High salt is a risk factor for cardiovascular and kidney diseases. What is next, fibrosis?

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In old age the flesh becomes tough, that is because the collagen increases in the connective tissue – the lime, you know, the most important constituent of the bones and cartilage. (Thomas Mann, ‘The Magic Mountain’, 1924)

In this issue of the Journal of Hypertension, Qian et al. have reported the results of a study showing that first morning voiding urine sample may be a valid low-burden, low-cost alternative for the estimation of mean population salt intakes [1]. They conclude that the International Study of Sodium, Potassium, and Blood Pressure (INTERSALT) formula may exhibit good performance in terms of mean 24-h sodium estimation for the hypertensive population living in northeast China. According to the World Health Organization, the systematic intake of excess salt in comparison with the physiological norm leads to an increase in blood pressure and, as a consequence, to a variety of heart and kidney diseases, stomach cancer, and osteoporosis [2]. The physiological norm for one person is 5 g of salt per day. In Europe and the United States, however, the average person consumes about 10 g [3]. The link between dietary sodium intake, hypertension, and progressive loss of cardiovascular and renal functions is strong and has been demonstrated in many epidemiological studies in humans [2–4]. In the prehistorical age (<10 000 years BC) our ancestors consumed <0.5 g/day, NaCl intake increased significantly due to food preservation with salt and reached 18 g/day. Following the invention of refrigerators, salt consumption dropped to 10 g/day but remained significantly greater than the amount recommended by the dietitians, NaCl intake (5–6 g/day) [4].

Remarkably, the results of Qian et al. demonstrate that INSERSALT, a program that previously used 24-h urine collection and blood pressure measurements in 10 079 adults from 32 countries, exhibited a good fit in estimating 24-h urinary sodium excretion [1]. INTERSALT has shown a direct relationship between salt intake as measured by daily urine sodium and blood pressure. This finding has been supported by numerous other large epidemiological studies [2]. Importantly, INTERSALT also found an association between salt intake and an increase in blood pressure with age, suggesting that, lowering salt levels may slow the increase in blood pressure with age [5]. In European countries, programs have been launched to explain the harmful consequences of salt abuse, in Finland, for example, it was possible to reduce salt intake by one-third, due to which the death rate from strokes and heart attacks decreased by 80% [6]. If doubts exist whether or not excessive salt intake harms, the arguments that moderate salt restriction does harm are weak. There are many conditions of different etiologies and pathogeneses which usually result in, but are not limited to the increases in blood pressure. However, very moderate blood pressure increases may be associated with severe vascular remodeling leading to end-organ damage [7]. Moreover, increased NaCl intake may damage the cardiovascular system without elevations of the blood pressure, that is, cause fibrosis [8]. With the results of Qian, we will get a confirmation in larger population groups of various ethnic backgrounds, and it will be possible to use spot urinary sampling for 24-h urinary sodium for prediction in thousands of aged hypertensive patients, patients with fibrosis of different origin, and ones with chronic kidney disease.

Many factors are involved in the genesis of fibrosis including cardiotonic steroids, like bufadienolides originally found in animals like toad Bufo marinus [9]. Cardiotonic steroids inhibit the Na/K-ATPase and regulate the monovalent ions balance and cell homeostasis. Moreover, by binding to the Na/K-ATPase, cardiotonic steroids can affect cell growth and differentiation, apoptosis and proliferation, glucose metabolism, and control of central nervous functions [9]. An important effect of cardiotonic steroids is their ability to function as pro-fibrotic factors, that is to start intracellular signaling cascades leading to a loss of elasticity and vascular fibrosis [10]. One of the mechanisms underlying the pro-fibrotic effect of marinobufagenin is the altered activity of Fli1, a nuclear transcription factor and a negative regulator of collagen-1 synthesis [10]. The inhibition of Fli1,
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Conflicts of interest

There are no conflicts of interest.

REFERENCES