and hypercalciuria in a famous clinical study published more than twenty years ago (73), and has been considered detrimental for stone formers ever since.

More recent investigations have actually pointed out that vegetarian diet does not increase oxalate excretion and lithogenic risk per se, but the global calcium/oxalate dietary content should be taken into account to define lithogenic risk. As a matter of fact, a balanced intake of calcium and oxalate can promote chelation in the intestinal tract, so that a smaller fraction of the two substances is excreted in urine. It is also important that the dietary intake of other substances able to chelate calcium, such as phytate, is low, making calcium available for chelation with oxalate. Therefore, the ability of a vegetarian diet to promote or prevent nephrolithiasis also depends on its composition in calcium, oxalate and phytate and on the timing of their ingestion (74). Simultaneous intake of highoxalate foods and high-calcium foods is the best way to limit the absorption of both substances (75). On the other side, simultaneous ingestion of calcium and substances with a high chelating power, such as fibres or rice bran, may result in a rise of lithogenic risk due to the higher excretion of oxalate, that leads to higher levels of calcium oxalate supersaturation index, even if stone recurrence rate is prospectively not affected (76,77).

It should also be noted that only a few vegetables have demonstrated to significantly raise oxalate excretion, if eaten regularly, such as spinach, rhubarb, beets and tomatoes (78). Moreover, even a massive dietary oxalate load results in a relatively mild increase in oxaluria (79): hyperoxaluria is indeed determined more frequently by genetic than environmental factors, and it generally affects only a small portion of calcium stone formers (4,80). Finally, both vegan and lacto-ovo-vegetarian diets have shown not to significantly affect calcium metabolism, bone turnover and calcium excretion on a short-term period, even if their effect for a long-term period is still poorly known (81).

Therefore, current evidence shows that a balanced lactoovo-vegetarian diet is generally not detrimental for kidney stone prevention and can on the contrary be protective, provided that there is an adequate and simultaneous intake of calcium and oxalate and that there is not an excessive intake in fibres. On the other side, the effects of vegan diet in kidney stone disease are not fully understood; the risks of micronutrient deficiencies and of hyperuricemia may outweigh benefits for kidney stone prevention. Thus, at the present state of knowledge, vegan diet should not be recommended for kidney stone prevention.

## **Mediterranean diet**

The traditional Mediterranean diet is characterized by a high intake of olive oil, fruits, vegetables and cereals, a moderate intake of fish, poultry and wine, and a low intake of dairy products, red meat and sweets (82). It is not properly a "fad" diet like the others discussed above, which have gained popularity for cultural or commercial reasons, but it should be instead considered an "evergreen" model of a healthy way of eating, recognized worldwide as one of the cornerstones of nutrition.

Mediterranean diet, as a matter of fact, has been extensively studied, especially in recent years. A huge amount of evidence has shown that it has protective effects against cardiovascular disease (83), hypertension (84), metabolic syndrome (85), cancer (86,87), neurological diseases like stroke and cognitive decline (88) and kidney function (89). Mediterranean diet has also been linked to biochemical and genic parameters of a successful aging (90).

However, the epidemiologic and biochemical impact on urinary stone risk factors of this diet has not been studied yet in literature, even if our research group has published a 5-year trial demonstrating the efficacy of normal calcium, low salt, low protein diet very close to a traditional Mediterranean diet (35). There are indeed no studies, at the current state of knowledge, comparing Mediterranean diet with the usual Western diet focusing on urine composition and the risk of stone relapse. Nevertheless, the composition of the traditional Mediterranean diet highly fits with the main dietary recommendations for nephrolithiasis prevention, such as the low intake of animal proteins and the high intake of fruits and vegetables. For many aspects, Mediterranean diet is very similar to DASH diet, which has proven to be effective in the prevention of kidney stone onset and relapse (69,70).

An aspect of Mediterranean diet that has been particularly emphasized is the high content of antioxidant substances, such as beta-carotene and vitamin E. These substances have been overall associated with a better health-related quality of life, both from a mental and physical point of view (91). In the nephrolithiasis field, there are some evidences stating that low levels of antioxidants such as alpha-carotene, beta-carotene and beta-cryptoxanthin are associated in general population to a history of kidney stones, thus indicating a possible protective role of these substances in stone prevention (92). There are also reports showing that antioxidants may prevent renal cell injury and stone formation in idiopathic calcium nephrolithiasis