

# **Section I**

## **Early Colorectal Cancer**



## CHAPTER 1 SETTING THE SCENE

### 1.1 Colorectal Cancer in Australia

Colorectal Cancer is unequivocally a major health problem in Australia. It is the most common cancer reported to Australian cancer registries and was responsible for 13% of cancer deaths in 2001,<sup>1</sup> the latest year for which national figures are available. Only lung cancer, which caused 19% of deaths, was a more common cause of cancer death.

Each year there are about 12,600 new cases of Colorectal Cancer and 4,700 deaths. About one in 21 Australians is likely to develop Colorectal Cancer during his or her lifetime, with the risk increasing after 40 years of age, and rising sharply and progressively from the age of 50.<sup>1</sup>

In 2001, premature death from Colorectal Cancer was responsible for an estimated 29,058 life-years lost before 75 years of age. This made it second only to lung cancer as a cause of lost life-years.<sup>1</sup>

In the same year, Colorectal Cancer was the most commonly diagnosed invasive cancer after non-melanocytic skin cancers, accounting for some 14% of all invasive cancer diagnoses.<sup>1</sup> Australian incidence rates are towards the higher end of the scale internationally, alongside those for North America and New Zealand.<sup>1,2</sup>

The lifetime risk of Colorectal Cancer before the age of 75 is about one in 17 for males and one in 26 for females,<sup>1</sup> with incidence and mortality increasing progressively with age. (Table 3.1) Fewer than 1% of cases are diagnosed in people under 35 years of age.<sup>1</sup>

Australian data for the period 1999–2001 show:

- for females, little evidence of a change in incidence (+0.1% per annum), but a slight decline in age-standardised (world population) Colorectal Cancer mortality (-1.6% per annum)
- for males, an increase in incidence (+0.3% per annum), and a slight decrease in the mortality rate (-1.2% per annum).<sup>1</sup>

A national Colorectal Cancer care survey in Australia has reviewed all cases registered at each cancer registry within Australia between February and April 2000. This study gives a snapshot of the management plan currently used in Australia. The results show a high concordance of current practice with evidence-based NHMRC guidelines.<sup>3</sup>

### 1.2 Aetiology and pathogenesis

Colorectal Cancer is a malignant tumour that starts in the bowel wall and is usually, but not always, confined locally for a relatively long period before spreading through the bowel wall and metastasising to lymph nodes and other parts of the body. Survival rates are significantly improved when the disease is detected and treated early.

The aetiology of Colorectal Cancer is complex and appears to involve interactions between inherited susceptibility and environmental factors.<sup>4-6</sup>

Most Colorectal Cancers are thought to develop from benign precursor lesions, or adenomas,<sup>7</sup> which may vary from tiny nodules to tumours up to 12 cm across.<sup>8</sup> Colorectal Cancers can arise in a pre-existing adenoma or *de novo*, but the relative importance of these two pathways is unclear. Colorectal Cancer develops from areas of dysplasia. Adenomas and carcinomas often coexist, and adenomatous remnants are frequently found in carcinomas.<sup>9</sup> *De novo* cancers have, however, been observed to arise in flat mucosa,<sup>10</sup> and flat elevated cancers may originate from a pathway different from the adenoma–carcinoma sequence.<sup>11</sup>

Adenomatous polyps (adenomas) are benign tumours that develop on the lining of the bowel. Some become malignant over time. Most evidence suggests that adenomas are precursors for a substantial proportion of Colorectal Cancers. This has prompted considerable interest in removal of adenomas to prevent the development of Colorectal Cancer.<sup>12</sup> However, it usually takes many years for Colorectal Cancer to develop from small adenomas.<sup>13</sup>

### **1.3 Treatment**

There are a number of treatment options for Colorectal Cancer, and the evidence for these will be presented in subsequent chapters. Usual curative treatment options consist of surgical resection with or without adjuvant chemotherapy or radiotherapy. In advanced-stage disease, neoadjuvant therapy for T4 rectal tumours may allow subsequent resection. Palliative care programs provide benefit for patients with advanced disease (Chapter 19). Efforts over recent years to improve survival have focused on earlier (presymptomatic) diagnosis, adjuvant chemotherapy, intensive follow up and modifications of surgical technique.

### **1.4 Case survival**

Case-survival rates in Australia, as in the United States and the Netherlands, exceed those reported from most European countries. They range from about 90% five-year survival for people whose cancers were detected at the earliest (localised) stage, to 7% for people diagnosed with distant metastatic cancer.

South Australian data for 1977–94 showed a five-year survival from Colorectal Cancer of 53%;<sup>14</sup> 1993–2001 data showed a survival rate of 58% (Colin, Luke. (2004) personal communication). Based on United States SEER (surveillance, epidemiology and end results) data, it is estimated that 15-year survival would be about 47%.<sup>15</sup> For the 1977–85 diagnostic period, the five-year case survival was 50%, rising to 56% for the 1986–1994 diagnostic period.<sup>14</sup> The South Australian figures, and the upward trend, are similar to data from the United States<sup>15</sup> and the Netherlands.<sup>16</sup>

The earlier the stage at diagnosis, the higher is the chance of survival. While population-based cancer registries in Australia do not collect data on Dukes stage or Australian clinicopathological stage (ACPS) (see Chapter 14), hospital-based registries for teaching hospitals in South Australia show that five-year Colorectal Cancer case survival varies with the ACPS: 88% for stage A (confined to the bowel wall), 70% for stage B (confined to the bowel wall), 43% for stage C (regional nodal involvement), and 7% for stage D (distant metastases).<sup>17</sup> This equates with international experience. Only 15% of these cancers in South Australia were diagnosed at stage A, suggesting that significant improvement in survival and a concomitant reduction in mortality could be achieved by a shift in diagnosis to the earlier, localised stage. Significantly lower survival from Colorectal Cancer has been found in lower socio-economic groups in the South Australian population,<sup>18</sup> and delay in seeking care has been proposed as a major contributing cause of such differences.<sup>19</sup>

### **1.5 Screening for Colorectal (bowel) Cancer**

Screening for bowel cancer based on faecal occult blood testing (FOBT) has been demonstrated to reduce mortality in population studies (Chapter 3). Pilot programs of FOBT for Colorectal Cancer have begun in three Australian states and are being evaluated.

## References

1. Australian Institute of Health and Welfare, Australasian Association of Cancer Registries. Cancer in Australia 2001. Canberra: Australian Institute of Health and Welfare, 2001.
2. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas D. Cancer incidence in five continents. International Agency for Research on Cancer 2003; VIII.
3. McGrath DR, Leong DC, Armstrong BK, Spigelman AD. Management of colorectal cancer patients in Australia: the National Colorectal Cancer Care Survey. ANZ J Surg 2004; 74: 55–64.
4. Reddy B, Engle A, Katsifis S, et al. Biochemical epidemiology of colon cancer: effect of types of dietary fiber on fecal mutagens, acid, and neutral sterols in healthy subjects. Cancer Res 1989; 49: 4629–35.
5. Fearon ER. Molecular genetic studies of the adenoma-carcinoma sequence. Adv Intern Med 1994; 39:123–47: 123–47.
6. Potter JD. Risk factors for colon neoplasia — epidemiology and biology. Eur J Cancer 1995; 31A: 1033–8.
7. Tierney RP, Ballantyne GH, Modlin IM. The adenoma to carcinoma sequence. Surg Gynecol Obstet 1990; 171: 81–94.
8. Morson B. President's address. The polyp-cancer sequence in the large bowel. Proc R Soc Med 1974; 67: 451–7.
9. Bedenne L, Faivre J, Boutron MC, Piard F, Cauvin JM, Hillon P. Adenoma — carcinoma sequence or 'de novo' carcinogenesis? A study of adenomatous remnants in a population-based series of large bowel cancers. Cancer 1992; 69: 883–8.
10. Shamsuddin AM, Kato Y, Kunishima N, Sugano H, Trump BF. Carcinoma in situ in nonpolypoid mucosa of the large intestine. Report of a case with significance in strategies for early detection. Cancer 1985; 56: 2849–54.
11. Hasegawa H, Ueda M, Watanabe M, Teramoto T, Mukai M, Kitajima M. K-ras gene mutations in early colorectal cancer ... flat elevated vs polyp-forming cancer. Oncogene 1995; 10: 1413–6.
12. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 1993; 329: 1977–81.
13. Potter JD. Reconciling the epidemiology, physiology, and molecular biology of colon cancer. JAMA 1992; 268: 1573–7.
14. South Australian Cancer Registry. Incidence and mortality 1994. Analysed by type and geographical location. Epidemiology of Cancer in South Australia. Incidence, Mortality and Survival 1977 to 1994. Adelaide: Openbook Publishers, 1996.
15. National Cancer Institute. SEER cancer statistics review, 1973–1991: tables and graphs. National Institute of Health Publications, 1994.
16. Coeburgh JWW, van der Heijden LH, Janssen-Heijnen MLG. Cancer incidence and survival in the southeast of the Netherlands, 1955–1994. Eindhoven: IKZ, 1995.

17. South Australian Cancer Registry. Incidence and mortality, 1996. Epidemiology of cancer in South Australia. Incidence, mortality and survival 1977 to 1996. Adelaide: Openbook Publishers, 1997.
18. Bonett A, Roder D, Esterman A. Determinants of case survival for cancers of the lung, colon, breast and cervix in South Australia. *Med J Aust* 1984; 141: 705–9.
19. Kogevinas M, Marmot MG, Fox AJ, Goldblatt PO. Socioeconomic differences in cancer survival. *J Epidemiol Community Health* 1991; 45: 216–9.
20. National Health and Medical Research Council (NHMRC). Using socio-economic evidence in clinical practice guidelines. Canberra: National Health and Medical Research Council, 2003.

