Etiology of lung cancer (C33–34) in Central and South America

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Tobacco smoking

Exposure to tobacco smoke, including second-hand smoke, is the most common cause of lung cancer; in high-income countries, smoking is estimated to account for about 90% of lung cancer cases among men and 80% of those among women [1]. Despite the joint efforts of the WHO and the Center for Disease Control Global Tobacco Surveillance System to obtain comparable adult smoking prevalence estimates in Central and Latin America, these are only available for Argentina, Brazil, Mexico, Panama, and Uruguay and information on temporal variations within countries is difficult to obtain. The Global Adult Tobacco Survey has been implemented in Argentina, Brazil, Mexico, Panama, and Uruguay since 2009 and showed that the highest smoking prevalence among men and women was in Uruguay and Argentina (31% and 29% in men and 20% and 16% in women, respectively) [2, 3]. Similar smoking prevalences were reported in a recent study conducted among 1550 adults aged 25–64 years in Barquisemeto (Venezuela), Buenos Aires (Argentina), Bogotá (Colombia), Lima (Peru), Mexico City (Mexico), Quito (Ecuador), and Santiago (Chile) [4]; the highest smoking prevalences were among men in Santiago and Quito and among women in Santiago and Buenos Aires.

The Pan-American Health Organization compiles smoking prevalence figures for countries in the region of the Americas [5] and these indicate that the highest adult smoking prevalence in Central America is in Cuba (31% in men and 16% in women) and that in South America is in Chile (44% among men and 38% among women); Chile and Nicaragua have the highest smoking prevalence among young people in their respective regions (35% and 25% for both sexes, respectively).

Occupation

Occupational exposures, including occupational agents and circumstances of exposure, play an important role in the etiology of lung cancer. The International agency for Research on Cancer (IARC) currently lists 28 substances/work situations/occupations that have been associated with lung cancer (group 1) [6]. The following industries or occupations that are relevant to the economies of many countries in the region have been associated with an increased risk for lung cancer: haematite mining, iron and steel foundries, aluminium production, coke production, carbon electrode production, painting, and rubber production. The increased risk for lung cancer in some of these activities has been recognized as being related to exposure to polycyclic aromatic hydrocarbons [7, 8]. Unfortunately, the investigation

of occupational exposures and the risk of lung cancer are complex in nature because detailed occupational history records are not widely obtained for patients with lung cancer.

De Stefani et al. [9] conducted a case–control study in men in Uruguay to evaluate the association between 22 occupations (i.e., farmer, electrician, forestry, butcher, tractor driver, painter, shoemaker, clerk, salesman, and medical worker), self-reported exposure to occupational carcinogens (wood dust, asbestos, silica dust, gasoline, strong acids, and formaldehyde), smoking history, and the risk of lung adenocarcinoma. They found that cases employed as a farmer, tractor driver, or painter for 1–20 years and those employed as a medical worker, mason or glass worker for more than 20 years had an increased odds of lung adenocarcinoma than controls *(P* for linear trend < 0.05) and also reported a synergistic interaction between smoking and employment as a tractor driver (*P* = 0.13), printer (*P* = 0.08), and medical worker (*P* = 0.03), but an antagonistic interaction for employment as a farmer (*P* = 0.02) and mason (*P* = 0.04). Furthermore, ever having been exposed to asbestos, silica dust, or formaldehyde was positively associated with the risk of lung adenocarcinoma, although the duration of exposure to formaldehyde was the only risk factor associated with an increased risk of lung cancer (*P* for linear trend = 0.004).These results suggest that smoking and selected occupational exposures are linked to lung adenocarcinoma among men in Uruguay.

Pezzotto et al. [10] conducted a study among men in Rosario, Argentina, and reported an increased risk of lung cancer among agricultural workers (odds ratio [OR],1.8; 95% confidence interval [CI], 1.1–3.1]), drivers (OR,1.9; 95% CI, 1.1–4.0),and construction workers (OR, 2.5; 95% CI, 1.0–5.9), and for the combination of agriculture–metallurgy (OR, 4.1; 95% CI, 2.0–8.1) or agriculture–construction (OR, 3.6; 95% CI, 1.1–12.4) compared with administrative staff (lawyers, teachers, and clerks). Similar results were reported for squamous cell carcinoma among agricultural workers (OR, 3.1; 95% CI, 1.5–6.9), construction workers (OR, 3.2; 95% CI, 1.2–10.9), and metal industry workers, particularly welders (OR, 2.9; 95% CI, 1.0–10.1), and carpenters had a higher risk of adenocarcinoma than administrative staff (OR, 4.7; 95% CI, 1.5–14.6). The association remained after comparing the mean duration of the occupation (33 years) and the risk of lung cancer (or squamous cell carcinoma).

The identification of cases of occupational cancer has been driven in many instances by the need for disability payments for occupational diseases and some progress in this aspect is slowly being achieved in the region. For instance, the Brazilian National Ministry of Health mandated by law the reporting of occupational lung cancer and other diseases related to work to the National Information System on Reportable Diseases [11]. In Colombia, the National Cancer Institute is currently working to establish an occupational cancer surveillance system to facilitate the identification of these diseases [Constanza Pardo, Instituto Nacional de Cancerología, Colombia, personal communication, 10 July 2014]. Chile established the National Plan to Eliminate Silicosis in 2009, which includes developing surveillance systems for exposed workers and for exposure assessments, an educational programme, and an exposure programme to regulate the risk of exposure to silica. The Chilean government also established the mandatory use of personal protective equipment [12]. The Occupational Research Centre in Canada

recently initiated a project to improve the surveillance of exposures to occupational carcinogens in the region by using the CAREX (CARcinogen EXposure) method at the request of the Pan-American Health Organization and in collaboration with Colombian institutions. The project includes the surveillance of exposures to known or suspected lung carcinogens in Canada such as diesel engine exhaust, crystalline silica, asbestos, nickel compounds, and hexavalent chromium to provide an overview of the most prevalent exposures linked to lung cancer and help to reduce or eliminate them [13].

Environmental and outdoor air pollution

On the basis of high-quality information from several countries, IARC classified outdoor air pollution and the particulate matter in outdoor air pollution as carcinogenic to humans [14]. Results from a recent meta-analysis revealed evidence for an association between an increased risk of lung cancer risk and particulate matter with a diameter of less than 10 microns [15]. An ecological time series study conducted in the region revealed that there was a high statistical correlation between lung cancer (and other types of cancer) and levels of particulate matter with a diameter of less than 10 microns in the city of São Paulo, Brazil [16].

Arsenic in the drinking-water

There is convincing evidence that the presence of arsenic – a naturally occurring metalloid in the earth's crust – in the drinking-water increases the risk of developing lung cancer [1, 17]. In Central and South America, the presence of arsenic in the drinking-water has been observed in Argentina, Chile, México, and Peru and the presence of arsenic due to mining activities was observed mainly in Bolivia, Chile, and Peru [18, 19].

The relationship between arsenic in the drinking-water and lung cancer has been widely studied in Argentina and Chile. In the province of Cordoba, Argentina, lung cancer mortality rates were much higher in districts where exposure to arsenic found naturally in the drinking-water was medium or high than in areas where exposure was low [20–22]. In Antofagasta, Chile, more than 250 000 people were exposed to high concentrations of arsenic in the drinking-water from 1958 until 1970, when a water treatment plant was installed; consequently, several studies revealed high incidence and mortality rates for lung cancer due to the high arsenic concentrations and, even 40 years later, increased lung cancer rates still persist [23–26]. The increase in lung cancer rates in Antofagasta, Chile, could also be related to the mining activity in this region. In Colombia, an elevated risk of mortality from lung cancer has been described in areas where high concentrations of arsenic are found in the drinking-water [27].

Radon

Exposure to radon – a radioactive gas formed naturally by the breakdown of uranium soils and rocks [17] – has been shown to be a risk factor for lung cancer [6]. High radon concentrations may occur in certain geological environments, mostly rocks and soils. Exhalation of radon from the environment and from radon-rich water can cause significant radon concentrations in tunnels, power stations, caves, public

baths, and spas. The average concentration of radon in houses is generally much lower than that in underground ore mines [28].

A retrospective study of lung cancer mortality among underground coal workers in Brazil concluded that the increased rates were associated with exposure to radon and radon daughters [29]. In a former gold mine in San Luis Province, Argentina, radon measurements exceeded the upper action level recommended for workplaces by approximately 3-fold [30]. In a study in Brazil, it was estimated that 16% of all lung cancer deaths at a specific location could be attributable to indoor radon exposure in the region [31].

Socioeconomic status

The socioeconomic gradient in lung cancer reflects differences in the prevalence of smoking, occupational and environmental exposures, air pollution, and dietary factors among people of different socioeconomic status [32]. Thus, socioeconomic differences in lung cancer incidence and mortality must consider the underlying differences in smoking prevalence. This relationship has been studied, although the question of whether tobacco smoking can explain the socioeconomic differences in lung cancer rates is complicated by collateral factors such as occupation and access to health care. In a recent meta-analysis of 16 studies on the socioeconomic differences in lung cancer incidence, Sidorchuk et al. [32] reported that incidence was positively related to educational level (risk ratio [RR], 1.61; 95% CI, 1.40–1.85 for low vs high), occupation (RR, 1.48; 95% CI, 1.34–1.65 for low vs high) and socioeconomic position (RR, 1.37; 95% CI, 1.06–1.77 for lowest vs highest income). They also presented pooled risk estimates for socioeconomic categories and lung cancer risk based on two studies conducted in Brazil, but the relationship was less clear. A study of poverty and cancer mortality in Argentina revealed that lung cancer mortality was inversely correlated with low socioeconomic status [33]. Different results were observed in a study in Pernambuco, Brazil, among the elderly which found a negative correlation between lung cancer mortality and social deprivation, indicating higher mortality risks in the highest socioeconomic class compared with the lowest socioeconomic class [34].

Diet

The expert panel from the World Cancer Research Fund concluded that fruit and foods containing carotenoids probably protect against lung cancer and that limited evidence suggests that red meat, processed meat, total fat, butter, pharmacological doses of retinol (in smokers only), and low levels of body fat are causes of lung cancer [35]. A series of studies on the relationship of diet and different foods and beverages has been carried out in Uruguay [36–42]. Mate, a traditional drink in some South American countries that is prepared by pouring very hot water onto the dried leaves of ‘yerba mate’ (*Ilex paraguariensis*), has been associated with the risk of most upper-aerodigestive tract cancers [43, 44]. One of the studies conducted in Uruguay in 1996 revealed that heavy mate consumption was associated with a 1.6-fold increase in lung cancer risk compared with light drinking, after adjusting for cigarette smoking [36].

Another study in Uruguay in 2002 indicated that total meat intake was positively associated with lung cancer (OR, 1.6; 95% CI, 1.2–2.2 for the highest quartile vs the lowest), whereas total vegetable and total fruit intakes were inversely related to lung cancer risk (OR, 0.62; 95% CI, 0.45–0.84 for the highest vs the lowest) [38]. Similarly, in a case–control study conducted among men in Uruguay revealed that red and processed meat may play a role in the etiology of lung cancer (OR, 2.90; 95% CI, 1.91–4.40 for high vs low meat consumption), while antioxidants were inversely associated with lung cancer risk (OR, 0.69; 95% CI, 0.51–0.96 for high vs low) [39].

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