C-REACTIVE PROTEIN, INTERLEUKIN-6, AND TUMOR NECROSIS FACTOR-α LEVELS IN OVERWEIGHT AND HEALTHY ADULTS

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Abstract. This study aimed to 1) compare levels of high sensitivity c-reactive protein (hs-CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) between overweight Thais and apparently healthy controls, and 2) investigate the association between serum hs-CRP, IL-6, and TNF-α levels and other biochemical parameters. A total of 180 health-conscious adults aged 25-60 years, who resided in Bangkok, participated in this study. No significant difference was found in age and sex between the overweight subjects and controls. Serum levels of hs-CRP, IL-6, TNF-α, glucose, lipid profile, body mass index (BMI), waist circumference (WC), hip circumference (HC) and waist hip ratio (WHR) were determined in these volunteers. The mean levels of white blood cells (WBC), uric acid, total cholesterol (TC), triglyceride (TG), and hs-CRP were significantly higher in the overweight subjects than those in the controls, whereas high density lipoprotein-cholesterol (HDL-C) values were significantly higher in the controls than the overweight subjects ($p<0.05$). Hs-CRP levels were significantly positively correlated with levels of TG, BMI, WC, HC and WHR. HDL-C levels were significantly negative correlated with hs-CRP levels. In conclusion, the prevalence of elevated serum hs-CRP levels was higher in overweight subjects than controls. However, more data in larger and other population groups are needed to confirm this study.

INTRODUCTION

Adipose tissue has long been known as a storage depot for fat, but now it is known to play a role in metabolism (Visser *et al*, 1999). Adipose tissue can secrete proinflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) (Hotamisligil *et al*, 1995). IL-6 released from adipose tissue may cause low-grade systemic inflammation in persons with excess body fat. C-reactive protein (CRP), a systemic marker for systemic inflammation can predict future risk of coronary heart disease (CHD) (Visser *et al*, 1999). Ramos *et al* (2003) reported that TNF-α and IL-6 are correlated directly to the degree of obesity. Vikram *et al* (2003) found TNF-α regulated the release of IL-6. Apart from this, a third of total circulating IL-6 levels originate from adipose tissue in healthy subjects (Mohamed-Ali *et al*, 1997). Ferranti and Rifai (2002) showed that IL-6 and TNF-α regulate the synthesis of CRP. IL-6 can stimulate the production of CRP in the liver. It was found that higher adipose tissue content of IL-6 has been associated with higher serum CRP levels in obese subjects (Das, 2001). Therefore, it is interesting to study the association of overweight persons with serum levels of CRP, IL-6, and TNF-α.

Thai people are highly inclined to be overweight, which can lead to non-communicable

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diseases, such as cardiovascular disease (CVD), hypertension (HT), and type II diabetes mellitus (DM). However, no data of TNF-α, CRP, and IL-6 levels, including their relationship to obesity, are available for adults. This study investigated serum CRP, IL-6, and TNF-α in overweight, compared with normal-weight, adults. These new data may highlight the benefit of these three tests for improving CHD risk assessment. The objectives of this study were to compare levels of serum high sensitivity c-reactive protein (hs-CRP), IL-6, and TNF-α between overweight subjects and healthy controls, and to study the association between biochemical, including anthropometric parameters and serum levels, of hs-CRP, IL-6, and TNF-α.

MATERIALS AND METHODS

Data collection was done between August 2003 and March 2004. The target population was health-conscious adult Thai males and females aged 25-60 years, who lived in Bangkok. They were 90 overweight subjects (44 males and 46 females) and 90 apparently healthy controls (46 males and 44 females). Venous blood samples were drawn after overnight fast for plasma glucose, lipid profile, serum IL-6, serum TNF-α and serum hs-CRP analysis. Serum total cholesterol (TC), triglyceride (TG) and high density lipoprotein-cholesterol (HDL-C) and plasma glucose were detected by enzymatic colorimetric method (Ashwood and Burtis, 1999). Low density lipoprotein-cholesterol (LDL-C) was calculated by subtraction of TC by HDL-C (Ashwood and Burtis, 1999). Sera for hs-CRP, IL-6, and TNF-α were stored at -70ºC until analysis. Hs-CRP was detected by particle enhanced turbidimetric test (Roche COBAS Integra; Roche Diagnostics, 2002). IL-6, and TNF-α were determined by a solid phase sandwich enzyme-linked immunosorbent assay (ELISA) (BD Biosciences 2003, 2004). The volunteers were interviewed for background characteristics using questionnaires. Subjects gave written consent to participate in the present study, which was approved by the Faculty of Tropical Medicine, Mahidol University. The inclusion criteria included having no diseases and no medical treatment. Anthropometric measurements were taken. Weight was measured using a standard balance scale. Weight was measured in light clothing and bare feet to the nearest 0.1 kg. Height was measured without shoes with the Frankfurt plane horizontal to the nearest 0.1 cm. In this study, normal weight referred to body mass index (BMI, weight in kilogram divided by height in meter^2) 18.5-24.9, and overweight as BMI ≥ 25 (WHO Expert Committee on Obesity, 2000).

Waist circumference (WC) was taken at the narrowest point between the lower rib border and the iliac crest recorded to the nearest 0.1 cm (Gibson, 1990). Hip circumference (HC) was taken at the point of maximum circumference over the buttocks in a horizontal plane. Then, the waist-hip circumference ratio (WHR) was calculated (Gibson, 1990). Blood pressure (BP) was measured using a standard mercury sphygmomanometer and a cuff of suitable size. The cut-point for hypertension was ≥140 mmHg systolic blood pressure (SBP) and ≥90 mmHg diastolic blood pressure (DBP) (WHO Expert Committee on Hypertension, 1996).

Statistical analysis

Odd ratios and their 95% confidence intervals were applied to test for an association between the categorical variables and overweight subjects. Levels of serum hs-CRP, IL-6, and TNF-α between overweight subjects and healthy controls were compared by *t*-test statistic. Pearson correlation was applied for testing the association between the factors involved, obesity and hs-CRP, IL-6, and TNF-α levels.

RESULTS

This study was conducted with 90 overweight subjects and 90 controls, in Bangkok. The univariate analysis of factors associated with overweight subjects is summarized in Table 1. Government employees were more likely to be overweight than those from private companies (OR =3.93, 95%CI = 1.55 - 9.98). Subjects who reported that they had a family income ≤10,000 baht were more likely to be overweight than those who had a family income more than 40,000 baht (OR = 4.88, 95% CI = 1.83 - 12.97). The result of multivariate analysis is summarized in Table 2. Variables that were significant on

Table 1
Background information of overweight subjects and healthy controls.

Variables	Overweight (n = 90)		Controls(n = 90)		OR	95%CI
	No.	%	No.	%		
Education						
Pratom 6	19	21.1	15	16.7	1.90	0.55-6.53
Mattayom 6	22	24.4	9	10	3.67	1.00-13.34
Vocational training	14	15.6	14	15.6	1.50	0.42-5.35
Bachelor degree	29	32.2	43	47.8	1.01	0.33-3.15
> Bachelor degree	6	6.7	9	10	1	
Occupation						
Housewife + others	7	7.8	10	11.1	1.34	0.40-4.48
Employee	35	38.9	17	18.9	3.93*	1.55-9.98
Government official	37	41.1	42	46.7	1.68	0.72-3.95
Private company	11	12.2	21	23.3	1	
Income (baht)						
≤ 10,000	26	28.9	16	17.8	4.88*	1.83-12.97
10,001-20,000	32	35.6	25	27.8	3.84*	1.53-9.62
20,000-40,000	23	25.6	22	24.4	3.14*	1.21-8.15
> 40,000	9	10	27	30	1	
Physical activity						
Regular	24	26.7	27	30	1	
Sometimes	35	38.9	42	46.7	0.60	0.28-1.31
No	31	34.4	21	23.3	0.57	0.28-1.15

*Significant at p-value ≤ 0.05

univariate analysis at a p-value ≤ 0.05 are included in the multivariate model. The risk of overweight was still significantly associated with subjects with family income ≤10,000 baht (Adjusted OR = 3.26, 95% CI = 1.11 - 9.57), 10,001 - 20,000 baht (Adjusted OR = 3.00, 95% CI = 1.12-8.02) and 20,001 - 40,000 baht (Adjusted OR = 2.85, 95% CI = 1.04 - 7.79).

Age, anthropometric parameters and blood pressures in overweight subjects and healthy controls are shown in Table 3. The mean ages of the controls and overweight subjects were similar. The mean values for BMI, WC, HC, WHR, SBP and DBP were significantly higher in the overweight subjects than those in the healthy controls ($p < 0.05$).

Hematological and biochemical findings for the overweight subjects and healthy controls are shown in Table 4. Hematological data showed a statistically significant higher white blood cell (WBC) count in overweight subjects than in healthy controls. The mean uric acid levels and

Table 2
Multivariate analysis of background information of overweight subjects and healthy controls.

Variables	Adjusted OR	95%CI
Occupation		
Housewife + others	1.04	0.03-3.68
Employee	2.33	0.82-6.62
Government official	1.15	0.46-2.90
Private company	1	
Income (baht)		
≤ 10,000	3.26*	1.11-9.57
10,001-20,000	3.00*	1.12-8.02
20,001-40,000	2.85*	1.04-7.79
> 40,000	1	

*Significant at p-value ≤ 0.05

hs-CRP levels were significantly higher in the overweight subjects than those in the healthy controls ($p < 0.05$). The TG and TC levels were significantly higher, whereas HDL-C levels were

Table 3
Age, anthropometric parameters and blood pressure in overweight subjects and healthy controls.

Parameters	Overweight subjects (No. = 90)		Healthy controls (No. = 90)		p
	Mean	SD	Mean	SD	
Age (year)	40	8.27	40	7.98	0.905
BMI (kg/m^2)	28.84	3.07	22.08	1.82	0.000*
WC (cm)					
M	94.2	7.2	79.7	5.1	0.000*
F	85.4	8.5	72.8	5.5	0.000*
HC (cm)					
M	104.3	7.0	93.6	4.2	0.000*
F	104.7	7.0	94.1	4.9	0.000*
WHR					
M	0.90	0.03	0.85	0.04	0.000*
F	0.82	0.05	0.77	0.05	0.000*
SBP (mmHg)	121	10	115	11	0.000*
DBP (mmHg)	77	6	75	7	0.000*

*Statistically significant difference at $p < 0.05$ tested by *t*-test
BMI = Body mass index, WC = waist circumference, HC = hip circumference, WHR = Waist hip ratio, SBP = systolic blood pressure, DBP = diastolic blood pressure

significantly lower in the overweight subjects compared to the healthy controls ($p < 0.05$).

When the association between age, BMI, WC, HC, WHR including blood pressure, were studied with hs-CRP, positive correlations between BMI,WC,HC,WHR and hs-CRP levels were statistically significant ($p < 0.05$) (Table 5).

The association between plasma glucose, total protein, albumin, lipid profile, uric acid, hs-CRP, IL-6 and TNF-α levels are shown in Table 6. Positive correlations between the level of TG, including uric acid in female group, and hs-CRP, was statistically significant ($p < 0.05$), while HDL-C was negatively correlated with hs-CRP. Il-6, it was significantly negatively correlated with serum TC and LDL-C.

DISCUSSION

This study reported serum hs-CRP, IL-6, and TNF-α in overweight Thais and healthy controls. Subjects willing to enroll in this study were carefully selected to exclude conditions that could interfere with hs-CRP, IL-6, and TNF-α levels (medication, diseases, etc).

The observations that raised concentrations of CRP in healthy subjects predicted the incidence of coronary heart disease (CHD) over a period of years suggested a role for inflammation in the initiation of atherosclerosis as well as in the precipitation of an acute event (Yudkin *et al*, 1999). Several trials have found that CRP increased in patients with a higher BMI (Ferranti and Rifai, 2002). Our study indicated a significantly higher prevalence of elevated serum levels of hs-CRP in overweight subjects than controls (Table 4). Overweight persons should prevent CHD in the future by reducing weight to normal status. Visser *et al* (1999) also reported that CRP levels were elevated in overweight adults, while Chandalia *et al* (2003) found Asian Indians as a group had significantly higher plasma hs-CRP levels than Caucasians. This indicates that there are different CRP levels in different races. Apart from the prevalence of elevated serum CRP in overweight adults, some reports indicate higher serum CRP levels in overweight children and adolescents as well. A study in the USA, which included a multi-ethnic population, showed elevated CRP levels in 7.6% of boys and 6% of girls. Apart from this, the prevalence of high CRP levels was three times higher among overweight subjects (Visser *et al*, 2001). A similar result was found in a study by Ford *et*

Table 4
Hematological and biochemical findings for overweight subjects and healthy controls.

Parameters	Overweight subjects (N = 44)		Healthy controls (N = 46)		p
	Mean	SD	Mean	SD	
WBC count (x 10^9 / l)	7.73	2.23	6.25	1.70	0.001*
Hemoglobin (g/dl)					
M	15.58	1.29	15.46	1.04	0.647
F	13.46	1.15	12.91	1.12	0.104
Hematocrit					
M	46.86	3.75	46.44	3.02	0.589
F	40.50	3.24	38.85	3.77	0.095
Mean corpuscular hemoglobin concentration (g/l)	33.23	0.55	33.27	0.37	0.643
Serum total protein (g/dl)	7.50	0.39	7.56	0.38	0.335
Serum albumin (g/dl)	4.54	0.36	4.54	0.32	0.981
Plasma glucose (mg/dl)	91.98	11.62	89.13	9.32	0.072
Uric acid (mg/dl)					
M	6.95	1.89	5.98	1.25	0.005*
F	4.47	1.89	3.75	1.01	0.028*
Serum cholesterol (mg/dl)	227.12	45.26	214.84	34.31	0.042*
Serum triglyceride (mg/dl)	148.32	127.85	103.64	52.34	0.002*
Serum HDL-C (mg/dl)	48.66	10.15	55.10	12.42	0.000*
Serum LDL-C (mg/dl)	134.14	39.29	134.37	36.49	0.969
Serum hs-CRP (mg/l)	1.80	1.28	1.01	0.96	0.000*
Serum IL-6 (pg/ml)	1.87	1.50	1.76	1.57	0.637
Serum TNF-α (pg/ml)	0.85	1.21	0.74	0.92	0.503

* Statistically significant difference at $p < 0.05$ tested by *t* test

al (2001), where high CRP was found in overweight subjects aged 6-18 years. However, these studies used different cut-points to define the elevated CRP levels. Vikram *et al* (2003) studied CRP levels in urban North Indians aged 14-25 years. The result revealed elevated CRP levels in adolescents and young adults having increased generalized and abdominal adiposity.

As mentioned previously, adipose tissue can secrete IL-6 and TNF-α (Hotamisligil *et al*, 1995). While most studies found IL-6 and TNF-α were significantly higher in overweight subjects than lean subjects, our study showed no difference in levels of IL-6 and TNF-α between overweight subjects and controls (Table 4). However, IL-6 and TNF-α values tended to be higher in the overweight subjects than the controls. The studies by Dandona *et al* (1998), Yudkin *et al* (1999), Zahorska-Markiewicz *et al* (2000), Berberoglu (2001) and Laimer *et al* (2002), displayed elevated serum TNF-α in obese subjects. However, data from two studies, by Kern *et al* (2001) and Pincelli *et al* (2001), found no correlation between serum TNF-α values and obesity. This was probably due to differences in mean BMI and age in each population studied. Most obese subjects in many research studies had higher mean BMI than this study. The mean age in our study was 40 years in both groups. One study in Japan found TNF-α was associated with BMI in Japanese subjects in their 60s, but not in those in their 20s and those aged 30-49 years (Suzuki *et al*, 2002). This is probably because older subjects tend to have more diseases than younger subjects. Apart from this, it was difficult to find volunteers to enroll in this study. Many obese persons had health problems that excluded them from the criteria of this research.

Our study found significantly positive correlations between hs-CRP levels and TG but a

Table 5
Correlation between age, anthropometric parameters, and blood pressure with hs-CRP, IL-6, and TNF-a levels.

Parameters	Hs-CRP		IL-6		TNF-α	
	r	p	r	p	r	p
Age	-0.03	0.756	0.08	0.279	-0.14	0.067
BMI	0.37*	0.000	0.03	0.726	0.06	0.392
WC						
M	0.27*	0.006	-0.05	0.313	0.12	0.130
F	0.43*	0.000	0.07	0.243	0.02	0.428
HC						
M	0.24*	0.013	0.00	0.493	0.15	0.089
F	0.46*	0.000	0.10	0.180	0.06	0.281
WHR						
M	0.20*	0.032	-0.12	0.135	0.03	0.390
F	0.21*	0.022	0.03	0.408	-0.04	0.347
SBP	0.12	0.108	-0.05	0.515	-0.02	0.782
DBP	0.02	0.822	-0.03	0.697	-0.02	0.841

* Statistically significant difference at $p < 0.05$ tested by Pearson correlation

Table 6
Correlation between plasma glucose, total protein, albumin, lipid profile, and uric acid with hs-CRP, IL-6, and TNF-α levels.

Parameters	Hs-CRP		IL-6		TNF-α	
	r	p	r	p	r	p
Plasma glucose	0.11	0.136	-0.06	0.456	-0.07	0.327
Serum total protein	0.06	0.451	-0.04	0.665	0.04	0.616
Serum albumin	0.08	0.334	-0.14	0.087	-0.07	0.421
Serum total cholesterol	0.14	0.062	-0.17*	0.024	-0.05	0.475
Serum triglyceride	0.28*	0.000	0.01	0.884	-0.01	0.895
Serum HDL-C	-0.16*	0.028	-0.003	0.973	0.08	0.263
Serum LDL-C	-0.04	0.566	-0.18*	0.02	0.05	0.494
Uric acid						
M	0.05	0.662	0.05	0.610	0.15	0.151
F	0.34*	0.001	0.10	0.363	-0.05	0.674

* Statistically significant difference at $p < 0.05$ tested by Pearson correlation

statistically significant negative correlation between hs-CRP and HDL-C (Table 6). Aronson *et al* (2004) also showed a positive correlation between CRP and fasting glucose, TG, and hypertension while a negative correlation was found between CRP and HDL-cholesterol in middle-aged subjects. This finding suggested that a proinflammatory effect may contribute to the adverse cardiovascular outcomes associated with dyslipidemia and impaired fasting glucose.

We confirmed the positive correlations between hs-CRP and BMI, WC, HC and WHR were statistically significance (Table 5). This is consistent with the largest data set on obesity and CRP in the Third NHANES of USA, in 1988 and 1994, which indicated obesity conferred an in-

creased odds ratio for increased CRP after controlling for other variables (Ferranti and Rifai, 2002). Saijo *et al* (2004) also found serum CRP had a significantly positive correlation with WC in Japanese subjects. Visser *et al* (1999) stated that human abdominal visceral adipose tissue releases more IL-6 than subcutaneous adipose tissue. Some studies suggested that abdominal adipose tissue was a major source of cytokines, including IL-6, which is an important determinant of hepatic CRP synthesis (Chambers *et al*, 2001).

We found no statistically significant association between levels of IL-6, including TNF-α, and BMI. Cottam *et al* (2004) mentioned that IL-6 and TNF-α are responsible for the dyslipidemia that is common in morbid obesity (BMI > 40).

The results of our study indicate that reducing overweight may be effective in decreasing hs-CRP and preventing the incidence of cardiovascular events. Moreover, the benefits of weight control affect one's health. If weight loss continues for 2 years, it can reduce blood pressure, improve dyslipidemia, and decrease the risk of DM (Sjostrom'*et al*, 1997). Ford (2001) indicated that a balanced diet and regular physical activity should be encouraged, because they showed an association with lower CRP levels in adults. Bruun *et al* (2002) found that obese subjects with a mean BMI 39 kg/m^2 had decreased plasma TNF-α after 20 weeks of weight reduction. Bastard *et al* (2000) found IL-6 levels dropped with weight loss. Therefore, regular physical activity and healthy dietary habits can help lower levels of hs-CRP, IL-6, and TNF-α and prevent obesity, including reducing potential cardiovascular inflammation. Data about CRP, IL-6, and TNF-α concentrations in representative populations from this study may be useful for the clinician and the general practitioner in assessing the risk of future cardiovascular events.

In summary, our study indicates a significantly higher prevalence of elevated serum hs-CRP in overweight subjects than controls. This supports findings that CRP is a strong predictor of cardiovascular events. CRP is a main acute phase protein, and a marker of systemic inflammation (Heinrich *et al*, 1990). Our results indicate that elevated CRP, a state of low-grade systemic inflammation, is found in overweight persons. Apart from this, we found significantly positive correlations between hs-CRP levels and TG, BMI, WC, HC and WHR. Further studies are needed to confirm these findings, especially in children, adolescents and the elderly.

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REFERENCES

Aronson D, Bartha P, Zinder O, *et al*. Association between fasting glucose and C-reactive protein in middle-aged subjects. *Diabet Med* 2004; 21: 39-44.

Ashwood ER, Burtis CA. Textbook of clinical chemistry. 3rd ed. Philadelphia: WB Saunders, 1999.

Bastard JP, Jardel C, Bruckert E. Elevated levels of IL-6 are reduced in serum and subcutaneous adipose tissue of obese women after weight loss. *J Clin Endocrin Metab* 2000; 85: 3338-45.

Berberoglu M. Evaluation of the correlation between serum tumor necrosis factor-alpha and relative body mass index (RBMI) in childhood. *J Pediatr Endocrinol Metab* 2001; 14: 543-7.

Biosciences BD. Human IL-6 ELISA KIT II. Instruction manual. Cat. No. 550799. Becton, Dickinson, 2004.

Biosciences BD. Human TNF ELISA KIT II. Instruction manual. Cat. No. 550610. Becton, Dickinson, 2003.

Bruun JM, Pedersen SB, Kristensen K, Richelsen B. Opposite regulation of plasma interleukin-8 and tumor necrosis factor-alpha by weight loss. *Obes Res* 2002; 10: 499-506.

Chambers JC, Eda S, Bassett P, *et al*. C-reactive protein, insulin resistance, central obesity, and coronary heart disease risk in Indian Asians from the United Kingdom compared with European whites. *Circulation* 2001; 104: 145-50.

Chandalia M, Cabo-Chan AV Jr, Devarajs, *et al*. Elevated plasma high-sensitivity C-reactive protein concentrations in Asian Indians living in the United States. *J Clin Endocrinol Metab* 2003; 88:

3773-6.

Cottam DR, Mattar SG, Barinas-Mitchell E, *et al*. The chronic inflammatory hypothesis for the morbidity associated with morbid obesity: implications and effects of weight loss. *Obes Surg* 2004; 14: 589-600.

Dandona P, Weinstock R, Thusu K, Abdel-Rahman E, Aljada A, Wadden T. Tumor necrosis factor-alpha in sera of obese patients: fall with weight loss. *J Clin Endocrinol Metab* 1998; 83: 2907-10.

Das UN. Is obesity an inflammatory condition? *Nutrition* 2001; 17: 953-66.

Ferranti SD, Rifai N. C-reactive protein and cardiovascular disease: a review of risk prediction and interventions. *Clin Chim Acta* 2002; 317: 1-15.

Ford ES, Galuska DA, Gillespie C, Will JC, Giles WH, Dietz WH. C-reactive protein and body mass index in children: findings from the Third National Health and Nutrition Examination Survey, 1988-1994. *J Pediatr* 2001; 138: 486-92.

Ford ES. Does exercise reduce inflammation? Physical activity and C-reactive protein among US adults. *Epidemiology* 2002; 13: 561-8.

Gibson RS. Principles of nutritional assessment. New York: Oxford University Press, 1990: 42-5, 165-71.

Heinrich PC, Castell JV, Andus T. Interleukin-6 and the acute phase response. *Biochem J* 1990; 265: 621-36.

Hotamisligil GS, Arner P, Caro JF, Atkinson RL, Spiegelman BM. Increased adipose tissue expression of tumor necrosis factor-alpha in human obesity and insulin resistance. *J Clin Invest* 1995; 95: 2409-15.

Kern PA, Ranganathan S, Li C, Wood L, Ranganathan G. Adipose tissue tumor necrosis factor and interleukin-6 expression in human obesity and insulin resistance. *Am J Physiol Endocrinol Metab* 2001; 280: E745-51.

Laimer M, Ebenbichler CF, Kaser S, *et al*. Markers of chronic inflammation and obesity: a prospective study on the reversibility of this association in middle-aged women undergoing weight loss by surgical intervention. *Int J Obes Relat Metab Disord* 2002; 26: 659-62.

Mohamed-Ali V, Goodrick S, Rawesh A, *et al*. Human subcutaneous adipose tissue secretes interleukin -6 but not TNF-α *in vivo*. *J Clin Endocrinol Metab* 1997; 82: 4196-200.

Pincelli AI, Brunani A, Scacchi M, *et al*. The serum concentration of tumor necrosis factor alpha is not an index of growth hormone- or obesity-induced insulin resistance. *Horm Res* 2001; 55: 57-64.

Ramos EJ, Xu Y, Romanova I, *et al*. Is obesity an inflammatory disease? *Surgery* 2003; 134: 329-35.

Roche Diagnostics. C-reactive protein (Latex). Application for C.f.a.s. Proteins. 04/2002, Version 1.2.

Saijo Y, Kiyota N, Kawasaki Y, *et al*. Relationship between C-reactive protein and visceral adipose tissue in healthy Japanese subjects. *Diabetes Obes Metab* 2004; 6: 249-58.

Sjostrom CD, Lissner L, Sjostrom L. Relationships between changes in body composition and changes in cardiovascular risk factors: the SOS Intervention Study. Swedish Obese Subjects. *Obes Res* 1997; 5: 519-30.

Suzuki K, Kobayashi S, Koyama T, *et al*. Relationships between light exercise-induced changes in TNF-a level and serum lipid components. *Health Evaluat Promot* 2002; 29: 904-9 (In Japanese).

Vikram NK, Misra A, Dwivedi M, *et al*. Correlations of C-reactive protein levels with an anthropometric profile, percentage of body fat and lipids in healthy adolescents and young adults in urban North India. *Atherosclerosis* 2003; 168: 305-13.

Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. *JAMA* 1999; 282: 2131-5.

Visser M, Bouter LM, McQuillan M, Wener MH, Harris TB. Low-grade systemic inflammation in overweight children. *Pediatrics* 2001; 107: E13.

WHO Expert Committee on Hypertension. Hypertension control. *World Health Organ Tech Rep Ser* 1996; 862: 1-83.

WHO Expert Committee on Obesity. Obesity: prevention and managing the global epidemic. *World Health Organ Tech Rep Ser* 2000; 894: 256.

Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? *Arterioscler Thromb Vasc Biol* 1999; 19: 972-8.

Zahorska-Markiewicz B, Janowska J, Olszanecka-Glinianowicz M, Zurakowski A. Serum concentrations of TNF-alpha and soluble TNF-alpha receptors in obesity. *Int J Obes Relat Metab Disord* 2000; 24: 1392-5.