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## Effects of Gene-Environment Interactions on Cardiovascular Risk Factors in Chinese Adolescent Twins

C.J. Chen<sup>1</sup>, B.H. Cohen<sup>2</sup>, E.L. Diamond<sup>2</sup>, T.M. Lin<sup>1</sup>, J.S. Chen<sup>3</sup>

*<sup>1</sup>Institute of Public Health, National Taiwan University College of Medicine, Taipei, Taiwan; <sup>2</sup>Department of Epidemiology, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland; <sup>3</sup>Department of Clinical Pathology, National Taiwan University Hospital, Taipei, Taiwan*

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**Abstract.** A population-based sample of 73 male and 77 female monozygotic (MZ), and 41 male and 33 female dizygotic (DZ) Chinese adolescent twin pairs were studied to assess effects of gene-environment interactions of systolic blood pressure (SBP), diastolic blood pressure (DBP), serum cholesterol and triglyceride levels. Intrapair concordance in BP levels was found to be significantly associated with the interaction of zygosity and salty foods preference and also with that of zygosity and vegetable preference. A consistently positive and statistically significant association was observed between the intrapair difference in serum cholesterol and the interaction of zygosity and animal organ preference; while intrapair concordance in serum cholesterol was associated with the interaction of zygosity and milk consumption. Intrapair difference in serum triglycerides was associated with the interaction of zygosity and fish preference, and a significant association was also found between the intrapair concordance in serum triglycerides and the interaction of zygosity and sweets preference. These observations suggest that the impact of these environmental agents may be influenced by the genotype.

**Key words:** Blood pressure, Cholesterol, Triglycerides, Diet, Gene-environment interaction, Twins

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### INTRODUCTION

Based on family studies, McKusick [33] indicated environment and heredity to be equally important in determining blood pressure. Pickering [41] also reported that environmental

factors account for 33% to 67% of total blood pressure variance. Several studies on serum cholesterol level also revealed the influence of both genetic and environmental factors [6, 9,36]. What is important is not only whether there is a genetic and/or an environmental factor, but also how strong these factors are, how they interact with each other, and how such risk factors can be eliminated or their effects modified.

Numerous functional and structural proteins are involved in the vasoregulatory system and the whole spectrum of serum lipids absorption, transportation, metabolism and monitoring. A better understanding of cardiovascular disease (CVD) necessitates a detailed description of the genetic loci implicated and their mode of action. However, as organisms live in an environment, a biochemical or a genetic description alone is inadequate. We need to know, in addition, how genetically different individuals interact with different environments.

Classical twin studies on mechanical ability did show different genotype and environment interaction on motor skill [7,34] and in a twin study on a musical aptitude test Stafford [43] found that "twin pairs with different amounts of music lessons indicated higher heritability compared to twin pairs with the same amount of music lessons". Interaction seems to exist in many situations.

This report presents the results of a twin study aimed to assess the possible effects of gene-environment interactions on CVD risk factors: systolic blood pressure (SBP), diastolic blood pressure (DBP), serum cholesterol and triglycerides levels.

## MATERIALS AND METHODS

### Data Collection

Twin sampling, zygosity determination, and data collection procedures have been extensively described elsewhere in this issue [8]. Shortly, blood pressure, serum cholesterol and triglyceride levels, as well as life style, personality profile, family background and early experience were assessed in 73 male and 77 female MZ and in 41 male and 33 female DZ pairs of Chinese adolescent twins.

### Methods of Analysis

Interactive effects of environmental and genetic factors were assessed by three different methods: additive effect model which used continuous intrapair differences as data input, and binary multiple linear regression [21] and binary multiple logistic regression [14] which dealt with dichotomous intrapair concordance of twin pairs.

#### Additive Effect Model

$$D_i = \beta_1 d_{i1} + \beta_2 d_{i2} + \dots + \beta_j d_{ij} + \dots + \beta_k d_{ik} + \beta_{k+1} (d_{i1} \cdot Z_i) + \beta_{k+2} (d_{i2} \cdot Z_i) + \dots + \beta_{k+j} (d_{ij} \cdot Z_i) + \dots + \beta_{2k} (d_{ik} \cdot Z_i) + e_i$$

for  $i = 1, 2, \dots, n$  and  $j = 1, 2, \dots, k$

where  $D_i$  = intrapair difference in CVD risk factor of the  $i^{\text{th}}$  twin pair;  
 $d_{ij}$  = intrapair difference in the  $j^{\text{th}}$  environmental factor of the  $i^{\text{th}}$  twin pair;  
 $Z_i$  = zygosity of the  $i^{\text{th}}$  twin pair: 0 for MZ and 1 for DZ;  
 $e_i$  = random error of the  $i^{\text{th}}$  twin pair.

Under this model, interaction terms (eg,  $d_{ij} \cdot Z_i$ ) were of non-zero value only when the intrapair difference in the  $j^{\text{th}}$  variable (ie,  $d_{ij}$ ) was non-zero and the zygosity of the twin pair was DZ. Intrapair differences of all related host and environmental factors were included in the regression equation, but only those interactions between zygosity and intrapair differences in dietary preference and beverage consumption were included.

As two twins of a given pair were randomized into two different groups, the intrapair differences in dependent variables might be positive, negative, or zero. The mean intrapair differences in CVD risk factors were thus zero for both MZ and DZ twins. Under this additive effect model, the main effect of zygosity on intrapair differences in CVD risk factor cannot be evaluated directly. However, the directionality of the association between CVD risk factor and environmental factor is preserved. The effect of intrapair difference in the  $j^{\text{th}}$  environmental factor for MZ twins was estimated by  $\beta_j$ , while the effect for DZ twins was estimated by both  $\beta_j$  and its interaction term with zygosity,  $\beta_{k+1}$ .

**Binary Multiple Linear Regression**

This model, employed to assess the effects of zygosity, environmental factors and their interactions simultaneously, is as follows:

$$C_i = \beta_0 + \beta_1 Z_i + \beta_2 c_{i1} + \beta_3 c_{i2} + \dots + \beta_{j+1} c_{ij} + \dots + \beta_{k+1} c_{ik} + \beta_{k+2} (c_{i1} \cdot Z_i) + \beta_{k+3} (c_{i2} \cdot Z_i) + \dots + \beta_{k+j+1} (c_{ij} \cdot Z_i) + \dots + \beta_{2k+1} (c_{ik} \cdot Z_i) + e_i$$

for  $i = 1, 2, \dots, n$  and  $j = 1, 2, \dots, k$

- where  $C_i$  = intrapair concordance in CVD risk factor of the  $i^{\text{th}}$  twin pair: 0 for concordant and 1 for discordant;
- $c_{ij}$  = intrapair concordance in the  $j^{\text{th}}$  environmental factor of the  $i^{\text{th}}$  twin pair: 0 for concordant and 1 for discordant;
- $Z_i$  = zygosity of the  $i^{\text{th}}$  twin pair: 0 for MZ and 1 for DZ;
- $e_i$  = random error of the  $i^{\text{th}}$  twin pair.

The main effect of zygosity was determined by the estimate of  $\beta_1$ ; the main effect of  $j^{\text{th}}$  environmental factor was determined by estimates of  $\beta_j$ ; and the interactive effect of zygosity and the  $j^{\text{th}}$  environmental factor was determined by the estimate of  $\beta_{k+2}$ .

**Binary Multiple Logistic Regression**

This model, employed to assess the possible non-linear effects of zygosity, environmental factors and their interactions on dependent variables, is as follows:

$$\ln(P_i/Q_i) = \beta_0 + \beta_1 Z_i + \beta_2 c_{i1} + \beta_3 c_{i2} + \dots + \beta_{j+1} c_{ij} + \dots + \beta_{k+1} c_{ik} + \beta_{k+2} (c_{i1} \cdot Z_i) + \beta_{k+3} (c_{i2} \cdot Z_i) + \dots + \beta_{k+j+1} (c_{ij} \cdot Z_i) + \dots + \beta_{2k+1} (c_{ik} \cdot Z_i) + e_i$$

for  $i = 1, 2, \dots, n$  and  $j = 1, 2, \dots, k$

- where  $P_i$  = probability that the  $i^{\text{th}}$  twin pair was discordant in the CVD risk factor and  $Q_i = 1 - P_i$ ;
- $c_{ij}$  = intrapair concordance in the  $j^{\text{th}}$  environmental factor of the  $i^{\text{th}}$  twin pair: 0 for concordant and 1 for discordant;
- $Z_i$  = zygosity of the  $i^{\text{th}}$  twin pair: 0 for MZ and 1 for DZ;
- $e_i$  = random error of the  $i^{\text{th}}$  twin pair.

or

$$P_i = \frac{e^{\beta_0 + \beta_1 Z_i + \dots + \beta_{k+1} c_{ik} + \beta_{k+2} (c_{i1} \cdot Z_i) + \dots}}{1 + e^{\beta_0 + \beta_1 Z_i + \dots + \beta_{k+1} c_{ik} + \beta_{k+2} (c_{ij} \cdot Z_i) + \dots}}$$

The main effect of zygosity was determined by the estimate of  $\beta_1$ ; the main effect of the  $j^{\text{th}}$  environmental factor was determined by the estimate of  $\beta_j$ , and the interactive effect of zygosity and  $j^{\text{th}}$  environmental factor was determined by the estimate of  $\beta_{k+2}$ .

**RESULTS**

**Additive Effect Model**

Table 1 presents the multiple correlation coefficients and the standardized regression coefficients of each interaction variable included in the stepwise multiple regression

analyses of intrapair differences in DBP, SBP, cholesterol and triglyceride levels of 224 adolescent MZ and DZ twins. After all the independent variables were included in the regression analyses of BP intrapair differences, the multiple correlation coefficients were 0.72 for SBP and 0.58 for DBP in males, and 0.76 for SBP and 0.78 for DBP in females.

Intrapair differences in SBP and DBP were significantly associated with some interaction terms. In females, SBP was negatively associated with zygosity  $\times$  sweet food preference, while DBP was positively associated with zygosity  $\times$  egg preference. In males, SBP was negatively associated with zygosity  $\times$  vegetable preference and with zygosity  $\times$  soft drinks consumption. In females, a positive association was found between DBP and zygosity  $\times$  tea consumption. In both males and females, DBP was negatively associated with zygosity  $\times$  alcoholic beverage consumption.

After including all the independent variables in the multiple regression analysis of intrapair difference in cholesterol level, the multiple correlation coefficients were 0.91 for males and 0.75 for females. The multiple correlation coefficients between intrapair difference in triglyceride level and all the independent variables were 0.86 for males and 0.79 for females.

Intrapair differences in cholesterol levels in males were associated with interactions of zygosity and intrapair differences in four dietary preferences: sweet foods, animal organs, eggs and vegetables. These associations were positive except for zygosity  $\times$  vegetable preference. In females, cholesterol was positively associated with zygosity  $\times$  animal organ preference. In males, cholesterol was positively associated with zygosity  $\times$  consumption of soft drinks, and negatively associated with zygosity  $\times$  tea and alcoholic beverages. In females, a positive association was found between cholesterol and zygosity  $\times$  milk consumption.

Intrapair difference in triglyceride level was associated with interactions of zygosity and intrapair differences in preferences for sweet foods, fried foods, fish and vegetables in males. These associations were positive except for vegetable preference. In females, positive associations between triglyceride level and zygosity  $\times$  fish preference, milk and soft drink consumption were observed. A negative association was observed between triglyceride level and zygosity  $\times$  tea consumption, which reached significance, however, only in males.

### Binary Multiple Regression Analyses

Table 2 shows the results of stepwise binary multiple regression analyses of concordance in DBP. Based on the binary multiple regression model, concordance in DBP was significantly associated with concordance in height, calcium level, exercise, salty food preference, and sweet food preference; and interactions of zygosity and concordance in milk consumption, salty food preference, fried food preference and vegetable preference, respectively.

The binary multiple logistic regression analysis of concordance in DBP also had a similar result. Significant associations were found between concordance in DBP and concordance in height, calcium level, exercise, salty food preference, and sweet food preference. Concordance in DBP was also associated with interactions of zygosity and concordance in milk consumption, salty food preference, fried food preference and vegetable preference.

Table 3 presents the stepwise binary multiple regression analyses of concordance in SBP. Based on binary multiple linear regression model, concordance in SBP was asso-

Table 1 - Multiple Regression Analysis of Twin Intrapair Differences in Cardiovascular Risk Factors Based on the Additive Effect Model

Independent variables	Male pairs			Female pairs				
	SBP	DBP	Cholest.	Triglyc.	SBP	DBP	Cholest.	Triglyc.
	0.72	0.58	0.91	0.86	0.76	0.78	0.75	0.79
	Multiple correlations							
	Standardized regression coefficients							
<b>Interaction variables</b>								
Zygoty x dietary preference								
Sweet foods	0.24	0.20	0.55**	0.39**	- 0.46*	- 0.04	- 0.02	0.16
Salty foods	0.13	0.13	0.00	0.27	0.27	0.14	0.05	0.06
Fried foods	0.10	0.16	0.30	0.83**	0.46	0.06	0.53	0.14
Meat	- 0.08	- 0.03	- 0.08	0.08	0.03	0.31	0.23	0.04
Fish	0.45	0.30	- 0.02	0.68**	0.07	0.26	0.18	0.50*
Animal organs	0.19	- 0.08	0.38**	0.09	0.01	0.21	0.68**	0.24
Eggs	0.35	0.28	0.42**	- 0.15	0.02	0.47*	0.26	0.04
Vegetables	- 0.67**	- 0.41	- 0.57**	- 0.54**	- 0.19	- 0.02	- 0.07	- 0.33
Zygoty x beverage consumption								
Milk	0.08	0.10	- 0.13	0.11	- 0.06	- 0.22	0.32*	0.50**
Soft drinks	- 0.51**	0.14	0.37**	- 0.07	0.07	0.03	0.06	0.34**
Tea	- 0.15	- 0.17	- 0.26**	- 0.19**	0.01	0.48**	0.30	- 0.15
Coffee	- 0.13	- 0.04	0.18	0.08	0.06	0.17	0.06	0.24
Alcoholic beverages	0.15	- 0.45**	- 0.64**	- 0.07	- 0.10	- 0.71**	- 0.09	0.12

\* P &lt; 0.05; \*\* P &lt; 0.01.

Table 2 - Stepwise Binary Multiple Regression Analyses of Twin Intrapair Concordance in Diastolic Blood Pressure

	Binary multiple linear regression <sup>1</sup>		Binary multiple logistic regression <sup>2</sup>	
	Regression coefficient	95% confidence limits of adjusted difference <sup>3</sup> in concordance rate	Regression coefficient	95% confidence limits of adjusted odds ratio <sup>4</sup> in concordance rate
Height	0.103*	- 0.01 - 0.22	0.497*	1.02 - 2.65
Weight	- 0.100	- 0.22 - 0.02	- 0.360	0.46 - 1.06
Serum calcium level	0.112*	0.01 - 0.21	0.492*	1.07 - 2.51
Neuroticism scale	- 0.074	- 0.19 - 0.04	- 0.336	0.46 - 1.10
Exercise	0.100*	0.00 - 0.20	0.703*	1.30 - 3.13
Sweet food preference	0.110*	0.01 - 0.21	0.600*	1.11 - 3.00
Salty food preference	0.186	0.05 - 0.32	1.546*	2.55 - 8.63
Vegetable preference	- 0.104	- 0.23 - 0.02	- 0.400	0.37 - 1.23
Interaction terms <sup>5</sup>				
Zygoty x milk consumption	0.168*	0.00 - 0.33	0.662*	1.06 - 3.55
Zygoty x salty food preference	0.249	0.02 - 0.48	1.129*	1.28 - 7.49
Zygoty x vegetable preference	0.197*	0.00 - 0.42	1.342*	1.61 - 9.10
Zygoty x fried food preference	- 0.180*	0.02 - 0.37	1.023*	1.47 - 5.27
Zygoty x egg preference	0.210	- 0.39 - 0.03	- 0.204	0.37 - 1.81

1. Dichotomous (concordant/discordant) independent variables were included in the stepwise regression equation if their F-values to enter the equation exceeded 1.65 ( $P < 0.20$ ).
2. Dichotomous (concordant/discordant) independent variables were those included in the stepwise binary multiple linear regression analyses.
3. The difference between concordance in dependent variable of twins who were concordant in a specific independent variable and that of twins who were discordant in that independent variable.
4. The ratio between concordance in dependent variable of twins who were concordant in a specific independent variable and that of twins who were discordant in that independent variable.
5. Interaction term was the product of zygoty (0 if MZ and 1 if DZ) and concordance in dietary preference or beverage consumption.

\* Regression coefficient was significantly different from zero with a P value at least less than 0.05.

Table 3 - Stepwise Binary Multiple Regression Analyses of Twin Intrapair Concordance in Systolic Blood Pressure

	Binary multiple linear regression		Binary multiple logistic regression	
	Regression coefficient	95% confidence limits of adjusted difference in concordance rate	Regression coefficient	95% confidence limits of adjusted odds ratio in concordance rate
Height	0.105	- 0.01 - 0.22	0.391*	1.01 - 2.17
Ponderosity	- 0.092	- 0.23 - 0.05	- 0.319	0.50 - 1.05
Serum uric acid	0.141*	0.03 - 0.26	0.434*	1.07 - 2.24
Animal organ preference	- 0.125	- 0.27 - 0.02	- 0.413	0.43 - 1.02
Egg preference	- 0.097	- 0.24 - 0.04	- 0.315	0.48 - 1.11
Tea consumption	- 0.107	- 0.25 - 0.04	- 0.394	0.43 - 1.06
Milk consumption	0.122*	0.01 - 0.23	0.426*	1.06 - 2.20
Interaction terms				
Zygosity x salty food preference	0.250*	0.04 - 0.46	0.745*	1.05 - 4.21
Zygosity x vegetable difference	0.236*	0.06 - 0.41	0.725*	1.17 - 3.65
Zygosity x tea consumption	0.221*	0.03 - 0.41	0.664*	1.09 - 3.46

See notes to Table 2.

Table 4 - Stepwise Binary Multiple Regression Analyses of Twin Intrapair Concordance in Serum Cholesterol

	Binary multiple linear regression		Binary multiple logistic regression	
	Regression coefficient	95% confidence limits of adjusted difference in concordance rate	Regression coefficient	95% confidence limits of adjusted odds ratio in concordance rate
Zygoty	0.140	- 0.02 - 0.30	0.388	0.89 - 2.45
Height	0.122*	0.02 - 0.23	0.570*	1.14 - 2.74
Serum calcium level	0.111*	0.01 - 0.21	0.410*	1.03 - 2.21
Sociability scale	- 0.095	- 0.20 - 0.01	- 0.297	0.50 - 1.10
Salty food preference	0.121*	0.00 - 0.24	0.490*	1.02 - 2.60
Fried food preference	0.169*	0.01 - 0.33	- 0.435	0.03 - 12.17
Fish preference	- 0.104	- 0.21 - 0.00	- 0.337	0.46 - 1.11
Vegetable preference	0.159*	0.05 - 0.27	0.668*	1.28 - 2.97
Milk consumption	- 0.111	- 0.23 - 0.01	- 0.385	0.38 - 1.21
<b>Interaction terms</b>				
Zygoty x milk consumption	0.242*	0.02 - 0.46	1.046*	1.27 - 6.39
Zygoty x fried food preference	0.246*	0.00 - 0.49	0.523	0.09 - 31.73

See notes to Table 2.

Table 5 - Stepwise Binary Multiple Regression Analyses of Twin Intrapair Concordance in Serum Triglycerides

	Binary multiple linear regression		Binary multiple logistic regression	
	Regression coefficient	95% confidence limits of adjusted difference in concordance rate	Regression coefficient	95% confidence limits of adjusted odds ratio in concordance rate
Zygosity	0.361*	0.15 - 0.57	1.016*	2.58 - 2.96
Height	0.143*	0.03 - 0.26	0.469*	1.11 - 2.31
Ponderosity	0.111	- 0.00 - 0.23	0.307	0.97 - 1.91
Serum calcium level	0.127*	0.01 - 0.24	0.392*	1.05 - 2.08
Neuroticism scale	0.198*	0.08 - 0.32	0.585*	1.26 - 2.56
Sleeping hours	- 0.112	- 0.23 - 0.01	- 0.305	0.52 - 1.05
Meat preference	- 0.082	- 0.24 - 0.07	- 0.283	0.45 - 1.27
Interaction terms				
Zygosity x sweet food preference	0.234*	0.03 - 0.44	0.659*	1.07 - 3.49
Zygosity x meat preference	- 0.210	- 0.48 - 0.06	- 0.461	0.28 - 1.42
Zygosity x tea consumption	- 0.163	- 0.36 - 0.04	- 0.470	0.36 - 1.09

See notes to Table 2.

ciated with concordance in milk consumption and uric acid level, and also with interactions of zygosity and salty food preference, vegetable preference and tea consumption, respectively.

Similar results were observed in the binary multiple logistic regression analysis. Concordance in SBP was associated with concordance in milk consumption and uric acid level and interactions between zygosity and salty food preference, vegetable preference and tea consumption, respectively. Although not significant in linear regression analysis, the association between concordance in height and SBP was significant in logistic regression analysis.

Table 4 illustrates the binary multiple regression analyses of concordance in cholesterol level. Based on binary multiple linear regression model, concordance in cholesterol level was associated with several independent variables: concordance in height, calcium level, preferences for salty food, fried food and vegetable; and interactions of zygosity and concordance in milk consumption and fried food preference.

### Binary Multiple Logistic Regression

In this analysis too, concordance in cholesterol level was associated with concordance in height, calcium level, salty food preference and vegetable preference, and also with interaction of zygosity and milk consumption. Although significant in linear regression analysis, the associations for concordance in fried food and its interaction with zygosity were not significant in logistic regression analysis.

Based on binary multiple linear regression model, concordance in triglyceride level (Table 5) was associated with zygosity, concordance in height, neuroticism and calcium level, and the interaction between zygosity and sweet food preference. Similar results were found in the binary multiple logistic regression analysis. Significant associations were found between concordance in triglyceride level and several independent variables: zygosity, concordance in height, neuroticism and calcium level, and the interaction between zygosity and sweet food preference.

## DISCUSSION

A significant interactive effect on blood pressure levels was found between zygosity and preferences for salty foods and vegetables. In other words, cotwins discordant in salty food preference (or vegetable preference) will more likely be discordant in blood pressure if they are DZ than if they are MZ. This finding is consistent with those of several studies which have shown a significant impact of interactions of environmental and genetic factors on blood pressure, eg, with regard to sodium intake and genetic susceptibility.

Studies of experimentally induced hypertension in animals have identified several mechanisms by which excessive sodium intake might increase vascular resistance and arterial pressure; these include structural changes in blood vessels, autoregulation of blood flow, alteration in trans-membrane ionic exchange in vascular muscle, salt-sensitive factors, and facilitation of sympathetic nervous system activity [5,11,18,20,22,24,45]. Moreover, several studies have revealed that, in animals, genotype is an important determinant of the vascular resistance and blood pressure response to excessive salt. Animals predisposed to hypertension developed increased vascular resistance and arterial pressure during high-salt diets, while animals without this predisposition did not [2,15,17].

Experiments on normotensive persons have shown that compensatory neurohumoral adjustment normally prevents an increase in vascular resistance during high dietary sodium intake [1,27,29,44]. Although normotensive subjects responded to high-salt diet with decreased vascular resistance, it seems likely that excessive sodium intake might produce a different pattern of vascular response in subjects with hypertension, possibly because of predisposing factors that might impair compensatory adjustment or exaggerate vasoconstrictor influences [30].

Epidemiological studies also provide some clue to the possible existence of an interaction of genetic predisposition with sodium intake. Some studies indicate an association between excessive sodium intake and the prevalence of hypertension [16,20,23,35,38,39,42,45]. However, other studies did not find significant correlations between elevated blood pressure and salt intake or urinary salt excretion [19,28,37]. It was found that correlation between blood pressure and sodium excretion was inversely related for those with a blood pressure of 175/115 mmHg or greater. In subjects with a blood pressure of 160/85 mmHg or less, sodium excretion was directly correlated with blood pressure [4].

The effects of interaction of genotype and sodium intake on the blood pressure levels were described by Page [40]: "Human populations undoubtedly vary in their genetic susceptibility to hypertension... One powerful determinant is habitual sodium intake. When all individuals in a population are habitually using very small amounts of sodium, blood pressure does not rise with age, and hypertension is virtually absent. When all members of the population are ingesting very large amounts of sodium, a high percentage, reflecting the maximum number of susceptible individuals, develop hypertension. Between these two extremes, the relationship between blood pressure and sodium intake is difficult to perceive because of wide variation in genetic susceptibility, and other types of 'noise' introduced by other variables". A possible parallel is found in the observations in this study: an interaction between zygosity and vegetable preference in relation to blood pressure. The precise mechanism involved requires further study.

The analysis of the interactive effects of genetic and environmental factors on serum cholesterol and triglyceride levels showed some interesting results. Under the additive effect model, a consistently positive, statistically significant relationship was found between cholesterol level and the interaction of zygosity and animal organ preference. The effect of the interaction of zygosity and milk consumption on serum cholesterol level also attained statistical significance in the binary multiple regression analyses.

With respect to the serum triglyceride levels, the interaction between zygosity and fish preference was positively associated with the levels under the additive effect model, while a significant interaction was found between zygosity and sweet food preference by all three methods applied.

Several cross-cultural studies of diet and plasma lipid levels show a significant association of serum cholesterol with dietary cholesterol and saturated fatty acid content and of serum triglyceride with saturate fatty acid consumption [13]. Berenson [3], using individual rather than group data, also showed a positive correlation between serum level of cholesterol and dietary content of cholesterol and saturated fatty acids. However, other studies could not find any relationship between serum cholesterol and diet [26,47].

Experimental studies on the human response to dietary manipulation suggest significant constitutional variability in the response of serum cholesterol to diet [12,25,

31,46]. In other words, while there was a mean decrease in serum cholesterol of groups when the diet was changed to one low in saturated fat and cholesterol, those individuals whose initial cholesterol levels were higher showed the most response to dietary manipulation, and those individuals whose initial cholesterol levels were normal responded to a lesser degree or did not respond at all. Experimental animal studies of the effects of diet and heredity on serum lipid levels also indicated constitutional differences in the response of serum lipid levels to dietary manipulation [10,32].

Consistent with the observations of other investigators, the findings of this study also showed significant interactive effects of genetic and environmental factors on serum cholesterol and triglyceride levels. However, the specific mechanism involved in this relationship is still unclear.

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**Correspondence:** Dr. Chien-Jen Chen, Institute of Public Health National Taiwan University College of Medicine, Taipei, Taiwan 100.