concentrations. These factors (including high uric acid) have been mentioned in one or more definitions of the metabolic syndrome [7]. Recently, much attention has been paid to the metabolic syndrome due to its possible role as a risk factor for the development of type 2 diabetes and cardiovascular disease. The worldwide increase in the prevalence of obesity and diabetes is a reason not only for the increasing prevalence of the metabolic syndrome but also of hyperuricaemia.

Hyperinsulinaemia and insulin resistance lead to elevated serum uric acid levels through both direct and indirect mechanisms, which include increased urate production as well as decreased renal urate excretion (probably due to the stimulating effect of insulin on urate reabsorption in the renal proximal tubule). Hypertension, use of some drugs (in particular diuretics) and renal disease are also associated with increased uric acid concentrations.

The link between uric acid and the progression of vascular disease has been examined not only in epidemiological studies but also with experimental investigations [8]. The possible mechanisms involved in this causal relationship are:
- uric acid may induce a thickening of the glomerular afferent arteriole, activation of the renin-angiotensin system, and hence hypertension;
- uric acid may contribute to endothelial dysfunction by inducing anti-proliferative effects on endothelium and impairing nitric oxide production;
- uric acid stimulates human vascular smooth muscle cell proliferation and synthesis of C-reactive protein;
- uric acid may increase platelet adheresiveness and platelet lysis (a platelet dysfunction may be linked to endothelial dysfunction);
- hyperuricaemia could promote thrombus formation;
- uric acid may have a role in oxidative stress and in the formation of free radicals;
- uric acid may enhance oxygenation of low-density lipoprotein cholesterol and lipid peroxidation.

An independent link between uric acid and endothelial function has been reported in patients with uncomplicated,
untreated essential hypertension, independent of traditional cardiovascular risk factors [9].

Renal excretion of urate is regulated by a member of the organic anion transporter superfamily (URAT1). A specific expression of URAT1 on human aortic vascular smooth muscle cells has been reported and this could be a mechanism by which uric acid enters the human vascular smooth muscle cell, eventually leading to cardiovascular disease [10].

In patients with congestive heart failure an increased production of uric acid is mediated by activation of xanthine oxidase, a producer of uric acid from xanthine and hypoxanthine. Xanthine oxidase is also a source of free radicals and may contribute to oxidative damage in the myocardium. It has also been reported that a high serum level of uric acid is an independent predictor of mortality in patients with congestive heart failure [11]. Therefore, xanthine oxidase inhibition could be a therapeutic strategy for heart failure and it may be important to measure serum uric acid as a marker of oxidative stress in patients with congestive heart failure.

Similarly to homocysteine (an amino acid that has been linked to increased risk of premature coronary artery disease and stroke), uric acid may have a toxic effect on the vasculature by inducing clotting abnormalities and oxidative stress. However, lowering of uric acid in patients with increased vascular risk has not always been accompanied by prevention of cardiovascular events [12].

In conclusion, a better understanding of the role of uric acid in health and in disease states may help physicians to improve their performance in preventing and treating cardiovascular disease.

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