Health Effects of Residence Near Hazardous Waste Landfill Sites: A Review of Epidemiologic Literature

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This review evaluates current epidemiologic literature on health effects in relation to residence near landfill sites. Increases in risk of adverse health effects (low birth weight, birth defects, certain types of cancers) have been reported near individual landfill sites and in some multisite studies, and although biases and confounding factors cannot be excluded as explanations for these findings, they may indicate real risks associated with residence near certain landfill sites. A general weakness in the reviewed studies is the lack of direct exposure measurement. An increased prevalence of self-reported health symptoms such as fatigue, sleepiness, and headaches among residents near waste sites has consistently been reported in more than 10 of the reviewed papers. It is difficult to conclude whether these symptoms are an effect of direct toxicologic action of chemicals present in waste sites, an effect of stress and fears related to the waste site, or an effect of reporting bias. Although a substantial number of studies have been conducted, risks to health from landfill sites are hard to quantify. There is insufficient exposure information and effects of low-level environmental exposure in the general population are by their nature difficult to establish. More interdisciplinary research can improve levels of knowledge on risks to human health of waste disposal in landfill sites. Research needs include epidemiologic and toxicologic studies on individual chemicals and chemical mixtures, well-designed single- and multisite landfill studies, development of biomarkers, and research on risk perception and sociologic determinants of ill health. *Key words*: epidemiology, hazardous waste, health effects, landfill, residence, review.
— *Environ Health Perspect* 108(suppl 1):101–112 (2000).
http://ehpnet1.niehs.nih.gov/docs/2000/suppl-1/101-112vrijheid/abstract.html

The disposal of wastes in landfill sites has increasingly caused concern about possible adverse health effects for populations living nearby, particularly in relation to those sites where hazardous waste is dumped. Studies on the health effects of landfill sites have been carried out mainly in North America and existing reviews focus entirely on this literature (*1,2*). Recent publications of large studies both in and outside North America warrant an update of evidence presented in previous reviews. Up-to-date knowledge about epidemiologic evidence for potential human health effects of landfill sites is important for those deciding on regulation of sites, their siting and remediation, and for those whose task it is to respond to concerns from the public in a satisfactory way.

We intend to present a critical discussion of all major epidemiologic studies published since 1980 on health effects related to residence near landfill sites in North America, Europe, and elsewhere. Special attention is paid to recent studies and studies outside the United States that have not been included in previous reviews.

Methods

Throughout this review the term landfill is used for any controlled or uncontrolled disposal of waste to land. Relevant papers were found through computerized literature searches on MEDLINE (MEDLINE Database, National Library of Medicine, Bethesda, MD) (*www.biomednet.com*) and BIDS Databases, Joint Information Systems Committee, University of Bath, Bath, UK (*www.bids.ac.uk*) from 1980 through to 1998 using keywords "landfill" and "hazardous waste site." In addition, articles were traced through references listed in previous reviews. All papers found in this manner that studied health effects in residents near waste landfill sites and that were published in journals available through the British Library and libraries of the University of London were included in this review. A few papers referred to in previous reviews could not be traced because they were published in local journals in the United States. Published reports of recent studies that have not yet appeared in peer-reviewed journals have been included in the review. A few abstracts of European studies have been included, although full research papers of these studies have not been published because they reflect growing concerns about landfill in Europe. A total of 50 papers, reports, and abstracts are reviewed in this article. Investigations of the health risks to those employed in the handling, transport, clean-up, or maintenance of substances at landfill sites are very scarce and have not been included in this review. Many chemicals or groups of chemicals potentially present in landfill sites, including organic solvents, polychlorinated biphenyls (PCBs), and heavy metals, have shown adverse effects on human health or in animal experiments. A discussion of findings from either epidemiologic or toxicologic research on health effects related to specific chemicals is beyond the scope of this review.

Epidemiologic Studies on Health Effects of Landfill Sites

The majority of studies evaluating possible health effects in human populations living near landfill sites investigate communities near one specific waste disposal site (single-site studies), frequently in response to concerns from the public about reported contamination from the site or reported clusters of disease. A small number of studies have addressed the risks of living near waste sites, independent of whether the sites caused concern, by a priori specifying a number of sites for study. These will be referred to as multisite studies. Single- and multisite studies have different methodologic problems and are therefore discussed separately in this paper. Most individual studies are discussed in detail in this article. Where appropriate due to common methodologic issues (e.g., in studies of self-reported health outcomes and clusters of disease) or due to a common landfill site of concern (e.g., in the Love Canal studies and Santa Clara County studies), less emphasis was put on individual studies and more on common issues. Studies included in the review are summarized in Table 1 (single-site studies) and Table 2 (multisite studies). Discussion of individual single- and multisite studies is preceded by a discussion of issues common to the interpretation of all landfill studies.

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This work was conducted under a research fellowship from The Colt Foundation. The project was funded specifically by the U.K. Environment Agency. The views expressed are those of the author and the Environment Agency accepts no liability for any loss or damage arising from the interpretation or use of the information or reliance on views contained herein. The author is grateful to H. Dolk and B. Armstrong for their comments on several drafts of this review.

Received 24 November 1998; accepted 7 June 1999.

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Table 1. Single-site studies.

Ref.	Study design	Study subjects	Exposure measure	Health outcomes studied	Reported findings
(7)	Geographical comparison	Love Canal census tract; comparison: New York State	Residence in Love Canal census tract	Cancer: liver, lymphomas, leukemia, other organ sites	No increased incidence
(8)	Cross-sectional	46 exposed residents; comparison: residents in adjacent census tract	Residence in houses where chemicals were detected	SCEs and CAs	No difference in frequency of chromosome changes
(9)	Cross-sectional	523 Love Canal children; 440 control children	Proximity to site; at least 5 months' residence in Love Canal area	Self-reported health problems: seizures, learning problems, hyperactivity, eye irritation, skin rashes, abdominal pain, and incontinence	Increased prevalence of all symptoms
(10)	Cross-sectional	428 Love Canal children; 493 control children	Born in Love Canal and more than 75% of life in Love Canal	Children's stature, weight, weight for stature	Shorter stature for Love Canal children. No difference in weight
(11)	Retrospective follow-up	174 births near site; 443 live births in rest of Love Canal area; all births in New York State	Residence in Love Canal area	LBW	Higher percentage of LBW in exposed area; excess in period of active dumping
(12)	Retrospective follow-up	239 exposed children; 707 unexposed	Residence in Love Canal area during pregnancy	LBW, birth defects	3-fold risk of LBW (homeowners only); increased risk for birth defects (homeowners and renters)
(26)	Retrospective follow-up	2,092 births in proximate area; 6,840 births in control area	Residence at birth in area closest to landfill	Average birth weight, LBW, preterm birth	Significantly lower average birth weight, higher proportion of LBW and prematurity during the time of heaviest pollution
(14)	Retrospective follow-up	25,216 births	Residence in census tract, proximate zone, and frequency of odor complaints	LBW, fetal mortality, infant mortality, prematurity	No difference over entire study period; moderate decrease in birth weight in high odor complaint zone in period of highest exposure
(27)	Case–control	7,977 LBW cases; 7,856 control births	Residence in areas adjacent to landfill and level of estimated exposure to landfill gas	LBW, very LBW, preterm birth, small for gestational age	Excess in LBW and small for gestational age births; no excess in very LBW or preterm birth
(21)	Geographical comparison	Residents of Montreal Island	Residence in areas adjacent to landfill and level of estimated exposure to landfill gas	Cancers of 17 organ sites for men; 20 organ sites for women.	Increase in incidence of stomach, liver, lung and prostate cancer for men, stomach and cervix–uteri cancer for women.
(15)	Cross-sectional	51 residents of exposed village incl. 11 children and 52 control persons	Residence in exposed village	SCEs	Higher frequency of SCEs in exposed population, particularly in children
(28)	Cross-sectional	47 children from exposed village; 45 unexposed children	Residence in exposed village and time of exposure	Chromosomal changes	Chromosome damage frequency returned to background levels after site remediation
(29)	Geographical comparison	Cancer deaths and birth defects compared to Pennsylvania and U.S.	Residence in counties surrounding waste site, incl. Clinton county, PA	Bladder cancer and cancers of other organ sites; birth defects	Increase in bladder cancer deaths in Clinton; increase in number of other cancers in Clinton and 3 surrounding counties; no excess in birth defects.
(16)	Cross-sectional	179 long-term exposed residents; 151 residents in comparison areas	Residence in area near waste site	14 self-reported diseases; 15 self-reported symptoms	Increased prevalence of skin problems and sleepiness
(17)	Cross-sectional	1,049 exposed; 948 unexposed residents	Residence in household close to site	36 self-reported health problems	Increased prevalence of minor respiratory symptoms (wheezing, cough, persistent cold), irregular heart beat, fatigue, bowel complaints
(30)	Retrospective follow-up	614 exposed households; 636 comparison households	Residence within 750 m of edge of site: long-/short-term residence	Self-reported health problems	Increased prevalence of mood disorders, narcotic symptoms, skin and respiratory disorders, eye problems, muscle weakness
(31)	Cross-sectional	403 exposed households; 203 comparison households	Residence in proximate area	19 self-reported diseases, 23 symptoms; mortality, cancer incidence, LBW, birth defects, spontaneous abortions	Increase in majority of self-reported diseases and symptoms. No significant association for mortality, cancer morbidity, reproductive effects
(32)	Cross-sectional	257 residents in exposed zones; 105 in comparison area	Distance based zones: zone 1: < 300 m zone 2: 300–1,000 m	Self-reported diseases and symptoms, miscarriages, stress levels	Increased reporting of majority of symptoms, miscarriages, stress
(18)	Follow-up survey	57 high-, 66 low-, 70 unexposed residents	Exposure zones based on odor zones	22 self-reported health problems	2-fold increase in 64% of reported symptoms
(33)	Cross-sectional	321 high-exposed persons; 351 persons with low/minimal exposure	Cumulative exposure index based on distance from sites and amount of chemicals present at sites	29 self-reported health problems	Excess in reporting of 11 of 29 symptoms: mainly neurologic symptoms

(*Continued*)

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Table 1. *Continued.*

Ref.	Study design	Study subjects	Exposure measure	Health outcomes studied	Reported findings
(*34*)	Cross-sectional	456 exposed residents; 481 comparison persons	Residence near site	14 self-reported health problems	Increased reporting of 11 of 14 symptoms.
(*19*)	Retrospective follow-up	694 residents	Individual exposure index based on concentration of pollutants and daily activity of study subjects	Amount of prescribed medication for selected diseases (respiratory, ophthalmologic, dermatologic, gastrointestinal, neurologic)	No relationship between individual exposure index and drug consumption
(*20*)	Case–control	432 cases; 384 controls	Individual exposure index based on concentration of pollutants and daily activity of study subjects	Dermatologic, respiratory, eye, gastrointestinal diseases, psychologic disorders and other conditions	Relationship between exposure level and existing cases of respiratory and psychologic conditions
(*38*)	Geographical comparison	Three counties adjacent to waste dump compared to whole region	Communities near dump; distance of community to dump	Leukemia, multiple myeloma, malignant lymphoma	Excess in leukemia incidence
(*39*)	Geographical comparison	Ward surrounding landfill compared to whole region	Residence in landfill ward, surrounding wards, area downwind from landfill	All childhood cancers	No excess of childhood cancer
(*40*)	Geographical comparison	5 wards near landfill compared to 22 wards elsewhere	Wards near landfill	Mortality rates, hospital admissions for asthma, cancer, and other conditions, spontaneous abortions, birth defects, drug prescriptions	No consistent differences in mortality rates, hospital admissions, spontaneous abortions. Excess in birth defects before and after start of the landfill. Increase in prescriptions for certain medications
(*41*)	Geographical comparison	Cancer rates in 8 counties in Illinois compared to national rates	Residence in town with contaminated wells	Bladder cancer	Excess in bladder cancer in town with contaminated wells
(*44*)	Geographical comparison	Woburn cancer rates compared to national rates	Residence in Woburn	Childhood leukemia	More than 2-fold excess in childhood leukemia
(*45*)	Case–control	20 leukemia cases; 164 control children	Exposure index based on fraction of water supply in household from contaminated wells	Childhood leukemia	Significant association with exposure index
(*45*)	Retrospective follow-up	4,396 pregnancies; 5,018 children under 18	Exposure index based on fraction of water supply in household from contaminated wells	Childhood disorders; adverse pregnancy outcomes: spontaneous abortions, perinatal death, LBW, birth defects	Increase in eye/ear anomalies, CNS/chromosomal/cleft anomalies; perinatal deaths; kidney/urinary tract disorders, lung/respiratory disorders
(*46*)	Cross-sectional	28 family members of leukemia cases; 30 healthy controls	Being a family member of a Woburn leukemia case	Immunologic abnormalities, medical examination	Immunologic abnormalities in family members
(*47*)	Retrospective follow-up	Births in exposed census tracts compared to births in the entire county	Residence in census tract served by contaminated water supply	Congenital heart defects	2-fold excess in cardiac anomalies
(*48*)	Retrospective follow-up	Pregnancies in exposed census tract; pregnancies in unexposed census tract	Residence in census tract served by contaminated water supply	Spontaneous abortions, birth defects, LBW	Increase in spontaneous abortions and birth defects; no excess in LBW
(*49*)	Retrospective follow-up	Pregnancies in 2 exposed census tracts; pregnancies in 2 unexposed census tracts	Residence in 2 census tracts served by contaminated water supply	Spontaneous abortions, birth defects, LBW	No excess in spontaneous abortions or malformations in new exposed study area
(*50*)	Retrospective follow-up	Pregnancies in 2 exposed census tracts	% water in census tract from contaminated well; estimated concentration of solvents	Spontaneous abortions, birth defects	No relation between abortion or malformation rate and estimated exposure
(*51*)	Case–control	145 cases with cardiac malformations; 176 nonmalformed control births	Mother's consumption of home tap water	Congenital heart defects	Elevated risk for consumption of more than 4 glasses of tap water compared to none
(*52*)	Retrospective follow-up	349 pregnancies in 1 exposed and 1 unexposed census tract	Mother's consumption of home tap water	Spontaneous abortions, birth defects	Spontaneous abortions: significant trend with number of glasses tap water per day. Birth defects: no trend
(*53*)	Retrospective follow-up	1,016 pregnancies in exposed and unexposed areas	Mother's consumption of home tap water	Spontaneous abortions, birth defects, LBW	Spontaneous abortions: 7-fold risk for any versus no tap water. Birth defects: nonsignificant increase. No association with LBW
(*13*)	Cross-sectional and follow-up	49 exposed residents; 57 unexposed residents	Use of contaminated well water	Liver function	Abnormalities in liver function in exposed residents. Returned to normal 2 months later.
(*54*)	Cross-sectional	676 exposed residents; 778 unexposed residents	Residence in high-exposure area based on groundwater flow	Self-reported disease: cancer, liver disease, respiratory illness, skin disease, seizures	Statistically significant increase in respiratory disease and seizures, not significant after accounting for smoking
(*55*)	Cross-sectional	65 exposed residents; 66 residents from control households	Residence in households with contaminated well water	15 self-reported health symptoms; 14 self-reported diseases	Increased reporting of eye irritation, diarrhea, sleepiness.

Abbreviations: CAs, chromosomal aberrations; CNS, central nervous system; LBW, low birth weight; SCEs, sister chromatid exchanges.

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Table 2. Multisite studies.

Ref	Study design	Study sties	Study subjects	Exposure measure	Health outcomes studied	Reported findings
(*56*)	Geographical comparison	593 NPL waste sites in U.S.	339 counties with waste site, more than 3,000 without	County with site	Cancer mortality	Increased rates of cancer of the lung, bladder, stomach, and rectum
(*57*)	Case–control	12 sites in New York State	339 deceased lung-cancer cases; 676 deceased controls	Residence in census tract with site; duration of residence	Lung cancer	No association
(*58*)	Case–control	38 sites with likely landfill gas migration in New York State	9,020 cancer cases; 9,169 deceased controls	Residence within 250 ft	Cancer of liver, lung, bladder, kidney and brain; non-Hodgkin lymphoma, leukemia	Excess of female bladder cancer and female leukemia
(*59*)	Case–control	300 sites in 1,072 census tracts in California	5,046 birth defects cases and 28,085 control births. 1,904,000 births for birth weight analysis	Residence in census tract with site and potential for human exposure	Birth defects, LBW	1.5-fold increase in risk of heart defects. Other malformations and birth weight not associated
(*60*)	Case–control	1,281 NPL sites in U.S.	17,407 births	Residence within 1 mile	Birth weight, birth defects, fetal deaths, infant deaths	No association between adverse pregnancy outcomes and living near a NPL site
(*61*)	Case–control	590 waste sites in New York State	9,313 live births with birth defects; 17,802 normal control births	Residence within 1 mile and hazard score of site	Birth defects	Increased risk for all malformations (12%), integument system, nervous system, musculoskeletal. Indications for dose–response relation with exposure risk
(*62*)	Case–control	643 waste sites in New York State	473 cases with central nervous system defects; 3,305 musculoskeletal cases; 12,436 control births	Ratings of exposure probability within 1 mile of each site	Central nervous system defects and musculo-skeletal defects	No association between two types of and proximity to waste sites
(*64*)	Case–control	317 waste sites in New York State	259 cases of end-stage renal disease and 259 controls	Residence within 1 mile, exposure probability; years of residence within 1 mile	End-stage renal disease	Nonstatistically significant increase in risk of renal disease for ever living within 1 mile, having lived within 1 mile for more than 12 years, and a medium/high probability of exposure
(*65*)	Case–control	105 NPL and 659 non-NPL sites in California	507 neural tube defects, 517 controls; 210 heart defects, 439 oral clefts, and 455 controls	Census tracts: no site, non-NPL site, NPL site; residence within 1 mile and residence within 1/4 mile	Birth defects: neural tube defects, heart defects, and oral clefts	No increased risks relating to residence in census tract with site. Small, nonsignificant increase in risk of NTD and heart defects for living within 1/4 mile
(*66*)	Case–control	21 sites in 5 European countries	1,089 cases with non-chromosomal birth defects; 2,366 control births	Residence within 3 km	Birth defects	Increased risk for all malformations (33%), NTD, cardiac defects

NTD, neural tube defect.

Issues Common to the Interpretation of Landfill Studies

A general problem in epidemiologic studies of landfill sites, whether studying single or multiple sites, is that there is insufficient information regarding potential human exposures from landfill sites. Although landfill sites are numerous and widespread, very few have been evaluated with respect to both the types of chemicals they contain and the extent to which they may be releasing chemicals. Most such work has been conducted in the United States under the Superfund program (*3*). In other countries, information is largely lacking. Moreover, although chemicals have been found to migrate off site at a number of sites that have been thoroughly investigated (*2*), we know very little about the extent to which residents living near a site are exposed to these chemicals. A few studies that have attempted to measure certain chemicals in blood and urine of populations near waste sites have generally not found increased levels of volatile organic compounds (VOCs) (*4*), mercury (*5*), or PCBs (*6*). Because knowledge of whether and to what extent substances from waste sites reach the human population is still largely lacking, and because resources are rarely available to carry out extensive exposure measurements or modeling, epidemiologic studies have based the assessment of exposure to landfills mainly on surrogate measures such as residence in an area close to a waste site or distance of residence from a waste site. The use of such surrogate, indirect exposure measurements can lead to misclassification of exposure which, if not different for diseased and nondiseased persons, will decrease the sensitivity of the study to find a true effect.

In addition to being hampered by insufficient exposure data, the study of landfill exposures is complicated by the fact that if residential populations are exposed to chemicals from landfill sites, it will generally be to low doses of mixtures of chemicals over long periods of time. Associations with such low-level environmental exposures in the general population are by their nature hard to establish. Low-dose exposures are generally expected to generate small increases in relative risk that will be difficult to distinguish from noise effects introduced by confounding factors and biases.

In most of the landfill studies reviewed in this article, residents near waste sites are studied without knowledge of the exact route(s) of exposure to chemicals from the site. Migration of hazardous substances into groundwater is often an important environmental concern in relation to landfill sites, which may represent a public health problem, especially when a site is located near aquifers supplying public drinking water. However, in many situations the drinking water supply of residents near waste sites does not originate

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from the local area. For people living in the vicinity of these sites, other routes of exposure may be of more concern. Landfill sites may be a source of airborne chemical contamination via the off-site migration of gases and via particles and chemicals adhered to dust, especially during the period of active operation of the site. Very little is known about the likelihood of air exposure from landfill sites through landfill gases or dust. At some of the sites described below, low levels of volatile organic chemicals have been detected in indoor air of homes near landfill sites (*7–13*), in outdoor air in areas surrounding sites (*14–20*) or in on-site landfill gas (*21*). Other possible routes of exposure include contamination of soil, ground, and surface water, which may lead to direct contact or pollution of indoor air in the case of evaporation of VOCs into basements of nearby houses. Contamination via the food chain may sometimes be of concern for nearby residents in the case of consumption of home-grown vegetables. Drinking water is a possible route of exposure only if water for domestic use is locally extracted. If this is the case, other domestic water uses (bathing, washing) may also lead to exposure via inhalation of evaporated VOCs and/or direct contact (*13*).

Some issues related to specific health outcomes should be noted in both single- and multisite studies. A general problem in studies of cancer incidence is the long latency period between exposure and clinical manifestation of the cancer. Studies may not always allow for a long enough latency period, which reduces their power to pick up long-term effects. Moreover, because of the long latency period, a considerable number of people may have migrated into or out of the exposed areas between time of exposure and time of diagnosis, which will lead to misclassification of exposures. Studies of chromosome changes (chromosome aberrations and sister chromatid exchanges) are undertaken with the assumption that such changes are related to the mechanisms underlying cancer and possibly birth defects. Chromosomal changes are studied as biomarkers of early response or effect of exposure to mutagenic and carcinogenic chemicals. Sorsa et al. (*22*) point out that theoretically it is reasonable to assume that chromosome damage is directly related to cancer etiology, but the number of agents clearly shown to induce such damage in humans is still limited. Increased frequencies of chromosome changes may indicate exposure to mutagens and carcinogens, but it is not clear at present how well they predict cancer risk. Low birth weight is thought to be relatively sensitive to effects of chemical exposures (*23*). It is also relatively easy to collect accurate information on birth weight from birth certificates. However, a large number of risk factors are associated with low birth weight (including smoking, socioeconomic status, nutritional factors, parental height) (*24*), and these may act as confounding factors, giving biased estimates of association with residence close to a site. Birth defects have fewer established risk factors than other reproductive outcomes such as low birth weight, and studies of birth defects may therefore be less affected by confounding factors, although unknown risk factors could still play a confounding role. Also, birth defects represent an etiologically very heterogeneous set of conditions; analyses of the total malformation rate (all defects combined) have the advantage of larger numbers but may not be sensitive enough to pick up increases in risk of specific defects. The grouping of malformations into groups that are etiologically similar is difficult because of lack of knowledge on causes of specific defects. Grouping therefore always entails a compromise between large enough numbers and etiologic specificity.

Single-Site Studies

The investigation of single landfill sites has been important as a response to community concerns; many of the single-site studies discussed below are prompted by public concerns, often under considerable political pressure. This means that they are prone to recall and reporting biases that may weaken the investigations and partly explain increases in reported health outcomes. Single-site studies have examined a vast range of possible health outcomes, often without a specific disease hypothesis being proposed a priori. Such "fishing expeditions" are thought to be of less scientific value than studies that start with a clear hypothesis (*1*). Including these fishing expeditions in evaluating the consistency of findings across multiple studies is important nevertheless when assessing evidence for health risks.

A less avoidable problem in single-site studies is that the size of populations living near waste sites generally is small and, especially when the outcome is a rare disease, this can seriously limit the statistical power of an investigation.

Single-site studies discussed in this section are grouped into those examining hard end points such as cancer and reproductive outcomes, those studying self-reported health outcomes and symptoms, those following up reported clusters of disease near landfill sites with geographic comparisons of disease rates, and those specifically investigating the contamination of well water used for drinking or other domestic uses in relation to health effects. These last studies were discussed separately to determine whether conclusions can be drawn about specific pathways of exposure.

Studies of cancers, reproductive outcomes, and chromosomal damage. Large quantities of toxic materials (residues from pesticide production) were dumped at the landfill of Love Canal, New York State, during the 1930s and 1940s, followed by the building of houses and a school on and around the landfill in the 1950s. By 1977 the site was leaking and chemicals were detected in neighborhood creeks, sewers, soil, and indoor air of houses. This led to one of the most widely known and publicized incidents of environmental pollution from landfill. Exposure of Love Canal residents, although not well understood, may have occurred via inhalation of volatile chemicals in home air or via direct contact with soil or surface water (*10*). The drinking water supply was not contaminated. Chemicals detected at Love Canal were primarily organic solvents, chlorinated hydrocarbons and acids, including benzene, vinyl chloride, PCBs, dioxin, toluene, trichloroethylene, and tetrachloroethylene. Several studies were conducted to detect whether Love Canal residents suffered adverse health effects.

Janerich et al. (*7*) compared cancer incidence for the Love Canal area with data for the entire state from 1955 to 1977 and found no increase in cancer rates at Love Canal for any organ site. This included leukemia, lymphoma, and liver cancer, which were thought to be the cancers most likely to result from exposures to the chemicals found at the site. The study is limited in that no information was available on confounding factors such as socioeconomic status and smoking. Subsequently, Heath et al. (*8*) compared the frequencies of chromosome changes (sister chromatid exchanges and chromosomal aberrations) in residents who lived in the first ring of houses adjacent to Love Canal in 1978 with those of control persons from socioeconomically similar census tracts. No differences in frequencies of chromosome damage were found. Chromosome changes were measured in 1981 and 1982, a few years after people were evacuated from the first ring of houses and therefore were no longer exposed. The authors point out that chromosome damage may be a reversible effect, which may explain the negative findings.

Infants and children have been the subject of other Love Canal studies. A cross-sectional study (*9*) reported an increased prevalence of seizures, learning problems, hyperactivity, eye irritation, skin rashes, abdominal pain, and incontinence in children living close to the Love Canal site compared to controls from other areas, as reported by the parents of the children. It has been noted in previous reviews (*1,25*) that this study was conducted in 1980, 2 years after the residents of Love Canal had become aware of the hazardous

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waste problem, when media and public interest were high, and people were being evacuated. This makes it likely that the results were biased by differential reporting of health problems. However, a similar population of children (spending 75% or more of their childhood in the Love Canal area) had significantly shorter stature for their age than control children after allowing for factors such as birth weight, socioeconomic status, and parental height (*10*). Vianna and Polan (*11*) found an excess of low birth weights (less than 2500 g) during the period of active dumping (1940–1953) in areas of Love Canal where exposure had been highest. Rates of low birth weight between 1960 and 1978 after the site had been closed were comparable to those in upstate New York as a whole. It is not clear whether exposure from Love Canal was highest during the active dumping period or during the period after the site was closed, when the building of houses near the site increased and the landfill was leaking. A study by Goldman et al. (*12*) reported a 3-fold risk of low birth weight for children exposed during gestational life to the Love Canal area compared to that for control children born elsewhere from 1965 to 1978. Data were analyzed separately for homeowners and renters so that groups of similar socioeconomic status were compared, and after allowing for confounding factors, the risk of low birth weight was significantly increased for homeowners only. This finding is difficult to interpret because there are no strong reasons to believe that homeowners would be more susceptible than renters to the effects of toxic chemicals. In the same study an increased risk of birth defects was observed for both homeowners and renters. Information on birth defects relied mainly on reports from parents. Some recall bias can therefore be suspected, in particular for defects of lesser severity, but this is unlikely to account for the entire association found for major birth defects.

Berry and Bove (*26*) studied birth weight at the Lipari Landfill in New Jersey, a site for municipal and industrial waste. Leachate from the site migrated into nearby streams and a lake adjacent to a residential area. Inhalation of volatile chemicals emitted from the landfill and contaminated waters was thought to be the most important exposure pathway. The site closed in 1971 after complaints of residents, but the heaviest pollution was estimated to have occurred during the late 1960s to the mid-1970s. The study found a convincing increase in proportion of low birth weight babies (< 2500 g) and a lower average birth weight in the population living closest (within a radius of 1 km) to the landfill in the time period when potential for exposure was thought to be greatest (1971–1975) compared to these factors in a control population. Although information on some confounding variables such as smoking, alcohol consumption, and socioeconomic status was not available, mothers in the exposed area were more highly educated and therefore appeared to be of higher socioeconomic status. One would expect higher birth weights in areas of higher socioeconomic status, so as the authors point out, confounding by socioeconomic status does not explain the lower birth weights found. In time periods before and after heavy dumping and off-site pollution, birth weights were higher in the area closer to the site than in the control area, which supports the hypothesis that pollution from the waste site may have been related to low birth weights in the community close to the site.

A range of reproductive effects including low birth weight was studied around the large BKK hazardous waste disposal site in Los Angeles County, California (*14*), after previous investigations of vital records found that trends in low birth weight and neonatal deaths corresponded closely with times and quantities of dumping at the landfill. Results for the whole study period showed no increase in adverse reproductive effects, but during the period of heaviest dumping, birth weights were significantly lower in exposed areas than in control areas using odor complaint frequency zones to classify exposure. All results were adjusted for education, income, and race. The decrease in mean birth weight found in the high-odor complaint zone was small (59 g) compared to that in the Lipari Landfill study (192 g) and was less than a third of birth-weight reductions caused by smoking during pregnancy (*26*). Odor complaint frequency zones corresponded better with vinyl chloride monitoring data and meteorology around the site than did census tract areas or distance-based (< 0.7 miles) exposure zones, and this was therefore thought to be the most accurate method for classifying exposure. Using census tract or distance-based exposure zones, smaller decreases in mean birth weight were found (35.2 g, $p = 0.02$ and 20.4 g, $p = 0.25$, respectively).

Miron Quarry, a large (the third largest in North America) municipal solid waste site in Montreal, Quebec has prompted studies on both reproductive outcomes (low birth weight and preterm births) (*27*) and cancers (*21*). Gas from the site was the main environmental and health concern and a range of VOCs, including a number of recognized or suspected human carcinogens, had been detected in the gas. An excess of 20% in low birth weight was found among babies of mothers who were living in the high-exposure area adjacent to the landfill at the time of delivery, taking account of confounding factors such as education and age of the mother. No excess was found in the low-exposure zone compared to a control area. Exposure zones were based on proximity to the site and accounted for the direction of dominant winds. Control areas were selected that were similar to exposure areas on a number of sociodemographic variables so as to limit the potential for confounding. The cancer study used the same exposure zones and control areas and increases were found in incidences of cancers of the stomach, liver, prostate, and lung for men, and stomach and cervix/uterus for women. Incidences of cancers of other organ sites were not increased in the exposed areas. Age and sex were the only confounders that could be controlled for directly and the authors admit that area matching for sociodemographic factors was based on fairly broad zones. The landfill started operation in 1968 and cancer incidence was studied between 1981 and 1988, which allowed a maximum latency of only 20 years among those residents in the area throughout the period.

In Mellery, Belgium, gases containing a complex mixture of VOCs escaped when the clay seal of a landfill site cracked. Because some of the detected chemicals were known mutagens and/or carcinogens, damage to chromosomes was studied and an increase in chromosome damage (sister chromatid exchanges) was found among Mellery residents but not in unexposed subjects in subgroups of both smokers and nonsmokers (*15*). In children 8–15 years of age, a more marked difference was found between exposed and unexposed groups than among adults. The findings indicated exposures similar to those of occupationally exposed populations. The adult unexposed comparison subjects were recruited from a volunteer blood donor list and may therefore have comprised a group with risk behavior and exposure to possible risk factors for chromosome damage different from those of the general population. They also reported less occupational exposure than the Mellery inhabitants. It is unclear how occupational exposure was defined and results have not been adjusted for it. A follow-up study after site remediation reduced the concentration of the atmospheric pollutants to background levels reported that chromosomal damages in Mellery children had returned to background levels and were no longer different from those for unexposed populations (*28*).

At the Drake Superfund Site, an industrial chemical dump in Pennsylvania, widespread on- and off-site contamination of groundwater, soil, and surface water with organic (benzene, chlorinated benzene, phthalates) and inorganic (arsenic, mercury) compounds prompted a

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cancer mortality and birth defects study (*29*) and a community health survey (*16*). Air monitoring near the site identified a small number of organic compounds, but the main exposure route was thought to be direct contact with surface waters and soil in recreational areas near the site. Budnick et al. (*29*) found an increase in mortality from bladder cancer (cancer of primary a priori concern because of aromatic amines detected on and off site) in the male population of one of the counties surrounding the waste site compared to average mortality rates in the entire state and the United States. Bladder cancer in females did not show such an effect. The authors point out that an occupational effect for males working in the Drake chemical plant may explain the fact that the association was found in men only. No excess in risk of birth defects was found. The subsequent health survey (*16*) found increased reporting of sleepiness and skin problems in the exposed community and concluded that it was difficult to say whether toxic chemicals from the site, overreporting of symptoms by the exposed community (reporting bias), or other factors such as stress and occupational exposure caused these symptoms.

Studies of self-reported health symptoms. A number of other community health surveys have investigated a wide range of health problems, including respiratory symptoms; irritation of skin, nose, and eyes; gastrointestinal problems; fatigue; headaches; psychological disorders; and allergies. These studies have been conducted in response to concerns from the public, often triggered by smells and odors from the sites. In a number of studies, self-reported health problems were increased in exposed populations (people living close to the waste sites) compared to control populations [Drake Superfund Site (*16*); Lowell, Massachusetts (*17*); Hamilton, Ontario (*30*); Stringfellow, California (*31*); Queensland, Australia (*32*); McColl waste site, California (*18*); Houston, Texas (*33*); Harris County, Texas (*34*)] (see Table 1 for details). The majority of these health surveys rely on residents reporting symptoms and diseases through questionnaires or interviews. The possibility exists that higher reporting rates of symptoms in exposed areas are at least partly explained by reporting and/or recall biases. From a public health point of view, the findings of high symptom reporting, whether or not due to differential self-reporting, may indicate the impact that stress and concerns related to landfill can have on ill health and/or perceived ill health. In the survey by Ozonoff et al. (*17*), residents who indicated they were worried about neighborhood pollution reported more symptoms than those who were not worried, both in the exposed and the control area. Although this does not eliminate the possibility of an effect of toxic chemicals from the site, it suggests that stress and/or recall bias may have been responsible for the findings. Miller and McGeehin (*34*) and Dunne et al. (*32*) found increased symptom prevalence only in residents who indicated they were worried about, or aware of, an environmental problem in their neighborhood. The study by Lipscomb et al. (*18*) showed a 2-fold risk in most symptoms for residents who were worried compared to those who were not worried among the exposed population. The authors concluded that being worried, rather than a toxicologic effect from the site, explained the symptoms. Hertzman et al. (*30*) used medical records to confirm certain symptoms and found no over- or underreporting. They concluded that this finding indicated limited reporting bias; however, only a small proportion of the respondents' records were reviewed. Moreover, seeing a physician (and therefore having a medical record) may itself be related to concerns about the site. Baker et al. (*31*) studied self-reported health problems as well as mortality, cancer incidence, and pregnancy outcomes from medical registers at the Stringfellow waste dump in California. Self-reported diseases and symptoms were the only outcomes that differed between exposed and unexposed areas. Again, a higher perception of threat was related to a higher risk of nearly all self-reported symptoms.

The complicated relation between worry, odor perception, and symptom reporting related to hazardous waste landfill sites is further discussed by several authors (*35–37*).

Two recent studies around the French landfill of Montchanin used records of prescribed medication (*19*) and cases from general practitioners (GPs) (*20*) to define health outcome, in order to avoid biases related to self-reporting of symptoms. Exposure classification in both studies was based on an individual index, taking into account the concentration of airborne pollutants and daily activities of study subjects. High concentrations of VOCs were detected in areas near the site and both leachates and air from the site were reported to be highly toxic in 1988 and 1989, shortly after site closure. Consumption of drugs prescribed for most conditions from 1987 to 1989 did not show a trend with exposure level, although a slight trend was found for drugs taken for ear, nose, and throat, and pulmonary conditions. In the second study, patients with conditions thought to be associated with dump emissions were compared to other GP patients and an association was found for respiratory symptoms and psychological disorders. Again, consulting a doctor for such conditions and subsequent diagnosis of the conditions by the physician may be related to fears of adverse effects from the landfill rather than to toxic chemical effects.

Cluster Investigations. In addition to the above papers, a number of reports are available of geographical comparison studies initiated after high rates (clusters) of specific diseases were reported in the vicinity of landfill sites. For example, increased rates of leukemia found in communities nearest a toxic waste dump in North-Rhine Westfalia, Germany, supported a GP report of a cluster near the site (*38*). A cluster of childhood cancer reported by residents near a landfill site in Walsall, England, was not confirmed in a geographical comparison of rates in the ward containing the site to expected rates based on the regional average (*39*). Only short reports of these two investigations have been published.Concerns from residents and a GP about increased rates of congenital abnormalities (specifically gastroschisis, a defect in the abdominal body wall) among the population living near the Welsh landfill of Nant-y-Gwyddon were supported by the finding that rates of congenital abnormalities in exposed wards were almost 1.9-fold those in unexposed wards over the period from 1990 to 1996 (*40*). However, rates in the exposed wards were already high (1.9-fold those of unexposed wards) between 1983 and 1987 before the site opened, and it is unlikely, therefore, that these increased rates were due to the landfill. Four cases of confirmed gastroschisis indicated a significant 9-fold excess in rates of gastroschisis among exposed wards between 1989 and 1996. A cluster of bladder cancer cases in one town in Illinois in the United States, was observed by researchers and subsequently linked to the presence of two contaminated wells close to a landfill site (*41*).

A general problem in the interpretation of all cluster investigations is that localized areas of high disease density may occur even as part of a random pattern of disease. It is difficult to distinguish clusters derived from this random pattern from those where there is a common underlying local cause (*42,43*). Also, areas with higher disease densities, although part of the random pattern of disease, may be selectively picked for study.

Studies of drinking water contamination incidents. The presence of chemicals in groundwater and drinking water is an important factor in determining the risk posed by landfill sites. However, it does not tell us what effect, if any, the consumption of contaminated water has on human health. Studies of adverse health effects prompted by the contamination of well water used for drinking water and other domestic uses by hazardous substances from waste disposal sites (mainly sites where chemical waste drums were buried) are discussed below. Literature on contaminated water and potential health effects is more extensive than that presented

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in this section, which focuses only on water contamination directly related to the disposal of waste. The 1991 review by the National Research Council (*2*) gives a more comprehensive review of studies on contamination of domestic water supplies and health effects and concludes that although the available literature is scanty and not conclusive, drinking water contamination could lead to adverse health effects. Most of the studies summarized below have been discussed extensively in previous reviews (*1,2*).

In Woburn, Massachusetts, toxic chemicals (industrial solvents, mainly trichloroethylene) from a waste disposal site were detected in municipal drinking water wells. Residents of Woburn reported a cluster of 12 leukemia cases in children, and a first study confirmed that this number was significantly higher than expected on the basis of national rates (*44*). The problems with cluster analyses are discussed above. Because of lack of information on exposure to the contaminated wells, it was not possible in this first report to link the leukemia cases with exposure to the well water. Lagakos et al. (*45*) followed up these findings by compiling an exposure score for residential zones in Woburn using information on what fraction of the water supply in each zone had come from the contaminated wells annually since the start of the wells. Childhood leukemia incidence, perinatal deaths, congenital anomalies, and childhood disorders were studied in relation to the exposure scores. A significant excess was found again comparing leukemia rates for Woburn with national rates, and an association was found between leukemia incidence and exposure scores. The pregnancy outcome survey found associations with eye/ear congenital anomalies and central nervous system/oral cleft/chromosomal anomalies (mostly Down syndrome) but not with low birth weight or most childhood disorders. Pregnancy outcomes were self-reported in this study, but because residents were not aware of their exact exposure scores, the authors conclude that it is unlikely that this led to substantial differential overreporting. Byers et al. (*46*) undertook a study of 28 family members of patients with leukemia in Woburn. Damage to the immune and nervous systems was found in exposed relatives but not in unexposed controls. Exposure in this study was not measured by exposure to contaminated well water but by being related to a leukemia patient in Woburn, which makes it difficult to interpret the findings. The authors point out that it is impossible to say whether the association is due to an inherited predisposition or to a common environmental exposure of family members to agents that damage the immune system.

A number of studies followed the contamination of two drinking-water wells in Santa Clara County, California, with chlorinated solvents that had leaked from an underground waste storage tank. Residents living near one of the contaminated wells reported a cluster of adverse pregnancy outcomes, mainly spontaneous abortions and congenital heart defects. A first investigation (*47*) confirmed a significant excess of cardiac anomalies in the service area of the water company that operated the contaminated well compared to those among residents of an unexposed area. The excess was found within the potentially exposed time period and not in an unexposed time period after the well was closed. The authors conclude that the solvent leak was an unlikely explanation for the excess of cardiac anomalies found because the excess occurred mainly in the first 12 months of the exposed time period, and there was a significant ($p = 0.03$) deficit of cases during the second 8 months corresponding to the time when exposure was thought to be more certain. However, it is unclear when the leak started and the potentially exposed period was defined beforehand as the full 20-month period. A second study in the same area reported an increased risk of all congenital malformations combined and spontaneous abortions (*48*). A follow-up study including a second exposed area did not observe an increase in either outcome in this second area, even though it was thought to have the same water exposure as the original area (*49*). An exposure study estimating monthly concentrations of solvents in each census tract found no difference in probability of exposure between women with adverse pregnancy outcomes and women with normal births (*50*). Subsequent studies investigating water consumption in Santa Clara County report significant associations between reported tap water consumption and risk of cardiac defects (*51*) and spontaneous abortions (*52,53*), regardless of whether women lived in areas that received contaminated water. As the authors of these studies point out, recall biases cannot be excluded.

In Hardeman County, Tennessee, well water used as drinking water by residents was found to be contaminated with high concentrations of carbon tetrachloride and other chlorinated compounds after complaints were received about the taste of the water. A nearby landfill where 300,000 barrels of pesticide waste had been buried was responsible for the contamination. Analysis of indoor air and bathroom air while showers were running both indicated detectable levels of carbon tetrachloride and other organic compounds in houses that received water from the contaminated wells. Carbon tetrachloride has been identified in toxicologic studies as a strong liver toxin. The investigation, conducted several months after the population had stopped using the water for drinking, showed abnormally high levels of liver enzymes (indicating liver damage) in residents who had used contaminated water compared to controls, who had not (*13*). The authors concluded that these high liver enzyme levels probably resulted mainly from exposure due to washing and toilet water uses, and possibly from previous exposure through drinking and cooking. Two months later, when use of the well had completely stopped, liver function in the exposed population had returned to normal. This study benefited from relatively well-documented exposure information and a clear hypothesis about the possible health effects (i.e., liver disease) related to exposure to carbon tetrachloride.

Leakage from an industrial dump of chemical waste drums in New Jersey caused contamination of groundwater and well water with organic chemicals (including benzene, toluene, trichloroethylene, and lead). Najem et al. (*54*) found higher self-reported prevalence of respiratory disease and seizures but not cancer, liver illness, and skin disease in people living in a high-exposure area estimated on the basis of groundwater flow patterns. Residents in the high-exposure area used private drinking-water wells, ate homegrown food, and smoked more often than populations living in unexposed areas, and when these factors were adjusted for, differences in health outcomes disappeared. Adjusting for possible exposure routes such as local food consumption and use of private wells may have led to overadjustment, however, which would explain why no differences in health outcome were found.

An ex-military base in Dauphin County, Pennsylvania contained drums of toxic chemicals, fly ash, and other waste; well water for homes located on the perimeter of the site was contaminated with trichloroethylene, PCBs, pesticides, and other chemicals (*55*). Residents were instructed to stop using the water. Higher rates of eye irritation, diarrhea, and sleepiness were reported by residents of households with contaminated well water than by residents of households not having contaminated water.

Multisite Studies

The problems with single-site studies prompted by community pressures have increasingly been recognized, and recently several large studies have investigated adverse health effects near sets of hundreds of sites selected independently of community concerns or reported disease clusters (Table 2). These studies have the additional advantage of large numbers of subjects, which would give them enough statistical power to detect

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small increases in risk of rare diseases such as birth defects and specific cancers. On the other hand, their large scale makes exposure assessment even more complicated than in single-site studies, as adequate information must be collected for each of many sites. A number of the studies discussed below have used the U.S. National Priority Listing (NPL) of hazardous waste sites developed by the U.S. Environmental Protection Agency (U.S. EPA) to select their sites. The NPL ranks all hazardous waste sites in the United States deemed to be of considerable threat to the environment or public health. NPL sites have been relatively well assessed with respect to the potential or actual migration of hazardous chemical substances from the sites through groundwater, surface water, and air (*2*). Most multisite studies, however, were not able to distinguish between different types and pathways of contamination and, in absence of better exposure data, based their assessments of exposure on distance of residence from the sites or residence in an area with a site. Exposure misclassification, if nondifferential, may be expected to dilute true effects in these investigations. Multisite studies mainly investigated cancers and reproductive outcomes.

Cancer studies. Griffith et al. (*56*) identified 593 NPL sites over the entire United States where contamination of groundwater used for drinking water had been detected by laboratory analyses. Cancer mortality rates for counties containing one or more of these NPL sites were compared to those for counties not containing sites and raised levels of lung, bladder, stomach, and rectum cancer were found. These results were not adjusted for confounding factors such as socioeconomic status and smoking and are therefore difficult to interpret.

A case–control study in New York State (*57*) examined lung-cancer in relation to residence in a census tract with a waste site. Twelve waste sites known to contain suspected lung carcinogens were studied. A questionnaire survey among next of kin of the deceased cases and controls attempted to collect information on factors such as smoking, diet, education, and residential history. Smoking was significantly more frequent among cases, but there was no association between having lived in or duration of living in an exposed census tract and risk of lung cancer. Low response rates (around 60%) and possible recall bias limit this study.

A recent study in New York State (*58*) investigated cancer risks near 38 landfills where migration of landfill gas through soil was likely. Migration of soil gas could result in indoor exposure in nearby houses to hazardous VOCs carried with the landfill gas. Potential exposure areas were defined around each site, and extended 250 ft from the landfill at 36 sites and 500 ft at 2 sites. Incident cases of cancer collected from the New York State Cancer Registry were compared with a random selection of deaths from causes other than cancer, matched by age and sex. Only cancers of the liver, lung, bladder, kidney, and brain, and non-Hodgkin lymphoma and leukemia were studied, as they were regarded potentially sensitive to chemical exposures. Statistically significant excesses in the defined exposure areas were reported only for bladder cancer in women and leukemia in women. The results were adjusted for sociodemographic characteristics of the areas of residence. No information was available on individual factors such as smoking or on how long cases and controls had been living at certain addresses. The use of deceased controls makes interpretation of this study extremely complicated. The deceased population from which controls were selected may differ from the population from which the cases were drawn on a number of variables, including their residence locations.

Studies of reproductive outcomes. Shaw et al. (*59*) conducted a study on the risk of congenital malformations and low birth weight in areas with landfills, chemical dump sites, industrial sites, and hazardous treatment and storage facilities in the San Francisco Bay, California area. Census tracts were classified as *a*) no hazardous site in area, *b*) hazardous site in area but no evidence of human exposure, and *c*) hazardous site and plume in the area with evidence of potential human exposure. A small increase (1.5-fold) in risk was found for heart and circulatory malformations in the areas with potential human exposure. This increased risk was present across chemical classes and exposure routes. Risk of other malformations or low birth weight was not significantly increased. Results were adjusted for some potential risk factors (maternal age, race, sex of child, birth order) but not for socioeconomic status.

Reproductive outcomes have been studied in a number of other multisite studies. Sosniak et al. (*60*) investigated the risk of adverse pregnancy outcomes for people living within 1 mile of a total of 1,281 NPL sites over the entire United States. The risk for low birth weight and other pregnancy outcomes (infant and fetal death, prematurity, and congenital anomaly) was not associated with living near a site after taking into account a large number of potential confounding factors, including socioeconomic variables collected through questionnaires. However, only around 63% of women originally sampled for the study returned the questionnaire and were included in the study. Also, it is unclear how congenital anomalies were defined, and no subgroups of malformations were studied.

Geschwind et al. (*61*) investigated the risk of congenital malformations in the vicinity of 590 hazardous waste sites in New York State. A 12% increase in congenital malformations was found for people living within 1 mile of a site. For malformations of the nervous system, musculoskeletal system, and integument (skin, hair, and nails), higher risks were found. Some associations between specific malformation types and types of waste were evaluated and found to be significant. A dose–response relationship (higher risks with higher exposure) was reported between estimated hazard potential of the site and risk of malformation, adding support to a possible causal relationship. However, a follow-up study of Geschwind's findings (*62*) found no relation between two selected types of malformations (central nervous system and musculoskeletal) and living near a hazardous waste disposal site. The study did report an increased risk of central nervous system defects for those living near solvent- or metal-emitting industrial facilities. Subjects for the first 2 years of this study were also included in Geschwind's study, and 2 more years were studied. Marshall et al. (*62*) attempted to improve the exposure measurement in the first study by assessing the probability of specific contaminant–pathway combinations in 25 sectors of the 1-mile exposure zones (*63*). The risk of particular pathways or contaminant groups could not be investigated, however, because of limited numbers of cases in each subgroup. Hall et al. (*64*) used the same method of exposure assessment to study renal disease near 317 waste sites in 20 counties in New York State. Increased risks were found for associations between renal disease and residential proximity to a site (within 1 mile), the number of years lived near a site, and a medium or high probability of exposure, although the associations did not reach statistical significance.

A study by Croen et al. (*65*) based exposure measurement on both residence in a census tract containing a waste site and distance of residence from a site. Three specific types of birth defects (neural tube defects [NTDs], heart defects, and oral clefts) were studied; little or no increase in the risk was found using either measure of exposure. Risks of neural tube (2-fold) and heart defects (4-fold) were increased for maternal residence within 1/4 mile of a site, although numbers of cases and controls were too small (between 2 and 8) for these risk estimates to reach statistical significance. Births were ascertained from nonmilitary-base hospitals only, and the authors point out that the increased risk of NTDs may have resulted from lower ascertainment of exposed controls than exposed cases where exposure zones included military bases. Military base residents with pregnancies

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affected by NTDs may have been more likely to deliver in nonmilitary hospitals than residents with unaffected pregnancies.

A first European multisite study recently reported a 33% increase in all nonchromosomal birth defects combined for residents living within 3 km of 21 hazardous waste sites in 10 European regions (*66*). Neural tube defects and specific heart defects showed statistically significant increases in risk. Confounding factors such as maternal age and socioeconomic status did not readily explain the results. The study included both open and closed sites that ranged from uncontrolled dumps to relatively modern controlled operations. This disparity makes it difficult at this stage to conclude, if indeed the association is causal, whether risks are related to landfill sites in general or whether specific types of sites may be posing the risks.

Conclusions

The presence of large quantities of mixtures of potentially hazardous chemicals in landfill sites close to residential populations has increasingly caused concern. Concerns have led to a substantial number of studies on the health effects associated with landfill sites. From this review we can conclude that increases in risk of adverse health effects have been reported near individual landfill sites and in some multisite studies. Although biases and confounding factors cannot be excluded as explanations for these findings, the findings may indicate real risks associated with residence near certain landfill sites.

For several reasons, evidence is limited for a causal role of landfill exposures in the health outcomes examined despite the large number of studies. Effects of low-level environmental exposure in the general population are by their nature difficult to establish. Also, existing epidemiologic studies are affected by a range of methodologic problems, potential biases, and confounding factors, making the interpretation of both positive (statistically significant increase in risk) and negative (no increase in risk) findings difficult (*67*). Lack of direct exposure measurement and resulting misclassification of exposure affects most studies and can limit their powers to detect health risks.

It is possible that studies not showing associations have been less likely to be included in this review because they may have been less likely to be submitted or selected for publication, thereby causing the review to be biased toward studies that did report positive associations. However, a number of so-called negative studies have been published and included in this review. We feel that most large, good-quality, epidemiologic investigations, particularly those starting with an a-priori hypothesis rather than a specific cluster, would have resulted in publication, whether or not the findings were positive.

An increase in self-reported health outcomes and symptoms such as headaches, sleepiness, respiratory symptoms, psychological conditions, and gastrointestinal problems has been found consistently in health surveys around sites where local concerns were evident (*9,16–18,30–34,54,55*). In these health surveys symptoms were usually reported by the exposed population without further confirmation of the diagnoses by medical examination. It is not possible at this stage to conclude whether the symptoms are an effect of direct toxicologic action of chemicals present in waste sites, an effect of stress and fears related to the waste site, or an effect of reporting bias (the tendency of exposed people to remember and report more symptoms than unexposed people). Several authors have discussed the possibility that odor complaints and related worry about a site may trigger symptoms of stress-related disease or lead to an increased awareness of existing symptoms (*36,37*). Further research in this area is urgently needed to improve our understanding of the impact of social factors and risk perceptions on both actual and perceived ill health in waste site communities. Issues of environmental equity and environmental justice must form an integral part of such research.

Evidence for a causal relationship between landfill exposures and cancers is still weak. Cancers are difficult to study because of long latency periods, as discussed in previous sections. Also, cancer studies have mainly compared incidence or mortality rates between geographic areas without collecting adequate information on confounding factors. Excesses in bladder, lung, and stomach cancer and leukemia were reported in more than one study (*21,29,41,45,56,58*). Well-designed studies with long follow-up and good quality information about confounding factors such as smoking are needed to confirm these findings.

A number of studies have suggested a relationship between residential proximity to landfill sites and adverse pregnancy outcomes. An increase in infants with low birth weights has been the most consistent finding in single-site studies (*11,12,14,26,27*). These were generally well-designed studies and low birth weight is thought to be a sensitive marker of effects of chemical exposures. Small increases in the risk of birth defects and certain specific birth defects (cardiac defects, central nervous system defects, musculoskeletal defects) have been reported, mainly in multisite studies (*12,59,61,65,66*). Studies are still too few, however, to draw conclusions regarding causality. Fetuses, infants, and children are generally thought to be more vulnerable and therefore experience toxic effects at lower doses than the adult population (*25*). The finding of shorter stature in Love Canal children (*10*) may also be an example of this.

An increased presence of chromosomal changes was reported in the vicinity of a landfill site in Mellery, Belgium (*15,28*), but not in Love Canal (*8*). Findings in Mellery were related to children in particular, which may again be an indication that children are more susceptible to low-level exposures from waste sites. It is not clear at present how well chromosomal changes predict cancer risk in humans.

Other adverse health outcomes such as abnormalities in liver function (*13*) and in renal disease (*64*) have also been reported in relation to hazardous waste exposure, although in single studies only.

For the future planning and regulation of landfill sites it is important to know which types of sites are most likely to entail risks. Landfill sites may differ enormously in the conditions that render them hazardous, and conditions that determine the exposure to and resulting health risks posed by any waste site are likely to be unique to that particular site. Such conditions may include the types, quantities, and age of the waste present; hydrogeologic and metereologic factors; and site management and engineering practices. We have not in this review attempted to relate technical aspects of waste disposal to health effects. Much of the existing epidemiologic work investigates large, old sites, uncontrolled dumps, and sites where heavy off-site migration of chemicals was detected. On the basis of current evidence, we cannot extrapolate findings for these individual sites to landfill sites in general or conclude which landfill sites are more likely than others to affect the health of nearby human populations.

It is also not possible to determine whether sites with airborne or waterborne exposures are more likely to pose a risk to human health. Although drinking water contamination is usually the primary concern related to landfill sites, in most cases local water supplies do not originate from the local area. Most studies, therefore, concern landfill sites where no local drinking-water wells were present and potential exposure was either airborne or through other routes such as direct contact and consumption of homegrown vegetables.

At present information regarding adverse health effects of exposure to landfill sites in European countries is largely lacking.

Further Research Needs

Research into the health effects of landfill sites is relatively immature, and further research could improve our current understanding (*1,2,25,68*). Future studies of landfill sites would greatly benefit from a more

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interdisciplinary approach, drawing from the fields of landfill engineering, environmental sciences, toxicology, and epidemiology.

Improvements in the base of toxicologic and epidemiologic data on effects of specific chemical exposures would improve our understanding of possible risks of the migration of these chemicals from landfill sites into the environment. Johnson and DeRosa (*69*), in a recent review of toxicologic hazards of Superfund waste sites, conclude that although a large body of toxicologic research is under way to assess the toxicity of chemicals commonly contaminating the environment surrounding waste sites, equally significant work is still to be done before these chemicals have adequate toxicity profiles that can be used by health and risk assessors. Johnson and DeRosa discuss data needs established by the Agency for Toxic Substances and Disease Registry and the U.S. EPA for research of individual chemicals and find these needs mainly in dose–response studies, reproductive studies, and immunotoxicology studies. Improved data on effects of individual chemical exposures would improve the quality of quantitative risk assessments that can be made for landfill exposures. However, quantitative risk assessments are based to a large extent on unverifiable assumptions, and therefore cannot negate the necessity for direct epidemiologic studies of people living near landfill sites.

More research into effects of chemical mixtures and possible interactions between single chemicals is needed to improve understanding of effects of multiple chemical exposures. Such research is complex, but new research initiatives are under way, mainly in the United States. For example, the U.S. EPA MIXTOX database, which contains toxicologic data on interactions of hundreds of pairs of chemicals, is a promising new development (*70*). Research developments and future directions in this field are discussed in detail by a number of authors (*70–72*).

The investigation of single landfill sites is important as a response to community concerns. More multisite studies with large study populations should also be conducted to draw conclusions about more general risks. Ideally, such multisite studies should attempt to classify sites in such a way that risks related to specific site characteristics can be investigated. However, systematic site assessments needed to underpin such classifications are at present totally lacking in Europe. There is little detailed information on waste inputs, especially for old landfills, and monitoring practices vary hugely for factors such as frequency of monitoring, the environmental media monitored, and types of chemicals monitored. Standardized waste-input recording systems and monitoring practices across European countries and the availability of summary reports of waste inputs and monitoring results would aid site classifications for epidemiologic studies as well as risk assessments. A recent report evaluating the use of a risk assessment tool on two U.S. and three U.K. landfill sites concluded that in the United Kingdom it is not possible to characterize the majority of landfills, even to the level at which a simple risk assessment framework can be employed on a site-specific basis. This particularly applies to the characterization of emplaced waste (*73*).

Epidemiology has increasingly made use of so-called biomarkers—biological monitors of either the internal dose of a chemical (biomarkers of exposure) or the biologic response to exposure (biomarkers of early effect). Biomarkers of the first type measure levels of chemicals in human tissue and fluids (e.g., blood, urine). These techniques can generally measure only a small number of chemicals, and their use is limited to situations in which environmental monitoring data indicate specific landfill chemicals that are of particular concern. The presence of chemicals in the body is currently difficult and costly to measure, but this may change. Biomarkers of the second type measure biological responses such as chromosomal changes (sister chromatid exchanges) and molecular changes (DNA adducts), and could be seen as early effect manifestations. Interpretation of these effect biomarkers is difficult; their link with clinically overt disease remains unclear, but their use could give studies much greater statistical power than studies of rare disease outcomes. Biomarker techniques have been used mainly in occupational settings and there has been less discussion of their use in environmental studies (*74,75*). Collaboration is required between epidemiologists and basic scientists to further develop biomarker techniques for use in studies of environmental exposures.

Specific areas of further research likely to prove most useful are

- The study of vulnerable groups—groups of the population likely to develop adverse health effects at levels of exposure lower than those of the general population. Such groups include: fetuses, infants, and children; elderly people; and people with impaired health.
- The study of people with higher exposures, for example, children (because they come into higher contact with potentially contaminated soil); people who eat local food products; workers at waste sites; people with life-styles (possibly socioeconomically determined) that lead to higher exposures.
- The study of worst-case landfills. In the absence of adequate exposure data, it is difficult to define worst-case sites. Ranking systems are in use, e.g., in the Superfund program (*76*), to rank waste sites according to their hazard potential, but their application generally requires extensive site investigations. Few epidemiologic studies would have the resources to carry out such investigations. It could be argued that identification of worst-case landfills should form part of regulatory practice in Europe. However, in the absence of systematic investigation of this kind, the study of sites where high off-site contamination has been detected and sites that have been subject to less regulation (possibly sites in developing countries or Eastern Europe) could be suitable for the study of worst-case scenarios provided appropriate health data can be collected.

It is possible with suitable investment to improve levels of understanding about risks of hazardous wastes to human health. However, because of the complicated nature of the exposure, it is likely that there will always remain a degree of uncertainty regarding health effects of landfill sites.

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