X. Surveillance for Work-Related Adverse Reproductive Outcomes

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Introduction

The NIOSH list of 10 leading work-related diseases and injuries in the United States includes disorders of reproduction.[1] Based on the proposed national strategy by NIOSH and the Association of Schools of Public Health for the prevention of disorders of reproduction, it is apparent that surveillance for these disorders—like the epidemiology and toxicology of reproductive disorders—is in an early stage of evolution.[2] Because of an increasing awareness of work-related disorders of reproduction and a perception of risk by the population, a call for action, concerted coordination, and commitment by the public health community are indicated to address these issues.

National strategies for surveillance of reproductive disorders are presently fragmentary and poorly coordinated. A need exists to develop, expand, integrate, and link current surveillance activities in the government, private industry, unions, and academia. In addition to developing existing sources of surveillance information, new and creative surveillance systems for reproductive disorders should also be developed.

There are two possible types of surveillance: surveillance for work-related disorders of reproduction and surveillance for physical and chemical hazards to reproductive health.[2] Disorders of reproduction can be prevented when hazards to reproductive health are controlled. The strategy relies on identifying risks to reproductive health through hazard surveillance.[3] When hazard surveillance identifies the source of a problem and controls are instituted, surveillance for work-related disorders of reproduction can document success in eliminating the hazard.

Surveillance for work-related disorders of reproduction documents the occurrence of these disorders in working populations. Surveillance for hazards to reproductive health identifies potential exposures to the population at risk. This paper covers surveillance for work-related disorders of reproduction; two companion papers in this monograph address hazard surveillance for identifying populations at risk (see chapters VI and VII). We will assume a generic population at risk for the surveillance system discussed here. Thus, when we refer to industry-based surveillance, we assume that an industrial population at risk has been identified.

At the meeting of the NIOSH Surveillance Evaluation Group in December 1987, surveillance activities of NIOSH, other health agencies, state health departments, and private industry were discussed, and modest recommendations were made. The chapter relates to previous NIOSH efforts by focusing on the NIOSH strategy as a guide for reviewing the state of surveillance for reproductive disorders. Because the counting of work-related injuries and illnesses is a difficult task,[4] we cannot hope to address all areas but only expect to focus the thoughts of readers.

Disorders of Reproduction

The spectrum of reproductive disorders that may be associated with parental (maternal, paternal, or both) exposures to environmental agents includes infertility, early fetal loss (spontaneous loss), altered sex ratio, late fetal death, neonatal death, low birthweight, birth defects, developmental disabilities, childhood malignancies, and childhood mortality. This paper will focus on the general concept of surveillance for disorders of reproduction as a counting of reproductive outcomes (whatever their nature) that result from events occurring before or after conception.

Surveillance can be achieved for some disorders through the registration of vital events, such as fetal deaths and births. If relevant information on industry and occupation is incorporated on vital records and is coded, then endpoints such as

NOTE: Author affiliations and addresses are listed on p. 7.

altered sex ratio, late fetal death, neonatal death, low birthweight, and some birth defects can be used to evaluate the experience of individuals in broad industry and occupation categories. Otherwise, vital statistics systems provide only nonspecific, work-related baseline incidence rates. With respect to the vital statistics systems, however, the further the outcome is from the time of exposure, the harder it may be to relate the event to parental workplace exposures. This temporal consideration may limit the usefulness of data on developmental disability, childhood malignancies, and mortality.

Surveillance of early endpoints that occur close to the time of conception or attempted conception—such as infertility and spontaneous abortions—is potentially more informative because of the temporal proximity to exposure in the workplace. On the other hand, early endpoints such as very early fetal death may be difficult to ascertain and therefore difficult to count. Buffler and Aase recommend monitoring populations for spontaneous abortions in conjunction with the use of specific tests to determine the frequency of anomalies among these spontaneous abortions.[5] Various hazards to reproductive health potentially increase the frequency of spontaneous abortions. These include hazards that alter the post-conception maternal environment, impair the preconception ovum genetically, produce genetic or cytologic damage to the early embryo, and damage the sperm. Although the completeness of reporting is still under study, industry-based systems could potentially monitor the early occurring reproductive disorders, such as spontaneous abortion, and vital statistics systems could monitor the late occurring reproductive disorders, such as birth defects and infant mortality.

Historical Background

The public health importance of disorders of reproduction to the growth of society can be traced to the beginning of epidemiologic history. In the 17th century, John Graunt and William Petty suggested:

> "By the proportion between marriages and births, and of mothers to births, may be learnt *what hindrance abortions* and long suckling of children is to the speedier propagation of mankind..."[6]

In the 19th century, William Farr measured the impact of reproductive disorders on population growth by counting their occurrence.[7] Farr aptly observed that reproductive outcomes affect the underlying economic and social fabric of a nation, and their influence can be measured by the actuarial laws and principles that govern the growth of a population. Even though William Farr may have worked out the actuarial effect of reproductive disorders, the process of how to collect surveillance data remains problematic. Disorders of reproduction, such as infertility or spontaneous abortions, may not receive medical treatment and may not be recorded in medical or registration systems. In addition, some disorders of reproduction are not uniformly defined. For example, reduced fertility is difficult to define, and the data required to evaluate fertility are often personal and time-consuming to collect.

Based on the success of traditional public health systems for surveillance of infectious diseases, surveillance for work-related disorders of reproduction is an obvious and necessary step toward understanding the nature and characteristics of work-related disorders of reproduction. Indeed, the goals of surveillance for disorders of reproduction resemble those of surveillance for infectious diseases. The epidemiologic study of infectious diseases depends on surveillance systems that identify and report cases of disease to measure the frequency and impact of infectious pathogens. Similarly, surveillance for work-related disorders of reproduction would provide a method for both detecting their occurrence and monitoring progress toward eliminating the hazard. Once hazard surveillance identifies the population at risk, then surveillance for reproductive disorders can identify adverse reproductive effects in the population. Surveillance for reproductive disorders can be used to construct baseline incidence levels for reproductive disorders just as surveillance for infectious diseases documents baseline endemic disease levels. A major difference between surveillance for disorders of reproduction and surveillance of infectious diseases is the clear association of pathogens with infectious diseases and the lack of known causes for most work-related disorders of reproduction.

Thus, surveillance for disorders of reproduction challenges the traditional public health methods for surveillance of communicable diseases. The ideas of one system cannot simply be adopted to develop the other system. Neither the ease of displaying some of the epidemiologic determinants of person, place, and time (such as age, race, sex, time of onset) for infectious data nor the relative ease of recognizing and reporting infectious diseases holds true in the surveillance of disorders of reproduction.

Obtaining the epidemiologic determinants for counting person, place, and time in work-related disorders of reproduction is more difficult because the surveillance process is confounded by a need to consider both occupational and nonoccupational agents, rank the incidence rate relative to background incidence rates (that may not even exist), and attribute exposure to an event occurring before conception or during pregnancy. Even if a given hazard is known to produce a specific effect and it can appropriately be measured through surveillance, it may not be the only hazard that produces that effect. Questions about the interpretation of surveillance statistics undoubtedly also cloud the issue of how to develop surveillance systems. For example, even if disorders of reproduction were defined unambiguously, the following epidemiologic considerations would still limit interpretation of surveillance results.

- Distinguishing the work-relatedness of disorders of reproduction is complicated because workplace exposures to hazards can be mixed with nonoccupational, environmental exposures and can also be influenced by personal behaviors (e.g., cigarette smoking, alcohol consumption).[8]
- Disorders of reproduction represent an interaction between individual genetic makeup; environmental conditions; and the intensity, duration, and timing of exposure to those conditions. All individuals will not respond in the same way to exposures, and this further complicates the determination of etiologies. Neither gender can be said to be the more vulnerable to reproductive toxicants.
- The causes of these disorders are largely unknown. An agent may be chemical, physical, or biologic and may act independently or in combination with other agents. Any given agent may act as a reproductive toxicant affecting postpubertal reproductive or sexual function, or it may be a developmental toxicant affecting growth, development, or acquisition of normal organ function between conception and puberty.

- Establishing a causal association between workplace conditions and reproductive health is difficult. Most associations studied are nonspecific; a single toxicant can produce a variety of adverse outcomes, or a class of outcomes can result from a variety of different agents.

Historically, the value of surveillance has been in its simplicity and in its capacity to provoke ideas and promote new avenues of thought. Because disorders of reproduction cover a complex spectrum of events, a single surveillance system may not provide adequate data on all outcomes. Nevertheless, several simple systems of surveillance have been used successfully to deal with simple issues of infectious diseases, and these might be considered for reproductive health. In-depth epidemiologic studies should be distinguished from surveillance activities that focus on events rather than on individuals and require timely reporting and feedback.

No historical precedent exists for implementing a national surveillance system for disorders of reproduction. Precedents now being established will be discussed in the following sections. Earlier in this decade, the World Health Organization (WHO) assessed the difficulties involved in addressing reproductive hazards in the workplace. WHO recognized a definite lack of surveillance systems for reproductive disorders; only one published paper among the nearly 200 references cited in the WHO report mentioned surveillance in the title.[9]

NIOSH Surveillance

In 1985, NIOSH discussed reproductive disorders among 10 leading causes of work-related diseases and injuries.[10] This was not the first NIOSH initiative on reproductive disorders; in 1978, NIOSH had stated a commitment to conduct research that would "identify and eliminate reproductive effects due to workplace hazards to workers of either sex."[11] Despite some attempts to develop a national surveillance system, none has yet been developed, and NIOSH typically learns about work-related disorders of reproduction when clusters of specific events, such as spontaneous abortions, occur among employees in a particular work environment[12,13] or, less commonly, through established mechanisms for reporting disorders of reproduction to specialized registries, such as the CDC Birth Defects Monitoring Program.[14] Investigating these reports is difficult because comparative national data for assessing the significance of events are not readily available.[15]

Current NIOSH surveillance of reproductive disorders in employed populations emphasizes development of methods for adapting existing data sources to provide reliable information on maternal and paternal occupation and industry, promote national and state population-based systems, and link data sources. Existing national and regional systems have been improved by standardizing the coding of industry and occupation on vital and health survey records.

NIOSH developed and awarded Surveillance Cooperative Agreements between NIOSH and States (SCANS) to develop capacity within the states for coding industry and occupation on death certificates.[16] Developing the use of existing and new data through programs like SCANS involves standardizing the coding of outcome and employment, increasing reporting, and managing data. Programs like SCANS may have substantial impact because of the population base covered by vital statistics data.

Through the NIOSH SCANS program, coders have been trained to incorporate industry and occupation data in national vital statistics systems. Under these agreements, three states have directed part of their state's activity to vital statistics records on reproductive outcomes. For coding fetal death and birth certificates, interest focuses primarily on the industry and occupation at the time of the event, whereas for coding death certificates, attention centers on the usual industry and occupation of decedents. The occupation and industry of the mother and father would be more relevant for reproductive surveillance involving infant and early childhood deaths. Utah and New York State have analyzed a subset of their data, and Maine is currently evaluating the quality of information on occupation and industry collected and recorded on birth certificates. In addition the State of Washington is currently conducting a review of disorders of reproduction and parental occupation based on vital registration information.

Adapting data from existing vital statistics systems (live births, fetal death, and infant deaths) to define background incidence rates and identify groups of workers with abnormal rates of reproductive disorders is difficult because parental industry and occupation are not routinely coded in national systems of vital statistics data, except in the case of fetal deaths.‡ National data systems offer the advantage of providing population-based estimates for certain disorders of reproduction.

NIOSH has successfully used both the National Maternal and Infant Health Survey[17] and the National Survey of Family Growth,[18] conducted periodically by the National Center for Health Statistics, to calculate national background incidence rates for certain adverse reproductive outcomes.‡‡ The National Maternal and Infant Health Survey is a follow-back survey of live births and fetal deaths reported in vital statistics systems and includes additional information about events and exposures that may be associated with characteristics of live births and fetal deaths. The National Survey of Family Growth is a follow-up survey of women of reproductive age who have been interviewed in the National Health Interview Survey. Additional information is obtained during this follow-up about fertility, pregnancies, and factors associated with fertility and pregnancy outcomes. NIOSH has also used data from state and local health departments to calculate local rates.[19] The 1980 National Natality Survey[20] and the National Fetal Mortality Survey[21] have been used to characterize the occupations of mothers during the year before their deliveries.

State and Hospital-Based Surveillance

The states are in various stages of developing birth defects registries.[14] Currently, one-half of the states have operating systems, one-fourth are developing systems, and the remaining one-fourth have no systems. The operating and developing systems are characterized by diversity, and their purposes range from epidemiologic study to program man-

‡Lalich NR, Salg J, Shilling S: Data sources for adverse reproductive outcomes surveillance: Occupational data. Paper presented at the National Environmental Public Health Conference, 1986.

‡‡Lalich NR, Shilling S: Maternal occupation and industry, and pregnancy outcome in the United States, 1980. Paper presented at 111th annual meeting, American Public Health Association, November 13–17, 1983, Dallas, Texas.

agement. The bulk of the effort, however, is in the surveillance of birth defects.

In addition to developing registries for birth defects, Arkansas has developed a registry for spontaneous abortions. Potential problems may exist in using data from state surveillance systems because these systems differ in their organization, funding authority, populations covered, outcomes surveyed, geographic area covered, method of surveillance, sources of data, analytic methods, and reporting of data. The usefulness of these systems and the importance of data consistency are currently under discussion.

The CDC Birth Defects Monitoring Program compiles discharge data on patients from approximately 1200 hospitals in the United States.[15] The program, which was established in 1974 and relies on voluntary reporting, is the single largest source of information on birth defects in the United States. However, the program does not cover early miscarriages and has no provisions for prospective follow-up of pregnancies. Another surveillance system for birth defects is the Metropolitan Atlanta Congenital Birth Defects Program, also managed by CDC. Since 1967, CDC has tried to record all live and stillborn infants with structural and biochemical congenital defects born to mothers residing in the five-county metropolitan Atlanta, Georgia, area.[22] The value of this system was demonstrated in the study of birth defects associated with occupational exposures among Vietnam veterans.[23,24] Currently, researchers in the Birth Defects and Developmental Disabilities Division of the CDC Center for Environmental Health and Injury Control are seeking to standardize surveillance methods by defining the minimum information needed for all surveillance data sets.

Industry-Based Surveillance

Surveillance systems may be sponsored and implemented by individual companies within a given industry, such as the petroleum refining industry. Although these systems are in their infancy, they are potentially valuable for the surveillance research objective. Industry-based surveillance offers the distinct advantage of conducting surveillance directly where problems exist in the work environment instead of relying on secondary reporting sources in which events may only be reported as a result of medical treatment.

Several investigators have already advocated the use of industry-based surveillance.[5] They suggest that data on fertility, fetal death, congenital malformations, low birthweight, and altered sex ratios can be calculated from existing or slightly modified company databases and compared with available population-based rates that were developed using data systems from the national surveys of the National Center for Health Statistics.

Although industry-based surveillance is a promising new source of data, members of the workforce may be reluctant to provide personal information routinely about either themselves or their spouses on pregnancy status, fertility problems, early fetal loss, or semen characteristics. They are concerned that employers may be tempted to use the data for other purposes, for example, to guide decisions on promotions, transfers, or even terminations. Considering the novel idea of industry-based surveillance and its current use in several industries, appropriate safeguards must be developed to protect the privacy and rights of the workforce so that surveillance can prevent the tragedies of work-related disorders of reproduction.

Recommendations

A major overall recommendation is to use the NIOSH proposed national strategy[3] to guide and focus efforts. This national strategy for achieving reproductive health recommends: 1) increased communication among public health and occupational constituencies, and 2) creativity in approaches, and examination and expansion of existing systems. Specific tasks should be considered as combined activities of government, industry, and labor and of volunteer organizations and university investigators. Reaffirming traditional public health methods for surveillance of communicable disease, these tasks include timeliness of reporting results, focusing on disease events rather than individuals, testing creative approaches for gathering data, coordinating the gathering of data, and evaluating existing systems.

- **Increasing the Quality of Communication**

A national network of public health professionals who are involved in surveillance for reproductive disorders should be augmented by developing a newsletter that reports the results of surveillance. Responsibility for developing the newsletter and a mailing list should be assigned to an agency. Such a vehicle for sharing information gathered through surveillance systems could provide regular reports on surveillance efforts in government agencies, industry, labor groups, volunteer organizations, universities, and others. Over time, the newsletter could evolve into a more formal report that solicits contributions, attempts to review findings in the literature objectively, presents and contrasts more lengthy reports, and presents surveillance data collected from available sources. This activity could also begin to build an archive of tables as a basis for calculating national rates and other measures of reproductive disorders by industry, occupation, environmental factors, and other population characteristics and peculiarities.

- **Encouraging the Development of New and Creative Surveillance Mechanisms**

At this time, a testing of ideas and developing of new systems is appropriate and investigators should try new surveillance mechanisms and compare results with existing systems. They should select an industry-based surveillance system in an area that also has a nonindustry-based surveillance system, monitor the industry-based surveillance system and note its progress and problems, and compare results of the industry-based surveillance with locally collected surveillance data. For example, some companies and some industries have already expressed interest in conducting surveillance for disorders of reproduction following the Digital Equipment Corporation report.[5]

Conclusions

Methods for preventing reproductive disorders in the population as a whole substantially parallel those found in the workplace. As a corollary, a system for surveillance of disorders of reproduction—work-related or not—can be helpful in understanding the epidemiology of work-related reproductive disorders.

Any delay in developing and implementing surveillance for disorders of reproduction may stem in part from a lack of specific outcomes or specific populations at risk identified by hazard surveillance. Diversity in the NIOSH goals and purposes for baseline surveillance of disorders of reproduction reflects a need to consider surveillance as an action item rather than a research need in the NIOSH national strategy.

Surveillance for reproductive disorders is not yet part of the action plan that includes conducting detailed epidemiologic investigations, conducting detailed surveillance for hazardous agents, and encouraging occupational health professionals to work with public and private health organizations to provide educational materials.

Whether trends are identified or disorders of reproduction remain anecdotal may depend in part on the degree of communication within a given industry, the awareness by labor organizations of the problems, or the awareness by investigators of similar problems reported in the literature.

Congress has suggested that surveillance for occupational disease is far behind other disease reporting mechanisms.[25] Surveillance for communicable diseases appears to have all strategic elements in place, such as networks of health departments, lists of notifiable disease, and collaborating laboratories. Unlike systems for communicable diseases, however, surveillance for occupational hazards to reproduction is confounded by hazards in other environments. To build a network for reliable surveillance of work-related disorders of reproduction is a large and challenging task, but clearly current efforts will need to be focused and coordinated.

A first step will be to build a collaborative scientific surveillance community that can evaluate the quality of the data, refine measures of effect and exposure, and develop criteria for interpreting these measures. Passions, prejudices, and opinions may be a source of confusion if they promote an interpretation of events favorable to certain views while weakening the participation of contrary opinions.[26] Quality surveillance can usually dispel illusions that are founded on daily experiences but exaggerated by fears and hopes.

REFERENCES

1. Centers for Disease Control: Leading work-related diseases and injuries—United States. MMWR 1983; 32:24–26, 32.
2. ASPH/NIOSH (The Association of Schools of Public Health under a cooperative agreement with the National Institute for Occupational Safety and Health): Proposed National Strategies for the Prevention of Leading Work-Related Diseases and Injuries, Part 1. Washington, DC: The Association of Schools of Public Health, 1986.
3. National Institute for Occupational Safety and Health: Surveillance in the prevention of leading work-related diseases and injuries: an excerpt of the role of surveillance from the proposed national strategies for the prevention of work-related diseases and injuries. Cincinnati, OH: NIOSH, January 1987.
4. National Academy of Sciences: Counting Injuries and Illnesses in the Workplace: Proposals for a Better System. Washington DC: National Academy Press, 1987.
5. Buffler PA, Aase JM: Genetic risks and environmental surveillance: epidemiologic aspects of monitoring industrial populations for environmental mutagens. JOM 1982; 24:305–314.
6. Greenwood M: Medical Statistics from Graunt to Farr: The Fitzpatrick Lectures for the Years 1941 and 1943, Delivered at the Royal College of Physicians of London in February 1943. Cambridge: Cambridge University Press, 1948.
7. Humphreys NA (ed): William Farr: Vital Statistics, a Memorial Volume of Selections from the Reports and Writings of William Farr. (London: Offices of the Sanitary Institute, 1885). Reprinted with introduction by Susser M and Adelstein A. Metuchen, NJ: Scarecrow Press, 1975.
8. US Congress, Office of Technology Assessment: Reproductive health hazards in the workplace. Pub. No. OTA-BA-266. Washington, DC: US Govt Printing Office, December 1985.
9. El Batawi MA, Fomenko V, Hemminki K, Sorsa M, Verieva T (eds): Effects of Occupational Health Hazards on Reproductive Functions. (WHO/OCH/87.2). Geneva: World Health Organization, 1987.
10. Centers for Disease Control: Leading work-related diseases and injuries—United States. MMWR 1985; 34:537–540.
11. National Institute for Occupational Safety and Health. Proceedings of a workshop on methodology for assessing reproductive hazards in the workplace. April 19–22 1978. NIOSH Pub. No. 81–100. Available from National Technical Information Service, Springfield, VA. No. PB-81–223–521/A18.
12. National Institute for Occupational Safety and Health. Hazard evaluation: immunology branch laboratory. HETA # 82–089–1213. Available from National Technical Information Service, Springfield, VA. No. PB-84–172–535/A03.
13. National Institute for Occupational Safety and Health. Hazard evaluation: Southern Bell. HETA # 83–329–1498. Available from National Technical Information Service, Springfield, VA. No. PB-85–208–379/A02.
14. Flynt JW, Norris CK, Zaro S, Kitchen SB, Kotler M, Ziegler A: State surveillance of birth defects and other adverse reproductive outcomes. Washington DC: Macro Systems, Inc., April 1987.
15. Child Trends Inc: Improving assessment of the effects of environmental contamination on human reproduction: report of findings and recommendations. Grant Number SES-8501616. Washington, DC: National Science Foundation, 1986.
16. Kelly BC, Gute DM: Surveillance Cooperative Agreement between NIOSH and States (SCANS) Program: Rhode Island, 1980–82. NIOSH Pub. No. 86–107. Available from National Technical Information Service, Springfield, VA. No. PB-86–236–163/A04.
17. Banach J, Placek P, Simpson G: AMRA's Role in the 1988 National Maternal and Infant Health Survey. J AMRA 1988;59(10):28–33.
18. NCHS: National Center for Health Statistics Data Line. Survey of Reproductive Health. Public Health Rep 1987;102(6):703–704.
19. Key MM: State and local health departments: forgotten resources in occupational safety and health. JOM 1985; 27:379–385.
20. NCHS, Keppel K, Hensar R, Placek PJ, *et al:* Methods and Response Characteristics—1980 National Natality and Fetal Mortality Surveys. Viral and Health Statistics, Series 2, #100. DHHS Pub. No. (PHS) 86-1374. Washington, DC: Govt Printing Office, September 1986.
21. Ibid.
22. Edmonds LD, Layde PM, James LM, *et al:* Congenital malformations surveillance: two American systems. J Epidemiol 1981; 10:247–252.
23. Flynt JW, Ebbin AJ, Oakley GP, Falek A, Heath CW: Metropolitan Atlanta Congenital Defects Program. *In:* Hook EB, Janerich DT, Porter IH (eds): Monitoring Birth Defects and Environment. New York: Academic Press, 1971.
24. Erickson JD, Mulinare J, McClain PW, *et al:* Vietnam veterans' risks of fathering babies with birth defects. JAMA 1984; 252:903–912.
25. US House of Representatives, Committee on Government Operations, 99th Congress, 2nd session: Occupational health hazard surveillance: 72 years behind and counting. House report 99–879. Washington, DC: Govt Printing Office.
26. DeLaplace M, Essai: Philosophique sur les probabilities, 6th ed. Imprimerie Librarie de Bachelier de L'Ecole Polytechnique, 1840.