

## CHAPTER I

### INTRODUCTION

#### Rationale and background

Laryngeal carcinoma is one of the common cancers in Thailand. At present, although there is no system to find out the exact incidence of this tumor in our community, it is estimated to be 1-2 / 100,000 population.<sup>(1-5)</sup> In Siriraj hospital, this malignancy is placed among the top ten leading cancers in males<sup>(5)</sup> and most of the cases ( 80% ) are classified as advanced cancer which requires a combined treatment of radical surgery and radiotherapy.<sup>(6)</sup>

Since rehabilitation after total laryngectomy such as esophageal speech, electrolarynx and tracheoesophageal speaking shunt is not feasible or accessible by most laryngectomized patients in Thailand<sup>(7)</sup>, many patients with laryngeal carcinoma refuse treatment and those who receive therapy may suffer the rest of their life with poor quality of life events. As a result, the outcome of treatment for this disease from the patient's perspective and with respect to long term follow up are unimpressive. To overcome this problem, several strategies should be simultaneously employed such as the development or modification of more accessible and less expensive speaking device; the promotion of public health education to diagnose early cancer cases and, most importantly, to improve cancer prevention. To reduce the incidence of laryngeal cancer, an

epidemiological study to identify possible risk factors is needed. Hopefully, intervention to minimize this top ranking cancer can be found and effectively applied in the community.

The hospital records of 437 laryngeal cancer cases diagnosed/treated at Siriraj Hospital from 1984 to 1991 were reviewed to determine their demographic characteristics and possible risk factors. Although there were no obvious associations between ethnicity, religion or occupation and the disease, this reviews showed a preponderance in males (90%)<sup>(5)</sup> and some association with tobacco consumption especially hand - rolled cigarettes ( 53.1% among smokers ).<sup>(8)</sup>

In Thailand , the tobacco used for hand - rolled cigarettes is obtained from tobacco leaves which are cut and cured by exposure to the sun and air , after which the leaves are tied into bundles for sale. There are different kinds of local tobacco available in the market; for example; Yamuan Prae ,Yamuan Nan, Yamuan Payao, Red bull etc. Hand - rolled cigarettes are made by hand rolling the finely cut tobacco into a tobacco wrapper which are made from either a square of sun dried banana leaf or paper sheet.<sup>(9,10)</sup>

The purpose of this study is to demonstrate the potential risk of this local tobacco smoking in developing laryngeal cancer and to compare this risk to the risk from manufactured cigarettes which are reported by most epidemiological studies as the important factor increasing the risk of laryngeal cancer.

## Review of the related literatures

Laryngeal cancer is a multifactorial disease. A considerable amount of epidemiological evidence has implicated chronic consumption of tobacco, excessive alcohol drinking, certain occupational exposures, and dietary insufficiency as the risk factors of this disease. <sup>(11-32)</sup>

### Alcohol and Tobacco

Epidemiological studies <sup>(13-15)</sup> have shown a relationship between excessive tobacco usage and laryngeal cancer, and the risk has been related to the amount of tobacco consumed per day. Sancho - Garnier and Theobald <sup>(16)</sup> reviewed two case - control studies from European countries and Uruguay and indicated that black tobacco smokers had an approximately 2 fold risk of laryngeal cancer as compared with blond tobacco smokers. A similar study from Spain <sup>(15)</sup> has also confirmed this finding. Whereas some studies <sup>(14,17)</sup> have shown that the risk of laryngeal cancer is increased with non-filter cigarettes compared to filter cigarettes; one study has shown no significant increase in risk. <sup>(16)</sup> In the non-industrialized countries, smoking other than manufactured cigarettes such as bidi smoking <sup>(18)</sup>, khiyo <sup>(10)</sup> and hand-rolled tobacco <sup>(19)</sup> has been shown to be associated with an increased risk of laryngeal cancer, with this risk claimed to be higher than the risk from smoking commercial cigarettes.

Mitacek and coworkers has shown that there are significant higher levels of tar, nicotine and carbon monoxide in some of Thai hand - rolled cigarettes than in local Thai and imported manufactured cigarettes.<sup>(9,10)</sup>

Excessive alcohol consumption in the presence of tobacco use is an additional risk factor, but the effects of heavy drinking have not been consistent in many epidemiological studies.<sup>(20-22)</sup> One of the main problems in most reports is that the amount of alcohol consumed by each individual is difficult to measure and has usually been measured by different methods. At present, the joint effect of alcohol and tobacco remains unclear whether it is additive or multiplicative.<sup>(14, 21-23)</sup> A study from France<sup>(24)</sup> where people commonly had high daily alcohol consumption indicated that the risk of alcohol use for laryngeal cancer is usually site specific (supragottis more than glottis) and the amount of ethanol used exceeded 80 gram per day in this disease. Wynder<sup>(13)</sup> reported in his study that there was no increased risk for laryngeal cancer among non - smoking heavy drinkers. It appears that there are no carcinogenic ingredients in alcoholic beverages per se. However, in certain part of the world, for instance, Africa, brewing or storage practices might add carcinogens to the alcoholic beverage.<sup>(13)</sup>

### Occupational Exposure

It is recognized that exposure to certain agents in the occupational environment may play an etiologic role in laryngeal cancer. Investigation of specific exposure in many case - control studies by means of the job exposure

matrix or in cohort studies of specific occupational groups have suggested associations between laryngeal cancer and exposures to asbestos, nickel, rubber products and wood dust.<sup>(25-27)</sup> Increased risk has also been noted for employment as construction workers, carpenters, drivers, plumbers, pipefitters and farmer.<sup>(25,27)</sup> However, these findings are still controversial. Muscat and Wynder<sup>(28)</sup> recently found no significant association between primary laryngeal cancer and exposures to asbestos, rubber product, wood dust and diesel fumes.<sup>(29)</sup> Wortley and colleagues<sup>(25)</sup> showed that no single occupation could explain its association with laryngeal cancer definitely and no striking difference was found for any specific occupation.

### Dietary Insufficiency

Association between low intake of fruits, vegetables and laryngeal cancer has been shown in studies from Uruguay and China.<sup>(19,20)</sup> Meanwhile, reports from Italy and USA<sup>(30,31)</sup> has emphasized that some specific substances or elements (for example carotene, iron, zinc, calcium) may be protective agents for this disease. Freudenheim and colleagues<sup>(32)</sup> indicated that high intake of dietary fat will increase the risk of developing laryngeal cancer 2 - 3 fold. Also, De Sstefani<sup>(33)</sup> has reported that past and current consumption of salted meat was associated with increased risk of this disease. But at present, the evidences to support the diet etiology have not been well confirmed.

## Miscellaneous Factors

Genetic susceptibility to cancer is suspected as another risk factor. Human glutathione S-transferase mu deficiency among smokers is believed to increase the risk of developing laryngeal cancer.<sup>(34)</sup> This enzyme is dominantly inherited and its prevalence in population is approximately 60%. However, the mechanism of developing cancer is unclear. Trell and colleagues<sup>(36)</sup> reported that the activity of the enzyme aryl hydroxycarbon hydroxylase is increased among smokers who developed cancer and concluded that the higher this genetically determined enzyme activity, the higher the cancer risk.