

## Use of selenium in chemoprevention of bladder cancer

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The anticarcinogenic potential of selenium was first identified nearly 40 years ago in geographical studies that reported lower death rates for cancer in regions with high levels of selenium. Cancer of the bladder was one of the body sites found to share this inverse association. Although many subsequent studies have been done on selenium and cancer, only a few have specifically assessed the relation with bladder cancer. However, the high recurrence rate and ability to monitor bladder urothelial-cell carcinoma make selenium a good candidate for chemoprevention. Evidence suggests that selenium is a biologically plausible, safe, and efficacious potential chemoprevention agent for bladder cancer. Large tertiary chemoprevention trials are needed to further investigate the role of selenium in the prevention of bladder cancer. Future studies should assess the best dose and form of selenium, and whether the protective effect of selenium differs between the sexes.

### Introduction

Bladder cancer is a major health problem and ranks the ninth most common cancer for both sexes worldwide.<sup>1</sup> In 2002, 357 000 new cases and 145 000 deaths were attributed to the disease.<sup>1</sup> About 90% of bladder cancer cases are transitional or urothelial-cell carcinomas, with the remainder comprising adenocarcinomas, small-cell carcinomas, and squamous-cell carcinomas.<sup>1</sup> Cancer of the bladder affects mainly elderly people, with a median age at diagnosis of 65–70 years.<sup>2</sup> This cancer is more common in men (77% of bladder cancer cases) and 63% of cases are from high-income countries.<sup>1</sup> Clinically, two types of bladder cancer are evident: papillary and invasive. Papillary bladder cancer is derived from superficial tumours (stage Ta–T1) and confined to the urothelium (figure 1).<sup>3</sup> Although rarely lethal, papillary bladder cancer recurs in up to 75% of patients.<sup>3</sup> Only a few of these patients progress to invasive bladder cancer, which develops through carcinoma in situ.<sup>3</sup> This type of bladder cancer has the potential to be highly malignant and progressive, and can metastasise and lead to death (figure 2).<sup>3</sup>

Most cases of bladder cancer are sporadic, and involve no known family history.<sup>4</sup> Long-term exposure of the urothelium to carcinogens is thought to cause bladder cancer.<sup>4</sup> Cigarette smoking is reported to be the major risk factor for the disease.<sup>5</sup> Other factors have also been implicated in its cause, such as radiation, schistosomal infections, and exposure to chemicals (eg, aromatic amines and polycyclic aromatic hydrocarbons).<sup>6</sup> Polymorphisms of genes involved in the metabolism of carcinogens—glutathione S transferase (*GST*), N-acetyltransferase (*NAT*), and sulphotransferase (*SULT*)—are thought to modify an individual's susceptibility to carcinogens and hence their potential risk to cancer.<sup>7</sup> From a dietary perspective, high consumption of meat and fat, and high total fluid intake have also been associated with bladder cancer.<sup>8</sup> However, results from studies investigating these dietary factors have been inconsistent and inconclusive.<sup>8</sup> From existing information on the nutritional factors that are thought to reduce the risk of bladder cancer, several studies<sup>8–10</sup> have reported that a diet high in fruit, vegetables, vitamins A, C, and E, and the trace element selenium might be protective.

Because geographical studies<sup>11,12</sup> done in the 1970s reported a possible inverse association between selenium and cancer mortality, epidemiological studies have focused on investigating the anticarcinogenic properties of this nutrient. Two key findings that emerged from these early studies were the inverse association between selenium and cancer seemed to be both sex and site specific. A larger difference in the reduced death rates was reported for men than for women in regions with high levels of selenium, and mortality was significantly lower for some types of cancer (eg, bladder cancer).<sup>11,13</sup> We reviewed the available published work to determine whether selenium is a suitable chemoprevention agent for bladder cancer.

### Sources of selenium

Selenium is an essential trace element that is present in a wide range of foods, including grains, meat, poultry, fish, eggs, and dairy products.<sup>14</sup> Large variations in selenium intake exist between populations. The soil

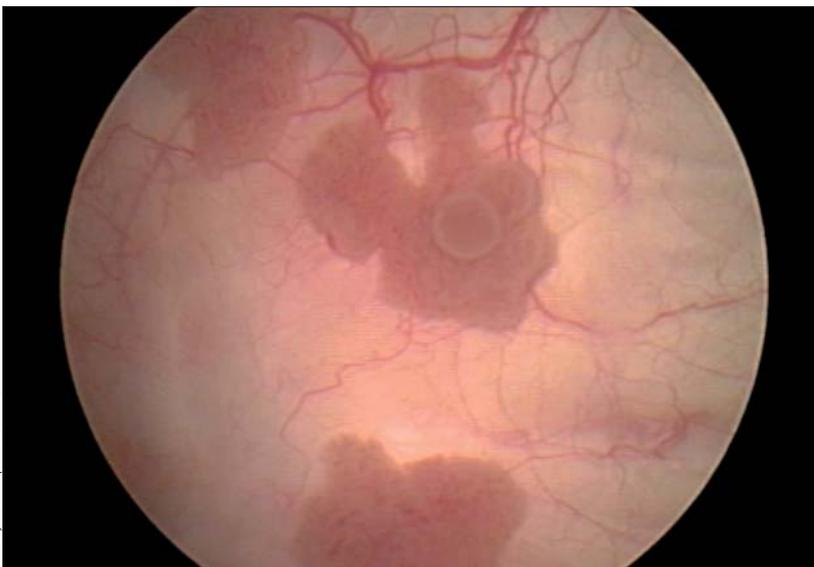


Figure 1: Endoscopy of three separate lesions of typical low-grade bladder urothelial-cell carcinoma with feeding blood vessels and papillary morphology