review

The emerging epidemic of environmental cancers in developing countries

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In overviews concerning environmental cancers, the definition of ‘environmental’ can vary considerably in terms of the list of exposures considered, due to differences in inclusion criteria, and the articles tend to focus mainly or exclusively on Western populations. International agencies such as World Health Organisation, that have had considerable success in fighting infectious diseases, seem to be weaker when considering the relevance of environmental carcinogens, particularly in developing countries, and in identifying the exposed populations. The purpose of this paper is to reexamine the issue with a specific focus on developing countries. There are good reasons to believe that the burden of environmental cancers in such countries is high and has been underestimated in previous analyses. We examine the most common pollutants (aflatoxins, arsenic, air pollutants, biomass fuel and coal, polychlorinated biphenyls and wastes). A systematic review was not possible given the sparse nature of the data, but we suggest that the burden of environmental exposures to carcinogens can be substantial in developing countries.

Key words: cancer burden, developing countries, environmental risks

introduction

The generally good health and long life expectancies experienced by Western populations owe much to the advent of large-scale public health measures in sanitation and advances in microbiology during the 19th century. This had led to a dramatic decrease in infectious diseases and marked gain in population health. Could such a dramatic improvement be achievable for today’s predominant diseases on a global scale and specifically for cancer? In overviews concerning ‘environmental cancers’ (see for example [1–6]), the definition of ‘environmental’ can vary considerably in terms of the list of exposures considered due to differences in inclusion criteria. The methodological difficulties encountered in the investigation of environmental causes of disease are often neglected in these publications, which tend to focus mainly or exclusively on Western populations. The purpose of this paper is to reexamine the issue with a specific focus on developing countries.

definition of environmental exposures

The interpretations of the word ‘environment’ differ between researchers: for example, in the ‘gene–environment interactions’ field, by environment researchers just mean nongenetic (inherited) determinants. For the sake of clarity, we will use the term environment in a more restricted way, meaning ‘pollutants’ of air, food, water and soil. We are thus excluding many nongenetic external causes, like tobacco smoking, alcohol and dietary habits. We will also exclude occupational exposures for which considerable work has already been done [7]. For the same reason, we also exclude infectious or parasitic causes of cancer, which explain ~15% of all cancers (a figure that is based on sound evidence [8]).

We focus on prospective cohort studies whenever possible. Controversial exposures with limited evidence are also exempt from this overview; such examples include electromagnetic fields [9], nonoccupational exposure to pesticides [10, 11], disinfection by-products [12] and exposure to solvents (except benzene) [13]. Although considerable evidence does exist for some of these exposures, it often comes predominantly from case–control studies and is therefore less persuasive than prospective cohort studies. We have also excluded UV light, although it is a well-established carcinogen, and focused on chemical exposures.

This is not a systematic review because evidence is still sparse and almost anecdotal, particularly for the size of exposed populations and thus we have not attempted a systematic estimate of attributable risks.

environmental exposure to arsenic in drinking water

Despite being a highly prevalent human exposure, arsenic was not included in some recent publications from World

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Health Organisation (WHO) and International Agency for Research on Cancer (IARC) on the burden of environmental cancer [1, 2]. The predominant source of arsenic exposure is from contaminated drinking water. Chronic exposure to arsenic is known to cause nonmelanocytic skin and internal tumours in humans, exhibiting dose-dependent effects. In a study assessing the potential burden of internal cancers due to arsenic exposure in Bangladesh, Chen and Ahsan estimated excess lifetime risks of death from liver, bladder and lung cancers using exposure distribution, death probabilities and cancer mortality rates from Bangladesh and dose-specific relative risk (RR) estimates from Taiwan. Their results indicated at least a doubling of lifetime mortality risks from liver, bladder and lung cancers (229.6 versus 103.5 per 100,000 population) in Bangladesh that were attributable to exposure to arsenic in drinking water [14].

Overall, it has been estimated that at least 137 million people in the world, including the 70 million or so that reside in the Padma-Meghna plain in Bangladesh and adjoining parts of India, are exposed to arsenic through drinking water [15].

indoor exposure to biomass fuel and coal
Biomass, including wood, crop residues and dung, is largely used for cooking in developing countries, in addition to coal. The burning of these materials gives origin to heavy exposure to polycyclic aromatic hydrocarbons (PAHs) and other airborne carcinogens. Zhang and Smith [16] reviewed to polycyclic aromatic hydrocarbons (PAHs) and other airborne carcinogens. Zhang and Smith [16] reviewed publications in both Chinese- and English-language journals which reported health effects and exposure characteristics. In addition, the odds ratios (ORs) for lung cancer associated with indoor coal use have been summarised in a recent meta-analysis by Smith et al. [17]. In such analysis, tobacco smoking status was either included as adjustment variable or the analyses were restricted to nonsmokers only. The overall OR estimates, adjusted for smoking and chronic respiratory disease, for men and women combined were 1.86 (95% confidence interval (CI) 1.48–2.35) and 2.55 (95% CI 1.58–4.10), respectively.

Early studies in Africa seemed to implicate nasopharyngeal cancer with wood smoke, but this association was not confirmed by later, more detailed studies in Asia [18]. One study in Brazil has shown a strong relationship with upper aerodigestive tract cancers, with an adjusted OR of 2.7 [19].

The estimate of the number of people exposed to biomass fumes is (conservatively) at least one-third of the total population in developing countries, i.e. at least 600 millions (according to the definition of developing countries given by the World Bank; we have only considered age >30). The total number of estimated lung cancer deaths in developing countries is about 600,000 per year [20]. If the OR of 1.8 for lung cancer applies, the preventable fraction in the exposed is (1.8 – 1)/1.8 = 0.45. Thus, at least 90,000 of 200,000 deaths from lung cancer occurring in the exposed population would be preventable each year in developing countries. But, of course, this estimate is very inaccurate because it does not consider, for example, the effect on adult cancer of exposures in utero or in infancy.

aflatoxins
Aflatoxins are a class of toxic metabolites produced by certain species of fungi, including *Aspergillus flavus*, which can contaminate groundnuts, tree nuts and grains. Laboratory studies have demonstrated the carcinogenicity of aflatoxins in rodents, primates and fish [21]. Hepatocellular carcinoma (HCC) has been observed in numerous species indicating the liver as a primary target organ. HCC is one of the most common cancers worldwide with a large geographic variation in incidence [22]. There have been two major cohort studies reported to date addressing the relationship of aflatoxin exposure and viral infection to HCC incidence. The first comprises of a study of >18,000 people in Shanghai from whom urine and blood samples were collected [23]. The data revealed an RR of 3.4 for HCC cases whose urine had detectable aflatoxin biomarkers. The RR of developing HCC in people who tested positive for hepatitis B virus (HBV) infection was 7.3. But more remarkably, individuals with both urinary aflatoxins and positive HBV status had an RR of 59 for developing HCC.

A nested case–control study in a cohort investigation carried out in Taiwan (of >15,000 people) found that in HBV-infected males, the adjusted ORs were 2.8 for detectable compared with nondetectable aflatoxin–albumin adducts and 5.5 for high compared with low levels of aflatoxin metabolites in urine [24]. A second cohort study in Taiwan observed a dose–response relationship between urinary AFB1 levels and HCC in chronic HBV carriers [25].

The number of people exposed to high levels of aflatoxin worldwide is unknown but it is likely to be at least 0.5 billion. One source reports the appalling figure of 4.5 billions, on the basis that most of the population in areas with particular conditions of humidity (that facilitate the growth of fungi) would be exposed chronically [26]. If we assume an RR of about 2, then it follows that the number of preventable deaths from liver cancer would be at least 50% of the total of the 125,000 occurring every year in populations exposed in developing countries, i.e. 60,000 (125,000 has been estimated as one fourth of all liver cancer deaths occurring in developing countries [20]).

exposure to air pollutants
Environmental tobacco smoke (ETS) and traffic-related air pollution share a number of characteristics: they are widespread exposures in both developed and developing countries; they have several chemical components in common (in particular PAHs) and they have been associated with increased risks of lung cancer and other diseases [27].

ETS has been considered as a human carcinogen (for the lung) by a Working Group of the IARC Monographs [28], with an overall RR for lung cancer of ~1.25. ETS exposure has an estimated prevalence level in developed countries of between 20% and 70%, although this is rapidly decreasing thanks to the new public health interventions against smoking in public places. The proportion of lung cancers attributable to ETS has been estimated as between 1.5% and 8% in developed countries.

Concerning air pollution, at least in the case of lung cancer we have now rather sound evidence: in fact, six cohort
studies (three in the United States and three in Europe) are consistent in reporting RRs in the order of 1.25 for higher versus lower levels of exposure in developed countries [29].

Also in this case, like in the case of ETS, molecular mechanisms that provide biological plausibility have been proposed. To arrive at an overall estimate for the attributable risk for developed countries is difficult due to the widespread nature of this exposure. However, it is usually considered that 30% of the population receive the highest levels of exposure (\(>30 \mu g/m^3\) of PM10 or NO\(_2\)). In a prospective study, 5%-7% of lung cancers in never smokers and ex-smokers were estimated to be attributable to high levels of air pollution as expressed by NO\(_2\) or proximity to heavy traffic roads [30]. In a systematic review, Cohen et al. [31] suggested the figure to be between 5% and 6% for the general Western population.

While estimates of the health effects of air pollution from developing countries are sparse, they tend to be much larger in magnitude than those obtained for developed countries [32]. Using the conservative estimates of 5% lung cancers due to ETS and 5% due to air pollution—coming from Western countries—we estimate that 40 000 of 400 000 total lung cancers deaths in developing cancers [20] could be prevented. Taking into account the additive action and the large overlap in exposure between the two hazards, a more conservative estimate is likely to be \(\sim25\ 000\). However, these figures do not consider the late effects of exposure in utero or in infancy.

Very little can be said on air pollutants deriving from industrial activities. Many of them are listed in Table 1 (see below), but a systematic survey is almost impossible given the extremely heterogeneous nature of exposures and locations.

**asbestos (nonoccupational)**

Nonoccupational asbestos exposure in developed countries, when it was addressed in credible epidemiological studies, turned out to be a more important issue than previously believed. A meta-analytical RR of 7.0 (95% CI 4.7–11) associating neighbourhood high-level exposure to asbestos and malignant mesothelioma has been reported [33]. This is a conservative estimate because it does not include studies from Wittenoom and South Africa [34]. Populations in developing countries may be extensively exposed to asbestos since production as well as associated health hazards have been transferred over from the Western countries where protective legislations had been introduced. However, the number of potentially exposed people is unknown [35].

**polychlorinated biphenyls**

Recent evidence strongly indicates that polychlorinated biphenyls (PCBs), and specifically some congeners, are involved in the aetiology of non-Hodgkin’s lymphomas (NHLs). PCBs have been found to widely contaminate soils, waters and foods in Western countries since the 1940s. Three cohort studies and, more recently, a large case–control study identified serum or plasma PCB congeners as related to NHL. In the case–control study [36], the OR for the highest versus the lowest quartile of PCB measurements was 1.83 (95% CI 1.18–2.84). In another study, prediagnostic serum or plasma concentrations of selected PCB congeners were measured among NHL cases and controls from three cohorts, one in Norway and two in the United States [37]. The ORs and 95% CIs for increasing quartiles of concentration of congener 118 relative to the lowest quartile were 2.4 (0.9–6.5), 4.9 (1.6–15.3) and 5.3 (1.5–18.8; \(P\) (trend) < 0.005) in Norway and 8.1 (1.0–68.9), 6.6 (0.7–59.0) and 13.0 (1.6–106.8; \(P\) (trend) < 0.05) in the United States.

Virtually nothing is known about exposures and risks in developing countries.

**other exposures**

Table 1 shows exposures with an environmental relevance that have been classified as human carcinogens (group I) or ‘probable human carcinogens’ (group II A) by IARC Monographs Working Groups (www.iarc.fr). In addition, a number of occupational carcinogens that can contaminate the general environment are listed according to a review by Siemiatycki et al. [38]. The list is likely to be incomplete because information on the occurrence of environmental exposure is often far from comprehensive, particularly in developing countries. We wish to draw attention to 1,3 butadiene, formaldehyde and metals (nickel, chromium, cadmium) as the most significant in terms of health implications, both because they are human carcinogens and because these exposures are likely to be widespread.

**waste landfill sites in developed and developing countries**

Information from some developed countries [39–41] indicates that illegal landfill sites involve exposure to carcinogens such as dioxins, PCBs, arsenic, cadmium, nickel, PAHs and solvents (including benzene), among others [40]. Illegal landfill sites in developing countries are probably more widespread, more frequently polluted with toxic chemicals and closer to dwellings than in developed countries. Food and Agriculture Organization of the United Nations has estimated that 120 000 of the 500 000 tonnes of toxic wastes produced in the world are actually stored in Africa.

**methodological issues**

Most epidemiological estimates are based on surrogate markers of exposure, such as through questionnaire interviews. It is not surprising that such measures can lead to inaccurate estimates. Although bias can occur in both directions (i.e. overestimations as well as underestimations are possible), the most likely implication of inaccuracy in prospective studies (in which exposure data are collected long before disease data) is underestimation of the risks. Several authors have shown that sources of underestimation in epidemiology may outweigh sources of overestimation (Table 2, courtesy of P. Grandjean).

When methods of biomarker measurements become available to improve accuracy in exposure assessments, estimates of risk for the same risk factors can increase substantially. For example, when sexual habits were used as a surrogate to investigate the relationships between human papilloma virus (HPV) infection and sexual habits, the RRs for cervical cancer were estimated to be in between 2 and 8. This increased to up to 500 when specific strains of HPV were considered [42].
Table 1. Environmental carcinogens according to the IARC Monographs (www.iarc.fr) and reference 38 (in italic typeface)

<table>
<thead>
<tr>
<th>Exposure name</th>
<th>Evaluation Routes of exposure</th>
<th>Exposed number and details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group I (human carcinogens)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzo[a]pyrene</td>
<td>ND S</td>
<td>Inhalation (mainly of tobacco smoke) and ingestion. Ubiquitous product of incomplete combustion of fossil fuels (engine exhausts, coal/oil stoves/heating). Also in tobacco smoke, contaminated urban ambient air and water. Present in some foods, processes such as curing and cooking increase levels. Last updated 1998, reevaluated in 2008 (not summarised here).</td>
</tr>
<tr>
<td>Radon-222 and its decay products</td>
<td>S S</td>
<td>Inhalation of decay products from soil, rocks (granite) and groundwater. Naturally occurring radon and radon daughters are ubiquitous in soil, water and air. Accumulation may occur in indoor and confined spaces such as mines in the absence of adequate ventilation. Radon-enriched groundwater can lead to conversion to gaseous state and infiltrate into buildings above the ground.</td>
</tr>
<tr>
<td>X- and gamma (γ)- radiation</td>
<td>S S</td>
<td>Irradiation from natural and man-made sources. Ionising radiation from natural terrestrial and man-made sources (nuclear facilities and accidents). Seven million of the world’s population is considered having been exposed in the past from mainly nuclear facility accidents and military actions. Main environmental exposures from cosmic radiation or naturally occurring radioactive elements (also see radon).</td>
</tr>
<tr>
<td><strong>Mixtures</strong></td>
<td></td>
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</tr>
<tr>
<td>Household combustion of coal, indoor emissions from</td>
<td></td>
<td>Arsenic is naturally occurring, its salts are soluble in groundwater and surface water, with levels usually &lt;10 μg/L. Approximately 160 million people are thought to be exposed to higher than usual concentrations, such areas are found in Argentina, Bangladesh, Chile, China, Taiwan, Bengal India, Mexico and parts of the South West United States.</td>
</tr>
<tr>
<td>Arsenic in drinking-water</td>
<td>S L</td>
<td>Inhalation or ingestion of contaminated ground and surface water.</td>
</tr>
<tr>
<td><strong>Likely environmental; defined as occupational carcinogens by Siemiatycki et al., 2004, ref. 38</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asbestos (vol. 14; Suppl 7; 1987)</td>
<td>S S</td>
<td>Mainly inhalation of fibres; also ingestion of contaminated water. Natural mineral, mined and used in construction. Occurrence in indoor air from asbestos-containing building/insulating materials. Domestic exposure from asbestos workers’ clothing and equipments and residents in proximity of mines and factories.</td>
</tr>
<tr>
<td>Benzene (vol. 29; Suppl 7; 1987)</td>
<td>S S</td>
<td>Inhalation of ambient air and ingestion of water contaminated from gasoline processes. Natural constituent in crude oil. General exposures occur at higher ambient air levels around petrol stations, storage, loading and transport facilities. Also present in tobacco smoke (47–64 ppm) and food (cooked): US National Research Council estimates daily dietary intake to be ~250 μg.</td>
</tr>
<tr>
<td>Beryllium and beryllium compounds (vol. 58; 1993)</td>
<td>S S</td>
<td>Inhalation. An abundant natural element in Earth’s crust, occurs in rocks. Most important environmental exposure is from burning of coal which releases airborne beryllium oxide (1.8–2.2 mg/kg dry weight). Also occurs in tobacco smoke, water and soils.</td>
</tr>
<tr>
<td>1,3-Butadiene (vol. 71, vol. 97; in preparation)</td>
<td>L S</td>
<td>Inhalation. Used industrially, most general population exposures occur as contaminated air from industrial release, tobacco smoke and automobile exhaust. Urban air concentrations range from &lt;1–10 ppb.</td>
</tr>
<tr>
<td>Cadmium and cadmium compounds (vol. 58; 1993)</td>
<td>S S</td>
<td>Inhalation of fumes and dusts and ingestion of contaminated foods. Natural element, general exposure occurs in tobacco smoke and contaminated foods. High-level airborne cadmium oxide can be found during burning of materials containing cadmium, around waste incinerators. Industrial facilities waste disposal and wash off from areas where cadmium-containing fertilisers are used can contaminate waterways.</td>
</tr>
</tbody>
</table>
Table 1. (Continued)

<table>
<thead>
<tr>
<th>Exposure name</th>
<th>Evaluation</th>
<th>Routes of exposure</th>
<th>Exposed number and details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromium[VI] (vol. 49; 1990)</td>
<td>S S</td>
<td>Inhalation, ingestion and skin contact</td>
<td>General exposures from higher ambient air and water levels from natural weathering and around industrial installations. Also present in food and soil, human daily intake averages ~80 μg.</td>
</tr>
<tr>
<td>Erionite (vol. 42, Suppl. 7; 1987)</td>
<td>S S</td>
<td>Inhalation</td>
<td>A major constituent in many sedimentary rocks and volcanic tuffs. Deposits found in &gt;40 countries with high purity deposits in Nevada, United States and Japan, while smaller ones are found in Kenya, New Zealand Tanzania and Yugoslavia. When ground to a powder, erionite particles resemble amphibole asbestos morphologically. Population exposures occur as result of re-suspension of erionite in dusts and agricultural soils (reported in Anatolian region, Turkey).</td>
</tr>
<tr>
<td>Formaldehyde (vol. 88; 2006)</td>
<td>S S</td>
<td>Main general exposure through inhalation</td>
<td>Volatile compound, considered ubiquitous in general environment. Vapours occur in ambient air from vehicle emissions and in residential indoor air from building and decoration materials, tobacco smoke, disinfectants, food and cooking. Indoor exposure can be 10 times as high as outdoor air.</td>
</tr>
<tr>
<td>Nickel compounds (vol. 49; 1990)</td>
<td>S S</td>
<td>Mainly inhalation; also ingestion</td>
<td>Widespread commercial use. Air contamination occurs around power stations, mining and refineries and waste incinerators. Also present in tobacco smoke, contaminated water. Some beverages and food naturally contain nickel, estimated daily intake is ~160 mg.</td>
</tr>
<tr>
<td>Neutrons (vol. 75; 2000)</td>
<td>I S</td>
<td>Mainly from natural outdoor irradiation</td>
<td>Natural worldwide exposure from cosmic background radiation. Also from man-made sources such as nuclear fusion/fission reactors and some medical instruments. Evaluation on the basis of carcinogenicities of reaction products (α- and β-particles and γ-radiation). Population groups considered exposed include high-altitude cities, nuclear workers and atomic bomb survivors, aircraft crew and passengers.</td>
</tr>
<tr>
<td>Silica, crystalline (vol. 68; 1997)</td>
<td>S S</td>
<td>Inhaled in the form of quartz/cristobalite or ingestion</td>
<td>Naturally occurring crystalline mineral. Quartz form occurs as suspended particulates in water dissolved from surrounding rocks. Presence worldwide, ingestion of contaminated water could occur daily. Also present (sometimes unintentionally) in consumer products such as tobacco.</td>
</tr>
<tr>
<td>Solar radiation (vol. 55; 1992)</td>
<td>S S</td>
<td>Natural outdoor terrestrial irradiation</td>
<td>Consist of UVA, UVB and UVC subtypes. High doses received by populations in mid-latitudes (40–60°N). Individual dose levels depend on factors such as cultural and social behaviour, clothing and outdoor activities. Exposure can also occur under indoor fluorescent lighting.</td>
</tr>
<tr>
<td>2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) (vol. 69; 1997)</td>
<td>L S</td>
<td>Ingestion of contaminated foods and inhalation</td>
<td>Contamination occurs in agricultural products and foods. Ingestion contributes to 90% body burden of TCDDs. It is lipophilic and undergoes bioaccumulation in fish, meat, milk, eggs and fats. Human dietary intake was ~88 pg TEQ/day in 1992.</td>
</tr>
<tr>
<td>Mixtures</td>
<td>S S</td>
<td>Ingestion of contaminated foods</td>
<td>Product of fungi, ubiquitous in world regions of hot humid climates: sub-Saharan Africa and south-east Asia (daily levels measured range: 3–200 ng/kg/day). Most dietary staples found to be contaminated (especially maize and groundnuts); also contaminates animal products through aflatoxin-tainted feed (i.e. milk). Cannot be broken down by normal cooking conditions. Exposure is often chronic in nature.</td>
</tr>
</tbody>
</table>
Some human cancers may take 20–30 years or longer from the time of first exposure to clinical manifestation. Waiting for high incidences of such cancers is not an ethically acceptable method for identifying human carcinogens. For several agents, carcinogenicities in animals were later confirmed once reliable human epidemiological data became available. This is well illustrated by the case of 1,3-butadiene, whose carcinogenicity has been recently confirmed by a review of the Working Group of the IARC Monographs [43]. It would be unwise to ignore health effects data derived from animal studies [44]. Trans-species extrapolations of health risks can be refined further by taking into account relevant information regarding the range and distribution of factors which enable more accurate prediction of responses in human populations.

**Conclusions: need for an effective strategy**

The burden of cancers due to environmental exposures in developing countries is unknown, but it can sum up to several hundred thousands, if we just limit our estimates to the main

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### Table 1. (Continued)

<table>
<thead>
<tr>
<th>Exposure name</th>
<th>Evaluation</th>
<th>Routes of exposure</th>
<th>Exposed number and details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involuntary smoking (exposure to second-hand or ‘environmental’ tobacco smoke) (vol. 83; 2004)</td>
<td>S</td>
<td>L/S</td>
<td>Inhalation of contaminated air</td>
</tr>
<tr>
<td>Iron and steel founding (vol. 34, Suppl 7; 1987)</td>
<td>S</td>
<td>ND</td>
<td>Inhalation of contaminated air at or near foundries</td>
</tr>
<tr>
<td>Rubber industry (vol. 28, Suppl 7; 1987)</td>
<td>S</td>
<td>ND</td>
<td>Inhalation of dusts, fumes, skin contact</td>
</tr>
<tr>
<td><strong>Group II A (probable human carcinogens)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lead compounds, inorganic (vol. 87; 2006)</td>
<td>L</td>
<td>S</td>
<td>Inhalation and ingestion</td>
</tr>
<tr>
<td>5-Methoxypsoralen (vol. 40, Suppl 7; 1987)</td>
<td>S</td>
<td>I</td>
<td>Inhalation and skin contact</td>
</tr>
<tr>
<td>Nitrate or nitrite (ingested) under conditions that result in endogenous nitrosation (vol. 94; in preparation)</td>
<td>ND</td>
<td>S</td>
<td>Ingestion and inhalation, in vivo reactions</td>
</tr>
<tr>
<td><strong>Likely environmental; defined as occupational carcinogens by Siemiatycki et al., 2004 (38)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diesel engine exhaust (vol. 46; 1989)</td>
<td>L</td>
<td>S</td>
<td>Inhalation of outdoor ambient air</td>
</tr>
<tr>
<td>Polychlorinated biphenyls (vol. 18, Suppl 7; 1987)</td>
<td>L</td>
<td>S</td>
<td>Ingestion of contaminated foods and inhalation</td>
</tr>
</tbody>
</table>

Classification key, level of evidence: I, insufficient; L, limited; S, sufficient; ND, no adequate data.
known carcinogenic exposures (arsenic, air pollution, aflatoxin, PCB, asbestos). The effects of additional exposures such as metals (chromium, cadmium, nickel, beryllium) and other known human carcinogens are difficult to quantify because virtually no information is available on the number of exposed people.

A recent document released by WHO [1] has estimated the worldwide risk for different diseases attributable to environmental exposures. The proposed value for cancer was 19% [1], on the basis of previously published results and expert opinions. Conversely, Boffetta et al. [2], from the International Agency for Research on Cancer (a WHO agency), propose a much more conservative figure of ~1%–3%. What is surprising is not only the large discrepancy between the two estimates but also the general lack of sound information behind the figures, especially for developing countries. In fact, Boffetta et al. extrapolated their global estimate from a figure that was originally proposed by Doll and Petö [3] for the United States in the late 1970s.

The development of an effective strategy goes beyond the scope of this paper. However, it is clear that such a strategy involves (i) a survey of the number of people potentially exposed in developing countries, (ii) a strict international policy about transfer of hazardous contaminants from developed to developing countries and (iii) an international programme for early detection of potential carcinogens through in vitro tests and animal experiments.

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references
17. Smith KR. Inaugural article: national burden of disease in India from indoor air pollution. PNAS 2000; 97: 13286–13293.