

Contributions to the epidemiological study design on mercury pollution in Amazon*

Contribuições para o desenho de estudos epidemiológicos sobre poluição por mercúrio na Amazônia

Volney de Magalhães Câmara^{1,2}

¹ Universidade Federal do Rio de Janeiro, Faculdade de Medicina, Rio de Janeiro, Rio de Janeiro, Brasil

² Universidade Federal do Rio de Janeiro, Instituto de Estudos em Saúde Coletiva, Rio de Janeiro, Rio de Janeiro, Brasil

For some researchers, the design of epidemiological studies is considered to be highly complex. Because it uses statistics of different levels in its analyzes, which evaluate the presence of certain effects on the population's health or the low probability of occurring, possibly, association between exposure to some factor and the emergence of health effects. Owing to this complexity, an opinion article on Epidemiology, related to the design of studies on the exposure and effects of mercury in the Amazon, should have the main purpose of discussing specific points of this connection and / or serving as an first step of the reader with this relevant topic in Brazilian Collective Health. Studies on metallic mercury and methylmercury, in the Legal Amazon, show exposed people in gold mining areas, riverside populations, indigenous groups and even populations in urban areas by indoor pollution^{1,2,3,4,5}.

One of the main decisions for defining the research design is the choice of which kind of mercury will be the object of the study. Metallic mercury found into the atmosphere by burning gold-mercury amalgam, and methylmercury originated by the biological chain in specific situations of river sediments, are completely different for the design of epidemiological studies. Urine samples are the most used in the evaluation of exposure levels for the metallic form; while hair samples are used for the methylated form.

The second decision refers to the most appropriate type of epidemiological study. In the case of mercury, descriptive studies, as the title indicates, describe how the mercury effects occur in the population - occurrence by gender, age, occupation, time, location, and others. Analytical study is another kind of epidemiological study that uses hypothesis testing that may relate exposure to mercury with some health effect (searching for a cause-effect relationship), such as assessing whether

mercury exposure may be related to hematological changes or a specific effect on hearing, vision, etc.

Most of the time, the researcher will need to go to the field in order to know about the levels of mercury exposure and also the possible effects need to be investigated. However, there are information systems available that can help for searching health effects, such as the Mortality Information System (SIM), Live Birth Information System (SINASC); National System of Toxic-Pharmacological Information (Sinitox); Notifiable Diseases Information System (Sinan) and the Hospital Information System of the Unified Health System (SIH-SUS). Others, such as the National Household Sample Survey of the Brazilian Institute of Geography and Statistics, include specific questions about the population's morbidity. For studies in the Amazon Region, even due to the huge geographical area and little capillarity of SUS, it can be assumed that the data on effects on the population health of this region in these systems do not express the real situation. The choice of secondary or primary data is the researcher's decision who must decide which data is more appropriate for his research⁶.

Descriptive studies are important for the health area and, of course, for epidemiological studies. What professionals in this field currently know about the clinical manifestation of mercury poisoning, for case definition, come from many of these studies.

Regarding variables on people, these surveys in the Amazon can show how different variables occur in intoxication; among them, the main ones are gender, age, type of food, profession, cultural habits, religion, consumption pattern (in this case, the consumption of fish becomes relevant), income, education and others.

Time is another relevant variable for any descriptive study. It is known that, in the rainy season in the Amazon,

* Opinion article written by Speaker for the II International Scientific Meeting of Instituto Evandro Chagas, held from October 25 to 27, 2017, in Ananindeua, Pará, Brazil. All the articles of this modality were analyzed by the Scientific Committee of the Event and, later, by the Editors of RPAS.

Correspondence / Correspondência:

Volney de Magalhães Câmara

Universidade Federal do Rio de Janeiro, Faculdade de Medicina

Av. Brigadeiro Trompowsky, s/n; Praça da Prefeitura Universitária; Ilha do Fundão. Bairro: Ilha do Fundão. CEP: 21949-900 – Rio de Janeiro, Rio de Janeiro, Brasil – Tel.: +55 (21) 2598-9328

there is a reduced metallic mercury exposure due to the impossibility of mining activities in some places. Acute intoxication can occur because of increased exposure to metallic mercury, and it can present cases of intoxication in a short period of time. However, for both metallic and methyl forms, the adverse health effects related to mercury are of chronic appearance because of the exposure to this metal over a long period of time.

The location is another important variable, since it can direct efforts and, thus, maximize surveillance activities to mitigate and prevent new cases.

The majority of epidemiological studies are descriptive and, among them, those that assess the prevalence of

the mercury effects in the population. As can be seen in Table 1, the incidence study is long-term experiment and, for this reason, more difficult to be conducted on mercury exposure⁷. Initially, a group of people to be studied is selected, and, after a certain period of time, all new cases of the mercury effects defined for the study are observed. As these effects are insidious and chronic, it is necessary to wait a long time for a relevant number of cases to be obtained. Prevalence studies, on the other hand, are short-term experiment and can be performed up to one day, it is more viable for the researchers. In these latter studies, all prevalent cases, whether new or old, are included.

Table 1 – Characteristics selected for the design of epidemiological studies in environmental health and worker health

Types	Examples of study design	Feasibility
Observational / Descriptive		
Incidence	Identification and monitoring of a population exposed to an environmental pollutant during a period of time in which new cases of poisoning by the pollutant to be studied are registered.	Long-term study is most appropriate for acute diseases.
Prevalence	Identification of a population exposed to an environmental pollutant and immediate calculation of all existing cases of poisoning by the pollutant.	Short-term study is most appropriate for chronic diseases.
Observational / Association between variables		
Ecological	Correlation between records of a particular pathology and those of levels of exposure to a pollutant over a period of time.	Not very practicable due to the absence of records of pollutants and disease.
Cross-sectional	Organizing a group of people exposed (census or a sample) to the environmental factor (Study Group) and another group of people not exposed (Comparison Group). Then, comparing the prevalence of effects between the two groups.	Very practicable. Short-term study and it is indicated to chronic effects.
Observational / Comparative / Evidence of causality		
Cohort	Organizing two groups: Study and Comparison (same as cross-sectional studies); then, comparing the incidence or mortality of the effects between the two groups over a certain period.	Not very practicable. Long-term study and it is indicated acute effects and stable populations.
Historical cohort	Through registration data, exposed (Study) and unexposed (Comparison) groups are formed at a certain point in the past. Soon after, the incidence / mortality of the effect to be studied between the two groups is compared, from the past to the present moment.	Not very practicable due to the absence of records.
Case control	A group of people is formed that have the effects that one wants to study (Study Group) and another similar group that does not have this effect (Control Group). The second step is to compare the proportion of people exposed in the past between the two groups.	Practicable. Short-term study. Ideal for chronic diseases and low prevalence. It is necessary reliable records of the effect.
Interventional/Experimental		
Experimental	Selecting a group of people who will undergo a certain type of intervention – for example, the use of new drugs or new technologies (Study Group) – and a similar group without the intervention (Comparison Group); and monitoring, over a period of time in order to compare the incidence of effects between the two groups.	Not very practicable due to ethical issues. Ideal for assessing the impact of a drug to be tested or protective equipment on the workplace environment.

Source: Câmara e Tambellini, 2003⁷.

The ecological type study may be impractical in Brazil and particularly in the Amazon Region. Records of mercury exposure and cases of health effects over long periods of time are necessary to calculate a correlation between these two variables (see explanation in Table 1). Among the main characteristics of ecological studies, they highlight the fact that the individual is not included to be interviewed or clinically evaluated, but rather populations, through much information that can be accessed in the systems mentioned above (mortality, morbidity and others).

Analytical studies are generally comparative between groups according to the exposure or the presence of a health effect. The first step in conducting such studies, for any researcher, is to define the hypothesis to be tested. The alternative hypothesis is the one that has to be proven. If the statistical tests show any "statistical difference", the null hypothesis is dropped (when there is no difference between the study groups) and the alternative hypothesis is used. The two groups need to be as similar as possible and undergo the same procedures. It is applied to all analytical studies. Selection errors (eg, choosing the population to be studied) and measurement (eg, uncalibrated equipment) should be avoided. The presence of interference variables (confounding) also distorts the exposure-disease association. As examples of bias, it can be mentioned: a) if an older population is included in the Study Group, a higher proportion of neurological effects may be associated with this age profile; b) the excess of hand tremors in a group, instead of being an indicator of a higher proportion of neurological injury, may be due to the fact that one of the groups includes more alcoholic individuals.

The sectional study is considered by many authors to be an analytical study. It is perhaps the most doable to be conducted. Initially, individuals from the Study Group are chosen (in this case, those exposed to mercury) and a Group Comparison, those not exposed to mercury (it is necessary to repeat that these groups must be as similar as possible). Right after (it may be a few days), it is compared the proportion of people with effects between the two groups, using statistical tests in order to assess the probability that this difference is not by chance. The problem with cross-sectional studies is that, in the Study Group, there may be people who showed

effects to be tested before mercury exposure and, therefore, could not be associated with this metal. A possibility, to minimize this problem, could be the use of an instrument, such as, a well-designed questionnaire, which could identify whether the effect arose after mercury exposure.

The cohort analytical study is the most appropriate research to assess risks, because, when monitoring the groups studied, the researcher will identify the cases that arose after mercury exposure. However, it is the most difficult to be carried out for studies on this metal in areas of great migratory movement, such as the Amazon. The selection of the Study and Group Comparison is similar to the sectional study; however, the difference is that only new cases that appear in a certain period of time are analyzed for group comparisons. An evaluation of studies on environmental pollutants in Brazil found that few studies, such as the cohort type, are conducted out in the country⁸.

Another difficult option is the historical cohort or retrospective cohort, in which, from a date in the past, the Study or Comparison groups are created; and, from that date until the present moment, the proportions of effects can be compared.

The case-control studies are different from all the analytical studies that have been described previously. A Study Group is formed by people who have the effect related to mercury, which is the object of study, and a Control Group is formed by those who do not have this type of effect. Then, the proportions of individuals who have been exposed to mercury in the past are compared using statistical tests between these two groups.

Finally, in experimental studies, in which the researcher intervenes, such as, testing a medication to reduce the effects of mercury, the question of ethics in research needs to be evaluated. The research must wait a long time for its approval, since it is necessary to be sent to higher authorities in Brasilia.

This is just a superficial view at the different types of epidemiological studies that can be used in research on mercury in the Amazon. The researcher, according to the adverse health effect to be investigated, needs to choose the type of study that can give answer to the research, considering the time, material and human resources that are available to.



REFERENCES

- Jesus IM, Brabo ES, Lima MO, Faial KRF, Moraes LLCS, Mendes RA, et al. Contribuição pioneira do Instituto Evandro Chagas para a saúde ambiental na Amazônia em 25 anos da Seção de Meio Ambiente. *Rev Pan-Amaz Saude*. 2016 dez;7 n. esp:83-92.
- Passos CJS, Mergler D. Human mercury exposure and adverse health effects in the Amazon: a review. *Cad Saude Publica*. 2008;24 Suppl 4:S503-20.
- Malm O, Dórea JG, Barbosa AC, Pinto FN, Weihe P. Sequential hair mercury in mothers and children from a traditional riverine population of the Rio Tapajós, Amazonia: seasonal changes. *Environ Res*. 2010 Oct;110(7):705-9.
- Marques RC, Abreu L, Bernardi JVE, Dórea JG. Neurodevelopment of Amazonian children exposed to ethylmercury (from Thimerosal in vaccines) and methylmercury (from fish). *Environ Res*. 2016 Aug;149:259-65.

- 5 Câmara VM, Tavares LMB, Filhote MIF, Malm O, Perez MA. A program for the control of indoor pollution by metallic mercury. *Environ Res.* 2000 Jun;83(2):110-6.
- 6 Rothman KJ, Greenland S, Lash TL. *Modern epidemiology.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008.
- 7 Câmara VM, Tambellini AT. Considerações sobre o uso da epidemiologia nos estudos em saúde ambiental. *Rev Bras Epidemiol.* 2003 jun;6(2):95-104.
- 8 Froes Asmus CIR, Camara VM, Landrigan PJ, Claudio L. A systematic review of children's environmental health in Brazil. *Ann Glob Health.* 2016 Jan-Feb;82(1):132-48.

Received / Recebido em: 2/10/2017

Accepted / Aceito em: 11/10/2017

Article originally published in Portuguese (<http://dx.doi.org/10.5123/S2176-62232017000400004>)

Translated by: Patrícia Campelo Haick