

Letters

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High Levels of Carcinogenic Polycyclic Aromatic Hydrocarbons Present Within Food from Linxian, China may Contribute to that Region's High Incidence of Oesophageal Cancer

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OESOPHAGEAL CANCER is a common fatal cancer worldwide and the fourth leading cause of cancer death in China [1, 2]. In the U.S.A. oesophageal cancer is the fourth most common cause of cancer death in black men and the eighth leading cause of cancer death in men of all races [3]. Most squamous cell carcinomas of the oesophagus in low risk populations are attributable to alcohol and tobacco consumption, but the aetiological agents in high risk populations are less clear [4, 5].

The county of Linxian, Henan province, in north-central China, has some of the highest rates of oesophageal cancer in the world, with annual age-adjusted mortality rates up to 169 per 100 000 and cumulative death rates of 20% for females and 32% for males [6]. Several aetiological possibilities, including nitrosamines, nutritional deficiencies, fermented and moldy foods and the inhalation of polycyclic aromatic hydrocarbons (PAH), have been considered, but none has been convincingly linked to the high rates of oesophageal

cancer [7]. PAHs, such as benzo(a)pyrene (B(a)P), are formed during the incomplete combustion of soft coal. The inhabitants of Linxian use soft coal extensively in unvented dwellings for cooking and heating. A recent 2-year feeding study in mice conducted by the National Center for Toxicological Research identified a striking dose-response relationship between B(a)P food levels and oesophageal cancer incidence (Dr Sandra J. Culp, National Center for Toxicological Research, Jefferson, Arkansas, U.S.A.) and several human studies have associated high-level environmental PAH exposure with an increased incidence of lung and gastrointestinal cancers [8, 9].

To investigate the possibility that Linxian's high rates of oesophageal cancer may be related to long-term, high-level environmental exposure to PAHs via ingestion of food cooked with soft coal or food that has been contaminated by the environmental pollution produced by soft coal combustion, we analysed 77 staple food samples from Linxian for the presence of B(a)P by fluorescence detection, after ethanolic KOH saponification, isooctane extraction and column chromatography, using thin-layer chromatography [10]. The food samples consisted of 25 g each of raw corn ($n=18$), raw wheat ($n=20$), cooked food made from corn ($n=20$), and cooked food made from wheat ($n=19$) collected from 32 households.

High levels of B(a)P were found in almost every food sample. The median values were: raw wheat 13.8 ng B(a)P/g food (ppb) (10-90% range 2.4-49.9); raw corn 3.1 (0.1-53.7); cooked wheat food 4.6 (1.3-27.8); and cooked corn food 4.9 (0.9-21.7). The concentration of B(a)P in the Chinese food samples was in the same range as the levels found in very well-done charcoal-broiled red meat, which is a food type that generally has some of the highest PAH levels (e.g. 2.6-25.2 ppb) [10, 11], and was substantially higher than the mean B(a)P level of 0.12 ppb found in several wheat and corn products obtained from two major food chains in the U.S.A. (data not shown).

This represents the first report of high levels of B(a)P in raw and cooked foods from Linxian, China. This finding suggests that the inhabitants of Linxian may be ingesting high levels of carcinogenic PAHs and that this exposure may be associated with this region's high rates of oesophageal cancer.

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Isolated Leptomeningeal Metastasis from Ovarian Carcinoma: an Unusual Event

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OVARIAN CARCINOMA is the third highest cancer-related cause of mortality in women. A review of 255 patients with epithelial ovarian carcinoma revealed that metastasis develops in 40% of patients (50% if autopsy is performed) at some time during the natural history of their disease [1]. Distant metastasis seldom occurs in the absence of intra-abdominal disease. The liver, lung and distant lymph nodes are the most common sites of metastatic disease, along with malignant pleural effusion. Bone metastasis and central nervous system (CNS) metastasis are rare and occur late in the evolution of the disease. Less than 2% of patients develop clinical evidence of cerebral disease. Such lesions usually exhibit contrast uptake on computed tomography (CT) scans and are located in the cerebral hemispheres [2, 3]. Leptomeningeal metastasis, presenting as a single lesion of the CNS and negative on magnetic resonance imaging (MRI) or CT scan, is exceptional and more frequently reported in breast cancer and lung cancer [4]. This situation has recently been described in only one of 23 patients with CNS metastasis from ovarian carcinoma [5]. 2 other cases have been mentioned in older studies [6, 7]. Here we present a case report from our institute. A 57-year-old woman was diagnosed as suffering from a FIGO stage III B adenocarcinoma of the ovary in November 1987. She underwent a hysterectomy and bilateral salpingo-oophorectomy. Postoperatively, she received six courses of chemotherapy combining carboplatin and cyclophosphamide. A

second laparotomy was performed and no microscopic residual disease was found in the omentum. The patient received abdominopelvic irradiation as consolidation. In September 1991, generalised peritoneal carcinomatosis was found. Salvage chemotherapy combining cisplatin and doxorubicin was administered and a clinical and biological complete remission was obtained, but with grade II peripheral neuropathy.

Between November 1996 and March 1997, she received seven cycles of paclitaxel, due to isolated elevation of serum Ca 125. The patient was well until April 1997, when she began to complain of increasing paresthesia and deafness and Ca 125 increased again. Examination of the head and neck and CT scan led to the diagnosis of maxillary infection and otitis which were effectively treated with antibiotics. Only peripheral neuropathy was found at neurological examination. No parenchymal lesion was detected on the brain CT scan. Consequently, chemotherapy-related toxicity was suspected.

Blurred vision confined to the left eye, dizziness and unsteady gait appeared 4 weeks later. The patient was finally hospitalised in the emergency unit because of severe headaches and radicular pain, without nuchal rigidity. An MRI was performed, but no evidence of brain or leptomeningeal metastasis was found. The diagnosis of meningeal carcinomatosis was finally confirmed when malignant cells were detected in the cerebrospinal fluid. Intrathecal injections of methotrexate were initiated, but the patient rapidly presented mental confusion, nuchal rigidity and deterioration of her general condition. She finally died 2 days later in a context of intravascular coagulation. At the time of death there was no evidence of recurrent peritoneal carcinomatosis. No sign of infection nor secondary cancer was found at complete clinical examination. An autopsy was not performed.

CNS metastasis from ovarian cancer is uncommon, while leptomeningeal metastases are even more rare. Advances in surgery and chemotherapy have led to higher remission rates and a trend towards a longer median survival. With effective combination chemotherapy with new drugs and longer survival, hitherto occult CNS metastases are probably becoming apparent. The CNS may be a 'pharmacological sanctuary', which is not always readily accessible to drugs, even when high intravenous doses are administered. However, adequate concentrations of cisplatin have been found in the CNS and a complete remission of cerebral metastasis from ovarian carcinoma has been reported after carboplatin [8]. To date, only minute traces of paclitaxel are reported have penetrated the brain and cerebrospinal fluid [9]. This could be the reason why leptomeningeal metastases are detected during paclitaxel single-agent therapy [10], although the disease appears to be controlled elsewhere.

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