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Letter to the editor

Occupational exposures, anatomic location, and geographic distribution of laryngeal cancer

Re: Berrino *et al.* (2003) Occupation and larynx and hypopharynx cancer: a job-exposure matrix approach in an international case–control study in France, Italy, Spain, and Switzerland. *Cancer Causes Control* **14**: 213–223.

We read the article by Berrino *et al.* [1] with great interest. In this well-designed and interesting population-based case–control study, Berrino *et al.* evaluated the relationship of laryngeal and hypopharyngeal cancers with specific occupational exposures and found excess risk with solvent exposure for both. Overall results, except solvent exposure, were consistent with our previous observation on occupational exposures and laryngeal cancer. We observed a dose–response relationship with silica, cotton dust exposures [2], as well as diesel exhaust exposure [3].

Laryngeal cancers are usually evaluated based on anatomic location of tumors such as in the supraglottic and glottic region, and there is an observed difference in anatomic distribution of tumor [4] and related occupational factors [5]. Berrino *et al.* described the number of cases with tumors that originated from glottis, supraglottis, and hypopharynx; however, in the actual analysis they aimed to distinguish inhaled agents from ingested agents and combined all cases into two categories: endolarynx (including supraglottic and glottic tumors) presumably affected by inhaled agents and epilarynx/hypopharynx, which was affected by ingested agents. Although this approach is correct based on gross anatomy and physiology, our experience showed that odds ratios for cancer with inhaled exposure agents vary by anatomic subsections of the larynx [2, 3]. We do believe that given anatomic, histologic, and dynamic variation, particle deposition as well as particle–tissue interaction probably differs between supraglottic and glottic regions. There is a significant anatomic difference between these sections (Figure 1) [6]. The average length of an adult larynx is 36–44 mm, with a 41–43 mm transverse measurement and a 26–36 mm antero-posterior diameter, and the narrowest part of the laryngeal cavity is the glottic opening (rima glottidis); in the condition of rest or in a relaxed respiration the transverse diameter of the glottis is about 8 mm [7]. This anatomic detail leads us to an interesting link between the larynx and fluid mechanics. According to Bernoulli's principle, as the radius of the tube decreases the speed of flow increases, so more energy is used up as the molecules accelerate, which leaves less energy to exert pressure [8]. Based on this dynamic principle, we suggest that comparing with glottis, particle pressure would be much higher in supraglottic region; particle-tissue interaction induced molecular and histopathologic changes will possibly be much more significant in supraglottic region. Besides these anatomic and dynamic variations, there is also a histologic difference in the laryngeal mucosa [7, 9]. Since Berrino *et al.* seemed to have had a sufficient number of cases, we would have liked to have seen the results of an analysis for glottic and supraglottic laryngeal cancers separately.

Although laryngeal cancer is not one of the leading cancers in Western Europe, Central Europe nor The United States, this cancer has one of the highest incidence rates in men of Eastern Europe and the Mediterranean area [10, 11]. It is also common in younger men; in our study 59.2% of all cases were below age of 55 [5]. Spain, Italy, and France are among those countries with higher incidence rates but Switzerland does not fit this cluster (Figure 2) [11]. Though the controls in each center were selected as an age and gender stratified random sample of the general population, Berrino *et al.* did not conduct stratification by country. We would have liked to have seen them examine the possibility that the association between occupational exposures and the risk of cancer may differ by country. They might have included this variability by using conditional logistic regression analysis or they might have compared their results from Spain, Italy, and France with data from Switzerland to analyze possible different etiologic factors in different geographic locations.

In occupational and cancer epidemiology, scientists should look for opportunities to examine anatomical, physical, and dynamic differences in the human body, as well as to the geographic distribution of diseases. Following this interesting study, we would like to see

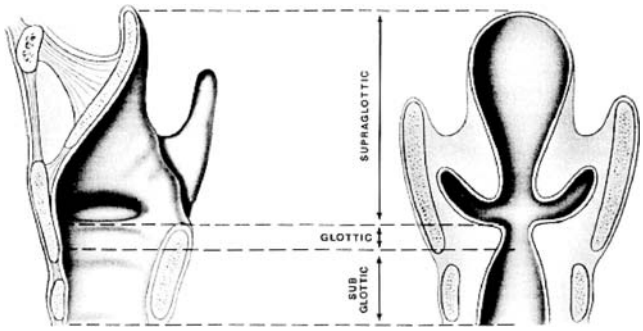

Fig. 1. Saggital and coronal sections of larynx [6].

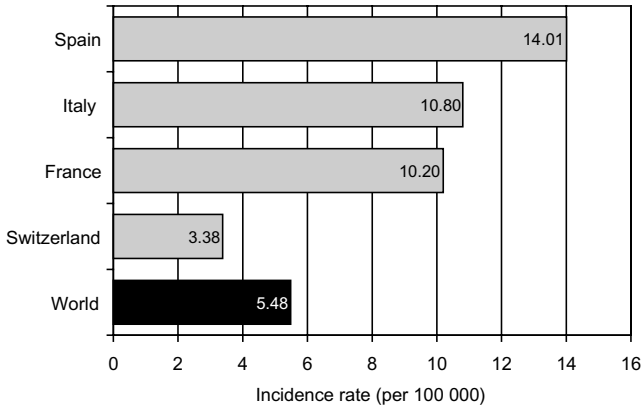

Fig. 2. Age-adjusted incidence of laryngeal cancer in 2000 [10].

Berrino *et al.* re-evaluate their data considering anatomic and geographic variation of the cancer. Detailed future investigations of bio-mechanical sciences, gene environment interactions, and occupational and environmental factors on laryngeal cancer in the Mediterranean area and in Eastern Europe will also be highly valuable for public health and the scientific community.

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