# Relation of low-grade inflammation and endothelial activation to blood pressure in obese children and adolescents

**Anhelli Syrenicz [1], Barbara Garanty-Bogacka [2], Małgorzata Syrenicz [2], Aneta Gębala [2], Grażyna Dawid [3] & Mieczysław Walczak [3]**

[1] Department of Endocrinology, Arterial Hypertension, and Metabolic Diseases, Pomeranian Medical University, Szczecin, Poland
[2] Independent Laboratory of Children's Diseases, Pomeranian Medical University, Szczecin, Poland,
[3] Department of Children's Diseases, Pomeranian Medical University, Szczecin, Poland

*Correspondence to:* Anhelli Syrenicz
Department of Endocrinology, Arterial Hypertension, and Metabolic Diseases, Pomeranian Medical University
4 Arkońska Street, 71-455 Szczecin, POLAND
PHONE: +48 91 4316241; FAX: +48 91 4316243
EMAIL: anhelli@asymed.ifg.pl

*Submitted: July 1, 2006* *Accepted: July 17, 2006*

*Key words:* **inflammation; endothelial activation; blood pressure; obesity; children**

Neuroendocrinol Lett 2006; **27**(4):459–464 **PMID:** 16891995 NEL270406A19  **www.nel.edu**

## Abstract

**OBJECTIVE:** To determine the role of low-grade, systemic inflammation and endothelial activation in the modulation of blood pressure (BP) independently of other traditional risk factors in obese children and adolescents.
**DESIGN:** We surveyed 281 obese subjects, aged 6–18 years to investigate the relationship of serum inflammation and endothelial activation markers and blood pressure.
**MEASUREMENTS**: Clinical variables, indices of obesity, ambulatory 24-h blood pressure and serum concentrations of C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-1 β (IL-1 β), intercellular cell adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), glucose and insulin. HOMA IR was used as a marker of insulin resistance (IR).
**RESULTS:** CRP, IL-6, IL-1 β, and ICAM-1 correlated significantly with mean 24-h systolic BP, whereas CRP and IL-6 was positively correlated with mean 24-h diastolic BP. Multiple regression analysis showed that serum IL-6 ($P < .001$) concentration, HOMA IR ($P < .01$), and waist to hip ratio ($P < .05$) were the significant determinants of systolic BP, whereas CRP ($P < .05$) level was the only predictor of diastolic BP. There were no significant associations of cell adhesion molecules with BP.
**CONCLUSIONS:** These results indicate that low-grade inflammation may play a role in the modulation of arterial BP relatively early in life.

ORIGINAL ARTICLE

## Introduction

Hypertension is a major health problem in adults, and contributes to cardiovascular disease. In addition, it is now recognized that the origins of hypertension are rooted in the young. Children and adolescents with blood pressure (BP) levels in the higher range of the BP distribution are at risk of developing hypertension and cardiovascular disease as young adults [21]. Obesity is a leading risk factor for essential hypertension but the mechanism involved in the development of obesity-related hypertension have not been clearly identified [7,10,11,19,25]. It is now clear that adipose tissue secretes various bioactive substances including leptin, tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) and adiponectin, and that dysregulation of these adipocytokines directly contributes to obesity-related disorders [10,20,26].

It is commonly accepted that long term impact of proatherogenic factors on vascular endothelium results in chronic, subclinical inflammation with a consequent rise in vascular and plasma concentrations of several acute-phase reactans such as IL-6 [24]. Persons with hypertension who are free of any other disorders have higher circulating levels of intercellular cell adhesion molecule-1 (ICAM-1), IL-6, TNF-α, and fibrinogen than non-hypertensive individuals, supporting a possible role of hypertension as a proinflammatory stimulus [5,16]. It has been suggested that a rise in blood pressure activates a vicious cycle, causing chronic inflammation of the endothelium, which in turn might be responsible for a further damage of endothelium and worsening of BP control. In addition, several metabolic abnormalities including insulin resistance (IR), dyslipidemia, type 2 diabetes, and obesity cause endothelial inflammation, and through this mechanism can cause a rise in arterial blood pressure [2,18]. There is growing evidence that proinflammatory cytokines such as IL-6, interleukin-1 β (IL-1 β), and TNF-α affect arterial BP control [8,23]. These results suggest that chronic, low-grade inflammation is a link between cardiovascular risk factors and hypertension, and may act as an independent determinant of arterial blood pressure. However, the relationship of inflammation and endothelial activation markers with blood pressure has never been investigated in obese children and adolescents.

The purpose of this study was to determine if BP level was associated with serum inflammatory markers and soluble cell adhesion molecules in a relatively large sample of obese children and adolescents.

## Material and methods

The study was conducted in 281 obese children and adolescents (151 boys and 130 girls), aged 6–18 y. Obesity was recognized on the basis of BMI greater than 97th percentile for age and sex according to the percentile charts for Warsaw population of children and adolescents [22]. None of the children had acute or chronic infections, cancers, autoimmunological diseases, hormonal abnormalities as well as hepatic or renal dysfunction. A positive family history of arterial hypertension (AH) was determined by parental report of hypertension in a first-degree relative.

Anthropometric measurements (weight, height, waist and hip circumferences) were performed using standarized methods and devices [22]. BMI and waist to hip ratio (WHR) were calculated. Since BMI changes with age, the BMI-SD score was also calculated. Measurement of body composition was performed by means of bioelectrical impedance (Bioelectrical Impedance Analyzer Tanita 131, Japan) with an applied current of 0.8 mA at a fixed frequency of 50 kHz.

Ambulatory blood pressure monitoring was performed using Mobil-O-Graph device, which uses the oscillometric method. Each patient was attached to the device for 24 h during a normal activity. The patients and parents were instructed to avoid vigorous arm movements during blood pressure measurements. The cuff was attached to the patient's left arm and chest electrodes were affixed by a skilled technician. Systolic and diastolic blood pressures were measured with an interval of 60 min between $23^{00}$ h and $07^{00}$ h, and 30 min between $07^{00}$ and $23^{00}$h. The data were edited to a limited extent, deleting all readings of 0, and readings where the difference between the systolic and diastolic blood pressures was <10 mm Hg.

Blood samples were obtained in the morning after an overnight fast. Circulating IL-6, IL-1 β, ICAM-1 and vascular cell adhesion molecule-1 (VCAM-1) levels were determined by ELISA with the use of the Quantikine high-sensitivity kit (R & D Systems, Minneapolis, MN, USA). The minimum detectable concentrations were 0.10 pg/mL for IL-6, 0.01 pg/mL for IL-1β, 0.35 ng/mL for ICAM-1 and 2.0 ng/mL for VCAM-1, and the interassay coefficient of variation was 7.0% for all kits. CRP was measured by immunoturbidimetric method (CRP-Latex, Olympus). Serum glucose levels were measured by an enzymatic colorimetric assay using a modified glucose oxidase-peroxidase method and a Glucose HK analyzer (Olympus). Free insulin concentrations were determined by double-antibody RIA (Pharmacia RIA kit). Total cholesterol (T chol) and triglycerides (TG) levels were measured in serum by automated enzymatic procedures (Olympus). LDL cholesterol (LDL chol) was measured after separating LDL-fraction from fresh fasting sera by sequencial ultracentrifugation. HDL cholesterol (HDL chol) was determined automatically by routine laboratory test (Olympus).

The homeostasis model was used to assess insulin resistance (HOMA IR). The formula for HOMA IR is as follows: insulin resistance (HOMA IR) = fasting insulin (mU/ml) × fasting glucose (mmol/L)/ 22.5

All statistical analyses were performed with the version 9.0 of the SPSS for Windows software (SPSS Inc., Chicago, Ill., USA). All values were expressed as means

± standard deviation (SD) or as median with range. Comparisons between two groups were tested with Mann-Whitney U-test. Parameters with skewed distributions were log-transformed for analyses. Association of biochemical and clinical variables were examined by Pearson's correlation. In addition, multivariate linear regression analyses were used to test the independent association of inflammation and endothelial activation markers and components of the IR syndrome with systolic and diastolic blood pressure. A P-value less than 0.05 was considered statistically significant.

The study was approved by the Ethical Committee of the Pomeranian Medical University and informed consent as well as assent were obtained.

## Results

The clinical and biochemical characteristics of the study subjects are presented in Table 1 and Table 2.

Table 2 provides the medians and ranges of biochemical parameters in the study group according to gender.

The mean cholesterol level in the whole group was 4.78 ± 0.95 mmol/L, LDL cholesterol – 2.80 ± 0.84 mg/dL, HDL cholesterol – 1.31 ± 0.32 mg/dL, and triglycerides – 1.19 mmol/L (0.33 – 5.18). There were no differences in lipid levels between genders.

Results of 24-h monitoring blood pressure are presented in Table 3.

In correlation analyses (Table 4) after adjustment for age, gender, pubertal stage, BMI and fat mass, mean (24-h) systolic blood pressure was associated with

**TABLE 1.** Clinical characteristics of studied children

| Parameter | Boys (n=151) | Girls (n=130) | P value |
|---|---|---|---|
| | Mean ±SD | | |
| Age (years) | 12.2±2.6 | 13.6±2.3 | NS |
| BMI (kg/m2) | 28.2±3.7 | 29.0±4.0 | NS |
| BMI-SD score | 3.2±1.2 | 3.7±1.4 | NS |
| %FAT | 31.4±6.9 | 36.5±5.0 | <.01 |
| Fat mass (kg) | 22.3±8.3 | 26.3±9.4 | <.01 |
| WHR | 0.99±0.05 | 0.93±0.07 | <.01 |
| | n,(%) | | |
| Tanner stage 1 | 58 (38.4) | 23 (17.7) | <.01 |
| Tanner stage 2-5 | 93 (61.6) | 117 (82.3) | <.05 |
| Positive family history of hypertension | 49 (32.5) | 41 (31.3) | NS |

**TABLE 2** Biochemical characteristics of studied children.

| Parameter | Boys (n=151) | Girls (n=130) | P value |
|---|---|---|---|
| | Median (range) | | |
| Glucose (mmol/L) | 4.9 (3.1–6.1) | 4.8 (3.3–7.9) | NS |
| Insulin (pmol/L) | 98.5 (20.3–829.8) | 119.8 (22.0–463.4) | <.01 |
| HOMA IR | 3.01 (0.6–28.3) | 3.6 (0.1–15.3) | <.05 |
| CRP (mg/dL) | 0.97 (0.0–3.8) | 1.19 (0.0–3.5) | <.05 |
| IL-6 (pg/mL) | 1.4 (0.1–14.8) | 1.5 (0.1–10.8) | NS |
| IL-1 β (pg/mL) | 0.4 (0.1–11.0) | 0.4 (0.8–3.8) | NS |
| ICAM-1 (ng/mL) | 276.0 (53.0–654.0) | 246.0 (45.0–650.0) | NS |
| VCAM-1 (ng/mL) | 1331 (145–1650) | 1272 (176–1649) | NS |

**TABLE 3.** Blood pressure in the study group

| Parameter | Boys (n=151) | Girls (n=130) | P value |
|---|---|---|---|
| | Mean ± SD | | |
| SBP, day (mm Hg) | 116.9 ±10.2 | 116.7 ± 11.8 | NS |
| DBP, day (mmHg) | 67.1 ± 7.6 | 66.9 ± 8.6 | NS |
| SBP, night (mm Hg) | 104.8 ± 11.3 | 103.7 ± 11.3 | NS |
| DBP, night (mmHg) | 56.4 ± 6.9 | 57.7 ± 9.7 | NS |
| Mean (24-h) SBP (mmHg) | 113.2 ± 10.1 | 113.0 ± 11.3 | NS |
| Mean (24-h) DBP (mmHg) | 63.9 ± 7.3 | 64.0 ± 8.9 | NS |

SBP – systolic blood pressure DBP – diastolic blood pressure

**TABLE 4.** Pearson's correlation between systolic and diastolic blood pressure, and inflammatory markers and cell adhesion molecules

| Variable | SBP (day) | DBP (day) | SBP (night) | DBP(night) | (24-h) SBP | (24-h) DBP |
|---|---|---|---|---|---|---|
| | | | r | | | |
| CRP | 0.21** | 0.18* | 0.18* | 0.20* | 0.23** | 0.18* |
| IL-6 | 0.28*** | 0.17* | 0.28*** | 0.24** | 0.32*** | 0.16* |
| IL-1β | 0.21* | –0.20* | –0.09 | –0.19* | 0.19* | –0.19* |
| ICAM-1 | 0.22** | 0.10 | 0.21** | 0.19* | 0.22* | 0.11 |
| VCAM-1 | 0.12 | 0.09 | 0.22* | 0.23** | 0.15 | 0.09 |

All inflammatory markers were log-transformed for statistical analysis
***P<0.001 ** .001<P<.01 *.01<P<.05

**TABLE 5a.** Linear multiple regression analyses with systolic and diastolic blood pressure as dependent variables – model1

| Model 1 | Systolic blood pressure | | | | Diastolic blood pressure | | | |
|---|---|---|---|---|---|---|---|---|
| | beta | r | t | P | beta | r | t | P |
| Age | 0.21 | 0.17 | 2.17 | 0.0314 | 0.18 | 0.14 | 1.70 | 0.0903 |
| Sex | 0.03 | 0.03 | 0.32 | 0.7490 | 0.11 | 0.10 | 1.21 | 0.2265 |
| BMI-SD | 0.19 | 0.15 | 1.92 | 0.0562 | 0.17 | 0.12 | 152 | 0.1311 |
| Fat mass | 0.10 | 0.07 | 0.82 | 0.4137 | 0.08 | 0.05 | 0.62 | 0.5365 |
| WHR | 0.13 | 0.12 | 1.45 | 0.1501 | 0.18 | 0.15 | 1.82 | 0.0701 |
| HOMA IR | 0.27 | 0.26 | 3.34 | 0.0010 | 0.15 | 0.14 | 1.68 | 0.0946 |
| CRP | 0.08 | 0.08 | 1.01 | 0.3145 | 0.19 | 0.17 | 2.10 | 0.0373 |
| IL-6 | 0.29 | 0.27 | 3.44 | 0.0007 | 0.05 | 0.04 | 0.52 | 0.6059 |
| IL-1β | –0.19 | –0.16 | –1.91 | 0.0582 | –0.14 | –0.15 | –1.67 | 0.0834 |
| HDL chol | –0.05 | –0.05 | –0.66 | 0.5124 | –0.05 | –0.05 | –0.57 | 0.5677 |
| LDL chol | 0.03 | 0.03 | 0.37 | 0.7130 | 0.05 | 0.05 | 0.63 | 0.5288 |
| TG | 0.01 | 0.01 | 0.11 | 0.9113 | 0.02 | 0.02 | 0.27 | 0.7876 |
| AH in family | 0.04 | 0.05 | 0.63 | 0.5285 | 0.11 | 0.12 | 1.44 | 0.1531 |

A significant P value are bolded.

**TABLE 5b.** Linear multiple regression analyses with systolic and diastolic blood pressure as dependent variables – model2

| Model 2 | Systolic blood pressure | | | | Diastolic blood pressure | | | |
|---|---|---|---|---|---|---|---|---|
| | beta | r | t | P | beta | r | t | P |
| Age | 0.09 | 0.07 | 0.75 | 0.4543 | 0.20 | 0.17 | 1.82 | 0.0714 |
| Sex | 0.05 | 0.04 | 0.45 | 0.6515 | 0.08 | 0.06 | 0.67 | 0.5050 |
| BMI-SD | 0.03 | 0.02 | 0.26 | 0.8023 | 0.08 | 0.05 | 0.55 | 0.5856 |
| Fat mass | 0.16 | 0.10 | 1.05 | 0.2957 | 0.09 | 0.06 | 0.58 | 0.5618 |
| WHR | 0.27 | 0.21 | 2.23 | 0.0278 | 0.20 | 0.16 | 1.72 | 0.0876 |
| HOMA IR | 0.24 | 0.21 | 2.26 | 0.0257 | 0.06 | 0.05 | 0.53 | 0.5940 |
| ICAM-1 | 0.04 | 0.03 | 0.29 | 0.7707 | 0.09 | 0.06 | 0.66 | 0.5092 |
| VCAM-1 | 0.01 | 0.01 | 0.09 | 0.9291 | 0.02 | 0.02 | 0.17 | 0.8658 |
| HDL chol | –0.03 | –0.02 | –0.24 | –0.8109 | –0.23 | –0.20 | –2.06 | 0.0420 |
| LDL chol | 0.04 | 0.03 | 0.36 | 0.7214 | 0.11 | 0.10 | 1.05 | 0.2957 |
| TG | 0.03 | 0.02 | 0.26 | 0.7991 | 0.11 | 0.09 | 0.93 | 0.3555 |
| AH in family | 0.03 | 0.02 | 1.18 | 0.2406 | 0.16 | 0.17 | 1.73 | 0.0862 |

A significant P value are bolded.

serum concentrations of all inflammatory markers and ICAM-1. Mean (24-h) diastolic blood pressure was positively correlated with plasma CRP and IL-6. The correlation's coefficients were higher for systolic than diastolic blood pressure. Moreover, only CRP and IL-6 correlated simultaneously with mean daily systolic and diastolic blood pressure, mean SBP and DBP at night as well as mean (24-h) SBP and DBP.

The predictive role of low-grade inflammation on 24-h systolic and diastolic BP after adjusting for age and sex was tested in multivariate analyses (Table 5a and 5b). In particular, we tested the independent association of serum CRP, IL-6, IL-1β, BMI-SD score, fat mass, WHR, HOMA IR, lipids and positive family history of arterial hypertension (AH) with SBP and DBP (model 1) after adjusting for age and gender. In such

analysis, only serum IL-6 level, HOMA IR, and age were independently associated with SBP. There was a trend for association between SBP and BMI-SD score (Table 5a). In model 2 the independent relation of soluble cell adhesion molecules, BMI, fat mass, WHR, HOMA IR and lipids to SBP and DBP was investigated. In these analyses, only HOMA IR and WHR were independent determinants of SBP, whereas HDL cholesterol was predictor of DBP. No association was found between soluble cell adhesion molecules and BP (Table 5b).

## Discussion

Our study demonstrates for the first time that low-grade systemic inflammation is independently associated with blood pressure in obese children and adolescents. The effect of inflammatory markers was particulary evident on SBP, whereas almost trivial on DBP.

The relationship between arterial blood pressure and chronic, subclinical inflammation is complex and not fully understood. Several studies have pointed out that BP may exert a proinflammatory effect on the arterial wall by two different possible mechanisms. Firstly, increased BP promotes atherogenesis by modulating the biomechanical stimuli of the pulsative blood flow (increased hydrostatic pressure or cyclic strain), which in turn affects endothelial cell gene expression [9]. Secondly, hypertension may cause enhanced endothelial responsiveness to factors promoting monocytes adhesion and subsequent atherosclerosis.

It is well-known that at early stages of atherosclerosis and inflammation, endothelial cell activation by various inflammatory stimuli results in the synthesis of adhesion molecules and increases the adherence of monocytes. An increased sICAM expression and greater monocyte adhesion were found in spontaneously hypertensive rats compared with normotensive rats [17]. However, the hypothesis that blood pressure is the main cause of arterial wall inflammation is somewhat limiting since several pathologic conditions such as hiperinsulinemia/insulin resistance, dyslipidemia, obesity, and depression may cause inflammatory response in vessel wall, and through this mechanism, may influence BP regulation [2,15].

In the present study we demonstrated the significant association of all inflammatory markers and cellular adhesion molecules with ambulatory 24-h blood pressure in obese children, even after adjustment for age, sex, BMI and fat mass. Barbieri and co-workers also found significant correlation between proinflammatory cytokines, such as IL-6, IL-1β, and blood pressure in elderly subjects [1].

Neverthless, in a multiple regression analyses, we found that serum IL-6, age, insulin resistance indices, WHR, and degree of obesity were significant determinants of mean 24-h systolic blood pressure. Previous studies in adults have shown that age and degree of atherosclerosis are significant determinants of SBP, whereas clustering variables of insulin resistance syndrome is a significant determinant of both SBP and DBP [1,2]. In the study by Daniels and co-workers, fat distribution was a significant correlate of systolic BP in children, stronger than percent body fat, which is an overall measure of obesity [6]. With regard to hyperinsulinemia/insulin resistance, Ighetti et al did not find any relationship between fasting insulin and blood pressure in obese children [13].

The significant effect of serum IL-6 on arterial BP was not unexpected. Interleukin-6, the primary stimulator of hepatic CRP production, promotes vascular smooth muscle cell proliferation, a hallmark of the early stage of hypertension and atherosclerosis [14]. Moreover, the IL-6 – 174 promoter polymorphism, which has been demonstrated to affect serum IL-6 concentrations in women [3], was associated with SBP in men [12]. Barbieri et al found that IL-6 was a predictor of systolic BP independently of age, sex, insulin resistance score and the IL-6-174 polymorphism [1].

Our findings also suggest that chronic, systemic inflammation exerts a modulator effect on diastolic BP, given that serum CRP concentration was a significant determinant of the rise in DBP. Such data are in agreement with previous study conducted in adults [1].

It is noteworthy that in a multiple regression analyses we did not find significant relationship between serum IL-1β and BP, although the results might suggest the lowering effect of serum IL-1β on diastolic BP. Barbieri et al. demonstrated the significant lowering effect of IL-1β on both systolic and diastolic BP in elderly subjects [1]. Such effect may be supported by the observations that IL-1β downregulates sympathetic nervous system activity, and this modulation is mediated by increased local expression of neuronal nitric oxide synthase (NOS) mRNA [12] as well as that angiotensin II-mediated increased in arterial blood pressure is caused by inhibition of the expression of IL-1β and neuronal NOS at the brain level [4].

In our study we demonstrated the lack of a significant effect of serum soluble cell adhesion molecules on arterial BP. On the contrary, Chae et al. demonstrated the increased levels of ICAM-1 in adult patient with essential hypertension, which indicates the possible role of cell adhesion molecules in the modulation of BP [5]. An explanation for such apparent discrepancy might be that soluble cell adhesion molecules could be more useful as markers of endothelial dysfunction but as less powerful determinants of change in BP, at least in youth.

In conclusion, our findings support the hypothesis that low-grade inflammation is the common link between different pathologic conditions, such as insulin resistance and the development of hypertension in obese children and adolescents. Further studies are needed to confirm our results in a longitudinal prospective and to gain insight into the mechanisms by which chronic inflammation affects BP over the course of growing process.

REFERENCES


1 Barbieri M, Ferrucci L, Corsi AM, Macchi C, Lauretani F, Bonafe M, Olivieri F, Giovagnetti S, Franceshi C, Paolisso G. Is chronic inflammation a determinant of blood pressure in the elderly? Am J Hypertens 2003; **16**: 537–543.

2 Bjorntorp P, Holm G, Rosmond R, Folkow B. Hypertension and the metabolic syndrome: closely related central origin. Blood Press 2000; **9**:71–82.

3 Bonafe M, Olivieri F, Cavallone L, Giovagnetti S, Marchegiani F, Cardelli M, Pieri C, Marra M, Antonicelli R, Lisa R, Rizzo MR, Paolisso G, Monti D, Franceshi C. A gender dependent genetic predisposition to produce high levels of IL-6 is detrimental for longevity. Eur J Immunol 2001; **31**: 2357–2361.

4 Campese VM, Ye S, Zhong H. Down regulation of neuronal nitric oxide synthase and interleukin-1 beta mediates angiotensin II-dependent stimulation of sympathetic nerve activity. Hypertension 2002; **39**: 519–524.

5 Chae CU, Lee RT, Rifai N, Ridker PM. Blood pressure and inflammation in apparently healthy men. Hypertension 2001; **38**: 399–403.

6 Daniels SR, Morrison JA, Sprecher DL, Khoury P, Kimball TR. Association of body fat distribution and cardiovascular risk factors in children and adolescents. Circulation 1999; **99**: 541–545.

7 DeSouza CA, Van Guilder GP, Greiner JJ, Smith DT, Hoetzer GL, Stauffer BL. Basal endothelial nitric oxide release is preserved in overweight and obese adults. Obes Res 2005; **13**: 1303–1306.

8 Fernandez Real JM, Vayreda M, Richart C, Gutierrez C, Broch M, Vendrell J, Ricart W. Circulating interleukin-6 levels, blood pressure, and insulin sensitivity in appoarently healthy men and women. J Clin Endocrinol Metab 2001; **86**: 1154–1159.

9 Gimbrone MA, Nagel T, Topper JN. Biomechanical activation: an emerging paradigm in endothelial adhesion biology. J Clin Invest 1997; **99**: 1809–1813.

10 Hall JE, Hidebrandt DA, Kuo J. Obesity hypertension: role of leptin and sympathetic nervous system. Am J Hypertens 2001; **14** (Part 2): 103S–115S.

11 Hall JE. The kidney, hypertension, and obesity. Hypertension 2003; **41**: 625–633.

12 Humpries SE, Luong LA, Ogg MS, Hawe E, Miller GJ. The interleukin-6-174G/C promoter polymorphism is associated with risk of coronary heart disease and systolic blood pressure in healthy men. Eur Heart J 2001; **22**: 2243–2252.

13 Ighetti L, Bedogni G, Ferrari M. Is fasting insulin associated with blood pressure in obese children? Ann Hum Biol 2000; **27**: 499–506.

14 Ikeda U, Ikeda M, Oohara T, Ohuchi A, Kamitani T, Tsuruya Y, Kano S. Inteleukin-6 stimulates growth of vascular smooth muscle cells in a PDGF dependent manner. Am J Physiol 1991; **260**: H1713–H1717.

15 Lesperance F, Frasure-Smith N, Theroux P, Irwin M. The association between major depression and levels od soluble intercellular adhesion molecule-1, interleukin-6, and C-reactive protein in patients with recent acute coronary syndrome. Am J Psychiatry 2004; **161**: 271–277.

16 Li JJ, Fang CH, Hui RT. Is hypertension an inflammatory disease? Med Hypotheses 2005; **64**: 236–240.

17 Liu Y, Liu T, McCarron RM, Spatz M, Feuerstein G, Hallenbeck JM, Siren AL. Evidence for activation of endothelium and monocyte in hypertensive rats. Am J Physiol 1996; **270**: H2125–H2131.

18 Manrique C, Lastra G, Whaley-Connell A, Sowers JR. Hypertension and the cardiometabolic syndrome. J Clin Hypertens (Greenwich) 2005; **7**: 471–476.

19 Mark AL, Correia M, Morgan DA, Shaffer RA, Haynes WG. Obesity-induced hypertension. New concepts from the emerging biology of obesity. Hypertension 1999; **33**: 537–541.

20 Meyer AA, Kundt G, Steiner M, Schuff-Werner P, Kienast W. Impaired flow-mediated vasodilatation, caroid artery intima-media thickening, and elevated endothelial plasma markers in obese children: the impact of cardiovascular risk factors. Pediatrics 2006; **117**: 1560–1567.

21 National High Blood Pressure Education Programme Working Group on Hypertension Control in Children and Adolescents. Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: a working group report from the National High Blood Pressure Education Programme. Pediatrics 1996; **98**: 649–658.

22 Palczewska I, Niedźwiecka Z. Somatic development indices in children and youth of Warsaw. Developmental Period Medicine 2001; **2** (suppl. 1): 113–114.

23 Peeters AC, Netea MG, Janssen MC, Kullberg BJ, Van Der Meer JW, Thien T. Pro-inflammatory cytokines in patients with essential hypertension. Eur J Clin Invest 2001; **31**: 31–36.

24 Ross R. Atherosclerosis: an inflammatory disease. N Eng J Med 1999; 340: 115–126.

25 Williams IL, Chowienczyk PJ, Wheatcroft SB, Patel AG, Sherwood RA, Momin A et al. Endothelial function and weight loss in obese humans. Obes Surg 2005; **15**: 1055–1060.

26 Yudkin JS. Adipose tissue, insulin action and vascular disease: inflammatory signals. Int J Obes 2003; **27**: S25–S28.