

**Review of Epidemiologic Studies of Cancer, Reproductive Outcomes,  
and Health Symptoms Among Populations in the Amazon Region of  
Ecuador**

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## Summary

I am an epidemiologist specializing in occupational and environmental health. I received my doctoral degree in epidemiology from the University of California, Los Angeles (UCLA) School of Public Health and I have worked over 20 years in this field. I was asked by representatives of Chevron Texaco to review epidemiologic investigations of populations residing in the Amazon or “Oriente” region of Ecuador.

Dr. San Sebastian and his colleagues have conducted several epidemiologic surveys of cancer, reproductive outcomes, and various general health symptoms among communities in the Oriente region. To interpret epidemiologic studies, it is important to consider the quality and accuracy of the exposure and health data, whether these studies accounted for other important known causes of disease, and other limitations such as statistical uncertainty, participation factors, and other study design issues.

The studies of Dr. San Sebastian and his colleagues lack specific petroleum exposure information and the estimates of cancer occurrence or other disease data is subject to inaccuracies. The number of cancers identified in the community of San Carlos is very small, involve unrelated cancers, and do not provide sufficient information to determine whether living near petroleum facilities has caused cancer among community members. The studies of reproductive outcomes and health symptoms among women rely on self-reported information that has not been clinically validated, and is likely inaccurate. Potential selective participation of women from the studied communities is also a concern. For all of the diseases studied, numerous other factors such as other exposures (e.g. pesticides, human papillomavirus, HPV), diet and generally poor living conditions associated with disease are not addressed.

All of these potential limitations are acknowledged but not adequately accounted for in the various publications prepared by Dr. San Sebastian and collaborators. Given the many serious limitations, the epidemiologic studies conducted among communities in the Oriente region are not sufficient for assessing whether residence near petroleum facilities

has caused disease and do not provide any evidence that there is an association between potential exposure to petroleum and disease.

## **Background**

I am an epidemiologist specializing in occupational and environmental health. I have worked over 20 years in this field. I received my doctoral degree in epidemiology from the University of California, Los Angeles (UCLA) School of Public Health. Currently I work as a consultant for a scientific research, engineering, environmental and health consulting company. I am also an adjunct professor at UCLA School of Public Health, Department of Epidemiology where I teach courses in occupational and environmental epidemiology. I have performed epidemiologic studies on a wide variety of occupational and environmental health topics in the U.S. and Latin America.

I was asked by representatives of Chevron Texaco to review recently published studies and unpublished reports of epidemiologic investigations of populations residing in the Amazon or “Oriente” region of Ecuador. This report briefly summarizes my independent assessment of the usefulness of these studies in assessing whether potential exposure to petroleum materials generated as part of the petroleum extraction processes in the Amazon region have produced adverse health impacts among the local population.

Epidemiology is the science that characterizes the occurrence of disease with respect to person, place and time and evaluates potential risk factors or causes of disease. In conducting my assessment of the epidemiologic studies, I draw upon standard epidemiologic principles that are routinely applied to the evaluation and interpretation of environmental health studies.

## Studies Reviewed

I reviewed the following studies for the preparation of this report:

San Sebastian, M; Cordoba JA. "Yana Curi" Report: The impact of oil development on the health of the people of the Ecuadorian Amazon. Vicariato Apostolico de Aguarico June 1999

San Sebastian M, Armstrong B, Stephens C. La salud de mujeres que viven cerca de pozos y estaciones de petroleo en la Amazonia ecuatoriana. Rev Panama Salud Publica 2001; 9(6): 375-384

San Sebastian M, Armstrong B, Cordoba JA, Stephens C. Exposures and cancer incidence near oil fields in the Amazon basin of Ecuador. Occup Environ Med; 2001; 158:517-522

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Hurtig AK, San Sebastian. Geographical differences in cancer incidence in the Amazon basin of Ecuador in relation to residence near oil fields. Int J Epidemiol 2002; 31: 1021-1027

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Quizhpe E, San Sebastian M, Hurtig KA. Prevalencia de anemia en escolares de la zona amazonica de Ecuador. Pan Am J Public Health 2003; 13: 355-361

Hurtig AK, San Sebastian M. Incidence of childhood leukemia and oil exploitation in the Amazon basin of Ecuador. Int J Occup Environ Health: 2004; 10:245-250

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San Sebastian M, Hurtig AK. Oil development and health in the Amazon basin of Ecuador: the popular epidemiology process. Soc Science & Medicine 2005; 60: 799-807

## Overview of Amazon Epidemiologic Studies

Dr. San Sebastian and his colleagues have conducted several basic epidemiologic studies of cancer (San Sebastian et al., 2001; Hurtig and San Sebastian 2002, 2004; San Sebastian and Hurtig 2004a, 2004b), reproductive outcomes (San Sebastian et al., 2002), and various general health symptoms (San Sebastian et al., 2001) among communities in the Oriente region. Dr. San Sebastian's studies are only descriptive and are not the type of studies that can provide information about disease causation, a point he acknowledges in many of his published studies.

Most epidemiologic studies are observational; that is, researchers observe events that will happen (*i.e.*, a prospective study) or have already happened (*i.e.*, a retrospective study). Cohort studies and case-control studies are the two most common types of analytical observational studies used to test for an association between an exposure and a disease. In cohort studies, the investigator selects exposed individuals and non-exposed individuals, and follows both groups over time to compare disease incidence rates or disease-specific mortality rates in the two groups. In case-control studies, subjects are divided into two groups based on disease status. One group (cases) is comprised of people who have the disease and the other group (controls) is comprised of people who do not have the disease. Data regarding past exposures in both groups are then obtained and compared. None of the types of studies conducted by Dr. San Sebastian and colleagues involved a cohort or case-control design, rather they are "ecological" studies or cross-sectional surveys.

In understanding and interpreting epidemiologic studies, it is important to consider the quality and accuracy of the exposure and health data, whether these studies accounted for other important known causes of disease, and other limitations such as statistical uncertainty, participation factors, and other study design issues. In addition, each study's findings should be considered in the context of existing scientific knowledge from research to determine how consistent the study findings are with previous research.

Dr. San Sebastians' studies are not the type that can provide information about disease causations, a point he acknowledges in many of his published studies. There are several problems in all of these studies that severely limit their ability to determine what caused the observed health effects. First, there is no specific exposure information provided for individuals in the studies that could give us an indication of concentration or duration of potential exposure. This is important because in order to infer causation, there needs to be evidence of exposure to a sufficient amount. More detailed exposure information also allows researchers to examine their findings for a potential dose-response relationship. The presence of an increasing dose response relationship is one of several important criteria in evaluating whether exposure to petroleum has caused cancer or other diseases. Simply stated, dose response refers to the situation where more exposure is associated with higher rates of disease. Secondly, there are concerns about the accuracy of the estimates of disease rates because of a variety of technical difficulties. Third, important risk factors for the health conditions studies have not been taken into account in the analysis. All of these limitations can result in misleading results, particularly regarding what has caused the reported health conditions.

### **San Carlos Study**

Epidemiologic studies focus on the patterns of disease and exposure in populations. By accurately measuring both exposure and disease among all individuals in a population, researchers can analyze whether a particular exposure is associated with a particular disease. For a study of cancer, considering the population size and the follow-up period, the San Carlos study is a very small study. Dr. San Sebastian observed a total of ten cancer cases. (8 among males, 2 among females), with only one type of cancer (stomach cancer) that had more than 1 case reported (San Sebastian et al., 2001). If a single environmental agent was responsible for an elevated incidence of cancer in San Carlos, the elevation would have to occur in one or two specific types of cancer. However, Dr. Sebastian reported eight different types of cancer. It is highly unlikely that a single environmental agent can cause these very different cancers. Furthermore, the consensus among scientists is that exposure to crude oil does not cause the type of cancers

reported in San Carlos. A finding based on only a single cancer case, or even a handful of cases, simply cannot provide information about cancer causes. Stomach cancer is the most common type of cancer reported among males in all of Ecuador. So given the population size (~1,000) and the ten years of follow-up observation, a few cases of stomach cancer would be expected to occur. In addition, based on comprehensive review of the epidemiologic studies, petroleum materials have not been shown to cause stomach cancer (Wong et al., 2000). In fact, the strongest suspected cause of stomach cancer is diet and San Sebastian's study does not address this point. The rates of stomach cancer vary significantly across different countries and studies that have shown diets with higher intakes of salted foods, preserved meats, and food with higher starch levels are associated with higher rates of stomach cancer. Further, diets with higher intake of fresh fruits and vegetables and the introduction of refrigeration are associated with lower stomach cancer risks (Nomura, 1996).

Another observation from this study is that there was no excess cancer among women. If an environmental factor were causing cancer in this community, we would expect it to show up in women as well as men. However, this observation is based on two observed cases, and may reflect the uncertainty inherent in this small study. As Dr. San Sebastian and coauthors state in their report (with respect to studying potential disease clusters): "...statistical results should be interpreted very cautiously." and regarding chance and small numbers they state: "However the high risk of cancer was based on small numbers ... making it difficult to reject the possibility of chance". I should point out that although Dr. San Sebastian claims a "high risk of cancer", it is not correct to characterize a finding as demonstrating "high risk" when it is based on only one observed occurrence of cancer.

In addition, the comparison with Quito population is likely not appropriate without statistical adjustment given the notable differences in access to care, race, and economic differences between the two populations. The justification for making this comparison because the cancer data are available in Quito does not overcome the lack of comparability between the two populations.

As previously mentioned, a significant limitation across all of the epidemiologic studies conducted by San Sebastian and colleagues in the Oriente region was the lack of any specific exposure information. This is true of the San Carlos study as well. Without more detailed exposure information, it is not possible to link the cancer cases to the petroleum exposure as hypothesized by San Sebastian.

### **Childhood Cancer Study**

Dr. San Sebastian's study of childhood cancer was conducted in a wider geographic area than the San Carlos study (Hurtig and San Sebastian 2004). Within four provinces in the Oriente, four cantons were labeled as "exposed" and eleven were labeled as "unexposed" based on proximity to oil production sites. This assignment of broad geographic areas as exposed and unexposed and the calculation of disease rates at the same geographic level is referred to in epidemiology as an "ecologic" study. Actual exposure of individuals is unknown; residential history is unknown and any other individual factors potentially related to disease and exposure are unknown. Lack of this important information is the critical limitation of this study design and precludes its use in trying to determine causes of disease.

Another important limitation of this study was that diagnosis of leukemia or cancer required that patients travel to Quito (a 12 hour drive). If cases from the alleged exposed region were more likely to travel to Quito than cases from the unexposed region, the higher reported cancer rates could be due to this and not have anything to do with potential exposures or living closer to the petroleum facilities. Given the concern residents of the petroleum producing areas have voiced, it is very likely these residents would be more willing to travel to Quito when they suspected they had cancer than people living in the non-petroleum producing areas. This practice would make it look like there was more cancer in petroleum producing areas.

Dr. San Sebastian and his coauthors describe several limitations of the study in their publication on childhood cancers: "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 the ecologic analyses” (pg. 248) On the following page they note: “The results suggest a relationship between leukemia and living in proximity of oil fields, although this ecologic study cannot lead to a casual inference” (pg. 249). In addition they state: ”It is possible that the exposed counties had had more rapidly increasing populations compared with non-exposed ones ...” This would lead to overestimating disease rates in the communities labeled as exposed.

These results do not suggest a relationship between leukemia and living in proximity to the petroleum fields because of all of the limitations mentioned above and those that Dr. San Sebastian and his coauthors acknowledge. Furthermore, in addition to the limitations discussed above, the type of leukemia found to be significantly elevated was acute lymphoblastic leukemia (ALL), which is the most common form of childhood leukemia, and is not related to petroleum or benzene exposure. Given all of these considerations, the study results do not allow for any causal interpretation between the reported childhood cancer data and living in an area with oil production activities.

### **Other Studies of Adult Cancers**

There were three other cancer studies conducted among populations in the Oriente region. In one study, they compared the cancer rates of four cantons, classified as “exposed” to eleven cantons classified as “unexposed” (Hurtig and San Sebastian 2002). As previously discussed, this is an ecologic study design, involving the assignment of broad geographic areas as exposed and unexposed and the calculation of disease rates at the same geographic level. Actual exposure of individuals is unknown; residential history is unknown and any other individual factors potentially related to disease and exposure are unknown. In a second study of adult cancers, San Sebastian and Hurtig compared cancer rates among indigenous populations to those of non-indigenous people living in the Oriente region (San Sebastian and Hurtig, 2004). In a third study, Hurtig and

San Sebastian report on gynecological and breast cancer rates in the region (Hurtig and San Sebastian, 2002).

The first study, which compared cancer rates in “exposed” and “unexposed” cantons, used the same ecologic study design as the childhood cancer study. As previously noted, with this design, the actual exposure of individuals is unknown; residential history is unknown, and any other individual factors potentially related to disease are unknown. The study examines over 20 different specific cancers and finds roughly equal numbers of cancers with risk ratio estimates above 1.0 and risk estimates below 1.0.

The relative risk (RR) is an estimate of the association between the exposure and the disease in the general population. A relative risk above the value 1.0 suggests an association (that may or may not be causal) between the exposure and the disease. A relative risk near 1.0 suggests no association between the exposure and the disease. A relative risk below 1.0 suggests that the risk of disease in the exposed group is less than that found in the unexposed group.

Similar to the rest of Ecuador, stomach cancer was the most common type of cancer in men and was reported to have an increased risk in the four cantons. Cervical cancer was the most common cancer among women and also had an increased risk. Cervical cancer is the second most common cancer among women worldwide, and in many cases is the most common female cancer in developing countries. Researchers report that human papilloma virus is associated with a large majority of cervical cancers cases (Schiffman et al., 1996).

As previously described, differences in how frequently cancers are reported and registered in the Quito cancer registry could explain the excess of cancers reported in the “exposed” cantons. This potential reporting difference was also discussed by San Sebastian and Hurtig in their analysis that compared cancer risk for indigenous populations, where they suggest cancer reporting to the Quito registry is lower compared to the non-indigenous populations in the region. The indigenous populations also had a

different pattern of cancer occurrence than non-indigenous populations. And there is no evidence that this difference is related to exposure to petroleum materials.

As with the childhood cancer study, Hurtig and San Sebastian noted the same significant limitations in their analyses of adult cancers: They note with respect to use of the ecologic study design: “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 the ecologic analyses” (page 1025 Hurtig and San Sebastian, 2002). On the same page they also note the problem of disease reporting: “Because of geographic 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”. They also note: “Errors in population estimates including differential migration patterns, might bias estimates of risk”.

Given all of these limitations it is not possible to make a causal assessment between cancer occurrence and petroleum facilities based on the studies by Drs Hurtig and San Sebastian.

### **Reproductive Outcomes**

Dr. San Sebastian and his colleagues conducted a study of spontaneous abortions and stillbirths among women aged 17-45 years in the Amazon region (San Sebastian et al., 2002). Because of a series of limitations, this study does not demonstrate that petroleum-producing activities caused adverse pregnancy outcomes. The study recruited women from two areas – those living within 5 km of an oil field versus women from communities at least 30 km from any oil field. These women were asked about their pregnancy histories (focusing on the last three pregnancies). They compared the rates of stillborns and spontaneous abortions (SA) between those groups of women. There are several important limitations of this study.

The identification of spontaneous abortion relies on women's self-report and recall. Given the publicity of environmental issues and the petroleum facilities, women from these areas may be more aware of SAs and/or more inclined to report SA events than women in areas that are more removed from the facilities. This pattern of biased recall has been shown in other studies. In support of this statement is the observation that the miscarriage rate in the unexposed communities appears very low compared to the average in other regions (e.g. the average for all of Ecuador). On the other hand, the miscarriage rate among women in the communities within 5 km of facilities was near the average rate for the rest of Ecuador and other South American communities. Thus, it appears that SAs were under-reported in the non-petroleum producing areas rather than evidence of an excess in those areas that were involved in petroleum production.

The study also has problems with potential exposure misclassification – many women within 5 km are probably not exposed to petroleum producing activities in any way. In fact only a small portion of women (7%) drank from the river, only 28% bathed, and 36% washed in river – thus, a majority did not report an opportunity for actual exposure. There are also additional concerns about who was initially selected to participate in this survey and who among those selected, who eventually participated. Community leaders were relied upon to identify and select to women to participate. These women may have been selected on the basis that the leaders perceived that they were more likely to have health problems. In addition, this study had relatively low response rates (59% and 64% for “exposed” and “unexposed” group), which can lead to problems because the large portion of eligible women who did not participate may have had different reproductive histories than the women who did participate. Of concern would be a pattern where women who have not had any reproductive problems chose not to participate. In addition, in situations where more than one spontaneous abortion has occurred in the same person, the SAs should not be considered as statistically independent events. The analyses of Dr. San Sebastian did not account for this in his analyses; consequently his results may not be scientifically valid.

Given these limitations, we cannot rely on this study to tell us anything about an association between potential exposures from petroleum facilities and reproductive outcomes.

### **Study of Women's General Health**

This study used interviews to ask women about health symptoms in the last two weeks and in the last twelve months. Women living within 5 km downstream of petroleum facilities were classified as “exposed” and women living more than 30 km upstream from petroleum facilities were classified as “unexposed”. Study participants were selected in several steps: first, communities meeting the location criteria were selected, then a subset of these communities were selected and women who resided for at least three years were identified and asked to participate (San Sebastian et al., 2001).

Results were reported for 23 different symptoms. For symptoms occurring within the last two weeks, with only one (skin mycoses) was statistically higher in the “exposed” communities. For reporting of symptoms during the last 12 months, there were two symptoms (nasal irritation and sore throat) that were statistically higher in the “exposed” communities. As Dr. San Sebastian notes, given the many symptoms assessed, this result may be simply due to chance. However, other important limitations are also present:

- None of the reported symptoms were validated with more objective clinical data;
- Because there are increases (although not statistically significant) for many symptoms that from a biological perspective would not be associated with exposure to petroleum materials, this suggests that women from “exposed” regions, because of their awareness and beliefs regarding environmental causes of disease, are likely over-reporting symptoms relative to ‘unexposed’ women;
- Symptoms reported over the last twelve months are subject to inaccuracies in recall;
- These symptoms have many other potential causes;
- The prevalence of symptoms in both groups of communities are very high making the detection of potential minor differences difficult and not reliable;

- No specific information on actual exposure is provided in this study.

In summary, this study cannot be interpreted as providing evidence of an elevation of adverse health conditions due to the petroleum facilities. Rather, at most it reflects a very high prevalence of health symptoms among women in the Oriente region.

## **Conclusions**

Taking into consideration all factors related to the epidemiologic studies of populations in the Oriente region, what can be concluded about the relationship between petroleum-related materials and potential exposures and the health effects observed? I recognize the difficulties in conducting epidemiologic research in these areas and under difficult conditions. At the same time, when assessing whether a potential exposure has caused disease, this does not mean that these studies should be reviewed or judged any differently than studies conducted in other parts of the world. In order to perform epidemiologic studies that can provide insight into the cause of disease, these studies must be conducted in a scientifically sound manner. I am sympathetic to the public health problems in the region. However, conducting epidemiologic studies with the objective of demonstrating that the cause of disease is living near petroleum facilities rather than conducting this research in an unbiased, objective and scientific manner has led to inaccurate results and conclusions. Given the many serious limitations that I have discussed, namely the lack of specific exposure information, the potential inaccuracies in disease assessment, and other potential causes of disease that are not evaluated, the studies conducted among communities in the Oriente region do not provide evidence of excess disease caused by activities associated with petroleum facilities and materials.

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