $P < 0.05$) of *unhealthy* lifestyles determining a bipolar high risk for elevated or suppressed IgE levels which in turn may result in allergic diseases or immuno-suppression. Maintenance of *healthy* lifestyles may prove beneficial for reducing the prevalence of allergic disorders.

Key words: allergy; health practices; immunoglobulin E; lifestyle; multiple logistic analysis.

Accepted for publication 16 January 1991

IgE is unique among the immunoglobulins (Ig) in its relationship to the genesis of allergic diseases, such as bronchial asthma, dermatitis and rhinitis, in economically developed societies (22). Early interest was focused on the relationship of IgE levels to genetic backgrounds (19). A large number of cross-sectional studies (2, 6, 10, 12-15, 24, 30) have documented a variety of factors affecting IgE levels. These include sex (2, 10, 15, 30), race (24), age (2, 6, 10, 12-15, 24, 30) and smoking habits (6, 10, 12-14, 24). However, findings from this area of research continue to be controversial (3, 8). To control for the various factors which may influence findings at a single point in time in cross-sectional studies, Barbee et al. (3) conducted an 8-year

follow-up cohort study in Arizona, USA. This study, the results of which are also controversial, found that IgE levels in non-atopic subjects are neither age- nor sex-related, but that smoking is associated with higher IgE levels in males regardless of atopic status.

The discrepancies in results between the above studies have arisen, we believe, because the effects of "comprehensive lifestyles" on IgE levels have not been accounted for. Since the time Breslow et al. (5) demonstrated that lifestyles unquestionably play a role in determining age-adjusted mortality rates within the general population, much interest has been focused on the relationship of lifestyle to development of several chronic diseases, including coronary

Table 1
Subject profiles

	Exposure	No. cases	Age (yr)			
			< 30	30-39	40-49	> 50
Male	No	239	75	78	55	31
	Yes	331	84	89	84	70
Female	No	113	56	18	28	11
	Yes	23	1	2	15	5

heart disease, strokes and cancers (4). The determination of the relationship of blood pressure and serum cholesterol level to the etiology of cardiovascular diseases has also been a striking result of studies of how lifestyle can affect the biological mediators of health and disease (9). Although the prevalence of allergic diseases has doubled from a few percent to more than 10% within the last two decades (22), and the relationship of individual health practices - including smoking (6, 10, 12-14, 24), nutrition (25) and exposure to various types of stress (20) or environmental factors (air pollution, indoor pollution, occupational dust exposure and respiratory infections) (21, 28, 31) - to allergic diseases has been investigated, individual health practices have not been considered part of overall "comprehensive lifestyles" that are themselves possibly determinative of IgE levels.

The purpose of this study was therefore to determine the combined impacts of comprehensive lifestyles responsible for total IgE levels at any given life-stage while controlling for some confounding variables. This approach offers new insight into the dynamics of the relationship between IgE levels and lifestyles, and enables us to further protect ourselves from allergic diseases that are exhibiting an upward trend (22).

MATERIAL AND METHODS

Subjects and their work environment

A sample population of 733 subjects was selected from among workers 18 years of age or older at a hard metal plant (18, 26). Twenty-

seven (3.7% of the above) atopic subjects were excluded from participation because they had symptoms, positive histories of allergic diseases or positive skin reactivity identified during testing done prior to starting work in the plant. A total of 570 male and 136 female workers were available as subjects for the present study.

Details of the environmental studies conducted within the plant have been described in previous reports (18, 26). Briefly, during a 6-h period air samples of total dust and vapour were collected at intervals from the working zones, using a dust sampling pump (Dupont P-6000). The cobalt concentration was determined by atomic absorption spectrophotometry. The subject's duration of exposure was ascertained at individual interviews. Subject profiles are summarized in Table 1.

Serological analysis

Serum samples were collected from each of the subjects and frozen at -80°C until tests were conducted. Total serum IgE was determined in duplicate using Phadebas PRIST (2-6, 8, 12-14, 24, 30), a technique in which the most precise and specific measurements are too low (< 10 IU/ml) IgE levels (2, 3, 6, 8, 10, 12-15, 24, 30).

Questionnaire and data analysis

We designed a questionnaire composed of both physical and mental health-related items similar to that of Berkman & Breslow (5). After a series of preliminary studies conducted within the general population of Tokyo metropolitan area, 17 habit items from five major areas of health concern were collected in a questionnaire. These items were related to eating habits (regularity of eating, salt consumption, nutritional balance, eating breakfast and snacking), mental qualities (enjoying hobbies, feeling busy, subjective mental stress, life satisfaction), physical qualities (physical exercise, condition compared with that of 6 months ago), tastes (smoking status, alcohol consumption and tea or coffee

consumption) and basic way of living (working time, regularity of daily life, sleeping time). An obesity index was also calculated for each subject according to BMI (Body Mass Index) (7).

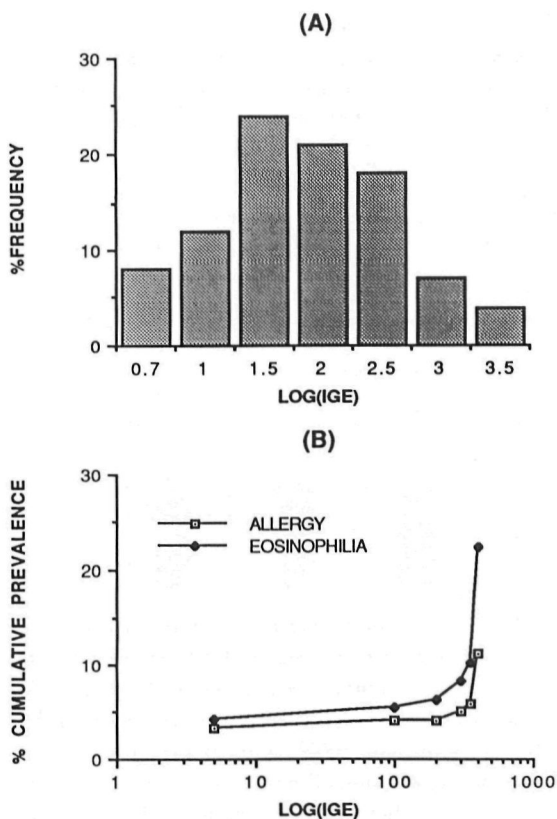


Fig. 1. A. Frequency distribution of log(IgE) for male subjects without hard metal exposure. Total IgE was determined by Pharmacia PRIST [2, 3, 6, 8, 10, 12–15, 24, 30]. A normal distribution was found after logarithmic conversion with a geometric mean of 43.5 IU/ml, slightly lower than that (45.5 IU/ml) of the female workers because of higher frequencies of younger female subjects. B. % cumulative prevalences of allergy (bronchial asthma, dermatitis, rhinitis and conjunctivitis) and eosinophilia in the non-exposed male subjects. Diagnoses were made using international criteria [22]. Abrupt increases of cumulative prevalence of allergy (from 5.2 to 11.2%) and eosinophilia (10.1 to 22.3%) in the atopic subjects with > 400 IU/ml, as well as significantly ($P < 0.05$) lower prevalences of them (2.3, 4.4%, respectively) in the IgE-suppressed subjects with < 5 IU/ml compared with those (4.2, 6.3%, respectively) of normal (5–400 IU/ml) subjects, warranted our determination of the cut-points for the high risk status in the multiple logistic analysis (see Table 3).

Subjects responded to the questionnaire during medical examinations. Incomplete answers, received from seven subjects, were eliminated from further analyses and response data were analyzed using the Osaka University ACOS-6 NEC computer system with the SPSSX (Statistic Package for Social Sciences extension, version 2.2) program, including Probit (multiple logistic analysis), oneway/polynominal (MANOVA) commands (27). The partial correlations for each of the 17 health practices with one another, while controlling for sex and age, were generally small, except those between regularity of daily life and eating patterns (regularity of eating breakfast, snacking) and between enjoying hobbies and some mental or physical qualities. Strong ($> 98\%$) questionnaire reliability was demonstrated in a pilot study of 54 workers in a branch plant who completed essentially the same questionnaire once and then again 2 months or a year later. The validity of collected data was evaluated by comparing answers received in the self-administration-questionnaire with those obtained following personal interviews with our staff. About 95% of respondents gave identical answers on the two occasions.

RESULTS

Serological analysis

Following logarithmic conversion, the distribution of log(IgE) for male subjects became Gaussian (Fig. 1A) with a mean log(IgE) of 1.72 IU/ml and a geometric mean of 52.5 IU/ml. A slight left skew is still apparent in the curve for female workers because of a higher frequency of younger individuals among them. The geometric means IgE for the non-exposed male (33.5 IU/ml) and female (32.5 IU/ml) subjects were consistent with those (25–35 IU/ml in this kit) established in previous studies (2, 3, 6, 8, 10, 12–15, 24, 30).

Effect of environmental exposure on total IgE levels

Hard metal (cobalt) exposure was associated with significantly ($P < 0.05$) higher total log

Table 2

Mean log(IgE) levels by lifestyle category in the non-exposed male subjects while controlling for age. Note that similar results were obtained in the exposed male subjects after controlling for exposure doses

		Healthy lifestyle		Unhealthy lifestyle	
	Health practice	Category	Mean log(IgE)	Category	Mean log(IgE)
1	Regularity of daily life	regular \$	1.63±0.83	irregular	1.63±0.85
2	Enjoying hobbies	yes \$	1.65±0.84	no	1.49±0.75
3	Feeling busy	no \$	1.48±0.97	yes	1.65±0.83
4	Physical exercise	≥ 2/wk (14)	1.64±0.81	≤ 1/wk	1.64±0.87
5	Alcohol consumption	not everyday (15)	1.53±0.84	everyday	1.77±0.83(*)
6	Smoking habits #	never (15)	1.58±0.91	present/former	1.69±0.76
7	Sleeping pattern	7-8 h (15)	1.66±0.83	≤ 6 h, ≥ 9 h	1.59±0.81
8	Regularity of eating	regular \$	1.65±0.86	irregular	1.59±0.80
9	Nutritional balance	good \$	1.65±0.68	poor	1.63±0.88
10	Eating breakfast	every morning (15)	1.63±0.82	not every morning	1.66±0.91
11	Tea or coffee	≤ 5 cups/day (16)	1.64±0.84	≤ 5 cups/day	1.60±0.85
12	Working pattern	≤ 10 h \$\$	1.69±0.83	> 9 h	1.47±0.83(*)
13	Subjective mental stress	mild \$\$	1.66±0.89	strong/weak	1.59±0.76
14	Condition change in last 6 mo	better/ no change \$\$	1.63±0.86	worse	1.64±0.68
15	Life satisfaction	good \$\$	1.62±0.81	poor	1.64±0.85
16	Snacking	no (15)	1.60±0.79	everyday/often	1.65±0.87
17	Salt consumption	good control \$	1.61±0.80	poor control	1.65±0.87

* $P < 0.05$, Student t test

() Determination of category. See references, (\$) dichotomized questions, (\$\$) on the basis of log(IgE) distribution
 # log(IgE) for those who formerly had smoked (1.87) were as high as those (1.73) determined for subjects still smoking. In our criteria, therefore, an old history of smoking was placed in the *poor* category.

(IgE) (1.64 ± 0.83 vs 1.83 ± 0.80) among the male subjects than was the non-exposed condition. However, there was no correlation between total IgE levels and duration ($r = 0.178$, $P = 0.11$) or intensity ($r = 0.149$, $P = 0.89$) of exposure. Among female subjects, no significant differences in IgE levels between exposure levels were found, although IgE levels were somewhat higher in the exposed group.

Lifestyle effect on total IgE levels

Questionnaire items each had 2 to 6 possible answers and each of these was categorized as typical of a lifestyle promoting *good* or *poor* health according to the criteria and method recommended by Berkman & Breslow (4) with slight modification on the basis of the IgE distribution (Table 2). Only a few factors (alcohol consumption and working time for non-exposed subjects, subjective mental stress for exposed subjects) were associated with significantly

($P < 0.05$) different serum total IgE as a function of *good* or *poor* category. However, subjects with good category responses were found to have each had higher or lower mean log(IgE) levels than had those with poor category responses after controlling for sex, age, exposure dose and other health practices. Five factors tending to normalize IgE upward (UNF): enjoying hobbies, working time, physical exercise, sleeping patterns and subjective mental stress, and three tending to normalize IgE downward (DNF): feeling busy, alcohol consumption and smoking habits, were extracted from a total of 18 items using MANOVA analysis (27) and were assigned dichotomized values of 0 (*poor*) or 1 (*good*), after holding confounders constant (Fig. 2).

To augment and clarify the cumulative effect of these two types of factors, we constructed a HIPA (Health Practive Index in Allergic reaction) composed of the above eight factors. Every respondent received a HPIA score between 0 and 8 based on the formula: HPIA = No. of

DNF + (5 - No. of UNF). Within each sex, a gradient of log (IgE) from high to low HPIA scores is apparent following classification into three categories (0-4, 5-6, 7-8).

A significant ($P < 0.05$) trend for total serum IgE to decrease with scores of the modified HPIA was identified within age strata among non-exposed subjects. There was also an evident, but non-significant ($P = 0.09$) tendency for serum IgE to decrease with age among non-exposed females. An age-related decline became

apparent when three categories of HPIA were controlled for. The same phenomena were demonstrated for the exposed subjects when some male workers in their third decade were excluded from analysis.

Further clarification of the effect of age on serum IgE was achieved with a oneway/polynomial analysis (27), which demonstrated a significant ($P < 0.05$) trend of linearity among male subjects with higher scores. In agreement with the results of the Arizona cohort study (12), sex-related differences in total IgE levels were not found within our population aged 20 years and older even after controlling for HPIA score.

Higher total IgE levels are often predictive of a subsequent development of allergic disease (2, 3, 6, 8, 10, 12-15, 19, 22, 24, 30), while low IgE levels may be related to the development of recurrent respiratory infections (17, 29) or to a higher prevalence of cancers (1, 11, 16). We therefore examined, using multiple logistic analysis (4), the role that the *unhealthy* categories of each lifestyle play in determining high risks for elevation or suppression of IgE levels. Seventeen health practices as well as three confounders (sex, age, cobalt exposure) were dichotomized and scored as 0 (low risk) or 1 (high risk).

The cutpoints of total IgE for high risk status (> 400 IU/ml or < 5 IU/ml) were determined as 1) 2 SD above or below mean levels of IgE in a general population established by Phadebas PRIST (6, 9), and 2) significantly more or significantly less likelihood of skin-test reactivity or allergic diseases and eosinophilia ($> 200/\text{mm}^3$) as previously reported (3, 14, 23) or in our subjects (Fig. 1B).

As shown in Table 3, four (smoking habit, alcohol consumption, regularity of daily life, nutritional balance) and six (subjective mental stress, sleeping pattern, working time, physical exercise, regularity of daily life, nutritional balance) health practices had substantial [relative risk (RR) = 1.1-1.8] but non-significant association with risk of elevated or suppressed IgE level, respectively. The RR ranged from 1.6 to 3.1, and cobalt exposure had the highest contribution to a risk of elevated IgE. Age and sex

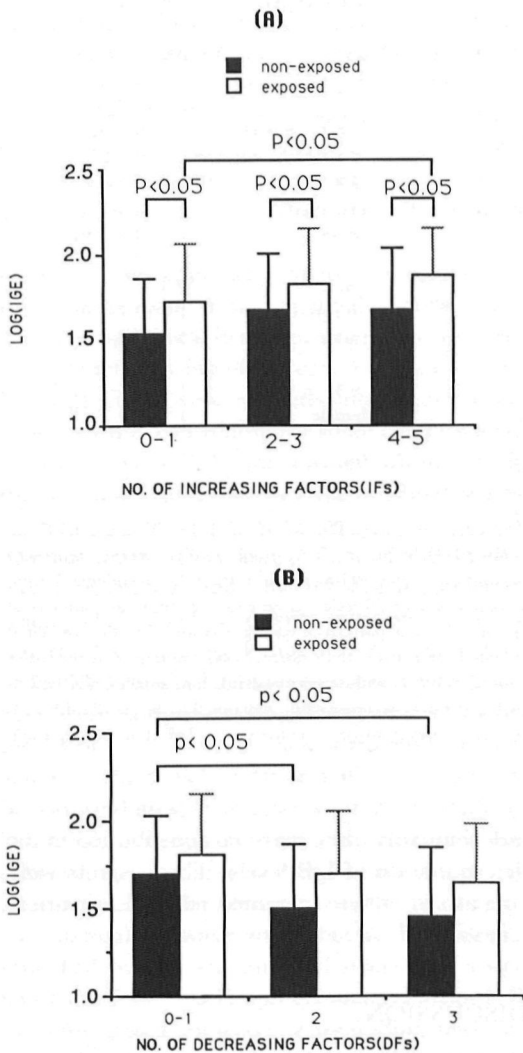


Fig. 2. Schematic presentation of the cumulative effects of health practice on total IgE levels: DNF (A) and UNF (B) were extracted from 17 items in the questionnaire using MANOVA analysis [27].

Table 3

Risk of elevated or suppressed IgE related to health practice, HPIA categories, age, sex, and hard metal exposure. Multiple logistic analysis. Cutpoints of total IgE for high risk status (> 400 IU/ml or < 5 IU/ml) were determined as 1) 2SD above or below mean levels of IgE in a general population established using Phadebas PRIST (2, 3), and 2) significantly higher or lower likelihood of skin-test reactivity, allergic diseases or eosinophilia as previously reported (31) or in our subjects (21).

		Elevated IgE (> 400 IU/ml)		Suppressed IgE (< 5 IU/ml)	
		High risk ^d	Relative risk ^a	High risk	Relative risk
Bipolar factors ^e			1.8 (0.8-3.0)		1.9 (0.8-3.3)
regularity of daily life	irregular		1.3 (0.4-3.6)	irregular	1.3 (0.4-4.0)
nutritional balance	poor		1.6 (0.4-4.4)	poor	1.8 (0.5-4.8)
Downward normalizing (DNF)			2.4 (1.2-4.4)*		
alcohol consumption	EVERYDAY		1.6 (0.5-2.2)	not everyday	1.0 (0.4-2.2)
skoking patterns	PRESENT/PAST		1.4 (0.5-2.5)	never	1.0 (0.3-2.2)
feeling busy	YES		1.0 (0.4-2.1)	no	NS
Upward normalizing (UNF)					2.6 (1.3-4.8)*
sleeping pattern	7-8 h		1.0 (0.4-1.9)	≤ 6 h, ≥ 9 H	1.6 (0.4-4.0)
physical exercise	≥ 2 wk		1.0 (0.3-1.9)	≤ 1 wk	1.2 (0.5-3.3)
working time	≤ 10 h		1.0 (0.4-1.8)	≥ 9 h	1.3 (0.4-4.0)
subjective mental stress	weak, mild		1.1 (0.4-2.0)	STRONG	1.2 (0.5-3.2)
enjoying hobbies	good		NS ^b	POOR	1.0 (0.4-2.0)
HPIA category ^c					
	high		1.0	low	1.0
	MEDIUM		1.8 (0.8-3.2)	MEDIUM	1.6 (0.7-2.9)
	LOW		6.3 (3.3-10.2)**	HIGH	3.6 (1.9-5.0)*
Age	< 35 yr		1.1 (0.4-3.2)	≥ 35 yr	1.1 (0.4-2.3)
Sex	male		1.1 (0.4-2.2)	female	1.1 (0.4-2.3)
Hard metal exposure					
in the exposed ^f	exposed		3.8 (2.0-5.3)**		
	high concentration		2.0 (1.0-3.8)*		
	high doses		2.0 (1.0-3.9)*		

^aOdds ratio between low-risk and high risk; ^bRelative risk < 1.0; ^clow (0-4), medium (5, 6), high (7, 8); ^dCapitals represent UNHEALTHY lifestyle; ^eHigh concentration was > 50 µg/m³ and high dose was 400 µg yr/m³ (20); ^f95 % confidence limits; * *P* < 0.05, ** *P* < 0.01; ^gPartial correlations demonstrated that among *unhealthy* lifestyle, those causing irregular patterns of daily life may suppress total IgE levels, while no clear factor except an irregular pattern of eating was found to be associated with a risk for elevated IgE. Suppressed IgE was found to be associated with lower than normal body weight. On the other hand, overweight subjects were likely to have elevated IgE levels, for 1) subjects with suppressed IgE had smaller (19.8±2.3, *P* < 0.01) mean BMI (7) than those within the normal BMI range (22.3±2.7) or those with elevated IgE levels (22.4±2.7), and 2) a higher prevalence (50 %) of obese men (index > 10 %) was found among subjects with elevated IgE than among the normal IgE group (39 %).

may not exert effect independently (RR = 1.1) on development of either risk status in the model used for the present study. Two factors (regularity of daily life, nutritional balance) had bipolar association with total IgE levels. In contrast, a strong increase in risk status associated with combinations of health practices (UNF, DNF and HPIA) and a dramatic enhancement of RR among HPIA categories confirm that health practices combined have cumulative impacts on IgE levels, while,

independently, they make no contribution to the determination of IgE levels. These results were similar to those obtained using univariate analyses.

DISCUSSION

Our first approach can be characterized as an assessment of the effect of antigen exposure on total IgE levels. This required individually quantitated IgE-relationships. For this reason,

we could not study subjects using tests with common airborne antigens such as mites or pollens because of our inability to determine to what extent and for how long each subject might previously have been exposed to them. We therefore chose a particular occupational population (hard metal workers). Hard metal exposure results in significant elevation of total IgE antibodies above normal in male subjects without any correlation to duration or intensity of exposure. Similar phenomena have been documented for reagins specific to some chemical agents (28). Thus, some environmental factors may elevate total IgE levels; this adjuvant effect of such factors in determining total IgE level might be due to damage to airway mucosa (31) or to long-term deposition of particles in the lung tissues with considerable adhesion of allergens, as is the case for diesel-exhaust particles (21).

Our second approach was to develop a questionnaire for evaluating individual lifestyles composed of individual health practices and to evaluate the relationship of scores to total IgE levels. Eight practices were extracted using univariate analysis while controlling for some confounders. A new index, HPIA, was created within which each of these health practices was weighted equally. Some of these practices are well known to increase (current smoking) (3, 6, 12-14) or decrease (mental stress) (20) IgE levels, and our results were consistent with those of previous reports. However, we found no significant effect of smoking on IgE levels when other health practices were controlled for. Discrepancies in the results of studies of the effect of smoking on IgE levels might therefore be due to differences in background lifestyle among populations studied. We think it necessary that in such studies the effect of age, sex and race should be considered after controlling for lifestyles. An age-related decline in total IgE was evident, but no difference in total IgE by sex was found: females had lower levels (32.5 vs 33.5 IU/ml geometric mean IgE in non-exposed subjects). This finding may reflect an antagonistic effect of the larger numbers of DNF and UNF for male subjects than for females. Under these conditions there was a significant trend for IgE to increase with HPIA

category. The results in exposed males were similar to those obtained from non-exposed subjects regardless of exposure dose. These results provide new evidence that "comprehensive lifestyles" have significant impact on total IgE levels even when sex, age and exposure dose are controlled for.

We found further support, using multiple logistic analysis, for the potent role of health practices in determining high risk for elevated (> 400 IU/ml) or suppressed IgE (< 5 IU/ml) levels. The RR (1.1-1.8) of these eight practices as well as of sex and age were too small to make independent contributions to increasing or decreasing total IgE levels and therefore the equal weighting assigned to each in the HPIA was warranted. In contrast, a dramatic synergism of unhealthy lifestyles (DNF, UNF, HPIA) was associated with IgE level elevations or suppressions into high risk status (RR > 2.0 , $P < 0.05$ in Table 3). This may account for the longitudinal changes in and the sudden development, exacerbation, disappearance or remission of allergic diseases. In applying our results to the prevention of allergic disorders, patient lifestyle as well as family histories and environmental conditions must first be determined. They should be advised to avoid the poor health practices considered in this study. Quitting drinking, for example, is as important as quitting smoking, and to make efforts to relax is important for decreasing total IgE.

Similar interest has been focused on the relationship between lifestyle and mortality risk for those chronic adult diseases for which each unhealthy practice has a *unipolar* potential to increase mortality risk (4, 5, 9). Previously, health practices had been thought to have *unipolar* potentials for inducing high risk of cancers (4, 5), cardiovascular diseases (9) or allergy (3, 6, 8, 10, 12-14, 20, 24, 25). Only nutritional intake had previously been discussed as a health practice related to *bipolar* induction of high risks for strokes (under-intake) or coronary heart diseases (over-intake) (9). The results of our study, however, suggest the new hypothesis that many health practices have *bipolar* potentials to increase or decrease total IgE levels as a function of lifestyle (see Table 3). This implies that even healthy lifestyles may have the potential to elevate or

suppress IgE levels. We have documented no cumulative effects of healthy lifestyles similar to those found for unhealthy lifestyles (UNF and DNF).

There are, however, two other possibilities of interpretation not excluded by our results: 1) a given health practice may decrease IgE in some individuals, while increasing it in others, or 2) a health practice may decrease or increase an individual's IgE level depending upon his or her lifestyle at a given age.

In conclusion, the present results suggest that IgE functions other than as a simple mediator of allergic reactions; it may be an immunologic determinant whose level can be used to assess an individual's "health" status.

It should be noted that this study's particular questionnaire items, its categorization of variables, its limitation of subjects to those aged 18-64 years, and its form of analysis may have influenced its findings and the determination of associations between lifestyle, hard metal exposure and IgE levels. Further work is therefore needed to corroborate and extend our findings. There is an urgent need to undertake extensive longitudinal studies using a well-designed questionnaire.

ACKNOWLEDGEMENTS

We authors thank Drs. N. Fujimura, M. Kato and S. Heki (Takatsuki Red Cross Hospital) for their support of our immunological studies, and Dr. Y. Kusaka (Department of Hygiene, Jichi Medical College) for his kind offer of environmental analysis. We also thank Prof. S. L. Breslow (Center for Health Promotion/Disease Prevention, UCLA), B. MacMahon (Department of Epidemiology, Harvard University) and B. Burrows (Department of Medicine, University of Arizona) for their encouragement of our studies.

REFERENCES

- Allegra J, Lipton A, Harway H, et al. Decreased prevalence of immediate hypersensitivity (atopy) in cancer population *Cancer Res* 36, 74, 1976.
- Barbee RA, Halonen M, Lewowitz M, Burrows B. Distribution of IgE in a community population sample. *J Allergy Clin Immunol* 68, 106-111, 1981.
- Barbee RA, Halonen M, Kaltenborn W, Lebowitz M, Burrows B. Longitudinal study of serum IgE in a community cohort. *J Allergy Clin Immunol* 79, 919-927, 1987.
- Berkman LF, Breslow L (eds.). *Health and ways of living*. Oxford University Press, NY, 1983.
- Breslow L, Enstrom J. Persistence of health habits and their relationship to mortality. *Prev Med* 9 460-466, 1980.
- Burrows B, Halonen M, Barbee RA, Lebowitz MD. The relationship of serum immunoglobulin E to cigarette smoking. *Am Rev Respir Dis* 24, 523-525, 1981.
- Burton BT, Foster WR, Hirsch J, Van Itallie TB. Health implication of obesity; an NIH consensus in Development Conference. *Int J Obesity* 9, 155-169, 1985.
- Cline MG, Burrows B. Distribution of allergy in a population sample residing in Tucson, Arizona. *Thorax* 44, 425-431, 1989.
- Dowber TR (ed.). *In Framingham study*. Harvard University Press, Cambridge, 1980.
- Friedhoff LR, Meyers DA, Marsh DG. A genetic epidemiologic study of human immune responsiveness to allergens in an industrial population. *J Allergy Clin Immunol* 73, 490-499, 1986.
- Galoppin L, Noirot C, Wastiaux JP, Scheinmann P, Papue J, Burtin C. Comparison between number of basophils, blood histamine, and histamine release in cancer and noncancer patients. *J Allergy Clin Immunol* 184, 501-506, 1989.
- Gerrard JW, Heiner DC, Ko CG, et al. Immunoglobulin levels in smokers and nonsmokers. *Ann Allergy* 44, 261-262, 1980.
- Grundbacher FJ, Massie FS. Levels of immunoglobulin G, A, M and E at various ages in allergic and non-allergic black and white individuals. *J Allergy Clin Immunol* 75, 651-655, 1985.
- Halonen M, Barbee AR, Lewowitz MD, Burrows B. An epidemiologic study of the interrelationships of total serum immunoglobulin E, allergy skin-test reactivity, and eosinophilia. *J Allergy Clin Immunol* 69, 221-228, 1982.
- Holford-Streven V, Warren P, Wong P, Manfreda J. Serum total immunoglobulin E levels in Canadian adults. *J Allergy Clin Immunol* 73, 516-522, 1982.
- Jacobs D, Hourii M, Landon J, Merrett TG. Circulating levels of immunoglobulin E in patients with cancer. *Lancet* ii, 1059-1061, 1982.
- Kanok JM, Steiberg P, Cassidy JT, et al. Serum IgE levels in patients with selective IgA deficiency. *Ann Allergy* 41, 220-223, 1978.
- Kusaka Y, Yokoyama K, Sera Y, et al. Respiratory diseases in hard metal workers; an occupational hygienic study in a factory. *Br J Ind Med* 43, 474-485, 1986.
- Marsh DM, Hsu SH, Hussain R, et al. Genetics of human immune response to allergens. *J Allergy Clin Immunol* 65, 322-332, 1980.
- Monjan AA, Collector MI. Stress-induced modulation of immune response. *Science* 196, 307-308, 1977.
- Muranaka M, Suzuki S, Kizumi K, et al. Adjuvant activity of diesel-exhausted particles for the production of IgE antibody in mice. *J Allergy Clin Immunol* 77, 616-623, 1986.
- O'Connor GT, Weiss ST, Speizer FE. In Gershwin ME, (ed.): *Bronchial asthma* pp. 3-18. Grune & Stratton, Orland CA, 1986.
- Pertonen L, Havu VK, Mattila L. Serum IgE in non-atopic adults and in dermatitis patients. *Allergy* 43, 152-158, 1988.

24. Rawle MA, Burr ML, Platts-Mills TAE. Long-term falls in antibodies to dust mite and pollen allergens in patients with asthma or hay fever. *Clin Allergy* 13, 409-417, 1983.
25. Reyes MA, Saravia NG, Watson RR, McMurray DN. Effect of moderate malnutrition on immediate hypersensitivity and immunoglobulin E levels in asthmatic children. *J Allergy Clin Immunol* 70, 94-100, 1982.
26. Shirakawa T, Kusaka Y, Fujimura, et al. Occupational asthma from cobalt sensitivity in workers exposed to hard metal dust. *Chest* 95, 29-37, 1989.
27. SPSSX User's Guide, 2nd ed. SPSS, Chicago IL, 1986.
28. Venables KM, Topping MD, Howe W, et al. Interaction of smoking and atopy in producing specific IgE antibody against a hapten protein conjugate. *Br Med J* 290, 201-204, 1985.
29. Welliver RC, Wong DT, Sun M, Middleton Jr E, Vanghan RS, Ogra PL. The development of respiratory syncytial virus-specific IgE and release of histamine in nasopharyngeal secretion after infection. *N Engl J Med* 305, 841-846, 1981.
30. Witting HJ, Belloit J, Fillippi ID, Royal G. Age-related serum immunoglobulin E levels in healthy subjects and in patients with allergic diseases. *J Allergy Clin Immunol* 66, 305-313, 1980.
31. Zetterstrom O, Osterman K, Machado L, Johansson SGO. Another smoking hazard: raised serum IgE concentration and increased risk of occupational allergy. *Br Med J* 283, 1215-1217, 1981.

Address:

Dr. T. Shirakawa

Nuffield Department of Clinical Medicine

John Radcliffe Hospital

Oxford OX3 9DU

England

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.