

## CANCER

# Geographical differences in cancer incidence in the Amazon basin of Ecuador in relation to residence near oil fields

Anna-Karin Hurtig and Miguel San Sebastián

<b>Background</b>	Since 1972, oil companies have extracted more than 2 billion barrels of crude oil from the Ecuadorian Amazon, releasing billions of gallons of untreated wastes and oil directly into the environment. This study aimed to determine if there was any difference in overall and specific cancer incidence rates between populations living in proximity to oil fields and those who live in areas free from oil exploitation.
<b>Methods</b>	Cancer cases from the provinces of Sucumbios, Orellana, Napo and Pastaza during the period 1985–1998 were included in the study. The exposed population was defined as those living in a county (n = 4) where oil exploitation had been ongoing for a minimum of 20 years up to the date of the study. Non-exposed counties were identified as those (n = 11) without oil development activities. Relative risks (RR) along with 95% CI were calculated for men and women as ratios of the age-adjusted incidence rates in the exposed versus non-exposed group.
<b>Results</b>	The RR of all cancer sites combined was significantly elevated in both men and women in exposed counties. Significantly elevated RR were observed for cancers of the stomach, rectum, skin melanoma, soft tissue and kidney in men and for cancers of the cervix and lymph nodes in women. An increase in haematopoietic cancers was also observed in the population under 10 years in the exposed counties in both males and females.
<b>Conclusion</b>	Study results are compatible with a relationship between cancer incidence and living in proximity to oil fields. An environmental monitoring and cancer surveillance system in the area is recommended.
<b>Keywords</b>	Crude oil, cancer, Amazon, Ecuador
<b>Accepted</b>	20 November 2001

The Amazon basin of Ecuador, known as the 'Oriente', consists of more than 40 million hectares of tropical rainforest lying at the headwaters of the Amazon river network. The region contains one of the most diverse collections of plant and animal life in the world.<sup>1</sup>

In 1967, a Texaco-Gulf consortium discovered a rich field of oil beneath the rainforest, leading to an oil boom that has permanently reshaped the region. Since then, foreign companies together with Ecuador's national oil company have extracted more than 2 billion barrels of crude oil from the Ecuadorian Amazon. During this process, millions of gallons of untreated toxic wastes, gas and oil have been released into the environment.<sup>2</sup>

Indigenous federations, peasants movements and environmental groups in Ecuador have organized in opposition to unregulated oil development, charging that contamination has caused widespread damage to both people and to the environment.<sup>3–5</sup>

Oil development activities include several contaminating processes. In the Amazon basin of Ecuador, exploration for crude oil has involved thousands of miles of trail-clearing and hundreds of seismic detonations that have caused erosion of land and dispersion of wildlife. Each exploratory well that is drilled produces an average of 4000 m<sup>3</sup> of drilling wastes (drilling muds, petroleum, natural gas and formation water) from deep below the earth's surface. These wastes are deposited into open, unlined pits called separation ponds, from which they are either directly discharged into the environment or leach out as the pits degrade or overflow from rainwater.<sup>2,3</sup>

Instituto de Epidemiología y Salud Comunitaria 'Manuel Amunárriz', Apdo. 17-10-7410, Quito, Ecuador. E-mail: sandyura@ecuanex.net.ec

If commercial quantities of oil are detected, the production stage starts. Beneath the earth's surface oil is mixed with gas and liquid substances. It is not possible to separate the oil from these other components during extraction, this is instead done at a later stage in a central facility. At each facility, over 4.3 million gallons of liquid wastes are generated every day and discharged without treatment into pits. Roughly 53 million cubic feet of 'waste' gas from the separation process is burned daily. The gas is burned without temperature or emissions control, and contaminants from the gas flares pollute the air. Additional potential contamination of the air is generated at pits and oil spills by hydrocarbons coming from standing oil slicks.<sup>2</sup>

Routine maintenance activities at over 300 producing wells discharge an estimated 5 million gallons of untreated toxic wastes into the environment every year. Leaks from wells and spills from tanks have been common.<sup>6</sup> According to a study conducted by the government in 1989, spills from flow lines alone were dumping an estimated 20 000 gallons of oil every 2 weeks.<sup>7</sup>

Overall, more than 30 billion gallons of toxic wastes and crude oil had been discharged into the land and waterways of the 'Oriente' up until 1993.<sup>3</sup> This compares to the 10.8 million gallons spilled in the Exxon Valdez disaster in 1989. For instance, in 1989 at least 294 000 gallons and in 1992, about 275 000 gallons of crude oil caused the Napo river (1 km wide) to run black for 1 week.<sup>8</sup>

In 1994, the Ecuadorian environmental and human rights organization *Centro de Derechos Económicos y Sociales* (Centre for Economic and Social Rights), released a report documenting dangerous levels of toxic contamination.<sup>9</sup> Concentrations of polynuclear aromatic hydrocarbons (PAH) were found in drinking, bathing and fishing waters. These were 10 to 10 000 times greater than the US Environmental Protection Agency guidelines. In 1999, the *Instituto de Epidemiología y Salud Comunitaria 'Manuel Amunárriz'* (IESCMA), a local non-governmental organization concerned with health, undertook water analysis for total petroleum hydrocarbons (TPH) in communities in the proximity of oil fields and communities far away from them. Water analyses showed high exposure to oil-derived chemicals among the residents of the exposed communities.<sup>10</sup> In some streams hydrocarbon concentrations reached 144 and 288 times the limit permitted by European Community regulations.<sup>11</sup> The same year, a report from the Ministry of Environment supported these results when concentrations of TPH over 300 times the limit permitted were found in the streams of one of the communities of the previous study.<sup>12</sup>

Although several studies have focused on residents exposed to major oil spillages,<sup>13–15</sup> epidemiological studies of communities exposed to oil pollutants near oil fields are scarce.<sup>10</sup> Few studies have been conducted in petroleum exploration and producing workers. In one of two case-control studies, an excess risk for testicular cancer was observed among petroleum and natural gas extraction workers.<sup>16</sup> No such excess was found in the other study.<sup>17</sup> In a case-control study of cancer at many sites, an association was observed between exposure to crude oil and rectal and lung cancer, however the association was based on small numbers.<sup>18</sup> A study carried out in producing and pipeline workers in the US did not find significant differences for any major cause of death.<sup>19</sup> Sathiakumar *et al.*<sup>20</sup> conducted an epidemiological study in oil and gas field workers in the US which showed a positive association between work and acute

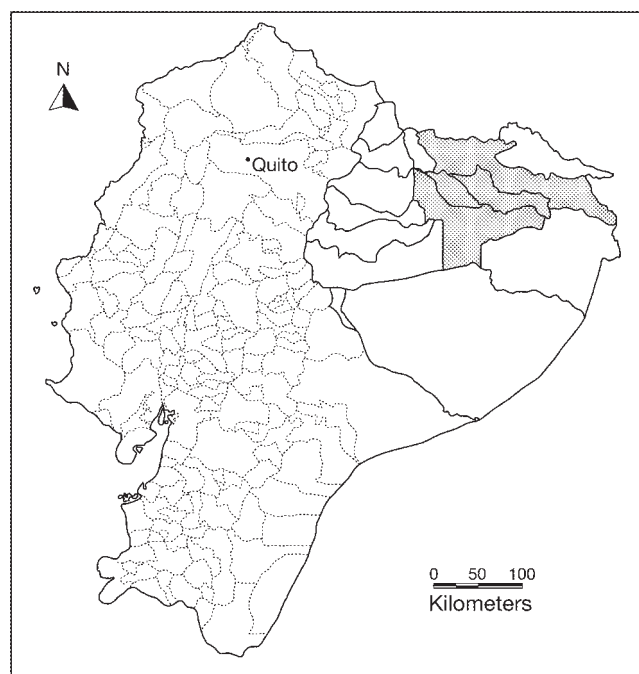
myelogenous leukaemia. A study from China has also reported increased incidences of leukaemia in oil-field workers.<sup>21</sup> A recent update of a study of crude oil production workers showed a lower mortality risk for these employees compared with the general US population (perhaps a reflection of the 'healthy worker effect'). An increased mortality from acute myelogenous leukaemia was found in those people who were first employed before 1940 and who were employed in the production of crude oil for more than 30 years.<sup>22</sup>

In a recent study in the Amazon basin of Ecuador, an excess of cancers was observed among males in a village located in an oil producing area.<sup>23</sup> The objective of this study was to determine if there was any difference in overall and specific cancer incidence rates between populations living in the proximity of oil fields and those who live in areas free from oil exploitation in the Amazon basin of Ecuador.

## Population and Methods

### Area of study

The study was carried out in the provinces of Sucumbios, Orellana, Napo and Pastaza, situated in the eastern part of Ecuador (Figure 1). Each province is divided into counties (cantones). The study area has a total population of approximately 280 000 indigenous people and peasants.<sup>24</sup> The indigenous people live in small communities scattered along the rivers, making their living by hunting, fishing and subsistence agriculture. The peasants arrived in the area in the 1970s following the paths opened by oil companies. They make their living mainly by agriculture and cattle-raising. In oil producing areas approximately 2% of the working population is employed by the oil industry.<sup>25</sup> Physical infrastructure in the region is poor. Few villages and small towns (10–15 000 citizens) have electricity



**Figure 1** Map showing counties included in the study; exposed counties in grey

and piped drinking water and the majority of the inhabitants live without these facilities. Many of the roads in oil producing counties are paved by crude oil to reduce the amount of dust otherwise produced in this tropical climate. In each province there is a provincial hospital and the counties have health centres. The hospitals have no histopathological services and no access to radio- or chemotherapy treatment. Two mission hospitals with efficiently functioning infrastructure are located in the counties Mera and Archidona—these are not oil producing areas. Oil producing areas have no better medical facilities than those areas where no such industry is present. Qualified personnel in the oil industry are contracted from the capital or abroad and flown out in the case of health problems. Only recently have some oil companies included health expenditure in their contracts with residents. Two counties, Sachas and Shushufindi, are producing and processing palm oil. There are no other major industries in the region apart from oil.

### Cancer data

No cancer registry is available in the Amazon region. Suspected cancer cases are referred from these provinces to Quito, the capital. All cases diagnosed in Quito are registered in the National Cancer Registry.<sup>26</sup> This register was used for the purpose of our study. In all, 985 cases of cancer were reported to the National Cancer Registry from the provinces of Sucumbios, Orellana, Napo and Pastaza during 1985–1998. The National Cancer Registry contains personal identification, gender, age at diagnosis, cancer site, histology (Ninth International Classification of Diseases), year of diagnosis, residence at diagnosis and education.

### Population data

Population data from the counties of the four provinces by gender and 5-year age strata for the year 1992 were used. These were projections of the National Institute of Statistics and Census based on the 1990 National Census.<sup>27</sup>

### Exposure status

The study was ecologic and the exposure status defined at a county level. The exposed population was defined as those living in a county where oil exploitation had been ongoing for a minimum of 20 years to the date of the study. The non-exposed were identified as those counties without oil development activities (excluding seismic studies during the late 1990s with no exploitation activities). Four counties (Lago Agrio, Shushufindi, Orellana and Sachas) (118 264 people; 55.0% males) were defined as exposed and 11 as non-exposed (Cascales, Pto El Carmen, La Bonita, Lumbaqui, Aguarico, Tena, Archidona, El Chaco, Baeza, Puyo, Mera) (155 710 people; 52.4% males).

### Statistical analysis

Incidence rates for overall and specific sites were calculated and age-adjusted to the world standard population.<sup>28</sup> Relative risks (RR) along with 95% CI were calculated for men and women as ratios of the age-adjusted incidence rates in the exposed versus non-exposed group.

## Results

In all, 473 cancer cases (39.1% in males) were identified in exposed counties and 512 (40.2% in males) in non-exposed

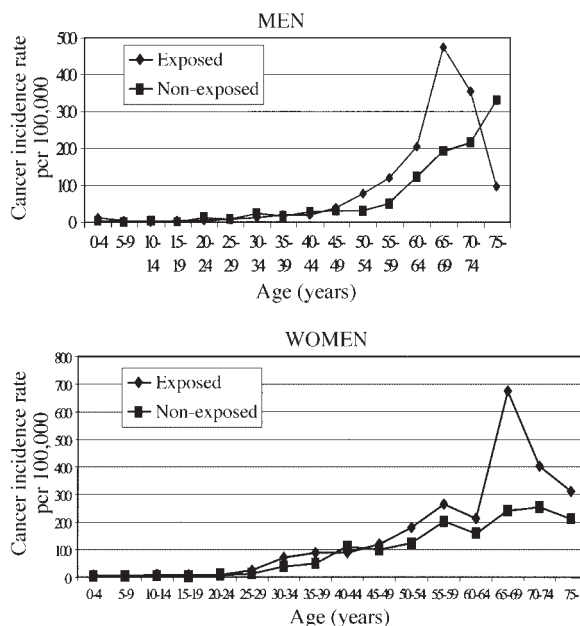
counties. An increased incidence for all sites combined by age was observed in both men and women (Figure 2). The RR of all cancer sites combined was significantly elevated in both men (RR = 1.40; 95% CI: 1.15–1.71) and women (RR = 1.63; 95% CI: 1.39–1.91) in exposed counties (Table 1). Significantly elevated RR were observed for cancers of the stomach (RR = 2.51; 95% CI: 1.60–2.94), rectum (RR = 10.40; 95% CI: 1.16–12.98), skin melanoma (RR = 10.15; 95% CI: 2.91–46.97), soft tissue (RR = 15.59; 95% CI: 1.74–139.30) and kidney (RR = 9.2; 95% CI: 1.03–82.20) in men and for cancers of the cervix (RR = 4.01; 95% CI: 2.97–5.41) and lymph nodes (RR = 4.74; 95% CI: 1.89–11.88) in women. Four cases of larynx cancer were found in males in exposed counties but none in the non-exposed countries (Table 1).

An increase in haematopoietic cancers was also observed in the population under 10 years in the exposed counties both in males (cases in exposed group: 10; RR = 2.63; 95% CI: 0.90–7.69) and females (cases in exposed group: 8; RR = 3.60; 95% CI: 0.95–13.57).

## Discussion

This study compared cancer incidence in counties with oil development and those without such activities in the Amazon basin of Ecuador (1985–1998). The results showed considerable geographical differences in the incidence of several cancers. Epidemiological studies have reported the same types of cancer being associated with occupational or residential exposure to oil pollutants.<sup>20,21,29–33</sup>

Crude oil is a complex mixture of many chemical compounds, mostly hydrocarbons. The petroleum hydrocarbons of most toxicological interest are volatile organic compounds (benzene, xylene and toluene) and PAH.<sup>34</sup> Studies on mice have reported skin tumours after application to the skin of crude oil.<sup>35–37</sup> However, a review concluded that there is limited evidence for



**Figure 2** All sites cancer incidence by age group in men and women, Amazon basin of Ecuador, 1985–1998

**Table 1** Risk of all cancers and specific cancers for category of exposed versus non-exposed to oil pollution, Amazon region, 1985–1998

Site (ICD-10)	Men			Women		
	Cases in exposed group	RR <sup>a</sup>	95% CI	Cases in exposed group	RR <sup>a</sup>	95% CI
All (C01–C80)	185	1.40	1.15–1.71	288	1.63	1.39–1.91
Mouth (C01–C10)	4	1.22	0.27–5.45	1	1.02	0.11–9.80
Oesophagus (C15)	2	0.82	0.15–4.48	1	0.85	0.35–2.04
Stomach (C16)	49	2.51	1.60–3.94	13	0.90	0.46–1.77
Colon (C18)	7	1.50	0.51–4.46	1	0.064	0.007–0.53
Rectum (C20)	4	10.40	1.16–12.98	2	–	–
Liver (C22)	4	1.53	0.34–6.83	3	1.52	0.31–7.52
Gallbladder (C23)	1	0.41	0.04–4.51	4	1.00	0.37–2.70
Pancreas (C25)	2	2.58	0.36–18.32	–	–	–
Larynx (C32)	4	–	–	–	–	–
Bronchus and lung (C34)	7	1.54	0.54–4.39	2	1.65	0.23–11.72
Haematopoietic, retic. endothel syst. (C42)	23	0.90	0.56–1.44	22	1.29	0.70–2.36
Skin melanoma (172)	9	10.15	2.19–46.97	–	–	–
Skin (C44)	16	1.12	0.58–2.15	14	1.24	0.62–2.48
Connective, subcut., other soft tiss. (C49)	4	15.59	1.74–139.30	2	0.56	0.12–2.58
Breast (C50)	–	–	–	19	1.17	0.65–2.09
Cervix (invasive) (C53)	–	–	–	96	4.01	2.97–5.41
Corpus uteri (C54)	–	–	–	4	2.65	0.59–11.85
Ovary (C56)	–	–	–	5	0.74	0.25–2.17
Placenta (C58)	–	–	–	4	1.80	0.40–8.05
Penis (C60)	2	0.39	0.071–2.13	–	–	–
Prostate (C61)	6	0.46	0.18–1.17	–	–	–
Testis (C62)	4	0.45	0.15–1.38	–	–	–
Kidney (C64)	4	9.2	1.03–82.20	1	0.37	0.02–5.91
Bladder (C67)	–	–	–	1	0.54	0.03–8.62
Eye (C69)	4	0.87	0.22–3.48	–	–	–
Brain (C71)	1	0.14	0.015–1.34	1	3.80	0.24–60.65
Thyroid (C73)	2	0.71	0.12–4.24	6	0.48	0.17–1.38
Lymph nodes (C77)	17	1.15	0.62–2.12	13	4.74	1.89–11.88

<sup>a</sup> Relative risk.

carcinogenicity of crude oil in experimental animals. The same review concluded that there was inadequate evidence for carcinogenicity of crude oil in humans.<sup>34</sup>

Benzene is a well known cause of leukaemia,<sup>38,39</sup> and perhaps other haematological neoplasms and disorders.<sup>40,41</sup> No adequate data on the incidence of cancer after human exposure to the other volatile organic chemicals exist.<sup>42</sup> A population-based case-control study carried out in Montreal showed limited evidence of increased risk for the following associations: oesophagus-toluene, colon-xylene, rectum-toluene, rectum-xylene and rectum-styrene.<sup>43</sup> An ecological study performed to examine the relation between the incidence of leukaemia and the occurrence of volatile organic chemical (VOC) contamination of drinking water supplies suggested that drinking water contaminated with VOC might increase the incidence of leukaemia among exposed females.<sup>44</sup> Different epidemiological studies have reported direct evidence of the carcinogenic effects of PAH in occupationally exposed subjects. Strong evidence of the carcinogenic effects of PAH on the skin, bladder and scrotum has been found.<sup>29,30,44–46</sup> Workers in several industries with significant PAH exposure have also been shown to be at risk of lung cancer.<sup>29–31,45</sup>

There have been few studies of residents near oil fields or petrochemical industries. In the US, an ecological study found an association in both sexes between residential exposure to petroleum and chemical air emissions and cancer of the buccal cavity and pharynx. In males, increased age-adjusted incidence rates for cancers of the stomach, lung, prostate and kidney and urinary organs were also associated with petroleum and chemical plant air emission exposures.<sup>47</sup> A study in the same country found high rates of cancer of the lung, nasal cavity and sinuses, and skin among the resident male population.<sup>48</sup> Other studies in the US have suggested high rates of lung cancer and an elevated risk of brain cancer among people living near petrochemical plants.<sup>49,50</sup> Studies from the US have also reported negative results.<sup>51</sup> Studies conducted in Taiwan have reported an excess rate for liver and lung cancer<sup>52,53</sup> and an excess of cancer (bone, brain, and bladder) deaths in young adults associated with residence near petrochemical industries.<sup>54</sup>

The increase in haematopoietic cancers found among children under 10 years old is troubling. Childhood leukaemia and other childhood cancers have been geographically associated with industrial atmospheric effluent, for example with petroleum derived volatiles in the UK.<sup>32,33</sup> By contrast, a study from

Wales did not find an association between incidence of leukaemia and lymphomas in children and young people in the area around the BP Chemical site at Baglan Bay, South Wales.<sup>55</sup> A recent report around all industrial complexes that include major oil refineries in the UK found no evidence of association between residence near oil refineries and leukaemia or non-Hodgkin's lymphoma.<sup>56</sup>

The findings of this study are consistent with earlier reports from the area evidencing severe contamination of water sources and an apparent excess of cancer morbidity and mortality in males in a village located in an oil producing area.<sup>23</sup> The type of cancers found in that village, ampulla of Vater, stomach, larynx, liver and melanoma in males, lymphoma and cervix in women and leukaemia in children, are similar to those found in this study.

Because they reflect group rather than individual characteristics and exposures, ecologic studies must be interpreted cautiously. The use of aggregated data instead of the joint distributions of exposure, outcome, and covariates at the individual level, may lead to severe bias in ecologic analyses.<sup>57</sup> Using narrow exposure data and small units of analysis (parishes) could have minimized the effect of this bias but this could not be carried out due to the lack of data. Overall, it is difficult to measure the impact of the ecologic bias in the study.

Because of geographical and socioeconomic difficulties in accessing adequate health care, it is likely that many cases of cancer were never referred to Quito from the study area. Health services are poor in both exposed and unexposed counties, but factors such as diagnostic skills and transport facilities might influence referral patterns. It is also possible that on a county level there are differences in racial composition and lifestyle patterns between exposed and unexposed populations that might confound risk estimates. However, no information was available on the distribution of these potentially important confounders.

Several limitations in the data and methods also need to be considered. Population data relied on county census estimated from the 1990 National Census. Errors in population estimates, including differential migration patterns, might bias estimates of risk. It is possible that exposed counties have had a more rapidly increasing population compared to non-exposed, providing a relatively greater underestimate of population denominators for these counties. However, population projections from the National Institute of Statistics and Census give no evidence that this is the case.<sup>27</sup> Cancer rates were based on county of residence at time of diagnosis without information as to length of time at current residence. Because the latency period for cancer

can be long, an assessment of migration into and out of counties as well as residence time in the county would have been useful, but no data were available.

Furthermore, the study design did not allow for measurement of relevant exposure over time. Although there is documented contamination of water sources used by the population in exposed areas, the relevant exposure period for cancers may extend one or two decades further back. However, in the four counties defined as exposed there is a commonly known history of heavy oil development activities since the early 1970s.<sup>2,4,6</sup>

One possibility that may explain any excess risk near an industrial source is that it reflects occupational rather than environmental factors. Individual occupational data were not available. Two exposed counties also have palm oil industries where pesticide use is common. The impact of this exposure on the results presented could not be measured.

The results suggest a relationship between cancer incidence and living in proximity to oil fields, although this ecologic study cannot lead to causal inference. However, the possibility of a causal relationship is supported by several criteria. First, the strength of the association between the outcome and the exposure. Second, there has been considerable attention devoted to the biological mechanism by which some of the components of crude oil (benzene, PAH) could increase cancer risk.<sup>58–62</sup> Third, consistency with other investigations is apparent after reviewing the body of literature that associates oil pollutants and cancer. Fourth, by using surrogate data that are representative of several decades of oil pollution exposure, a plausible time sequence from exposure to development of disease can be inferred.

Further research is necessary to determine if the observed associations do reflect an underlying causal relationship. A next step could be epidemiological studies at the individual level. Meanwhile, an environmental monitoring system to assess, control and assist in elimination of sources of pollution in the area, and a surveillance system to gain knowledge of the evolution of cancer incidence and distribution in the area, are urgently recommended.

## Acknowledgements

We are grateful to Dr Pepe Yopez from the National Tumour Registry of Ecuador for providing the cancer data and Dr Ben Armstrong for valuable comments on an earlier draft. This study was supported by a grant from Medicus Mundi Gipuzkoa, Capuchinos-Navarra and Fundación para los Indios del Ecuador.

### KEY MESSAGES

- Since the early 1970s millions of gallons of untreated toxic wastes, gas and oil have been released into the environment in the Amazon basin of Ecuador during oil exploration activities.
- Our study shows significantly higher incidence of cancer for all sites combined in both men and women living in proximity to oil fields.
- Significantly higher incidences were observed for cancers of the stomach, rectum, skin melanoma, soft tissue and kidney in men and for cancers of the cervix and lymph nodes in women.
- There have been few studies of those resident near oil fields, further research is necessary.
- An environmental monitoring and cancer surveillance system in the region are urgently recommended.

## References

- 1 Myers N. *The Primary Source: Tropical Forests and Our Future*. New York: Norton Press, 1984.
- 2 Kimerling J. *Amazon Crude*. New York: Brickfront Graphics Inc, 1991.
- 3 Jochnick C, Normand R, Zaidi S. Rights violations in the Ecuadorian Amazon: the human consequences of oil development. *Health Human Rights* 1994;**1**:82–100.
- 4 Garzón P. Impacto socioambiental de la actividad petrolera: estudio de caso de las comunidades San Carlos y La Primavera. In: Varea A, Ortiz P (eds). *Marea Negra en la Amazonía: Conflictos Socioambientales Vinculados a la Actividad Petrolera en el Ecuador*. Quito: Abya-Yala, 1995, pp. 265–94.
- 5 Kimerling J. *Oil Development in Ecuador and Peru: Law, Politics and the Environment*. Draft paper presented at Amazonia 2000: Development, environment and geopolitics. London: Institute of Latin American Studies, University of London, 1998.
- 6 Almeida A. Reseña sobre la historia ecológica de la Amazonía ecuatoriana. In: Martínez E (ed.). *Ecuador Post Petrolero*. Quito: Acción Ecológica, 2000.
- 7 Dirección General de Medio Ambiente. *Estudio de Impacto Ambiental 42*. Quito: Dirección General de Medio Ambiente, 1989.
- 8 Rainforest Action Network News. [http://www.ran.org/ran/ran\\_campaigns/amazonia/texaco\\_ecuador.html](http://www.ran.org/ran/ran_campaigns/amazonia/texaco_ecuador.html), 1998.
- 9 Centro de Derechos Económicos y Sociales. *Violaciones de Derechos en la Amazonía Ecuatoriana*. Quito: Abya-Yala, 1994.
- 10 San Sebastian M, Armstrong B, Stephens C. La salud de mujeres que viven cerca de pozos y estaciones de petróleo en la Amazonía ecuatoriana. *Rev Panam Salud Pública* 2001;**9**:375–84.
- 11 Zehner R, Villacreces LA. *Estudio de la Calidad de Aguas de Río en la Zona de Amortiguamiento del Parque Nacional Yasuní. Primera Fase: Monitoreo de Aguas—Screening Octubre de 1997*. Coca, Ecuador: Laboratorio de Aguas y Suelos P. Miguel Gamboa-Fepp, 1998.
- 12 Ministerio de Medio Ambiente. *Informe de Inspección Ambiental al Área de las Comunidades Flor de Manduro y Centro Manduro Ubicadas en el Bloque Siete Operado por la Compañía Oryx*. Quito: Ministerio de Medio Ambiente, 1999.
- 13 Campbell D, Cox D, Crum J *et al*. Initial effects of the grounding of the tanker Braer on health in Shetland. *Br Med J* 1993;**307**:1251–55.
- 14 Palinkas LA, Petterson JS, Russell J *et al*. Community patterns of psychiatric disorders after the Exxon Valdez oil spill. *Am J Psychiatry* 1993;**150**:1517–23.
- 15 Lyons RA, Temple MF, Evans D *et al*. Acute health effects of the Sea Empress oil spill. *J Epidemiol Community Health* 1999;**53**:306–10.
- 16 Mills PK, Newell GR, Johnson DE. Testicular cancer associated with employment in agriculture and oil and natural gas extraction. *Lancet* 1984;**i**:207–10.
- 17 Sewell CM, Castle SP, Hull HF *et al*. Testicular cancer and employment in agriculture and oil and natural gas extraction. *Lancet* 1986;**i**:553.
- 18 Siemiatycki J, Dewar R, Nadon L *et al*. Associations between several sites of cancer and twelve petroleum-derived liquids. Results from a case-referent study in Montreal. *Scand J Work Environ Health* 1987;**13**:493–504.
- 19 Divine BJ, Barron V. Texaco mortality study III. A cohort study of producing and pipeline workers. *Am J Ind Med* 1987;**11**:189–202.
- 20 Sathiakumar N, Delzell E, Cole P *et al*. A case-control study of leukemia among petroleum workers. *J Occup Environ Med* 1995;**37**:1269–77.
- 21 Yang C, Zhang X. Incidence survey of leukemia in China. *Chin Med Sci J* 1991;**6**:65–70.
- 22 Divine BJ, Hartman CM. Update of a study of crude oil production workers 1946–94. *Occup Environ Med* 2000;**57**:411–17.
- 23 San Sebastian M, Armstrong B, Stephens C. Environmental exposure and cancer incidence near oil fields in the Amazon basin of Ecuador. *Occup Environ Med* 2001;**58**:517–22.
- 24 Fundación José Peralta. *Ecuador: su Realidad*. Quito: Fundación de Investigación y Promoción Social José Peralta, 1999.
- 25 UNICEF. *Situación de las Madres y los Niños en Zonas de Grandes Proyectos*. Quito: United Nations Childrens Fund, 1992.
- 26 Sociedad de Lucha contra el Cáncer. *Cáncer en Quito; Anuario 1995–1996*. Quito: Sociedad de Lucha contra el Cáncer, 1998.
- 27 Instituto Nacional de Estadísticas y Censos del Ecuador. *V Censo de Población y IV de Vivienda*. Quito: INEC, 1990.
- 28 Smith PG. Comparison between registries: age-standardized rates. In: Parkin DM, Whelan SL, Ferlay J, Raymond L, Young J (eds). *Cancer Incidence in Five Continents, Vol. VII*. Lyon, France: International Agency for Research on Cancer, 1997.
- 29 Mastrangelo G, Fadda E, Marzia V. Polycyclic aromatic hydrocarbons and cancer in man. *Environ Health Perspect* 1996;**104**:1166–70.
- 30 Boffetta P, Jourenkova N, Gustavsson P. Cancer risk from occupational and environmental exposure to polycyclic aromatic hydrocarbons. *Cancer Causes Control* 1997;**8**:444–72.
- 31 Nadon L, Siemiatycki J, Dewar R *et al*. Cancer risk due to occupational exposure to polycyclic aromatic hydrocarbons. *Am J Ind Med* 1995;**28**:303–24.
- 32 Knox EG, Gilman EA. Hazard proximities of childhood cancers in Great Britain from 1953–80. *J Epidemiol Community Health* 1997;**51**:151–59.
- 33 Knox EG, Gilman EA. Migration patterns of children with cancer in Britain. *J Epidemiol Community Health* 1998;**52**:716–26.
- 34 International Agency for Research on Cancer. Monographs on the evaluation of the carcinogenic risk of chemicals to man: occupational exposures to petroleum refining: crude oil and major petroleum fuels. Lyon, France: IARC, Vol. 45, 1989.
- 35 Grimmer G, Dettbarn G, Brune H *et al*. Quantification of the carcinogenic effect of polycyclic aromatic hydrocarbons in used engine oil by topical application onto the skin of mice. *Int Arch Occup Environ Health* 1982;**50**:95–100.
- 36 Clark CR, Walter MK, Ferguson PW *et al*. Comparative dermal carcinogenesis of shale and petroleum-derived distillates. *Toxicol Ind Health* 1988;**4**:11–22.
- 37 Wilson JS, Holland LM. Periodic response difference in mouse epidermis chronically exposed to crude-oils or BaP: males vs. females. *Toxicology* 1988;**50**:83–94.
- 38 Wong O. An industry wide mortality study of chemical workers occupationally exposed to benzene. I. General results. *Br J Ind Med* 1987;**44**:365–81.
- 39 Austin H, Delzell E, Cole P. Benzene and leukemia. A review of the literature and a risk assessment. *Am J Epidemiol* 1988;**127**:419–39.
- 40 Hayes RB, Yin SN, Dosemeci M *et al*. Benzene and the dose-related incidence of hematologic neoplasms in China. *J Natl Cancer Inst* 1997;**89**:1065–71.
- 41 Savitz DA, Andrews KW. Review of epidemiologic evidence on benzene and lymphatic and hematopoietic cancers. *Am J Ind Med* 1997;**31**:287–95.
- 42 Gerin M, Siemiatycki J, Desy M *et al*. Associations between several sites of cancer and occupational exposure to benzene, toluene, xylene, and styrene: results of a case-control study in Montreal. *Am J Ind Med* 1998;**34**:144–56.
- 43 Fagliano J, Berry M, Bove F *et al*. Drinking water contamination and the incidence of leukemia: an ecologic study. *Am J Public Health* 1990;**80**:1209–12.
- 44 Everall JD, Dowd PM. Influence of environmental factors excluding ultra violet radiation on the incidence of skin cancer. *Bull Cancer* 1978;**65**:241–47.

- <sup>45</sup> International Agency for Research on Cancer. Monographs on the evaluation of the carcinogenic risk of chemicals to man: polynuclear aromatic hydrocarbons. Lyon, France: IARC, 1983, Vol. 34.
- <sup>46</sup> Bonassi S, Merlo F, Pearce N *et al.* Bladder cancer and occupational exposure to polycyclic aromatic hydrocarbons. *Int J Cancer* 1989;**44**: 648–51.
- <sup>47</sup> Kaldor J, Harris JA, Glazer E *et al.* Statistical association between cancer incidence and major-cause mortality, and estimated residential exposure to air emissions from petroleum and chemical plants. *Environ Health Perspect* 1984;**54**:319–32.
- <sup>48</sup> Blot WJ, Brinton LA, Fraumeni JF *et al.* Cancer mortality in U.S. counties with petroleum industries. *Science* 1977;**198**:51–53.
- <sup>49</sup> Gottlieb MS, Shear CL, Seale DB. Lung cancer mortality and residential proximity to industry. *Environ Health Perspect* 1982;**45**:157–64.
- <sup>50</sup> Olin RG, Ahlbom A, Lindberg-Navier I *et al.* Occupational factors associated with astrocytomas: a case-control study. *Am J Ind Med* 1987; **11**:615–25.
- <sup>51</sup> Hearey CD, Ury H, Siegelaub A *et al.* Lack of association between cancer incidence and residence near petrochemical industry in the San Francisco Bay area. *J Natl Cancer Inst* 1980;**64**:1295–99.
- <sup>52</sup> Yang CY, Chiu HF, Chiu JF *et al.* Cancer mortality and residence near petrochemical industries in Taiwan. *J Toxicol Environ Health* 1997; **50**:265–73.
- <sup>53</sup> Yang CY, Cheng MF, Chiu JF *et al.* Female lung cancer and petrochemical air pollution in Taiwan. *Arch Environ Health* 1999;**54**:180–85.
- <sup>54</sup> Pan BJ, Hong YJ, Chang GC *et al.* Excess cancer mortality among children and adolescents in residential districts polluted by petrochemical manufacturing plants in Taiwan. *J Toxicol Environ Health* 1994;**43**:117–29.
- <sup>55</sup> Lyons RA, Monaghan SP, Heaven M *et al.* Incidence of leukaemia and lymphoma in young people in the vicinity of the petrochemical plant at Baglan Bay, South Wales, 1974 to 1991. *Occup Environ Med* 1995;**52**: 225–28.
- <sup>56</sup> Wilkinson P, Thakrar B, Walls P *et al.* Lymphohaematopoietic malignancy around all industrial complexes that include major oil refineries in Great Britain. *Occup Environ Med* 1999;**56**:577–80.
- <sup>57</sup> Dos Santos Silva I. *Cancer Epidemiology: Principles and Methods*. Lyon, France: International Agency for Research on Cancer, 1999.
- <sup>58</sup> Smith MT, Robertson ML, Yager JW, Eastmond DA. Role of metabolism in benzene-induced myelotoxicity and leukemogenesis. *Prog Clin Biol Res* 1990;**340B**:125–36.
- <sup>59</sup> Smith MT. The mechanism of benzene-induced leukemia: a hypothesis and speculations on the causes of leukemia. *Environ Health Perspect* 1996;**104**(Suppl.6):1219–25.
- <sup>60</sup> Whysner J. Benzene-induced genotoxicity. *J Toxicol Environ Health A* 2000;**61**:347–51.
- <sup>61</sup> Burczynski ME, Penning TM. Genotoxic polycyclic aromatic hydrocarbon ortho-quinones generated by aldo-keto reductases induce CYP1A1 via nuclear translocation of the aryl hydrocarbon receptor. *Cancer Res* 2000;**60**:908–15.
- <sup>62</sup> Dertinger SD, Lantum HB, Silverstone AE, Gasiewicz TA. Effect of 3'-methoxy-4'-nitroflavone on benzo[a]pyrene toxicity. Aryl hydrocarbon receptor-dependent and -independent mechanisms. *Biochem Pharmacol* 2000;**60**:189–96.

## Commentary: Epidemiology on the side of the angels

Jack Siemiatycki

Hurtig and San Sebastián<sup>1</sup> have examined cancer incidence rates in a region of the Amazon basin of Ecuador and ostensibly found higher cancer rates in the area closer to oil extraction sites than in the area further away; they concluded that this should lead to the establishment of systems of environmental monitoring and control, and of cancer surveillance. The conduct and publishing of this work raise several issues, of which I will comment on three: the strength of evidence that this study affords, the replicability of this study; and the public health recommendations that can be made.

### Strength of evidence from this study

Research on cancer in developing countries is difficult. Among the major problems is the fact that diagnosis of cancer is a fairly

high-tech and expensive enterprise, not readily available to the majority of inhabitants of many developing countries. Available statistics on cancer incidence and mortality in most developing countries are probably incomplete, of questionable validity, and biased in their representation of variation by social class, geographical sub-region and other factors that may influence access to diagnostic services.

This study's limitations are clear and are partly acknowledged by the authors. Stripped to its essence, it is a geographical correlation study with: an n of 2, a real possibility of bias in ascertainment of the outcome between the two study areas, a real possibility of confounding by a plethora of ethnic and social factors, and the crudest of measures of exposure. While the overall cancer incidence was ostensibly higher in the 'exposed' area, the cancer site distributions did not exhibit a pattern that would obviously throw suspicion on aetiological agents coming from the oil industry pollution. Namely, the greatest excess in the exposed area, representing virtually all of the observed

excess among females, was for cancer of the cervix. The only other cancer site which exhibited more than a handful of excess cases in the exposed area was stomach cancer. Given the limitations of the study design and the lack of clear, strong results, this study provides no more than a hint that there may be a cancer problem in the area around oil fields.

## Replication of studies—consistency of evidence

Because of the capricious nature of biases that can arise in epidemiological research, the need for multiple pieces of epidemiological evidence to support a hypothesis is well grounded and well recognized.<sup>2</sup> But what about causal inferences when there is little opportunity for replication?

No observational epidemiology study is perfectly replicable, in the sense that a laboratory experiment should be perfectly replicable. Differing social/environmental contexts and differing study methods are inevitable even when two studies seem to be similar in objectives and study design. Still, some issues entail a fair degree of replicability. Smoking and lung cancer can be studied in a variety of populations and despite some real differences in the nature of the exposure variable (e.g. type of tobacco, smoking habits) and differences in the nature of the genetic make-up and social covariables, the pattern of results from different studies can be juxtaposed to draw some generalized inferences about smoking and lung cancer. There are many such circumstances that allow us to invoke the criterion of consistency of findings in evaluating causality. However, there are other issues, and this is particularly a problem in environmental epidemiological studies, where the nature of the exposure circumstances or of the covariable circumstances is so unique, that there is no realistic expectation that other epidemiological evidence could be assembled that would be directly informative for the hypothesis under study.

Rare environmental disasters and residential proximity to toxic waste dumps or industrial sources of pollution can be so unique in their chemical make-up and in their ability to pollute neighbouring human habitats, that there may be little or no hope of finding circumstances similar enough elsewhere to conduct studies to replicate what is found in one location.

Most epidemiological studies fall somewhere on the continuum from a completely unique non-replicable exposure and covariate situation to a completely generic and generalizable exposure and covariate situation. In general, the closer the study is to the 'unique situation' end of the continuum, the stronger the evidence needs to be on other causal criteria (strength of association, 'dose-response', likely absence of known biases, plausibility, temporality). These various causal criteria should not be seen as a checklist of disconnected items that need to be satisfied in abstraction, one after the other. Each one provides an opportunity to support the causal hypothesis on a continuous rather than binary scale. That is, weaker evidence on one or more of these criteria can be compensated by stronger evidence on other criteria. It is possible to derive an inference of causality even when there is no opportunity to assess consistency; but the evidence should be compelling. Cancer risks following the atomic bombs in Japan provide one example.<sup>3</sup> A more recent example comes from an outbreak of tumours of the ureter found among a group of Belgian women who had taken high

doses of a Chinese herbal medicine as part of a weight loss regimen.<sup>4</sup>

Insofar as pollution due to oil extraction processes is concerned, the nature of any human exposure that might occur would depend critically on the engineering processes, control measures, the local geography, and the local human population habits and characteristics. It is questionable whether studies could be mounted in different places that would provide a reasonable estimate of the consistency of the epidemiological evidence for the hypothesis that residence near oil fields in Ecuador causes cancer. In any case, at this time there does not appear to be such evidence. What we are left with is this study in this locale on this population, and some indirect evidence concerning exposure to petroleum products in very different (mainly occupational) circumstances.

## Justification for public health recommendations

If the evidence from this study does not provide convincing evidence of health effects due to an environmental exposure, should one use the study as a basis for public health recommendations?

Hurtig and San Sebastian call for further research, possibly at the individual level, to examine cancer risks in relation to oil industry pollution, and for the establishment of a cancer surveillance system in the area. These are reasonable recommendations that flow from the inconclusive study that they carried out.

They also call for 'an environmental monitoring system to assess, control and assist in elimination of sources of pollution in the area'. Given the graphic descriptions of the extent of environmental pollution in the area, this recommendation is difficult to resist. However, it does not flow as a consequence of this study.

There is some tension between two views of the essential nature of epidemiology. One view holds that epidemiology is a scientific discipline whose *raison d'être* is to describe nature in its sphere of competence (distribution and determinants of health and illness) and another holds that epidemiology is that branch of public health which provides the empirical underpinnings of public health policy. These views are certainly not mutually exclusive, but neither are they perfectly congruent. The 'scientific' and 'activist' visions occasionally confront each other.

Environmental monitoring and control of pollution from oil fields seem like elementary public health needs irrespective of whether pollution can be demonstrably linked to cancer among local residents. At the very least, the case for monitoring should not depend on whether or not the link to disease has been demonstrated. Indeed, one of the reasons why it is so hard to demonstrate a link is precisely because the epidemiological database does not include adequate information on human exposures.

Epidemiological research is sometimes used as a cover of scientific legitimacy in calling for sensible public health precautions. While this definitely puts epidemiologists 'on the side of the angels', it also risks compromising the scientific credibility of epidemiology. The paper by Hurtig and San Sebastian does not represent the most egregious example of such a tendency. But the apparent reach for suggestive results where such suggestions are at best hints, and the ease with which public health

recommendations are made, suggest that the authors may have been leaning on the recommendations before the data were in and the evidence assessed. On the other hand, in the real world of lobbying and public policy, it seems that epidemiologists are sometimes 'caught between a rock and a hard place' when they try to simultaneously satisfy their rigorous scientific principles and their public health principles.

### General remarks

Research on cancer in developing countries can be very helpful in elucidating potential environmental hazards, either in situations where the observed associations are so strong that they are unlikely to be explained by potential biases,<sup>5</sup> or in situations where the quality of data and strong design permit reasonable inferences to be drawn even in the absence of strong associations.<sup>6</sup> Epidemiology is an eclectic discipline, using an ever-expanding panoply of methods. In assessing methodological quality, we must make allowances for the resources and local conditions in which the investigators find themselves. To require the same standards of research design everywhere would lead to pockets of the world where there is no information at all on various issues.

The study by Hurtig and San Sebastian represents a bold attempt to use imperfect data to derive scientific knowledge; it

is useful in highlighting the issue and drawing attention to the limitations of the data. But it does not provide strong evidence in favour of the hypothesis. Nevertheless, given the complexity of disease aetiology, and the need to discover both universal and local facets of disease aetiology, we should encourage the conduct of research such as this.

### References

- <sup>1</sup> Hurtig A-K, San Sebastián M. Geographical differences in cancer incidence in the Amazon basin of Ecuador in relation to residence near oil fields. *Int J Epidemiol* 2002;**31**:1021–27.
- <sup>2</sup> Hill AB. The environment and disease: association or causation? *Proc R Soc Med* 1965;**58**:295–300.
- <sup>3</sup> Thompson DE, Mabuchi K, Ron E *et al.* Cancer incidence in atomic bomb survivors. Part II: Solid tumors, 1958–1987. *Radiat Res* 1994;**137**:S17–67.
- <sup>4</sup> Nortier JL, Martinez MC, Schmeiser HH *et al.* Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *N Engl J Med* 2000;**342**:1686–92.
- <sup>5</sup> Peers F, Gilman G, Linsell C. Dietary aflatoxins and human liver cancer. A study in Swaziland. *Int J Cancer* 1976;**17**:167–76.
- <sup>6</sup> Wesseling C, Antich D, Hogstedt C, Rodriguez AC, Ahlbom A. Geographical differences of cancer incidence in Costa Rica in relation to environmental and occupational pesticide exposure. *Int J Epidemiol* 1999;**28**:365–74.