

# UC Irvine

## UC Irvine Previously Published Works

### Title

Banking of human tissue for biomonitoring and exposure assessment: utility for environmental epidemiology and surveillance.

### Permalink

<https://escholarship.org/uc/item/0tq184c5>

### Journal

Environmental Health Perspectives, 103(Suppl 3)

### Authors

Goldman, L R  
Anton-Culver, H  
Kharrazi, M  
et al.

### Publication Date

1995-04-01

### Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

---

# Banking of Human Tissue for Biomonitoring and Exposure Assessment: Utility for Environmental Epidemiology and Surveillance

Lynn R. Goldman,<sup>1</sup> Hoda Anton-Culver,<sup>1,2</sup> Martin Kharrazi,<sup>1</sup> and Elinor Blake<sup>1</sup>

<sup>1</sup>California Department of Health Services, Emeryville, California; <sup>2</sup>University of California, Irvine, California

Human tissue banking could provide a tool to address a number of public health concerns. We can potentially use it to monitor trends in human exposures, serve as an early warning system for new environmental exposures, assess low-level exposures around hazardous waste and other point sources of pollutants, evaluate the effectiveness of regulatory programs, and study etiologies of diseases (e.g., childhood cancer and birth defects) that are likely to be related to the environment. This article discusses opportunities to establish human tissue banks in connection with pre-existing public health surveillance programs for cancer and adverse reproductive outcomes. This is a cost-effective way to conduct surveillance and enhances the ability to carry out epidemiologic studies. The article also discusses ethical issues that are particularly important for public health practice. One is the issue of risk communication and the need to explain risks in a way that provides people with the information they need to determine appropriate action on the individual and community levels. Second is the issue of environmental justice. We recommend early involvement of communities that are likely to be involved in tissue-banking projects and full explanation of individual and group social risks from their participation. — *Environ Health Perspect* 103(Suppl 3):31–34 (1995)

Key words: surveillance, environmental health, human tissue banking, reproductive outcomes, childhood cancer

---

## Introduction

Some environmental epidemiologic and health surveillance needs can be addressed by using human tissue banking. There are opportunities for developing tissue banks in the context of existing public health studies and health surveillance systems. This not only offers possible cost savings but also the opportunity to provide data for future epidemiologic studies. However, human tissue banking raises specific ethical concerns on a community level. This article discusses these issues and gives examples of potential applications.

## Uses of Human Tissue Banks in Public Health Surveillance and Epidemiology

Human tissue banking holds great promise for improving epidemiologic surveillance of environmental exposures. Surveillance is defined as “the ongoing systematic collection,

analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know. The final link in the surveillance chain is the application of these data to prevention and control” (1). At a minimum, a surveillance system should allow examination of trends over time and comparison of data between representative subgroups or geographic areas.

Public health surveillance for environmental health is limited to blood lead reporting (2), diseases believed to be possibly of environmental origin such as birth defects (3), and environmental databases designed primarily for other purposes (4,5). Blood lead reporting is usually carried out by states, using requirements of clinical laboratories to report all or elevated blood lead levels. Birth defects registries exist in only a few states. Some use passive surveillance methods, obtaining data from vital records or hospital discharges only, while others use active surveillance methods involving abstraction of full hospital records. Environmental databases are usually developed by regulatory programs to track the results of monitoring and compliance activities, and are of varying usefulness in conduct of environmental surveillance (5). No longer in existence is the National Human Monitoring Program

(NHMP). The purpose of the NHMP, established in 1967, was to monitor chemical exposures in the population. It included the National Human Adipose Tissue Survey (NHATS), which collected adipose tissues from metropolitan areas in the United States from 1970 to 1990 and monitored chlorinated organic compounds, such as the organochlorine pesticides and the polychlorinated biphenyls (6). The National Health and Nutrition Examination survey (NHANES), a periodic, population-based survey carried out by the National Center for Health Statistics, has been useful for monitoring trends in blood lead levels (7) and special studies of pesticides and volatile organic compounds. A number of reviews have been conducted of these surveillance systems; these have concluded that at present environmental health surveillance is fragmentary and in an early stage of development (4–6). Human tissue banking—collection and storage of tissues or blood samples from special groups or the general population—would enhance this current environmental health surveillance system.

What would be wanted for environmental surveillance of human exposures? An environmental health surveillance system should:

- integrate with other data sources that contain information on disease or disability;

---

This paper was presented at the Conference on Human Tissue Monitoring and Specimen Banking: Opportunities for Exposure Assessment, Risk Assessment, and Epidemiologic Research held 30 March–1 April 1993 in Research Triangle Park, North Carolina.

Address correspondence to Dr. Lynn R. Goldman, U.S. Environmental Protection Agency, 401 M Street, S.W. (TS-788), Washington, DC 20460. Telephone (202) 260-2902. Fax (202) 260-1847.

- identify pollutants and populations of exposed individuals that require more urgent public health intervention;
- be useful for planning and evaluation of intervention programs;
- provide “early warning” of new environmental problems;
- provide data for analytic epidemiologic studies; and
- contribute to the knowledge base of “background” levels of contaminants in the population to help interpret findings from specific population studies.

### Integration with Health Surveillance Systems

Any system of environmental exposure surveillance, including a tissue bank, should collect data in a manner that will allow integration of information with information in health surveillance systems, e.g., vital records, registries of cancers and birth defects, and hospital discharge data. Such data integration allows for population-based, hypothesis-generating studies, and for linkages for performing epidemiologic studies (5).

### Priority Setting

Knowledge about exposures should help establish relative priorities to be addressed by public health and environmental regulatory programs. Current environmental surveillance programs do not give sufficient information about individual exposures, particularly exposures to population subgroups of special concern like children, pregnant women, and ethnic minorities.

### Program Evaluation

There is very little basis for evaluating the efficacy of environmental health and regulatory programs. Insofar as efficacy can be measured by decreases in human exposure, tissue banks can be a useful resource for this purpose in much the same way that reporting of measles cases is used to monitor the success of measles immunization programs.

### Early Warning

Public health agencies are expected not only to provide surveillance of known hazards but also to identify newly emerging hazards to assure that society can promptly and rapidly address them. A tissue bank can be a very useful resource for this purpose if the tissue banking activities are linked to the capability to use analytic techniques, not only for identifying known compounds and indicators of exposure, but also for broadly screening for new exposures. The finding of new chemicals or indicators of exposure,

either emerging over time or at a higher level in individual population groups, may warrant further study.

### Epidemiologic Studies

Tissue banks can potentially be useful for the conduct of epidemiologic studies. Little is known about the etiology of a number of diseases that are believed possibly to be caused by environmental exposures, for example birth defects and childhood cancer. The public expects that public health agencies can explain the causes of community outbreaks, or “clusters” of such diseases; but in many cases too little is known about etiology to even allow formation of specific hypotheses. At the same time, there are a number of exposures that convey “theoretical” risks but for which we have very little human epidemiologic evidence. While we would attempt to reduce the exposures based on the theoretical risks, a human tissue bank would increase the opportunities available to learn more about their effects in humans.

### Background Population Exposure Levels

We lack adequate information about “background” levels of exposure in the population. By background, we mean what a statistician would call “normal,” that is, the expected range of the exposures in the general population. Public health agencies often encounter situations in which measurements were taken by others and an interpretation is needed. For example, in 1990 a biological monitoring technique for urinary malathion metabolites was used to assess exposures of toddlers in a day care center in an area in Los Angeles County that was being treated with aerial applications of malathion. All existing information on urinary malathion metabolites was for pesticide workers. No data were available for the general population or for toddlers. There was no information on how to extrapolate from higher to lower exposures, nor on how malathion metabolism might differ in toddlers than in adults. Toxicologists who evaluated the data used a number of assumptions about malathion elimination in toddlers that resulted in extrapolated exposures that differed by more than an order of magnitude.

Examples of other types of situations for which “background” data on exposures are needed are hazardous chemical spills, chemical fires, pesticide drift exposures and other incidents of pesticide misuse, hazardous waste site exposure assessment and consumer product contamination episodes.

## Using Existing Surveillance Systems

As mentioned above, linkage of environmental with health surveillance offers a number of important advantages in terms of allowing assessment of health outcomes and in maximizing resources by using established population-based monitoring systems rather than creating new ones. Opportunities for human tissue banking exist in several areas using established public health surveillance programs. Two pilot studies have been conducted by the California Department of Health Services to take advantage of disease registries and genetic disease screening programs. By using pre-existing surveillance systems as a base, one can ensure that the sample is representative with respect to the general population of persons with diseases such as cancer or birth defects.

In planning any human tissue banking effort, one should consider what tissues might already or potentially be available, and their utility for tissue banking. There is much “throwaway” tissue that may be usable, such as discarded tissue blocks and serum samples. There are also diagnostic specimens from surgery that may require obtaining informed consent. Some of this tissue cannot be used for specific purposes. For example, formalin-preserved samples have altered chemical constituencies. However, with development of new analytical techniques, new uses may be found for any tissues that might be available. For example, the California Department of Health Services obtains a capillary blood spot on a piece of blotter paper for almost 100% of births; these blood spots have been retained and archived for years. Recently, methods have been developed to use them for DNA amplification studies. When linked with our birth defects surveillance program, this should prove to be a very valuable resource. Usability involves not only the ability to analyze the specimen but also the ability to secure, archive, and document the tissue.

Population-based birth defects and cancer registries are potentially of great usefulness. An enormous amount of effort is already expended to collect large amounts of data on persons with these diseases. Since 3% of births involve a birth defect and 25 to 30% of persons are expected to develop cancer, these registries cover a large number of people in the areas they serve. Childhood cancer has been a particular issue of concern in California, where childhood cancer “clusters” in the agricultural Central Valley have led to concerns about pesticides

and other environmental exposures. There are a wealth of epidemiologic studies that suggest potential roles for parental occupational exposures to solvents and pesticides for a number of specific cancer types, but most of these studies suffer from poor exposure assessments. Typically, exposures are based on paternal and maternal occupational codes; a few studies have used questionnaires and there are rarely measurements of chemicals or biologic markers of exposure. Birth defects are a major cause of infant mortality and account for many of total potential years of life lost. Although a number of chemicals can be shown to cause malformations in laboratory animals, there may not be concordance between the type of malformation caused in animals and the type caused in humans, so that we cannot rely solely on animal studies to identify human teratogens. Only a small fraction of childhood cancers and birth defects, less than 10%, can be attributed to known environmental and genetic etiologies.

California conducted a pilot study with the University of California at Irvine (UCI) Cancer Surveillance Program of Orange County (CSPOC) and the Children's Hospital of Orange County, to set up a tissue bank for childhood cancer cases for Orange County. We rapidly ascertained new cases of cancer at the childhood cancer center at UCI, which diagnoses and treats virtually all childhood cancer cases in Orange County. Ascertainment included identifying new cases and obtaining blood samples and tumor tissue from the patient before initiation of treatment. This was important because we wanted to avoid the biologic changes caused by chemotherapy and radiation treatment, which might be similar to markers of environmental exposures. We also obtained blood samples from parents and siblings and interviewed parents, not only because other family members might be expected to share environmental exposures, but also to look for genetic traits. UCI separated the lymphocytes and preserved them in a viable state. Later, chromosome breakage studies were undertaken. In the pilot study, it was possible to obtain comparable information from both hospital-based and "friend" controls and we suspect that it would also be possible to obtain population-based controls as well. Although we piloted this technique for childhood cancers, it would be a reasonable approach for birth defects as well. In that case, one would be less concerned about the timing of case ascertainment. Over time, such a resource would be useful for conducting population-based environmental and genetic etiologic studies.

Another area of much environmental epidemiologic interest is in looking at other reproductive outcomes. Vital records systems contain valuable information about birthweight; gestational age; fetal and neonatal death, age, ethnicity, and education of parents; and use of prenatal care. They also contain information about the mother's residence. However, they contain very little information about exposure. Increasingly, states carry out prenatal genetic disease screening programs. In California we conduct serum alpha fetoprotein (AFP) testing for about 60% of births. This test is performed at 15 to 19 weeks of gestation and is used to screen for neural tube defects and other disorders. All tests are carried out in large regional contract laboratories under supervision of the state laboratory. Typically, samples are discarded after confirmatory analyses are carried out.

Rather than discarding prenatal AFP samples, we banked all serum specimens from an 11-county area for a month (3699 samples). The area chosen was in the Central Valley of California which is ethnically diverse with an especially large Hispanic population. After linking these specimens with live birth or fetal death records, there are a number of analyses that are feasible. At present, we are using the specimens to study the relationship of birthweight and gestational age to mid-pregnancy cotinine and caffeine levels. It will be possible to look at not only active smoking but also environmental tobacco-smoke exposure. With very little extra cost, programs such as the genetic disease screening program could be modified to archive specimens on a routine basis. This could be useful not only for studies of reproductive outcomes but also for a number of other developmental outcomes that may be related to prenatal exposures. There are a number of chemicals that can be measured in serum, including some metals and a number of pesticides; and new methods are under development to measure other substances and to find better markers of exposure.

### Cluster Investigations

We also conduct studies of space-time clusters of diseases such as childhood cancer and birth defects. These studies usually result in inconclusive results. Tissue banking holds the promise of being able to look later for markers of exposure or pre-disease conditions that might help elucidate the cause of at least some of these space-time clusters. The experience with studying

genetic etiologies of cancer can serve as an example of the potential of this method.

### Ethical Concerns

Two interrelated ethical issues are particularly important for public health practice. One is the issue of risk communication and the need to explain risks in a way that provides people with the information they need to determine appropriate action on the individual and community level. Second is the issue of environmental justice, often referred to as environmental equity. Environmental justice advocates dislike the term "environmental equity" because, as Charles Lee of the United Church of Christ has said, "It sounds as if we all share the problem, it's OK" (8). It will be very important for any national program of adipose tissue banking, like any program of environmental surveillance, to over-sample in low income and various racial and ethnic communities. If past studies can serve as a guide, we can expect that we will be more likely to find higher exposures in these communities (9,10). Researchers, who rarely are from these areas, should not assume that they understand the needs for these communities or the consequences of their findings for the residents. Certainly, there is likely to be less access to education, poorer nutrition in low income areas, and cultural differences in understanding of health and disease. Such communities are also less likely than a white suburban community to have resident experts such as scientists, physicians, attorneys, and other trained professionals who can interpret the data for neighbors; and they have less access to such expertise overall. In consequence, these communities may have more difficulty in taking steps needed to deal with any problems that might be identified, or compelling the government to do so. In low-income communities, food, housing and child care may take precedence over the environmental problems. Moreover, identification of specific environmental exposures could worsen discriminatory practices, such as has been seen in "redlining" practices in neighborhoods with lead contamination. Early involvement and participation of members of these communities in any monitoring effort are essential to ensure sensitivity to cultural issues and the barriers to addressing any problems that may exist, and to identify ways to overcome those barriers.

Informed consent needs to include not only information about individual medical and privacy risks but also about social risks

for both the individual and the group as a whole. Although involving communities in this way may delay or even make it impossible to do studies that we would like to do, this is the only way to proceed ethically if the ultimate goal is the protection of public health. We have found that involving communities at the outset saves time in

explaining study results and provides for a better ultimate outcome.

In conclusion, human tissue banking will help address a number of public health concerns. We can potentially use it to *a*) monitor trends in human exposures; *b*) serve as an early warning system for new environmental exposures; *c*) assess low level

exposures around hazardous waste and other point sources of pollutants; *d*) evaluate the effectiveness of regulatory programs; and *e*) study etiologies of diseases (e.g., childhood cancer and birth defects) that are likely to be related to the environment.

---

## REFERENCES

1. CDC. Comprehensive Plan for Epidemiologic Surveillance. Atlanta:Centers for Disease Control 1986.
2. CDC. Surveillance of elevated blood lead levels among adults—United States, 1992. *MMWR* 41:285–287 (1993).
3. Thacker SB, Berkelman RL. Public health surveillance in the United States. *Epidemiol Rev* 10:164–190 (1988).
4. Sexton K, Selevan S, Wagener D, Lybarger J. Estimating human exposures to environmental pollutants: are existing data bases adequate and sufficient? *Arch Environ Health* 47:398–407 (1992).
5. Goldman L, Gomez M, Greenfield S, Hall L, Hulka B, Kaye W, Lybarger J, McKenzie D, Murphy R, Wellington D, Woodruff T. Use of exposure databases for status and trends analysis. *Arch Environ Health* 47:430–438 (1992).
6. National Research Council. Monitoring Human Tissues for Toxic Substances. Washington:National Academies Press, 1991.
7. Annett JL, Pirkle D, Makuc D, Neese JW, Bayse DD, Kover MG. Chronological trend in blood lead levels between 1976 and 1980. *N Engl J Med* 308:1373–1377 (1983).
8. Lavelle M. Residents want justice. The EPA offers equity. *Natl Law J*. September 21, 1992;S12.
9. Bullard RD. The threat of environmental racism. *Natl Res Environ* 7(3):23 (1993).
10. Mohai P, Bryant B. Race, poverty, and the distribution of environmental hazards: reviewing the evidence. *Race Poverty and the Environment*. Fall 1991/Winter 1992:3.