Chapter II

14

CERVIX UTERI

ICD-10 C53

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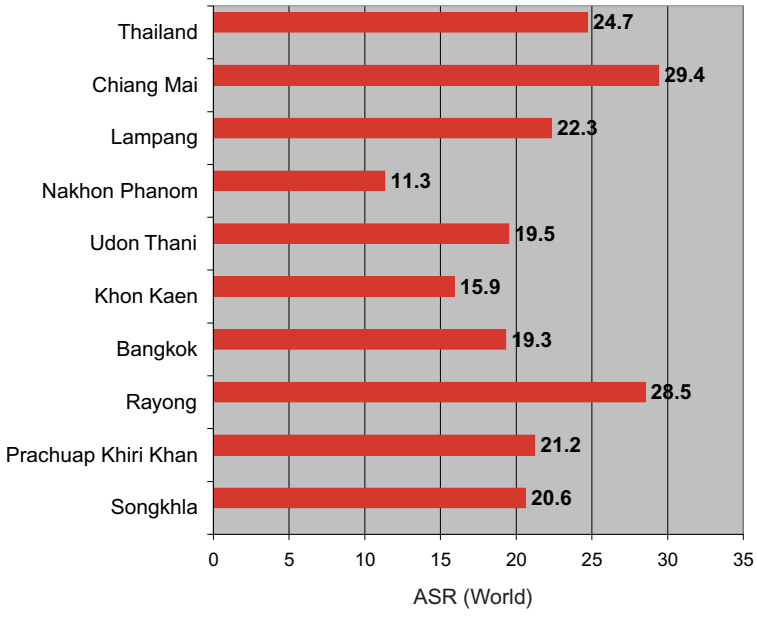
Incidence

Cervical cancer is the second most common cancer world-wide, with at least 493 243 new cases identified throughout the world each year. Eighty per cent (80%) of these cases occur in developing countries where some 273 505 women die as a result of cervical cancer every year (Ferlay *et al.*, 2004). Figures for developed nations are lower, but nevertheless cervical cancer remains a major cause of morbidity and mortality amongst women. The highest age-stan-dardized incidence rates of cervical cancer have been reported in Melanesia, Southern Africa, Central America, Eastern Africa, and South America. In all of these regions, the rates were over 40 per 100 000 women. For example, a study in Zimbabwe found an incidence rate of 54 per 100 000 and rates in Guinea were 46 per 100 000 (Chokunonga *et al.*, 2000; Koulibaly *et al.*, 1997). There is evidence that incidence rates are increasing in some parts of sub-Saharan Africa (Wabinga *et al.*, 2000).

Cancer of the cervix is the most common cancer in Thai women with an estimated 5 593 new cases in 1990 (Vatanasapt *et al.*, 1993), 5 462 new cases in 1993 (Deerasamee and Srivatanakul, 1999), 6 268 new cases in 1996 (Sriplung *et al.*, 2003) and 6 746 new cases in 1999. In 1999, the incidence is highest in Chiang Mai (ASR = 29.4) and Rayong (ASR = 28.5) and lowest in Nakhon Phanom (ASR = 11.3) and Khon Kaen (ASR = 15.9), the northeastern region of Thailand (Figure 2.14.1). In general, rates of this cancer are higher in economically developing societies. Rates are declining in those parts of the developed world with widespread screening programmes. In Nakhon Phanom, the incidence rate is the lowest, we have the organized low intensity cervical cytology programme on the years 1998-2002.

In most countries, the incidence of invasive cervical cancer is very low in women under age 25. Incidence increases at about 35 to 40 years, and reaches a maximum

Figure 2.14.1 *Cervical cancer in different regions, 1998-2000*

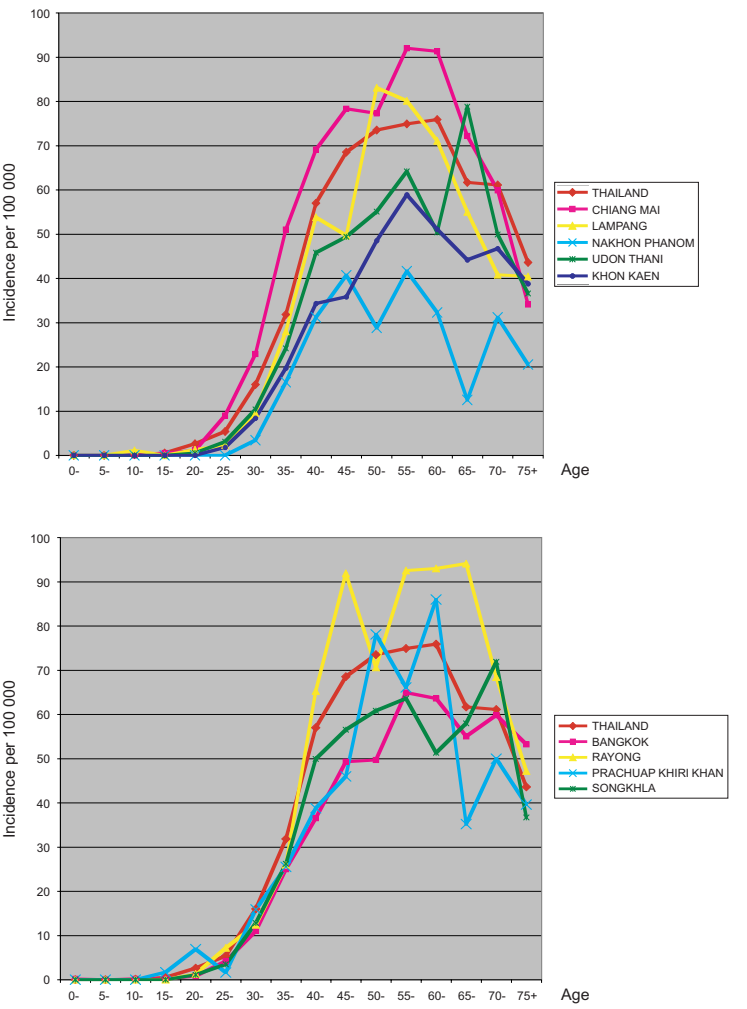


in women in their fifties and sixties (Miller, 1992). Data from cancer registries in developing countries indicate that approximately 80 to 90 percent of confirmed cases in these countries occur among women aged 35 or older. In Thailand, the age-specific incidence curves show a pattern of early increase (starting before age 20), with a steep rise to about ages 45-50, followed by a plateau and a decline (Figure 2.14.2).

Microscopic verification in all nine cancer registries are ranged from 68% (Rayong) to 98% (Chiang Mai). 73.8-83.6% of the cases are squamous cell carcinoma and 11.1-18% are adenocarcinoma (Figure 2.14.3).

It is clear that stage at diagnosis is often very advanced, compared with developed countries, i.e. Finland and U.S.A (Figure 2.14.4).

Figure 2.14.2 *Age-specific incidence rates of cervical cancer, 1998-2000*



Risk factors

The main causal agents of cervical cancer are sexually transmitted almost certainly the human papillomaviruses (HPVs) (Munoz and Bosch 1992; Munoz *et al*., 1992; IARC, 1995 Walboomers, 1999). Women infected with HPV-16 and HPV-18 have a 60-fold greater risk of developing cervical cancer than uninfected women; these two types have been identified in approximately 84% of cervical cancers (de Villiers, 1992). HPV-DNA was found in 82-91% of cervical carcinomas in Thai females (63-65% were HPV-16 and HPV-18), while HPV-DNA was found only 9.4% of normal cervical smears (Sukvirach *et al*., 1994; Bhattarakosol *et al*., 1996). The study of Chichareon *et al*., 1998 confirms the very high risks associated with HPV infection; OR of 119 (95% CI = 64-222) for squamous cell tumours and OR of 53 (95% CI = 17-163) for adenocarcinomas. Suppression of the immune system due to HIV infection also is an important risk factor because it makes the cells lining the lower genital tract (vulva, vagina and cervix) more easily infected by the cancer inducing types of HPV (Stentella *et al*., 1998). There is substantial evidence the HIV positive women are at increased risk of developing cervical cancer as well (Judson, 1992). In two studies, both from high HIV prevalence areas, a statistically significant association between HIV and CIN was reported (Maggwa *et al*., 1993; Miotti *et al*., 1996). Because the number of adolescents, as well as adults, with HIV is rising in most countries where cervical cancer is largely untreated, cervical cancer rates are expected to continue increasing, especially in areas where STI and HIV / AIDS rates are high.

Most HPV infections are transient, however, the body's defense mechanisms eradicate them, without progressing to cancer (Elfgren *et al*., 2000; Ho *et al*., 1998; Nobbenhuis *et al*., 1999). Approximately 5% to 10% of women infected with high-risk types of HPV develop persistent infections. Evi-

dence shows that these women have an increased risk of developing high-grade precancerous lesions, and cervical cancer (Bosch *et al.*, 2002; Ho *et al.*, 1998; Hopman *et al.*, 2000; Munoz and Bosch, 1996; Nobbenhuis *et al.*, 1999; Schiffman *et al.*, 1993; Walboomers *et al.*, 1999). HPV infection can lead to low-grade lesions. Most of these lesions either regress on their own or do not progress to high-grade lesions or cancer (PATH, 2000). Some high-grade lesions will progress to invasive cancer over a period of up to ten years.

HPV is the necessary but not solely sufficient precursor to cervical cancer. Men and women infected with HPV can harbor the virus both on the internal and external genitalia. Individuals can harbor HPV infection for long durations without knowing they are infected. The most promising approach to primary prevention of cervical cancer is through development of effective HPV vaccines. It is expected that prophylactic vaccines against HPV 16 and 18 (which account for about 70% of cervical cancer cases) are likely to become commercially marketed in some developing countries before 2010. Early data suggest that these vaccines are likely to be effective in preventing certain types of HPV infection and precancer (cervical intraepithelial neoplasia (CIN); their long-term impact on cancer rates will not be known for many years after introduction (Koutsky *et al.*, 2002).

It is important to recognize that less than five percent of women infected with HPV ultimately develop cervical cancer if they have no access to treatment. Natural history models and clinical data suggest that cervical cancer generally develops slowly from precursor lesions. Therefore, screening can take place relatively infrequently and still have a significant impact on morbidity and mortality. Screening every three years has almost as great an impact as screening every year. Even screening every 10 years can have a significant impact on cervical cancer incidence compared to no screening (IARC, 1986). Screening emphasis, then, should be on coverage rather than on frequency. Current understanding of cervical cancer natural history strongly suggests that, where resources are scarce, treatment of cervical lesions should focus on high-grade dysplasia, with follow-up mechanisms in place for women with low-grade dysplasia.

Figure 2.14.3 *Cervical cancer : percentage distribution of histological type among microscopically verified cases, 1998-2000*

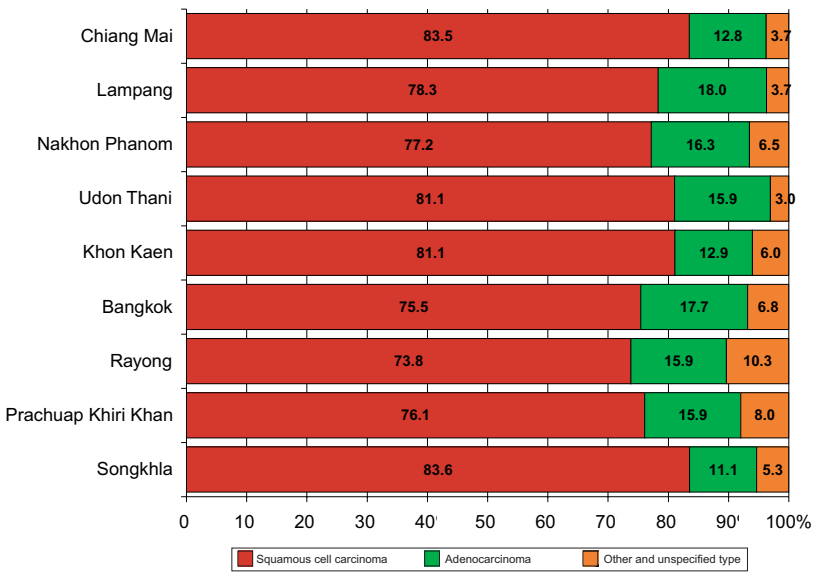


Figure 2.14.4 *Stage distribution of cervical cancer, 1998-2000*