SERUM CONCENTRATIONS OF URIC ACID AND C-REACTIVE IN MIDDLE SCHOOL AGED CHILDREN

By:

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To the Faculty of Washington State University:

The members of the Committee appointed to examine the master's project of Michelle Diane Crawford find it satisfactory and recommend that it be accepted.

_Ruth Bredlin_
Chair

_Angela G. Humeather_

_Kim D. Carter_
Journal Submission

A journal will be selected for its focus on research and endocrine issues in youth. Further refinement of this paper will be performed with the committee, with submission to follow.
Abstract

The prevalence of cardiovascular and metabolic diseases among adults is increasing. The health status of children also demonstrates increasing risks, particularly in middle school aged children. Uric acid and CRP may be helpful in determining children who are at risk, as these have been found to be elevated in many cardiovascular and metabolic conditions. The purpose of this literature review is to examine mean levels of uric acid and CRP in middle school aged children. Normal ranges need to be established as there are no accurate ranges for children. A review of literature found lower uric acid and CRP levels in children than adults. Uric acid levels were also higher in males than females but there were no gender differences in CRP. Results may contribute to applications of these biomarkers in clinical situations. Additional studies with larger samples need to be conducted.
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Serum Concentrations of Uric Acid and C-Reactive Protein in Middle School Aged Children

Over the past generation there has been a significant increase in obesity, type 2 diabetes, and cardiovascular disease amongst the adult population. The Centers for Disease Control and Prevention (CDC) (2008) stated that the prevalence of obesity increased from 15% in the 1970s to 32.9% in 2004, and is continuing to rise. Cardiovascular disease, which is directly related to obesity, is associated with more deaths than the next 5 causes of death combined, including cancers, diabetes, and accidental death (Armani & Becker, 2005). In addition, cardiovascular disease and obesity can significantly increase the risk of myocardial infarction, stroke, congestive heart failure, renal failure, and death (Alper et al., 2005).

The health status of children also demonstrates increasing risks, leading to much concern about the health of the coming adult generation. In 2006, it was found that the prevalence of overweight and obesity in American children had tripled in the past twenty years and that the rate currently exceeds 30% (Budd & Volpe, 2006; Retnakaran, Hanley, Connelly, Harris, & Zinman, 2006). Overweight children are at a higher risk of developing long term chronic conditions at an earlier age. Studies have shown that two-thirds of overweight children have at least one cardiovascular risk factor, and one-fourth have two or more risk factors (Bachman, Baranowski, & Nicklas, 2006). In addition to cardiovascular disease these children are at risk of type 2 diabetes mellitus, orthopedic disorders, and respiratory disease; all of these conditions result in an increased risk of morbidity and mortality in adulthood (Chu, Chang, & Shieh, 2003).

In order to help decrease the prevalence of chronic illnesses in adulthood, it is important to identify those children that may be at risk. Ford et al. (2003) stated that the pathogenesis of cardiovascular disease often starts in childhood and found the presence of early precursors of atherosclerosis such as intimal thickening and fatty streaks in the arteries at young ages. An age
group of particular interest is middle school aged children (ages 11-14). Since their bodies are starting to mature and early adolescents are beginning to make their own lifestyle decisions, this would be a very crucial time to identify health risks and aid them in lifestyle modifications that would carry over into their older adolescent years and adulthood.

Biomarkers may be helpful in determining those children who are at risk for early cardiovascular disease. Examples of biomarkers explored for use in both adults and children are serum uric acid and C-reactive protein (CRP). Although there have been some well established ranges for adult uric acid and CRP levels, there has yet to be any nationally recommended ranges for middle school aged children. When measuring laboratory values for these children, they are often placed on an adult range scale; however there is a lack of evidence for normal values in childhood. In order to accurately screen for cardiovascular and other related diseases, normal levels of uric acid and CRP for middle school aged children need to be established.

The purpose of this literature review is to examine and describe the mean levels of uric acid and CRP in middle aged school children. The aims include:

1. Describe the physiological metabolic processes of uric acid and CRP and discuss their significance in children.
2. Describe the mean levels or uric acid and CRP in middle school aged children found in the literature.
3. Analyze differences in uric acid and CRP according to gender.

Pathophysiology

Uric acid

Uric acid is synthesized in the body through purines which come from dietary metabolism and endogenous nucleic acids. Purine metabolism is influenced by both dietary and
genetic factors. The development of uric acid from purines and other substances is a complete system involving numerous enzymatic processes (see Figure 1). Uric acid is typically distributed throughout the body as sodium urate, and cleared from the plasma through the kidneys by glomerular filtration. About 90% of the uric acid is reabsorbed from the proximal renal system, where it is then actively secreted into the distal tubule and eliminated from the body (Johnson et al., 2003; Waring, Webb, & Maxwell, 2000). The normal adult range for serum uric acid is 3.0 to 7.0 mg/dL (Van Voorhees, 2007).

Elevations in uric acid have been found to be positively associated with a number of cardiovascular and metabolic conditions (Johnson et al., 2003; Oyama et al., 2006; Waring et al., 2000). Adenosine is a product released by cardiac and vascular myocytes that degenerates into uric acid. It contributes to the normal resting vascular tone through the involvement of smooth muscle and arteriolar vasodilatation. However, under conditions of hypoxia and ischemia, adenosine is synthesized at an unregulated rate and can lead to increased serum concentrations. This results in a rapid degeneration and serum elevation of uric acid. Thus, uric acid may act as a marker for tissue ischemia. This becomes very significant when ischemia is involved in transient coronary artery occlusion commonly seen in strokes and myocardial infarctions (Johnson et al. 2003; Waring et al. 2000).

Elevated insulin levels have also been shown to play a role in hyperuricemia (Ford, Li, Cook, & Choi, 2007, Waring et al., 2000). Circulating insulin causes a reduction of sodium and uric acid clearance by physiologically acting on the renal tubules (Waring et al. 2000). Elevated insulin levels have been commonly seen in disorders such as metabolic syndrome and diabetes. Thus, when there is an increase in plasma insulin there is a rise in uric acid, which makes uric acid a good biomarker for elevated levels of insulin.
Since uric acid is eliminated primarily through the kidneys, hyperuricemia has also been found to be associated with hypertension (Alper et al., 2005; Feig & Johnson, 2003; Johnson et al., 2003;). During instances of renal disease or poor renal function, there is a reduced glomerular filtration rate which in turn reduces the rate of urate excretion. Hypertension also contributes to decreased renal blood flow and results in microvascular disease, which decreases uric acid excretion, stimulates urate reabsorption, and may lead to local tissue ischemia of the kidneys (Johnson et al. 2003).

**C-Reactive Protein**

C-Reactive Protein (CRP) is produced by the liver during the acute phase response of the immune system. This response is commonly activated though an acute injury, infection, inflammation, or malignancy. Multisystem responses occur that release inflammatory mediators and enhance hepatic protein synthesis. The key functions of CRP within the immune system include: recognizing and binding to damaged walls found on bacteria, fungi and parasites; preparing bacteria debris for phagocytosis; activating the complement system which triggers phagocytic activity; and stimulating the production of cytokines as shown in Figure 2. Early in the acute phase response inflammatory mediators such as Interleukin (II) – 1, II-6, and tumor necrosis factor (TNF) – alpha initiate a response by the liver to produce CRP. CRP can then increase up to 10,000 times in response to an infection or injury; and it serves to activate the complement system. Thus, CRP levels are a direct and quantitative measurement of the overall acute phase response. CRP will remain elevated throughout the response and will only return to normal once normal tissue structure and function is restored. (Armani & Becker, 2005; Calabro, Chang, Willerson, & Yeh, 2005; Capuzzi & Freeman, 2007).
In addition to acute insults, studies have also found obesity to be associated with elevated levels of CRP (Calabro et al., 2005; Wu, Chu, Shen, & Chang, 2003; Yoshida, Kaneshi, Shimabukuro, Sunagawa, & Ohta, 2007). Adipose tissue secretes various bioactive substances called adipocytokines which have many inflammatory mediators; initiating inflammation. Some of these mediators include II-6, II-1, and TNF-alpha which activate both hepatic and extrahepatic production of CRP. Because obese individuals have a large amount of adipose tissue, they manifest enhanced inflammation and demonstrate increased CRP (Calabro et al. 2005).

Research has also demonstrated that CRP is a biomarker effective in evaluating cardiovascular and cerebrovascular risk in healthy adult men, women, and the elderly; and has been found to be a reliable predictor of future cardiovascular events (Armani & Becker, 2005; Capuzzi & Freeman, 2007; Wu et al., 2003; Yoshida et al., 2007). Because CRP is associated with inflammation, data suggest that chronic inflammation is a major factor that drives the progression of atherosclerosis and atherothrombosis (Armani & Becker). Vascular risk factors such as hypertension, dyslipidemia, and hyperglycemia, which are commonly seen in diabetes and metabolic syndrome; all cause damage to the vascular walls. This produces inflammation and initiation of endothelial dysfunction and atherosclerotic plaque formations. Progressive rises in CRP can reflect the stages of vascular inflammation (Capuzzi & Freeman, 2007).

Although typically CRP is not as significantly elevated in cardiovascular disease or obesity as in injury, infection, or acute inflammation, measuring small changes in CRP has been shown to be effective in evaluating risk. While the standard CRP assay is commonly used to evaluate elevations seen in the acute phase response, it has been found to be less accurate when measuring CRP levels lower than 10 mg/L. In order to more accurately measure small elevations in CRP presented in cardiovascular disease and obesity, high sensitivity CRP (hs-CRP) methods
have been developed. Two assays that have been shown to be effective in measuring hs-CRP are the latex hs-CRP method and enzyme-linked immunoabsorbent assay (ELISA) (Rifai, Tracy, & Ridker, 1999). Although these methods use different techniques, studies have shown both tools to be equally useful in evaluating small elevations of CRP. (Capuzzi & Freeman, 2007; Rifai et al. 2007).

The CDC and American Heart Association (AHA) have also supported the evaluation of CRP for cardiovascular risks using the hs-CRP method. In doing so, they have developed adult guideline reference ranges. A CRP of less than 1.0 mg/L is considered low risk; 1.0-3.0 mg/L is average risk, and greater than 3.0 mg/L is high risk (Wu, 2006).

Uric Acid and CRP in Children

Research has demonstrated that elevated uric acid and CRP are positively associated with many chronic conditions in adulthood. Several studies have found high uric acid and CRP levels in patients with cardiovascular disease, glucose intolerance, obesity, hypertension, and hyperlipidemia (Feig & Johnson, 2003; Alper et al., 2005). A number of studies have also identified associations of elevated levels and chronic conditions with children and adolescents. Ford, Ajani, & Mokdad (2005) found elevated CRP and uric acid levels to be strongly correlated with the prevalence of metabolic syndrome among US children and adolescents. The authors concluded that children and adolescents with metabolic syndrome are more likely than those without to show evidence of low grade inflammation.

Studies have also shown that uric acid and CRP levels are significantly increased with obesity and could be used as an obesity-related indicator in early adolescence (Oyama et al., 2006; Ford et al., 2005; Chu et al., 2003). Elevated uric acid levels in children have also been positively related to hypertension (Alper et al., 2005; Feig & Johnson, 2003).
suggested that early elevation in serum uric acid levels may play a key role in the development of hypertension. In addition, research has linked elevated CRP with adverse lipid profiles and cardiovascular risk factors in children and adolescents (Chu et al., 2003).

Although usual adult ranges of uric acid and CRP have been determined, research has shown that these are not accurate ranges for children and adolescents. Wilcox (1996) found that serum uric acid levels increase slowly throughout childhood. The levels during infancy, childhood, and adolescence reflect developmental changes in metabolism, renal function, endocrine function, diet, and energy expenditure. He also found that because renal tubular secretion is related to age, there is a progressive decrease in the fraction excretion and clearance of uric acid by the kidney with advancing age until adulthood. Thus, adult reference ranges would not be accurate even for adolescent children.

While CRP cardiovascular risk ranges in adults have been developed, research suggests they may be inaccurate for children. Since body and fat composition are different between children and adults, it may influence the relationship between adiposity, obesity, and CRP. Because children do not have as much adipose tissue, there is a lower release of adipocytokines which may result in a lower CRP than a normal adult (Cook et al., 2000). Cook and colleagues (2000) identified elevated levels of CRP in those who were developing breasts and having changes in adipose tissue compared to those children without such pubertal changes. In addition, studies have shown that inflammation increases with age, and differences in sex steroid hormone concentrations from children to adults may cause additional differences in CRP (Cook et al., 2000).

Because CRP and uric acid have been shown to be good predictors of numerous cardiovascular and obesity related conditions, it is important that normal ranges for middle
school aged children be established. While there has yet to be any nationally recommended ranges, the literature reports a variety of different mean levels of CRP and uric acid among the middle school aged population.

**Literature Review**

**Method**

In order to ensure a comprehensive review of the literature, a broad search strategy that covered several electronic databases and search engines was used. This included searches in CINAHL, PubMed, Ovid, Medline, Google, the CDC, and the Cochrane library. Key words used included “middle school,” “children,” “uric acid,” “C-reactive protein,” “levels,” and “ranges;” and searches were conducted using a variety of different key word combinations. Only those studies that were in the last 12 years (1996-2008) and included a general representation of healthy middle school aged children were selected.

**Uric acid**

A number of studies describe the mean uric acid levels of middle school aged children. Alper et al. (2005) conducted a study that examined 334 whites and 243 blacks enrolled in the Bogalusa Heart Study, which consisted of multiple cross-sectional surveys of children ages 5 to 17 years. Uric acid means ranged from 220.1 μmol/dL (3.7 mg/dL) in black females to 303.3 μmol/dL (5.1 mg/dL) in white males, averaging to 4.7 mg/dL in males and 3.9 mg/dL in females. (see table 1).

A cross-sectional analysis of 1370 males and females aged 12 to 17 years used data from the National Health and Nutrition Examination Survey (NHANES) of 1999-2000. Uric acid concentrations in this population ranged from 1.9 mg/dL to 12.1 mg/dL with a mean of 5.1
mg/dL. The 50th percentile had uric acid ranging from 4.88 mg/dL to 5.21 mg/dL (Ford, Li, Cook, & Choi, 2007).

Oyama et al. (2006) conducted a cross sectional study of Japanese children ages 9.1 to 15 years. The study consisted of 923 males and 806 females. None of these subjects had any chronic conditions or were on any medications. They found that the mean uric acid levels in males and females were 5.3 mg/dL and 4.3 mg/dL respectively; the range was 0.6 – 9.6 mg/dL in males and 0.2 – 7.7 mg/dL in females. In this study, males from 11 to 15 years had significantly higher means than females; 81 of 923 males (8.8%) had a serum uric acid value more than 7.0 mg/dL while only 5 of 806 females (0.6%) had these elevated levels. While the results demonstrated that the uric acid levels began to rise from age 11.1 to 12.0 years old, females tended to stabilize and males showed an upward trend throughout adolescence. This was attributed to the progressive decline in renal uric acid clearance during puberty. Because males tend to develop later than females, the elevation of male uric acid corresponded with their later onset of puberty.

A meta-analysis was conducted by Wilcox (1996). This study presented the changes in uric acid levels as children age into adulthood. Males of 12 years old were found to have a mean uric acid level of 4.4 mg/dL, while females had a mean of 4.5 mg/dL. It was then discovered that there was an increase in male uric acid levels as the children aged into their late adolescence with males and females at 5.6 mg/dl and 4.5 mg/dL at 15 years old; and 6.2 mg/dL and 4.0 mg/dL at 18 years. This may be attributed to the increase in weight of males as they age, and the hypouricemic effects of estrogen in females.

**C-reactive protein**

CRP mean levels have been investigated in several children and adolescent populations. Wu, Chu, Shen, & Chang (2003) conducted a study of children in the Taipei Children Heart
Study. The population consisted of 835 randomly selected children (410 boys and 425 girls) from Taipei, Taiwan junior high schools. Ages ranged from 12-16 years, with a mean age of 13.3 years. Using the latex high sensitivity method to calculate the CRP, the mean CRP in males was 0.301 mg/L and less than 0.188 mg/L for females (see Table 2).

Ford et al. (2003) used data from the NHANES 1999-2000 to describe the distribution of CRP of US children and young adults 3-19 years old. In order to calculate the CRP, the latex high sensitivity CRP method was used. There were a total of 3227 participants with a CRP less than 10 mg/L. The mean CRP for these participants was 0.8 mg/L, with a male mean of 1.2 mg/L and female mean of 1.9 mg/L. When looking at children from ages 10-15 years, there were 1347 participants and the mean was found to be 0.9 mg/L.

Morgan et al. (2005) conducted a random stratified sample study of youth in Minneapolis, MN. To calculate the CRP the ELISA method was used. Six subjects with a CRP greater than 5.05 mg/L were excluded from the analysis. The total participants ranged from 10-16 years old (mean of 13 years) and there were 189 males and 153 females. The mean CRP for the males was 1.10 mg/L and for females was 1.16 mg/L.

One study conducted a cross section survey by collecting sample of subjects aged 6 to 24 years who enrolled in the Columbia University BioMarkers Study. Subjects could not be ill with any current infections at the time of enrollment. There were a total of 95 males and 110 females in the study; 46 of the males and 49 females were from 10-14 years old. The ELISA method was used to calculate CRP levels. Among all ages, females had a mean CRP of 1.3 mg/L and males of 1.4 mg/L. The range throughout all ages was 0.6 – 9.63 mg/L for males and 0.4-10.27 mg/L for females. In children from 10-14 years, the mean CRP was 1.3 mg/L. The median for both boys and girls was 0.98 mg/L (Isasi et al., 2003).
Discussion

Elevated levels of uric acid and CRP have been positively associated with a number of cardiovascular and metabolic conditions. Some of these include ischemia that can lead to strokes and myocardial infarctions, obesity, insulin resistance, and hypertension. Although these chronic conditions are more prevalent in adulthood, studies have shown associations with elevated levels in children and adolescents.

While normal adult ranges have been established, research has shown that because children and adolescents have not grown to their full maturity, their uric acid and CRP levels should not be compared to adult ranges. Wilcox (1996) demonstrated that uric acid levels slowly increase throughout childhood based on a variety of metabolic and developmental changes. Studies also found that CRP levels in children could be related to percentage of adipose tissue, inflammation, and differences in sex steroid hormones (Cook et al. 2000).

While adult normal ranges for uric acid were found to be 3.0 to 7.0 mg/dL, the review of literature found means in young adults that range from 3.9 mg/dL to 5.3 mg/dL. While the highest for the studies means was 5.3 mg/dL, it appears to be significantly lower than the normal upper limit of an adult at 7.0 mg/dL. This can suggest that middle school aged children may have a lower normal range than adults.

Although a variety of different mean levels were found among the studies examined, each study focused on a different population which may account for these differences. While many of these studies had large sample sizes, there were only a very few studies that specifically examined middle school aged children. Wilcox et al. (1996) demonstrated a good representation of middle school aged children, by looking at specifically 12 year olds finding the mean levels of males and females to be 4.4 mg/dL and 4.5 mg/dL. These numbers also appear to be relatively
reliable as they are near the middle of the means found among all the studies. Oyama et al. (2006) examined subjects from 9 to 15 years old and found a mean of 5.3 mg/dL and 4.3 mg/dL in males and females, respectively. Although this study demonstrated the highest uric acid levels, there is no conclusive evidence about this finding. This was the only study with a Japanese population, so cultural variation may occur.

Other studies that may provide less accurate results for middle school aged children evaluated a larger age range for their studies. Ford et al. (2007) studied a more mature population with ages ranging from 12-17 years old. This may have contributed to the high uric acid mean level of 5.1 mg/dL found in both male and female populations. The lowest levels of uric acid were found in the study conducted by Alper et al. (2005). They found mean levels as low as 3.9 mg/dL. Although the population was significantly younger, with subjects as young as 5 years, it also had some of the oldest subjects at 17 years, so it may be difficult to assume this lower number is associated with the younger population.

Another variable that may have contributed to disparate results was population selection. In the literature, only the study conducted by Oyama et al. (2006) discussed removal of those subjects who had chronic conditions or were on any medications. Thus, outliers in the studies may have skewed the results to make them a less accurate representation of the entire population. While larger studies may be able to absorb some of the large numbers, smaller population studies could have been greatly affected.

Numerous studies have found that uric acid levels are higher in males than females though adolescence. When comparing gender the literature found that females ranged from 3.9 mg/dL to 4.5 mg/dL and males from 4.3 mg/dL to 5.3 mg/dL. This suggests that there could be a possible association between gender differences and uric acid levels. Oyama et al. (2006) study
found that male levels were significantly higher than female levels. Wilcox (1996) also
discovered that males tended to have higher levels than females during puberty and suggested
that it may be attributed to the increase in weight of males as they age and hypoureemic effects of
estrogen in females.

Regarding CRP levels, there was a great deal of variability among the studies. The lowest
CRP rating was found to be <0.19 mg/L and the highest was 1.3 mg/L. Although Wu et. al.
(2003) found significantly lower values than the rest of the studies; the fiftieth percentile in the
study conducted by Ford et al (2003) was 0.3 mg/L in ages 10-14 years, and median for both
males and females in the study conducted by Isasi et al (2003) was 0.98 mg/L. This suggests that
there may be a large degree of variability among the data collected in each study, and possibly
outliers that may have increased the mean number.

When comparing the levels found to adult ranges of CRP for cardiovascular risk which
included: less than 1.0mg/dL low risk; 1.0-3.0mg/dL average risk, and greater than 3.0mg/dL
high risk, all of the study means were in the low to low average risk. This may imply that CRP
levels may be lower on average in middle school aged children compared to adults. Thus, in
order to detect cardiovascular risk, these ranges may need to be adjusted lower to accurately
assess the middle school aged population.

While the studies gave a good representation of middle school aged children with
populations focusing on ages 10-14 years, there were a number of variables that may have
attributed to the variety of mean numbers found in the literature. One variable that played an
important role was how each study removed existing outliers that may have affected the results.
In the study presented by Ford et. al.(2003); CRP levels that were higher than 10 mg/L were
excluded from the study. In Morgan et al.’s study (2005) levels greater than 5.5 mg/L were
removed. The study by Isasi et al. (2003) only removed those subjects that were ill with infections, and did not have any specific CRP level cut off. Because each method was different, each study would have found different means. This may have also contributed to why Isasi et al. (2003) study had such a high mean CRP level, especially since it has a smaller population so a few high CRP levels could have increased the mean number significantly.

Some other variables that may have affected the results were the population of study. While Wu. et al. (2006) only studied subjects in Taipei, Taiwan, all the other studies were based on a US population. This may help explain why their CRP levels were markedly lower than the rest of the studies. Also some of the studies used very large populations while others had smaller numbers which could affect the final results of the study.

In addition, the way CRP was calculated may have played a minor role in the data found. While studies conducted by Ford et al. (2003) and Wu et al. (2006) used the latex high sensitivity assay method to determine their CRP, the other two studies used the ELISA method. Although research has shown both these studies to be similar in their results, this could have accounted for minor differences in the outcomes (Rifai, Tracy, & Ridker, 1999).

When comparing males to females there appears to be no significant differences. Although each study had different levels for each gender, two studies had the females being higher, another had higher values with males, and the last study has no comparison. Thus, no trends associated with gender and CRP can be accurately stated.

Conclusion

Research has demonstrated the differences in uric acid and CRP in middle school aged children and adults. Most of the literature has suggested that middle school aged children may have lower levels of these biomarkers than adults, thus implying the inaccuracy of using adult
Serum Concentrations

normal ranges. Uric acid and CRP may play an important part of determining those children who may be at risk, so defining normal levels would aid health care providers in identifying those children who are at risk. They are additional tests that would help detect inflammatory risk in these children at an early age, especially those with a positive family history or associated symptoms. This comprehensive profile provides information to develop interventions and life style modifications for children at risk. This would benefit the child’s well being, help establish healthy life styles changes that they could carry over into adulthood, and improve their health outcomes as adults.

In order to accurately determine those children who may be at risk for cardiovascular and metabolic disease associated with elevated levels, more studies need to be conducted. Studies that have a narrow range of focus on just the middle school aged population with a very large sample size would be the most beneficial in determining the normal ranges for uric acid and CRP in middle school aged children. Also studies that look at specific gender populations may need to be conducted as uric acid levels in males and females have been found to vary. Through these larger studies, normal ranges of uric acid and CRP can be better defined and more accurate at determining those children who may be at risk. Thus, it would be one more step in fighting the battle of cardiovascular disease, obesity, and metabolic diseases that claims an increasing number of lives each year.
References


Table 1.

**Mean Uric Acid Levels**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Type of study</th>
<th>Population</th>
<th>Age (years)</th>
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<th>Females</th>
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<td>Cross sectional</td>
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<td>9-15</td>
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<td>Meta-analysis</td>
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Table 2.

Mean C-Reactive Protein Levels

<table>
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<th>Mean (mg/L)</th>
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<td>Males</td>
<td>Females</td>
<td></td>
<td></td>
<td>Males</td>
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<td>Wu et. al.</td>
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<td>425</td>
<td>Random selection</td>
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<td>10-14</td>
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PRPP = phosphoribosylpyrophosphate

*Figure 1.* Production and excretion of uric acid. Purine nucleic acids are broken down to eventually produce uric acid. It is then excreted through the kidneys and gastrointestinal track (Wilcox, 1996).
Figure 2. Functions of C-reactive protein. The key functions of CRP within the immune system include: recognizing and binding to damage walls found on bacteria, fungi and parasites; preparing bacteria debris for phagocytosis; activating the complement system which triggers phagocytic activity; and stimulating the production of cytokines (Hengst, 2003).