

Oil Contamination and Health Effects in the Ecuadorian Amazon Basin:

A review of recent reports and publications

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What is the main theme of the studies?

Exposures of native populations to contamination from oil production leads to adverse health effects due to those exposures. Health effects attributed to oil exposure include cancers (of multiple sites), spontaneous abortions, dermatitis, and a variety of symptoms. Some reports include discussions of malnutrition and infant mortality as if they were considered to be due to contamination.

What are potential issues with respect to the design and conduct of the studies reviewed?

- Bias, both selection bias and information bias, and residual confounding.
- Socioeconomic differences between exposed and non-exposed communities.
- Differences between communities in ethnicity, indigenous versus mestizo.
- The communities assigned to exposed and non-exposed groups are not always clearly defined.
- Case reports/series includes no consideration of frequencies of outcomes in comparison populations.
- Little evidence that the literature cited on health effects of occupational exposures to petrochemical industry is relevant to environmental exposures to contamination from oil fields.

What are the key issues in interpreting the studies?

There is little or no evidence that would support a causal relationship between oil contamination and health effects. Even some of the evidence suggesting an association is highly questionable due to potential problems of case ascertainment, exposure determination, bias, and confounding. The larger agenda of social activism with respect to lack of public health programs and medical services is potentially being used to argue, speciously, for attributing the poor health of members of marginalized and disenfranchised communities to oil contamination. Review of the documents related to health status and human rights in Ecuador in general suggests that the problems observed are unrelated to oil contamination. The documents that put the health problems into the context of oil contaminated communities versus others tend to ignore potentially important differences between these types of communities in factors other than oil contamination. These include ethnicity, migrant versus sedente status, and socioeconomic conditions in general, to name a few. Any and all of these could contribute to differences in patterns and rates of adverse health outcomes.

An example to illustrate how some of these variables could be relevant comes from the literature on childhood leukemia. Kinlen (1995) and others have put forward data to support the importance of population mixing in contributing to high rates of leukemia in some parts of the United Kingdom and other locations in multiple countries. Kinlen argues that high rates of leukemia in several “new

towns” established during the war years in the UK were the result of residents from different areas coming together to establish new populations that were heterogeneous with respect to their disease/exposure histories. This created a set of conditions that led to the occurrence of cases of childhood leukemia. The fact that the Ecuadorian oil communities are made up, predominantly, of migrants from the coastal and mountain areas of Ecuador while the non-oil communities consist of large proportions of indigenous peoples suggests the possible relevance of Kinlen’s hypothesis to the occurrence of childhood leukemia in the oil communities of Ecuador.

The heterogeneity of the types of cancer reported in the San Carlos “cluster” makes it difficult to believe that those cancers are related to a common etiologic agent. In addition, the generation of the standardized incidence ratios based on observed single cases of a variety of specific types of cancer is particularly problematic. The only cancer for which more than one case was observed was stomach cancer. Neoplasms are the second overall cause of mortality in Ecuador (PAHO, 2002). In 1999 stomach cancer was the leading cause of cancer deaths (PAHO, 2002).

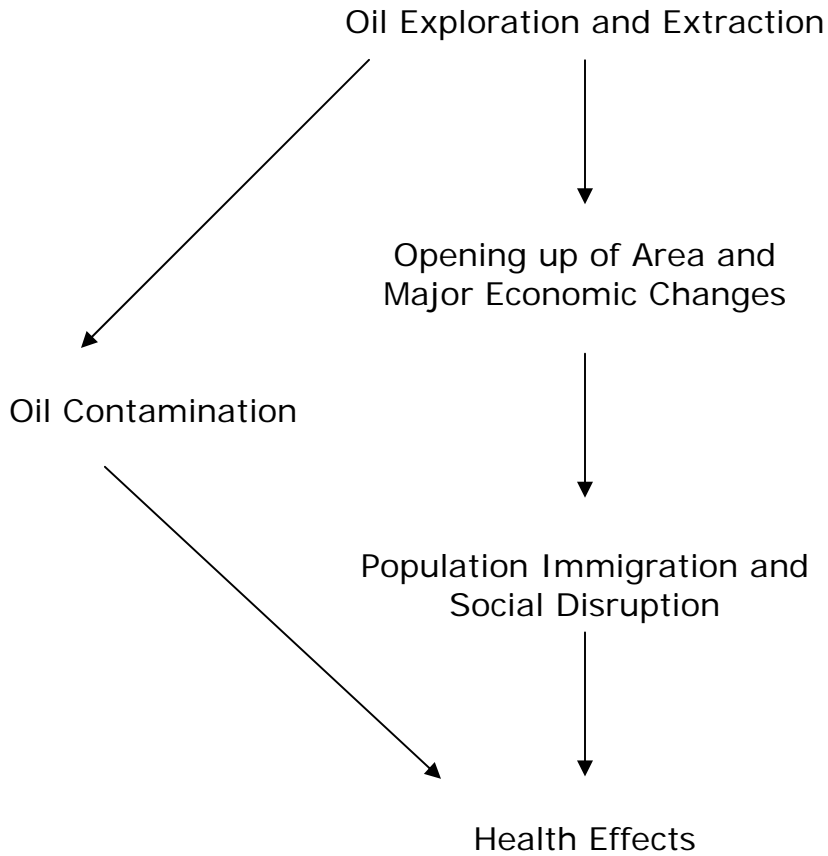
In a 2004 study of cancer incidence in multiple communities in Ecuador, marked differences in rates between indigenous and immigrant populations are reported (San Sebastian and Hurtig, 2004). The oil contaminated communities have a higher percentage of immigrants. This study noted the potential under-diagnosis and under-reporting of cancer in the indigenous populations of Ecuador. If this is indeed the case, this could lead to apparently increased rates in the oil contaminated communities which are reported to be made up of immigrants from the coastal and mountain areas of the country. Rather than there being an excess of cases among the populations of the oil contaminated communities – predominantly immigrants – there may be underreporting of cancers in the uncontaminated communities – primarily indigenous – which is suggested by the 2004 publication by San Sebastian and Hurtig.

A proposed model for understanding the suggested relationships between oil exploration and extraction and health effects

The following figure illustrates how there could be apparent relationships between oil exploration and extraction and health effects due to confounding by socioeconomic conditions. Below I review the individual reports and publications that have been used to support a causal relationship between exposures to crude oil and oil products. This model is supported by many points in the discussion which follows.

Figure 1

**The Potential Confounding Effects of Socioeconomic Conditions
on the Described Associations between Oil Contamination
and Health Effects in the Ecuadorian Amazon Basin**



Reviews of Individual Publications

CESR Rights Violations in the Ecuadorian Amazon The Center for Economic and Social Rights, New York 1994

The nature and focus of this report are clearly established in the objectives of the CESR team which are stated in the executive summary “(i) to collect data on contamination levels and associated health effects and (ii) to integrate these data into a human rights report assessing the conduct of policies of the government of Ecuador.” It seems clear that any information on possible health effects could have been importantly influenced by the second of these objectives. This is reflected in the discussion of the results of the CESR survey in the executive summary where CESR states “The presence of high levels of toxic compounds and oil-related injuries indicate that the exposed population faces an increased risk of serious and non-reversible health effects such as cancers and neurological and reproductive problems.”

In discussing the situation in the Oriente region, the authors of the report note that settlers from outside have flooded into the area because of the established network of roads, built by oil companies, and have cleared vast regions of the rainforest and displaced the indigenous inhabitants. Thus, there have been important ecological changes that can affect the immigrants' health. This is further supported in the report where the authors note that the settlers “cluster in desperate and squalid oil towns, with little running water, sanitation, or basic health facilities.” It does not seem scientifically reasonable to attribute health problems in these communities to oil contamination.

As an example of the potentially biased approach to the health issues of the communities, much of the discussion of health effects in the report seems to focus on supporting “local reports that oil contamination has damaged people's health.” The authors note a rise in child mortality as a result of oil-related accidents and contaminated drinking water, but this is much more likely to be due to poverty and social disorganization in these areas. This is supported by the reference to high rates of child malnutrition in areas impacted by oil development. The health conditions reported are unlikely to be related to oil production per se. Similarly, in discussing the findings of a study by UPPSAE (reviewed below) they reported that ten percent of the people surveyed were ill due to bathing in oil contaminated waters, occupation-related exposures or non-occupational accidents. This clearly suggests an over-interpretation of the findings as they relate to oil contamination.

Section III of this report reviews studies of “health effects of exposure to crude oil” but the actual scientific information on health risks from exposure of humans to crude oil and its constituents is quite limited. For example a long list of dermatologic conditions, none of which would appear to be pathognomic, is attributed to crude oil exposure. In addition, the skin conditions described

subsequently in the case series section of the report do not seem to be similar to those included here. One citation is provided for cancer associated with consumption of drinking water contaminated with oil – esophageal cancer in a community in Saudi Arabia. Inhalation of crude oil fumes is suggested to lead to effects on the nervous and respiratory systems, in the latter case leading to chemical pneumonitis, but there is no evidence that was found in the survey presented here. The authors cite single sources for possible associations between crude oil and reproductive and developmental effects (IARC, 1989) and between parental occupational exposure to petroleum products and childhood cancers, including leukemia and brain cancer (O’Leary et al., 1991). The discussion of the toxic constituents of crude oil focuses on the effects of PAHs and VOCs and includes risk estimates from the EPA and WHO.

The exposure and health study (Section IV) was based on matching levels of oil-related contaminants – PAHs and VOCs – and contamination-related illnesses – dermatitis. The authors believed that dermatitis, which was studied using a cross-sectional survey (“case finding approach”), can be used to demonstrate a risk for more serious chronic diseases. No evidence is given to support this assumption and no data are provided on the occurrence of dermatitis in comparison populations.

The authors report 12 cases of dermatologic problems that they attribute to oil exposure. It is not clear, however, how these cases are related to the contamination sampling data presented in their Figure #3. In addition, review of the case histories presented in Appendix IV suggests that most of these individuals attributed the appearance of their dermatitis to exposures following oil spills. It is unclear how exposures to spills are related to issues of general contamination. It is also quite possible that there is no real relationship between the dermatitis and the spills but that the spills provided a temporal marker to which the subsequent development of dermatitis could be tied.

It is interesting to note that in discussing the cases of dermatitis on page 19 of the report only one measurement of PAH concentration is linked to a case and this is one of the lowest levels reported in Figure #3. The authors suggest that exposure was more likely to be due to the oil covered road since residents usually walk barefooted. This seems to be a somewhat disingenuous attempt to explain why the outcome being examined was “associated” with a low level of the exposure measured and not with high-level exposure.

The authors dismiss any cause of the dermatoses observed other than crude oil exposures. They suggest that they may be attributable to either high dose episodic exposures from spills or to low dose long-term exposures. They do not cite any relevant published toxicological studies that would suggest that these two very different exposure scenarios would lead to the same outcomes. In addition, they do not cite any data to support their statement that the exposure-outcome relationship they postulated, on the basis of their case series, suggests

increased risks of more serious health effects, including cancers, neurologic and reproductive problems.

In the appendices discussing the methods of the health and exposure studies (Appendix III) and the detailed case studies (Appendix IV) the authors provided details behind the information presented in the report. It is important to note that in Appendix III it is stated that the groups studied have reported adverse oil-related health effects, which could lead to reporting bias. The authors state that “emphasis was placed on health effects relating to dermatosis and other skin rashes” without providing any rationale.

Appendix IV – “detailed case studies” – includes descriptions of selected cases. It is important to note that case studies do not provide evidence for associations between exposures and potentially common outcomes. There is no comparison population with which the cases observed in these communities, that have reported health problems attributed to the exposure, can be compared. Case series are usually relevant for hypothesis generation where there is an uncommon exposure and an unusual outcome. Appropriate examples of case studies in this context include:

- Case series of phocomelia linked to maternal use of the drug thalidomide;
- Case series of embryos exposed to isotretinoin, through maternal use, which exhibited a syndrome of multiple structural malformations.

This report provides little support for a relationship between oil contamination and health effects. It is more likely that the observed case series illustrates bias in the selection of subjects for evaluation and that the health effects observed are related to the generally low standards of hygiene and health and socioeconomic conditions in the communities. This assessment is supported by a second report from the Center for Economic and Social Rights (1998) “From Needs to Rights: Recognizing the right to health in Ecuador.” This report deals with the overall issues of poor public health programs and lack of services in Ecuador. It supports the idea that the major health problems are related to systematic programmatic failures. It can be used to argue that the differences between oil and non-oil communities, in terms of health, are most likely to be related to socioeconomic conditions and cultural differences between these two general categories of communities.

UPPSAE Report “Cultures Soaked in Oil” Union of Popular Health Promoters of the Ecuadoran Amazon, 1993

This report, according to the introduction, comes from a group of farmer health promoters who are fighting against the structure of poverty and working for the area’s health. The expressed concerns are:

- Disease levels are higher in areas of oil contamination;

- Miscarriages are more frequent in women who live close to contamination areas;
- There are higher infant mortality and malnutrition levels in preschool children in contaminated areas;
- Serious skin conditions are found among persons cleaning crude oil from pools.

The stated purpose of the study was to develop knowledge regarding socioeconomic, political and cultural factors in the area and to understand how these related to farmers' diseases. The authors state, however, that the chemicals from Texaco (Petroecuador) "cause cancer, miscarriages, monster babies, liver, kidney and brain diseases" without providing any scientific evidence to support their statement, except to note that certain institutions from the United States said they could.

Health promoters from the UPPSAE conducted a study based on seven communities where there are oil operations and three similar communities without. One of the initial steps was to collect data from clinical files in the communities for the preceding four years; based on these data they report miscarriages were 2 to 3 times more frequent in the oil-contaminated communities. The validity of these findings can be questioned since there is no indication of potential differences in the availability of health services in the two groups of communities, which would influence whether women do or do not seek medical care following a miscarriage (spontaneous abortion). Additionally, reporting that miscarriages were 2 to 3 times more frequent suggests that the information was quite inexact.

The investigators reported that they intended to study 1077 individuals in oil-contaminated communities and 388 where there was no contamination. Medical checkups were reportedly given to the entire family in their home. While the refusal rates in the contaminated and uncontaminated communities were comparable, the percentage of persons with incomplete data was higher in the contaminated than in the uncontaminated communities (13.9% versus 8.2%). The potential for serious bias is suggested by the authors' statement that they had the best participation where they explained things most extensively.

The authors report what appear to be major socio-demographic differences between the two groups of communities. For example, those living in contaminated communities have fewer years of education. There are also major differences between the communities in terms of their places of origin (migration history); families in oil contaminated communities come from 11 different provinces versus 6 provinces in the cases of the communities with no contamination. There were also differences between the communities in terms of the lengths of time the families had resided there:

	Contaminated	Non-contaminated
> 5 years	12	16
1-4 years	6	2
< 1 year	2	2

Much of the subsequent discussion in the report seems to have little to do with questions of petroleum production or oil contamination but, rather, with general conditions in the communities, covering topics such as work, marketing and economic conditions. The potential impacts of social disruption on health among members of the two groups of communities are illustrated by a two-fold difference between the oil communities versus the non-oil communities in the percentages of families who have been the victims of robberies. Similar differences are reported for malnutrition in children under five. There are also differences between the communities in the numbers of rooms in the houses, with more people per room in the contaminated communities. As the authors themselves state, the more people who sleep in the same room the easier it is to catch diseases. It is difficult to logically attribute these differences to oil contamination but such socio-demographic factors could certainly be confounders when examining health effects associated with oil contamination.

In addition to information regarding miscarriages that was collected from medical records as noted above, data on pregnancies, miscarriages, and stillbirths were collected as part of the health surveys. The authors note that women in the contaminated areas reported more miscarriages after they moved to the area than before but that ignores the potential relationship between miscarriage risk and gravidity (number of previous pregnancies). Interestingly, while the percentages of pregnancies resulting in miscarriages in women before and after they came to the area were similar (11.1% after versus 8.4% before) the percentages for stillbirths are quite different, with 14.5% of pregnancies resulting in stillbirths before coming to the area versus 8.6% after. These are extremely high proportions of pregnancies ending in stillbirths, with nearly a two-fold higher percentage among the women before they moved to the area, facts which are apparently ignored by the authors. The data presented in Figure 22 on the percentages of pregnancies among women less than 200 meters from contamination that result in miscarriages versus the percentages among women at greater than 200 meters do not seem to be consistent with the data presented on the overall percent of pregnancies resulting in miscarriages.

Data are also presented on infant mortality but it is impossible to differentiate between contaminated and non-contaminated communities. With respect to adult mortality, the authors state that there are more deaths in the communities where oil is produced than in the areas where it is not but the causes of death noted, particularly accidents and murders, are not likely to be attributable to oil contamination.

In describing cultural differences between communities, the authors note that they chose one community as part of the uncontaminated group which had three groups of persons of different cultures. The health outcome findings for this community were intermediate between the contaminated and the other uncontaminated communities. This supports that interpretation that the differences between contaminated and non-contaminated communities are related to cultural/ethnic differences between them and not to contamination per se.

The report goes on to compare the number of diseases per person in the two groups of communities, stating that there are almost three diseases per person in the contaminated communities compared with two per person in the uncontaminated ones. Review of the types of diseases of highest frequency in the contaminated communities – parasites, fungi, anemia, skin infections and malnutrition – suggests that the higher prevalence is unlikely to be related to oil contamination. The authors, however, state that “these diseases can be due to consumption of and bathing in contaminated water.” That oil contamination is likely to be a confounder in a relationship between poor socioeconomic conditions and disease is illustrated clearly by the data presented on tuberculosis, which is reported to be three times more frequent in contaminated than in uncontaminated communities. It is difficult to argue that oil contamination plays a role in the etiology of tuberculosis. It is much more likely that the excess is attributable to higher rates of crowding, as noted above. Similarly, the excess of anemia reported for the contaminated communities is most likely due to poverty and the reportedly higher frequency of malnutrition.

Data are also presented showing that white cell levels are reduced, but are similar in both groups of communities. If there is a proposed association between contamination and immune status it is not supported by these data.

The authors used water sources in contaminated communities as an indicator of exposure, comparing families who consumed water from springs or wells less than 200 meters from contaminated water with those who took their water from between 200 and 500 meters from any contamination. Their observations that the people using water from close to the contaminated course had more fungi, skin infections, tuberculosis and under-5 malnutrition supports the importance of socioeconomic variables in disease risk, versus contaminated water. It is essential to differentiate between a biological mechanism of disease causation and cultural factors affecting risk.

In their conclusions, the authors note a number of important socioeconomic and demographic differences between the communities that do and do not have oil production. Although they seem to attribute health effects to oil contamination, the data are much more compelling to support the importance of other factors such as illiteracy, poor quality of life, ethnic differences, and poor economic conditions. In the authors' own words “we suffer from diseases caused by all this

economic and social injustice.” Other data presented – the main cause of death is violence, the highest cause of infant mortality is the lack of care in deliveries and the second highest cause is diseases that can be avoided by immunization – support this assertion. Yet they go on the state “the risk of becoming ill is higher due to the crude oil.”

In epidemiologic terms, any association between oil production and health status is likely to be the result of confounding by low socioeconomic status and the poorer standard of living in the oil contaminated communities, rather than there being a causal association between oil contamination and the health effects studied.

Yana Curi Report “Impact of Oil Activity on the Health of Rural Populations in the Ecuadorian Amazon.” Dr. Miguel San Sebastian et al. 2000

Introduction

Some of the findings presented in the Yana Curi report have now been published in peer reviewed journals. Although the assessment here follows the structure and organization of the original report, the results and interpretations reported in the published papers are included as appropriate. Thus, this assessment covers the original report and two ensuing peer reviewed publications.

Background

This report begins with a review of the scientific evidence of health effects due to exposure to chemicals found in oil. It is not clear how relevant the data presented are to the Ecuadorian situation or how representative and complete the literature cited is. These issues are not addressed in my review, although it is my opinion that the data do not support the author’s assertion that “exposed populations have a high risk of severe, irreversible effects on their health.”

Study Objectives and Methods

Three health outcomes are suggested to be associated with oil contamination:

- An increase in specific symptoms;
- An usually high number of miscarriages;
- Higher-than-expected numbers of cancer cases (this was not based on an a priori hypothesis but developed during the study).

A cross-sectional study was conducted to address the first two issues. It should be noted that cross-sectional studies are considered to be weak epidemiologic study designs for reasons that have to do with temporality and hypothesis testing. In addition, there are serious problems with respect to ascertaining the two outcomes – symptoms and miscarriages – under investigation.

Two groups of communities were selected for study: contaminated communities in which the populations are considered to be exposed to contamination from oil wells and stations and control or uncontaminated communities. Although the author states that these two groups of communities are similar with respect to geographic and sociodemographic characteristics, this does not appear to be the case. Based on data from the Ecuadorian 2001 census, larger percentages of homes lack basic services – public water, public sewer, electricity – in the oil producing communities. This suggests that the exposed families are poorer than the unexposed families, which could increase disease risks. In addition to socioeconomic differences based on census data, there are also major differences in terms of ethnicity. The percentages of indigenous persons are much higher in the non-oil communities than in the oil communities, with the percentages of mestizos higher in the oil communities. This suggests potentially important differences between these two groups of communities in terms of both socioeconomic and demographic factors that could influence health status. It is of considerable interest in this regard to note that two other health studies among oil contaminated and non-contaminated communities, carried out by different investigators and of apparently different communities, also reported major socioeconomic and sociodemographic differences between the two types of communities (UPPSAE, 1993; and CESR, 1994, 1998).

The study population was defined as women between the ages of 17 and 45 with a minimum time of residence in one of the study communities of three years. The author reports that a list of all communities in the area was prepared – grouped as contaminated and uncontaminated – and the individual communities for study were randomly selected, resulting in 9 communities from the contaminated areas and 14 from the uncontaminated areas being included. Leaders of the communities were asked to identify the women who met the age and residence time requirements. The selection of the final study sample does not appear to have been random; the participants were identified by a community leader who may have been aware of health problems, suggesting the possibility of selection bias.

The discussion of data collection is somewhat confusing. Although the study sample was women, the author reports that a structured questionnaire was answered by the head of the family. It seems likely that the head of the family in these communities would be men. The data collected by questionnaire included sociodemographic information; the woman's medical history, including symptoms (not defined); and reproductive history, focusing on the last three pregnancies while resident in the study community. If there are differences between communities in gravidity (number of previous pregnancies), quite likely based on differences in socioeconomic status and ethnicity as noted above, this could potentially contribute to any observed differences in reproductive outcome. While three pregnancies per woman were studied to increase sample size (and resulting statistical power) it should be recognized that a woman's pregnancies are not considered by most epidemiologists to be independent events.

A recall period of 12 months was decided on for reporting symptoms and a list of 23 symptoms was included in the questionnaire. Pregnancy was defined as a subjective perception of the event by the participant. Pregnancy outcomes were categorized as miscarriage (fetal loss at 28 weeks gestation or earlier), still birth (fetal loss after 28 weeks gestation without evidence of life at birth), and pregnancy to term (live birth after 36 weeks). It is not clear from the authors' definitions how pre-term live births were handled. Only pregnancies which occurred during the residence period in the study communities were included.

Data were collected between January and April 1999. It is interesting to note that a male assistant was used to collect interview data; the principal investigator is also a male. It is somewhat unusual in many cultures to have males collect reproductive histories from female subjects. Since other members of the study team were female it would be informative to know if there were differences between interviewers in terms of the reproductive histories collected. It could also be problematic if women collected data in some communities and men in others; this is not clear in the report. In addition, both the male assistant and the main researcher were aware of both the exposure status of each community and the research objectives, and the sociopolitical agenda behind them. This suggests that interviewer bias is a distinct possibility.

In discussing the analysis of the miscarriage data (the technically preferable term is spontaneous abortion, which will be used in my subsequent discussion abbreviated as SAB), the authors state that history of prior SAB was examined but was not included in the statistical model, for reasons which although stated are unclear. My interpretation is that if the group included women who had SABs before moving to the contaminated area this would suggest that they were at increased risk in the absence of exposure.

There is a very brief discussion of environmental assessment. The authors summarize this by stating that residents are exposed to pollutants from oil activities at levels that significantly exceed international safety limits. They also note that reports have suggested that such contamination has occurred since the start of oil operations.

Results – General Findings

There appears to be possible inconsistency between the required length of residency as established in the methods section and as presented in the results. The authors state in the methods section (page 37 of the translation reviewed) that “all women who had lived in the community for at least 3 years were included in the sample.” On page 49 (results), however, they state “Sixty women (14.0%) in the contaminated area and 56 (16.1%) in the uncontaminated area were excluded from the study because they had lived in the communities for less than 4 years.” This may be an issue in translation, however, as in the peer reviewed publication (San Sebastian et al. 2002) these same numbers of

exclusions are reported to be based on living less than three years in the community.

The Yana Curi report and the published paper both report participation rates of 70.2% among the exposed and 79% among the unexposed women. Apparently only in the published paper is information presented on the availability of information from the questionnaire, available for 59.8% of the potential participants from the exposed communities and for 64.4% of the potential participants from the unexposed communities. This may explain why the demographics of the study population do not reflect the demographics of the communities, as noted.

In the results section the authors state that the exposed and unexposed communities show little difference in terms of ethnic groups and education level and that the indicators they used showed a higher economic level in the exposed communities. This is not consistent with the Ecuadorian census data or with the other studies in the area that have compared the two types of communities (UPPSAE, 1993; CESR, 1994, 1998). Since the distributions of the study populations by ethnicity are comparable, while the census data show major differences between the communities San Sebastian studied, questions can be raised about whether the subjects for whom questionnaire data were available were truly representative of the target populations.

The authors note that women in the exposed areas worked less in agriculture than those in the unexposed areas. This raises questions about potential differences between the areas in the types of agriculture practiced. For example, Addendum 1 of the Yana Curi report refers to pesticide exposure associated with the agro-industry that has developed in the oil areas. It seems likely that in the non-oil communities agriculture is mainly of the indigenous type – thus involving a large percentage of the women – while large scale agricultural production is found in the oil producing communities, where large areas of tropical forest have been cleared.

Results – Symptoms

In terms of symptoms reported by subjects within the previous two weeks, a statistically significant prevalence ratio was observed for skin fungi. It is difficult to envision a causal relationship between exposure to oil and skin fungi. Two other symptom categories – “other symptoms” and fatigue – were reported to be significantly increased in the exposed group. Since the reported 95% confidence intervals include 1.0 it is not possible to know on what evidence the statement of statistical significance is based.

With respect to symptoms during the previous 12 months, the exposed group reported a high frequency for 20 out of 23 categories. Because almost all of the symptoms, irrespective of the biological plausibility of their being associated with oil exposure, were reported to occur more frequently in the exposed women,

attention needs to be paid to the possibility of significant information bias. Since symptoms are subjective, i.e. self-reported rather than observed, their usefulness in assessing health effects related to environment exposures has been challenged (Sever, 1997). It should be noted, however, that the two symptoms reported to be statistically significantly more frequent among the exposed women – nose irritation and throat irritation – could plausibly be related to the substances of concern. Nonetheless, it can be argued that this does not support the authors' statement that "the increased prevalence of the symptoms can be explained by the environmental exposure to oil and its components through ingestion, inhalation or skin contact."

Results – Reproductive Health

The results of the reproductive outcome study are included in both the Yana Curi report and in a peer reviewed publication (San Sebastian, Armstrong and Stevens, 2002). A total of 1377 pregnancies was reported, with 7.5% ending in a SAB. The pregnancies of women living in the exposed areas were more likely to result in a SAB than were those of women in the unexposed areas (9.8% versus 4.4%). Since the authors had predicted a baseline prevalence of SABs at 10% for this area, consistent with usually accepted rates of observed loss, in calculating their sample size, the data seem to clearly suggest underreporting by the unexposed women.

While the crude prevalence ratios for SABs included in the Yana Curi report and the published study are identical (PR=2.34; 95%CI=1.48-3.71) the adjusted prevalence ratios are slightly different (PR=2.52; 95%CI=1.58-4.02 versus OR=2.47; 95%CI=1.61-3.79). These adjusted prevalence ratios are statistically significant. Note that in the Yana Curi report the technically correct designation, prevalence ratio, is used while in San Sebastian et al. (2002) this ratio is incorrectly referred to as an odds ratio.

When the last three pregnancies were analyzed separately the Yana Curi report states that a higher risk of miscarriage was found for each pregnancy, with the "penultimate and "antepenultimate" being statistically significantly higher. This is based on the crude ratios. For the adjusted ratios included in San Sebastian et al. (2002) only the penultimate prevalence ratio is statistically significantly elevated.

In the Yana Curi report, but not the published paper, it is noted that when a dose-response relationship was tested – based on the woman's time in the community – no increase based on the degree of exposure was observed.

Spontaneous abortions are difficult reproductive outcomes to study, even among urbanized "western" populations. Important questions revolve around definition and ascertainment, particularly as related to gestational age at termination. In addition, as noted earlier, it is problematic to consider multiple pregnancies in a

woman as independent events. San Sebastian et al. (2002) note this latter point; their stated justification for treating them as independent is unclear.

Two important issues that were not addressed in either report are whether gravidity is comparable between the two groups of women and, perhaps most importantly, whether the distributions of gestational ages at the time of SAB are similar. If there are differences between the groups in terms of gravidity this could influence their risk of having an SAB. If there are differences in terms of gestational ages this could be an indicator of potential recall bias.

Cancer Incidence in San Carlos

During a visit to the village of San Carlos, an oil contaminated community, cases of cancer were reported to the investigators. In addition to being discussed in the Yana Curi report a peer reviewed publication presents the results of this investigation (San Sebastian et al., 2001). It should be noted that this study was not based on an a priori hypothesis of an association between oil exposure and cancer risk but was carried out specifically because of expressed concern about cancer incidence. There is, in fact inconsistency between the Yana Curi report and the published report on this issue. As noted, the report states “the presence of several cases of cancer...in their family members was observed. They attributed this to their constant exposure to oil.” This is quite different than the statement in San Sebastian et al. (2001), discussing the relevance of the Texas sharp-shooter cluster phenomenon to their study: “This study was led by local concerns about overall health effects on their communities. This concern preceded identification of a cancer cluster.” It seems to me that although there was concern about health effects in general, cancer in this community was studied specifically because of the concerns about the number of cases – the Texas sharp-shooter.

The population of San Carlos is small, approximately 1000 persons, and people entered the area in the 1970's when oil activity opened access routes. Most of the people work in agriculture and livestock production. The author notes that the infrastructure of the community is “deficient” with no drinking water service or sewer system.

Based on local informants and clinical records a list was made of possible cases of cancer occurring during the ten year period 1989-1998. Histopathological confirmation of cancer type was obtained from hospital records in Quito, where cases were referred for treatment. Ten cases were confirmed during the years 1989-1998, nine in adults and one in a child. Of the nine adult cancers, three were of the stomach and the other six were in all different organ systems. The single childhood cancer case was acute lymphoblastic leukemia (ALL).

Table 2, in both the report and publication, presents information on the individual cancer cases. This includes sex, diagnosis, age at diagnosis, and the time of residence in San Carlos. The time of residence in San Carlos is somewhat

misleading; to be meaningful it should be time prior to diagnosis. Since for most individuals the time between diagnosis and death is short this is perhaps irrelevant but for those cases who survived it is of interest. For example, the single case of childhood cancer – ALL – was diagnosed at age five years but the time of residence was reported as seven years. Since this child apparently survived until the time the data were collected in 1998 five of the reported seven years would have been after the diagnosis was made.

As noted, the population of San Carlos was estimated to be 1000 persons, based on information from 1998. There is no indication of how representative this estimate is for the ten years from which the cases came. Census data from the district, stratified by five-year age groups and sex, were used to estimate the age- and sex-specific structure of the population. These data were used, along with the comparable age- and sex-specific cancer rates from Quito, to estimate expected cancer incidence as a basis for calculating a standardized incidence ratio (SIR)

Problems with this approach include the facts that the size of the population at one point in time was used to represent the entire ten year period and that the age-sex-structure of the district was used to establish that of a small community. Of potentially greater importance, there is no indication that the ethnic composition of San Carlos is similar to that of Quito. Although in the published paper the authors refer to the uncertainty of the comparability between Quito and San Carlos they do not mention the possible importance of ethnic differences.

The calculated SIR is potentially misleading. Since there are observed cases of eight different types of cancers, expected numbers are calculated for each of these eight. Because cancer-specific incidence rates are low the expected number of each of these cancers are consistently much less than one, leading to an inflated SIR for males, among whom eight of the total of 10 cases occurred. One of the two cancers observed in women was cervical cancer, which is common among Ecuadorian women and highly unlikely to be related to environmental contamination. For females the calculated SIR is 0.5, suggesting that oil exposure reduces cancer risk among women. This is particularly interesting, given the fact that the Yana Curi report states that women were selected for the symptom study because their exposure levels were higher than those of men (Section 4.2.4).

Data on cancer mortality among males are also included in both the Yana Curi report and the published paper. The data are presented along with a standardized mortality ratio (SMR) based on mortality rates for Quito. While the authors report that the mortality rate is 3.6 times higher than that of the comparison population this is probably meaningless because of issues of access to health care in San Carlos.

The authors conclude that there is a higher risk of cancer in San Carlos. They state that risk is particularly high for cancer of the larynx, liver and melanoma,

stomach and lymphoma. Note that for each of these cancers, except for stomach cancer which is reported to be common in Ecuador (PAHO 2002), there is a single case. For reasons stated earlier, it is difficult to assert that there is a high risk of cancer in the community based on single observed cases of cancers in multiple organ systems. The authors put forward what I consider to be a weak argument to link these multiple types of cancers to oil exposure.

Methodological Considerations

In concluding their report the authors come back to two central questions:

- Whether the general health condition of communities living near oil wells and stations is poorer than that of a comparable population;
- If so, is this poorer health condition related to contamination from such wells and stations?

Answering the first question requires identifying appropriate communities for comparison and accurately ascertaining the outcomes in identical ways in both groups of communities. As noted above, it is not clear that the communities are comparable, with respect to socioeconomic and demographic characteristics, nor is it clear that the data collected came from subjects who were representative of their populations. There also seems to be a serious potential for both selection and information bias.

As the authors note, addressing the second question is more complex but they present four reasons why they believe a causal association is supported. Here I will state these reasons and present counter arguments to them.

1. "Intense exposure to oil chemicals among the residents of communities near wells and stations." Environmental contamination does not equal individual exposure. There are no data presented at the level of individual subjects. In addition, in the report the authors state that they were not able to differentiate exposure levels; all can not be "intense."
2. "The connection between exposure to contamination and the poor health condition is solid. The results found, especially for miscarriages, are statistically significant...which indicates they are not attributable to chance." Statistical significance does not equal a solid connection between exposure and outcome. Statistical significance is not the same as biological significance and does not rule out chance. It simply states what the probability was of finding a difference as great as that observed, or greater, by chance alone. Of particular relevance to this study, it says nothing about the possible effects of bias. Although the prevalence ratios were adjusted for selected potential confounders, I believe that there is a high probability of confounding by other socioeconomic and demographic

variables; in epidemiologic terms “unrecognized or unmeasured confounding.”

3. “Both the studies carried out on animals and those conducted on human populations alert against the health risk caused by exposure to the various oil toxins and confirm the likelihood and consistency of the results obtained.” The latter part of this statement is somewhat confusing but it may be related to the translation. It is not clear that the other studies that the authors put forward to support their claims are entirely relevant. It is difficult to extrapolate from acute high dose animal studies to low dose chronic exposures in humans. The relevance of studies of workers in the petrochemical industry to studies of people living in the Amazon basin can be questioned. Many of the studies to date are of petrochemical workers who may be exposed to quite different agents than are present in crude oil in the Amazon basin.
4. “The general health condition and cancer results are specific to the known toxicological effects of exposure to oil.” It is somewhat difficult to determine how this differs from point #3 but that may relate to the translation. The findings with respect to symptoms are hardly specific to toxicological effects of any agent or category of agents. Many of the symptoms reported are likely to be due to the poor socioeconomic conditions present in the oil towns. The cancer findings are hardly specific as the types of cancers are heterogeneous and the estimates of excess risk are based on single cases of cancers in multiple organ systems.

Addendum 1 – Other Impacts Related to Oil Operations

This Addendum is important in that it describes four sets of conditions in the oil communities that I believe are more likely than crude oil exposure to be responsible for differences between communities in the frequency of health effects. I list each of these, as presented in the report, along with comments regarding their possible impacts on health.

1. Labor mobility. The authors note that oil exploration is accompanied by large numbers of workers coming into the area. These workers are, in turn, exposed to various health risks associated with poor living conditions. These conditions continue, as noted by the authors, and include new settlements without infrastructure and poor sanitation. That these factors could adversely affect health status seems to be self evident.
2. Colonization. A number of social and environmental changes associated with colonization of the Amazon basin are considered by the authors. Of particular importance is the statement that the ecosystem does not support agricultural production or livestock and 70% of school-aged children were malnourished. This seems to clearly represent health impacts independent of oil contamination.

3. Deforestation. With deforestation, related to road building and oil production facilities, major environmental changes have taken place. This can lead to changes in patterns of infectious diseases through several pathways, including changing the ecosystem to allow increases in vector populations and bringing human populations into more direct contact with infectious agents.
4. Agro-industry. The opening of the rainforest allowed for the development of an African palm industry. The authors note there is a high risk of exposure to pesticides in this area. Given the fact that, as the authors state, there are concerns about relationships between exposure to pesticides and cancer risk, immune system toxicity and reproduction, these exposures could act as important confounders. Evidence for human health effects of pesticides are much more firmly established (Keifer, 1997) than are effects from crude oil or petroleum production (Yana Curi report Addendum 2).

Addendum 2 – Health Impact of Exposure to Chemicals from Petrochemical Industries

This addendum presents a very brief review of health effect studies in the workplace and residential exposures of people who live near petrochemical industries. In sum, the findings from these studies are quite mixed. Of perhaps greatest importance, as mentioned earlier, it is not clear how comparable the potential exposures of people living in the Ecuadorian oil areas are to:

- Occupational exposures among petroleum and/or petrochemical workers;
- Residential exposures among persons living near petrochemical industries.

These caveats apply to two key components of toxicological risk assessment: the specific agents involved and the biologically effective doses received by individuals in the receptor population.

Hurtig and San Sebastian 2004 – Incidence of childhood leukemia and oil exploitation in the Amazon basin of Ecuador

This study examined rates of childhood leukemia (and other cancers) among residents of four provinces in the Amazon basin in Ecuador. The study was carried out to determine if there were differences in cancer incidence between populations living in proximity to oil fields and those living in areas free from oil exploration. Cases of leukemia (as well as other cancers) among children <15 who were residents of four exposed and 11 non-exposed communities were ascertained from the National Cancer Registry. The study was ecologic in design, with country of residence determining exposure status.

The exposed counties were those where oil exploration has been going on for at least 20 years.

This publication focuses on the findings with respect to 42 cases of leukemia; the incidence rates for all other cancers combined (49 cases) are also presented but none of these relative risks were statistically significantly elevated. Multiple comparisons of incidence rates – by age- and sex-strata separately and combined – were computed, with the following being statistically significantly higher in the contaminated communities:

- Age group 0-4 both genders combined RR=3.48 (95% CI=1.25-9.67)
- Age group 0-14 females RR=2.60 (95%CI=1.11-6.08)
- Age group 0-14 both genders combined RR=2.56 (95%CI=1.35-4.86)

In discussing their findings, Hurtig and San Sebastian refer to other studies that have been done of petroleum hydrocarbons and cancers. Although adult and childhood cancers are likely to be etiologically distinct, the authors do not clearly distinguish between them in their review of the literature.

The authors discuss some of the limitations of their study. In addition to the lack of individual-level information on exposure, the following are particularly important:

- No information on potential socioeconomic differences between the two groups of communities;
- No information on ethnic differences;
- No data on length of residence in the communities for cases or their parents;
- No information on migration patterns.

Hurtig and San Sebastian, recognizing the weakness of ecologic studies in demonstrating causation, suggest the possibility of causation is supported by three criteria:

- The strength of the association;
- The finding that only leukemia was at increased risk;
- Plausible time sequence from exposure to exposure to disease.

I will address only the second point. The epidemiology of childhood leukemia is complex. Two of the most widely discussed sets of possible risk factors, specific to childhood leukemia and particularly ALL are not discussed here: pesticides and infectious etiology due to population mixing. There is an extensive literature on both these topics. It is quite surprising that Hurtig and San Sebastian do not include these because both are directly relevant to the situation in the Amazon basin. I will briefly consider each of these groups of risk factors in this context.

The possibility of populations in the oil exploration areas of the Amazon basin being exposed to pesticides is described in Addendum 1 of the Yana Curi report. Associations between leukemia risk and pesticides have been suggested for both

parental occupational exposures (Zahm, Ward and Blair 1997; Daniels, Olshan and Savitz, 1997) and ambient exposures (Goldsmith et al. 2000; Renolds et al. 2002). On the basis of numerous studies, consideration should be given to the potential role of these types of exposures in relationship to childhood leukemia in the oil producing areas of the Amazon basin.

Of particularly greater importance in this setting are studies that show that rates of childhood leukemia are elevated in areas where there are rapid influxes of people into an area from different regions, leading to population mixing. These conditions are certainly characteristic of the oil producing communities. The population mixing hypothesis is perhaps most closely associated with Kinlen (1995) who postulated that childhood leukemia is an uncommon response to an infectious agent following influxes of people into isolated areas. This was the situation in the oil producing areas, where migrations of people from both the coastal and mountainous regions of Ecuador occurred. Studies from a number of countries, including the UK (Kinlen, 1995; Kinlen and Balkwill, 2001; Dickenson and Parker, 1999), Canada (Koushik, King and McLaughlin, 2001), Hong Kong (Alexander et al., 1997) and Greece (Petridou et al., 1997) have supported this hypothesis. This is an issue that deserves study in Ecuador and it is surprising that its potential importance was ignored by Hertig and San Sebastian.

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