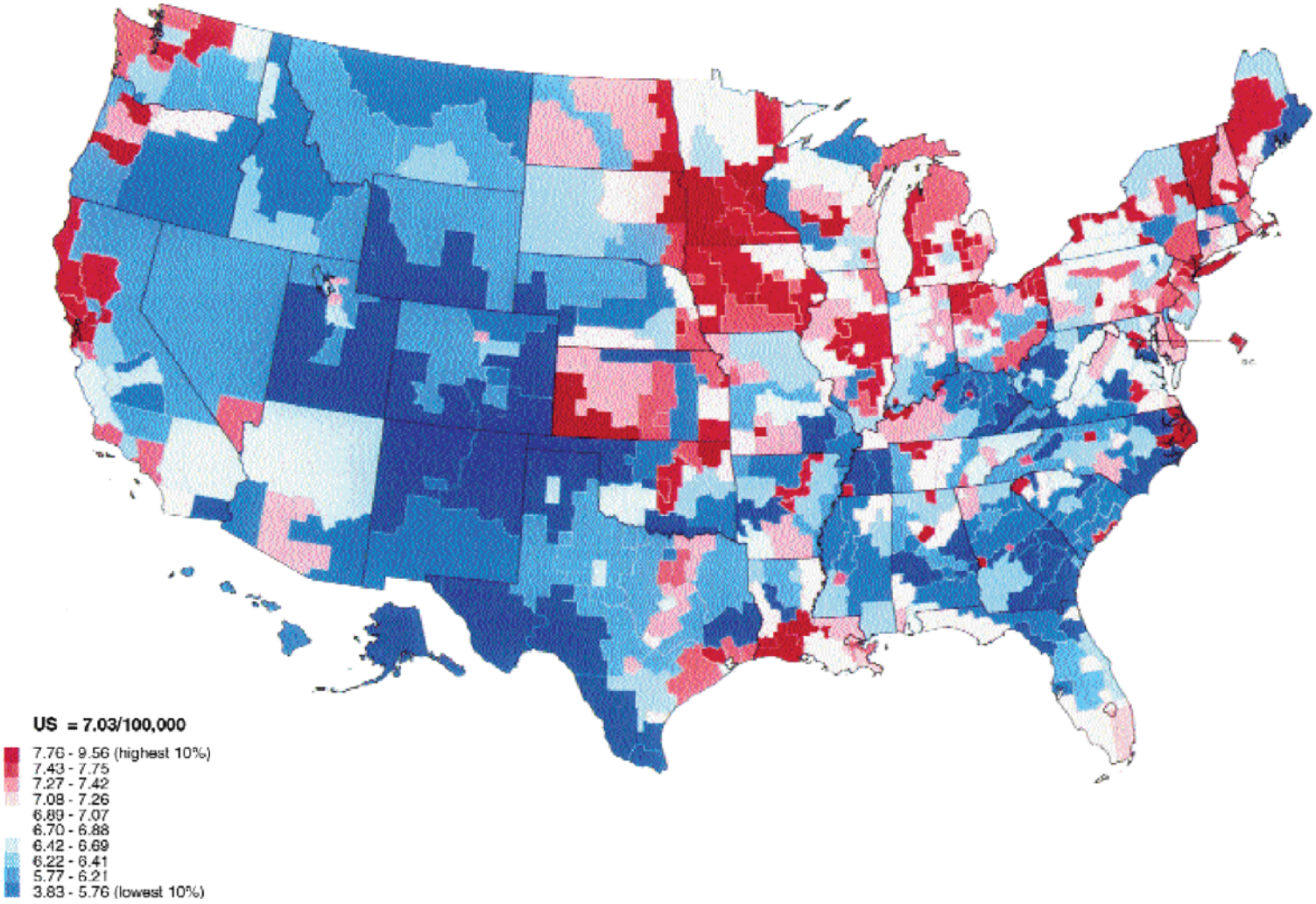
Do Pesticides Cause Lymphoma?

Lymphoma Foundation of America

Do You Live in a High-Lymphoma Area?



"Cancer Mortality Rates by State Econ. Area (Age-adj. 1970 U.S. Pop.), Non-Hodgkin's Lymphoma: White Males, 1970-1994." *Atlas of Cancer Mortality in the U.S.: 1950–94.* DeVesa, S.S.;et al., NIH Pub. #99-4564, NCI (1999).

RESEARCH REPORT

Do Pesticides Cause Lymphoma?

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Lymphoma Foundation of America®

A nonprofit charitable organization
helping cancer survivors and families since 1986

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Thank You

Thank you to the many scientists, doctors, lymphoma patients, and health professionals who read and reviewed this research report before it was published. We appreciate your comments and suggestions.

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Do Pesticides Cause Lymphoma?

Belita H. Cowan

This question is often asked by people who call our Foundation. They want to know — why did I get lymphoma? Where does it come from? What can I do to keep it from coming back?

The causes of cancer are complex and not altogether known. There are many things to consider: our heredity, viruses, our exposures to toxic substances in the environment (including chemicals that can cause cancer) and other factors. Anyone who could answer this question with certainty would surely win the Nobel Prize in Medicine.

And yet, there is so much we do know. Over the years, many researchers have done studies to see if pesticides cause lymphoma. Although they do not all agree, many scientists believe this is a serious problem.

We began our Pesticides Research Project last year. Our goal was to look at the worldwide medical and scientific literature on the subject of lymphoma and pesticides. During that year, many of you told us that you, too, wanted to know more about these studies.

We are pleased to make available to you this **Research Report**, which describes the most widely regarded studies on lymphoma and pesticides. We encourage you to use our **Research Report** as a first step in your own research. Because our Pesticides Research Project is ongoing, we welcome your comments and suggestions.

Belita H. Cowan
President
Lymphoma Foundation of America

Contents

Read This First

Most of us get our health information from magazines, TV news, and the Internet. We don't usually read scientific or medical journals. Therefore, we offer you this **Research Report** in plain English.

What causes lymphoma?

It would be so much easier if "somebody" could just "do a big study" and "find the answer" to the question of what causes lymphoma. Both fortunately and unfortunately, that isn't the way science works. One study doesn't usually "prove" anything. Instead, scientific knowledge develops by careful testing and retesting of theories through a gradual collection of evidence.

When a scientific study is finished, the most that can be claimed is that a statistical association between one or more factors and a certain outcome has been found — an association, but not necessarily the cause.

Of course, important breakthroughs do occur, and some research studies are better designed and produce more meaningful results than others. Still, any study that shows an association between factors must be reproduced by other scientists working independently, before the theory which is being tested gains favor in the scientific community.

What "Causes" Cancer?

All of us define "cause" differently, depending on whether we are considering "cause" from a medical, legal, religious, or everyday perspective. The definition of "cause" and the whole idea of causation are rarely mentioned by cancer researchers.

Common sense tells us that the cause of an event or an effect may be complex or unknown. In reading and evaluating research study results, we need to give some thought to the different definitions of "cause" and to the ways the author's point of view can affect research methods.

Question: Why does food get moldy after being left out on the kitchen counter for a few days?

Answer: Ask several people and you'll get several answers:

- Because mold is everywhere;
- Because a few days is too long to keep food at room temperature;
- Because Annie didn't cook it thoroughly;
- Because Jack didn't clean the countertop;
- Because the weather was hot and humid.

Of course, there may be other theories of what "causes" mold to grow. Any of them might be involved in the spoiled food problem. Obviously, your understanding of the "true cause" will depend to some extent upon your level of knowledge concerning mold growth, your experience with food preparation and storage, and whether you are Annie or Jack.

Your ideas about cancer may depend on whether you're a cancer patient, doctor, researcher or chemical company.

In that same way, your understanding of what causes cancer may depend on your knowledge of the ways in which cancer develops, as well as whether you are a cancer patient, friend of a cancer patient, cancer doctor or researcher — or a manufacturer of pesticides.

One of the most publicized stories about the "cause" of cancer is the ongoing drama of the cigarette companies and their attempts to show, in extended legal battles, that people develop lung cancer not from smoking, but from their own inherent problems and weaknesses.

You, the reader, need to understand that when lymphoma is discussed by researchers, there are many things to consider: heredity, viruses, our exposure to chemicals, and toxic substances in our air, water, and food. These factors and exposures may vary, depending in part on our chosen occupations and where we live. Any or all of these may weaken a person's immune system. These are only some of the possible — even probable — "causes" of cancer. It appears that pesticides may be one piece of a larger lymphoma puzzle.

Two studies in our **Research Report** (Faustini, 1996 and Figgs, 1998) show that exposure to 2,4-D (a commonly used weed killer) killed large numbers of lymphocytes in the people who were studied. These people's immune systems were weakened.

These people's immune systems were weakened.

Their lymphocyte counts improved only slowly. When the body is forced to form new lymphocytes after this kind of toxic injury to the immune system, mutated, abnormal cells may form in some cases, leading to the development of lymphoma.

As is typically the case when a question is studied for many years, there is some disagreement among authors of lymphoma/pesticides studies. Different scientists may look at the same statistics and conclude either "significant association," "limited evidence," or "no clear evidence."

You should be aware that some people are motivated to see "failure to prove cause" unless everyone, or almost everyone, who is exposed to a substance later develops cancer. For example, since cigarette smoking does not cause cancer as reliably as, say, smallpox virus produces smallpox, there are those who will say that cigarette smoking has little or no role in causing cancer. Jonathan Haar's book, *A Civil Action*, shows how some companies (and their scientists and lawyers) are motivated to "disprove" that chemicals cause cancer.

Research Methods: Do They Matter?

There are many different ways to do research studies. When we read the results of a study, we should look carefully at how the study was designed, carried out, and interpreted. Common sense tells us that a report which mentions only a few cases, occurring in one region within a limited time period, is only suggestive of a pattern, while a study with thousands of people observed over many decades has more power to show meaningful associations.

Here's what we looked for:

- ✔ Diagnosis of lymphoma must be accurate;
- ✔ Method of assessing exposure to the pesticides must be valid;
- ✔ Exposed populations and control groups must be the same except for their exposure to the pesticide;
- ✔ The number of people studied must be sufficiently large;
- ✔ Analyses and interpretation of results must be appropriately done.

When scientists study people in a particular occupation, there may be unidentified factors and/or exposures that confound the results.

Differences like these may affect a study's outcome:

- Farmers are exposed to sunlight, dusts, machinery, fuel, fumes, and animals, in addition to pesticides.
- With rare exceptions, studies fail to include any women.
- Though the latency period for lymphoma may be very long — easily 20 years after chemical exposures — some studies proclaim findings after only a few years.
- Mortality studies, which include only lymphoma deaths, ignore lymphoma survivors who are receiving treatment or who are in extended remission, and who may have different histories of pesticide exposure than those who have died.
- Some researchers carefully determine a person's exposure to potentially cancer-causing substances or factors. Other researchers use general categories, such as persons employed in a particular industry or living in a certain location.

Who Employs the Researchers? Who Pays For the Research?

While scientists may strive to remain impartial and unattached, they are human. So we need to consider: Who employs the researchers? Who is paying for the research? Naturally, these two questions are closely related.

The results are likely to differ depending on who is funding the research.

This idea — that the results of scientific research are likely to differ depending upon who is funding the research — is not just conjecture. A team of researchers who analyzed 70 articles concerning calcium-channel blocking drugs found a very close relationship between the authors' financial ties and their attitudes toward the drugs. In fact, 100% of those supporting the drugs had financial ties to drug companies, while only 43% of those critical of the drugs had such ties. There was a group who were considered "neutral" (neither for nor against the drugs), and of this group, 67% had drug company ties. Finally, it was discovered that in only 2 of the 70 articles did the authors disclose their corporate/drug company affiliations. ("Conflict of interest in the debate over calcium-channel antagonists," *New England Journal of Medicine*, Vol. 338, No. 2, pp. 101–106.)

Though some scientific and medical journals do show sources of research funding, this practice is not universal. In addition, there may be indirect sources of financial support which are not disclosed in such listings. In our **Research Report**, we have listed the authors' stated institutional/organizational affiliations and, when shown, funding sources. Since our information comes solely from the journal articles, we have no way of knowing all the affiliations nor funding sources of the authors, nor whether some have financial ties to the industries whose chemicals they are studying.

Even in instances where funding is available with few strings attached, there is a scientific "culture" that limits the types of research likely to be carried out by an agency or the scientific community as a whole. Also, studies with a "positive" result are more likely to be published than studies that don't show a correlation between the factors studied, even though a lack of findings is also an important piece of scientific evidence when a study is well-designed and well-executed.

Over the last 30 years there has been much more scientific interest in cancer chemotherapy, surgery, transplantation, immune therapies, and radiation than in alternative approaches, despite the public's great interest in them. The large role of drug companies in the funding of research may be part of the reason why so little money is spent on true cancer prevention (as opposed to detection) and the study of alternative treatments.

Hidden Bias

In November, 1997, the prestigious *New England Journal of Medicine* published an extremely negative review of a book written by Sandra Steingraber, *Living Downstream: An Ecologist Looks At Cancer and the Environment*. In that book, Dr. Steingraber cites evidence that the increase in lymphoma may be related to pesticides exposure. Why was the reviewer so highly critical of the book? Did he have a hidden bias?

The next month, the *New England Journal of Medicine* apologized publicly for failing to inform readers that the author of that negative book review was the medical director of W.R. Grace & Co., a Massachusetts corporation that had received extensive negative publicity for polluting ground water that may have contributed to higher than expected rates of leukemia among nearby residents.

Are Some Studies Better Than Others?

Some studies really are better than others. *Differences in study design are important.* Larger studies and those involving longer time periods may be more meaningful. The way a study is designed and carried out is critical.

Among the thousands of studies and articles which are published each year, not all bear the same weight or have equal influence in the scientific community nor in the public understanding. Those published in more prestigious journals are more widely read and respected.

Studies that are more highly publicized, or which catch the attention of the press because they address an interesting subject (like obesity or impotence), or are released on a day when there is little other news, get more publicity than others. That doesn't necessarily mean that they are more important or that we should base our decisions on what we read or hear in the news.

There are also differences among studies done in various countries. The conditions under which scientists work are not all the same. In some countries, especially in Northern Europe, extensive record keeping is required of all citizens and businesses, which gives scientists access to fairly accurate records showing which people worked where and under what conditions. Certain countries, such as Sweden, maintain national cancer registries which provide information on all cases and all types of cancer. This information can make it much easier for scientists working in these countries to obtain complete information about the people they are studying.

12 Words You Need to Know

1 Pesticide

A substance used to kill or reduce the numbers of unwanted forms of life in a particular environment. These life forms may be unwanted plants ("weeds"), fungi, insects, or animals such as rats. Most pesticides are man-made chemicals, though a few are naturally derived from plants. Though efforts are made to choose pesticides which are toxic only to the intended target and not to humans or other living things, often pesticides have more general toxicity. Pesticides are widely used in schools, factories, offices, homes, public and private lands, and in farming. The use of pesticides has greatly increased in recent times. Many pesticides persist in the environment and can be found in air, water, soil, plants and animals (including the food we eat), and in our own bodies.

2 Herbicide

A substance used to kill plants. Some herbicides kill all plants with which they come into contact; these are often called defoliants. Others are more specific, affecting only certain types of plants, such as crabgrass or plants that are not grasses. Herbicides are used widely in home lawn care, farming, and for weed control in public areas (parks, streets, golf courses, and highway areas).

3 Fungicide

A substance used to kill fungi ("funguses"). Yeasts, molds, mildew, and mushrooms are examples of fungi.

4 Insecticide

A substance used to kill insects. These are very widely used in nearly every kind of human environment, including homes, gardens, apartment buildings, schools, office buildings, restaurants, bakeries, and farms. They are also applied directly on adults, children, and pets. The term "insecticide" is sometimes used when the target is not, strictly speaking, insects, for example, worms.

5 Carcinogen

A substance that causes cancer. "Carcinogenic" means "causing cancer."

6 Chlorophenol

A type of manmade chemical that contains chlorine atoms and a ring-shaped carbon structure. Chlorophenols have some similarity to naturally-occurring substances, except for the chlorine atoms. These chemicals are toxic to living organisms, even in tiny concentrations. Chlorophenols vary in their nature, uses, toxicity, and tendency to cause cancer.

These chemicals are toxic to living organisms, even in tiny concentrations.

The phenoxy herbicides, frequently mentioned in our **Research Report**, are chlorophenols. So are DDT, PCB, TCDD, and many other chemicals now or formerly used in farming, landscaping, industrial processes, and home, school, and office pest control. These chemicals are sometimes called chlorinated (or halogenated — refers to the group of elements that includes chlorine) hydrocarbons, or organochlorines.

Even people who don't use these substances in their work may be exposed to them through drinking water, food, pesticide sprays used at home, school, work, home or business landscaping, and use on public lands such as parks and along highways. All people living in industrialized nations are exposed to these chemicals. We have residues of them in our body's own body fat, where such chemicals tend to persist. (See *dioxin/TCDD*, below)

7 Dioxin/TCDD

TCDD is 2,3,7,8-tetrachlorodibenzo-p-dioxin, also just called "dioxin." The numbers refer to the locations on the carbon structure where the four chlorine atoms are located. The term "dioxin" can also be applied to closely related chemicals.

One of the most toxic chemicals known, TCDD/dioxin occurs as a contaminant/byproduct when certain pesticides are manufactured.

It also gets into the air from incineration of chemical wastes and from certain industrial processes. Dioxin persists in the environment, breaks down very slowly, and tends to become concentrated in the fatty tissues of living animals and humans.

Unfortunately, we all have residues of chlorophenols in our own body fat.

Fish living in dioxin-contaminated waters contain much higher concentrations of dioxin than the water does.

Americans get 90% of their dioxin exposure by eating dairy products, meat, and fish. Since dioxin is concentrated in fatty tissues, it occurs in human breast milk. According to Dr. Sandra Steingraber, "a breast-fed infant receives its so-called "safe" lifetime limit of dioxin in the first six months of drinking breast milk." (Raffensperger, C. & Tickner, J., eds. *Protecting Public Health and the Environment*, Island Press, Washington, DC). Dioxin is also a hormone disruptor, even in concentrations much smaller than those that can cause cancer. Other health problems which some experts believe are linked to widespread dioxin contamination include the international epidemic of lowered sperm counts, the increase in breast cancer, and learning disabilities in children.

8 Case-control study

A study in which "cases" (people who have a disease) are compared with "controls" (people who don't have the disease). The differences between the two groups might reveal the cause of the disease. In our **Research Report**, "cases" are people with lymphoma; "controls" are people with no lymphoma. In designing a case-control study, scientists may consider such variables as age, gender, residence, occupation, race, military duty, etc. Sometimes several controls are selected for each case. Often the controls are selected at random from the same general population (hospital, state, etc.) where the cases are found. Good choice of cases and controls is a very important part of the design of all case-control studies.

9 Cohort study

A defined group of people (cohort) is followed up over time to observe their incidence of (or mortality from) a disease. The incidence or mortality in the cohort is compared either to the general population or to persons lacking the characteristic or exposure being studied.

10 Mortality study

A study of deaths from a particular disease (non-fatal cases are left out). A mortality study may have a cohort or case-control design. There is a weakness in the use of mortality studies for lymphoma, because many cases of lymphoma are not fatal. Since lymphoma survivors are ignored, the occurrence of lymphoma can appear lower than it really is.

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In some populations, exposure to carcinogens may increase the incidence of lymphoma at a relatively young age, resulting in higher than expected incidence but few deaths, since younger patients may better tolerate cancer treatments. Differences in access to treatment may affect mortality, and may differ from risk factors which affect incidence. Also, the cause of death recorded on a certificate sometimes does not reflect underlying illness. For instance, a death certificate may show the cause as kidney failure, but the kidney failure may have resulted from cancer chemotherapy. Still, mortality studies do provide useful information.

In the United States, it is often easier to conduct mortality studies than incidence studies because death records are easier to obtain than information about disease incidence. Norway, Finland, and England have complete records of every cancer case in their countries, making mortality studies less attractive as a study design (and incidence studies easier to carry out). These nations also have very complete data on the occupations of their citizens, which researchers can fairly easily match with cancer data for individuals.

NOTE: We have not attempted to define all types of study designs, but only to explain some of those which occur frequently in our

Research Report. For example, in a **meta-analysis**, a group of similar studies is evaluated for possible patterns or results not obtainable from the studies separately.

11 Odds ratio (OR)

Simply put, a measure of the risk of cancer for a study population (people exposed to a pesticide) divided by the risk for a population lacking the characteristic or exposure being studied (people not exposed to the pesticide). The odds ratio shows whether the group under study has more, less, or about the same chance of getting the disease as people who are not exposed to the pesticide.

12 Standard incidence ratio (SIR) and standard mortality ratio (SMR)

These, like the odds ratio, are ways of expressing the relationship of incidence (or mortality) from lymphoma in a study population to that in a reference group, except that in this case, the reference group is the whole population (of one country, usually).

Here's an example using *mortality figures*: Employees in certain pesticide factories had a SMR of 3.26 for non-Hodgkin's lymphoma. This means that 3.26 times as many people in that population died from non-Hodgkin's lymphoma as would have in a sample of the same size taken from the general population.

Here's an example using *incidence figures*: If in the population of the U.S., 15 cases of non-Hodgkin's lymphoma would be expected per 100,000 person-years, but in a study group of people exposed to a particular pesticide for a total of 100,000 person-years, 30 cases occurred, this would result in a SIR for non-Hodgkin's lymphoma in that group of 2.0 (twice the expected incidence).

The Choice Is Yours

It's Up To You

Every day you make choices that affect your health. Since there appears to be a relationship between pesticides and lymphoma, then this risk factor may be partially under your control. You can choose whether to make an effort to reduce your exposure to pesticides.

When U.S. Surgeon General Luther Terry first announced in 1964 that smoking causes lung cancer, his statement was considered controversial. There wasn't scientific consensus on the issue — many studies showed a strong link between lung cancer and cigarettes, while others did not. During the decades that followed, evidence that cigarette smoke is carcinogenic mounted slowly and is now overwhelming. Today, though tobacco companies continue to argue otherwise, most people believe that cigarette smoking is a major cause of disease and death.

What can we learn from this? Since it may take years to establish with some certainty whether pesticides cause lymphoma and other cancers, what are we, as lymphoma patients, friends, and family members, to do?

How important is it, really, to have a "perfect lawn"?

A sensible approach is to follow "the precautionary principle," a concept defined and developed in 1998 by an international group of scientists and environmental activists. This principle, meant to apply to public policy as well as to individual choices, reads in part:

"When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically."

Since we see from the studies in this Research Report that there is some evidence that links pesticides to non-Hodgkin's lymphoma, it makes sense for us to reduce our exposure to pesticides.

You have an opportunity to make a conscious choice in balancing the risks of pesticides against their possible benefits. How important is it, really, to have a "perfect lawn?" Do the ants that invade your kitchen each spring pose any danger, or are they just plain annoying? Is there really a danger of contracting Lyme disease in that weedy patch in the back of your property

(and if so, might it be better to mow the patch than to spray it with pesticides)? Would the manager of your apartment building, condo maintenance service, office building, or hotel/ motel consider reducing or eliminating their spraying schedules if you mention your concerns?

In the next few pages, we offer you some ideas to help you reduce your own and your family's exposure to pesticides.

What About Drinking Water?

You may be drinking a daily dose of pesticides without knowing it, even if you get your water from a city, town, or suburban water system. A report in USA Today (October 21, 1998) stated, "Powerful new pollutants imperil drinking water supply...from heartier bacteria to increasingly toxic industrial pollutants, pesticides, and fertilizers."

While federal regulations require water system operators to test for more than 80 substances, the rules are not enforced in many communities, and pesticide residues do appear in tap water. To learn more about the drinking water in your locality, you can call the EPA's Safe Drinking Water Hotline at 1 (800) 426-4791.

If you have a well on your property, its water, like that supplied by public water systems, may be contaminated by pesticides from nearby farms, lawns and gardens. The U.S. Department of the Interior states in its recent report, The Quality of Our Nation's Waters (p. 6): "At least one pesticide was found…in more than one-half of shallow wells sampled in agricultural and urban areas. Moreover, individual pesticides seldom occurred alone."

You might consider having your well water tested by a private laboratory, though this is expensive. An alternative is to use tap water for washing, and bottled or filtered water for drinking. Use caution, however — some brands of bottled water are not pure spring water, but city tap water placed into bottles. Look for the source of the water — it's printed on the label.

What About DDT?

DDT, a very toxic pesticide, was banned in the U.S. in 1970. Twenty-five years later in 1995, researchers were still able to find it in the fatty tissues and blood of nearly 100% of humans. So, we are all internally exposed to small amounts of DDT in addition to everything else we use, consume, or breathe. We — all people who live in industrialized nations — have dioxin and other chemical residues in our bodies. It's possible that this chemical insult to our immune systems is a partial or contributing cause for the epidemic of lymphoma that we see today.

Common Ways You Are Exposed to Pesticides in Daily Life

Home pest control

Do you use products in your home to kill fleas, cockroaches, ants, earwigs, flies, wasps, bees, termites, carpenter ants, silverfish, or spiders?

Exterminators

Have you hired an exterminator to rid your house of pests? Has your home been treated for termites or carpenter ants?

Apartments

Do you live in an apartment that is sprayed with pesticides by the building management?

Condo

Do you live in a condominium where the grounds are maintained by a landscaping service that uses weed killers and insect killers?

Garden

Do you use insect killers or weed killers in your garden? Do you plant tulip or daffodil bulbs with your bare hands? (Most floral bulbs have been drenched with fungicides before being sold.)

Lawn care

Do you use lawn fertilizers that have weed killers (which are herbicides) to get rid of crabgrass and other weeds? Have you hired a lawn service to keep your yard and lawn free of weeds and insects? Do you allow children or pets to play in pesticide-treated grass?

Neighbors

Do your neighbors spray their shrubs, trees, or lawns? (Sprays allow pesticides to drift beyond property lines.)

Workplace

Is your workplace treated with pesticides? (Many managers of office buildings and public buildings hire commercial exterminators to spray at regular intervals.)

Public areas

Do you use a park, golf course, playing field, or other public area? (Many parks and public areas, and virtually all golf courses, are treated with weed killers and/or insecticides. So are the green spaces near roads and highways.)

Drinking water

Do you drink water from a private well or public source that contains pesticides? (Don't assume that your city tap water is free of pesticides).

Hotels and motels

Do you stay in hotels or motels? (Most hotels and motels regularly spray the rooms with pesticides.

Certain foods

Do you eat fish caught in lakes (such as the Great Lakes) or streams that are contaminated with pesticides?

How Can I Minimize My Exposure to Pesticides?

10 Easy Steps To Take

1. To get rid of weeds in your lawn or garden, don't spray them — pull or dig them up, or leave them alone. Tolerate some weeds in your lawn — after all, they are green, like grass.

2. Keep your use of indoor pesticides — such as insect sprays and pest strips — to a minimum, eliminate them altogether, or use less toxic pesticides such as pyrethrins and boric acid.

3. If your workplace is sprayed with pesticides, find out whether your office or workspace can be spared this treatment. Often, there are no insects in office areas, especially if food is not stored or eaten there.

4. Try to avoid lawn fertilizers or treatments that contain pesticides. If you're not sure whether they contain pesticides, call the store where you bought them, or call the manufacturer (many stores are not familiar with all the pesticides and chemicals they sell).

5. If you hire a lawn care company, ask them not to use any pesticides. Even if you hire a "natural" lawn care company, check on all substances they plan to apply to your property. If the product kills weeds or insects, it's a pesticide.

6. If you live in an area where the local water supply is contaminated by farm runoff (this includes much of the Midwest, parts of California, and some other areas), consider drinking filtered or bottled water rather than city tap water or local well water. Be careful: not all filters effectively remove pesticides, and not all bottled water is free of chemical contamination. (Ask your dentist about possible fluoride needs, especially for children.)

7. Buy organically grown fruits and vegetables from a store you can trust. Look for the organic label. If you can't buy organic food, wash and/or peel fruits and vegetables. These fruits and vegetables are thought to have the highest pesticide residues: apples, grapes, green beans, peaches, pears, strawberries, spinach, and winter squash (squashes like butternut, acorn, spaghetti, pumpkin, golden). But continue eating lots of fruits and vegetables!

8. In animals and humans, pesticide residues concentrate in fat. If you do eat dairy products, use the low-fat kinds. (It is thought that young children may benefit from consuming some fat in their diet. Check with your pediatrician.)

9. Reduce your consumption of animal fat, which contains more pesticide residue than the muscle (meat) portions. Remove as much fat as possible from meat and poultry before cooking.

10. Don't eat fish caught in ponds, lakes, or rivers that are contaminated with runoff water from nearby farms.

The Studies of Pesticides and Lymphoma

Alavanja, M.C., Rush, G.A., Stewart, P., Blair, A. Proportionate mortality study of workers in the grain industry. *Journal of the National Cancer Institute* 78(2): 247–252 (Feb., 1987).

Grain workers' mortality rates from particular causes of death were studied using union insurance records. Information concerning pesticide use was also gathered. The authors found that pesticides used in the grain industry include aluminum phosphide (phosphine), carbon disulfide, carbon tetrachloride, ethylene dibromide, ethylene dichloride, Malathion, and methyl bromide. In this study of the deaths of 1,114 white males, findings indicated increased risk of lymphoma among grain mill workers (prompting a later study — see below). Mortality rates for several other types of cancer were also elevated. National Cancer Institute.

Alavanja, M.C.R.; Blair, A.; & Masters, M.N. Cancer mortality in the U.S. flour industry. *Journal of the National Cancer Institute* 82(10): 840–848 (1990).

Researchers looked at the causes of death of 22,938 white male flour mill workers. Both a cohort mortality study and a case-control study were done. Results showed increased risk of non-Hodgkin's lymphoma associated with work in flour mills, where pesticides are used frequently and heavily. The risk increased with the number of years employed in the flour industry; the OR for non-Hodgkin's lymphoma for white males followed for 25 years or more was 9.4 (9.4 times as many people from this group developed non-Hodgkin's lymphoma as from the control groups). The standard mortality ratio (SMR) from non-Hodgkin's lymphoma was 149 in flour mill workers (this means they had a 49% extra risk of dying from lymphoma compared to the general population). These findings point to pesticide exposure as a risk factor for non-Hodgkin's lymphoma. The authors have considered and ruled out other risk factors such as grain dusts and solvent exposures. National Cancer Institute.

Asp, S.; Riihimaki, V.; Hernberg, S.; & Pukkala, E. Mortality and cancer morbidity of Finnish chlorophenoxy herbicide applicators: an 18-year prospective follow-up. *American Journal of Industrial Medicine* 26: 243–253 (1994).

To follow up on their earlier study (see Riihimaki, 1982), the authors contacted 1,909 pesticide sprayers they had identified and studied previously, or proxies for those who had died. Though mortality figures were used in the initial study, in this follow-up total cancer incidence was studied, so survivors were included also. Only one case of non-Hodgkin's lymphoma appeared in the entire cohort, though 2.4 cases would have been expected with a 10-year latency period (elapsed time since exposure to the herbicides). The authors point out that their study was not powerful enough to detect an increase in incidence of non-Hodgkin's lymphoma unless it had increased to 4.5 times the level in the general population. Institute of Occupational Health, Helsinki, Finland.

Baris, D.; Zahm, S.H.; Cantor, K.P.; & Blair, A. Agricultural use of DDT and risk of non-Hodgkin's lymphoma: pooled analysis of three case-control studies in the United States. *Occupational and Environmental Medicine* 55: 522–527 (March 24, 1998).

To study the incidence of non-Hodgkin's lymphoma relative to DDT exposures, the

authors pooled data from three case-control studies of agricultural workers from four Midwestern states: Kansas, Nebraska, Iowa, and Minnesota. (See Cantor et al., 1992; Hoar et al., 1986; Zahm et al., 1990). Information on pesticide use and other risk factors was obtained by interview; non-farmers were used as a reference category. Results seemed to show a relationship between DDT exposure and non-Hodgkin's lymphoma, but when corrections were made for exposure to other pesticides (most agricultural workers are exposed to multiple pesticides; the study subjects were carefully questioned about pesticide use) the DDT effect was not statistically significant. [NOTE: Though the use of DDT was banned in the U.S. in 1970, it persists in living things and in the environment, so most Americans have residues of DDT in their tissues.] National Cancer Institute.

Becher, H.; Flesch-Janys, D.; Kauppinen, T.; Kogevinas, M.; Steindorf, K.; Manz, A.; & Wehrendorf, J. Cancer mortality in German male workers exposed to phenoxy herbicides and dioxins. *Cancer Causes and Control* 7(3): 312–321 (May, 1996).

These authors studied cancer deaths among 2,479 workers in four German chemical plants that manufactured phenoxy herbicides and chlorophenols. An increase in deaths from non-Hodgkin's lymphoma was noted (SMR of 326). These data are difficult to interpret because of small numbers (6 lymphoma deaths) and relatively short follow-up times (or lengths of time on the job) at some of the plants; in addition, non-fatal cases of lymphoma were not included. German Cancer Research Center, Heidelberg; Medical Center for Chemical Workers' Health, Hamburg; Finnish Institute of Occupational Health; IARC, Lyon, France. Funding: German Ministry of Research and Technology.

Bertazzi, P.A.; Zocchetti, C.; Pesatori, A.C.; Guercilena, S.; Sanarico, M.; & Radice, L. Ten-year mortality study of the population involved in the Seveso incident in 1976. *American Journal of Epidemiology* 129(6): 1187–1200 (June, 1989).

The impressive figure of 1,674,743 person-years of observation was reached in this study. The entire population in the region of Seveso, Italy was exposed to a variety of hazardous chemicals after a chemical plant safety valve pressure disk blew up, releasing a cloud of toxic chemicals, including chlorophenols. This report describes causes of death the researchers found after they followed up the residents for ten years. Death rates for females and males differed; in the most heavily exposed region, proportionately more females died of all causes than did males. Only seven lymphoma deaths occurred, though these were more than were expected. The results suggest, but do not prove, an increased risk of lymphoma. Institute of Occupational Health, Milano; Istituti Clinici di Perfezionamento, Clinica del Lavoro, Milano. Funding: Government of the Region of Lombardy and the Italian National Research Council.

Betta, P.G., Crosignani, P., Russa, A., Bottero, G., Bernardo, G., Pavesi, M., Pastonnerlo, M. Triazine herbicides and non-Hodgkin's lymphomas. A case-control study. *Proceedings of the Annual Meeting of the American Society for Clinical Oncology* 13: A534 (March 13, 1994).

The authors conducted a study in Italy, using small numbers (19 non-Hodgkin's lymphoma cases, 48 controls in similar rural areas) to determine the relationship, if any, between exposure to triazine herbicides and later development of non-Hodgkin's lymphoma. A significant relationship was found; persons with long-term exposure (over 18 years) had the highest incidence of non-Hodgkin's lymphoma. The authors concluded that their findings suggest a link between triazine exposure and non-Hodgkin's lymphoma. Santo Spirito Hospital, Montferrato, Italy; Division of Epidemiology, INT, Milan; City Hospital, Alessandria; Clinica del Lavoro Foundation, Pavia.

Blair, A.; Cantor, K.P.; & Zahm, S.H. Non-Hodgkin's lymphoma and agricultural use of the insecticide lindane. *American Journal of Industrial Medicine* 33: 82–87 (1998).

As in the Baris, et al. 1998 study (above), this was a pooled analysis of 3 studies previously done in Midwestern farming areas in Iowa, Kansas, Nebraska, and Minnesota. Results showed that farmers who had used lindane had a 50% higher incidence of non-Hodgkin's lymphoma than nonfarmers. Earlier, longer, and heavier use of lindane resulted in higher incidences. When the use of other pesticides, especially diazinon and 2,4-D, was considered, the effect of lindane on lymphoma incidence was weakened (1.2 or 1.3 times the control level, as opposed to 1.5 times). Lindane is not as widely used in agriculture today, but is still used on ornamental plants, Christmas trees, pecans, avocados, livestock sprays, dog shampoos, and shampoos for treating head lice in humans. National Cancer Institute.

Bloemen, L.J., Mandel, J.S., Bond, G.G., Pollock, A.F., Vitek, R.P., and Cook, R.R. An update of mortality among chemical workers potentially exposed to the herbicide 2,4-Dichlorophenoxyacetic acid and its derivatives. *Journal of Occupational and Environmental Medicine* 35(12): 1208–12 (Dec., 1993).

This is an update of a previous study of 878 chemical workers exposed to 2,4-D (a herbicide), compared with 36,804 unexposed workers from the same chemical factory as well as with the general population. In the previous study, exposures from 1945–1983 were tracked; this study provides an update through 1987. In the original study, 2 deaths from lymphoma were found with 1 expected; in the follow-up period, there were no deaths from lymphoma. The authors conclude that their study of workers exposed to the manufacture of 2,4-D "did not show patterns suggestive of a causal association with any particular cause of death, including cancer." However, since only 0.3 deaths from lymphoma would have been expected during the follow-up period, the study lacked sufficient power (was too small) to detect such patterns. Dow Chemical Company (five of the six authors), University of Minnesota School of Public Health.

Buckley, J.D.; Meadows, A.T.; Kadin, M.E.; Le Beau, M.M; Siegel, S.; & Robison, L.L. Pesticide exposures in children with non-Hodgkin's lymphoma. *Cancer 2000* 89: 2315-2321 (Dec. 1, 2000).

268 California children (ages 12 months – 20 years) with non-Hodgkin's lymphoma were matched with healthy controls. The children's parents answered a telephone questionnaire which included topics such as medications, X-rays, allergies, and others in addition to pesticide exposures. Parents were asked about their pesticide exposures at work, the mothers' exposures during pregnancy, and the use of pesticides in and around the home during the child's lifetime. Results showed a significantly increased risk of non-Hodgkin's lymphoma in children whose mothers had greater pesticide exposures during pregnancy, as well as in children who were exposed in the home. The more pesticide exposure the children had, the higher their lymphoma rates. In children whose parents reported pesticide use "most days," the OR was 7.3. When professional exterminations had been done in the home, the OR was 3.0. The authors include an excellent review of other studies on pesticides and lymphoma in their report. They note that although in this study all pesticides were considered, certain pesticides which are more capable of inducing lymphoma would be likely to produce a higher odds ratio. The investigators plan to conduct a larger case-control study in which the pesticides will be specifically identified. Children's Cancer Group. Funding: National Cancer Institute.

Bueno de Mesquita, H.B.; Doornbos, G.; Van der Kuip, D.A.; Kogevinas, M.; & Winkelmann, R. Occupational exposure to

phenoxy herbicides and chlorophenols and cancer mortality in the Netherlands. American Journal of Industrial Medicine 23(2): 289–300 (Feb., 1993).

Mortality records for employees at two chemical plants in the Netherlands were studied: 963 men exposed to phenoxy herbicides and 1,111 men who were not exposed. Time periods since earliest known exposure to the pesticides were fairly long (21 years and 30 years). Neither overall mortality nor cancer mortality was increased, but 2 cases of non-Hodgkin's lymphoma were observed in the exposed group (none in the non-exposed group), suggesting a possible increased risk. There were increased rates of other cancers in certain subgroups. National Institute of Public Health and Environmental Protection, The Netherlands; International Agency for Research on Cancer, Lyons, France.

Cantor, K.P. & Fraumeni, J.F. Jr. Distribution of non-Hodgkin's lymphoma in the United States between 1950 and 1975. *Cancer Research* 40 (8 Pt. 1): 2645–2652 (Aug., 1980).

Mortality rates for non-Hodgkin's lymphoma for all counties in the contiguous United States were studied. Trends that were found: increased rates of non-Hodgkin's lymphoma along with increased socio-economic status (SES); increased rates of non-Hodgkin's lymphoma in California coastal areas; decreased rates in the Southern United States (thought also to go with lower SES in many counties); increased rates of non-Hodgkin's lymphoma in counties with food packing industries, especially sugar beet processing; and a continuous increase in deaths from non-Hodgkin's lymphoma nationwide. The authors noted that food processing takes place most often in counties with extensive farming, and also that many of the death certificates listing non-Hodgkin's lymphoma as the cause of death were for persons employed as farmers, not as food canners. This finding helped to focus later research upon farmers. National Cancer Institute.

Cantor, K.P. Farming and mortality from non-Hodgkin's lymphoma: a case-control study. *International Journal of Cancer* 29(3): 239–247 (1982).

Death certificates of Wisconsin men with non-Hodgkin's lymphoma listed as the cause of death during the years 1968–1976 were matched with men whose death certificates showed other causes. The study examined whether non-Hodgkin's lymphoma occurred more frequently in farming communities. A limitation of the study, noted by the author, was that the analyses of data and the matching with controls were made according to the county of residence at the time of death, rather than the men's actual work histories. Results showed an increased rate of death from non-Hodgkin's lymphoma among men living in counties with higher rates of pesticide use. The farming group had an overall risk of non-Hodgkin's lymphoma of approximately 1.2 times that of the controls. Younger farmers in general had higher mortality from non-Hodgkin's lymphoma than older farmers (over 65). Though exposure to chicken and animal viruses has been proposed as a possible cause of non-Hodgkin's lymphoma, in this study the prevalence of animals or chickens in the various counties showed no correlation with lymphoma rates. National Institutes of Health. Funding (partial): Health Effects Laboratory, Environmental Protection Agency, Cincinnati, Ohio.

Cantor, K.P., Blair, A., Everett, G., Gibson, R., Burmeister, L.F., Brown, L.M., Schuman, L., and Dick, F.R. Pesticides and other agricultural risk factors for non-Hodgkin's lymphoma among men in Iowa and Minnesota. *Cancer Research* 52(9): 2447–55 (May 1, 1992).

622 white men (over age 30) with non-Hodgkin's lymphoma were matched with men who did not have non-Hodgkin's lymphoma (twice as many controls as cases) to measure the risks associated with farming and pesticide exposures. Data were obtained by interviewing the men directly, or family members of those who were unable to participate or had died.

Detailed farming and pesticide use histories were taken, including 23 animal insecticides, 34 crop insecticides, 38 herbicides, and 16 fungicides. A possible difficulty arises from the inability of the study subjects and/or their family members to recall exact pesticide usages, but this would tend to weaken rather than to strengthen the statistical association with non-Hodgkin's lymphoma. Extensive statistical data were generated concerning particular pesticides and their non-Hodgkin's lymphoma risks. "The chemicals most strongly associated with risk of non-Hodgkin's lymphoma were carbaryl, chlordane, DDT, diazinon, dichlorvos, lindane, malathion, nicotine, and toxaphene." National Cancer Institute, University of Iowa, University of Minn., Orlando Regional Medical Center.

Cantor, K.P., Blair, A., Brown, L.M., Burmeister, L.F., & Everett, G. Correspondence re: K.P. Cantor et al., Pesticides and other agricultural risk factors for non-Hodgkin's lymphoma among men in Iowa and Minnesota. *Cancer Research* 53(10): 2421 (May 15, 1993).

Following publication of Hoar et al. in JAMA, 1986, which found days per year of pesticide use to be a risk factor for NHL, Cantor et al. contacted the subjects from the previously conducted Iowa/Minnesota study to obtain days per year information. Many more cases than controls had died in the interim between the original study and the re-interview, so comparisons may have been biased. Because journal reviewers requested that these data not be included in the Cantor et al. 1992 paper, the authors published the data in this letter to the editor. No association with 2,4-D was observed based on the second interview data. National Cancer Institute, University of Iowa, Orlando Regional Medical Center.

Coggon, D.; Pannett, B.; Winter, P.D.; Acheson, E.D.; & Bonsall, J. Mortality of workers exposed to 2 methyl-4 chlorophenoxyacetic acid. *Scandinavian Journal of Work and Environmental Health* 12(5): 448–454 (Oct., 1986).

5,754 men who worked at a plant producing this particular phenoxy herbicide were included in this epidemiological study. Mortality figures were used primarily, with some cancer registry information. No increased risk of non-Hodgkin's lymphoma was found. The number of years of exposure, intensity of exposure, and years of follow-up varied widely, since all men employed during the period 1947–1975 were included in the study. Environmental Epidemiology Unit of the Medical Research Council, Southampton, United Kingdom; MRC Environmental Epidemiology Unit, Southampton General Hospital.

Coggon, D.; Pannett, B.; & Winter, P. Mortality and incidence of cancer at four factories making phenoxyherbicides. *British Journal of Industrial Medicine* 48(3): 173–178 (Mar., 1991).

Over 2,000 male workers in four chemical plants were studied using mortality records and cancer registry information. Twice the expected mortality from non-Hodgkin's lymphoma was found, but the number of non-Hodgkin's lymphoma deaths was two. Both occurred over 10 years after first exposure. The study group also had 1 non-Hodgkin's lymphoma survivor. No cases of Hodgkin's lymphoma were found. These findings are not strong enough either to show or to disprove increased risk of non-Hodgkin's lymphoma from such exposures. MRC Environmental Epidemiology Unit, University of Southampton, Southampton General Hospital, United Kingdom. Funding: International Agency for Research on Cancer (IARC).

Corrao, G., Calleri, M., Carle, F., Russo, R., Bosia, S. and Piccioni, P. Cancer risk in a cohort of licensed pesticide users. *Scandinavian Journal of Work and Environmental Health* 15(3): 203–209 (June, 1989).

25,945 male farmers in the southern Piedmont region of Italy, who had registered for licenses to buy and use pesticides of known toxicity, were the study subjects. The authors used hospital records to determine the incidence of various cancers. They also performed quality control studies to determine the reliability of the cancer diagnoses. The authors found an association between cancers of the lymphatic system and exposure to pesticides (SIR of 1.4 in the cohort as a whole; 45 cases found, 31.79 expected). The authors criticize their government's policy of requiring licenses for those substances that have high acute toxicity but not for those which pose long-term cancer risks. They also criticize the IARC working groups for failing to conclude that organic pesticides are carcinogenic. University of L'Aquila, Italy; University of Torino, Italy; Department of Worker Health Protection, Region Piedmont, Asti, Italy.

Dalager, N.A., Kang, H.K., Burt, V.L., and Weatherbee, L. (1991). Non-Hodgkin's lymphoma among Vietnam veterans. *Journal of Occupational Medicine* 33(7): 774–779 (July, 1991).

This analysis of the possible relationship between non-Hodgkin's lymphoma and military service in Vietnam showed no increased incidence in non-Hodgkin's lymphoma among Vietnam veterans. Service records of non-Hodgkin's lymphoma patients (men) treated in VA hospitals were compared with the service records of patients from VA hospitals who had other diagnoses. The authors note that their sampling methods, as well as changes in Veterans' Affairs policies concerning hospital treatment, might have affected the outcome of their study. Department of Veterans Affairs; Centers for Disease Control.

Dalager, N.A.; Kang, H.K.; Burt, V.L.; & Weatherbee, L. Hodgkin's disease and Vietnam service. *Annals of Epidemiology* 5(5): 400–406 (Sept. 1995).

The authors examined service statistics of those admitted to VA hospitals with Hodgkin's lymphoma, as well as controls with no cancer. They excluded from the study any veterans (both cases and controls) who were first hospitalized before 1975. (The Vietnam era is considered to be 1965 to March 1973, yet any cases occurring from 1965–1975 were not included.) The overall OR for Hodgkin's lymphoma among Vietnam veterans vs. those serving elsewhere was 1.28, but the authors do not consider this significant. They conclude that their data do not show a correlation between Hodgkin's lymphoma and Vietnam service, nor between Hodgkin's lymphoma and particular locations or types of service that might have resulted in more exposure to Agent Orange. Environmental Epidemiology Service, Dept. of Veterans Affairs; Centers for Disease Control, Natl. Center for Health Statistics; and VA Medical Center, Ann Arbor.

Dich, J., Zahm, S.H., Hanberg, A., & Adami, H-O. Pesticides and cancer. *Cancer Causes and Control* 8(3): 420–443 (1997).

These authors reviewed studies that cover the whole range of human and animal research on the carcinogenicity of pesticides. They conclude that organochlorine and organophosphorous compounds are associated with an increased risk of non-Hodgkin's lymphoma. The variable results obtained in studying both non-Hodgkin's and Hodgkin's lymphoma and other pesticides are discussed, as well as possible reasons for the variations in findings. Karolinska University Hospital, Stockholm, Sweden; U.S. National Cancer Institute; Karolinska Institute, Stockholm; Harvard School of Public Health.

Faustini, A.; Settimi, L.; Pacifici, R.; Fano, V.; Zuccaro, P.; & Forastiere, F. Immunological changes among farmers exposed to phenoxy herbicides: preliminary observations. *Occupational and Environmental Medicine* 53: 583–585 (1996).

Ten farmers who mixed and applied chlorophenoxy herbicides (including 2,4-D and 4-chloro-2-methylphenoxyacetic acid [MCPA]) were the subjects of this study. The researchers performed lymphocyte counts on the farmers' blood, using specialized methods to detect specific types of lymphocytes and their activity. This testing was performed before the pesticides were mixed and applied, one to 12 days after, and 50 to 70 days after. All ten of the farmers had reduced amounts of every type of lymphocyte in the days following their pesticide exposures. The greatest reductions occurred in lymphocyte types (CD8-DR, CTL, NK) which are thought to be important in cell protection and immunity to tumors. The ability of NK (natural killer) cells to carry out their functions was sharply reduced. By 50 to 70 days following pesticide exposure, all the lymphocyte test values had returned to normal limits, but had not reached the levels found before exposure. The authors conclude that exposure to these pesticides may cause immune system suppression and that more study is needed to clarify the health implications of this suppression, including cancer risk. Local Health Unit, Tarquinia (VT), Italy; Istituto Superiore di Sanita', Rome; Dept. of Occupational and Environmental Medicine, Linköping, Sweden; Epidemiologic Unit, Lazio Regional Health Authority, Rome.

Figgs, L.; Titenko-Holland, N.; Rothman, N.; Zahm, S.; Tarone, R.; Hill, R.; Smith, M.; Holmes, F.; & Blair, A. Occupational exposure to the herbicide 2,4-dichlorophenoxyacetic acid is associated with increased lymphocyte replicative index. Presented at the annual meeting of American Association for Cancer Research, Mar. 28–Apr. 1, 1998.

The researchers studied the lymphocytes of people who apply herbicides. They found that the lymphocyte replicative index (RI), a measure of the rate at which the body is producing lymphocytes, was significantly higher after spraying 2,4-D. (This means that many lymphocytes died after exposure to the pesticide, and had to be replaced rapidly. Rapid growth of lymphatic tissue in response to a toxic exposure, especially if the genetic content of the cells is damaged, may be related to the development of lymphoma.) The mean RI in these individuals was also significantly higher than that of controls (persons not exposed to the pesticide). St. Louis University; National Cancer Institute; Center for Disease Control and Prevention, Atlanta, GA; Univ. of California at Berkeley; Kansas Univ. Medical Center.

Fleming, L.E.; Bean, J.A.; Rudolph, M.; & Hamilton, K. Cancer incidence in a cohort of licensed pesticide applicators in Florida. *Journal of Occupational and Environmental Medicine* 41(5): 279–288 (April, 1999).

Men and women licensed to apply a wide variety of pesticides in Florida were studied. No increase in incidence of lymphoma was found, but a significant increase in genital cancers (testicular and prostate for men, cervical for women) occurred. The group studied was moderately large (34,211 persons over 18 years, totaling 279,397 person-years), and cancer incidence rather than mortality was used, but having a license to apply pesticides is only an indirect measure of pesticide exposure. University of Miami School of Medicine. Funding (partial): National Institute of Occupational Safety and Health.

Fontana, A.; Picoco, C.; Masala, G; Prastaro, C.; & Vineis, P. Incidence rates of lymphomas and environmental measurements of phenoxy herbicides: ecological analysis and case-control study. *Archives of Environmental Health* 53 (6): 384–387 (Nov./Dec. 1998).

This is a follow-up of Vineis et al. 1991, in which incidence of lymphoma relative to exposures to high levels of phenoxy herbicides in the soil was studied in certain regions of Italy. Besides updating data by locating newly-diagnosed cases, the authors conducted a case-control study, identifying occupations of people with lymphoma and controls who did not have cancer.

The study of residents of polluted areas again showed increased incidence of non-Hodgkin's lymphoma compared with areas that did not have high levels of pesticides in the soil. The case-control study showed the highest incidence of non-Hodgkin's lymphoma (OR = 4.3) in women who worked as rice weeders—an occupation which involves very high exposure to soil and the pesticides which, in that part of Italy, contaminate it. Local Unit of Public Health, Novara, Italy; Istituto di Anatomia Patologica dell'Universita Verona; IST, Genoa; Dipartimento di Scienze Biomediche e Oncologia Umana, Torino. Funding (partial): Europe Against Cancer programme; U.S. National Cancer Institute.

Gambini, G.F.; Mantovani, C.; Pira, E.; Piolatto, P.G.; & Negri, E. Cancer mortality among rice growers in Novara Province, northern Italy. *American Journal of Industrial Medicine* 31(4): 435–441 (April, 1997).

Mortality records of rice growers in a particular region of Italy were studied, since there is a known pattern of herbicide use in weeding rice fields (though data on individual exposures was not available). A slight excess of non-Hodgkin's lymphoma mortality was observed, all occurring among rice growers aged 65–79 who had been exposed to the herbicides for over 20 years. Numbers were small (4 deaths from lymphoma observed vs. just over 1 expected). The authors conclude that further long-term study is needed. Occupational Health Service, Ospedale Maggiore di Norvara, Italy; University of Turin, Italy; and the Institute of Pharmacological Research, Milan.

Garry, V.F., Danzl, T.J., Tarone, R., Griffith, J., Cervenka, J., Krueger, L., Whorton, E.B., & Nelson, R.L. Chromosome rearrangements in fumigant appliers: possible relationship to non-Hodgkin's lymphoma risk. *Cancer Epidemiology, Biomarkers & Prevention* 1(4): 287–291 (May/June 1992).

This highly technical study focused on chromosome breakage and rearrangements in circulating blood cells of pesticide appliers who were exposed to phosphine, a toxic gas used to fumigate grain storage facilities. Six of the appliers used phosphine almost exclusively in their work; the rest used multiple pesticides. Controls were healthy subjects not exposed to pesticides in their work. Men exposed mainly to phosphine and those exposed to multiple pesticides had significantly higher rates of chromosome rearrangement when blood was drawn during periods of pesticide application. Five of the six phosphine appliers chose to give up their work with this chemical, and the frequency of chromosomal rearrangements in these five individuals declined significantly after one year. Specific sites of breakage and rearrangement suggested to the researchers that this alteration of chromosomes may play a role in the increased risk of non-Hodgkin's lymphoma in people with occupational exposure to pesticides. Though the number of people studied was small and their occupational exposure to solvents and dusts may have been additional risk factors, the study provides evidence of chromosomal damage from pesticide exposure, possibly consistent in some cases with chromosomal changes found in non-Hodgkin's lymphoma cells (cancer cells). Univ. of Minn.; NCI; EPA; Univ. of Texas.

Green, L.M. A cohort mortality study of forestry workers exposed to phenoxy acid herbicides. *British Journal of Industrial Medicine* 48(4): 234–238 (April, 1991).

Men employed in the forestry industry in Ontario, Canada were studied. Instead of attempting to assess individual exposures, the author used employment in the forestry industry as an indication of exposure to phenoxy herbicides. No excess risk of non-Hodgkin's lymphoma—indeed, no mortality from non-Hodgkin's lymphoma—was found. The author notes that, because of the small size of the study group (1,222 men), "this study only had sufficient power to detect a sevenfold increase in

non-Hodgkin's lymphoma." The author concludes that the risk of non-Hodgkin's lymphoma from pesticide exposure is low and requires a long latent period, necessitating long-term studies with large numbers of people. Ontario Hydro (the electricity provider for the province of Ontario, Canada).

Hardell, L.; Eriksson, M.; Lenner, P.; & Lundgren, E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case-control study. *British Journal of Cancer* 43(2): 169–176 (Feb., 1981).

169 men diagnosed with lymphoma were matched with men from the community, using a 2:1 control:subject ratio. Pesticide exposures were ascertained using a questionnaire and/or interviewing relatives, as well as assessments of pesticide use in the pertinent industries and worksites. Results showed higher correlations between pesticide exposures and lymphoma than any previous studies (6-fold risk with exposure to phenoxyacetic acids or chlorophenols compared to non-exposure); analysis and reporting of data was very complex and somewhat fragmented. The author theorized that immunosuppressive and/or mutagenic effects of the pesticides and solvents might be involved. University Hospital, Umea, Sweden. Funding: Swedish Work Environment Fund.

Hardell, L. Relation of soft-tissue sarcoma, malignant lymphoma and colon cancer to phenoxy acids, chlorophenols and other agents. *Scandinavian Journal of Work and Environmental Health* 7(2): 119–130 (June, 1981).

In response to criticism of his earlier study, Hardell re-analyzed some of the data. A study of colon cancer, using similar methods, was undertaken to demonstrate that the questionnaire and interview methods used were sound and introduced no undue bias. The colon cancer study showed similar results to previous colon cancer studies. Hardell concluded that his original findings (significantly increased non-Hodgkin's lymphoma risk with exposure to phenoxy herbicides, chlorophenols, and solvents) were upheld. Dept. of Oncology, University Hospital, Umeå, Sweden.

Hardell, L. and Bengtsson, N.O. Epidemiological study of socioeconomic factors and clinical findings in Hodgkin's disease, and reanalysis of previous data regarding chemical exposure. *British Journal of Cancer* 48(2): 217–25 (Aug., 1983).

Hardell re-analyzed his data and included socioeconomic factors, as other studies have shown a correlation between Hodgkin's lymphoma in children and small family size/higher socio-economic status. He found no correlation between Hodgkin's lymphoma and social class, but did find an association between Hodgkin's lymphoma and exposure to phenoxy acids (such as herbicides), chlorophenols, and organic solvents (relative risks of 1.2 to 6.6, depending on level of exposure). The numbers used in this study were small (60 cases of Hodgkin's lymphoma, 335 controls). Dept. of Oncology, University Hospital, Umeå, Sweden. Funding: Research Foundation, Dept. of Oncology, University of Umeå, Sweden; Swedish Work Environment Fund.

Hardell, L.; Eriksson, M.; Degerman, A. Exposure to phenoxyacetic acids, chlorophenols, or organic solvents in relation to histopathology, stage, and anatomical localization of non-Hodgkin's lymphoma. *Cancer Research* 54(9): 2386–2389 (May 1, 1994).

Hardell and colleagues analyzed their 1981 data once again. When analyzed by broad occupational groups rather than by closer measures of pesticide exposure, the data show no significant correlation between non-Hodgkin's lymphoma and any kind of work, just as other studies done using occupational classifications to imply pesticide exposure have produced equivocal results.

An odds ratio of 5.5 was obtained for exposure to phenoxy herbicides, 4.8 for chlorophenol exposure, and 2.4 for solvents. Median latency periods ranged from 18 to 21 years. Örebro Medical Center, Örebro, Sweden.

Hardell, L. et al. A case-control study of non-Hodgkin lymphoma and exposure to pesticides. *Cancer* 85(6): 1353–60 (Mar., 1999).

Researchers studied 404 white males (both living and deceased) who had non-Hodgkin's lymphoma and 741 controls with no lymphoma, with regard to exposures to various pesticides, solvents, and other materials. Many kinds of pesticides, alone or in combination, appeared to increase the risk of non-Hodgkin's lymphoma; among the highest risks were fungicides (OR = 3.7) and the herbicide MCPA (a herbicide widely used as a weed killer, somewhat chemically similar to 2,4-D) (OR = 2.7 overall; 1.7 with lower exposures, 4.1 with higher exposures). Increased risk was also found with exposure to glyphosate, a herbicide used for home weed control in the U.S. (O.R. = 2.3, but based on a small number of cases). The highest risk of non-Hodgkin's lymphoma was seen 10 to 20 years after first exposure to pesticides, but lower risks were seen after 20 to 30 years or more. The authors suggest that the carcinogenic effect of these chemicals may be due to a combination of exposure to certain viruses in combination with a weakening of the immune system due to the chemical exposure. Department of Oncology, Örebro Medical Center, Sweden. Funding: Swedish Work Environment Fund, Swedish Medical Research Council, Örebro County Council Research Committee, Örebro Medical Center Research Foundation.

Hoar, S.K.; Blair, A.; Holmes, F.F.; Boysen, C.D.; Robel, R.J.; Hoover, R.; & Fraumeni, J.F. Jr. Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. *Journal of the American Medical Association* 256 (9), 1141–1147 (Sept. 5, 1986).

Cancer reporting is required by Kansas law, making it easier for researchers to find all cases of lymphoma there. The authors identified all newly-diagnosed cases (males only) of Hodgkin's and non-Hodgkin's lymphoma in the state from 1976–1982, and matched them with three controls each. All were interviewed carefully concerning pesticide use as well as other variables. Results showed that exposure to herbicides for over 20 days per year (in farm work) was associated with a sixfold increase in incidence of non-Hodgkin's lymphoma. Lesser increases were seen in farmers who had used herbicides for fewer days per year. Insecticides were also studied, and analyses suggested that herbicides, especially phenoxy herbicides such as 2,4-D, pose a greater risk for non-Hodgkin's lymphoma than do insecticides. National Cancer Institute.

Hoar Zahm, S., Weisenburger, D.D., Cantor, K.P., Holmes, F.F., & Blair, A. Role of the herbicide atrazine in the development of non-Hodgkin's lymphoma. *Scandinavian Journal of Work and Environmental Health* 19(2): 108–114 (1993).

Atrazine is the most commonly used pesticide in the U.S. and is considered a possible carcinogen. These researchers interviewed 993 white men with non-Hodgkin's lymphoma and 2,918 white men who did not have lymphoma in Iowa, Kansas, Minnesota, and Nebraska. Extensive statistical analysis, including correction for exposure to other pesticides, appears not to show a link between atrazine and non-Hodgkin's lymphoma. National Cancer Institute.

Hooiveld, M.; Heederik, D.J.J.; Kogevinas,M.; Boffetta, P.; Needham, L. L.; Patterson, D.G.; & Bueno de Mesquita, H.B. Second follow-up of a Dutch cohort occupationally exposed to phenoxy herbicides, chlorophenols, and contaminants. *American Journal of Epidemiology* 147(9): 891–901 (1998).

Workers in a chemical factory (1955–1985) were classified according to their chemical exposures. Some had been exposed to dioxin and other toxic chlorophenols released in an industrial explosion. The researchers also tested the blood dioxin levels of many of the workers. Results showed an increased incidence of cancer deaths in the group and an increased incidence of non-Hodgkin's lymphoma, though the number of cases was small (3 cases out of 140 workers). Two of these three cases of non-Hodgkin's lymphoma occurred in workers with high blood levels of dioxin. National Institute of Public Health and the Environment, The Netherlands; Wageningen Agricultural University; International Agency for Research on Cancer, Lyons, France; Institut Municiapal d'Investigació Mèdica, Barcelona; U.S. Centers for Disease Control. Funding: U.S. National Institute of Environmental Health Sciences.

Johnson, R.A., Mandel, J.S., Gibson, R.W., Mandel, J.H., Bender, A.P., Gunderson, P.D., & Renier, C.M. Data on prior pesticide use collected from self- and proxy respondents. *Epidemiology* 4(2): 157–164 (March, 1993).

In many studies of cancer and pesticide exposures, information is obtained by interviewing a spouse or family member (called a "proxy") if an individual under study is dead or incapacitated. In some studies, authors note differences in results from proxies vs. those obtained from actual patients. There are examples in which the risks from pesticides appear higher when proxies are questioned, and others where the risks appear lower when proxies are questioned. The authors conducted a study in which the responses of primary respondents were compared with the responses of proxies for the very same individuals. For this study, proxies might be spouses, other relatives, or friends and neighbors. Differences in response to interview questions were found, especially in the areas of specific pesticides used, time and mode of usage. These differences did affect ORs, though in varying ways. The authors cite the results of a study in which ORs were higher (Zahm et al Nebraska study) as evidence that the use of proxies must be studied, while results in which the ORs are lower, which the authors also mention, do not seem to concern them. MN Dept. of Health; Univ. of Minn; Park Nicollet Medical Center. Study supported in part by the Industry Task Force I on 2,4-D Research Data.

Keller-Byrne, J.E.; Khuder, S.A.; Schaub, E.A.; & McAfee, O. A meta–analysis of non-Hodgkin's lymphoma among farmers in the central United States. *American Journal of Industrial Medicine* 31(4): 442–444 (Apr., 1997).

Six studies of the incidence of non-Hodgkin's lymphoma in farmers from Iowa, Minnesota, Missouri, Illinois, and Ohio were selected for the meta-analysis. All studies had shown elevated ORs, but at varying levels (1.09 to 1.80). The OR for the six groups taken together was 1.34. When the oldest and largest study was omitted from the analysis, the OR was 1.39. The authors conclude that microorganisms or pesticides are responsible for an increase in non-Hodgkin's lymphoma incidence among American farmers. Medical College of Ohio, Toledo.

Khuder, S.A.; Schaub, E.A.; & Keller-Byrne, J.E. Meta-analyses of non-Hodgkin's lymphoma and farming. *Scandinavian Journal of Work and Environmental Health* 24(4): 255–261 (1998).

The authors selected 36 studies of non-Hodgkin's lymphoma and farming, and examined the results and differences among the studies. Case-control studies showed a higher correlation between non-Hodgkin's lymphoma and farming than did either mortality/incidence studies or cohort studies (relative risk of 1.19, 1.10, and 0.95 respectively). U.S. studies showed a higher risk (relative risk of 1.26) for farmers than foreign studies (relative risk of 1.02). Overall, the meta-analysis showed a

small but significant risk (1.10) of non-Hodgkin's lymphoma for farmers compared to the general population. Female farmers had a lower risk of developing non-Hodgkin's lymphoma (relative risk of 0.93). The authors suggest that multiple factors may affect farmers, including pesticides and infectious microorganisms; these factors may affect men more than women because of traditional divisions of labor on farms, resulting in higher exposures for men. Medical College of Ohio, Toledo.

Kogevinas, M.; Kauppinen, T.; Winkelmann, R.; Becher, H.; Bertazzi, P.A.; Bueno de Mesquita, H.B.; Coggon, D.; Green, L.; Johnson, E.; Littorin, M.; et al. Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols, and dioxins: two nested case-control studies. *Epidemiology* 6(4): 396–402 (July, 1995).

Only 32 cases of non-Hodgkin's lymphoma (found worldwide) were studied. They were matched with multiple controls. The authors evaluated the exposures of all these individuals to a long list of chemicals by using job records, company questionnaires, and company reports. Among people who had been exposed to phenoxy herbicides, they found an increase of soft tissue sarcomas (ORs of up to 11.27), but results for non-Hodgkin's lymphoma were less clear (some elevated ORs, but to a much lesser degree; highest OR was 1.85, and there were non-linear results with increasing exposures; sometimes lower ORs were found with higher exposures). The authors conclude that their results provide only weak evidence that exposed workers are at increased risk for non-Hodgkin's lymphoma, and note that exposure to multiple chemicals complicates the analyses. IARC, Lyon; Intitut Municipal d' Investigacio Medica, Barcelona; Institute of Occupational Health, Helsinki; German Cancer Research Center, Heidelberg; Clinica del Lavoro Luigi Devoto, Milan; National Institute of Public Health and Environmental Protection, Bilthoven; MRC Environmental Epidemiology, Univ. of Southampton; Ontario Hydro, Toronto; Tulane University Medical Center, New Orleans; Lund Univ., Sweden; Danish Cancer Registry, Copenhagen; National Institute for Occupational Safety and Health, Cincinnati; Menzies School of Health Research, Australia; Univ. of Vienna, Austria; Health and Safety Executive, UK; Wellington School of Medicine, New Zealand. Funding: Grant NO1-ES-9527, U.S. National Institute of Environmental Health Sciences.

Kristensen, P.; Andersen, A.; Irgens, L.M.; Bye, A.S.; & Sundheim, L. Cancer in offspring of parents engaged in agricultural activities in Norway: incidence and risk factors in the farm environment. *International Journal of Cancer* 65(1): 39–50 (Jan. 3, 1996).

Norway has a mandatory cancer case registry and a farm census with detailed information on farming practices. These records, considered highly accurate, allowed the authors to analyze the incidence of cancer in children of farmers and agricultural workers with regard to various farm-related exposures and farming practices. Many cancers were studied. The authors found a non-significant increase for Hodgkin's lymphoma in children of farmers and farm workers from farms with forestry activities, and an association between the mixed cell type of Hodgkin's lymphoma and chicken farming. For non-Hodgkin's lymphoma in these children, incidence levels followed a dose-response pattern (the more pesticides the parents purchased, the more lymphoma in their children). The authors state, "Our data suggest that parental use of pesticides in horticulture is a risk factor for non-Hodgkin's lymphoma in childhood." National Institute of Occupational Health, Oslo; Cancer Registry of Norway; Medical Birth Registry of Norway; Statistics Norway; Norwegian Crop Research Institute.

Kross, B.C.; Burmeister, L.F.; Ogilvie, L.K.; Fuortes, L.J.; & Fu, C.M. Proportionate mor-

tality study of golf course superintendents. American Journal of Industrial Medicine 29(5): 501–506 (May, 1996).

Golf course superintendents are exposed to many of the same chemicals and conditions as are farmers: pesticides, dusts, and years of exposure to sunlight. They were found in this study to have increased mortality from brain cancer and non-Hodgkin's lymphoma. The proportionate mortality ratio (PMR) for non-Hodgkin's lymphoma was 237 (approx. 2.37 times the incidence found in the general public). The authors note that their findings are consistent with other studies involving populations with occupational exposures to pesticides. University of Iowa.

Lampi, P.; Hakulinen, T.; Luostarinen, T.; Pukkala, E.; & Teppo, L. Cancer incidence following chlorophenol exposure in a community in southern Finland. *Archives of Environmental Health* 47(3): 167–175 (May-June 1992).

Järvelä, Finland was found to have a high concentration of chlorophenols in its drinking water and in a nearby lake. A local sawmill that used a fungicide on its lumber is thought to be the source of this chemical pollution. The authors studied various cancers. There was a significant increase in non-Hodgkin's lymphoma (over six times) among persons who had consumed the local drinking water and eaten fish from the polluted lake. The authors note that the levels of chlorophenols in the water were not far above the allowable levels in some countries, such as the United States and Canada. National Public Health Institute, Finland; Karolinska University Hospital, Stockholm; Finnish Cancer Registry, Helsinki.

Leiss, J.K. and Savitz, D.A. Home pesticide use and childhood cancer: a case-control study. *American Journal of Public Health* 85(2): 249–252 (Feb., 1995).

Pesticide exposures of 252 children diagnosed with cancer in the Denver area, plus 222 controls, were evaluated. Results were analyzed separately for exposure to home extermination, lawn treatments, and indoor pest strips, as well as for different types of cancer. The strongest association for lymphoma was exposure to yard insecticides (ORs of 1.2 to 1.8 depending on the age of a child at time of exposure). The number of cases was small, however. There was a relatively strong association between the use of pest strips and leukemias. State Center for Health and Environmental Statistics, Raleigh, NC; University of North Carolina, Chapel Hill.

Lynge, E. A follow-up study of cancer incidence among workers in manufacture of phenoxy herbicides in Denmark. *British Journal of Cancer* 52(2): 259–270 (Aug., 1985).

Lynge compiled data on men and women employed in two Danish chemical factories which make phenoxy herbicides. All workers were included, even those who made other chemicals and those who worked only in office jobs. She found an excess of soft tissue sarcomas in men (5 cases with only 1.84 expected) and no significant excess of lymphoma (7 cases with 5.37 expected). The study is rather small (3,390 men, 1,069 women), and there were wide variations in years employed at the chemical firms. No attempt was made to determine the amount of actual pesticide exposure. Institute of Cancer Epidemiology, Danish Cancer Society. Funding: Danish Work Environment Foundation.

Lynge, E. Cancer in phenoxy herbicide manufacturing workers in Denmark, 1947–87 – an update. *Cancer Causes and Control* 4(3): 261–272 (May, 1993).

Lynge added five more years of data to the previous study and focused on a single chemical factory. One person's disease was re-assigned as non-Hodgkin's lymphoma based on diagnos-

tic review. More detailed information on exact work sites/chemical exposures was obtained. Results were mixed: no increased incidence of non-Hodgkin's lymphoma was found among workers possibly exposed to phenoxy herbicides, but there was a "puzzling 3.5-fold excess risk" among workers employed in other manufacturing departments, including those producing dyes, pigments, and organic solvents. Increased risk for certain other tumors, including soft tissue sarcomas, was found. Lynge includes a 3-page table showing the results of studies of exposure to phenoxy herbicides and the risk of non-Hodgkin's lymphoma worldwide. Danish Cancer Society.

Lynge, E. Cancer incidence in Danish phenoxy herbicide workers, 1947–1993. *Environmental Health Perspectives* 106 (Supp. 2): 683–688 (April, 1998).

Five years later, Lynge published another update and concluded that her results showed no excess risk for non-Hodgkin's lymphoma among the workers, although they showed an increased risk of soft-tissue sarcomas. As before, the workers were considered "potentially exposed" based upon their assigned work areas in the factories. Actual exposures to the pesticides and other toxic chemicals were not determined. Danish Cancer Society.

McDuffie, H.H., Dosman, J.A., McLaughlin, J., Theriault, G., Pahwa, P., Choi, N.W., Fincham, S., Robson, D., Spinelli, J., Skinnider, L.F., & White, D. Non-Hodgkin's lymphoma (NHL) and pesticide exposure: Canada. *Proceedings of the American Association for Cancer Research* 35: A1721 (March, 1994). (Abstract only)

These researchers conducted a case-control study in Canada, obtaining information about pesticide exposures from 352 men with non-Hodgkin's lymphoma and 704 men who did not have lymphoma. A significantly higher incidence of non-Hodgkin's lymphoma was found in men with occupational exposures to any combination of herbicides, insecticides, fumigants, or fungicides. The risk of non-Hodgkin's lymphoma increased with increasing number of exposure hours per year. University of Saskatchewan, Canada.

Morrison, H.I., Semenciw, R.M., Wilkins, K., Yang Mao, & Wigle, D.T. Non-Hodgkin's lymphoma and agricultural practices in the prairie provinces of Canada. *Scandinavian Journal of Work and Environmental Health* 20(1): 42–47 (1994).

This is a follow-up to Wigle, et al. (see below). Records from the Census of Agriculture (Canada) were cross-referenced by computer with records from the Census of Population to look for any relationship between farm size, herbicide use, and non-Hodgkin's lymphoma. Results varied according to farm size, province, farming practices, and fuel and oil expenditures. The authors conclude that their findings show an association between herbicides and the risk of fatal non-Hodgkin's lymphoma. Laboratory Centre for Disease Control (Canada).

Mulder, Y.M., Drijver, M., & Kreis, I.A. Case-control study on the association between a cluster of childhood haemopoietic malignancies and local environmental factors in Allsmeer, The Netherlands. *Journal of Epidemiology and Community Health* 48(2): 161–165 (April, 1995).

The authors did a case-control study of a cluster of leukemia and lymphoma cases in a horticultural community. The number of subjects was small: 7 lymphoma cases and 7 leukemia cases. Age at diagnosis with lymphoma varied from 12 to 39. A questionnaire was used to identify risk factors. Several associations emerged; most notable was a history of swimming in a pond known to be polluted with DDT, polycyclic aromatic hydrocarbons, and benzene chemicals

associated with farming activities and with a nearby airport. There was a strong association between these cancers and the fathers' exposure to pesticides. Community Health Service Amstelland De Meerlanden; Community Health Service Zuid Kennemerland; National Institute for Public Health and Environmental Protection, The Netherlands.

Nanni, O., Amadori, D., Lugaresi, C., Falcini, F., Scarpi, E., Saragoni, A., and Buiatti, E. Chronic lymphocytic leukaemias and non-Hodgkin's lymphomas by histological type in farming-animal breeding workers: a population case-control study based on an a priori exposure matrices. *Occupational and Environmental Medicine* 53(10): 652–657 (Oct., 1996.)

In an earlier study, the authors noted a probable correlation between pesticide exposures and incidence of chronic lymphoctyic leukemia (CLL) and non-Hodgkin's lymphoma. In the present study, they analyzed numerous variables for 187 cases and nearly a thousand controls in an agricultural region of Italy. The methods were complex, involving ten different questionnaires depending upon which crops/animals were raised, plus estimates of types and amounts of exposures. The results were also complex. Increased ORs for CLL and non-Hodgkin's lymphoma were found with exposure to stannates (tin-containing compounds; OR of 2.44), arsenates (OR = 1.83), and to a lesser degree, for most other pesticides. When occupational titles alone were studied (for example, farmer vs. non-farmer), no correlations were found. Oncological Institute of Romagna, Italy; Medical Oncology Unit, Forli; Phytopathology Institute, Cesena; Department of Pathology, Forli; Epidemiology Unit, Center for Study and Prevention of Cancer, Firenze. Funding: Province of Forli; Emilia-Romagna Region; Italian League Against Cancer; Italian Association for Cancer Research; Ministry of Employment, Health, and Social Services, Rome.

O'Brien, T.R., Decouflé, P., & Boyle, C.A. Non-Hodgkin's lymphoma in a cohort of Vietnam veterans. *American Journal of Public Health* 81(6): 758–760 (June, 1991).

By examining the hospital records of a large cohort (18,313) of male Vietnam-era veterans who had died after discharge, the authors determined that Vietnam veterans had an increased risk of non-Hodgkin's lymphoma (7 fatal cases in Vietnam veterans vs. only 1 case in non-Vietnam veterans; similar numbers studied). None of the non-Hodgkin's lymphoma cases occurred in veterans who had served in areas thought to have Agent Orange exposure. The cause of the increased risk was unclear. Non-fatal cases of non-Hodgkin's lymphoma were not considered; neither were differences in socio-economic status, education, race, or wartime living conditions between Vietnam veterans and non-Vietnam veterans. U.S. Centers for Disease Control.

Olsson, H. and Brandt, L. Non-Hodgkin's lymphoma of the skin and occupational exposure to herbicides [letter]. *Lancet* 2(8246): 579 (Sep. 12, 1981).

Prompted by reports of a relationship between pesticides and cutaneous (skin) lesions as the site of non-Hodgkin's lymphoma, the authors report on their own lymphoma patients, from whom they obtained occupational histories. Of 5 male patients with skin lesions as the only detectable manifestation of non-Hodgkin's lymphoma, 4 (80%) had been actively spraying pesticides for 18 to 20 years. Of 118 male patients whose lymphomas had begun at other sites, only 7 (6%) had similar exposures. Though the numbers are small, this finding suggests a possible relationship between pesticide exposures and cutaneous non-Hodgkin's lymphoma. Dept. of Oncology, University Hospital, Lund, Sweden.

Pearce, N.E., Smith, A.H., Howard, J.K., Sheppard, R.A., Giles, H.J., & Teague, C.A.

Non-Hodgkin's lymphoma and exposure to phenoxyherbicides, chlorophenols, fencing work, and meat works employment: a case-control study. *British Journal of Industrial Medicine* 43(2): 75–83 (Feb., 1986).

Using the New Zealand Cancer Registry, the authors compared occupational exposures of 83 men who had non-Hodgkin's lymphoma with men having other cancers as well as with healthy men. A wide range of occupational and exposure variables were included, and the results were complex. Exposure to phenoxy herbicides did not result in significantly elevated odds ratios. Results in relation to chlorophenol exposure were unclear, since many of the men had been exposed to other chemicals as well. There was an increase in non-Hodgkin's lymphoma in men who had worked both in fencing (building and maintaining fences in rural areas) and in a meat processing plant (they had exposure both to arsenic compounds used in the treatment of fence posts, and exposure to various chemicals, animal viruses, etc. while processing meat and pelts). The authors noted possible synergistic effects of various exposures, and the difficulty in assessing multiple exposures. Wellington Clinical School of Medicine, Wellington Hospital, New Zealand; School of Public Health, Univ. of North Carolina, Chapel Hill; School of Public Health, Univ. of California, Berkeley. Funding: New Zealand Health Dept., War Pensions Medical Research Trust Board, Medical Research Council, Northern California Occupational Health Center.

Pearce, N.E., Sheppard, R.A., Smith, A.H., and Teague, C.A. Non-Hodgkin's lymphoma and farming: an expanded case-control study. *International Journal of Cancer* 39(2): 155–61 (1987).

In this follow-up study, the authors now included lymphosarcoma and reticulosarcoma patients, previously excluded, to facilitate comparisons with studies done by Hardell, 1981 and Hoar et al., 1986. No increased risk from exposure to phenoxy herbicides was found, but two groups – persons who had been engaged in both fencing work and meat works employment (OR 3.8), and orchard workers, (OR 3.7) showed rather sharply increased risks. The authors were puzzled as to the reasons why their results showed no increased risk from phenoxy herbicides, in contrast to earlier studies (such as Hardell, et al.). They felt that the high rates found in the fencing/meat workers and orchard workers might be a result of synergistic effects of co-carcinogens, including arsenic compounds which are used as pesticides in orchard work and in fencing. Univ. of North Carolina; Wellington Clinical School of Medicine, New Zealand; Univ. of Cal., Berkeley; Princess Alexandra Hospital, Australia.

Pearce, N. Phenoxy herbicides and non-Hodgkins lymphoma in New Zealand: frequency and duration of herbicide use. *British Journal of Industrial Medicine* 46: 143–144 (1989).

In this short update, Pearce added more subjects (all male, as before), and focused specifically on phenoxy herbicides. He found little increased risk of non-Hodgkin's lymphoma with increased numbers of years of exposure. A dose-response relationship between non-Hodgkin's lymphoma and numbers of days per year of using phenoxy herbicides was observed, but this finding was not consistent at the highest use level (over 20 days of use per year). Pearce's findings differed from those in the Swedish study (Hardell et al.), in which a strong correlation was found. He hypothesizes that differences in the spraying schedules may account for these differences. In Sweden herbicide use is concentrated in a 2 or 3 month period, but in New Zealand spraying is more intermittent. [An additional factor not mentioned is that in New Zealand, the workers were usually exposed to 2,4,5-T rather than to 2,4-D.] Wellington School of Medicine, New Zealand.

Persson, B., Dahlander, A., Fredriksson, M., Brage, H.N., Ohlson, C-G., & Axelson, O. Malignant lymphomas and occupational exposures. *British Journal of Industrial Medicine* 46: 516–520 (1989).

The authors found increased risks for both Hodgkin's lymphoma and non-Hodgkin's lymphoma in relation to exposure to phenoxy herbicides (a type of weed killer). However, the number of subjects was quite small; of all persons with lymphoma and controls (persons with no lymphoma) studied, only nine in total had been exposed to phenoxy herbicides. Increased risks were also found with welding work, exposure to solvents, exposure to wood (creosote suspected as a cause), and hairdressing as a career (hairdressers are exposed to manmade chemicals, including hair dyes). University Hospital and Örebro Medical Centre Hospital, Sweden.

Persson, B., Fredriksson, M., Olsen, K., Boeryd, B., & Axelson, O. Some occupational exposures as risk factors for malignant lymphomas. *Cancer* 72(5): 1773–8 (Sept. 1, 1993).

124 cases (a relatively small number) including both Hodgkin's lymphoma and non-Hodgkin's lymphoma, men only, were matched with men who did not have cancer. The number of occupational and other risk factors studied was large. The highest non-Hodgkin's lymphoma risks were found among lumberjacks (crude OR 7.0), workers exposed to raw wood (various occupations including sawmill workers, lumberjacks, and paper-pulp workers; OR 2.9) and persons exposed to phenoxy herbicides (crude OR 2.6). The authors note that their findings concerning elevated risks of non-Hodgkin's lymphoma in association with exposures to raw, untreated wood raise the question of whether naturally-occurring fungicides which are present in wood may be carcinogenic. Univ. Hosp., Linköping, Sweden. Funding: Local Cancer Fund, County of Östergötland; Swedish Cancer Society.

Riihimaki, V., Asp. S, & Hernberg, S. Mortality of 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid herbicide applicators in Finland. First report of an ongoing prospective cohort study. *Scandinavian Journal of Work and Environmental Health* 8(1): 37–42 (1982).

Using personnel records, the authors located 1,926 pesticide sprayers who had probably been exposed to 2,4-D and 2,4, 5-T. Causes of death were determined using the Finnish Central Statistical Office. Results showed no cases of non-Hodgkin's lymphoma in the group. The authors point out that their study cannot be used to show that phenoxy herbicides are or are not implicated in non-Hodgkin's lymphoma, because the number of people studied is too small, the exposures were brief and low, and the follow-up period too short. Institute of Occupational Health, Helsinki, Finland.

Ritter, L., Wigle, D.T., Semenciw, R.M., Wilkins, K., Riedel, D., & Mao, Y. Mortality study of Canadian male farm operators: cancer mortality and agricultural practices in Saskatchewan. *La Medicina del Lavoro* 81(6): 499–505 (1990).

73,538 male farm operators (the primary person who owns and operates a farm) in Saskatchewan, Canada were studied using census data and questionnaires. Mortality and cause-of-death data were obtained from the Canadian Mortality Data Base (non-fatal cases of lymphoma were not included). Although farm operators overall showed no increased risk of death from non-Hodgkin's lymphoma, certain subgroups had significant increases. Risk increased with the number of acres sprayed with pesticide in 1970 (a year for which data were available), and also with increasing annual fuel expenditure (up to a relative risk of 2.29 for farmers spending over $900 for fuel in 1970). An exception occurred with farms of over 1,000 acres sprayed with pesticide—risks were lower for this group than for farm operators with less

acreage. The authors speculate that when farms are quite large, spraying may be done by hired workers rather than by the farm operator. Fuel expenditures are possibly indicative of (1) increased exposure to pesticides due to extensive spraying using tractors and (2) exposure to diesel fumes, which could be significant alone or in conjunction with pesticide exposures. Environmental Health Directorate, Health Protection Branch, Laboratory Centre for Disease Control, Health and Welfare Canada, Ottawa.

Rothman, N., Cantor, K.P., Blair, A., Bush, D., Brock, J.W., Heizlsouer, K., Zaham, S.H., Needham, L.L., Pearson, G.R., Hoover, R.N., Comstock, G.W., & Strickland, P.T. A nested case-control study of non-Hodgkin lymphoma and serum organochlorine residues. *Lancet* 350: 240–244 (1997).

Using very sophisticated methods, these scientists compared the amounts of DDT and PCBs in the blood of persons who developed non-Hodgkin's lymphoma with the blood of healthy controls. An important factor in this study design is that the blood was obtained and frozen in 1974, before rather than after the disease had developed. Although increased incidence of non-Hodgkin's lymphoma with increased serum DDT was found, the results were not considered statistically significant. A stronger, significant relationship was detected between serum PCB levels and later development of non-Hodgkin's lymphoma. (Note: PCBs are mainly associated with electrical equipment rather than pesticides, but are similar in chemical nature to some organochlorine pesticides, and were sometimes mixed with pesticides as adhering or extending agents.) There was also a relationship between Epstein-Barr virus (in combination with PCBs) and non-Hodgkin's lymphoma. National Cancer Institute; Johns Hopkins University School of Hygiene and Public Health; National Center for Environ- mental Health, Centers for Disease Control and Prevention; and Georgetown University Medical School. Funding: Dept. of Health and Human Services grants CA60754 and ES03819; Research Career Award HL21670.

Saracci, R., Kogevinas, M., Bertazzi, P.A., de Mesquita, B.H.B., Coggon, D., Green, L.M., Kauppinen, T., L'Abbe, K.A., Littorin, M., Lynge, E., Mathews, J.D., Neuberger, M., Osman, J., Pearce, N., & Winkelmann, R. Cancer mortality in workers exposed to chlorophenoxy herbicides and chlorophenols. *Lancet* 338(8774): 1027–32 (October 26, 1991).

In this very large study (17,372 men, 1,537 women, and one person of unknown gender), 20 groups of workers employed in production or spraying of chlorophenoxy herbicides from 10 countries were included. Mortality was studied rather than incidence, so non-fatal cases of lymphoma were not included. No significant increase in death from lymphoma was found. The authors note that interpretation of the findings will be easier when the groups of workers have been followed for a longer time and more deaths have occurred. The authors are involved in epidemiological research and are employed by medical schools or government agencies. The primary author (Saracci) is associated with the Unit of Analytical Epidemiology, International Agency for Research on Cancer, Lyon, France. Funding: U.S. National Institute of Environmental Health Sciences.

Sathiakumar, N., Delzell, E., & Cole, P. Mortality among workers at two triazine herbicide manufacturing plants. *American Journal of Industrial Medicine* 29(2): 143–151 (Feb., 1996).

A slight increase in mortality from non-Hodgkin's lymphoma was found among workers directly exposed to triazines (triazine herbicides are widely used on corn crops). There were more deaths (3) among workers whose exposures were "definite or probable" than among those who had "possible" exposure (2 deaths).

The authors note two factors which might have weakened the study's ability to detect an increase in lymphoma: insufficient follow-up time and the omission of non-fatal cases. Dept. of Epidemiology, School of Public Health, University of Alabama at Birmingham.

Sathiakumar, N., & Delzell, E. A review of epidemiologic studies of triazine herbicides and cancer. *Critical Reviews in Toxicology* 27(6): 599–613 (1997).

The authors reviewed eleven studies on the relationship between triazine herbicides and cancer. They note that none of the studies included assessments of actual herbicide exposures; instead, the potential for exposure was assumed based on later questioning or on employment information. Most of the people who had used triazine herbicides had also been exposed to other pesticides. Although all the studies on non-Hodgkin's lymphoma and triazine herbicides showed excess incidence of the disease, and some showed increased incidence with increased years of exposure, these authors conclude that the associations are weak. No studies showed a relationship between triazines and Hodgkin's lymphoma. Dept. of Epidemiology, School of Public Health, University of Alabama, Birmingham.

Scherr,P.A.; Hutchison, G.B.; & Neiman, R.S. Non-Hodgkin's lymphoma and occupational exposure. *Cancer Research* 52(19 Suppl): 5503s–5509s (Oct. 1, 1992).

303 cases of non-Hodgkin's lymphoma (including patients, proxies, and parents) were interviewed, along with 303 controls, concerning their occupations, possible risk factors, and a wide range of general questions. Data were analyzed with regard to types of lymphomas. One unusual finding was a relative risk of 0.4 for Protestants as compared to all other religions and a relative risk of 3.1 for Jews (the risk in the total population would be expressed as 1.0, so Protestants only had 40% of the expected incidence of lymphoma, whereas Jews had over three times the expected incidence). [Ed. note: No theory or explanation is given for this finding. The authors did not report results for Roman Catholics or other religions.] For exposure to pesticides and insecticides, the authors found an increased risk for all lymphomas and a large risk for diffuse, large cell lymphoma in particular. There was a relative risk of 8.0 for diffuse large cell lymphoma for those having ever been exposed in their work to particles such as dust, sawdust, or fibers. This risk rose to 8.2 when adjusted for religion. Relative risk of 11.0 was found when all types of non-Hodgkin's lymphoma were correlated with a history of work as a carpenter or plumber; this risk rose to 13.2 when adjusted for religion. Mathematicians and programmers had a sharply decreased risk of lymphoma. The authors conclude that they "have found an increased risk of lymphoma among persons exposed to insecticides, pesticides, and particles such as dust" as well as people employed in the agriculture, forestry, fishing, construction, paper, wood, leather, and various building-material trades, such as carpenters, stone masons, etc. They note that in each of these occupations, workers had the possibility of exposure to chlorophenols or phenoxyacids (pesticides also associated with lymphoma in many other studies). Harvard School of Public Health; Boston University School of Medicine.

Smith, J.G. and Christophers, A.J. Phenoxy herbicides and chlorophenols: a case control study on soft tissue sarcoma and malignant lymphoma. *British Journal of Cancer* 65(3): 442–448 (March, 1992).

52 Australian men with lymphoma were matched with non-cancer and cancer controls, and interviews were conducted to determine pesticide exposures. The study took more than ten years to complete because of a poor response rate from prospective participants. Although results show increased risk of non-Hodgkin's lymphoma among those exposed to pesticides, with a dose-response effect, the authors conclude that with such a small sample,

their results do not support the hypothesis that exposure to chlorinated phenoxy herbicides or chlorophenols causes lymphoma. They found a correlation between smoking and lymphoma (though not between alcohol and lymphoma), but did not consider this to be significant either. Peter MacCallum Cancer Institute, Melbourne; University of Melbourne. Funding: Health Dept. of the State of Victoria, Australia.

Torchio, P.; Lepore, A.R.; Corrao, G.; Comba, P.; Settimi, L.; Belli, S.; Magnani, C.; & di Orio, F. Mortality study on a cohort of Italian licensed pesticide users. *Science of the Total Environment* 149: 183–191 (1994).

Using records of people who obtained licenses to apply pesticides and correlating these with death records, the authors studied death rates from various causes for a large number of people in a particular region of Italy. Overall, death rates were unusually low, due to what is called the "healthy worker effect." A slight increase in mortality from both Hodgkin's and non-Hodgkin's lymphoma was found in pesticide appliers (typically farmers) whose homes were in farmland areas, as opposed to woodland or village areas. The authors note that the mere possession of a license to apply pesticides is not indicative of exposure. They state that had they been able to limit the study to those who actually applied pesticides, the results might have showed a stronger association. University of L'Aquila, Italy; Istituto Superiore di Sanità, Roma; University Service of Cancer Epidemiology, Torino. Funding: Consiglio Nazionale delle Richerche [Italy] and the Piedmont Region [Italy].

Viel, J.F. and Richardson, S.T. Lymphoma, multiple myeloma and leukemia among French farmers in relation to pesticide exposure. *Social Science and Medicine* 37(6): 771–777 (1993).

By correlating mortality records for French farmers with amounts of pesticides used in 89 geographical areas ("départements"), the authors examined the effects of pesticide exposure on incidence of non-Hodgkin's lymphoma, leukemia, and multiple myeloma. Data were interpreted using complex statistical analyses. Results showed increased mortality with increased pesticide use for leukemia and for myeloma, but not for non-Hodgkin's lymphoma. The paper includes discussion of similar, earlier research worldwide. Public Health Department, Villejuif, France.

Vineis, P., Faggiano, F., Tedeschi, M., & Ciccone, G. Incidence of lymphomas and soft-tissue sarcomas and environmental measurements of phenoxy herbicides. *Journal of the National Cancer Institute* 83(5): 362–363 (March 6, 1991).

This study is unusual in that the authors had information concerning the levels of water and soil contamination with 2,4-D and 2,4,5-T (herbicides widely used in agriculture) in various regions of the Italian rice-growing provinces where their subjects live. A limited number of hospitals serves the area, so all cases of non-Hodgkin's lymphoma, Hodgkin's lymphoma, and soft-tissue sarcoma could be identified. Quite significant increases in non-Hodgkin's lymphoma incidence were found: (age-adjusted incidence rates of 5.7 to 18.2, compared to the rate of non-Hodgkin's lymphoma in the world population), with the highest rates of non-Hodgkin's lymphoma found in the "category B" area, which had the highest levels of pesticides in water and soil. Both males and females were included; males had a higher incidence of non-Hodgkin's lymphoma. The authors conclude that the excess of non-Hodgkin's lymphoma in this group is a result of the workers' exposures to the contaminated soil and water (in many nations, rice workers often walk barelegged through the wet fields). The authors plan to do a case-control study also (see Fontana et al.). Università di Torino, Italy. Funding: European Economic Community Europe Against Cancer Campaign, Associazione Italiana per le

Richerche sul Cancro, and Lega Italiana per la Lotta Contro i Tumori, Sezione Provinciale di Alessandria.

Weininger, R.B., Davis, G., & Hawks, C.D. Herbicides and cancer. *Journal of the American Medical Association* 257(17): 2292 (May 1, 1987).

This is a brief report on two neighboring rural counties in upstate New York. Using the local hospital tumor registry, the authors found that non-Hodgkin's lymphoma incidence was 15.3 new cases per 100,000 people per year, about 1 1/2 times that for the general U.S. population at that time. 2,4-dichloro-phenoxyacetic acid herbicides are widely used in their communities. The impetus for this study was Hoar et al. 1986. Columbia Memorial Hospital, Hudson, NY.

Weisenburger, D.D. Environmental epidemiology of non-Hodgkin's lymphoma in eastern Nebraska. *American Journal of Industrial Medicine* 18(3): 303–305 (1990).

The author, having noted an increase in non-Hodgkin's lymphoma (especially aggressive, diffuse large-cell subtype) in eastern Nebraska, conducted a study, using telephone interviews, of 201 men with non-Hodgkin's lymphoma and 725 controls. Results showed a 50% increased risk of non-Hodgkin's lymphoma with use of 2,4-D herbicide, with a threefold risk for those who were exposed to 2,4-D for 20 or more days per year. Increased risk of non-Hodgkin's lymphoma was also found for those exposed to organophosphates, carbamates, atrazine, or chlorinated hydrocarbons (all of these are pesticides). The paper also includes a discussion of contamination of the area's groundwater with pesticides and fertilizers. University of Nebraska Medical Center.

White, D., McDuffie, H.H., Pahwa, P., Gomez, S., Parker, R., & Dosman, J.A. Rural residence: a risk factor for non-Hodgkin's lymphoma in women? *Proceedings of the American Society for Clinical Oncology* 10: A390 (p. 131) (March, 1991). (Abstract only)

Since most researchers study men only, the authors began a study of women living in rural areas and also a case-control study of non-Hodgkin's lymphoma. Preliminary results show that rural women have significant exposure to grain dust, diesel exhaust, and pesticides, and that more non-Hodgkin's lymphoma cases occur in women living in rural areas than in the general population, with the most cases occurring among women spending the most years as rural dwellers. Saskatoon Cancer Clinic and Dept. of Medicine, University of Saskatchewan.

Wigle, D.T., Semenciw, R.M., Wilkins, K., Riedel, D., Ritter, L., Morrison, H.I., & Mao, Y. Mortality study of Canadian male farm operators: non-Hodgkin's lymphoma mortality and agricultural practices in Saskatchewan. *Journal of the National Cancer Institute* 82(7): 575–582 (April 4, 1990).

By linking government mortality records with farming census records, the authors studied the relationship between non-Hodgkin's lymphoma and variables which might be associated with differences in farmers' health, including acres sprayed with herbicides as well as many other factors. Overall death rate in this group of farmers was low, and individual exposures to pesticides could only be determined generally and indirectly. Still, increased risks of non-Hodgkin's lymphoma were associated with increased number of acres sprayed with herbicides in a "dose-response" relationship. The authors conclude that their results are consistent with an increased risk of non-Hodgkin's lymphoma in association with the spraying of herbicides. Laboratory Centre for Disease Control, Ottawa, Canada.

Wiklund, K., Dich, J. and Holm, L-E. Risk of malignant lymphoma in Swedish pesticide

appliers. *British Journal of Cancer* 56(4): 505–508 (1987).

Since 1965, Sweden has required pesticide appliers to complete a 4-day training course and obtain a license before handling toxic pesticides in agriculture. Records kept for this purpose allowed the authors to study 20,425 pesticide appliers. However, the mean follow-up time was only 12.2 years. The authors found a very small, non-significant increased risk of Hodgkin's lymphoma and no increased risk of non-Hodgkin's lymphoma. A slight increasing trend in risk for both non-Hodgkin's lymphoma and Hodgkin's lymphoma was found with increased time of holding a license to apply pesticides. It was noted that the majority of pesticide appliers were farmers. The authors note that persons with pesticide-applying licenses have higher exposures to phenoxy herbicides than do other farmers. They suggest that a longer time of follow-up would be of value. Depts. of Cancer Epidemiology and General Oncology, Karolinska Hospital and Institute, Stockholm, Sweden.

Wiklund, K., Lindefors, B.-M., & Holm, L.-E. Risk of malignant lymphoma in Swedish agricultural and forestry workers. *British Journal of Industrial Medicine* 45: 19–24 (1988).

Over 350,000 Swedish men employed in agriculture or forestry were followed for 18 years using a national cancer registry. Overall, the group showed no increased incidence of non-Hodgkin's lymphoma, nor did any of the subgroups. Increased incidence of Hodgkin's lymphoma was found in the "silviculture" (forestry maintenance) group and also among mink farmers and poultry breeders. The authors note that veterinarians have an increased incidence of Hodgkin's lymphoma, raising questions about a possible viral cause. Depts. of Cancer Epidemiology and General Oncology, Karolinska Hospital and Institute, Stockholm, Sweden.

Woods, J.S., Polissar, L., Severson, R.K., Heuser, L.S., and Kulander, B.G. Soft tissue sarcoma and non-Hodgkin's lymphoma in relation to phenoxyherbicide and chlorinated phenol exposure in western Washington. *Journal of the National Cancer Institute* 78(5): 899–910 (May, 1987).

In this case-control study, men with non-Hodgkin's lymphoma were identified through a state tumor registry and matched with controls of similar age who did not have cancer. Both groups were asked about their occupational backgrounds, health histories, and pesticide exposures. The authors performed an extensive array of statistical analyses and various breakdowns of the study groups. An increased risk of non-Hodgkin's lymphoma was found among men with certain occupational exposures to phenoxy herbicides (a type of weed killer), organochlorine insecticides (certain insect sprays), organic solvents (chemicals used to dissolve other substances), and other chemicals used in agricultural, forestry, or wood product work. Relationship of non-Hodgkin's lymphoma to immune system diseases, to past treatment with immunosuppressive drugs, to chloracne, and to exposure to routine weed spraying was also examined. The authors conclude that a compromised immune system is a very significant risk factor for non-Hodgkin's lymphoma, and speculate that prolonged exposure to phenoxy herbicides may contribute to the development of non-Hodgkin's lymphoma in individuals who have some additional challenge to their immune systems. Battelle Human Affairs Research Centers, Seattle; Fred Hutchinson Cancer Research Center, Seattle; Swedish Hospital Medical Center. Funding: National Cancer Institute. [Ed. note: Dow Chemical Company researchers Bloeman et al. (above), cite this study (Woods et al.) as an example of studies which do not support a possible association between non-Hodgkin's lymphoma and phenoxy herbicides].

Zahm, S.H., Weisenburger, D.D., Babbitt, P.A., Saal, R.C., Vaught, J.B., Cantor, K.P., &

Blair, A. A case-control study of non-Hodgkin's lymphoma and the herbicide 2,4-dichloro-phenoxyacetic acid (2,4–D) in eastern Nebraska. *Epidemiology* 1(5): 349–356 (1990).

By using cases of non-Hodgkin's lymphoma rather than mortality data, and by questioning cases and controls closely concerning use of and exposure to pesticides, these researchers eliminated some of the weaknesses affecting some other studies. 201 white men with non-Hodgkin's lymphoma were matched with three times as many controls. No correlation was found between simply working on a farm and non-Hodgkin's lymphoma, but men who mixed or applied 2,4-D had an elevated risk (1.5 times the risk of lymphoma as the controls). Farmers who failed to change into clean work clothes after using 2,4-D had higher risk of lymphoma than those who did change clothes; this is another example of how pesticide exposures may vary among individuals in ways that are not detected by measures such as occupational category or number of days working with the substance. Exposure to organophosphates (a type of pesticide used in farming) had an independent effect of increased non-Hodgkin's lymphoma risk. National Cancer Institute. Funding: National Cancer Institute and State of Nebraska Department of Health.

Zahm, S.H., Babbitt, P.A., Weisenburger, D.D., Blair, A., Saal, R.C., & Vaught, J.B. The role of agricultural pesticide use in the development of non-Hodgkin's lymphoma in women. *Archives of Environmental Health* 48(5): 353–358 (Sept./Oct. 1993).

This is one of only a few studies on pesticides and lymphoma that is focused on women. Many variables were examined, and the findings were complex. Merely living on a farm did not increase the risk of non-Hodgkin's lymphoma, but personally handling several types of pesticides (chlorinated hydrocarbons, organophosphates, and others) did. The highest rates of non-Hodgkin's lymphoma were found among women who had personally handled/applied pesticides and also had close relatives (mother, father, sister, brother) with histories of lymphatic or blood cancers. National Cancer Institute, University of Nebraska, Westat, Inc.

Zahm, S.H. Mortality study of pesticide applicators and other employees of a lawn care service company. *Journal of Occupational and Environmental Medicine* 39(11): 1055–1067 (1997).

Following publication of Dr. Zahm's 1986 study of Kansas farmers (see Hoar, 1986), ChemLawn Services asked the National Cancer Institute to study the mortality of their employees, many of whom are exposed to multiple pesticides in their work. Zahm examined records for about 32,600 employees. Preliminary results indicate a slight increase in deaths from non-Hodgkin's lymphoma over the expected numbers for this group. There were four deaths from non-Hodgkin's lymphoma, three of them men aged 24-35 who applied pesticides to lawns; two of these had been employed for three or more years. Zahm points out that, since the average age at diagnosis of non-Hodgkin's lymphoma is 64 years old in other studies, the young age of ChemLawn employees being studied may not have allowed the study to adequately assess the risks. As the study continues, the aging of the employee group will increase the study's future power to detect any excess of non-Hodgkin's lymphoma. National Cancer Institute.

Letters, Comments and Reports

Axelson, O. Seveso: disentangling the dioxin enigma? *Epidemiology* 4(5): 389–392 (Sept.1993).

These editorial remarks by a Swedish researcher offer a clear, open-minded overview of the ongoing issues concerning cancer and pesticide exposures.

Blair, A. and Zahm, S.H. Methodologic issues in exposure assessment for case-control studies of cancer and herbicides. *American Journal of Industrial Medicine* 18(3): 285–293 (1990).

This article is useful reading for anyone wondering why there are variations in results among the many case-control studies of pesticides and lymphoma. The authors discuss the factors and research challenges which may produce differing results, and note that in most instances, errors will fall in the direction of discovering less exposure to pesticides, and less correlation with cancer, than actually exist. National Cancer Institute.

Blair, A. Herbicides and non-Hodgkin's lymphoma: new evidence from a study of Saskatchewan farmers. *Journal of the National Cancer Institute* 82(7): 544–545 1990). [This is an editorial comment on Wigle et al.]

Commenting on the discrepancies among studies, as well as the "dilemma to the scientific community in how to draw conclusions regarding carcinogenicity of a substance when the epidemiologic and experimental data do not agree," Blair points out that exposure to a pesticide is difficult to measure (i.e., pesticides are absorbed through the skin, so studying amounts sprayed in the neighborhood may not tell the story), and that the cancer-causing mechanism of DNAdamage, studied experimentally, may not be the same mechanism by which phenoxy herbicides cause lymphoma. Yet, correlations between exposure to pesticides and lymphoma incidence and/or mortality are found. National Cancer Institute.

Blair, A., and Zahm, S.H. Overinterpretation of small numbers in the Dow 2,4-D cohort study. *Journal of Occupational and Environmental Medicine* 37(2): 126–127 (1995).

Blair and Zahm criticize Bloeman et al. (authors of a Dow Chemical Co. study) for drawing conclusions from the absence of deaths from lymphoma in their study. The Bloeman et al. study group was so small (878 people) that only 0.3 deaths from lymphoma would have been expected in a random population of the same size. Therefore, a doubling of deaths from lymphoma (for instance) would still possibly amount to no deaths at all, and it is misleading to note their absence as being meaningful. Bloeman et al. respond in turn that their article had not implied anything inappropriate. National Institutes of Health.

Coggon, D. and Acheson, E.D. Do phenoxy herbicides cause cancer in man? *Lancet* 1 (8280): 1057-1059 (May 8, 1982).

The authors review much of the worldwide scientific literature up to 1982, including the work of Hardell, who found a strongly increased risk of lymphoma among people exposed to certain pesticides. The main conclusion: some researchers have found an increased risk, so more studies are needed. University of Southampton, MRC Epidemiology Unit, Southampton, England.

Colton, T. Herbicide exposure and cancer. *Journal of the American Medical Association* 256: 9, 1176–1178 (Sept. 5, 1986).

This article is an editorial comment on the research to that date regarding the possible relationship between phenoxyacetic herbicides (such as 2,4-D) and various forms of cancer, including lymphoma. Colton discusses the work of Hardell in contrast to that of Hoar (a study headed by Hoar is published in the same issue), as well as the confusion regarding Agent Orange and Vietnam veterans. He gives a clear and useful explanation of the various study methods (such as case-control studies vs. proportional mortality studies), and discusses other factors related to study size and the difficulty of finding a large enough cohort to detect an increased incidence of non-Hodgkin's lymphoma, a disease which has a relatively low incidence in the general population. While he praises the methods used by Hoar et al., Colton states, "Perhaps the question will never be answered entirely satisfactorily." Boston University School of Public Health.

Cozen, W., and Bernstein, L. [untitled] Comments on Palackdharry [see below]. *Oncology* 8(8): 77–78 (August, 1994).

The authors agree with both Palackdharry and Longo concerning possible causes of the recent increase in the incidence of non-Hodgkin's lymphoma, with some exceptions and differing emphases. They note an increase in lymphomas which originate at sites other than lymph nodes, and the variability of results in studies of pesticide exposures and non-Hodgkin's lymphoma. They question whether exposure to specific animal viruses might also be a factor in some farm populations, and suggest immunosuppression resulting from exposure to ultraviolet radiation (sunlight) as a possible factor in non-Hodgkin's lymphoma. University of Southern California.

Crosignani, P., & Berrino, F. Re: "Role of the herbicide atrazine in the development of non-Hodgkin's lymphoma" by S. Hoar Zahm, D.D. Weisburger, K.P. Kantor, F.F. Holmes, & A. Blair. Scandinavian Journal of Work and Environmental Health 1993; 19:108–14. *Scandinavian Journal of Work and Environmental Health* 20(3): 223–226.

This article is a response to Hoar Zahm et al., same journal, 1993. The authors believe that the conclusions of the Hoar Zahm group were too conservative, and that the data could have been analyzed differently (more indicative of a causal relationship between atrazine and non-Hodgkin's lymphoma). Issues raised include confounding effects due to exposure to multiple pesticides and the likelihood of toxicity/mutagenicity based upon laboratory-based knowledge of atrazine. The authors also point out that measuring the farmers' exposure to atrazine by counting the number of days they spend applying it may be misleading, since atrazine stays in the fields for a long time and the farmers are also exposed to it while they are cultivating, harvesting, cleaning equipment, etc. The Hoar Zahm group responded that they had considered all of these issues. For the public, this kind of open discussion serves mainly to illustrate the difficulties involved in conducting and evaluating research. Epidemiology Unit, National Cancer Institute, Milan, Italy.

Gough, M. Human health effects: what the data indicate. *The Science of the Total Environment* 104(1–2): 129–158 (1991).

Mr. Gough reviewed much of the research through 1990 concerning pesticide-cancer links, and decided that there wasn't a significant causal relationship. He was particularly critical of Hardell's early work in Sweden, which was not replicated elsewhere for some years. Based upon the studies he cited, Gough questioned the links between dioxin and cancer. He did indicate (p. 152) a link between 2,4-D and lymphoma. His main concern is the near impossibility, in his view, of establishing a clear causal link to pesticide exposure in any particular case or cases of disease, failing stronger associations

and more consistent study results. Center For Risk Management, Washington, D.C.; later, Office of Technology Assessment, U.S. Congress.

Hardell, L. Malignant lymphoma of histiocytic type and exposure to phenoxyacetic acids or chlorophenols [letter]. *Lancet* 1(8106): 55–56 (Jan. 6, 1979).

This letter describes a study of 17 male patients with histiocytic lymphoma. 14 of the 17 worked in occupations involving pesticides. A table shows 11 patients with lymphoma (mostly in unusual sites), all of whom had been exposed to pesticides in the past, about 15 years before diagnosis. [Hardell published on similar subjects in 1977 — "describing several patients with soft-tissue sarcomas and previous exposure to phenoxyacetic acids" (Hardell, L., Läkartidningen 74: 2753, 1977) and "Malignant mesenchymal tumors and exposure to phenoxy acids—a clinical observation" (Hardell, L., Läkartidningen 74: 2853).] University Hospital, Umeá, Sweden.

Hardell, L. and Axelson, O. Phenoxyherbicides and other pesticides in the etiology of cancer: some comments on Swedish experiences. In: *Cancer Prevention. Strategies in the Workplace.* Becker, C.E. & Coye, M.J., eds. Washington, D.C.: Hemisphere Publishing Corporation: 107–119 (1986).

The Swedish authors discuss their research findings and the international debate concerning their validity. Included is a discussion of the methods used and whether they might have been subject to error. They note the longer latency periods in the Swedish studies compared to some of the American studies. The authors explain that the unusually complete information on cancer cases and pesticide use which is available in Sweden allows researchers to perform their studies using actual pesticide exposures rather than broad occupational categories. They suggest that some scientists who have been critical of the Swedish studies or who have questioned the results may have failed to understand these differences. The authors conclude that they have indeed uncovered significant cancer risks. University Hospital, Umeå, Sweden.

Hardell, L. and Eriksson, M. Non-Hodgkin's lymphoma and previous exposure to hexachlorophene: a case report [letter]. *Journal of Occupational Medicine* 34(8): 849–850 (Aug., 1992).

The authors found a cluster of 8 cases of non-Hodgkin's lymphoma in which all had been exposed to hexachlorophene through work exposure in the healthcare field. (Hexachlorophene was widely used as a skin cleanser before its toxicity was recognized.) Latency periods varied from 15 to 28 years. This finding may be relevant to the pesticide/non-Hodgkin's lymphoma issue, since hexachlorophene (formerly widely used as a skin cleanser) is an organochlorine and, like some pesticides, contains small amounts of dioxin (which occurs as a contaminant during the chemical manufacturing process) and also has direct toxic effects aside from the effects of the dioxin. Örebro Medical Center Hospital, Sweden.

Hardell, L. Phenoxy herbicides, chlorophenols, soft-tissue sarcoma (STS) and malignant lymphoma [letter/comment]. *British Journal of Cancer* 67(5): 1154–56 (1993).

This is a response to Smith and Christopher's study (1992). Hardell says that their conclusions should be regarded with caution because Smith and Christopher had very few cases; the response rate was low (only 56%–70% of those approached were willing to respond); and because Smith and Christopher did find increased risk among those who were exposed to phenoxyacetic acids or chlorophenols for over 30 days (compared to those who were exposed for fewer days). Referring to three other studies recently published in leading journals, Hardell

notes that there have been few significant results from studies which estimate exposures using occupational categories rather than assessing of actual pesticide exposures. Örebro Medical Center, Sweden.

Hardell, L.; Liljegren, G.; Lindstrom, G.; & van Bavel, B. Polychlorinated biphenyls, chlordanes, and the etiology of non-Hodgkin's lymphoma. *Epidemiology* 8(6): 689 (Nov., 1997).

Many pesticides and similar organic toxins are stored in fatty tissues. This letter elaborates on the results of a case-control study done earlier by this group of scientists in which the levels of some organochlorines (this chemical group includes several pesticides) in fatty tissues were compared in people with non-Hodgkin's lymphoma and in people who had no lymphoma. They found that people with non-Hodgkin's lymphoma had higher level of PCBs and chlordanes than the control group. PCBs (bichlorinated phenyls) are not pesticides; they are industrial chemicals formerly used in electrical equipment (such as transformers) and as coolants, etc. They may cause impairment of immune functioning. Their use was banned in 1977, but these chemicals have a strong ability to persist and are still found in the environment, in food, and in human tissues. Occupational exposures were not the cause of the increased levels of PCBs in the subjects of this study. Örebro Medical Center, Örebro, Sweden.

Hardell, L., Lindstrom, G., van Bavel, B., Fredrikson, M.; & Liljegren, G. Some aspects of the etiology of non-Hodgkin's lymphoma. *Environmental Health Perspectives* 106 (Supp. 2): 679–681 (April, 1998).

The researchers discuss various individual and environmental factors which have been found in association with increased incidence of non-Hodgkin's lymphoma, including exposures to certain pesticides; higher than usual levels of PCB's, dioxin, and chlordane in fatty tissues; blood transfusions; viruses; and various medical conditions which depress immune functioning. They suggest that impairment of immune response is a common thread linking all these possible causes of lymphoma, and that interactions between immune response and other factors should be further studied. Örebro Medical Center, Sweden.

Hoffman, W. Organochlorine compounds: risk of non-Hodgkin's lymphoma and breast cancer? *Archives of Environmental Health* 51(3): 189–192 (1996).

This is an overview of 42 epidemiologic studies and basic scientific studies on the possible relationship between organochlorine compounds (often used as pesticides) and cancer. (Ed. note: Basic scientific studies include a wide range of lab studies involving cell growth using either test tubes or animals, chromosome studies, etc., whereas epidemiologic studies focus on the actual occurrence of the disease among humans.) Mechanisms of cancer causation and/or promotion are also discussed. Hoffman notes the variations in findings when different study methods are used, including the findings of higher risks when more detailed measures of pesticide exposure are used. He concludes that organochlorines, in particular herbicides such as 2,4-D, pose a significant risk of non-Hodgkin's lymphoma as well as breast cancer. He recommends a ban on their use. School of Public Health/Dept. of Epidemiology, University of North Carolina at Chapel Hill. Funding: German Academic Exchange Organization in the "Sonderprogramm Epidemiologie".

IARC working group on the evaluation of carcinogenic risks. Occupational exposures in spraying and application of insecticides. *IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans* 53: 45–92 (1991).

This report on people's occupational exposures to insecticides describes what pesticides are used for—worldwide—their various application

methods, and the different amounts of insecticides that people are exposed to depending upon application methods used. Some studies of pesticides and various cancers are mentioned, including several on lymphoma and pesticides. The authors conclude that "there is limited evidence that occupational exposures in spraying and application of nonarsenical insecticides entail a carcinogenic risk." (Arsenic compounds are known to be carcinogenic.) International Agency for Research on Cancer (World Health Organization).

IARC working group on the evaluation of carcinogenic risks. Occupational exposures to chlorophenols. *IARC Monographs Eval Carcinog.Risk Chem. Hum.*41: 319–356 (1986).

This is a long and detailed overview of the kinds of exposures that workers may experience in the manufacture and use of chlorophenols, which are used as pesticides in many settings. (Chlorophenol compounds include 2,4-dichlorophenoxyacetic acid [2,4-D], 2,4,5-T, 2,4,6-T, and at least 14 others which are available commercially.) The authors reviewed some of the literature on lymphoma. Their final evaluation: "There is limited evidence for the carcinogenicity of occupational exposure to chlorophenols to humans." International Agency for Research on Cancer (World Health Organization).

IARC working group on the evaluation of carcinogenic risks. Occupational exposures to chlorophenoxy herbicides. IARC *Mongraphs Eval Carcinog Risk Chem Hum* 41: 357–406 (1986).

Covering much of the same ground as the monograph above (but with an emphasis on herbicides rather than chlorophenols in general), the authors discuss the structure, manufacture, and occupational exposures to phenoxy herbicides, including the use of Agent Orange in Vietnam. Urinary concentrations found in various categories of workers are included, as are the results of experiments in which volunteers ingested phenoxy herbicides or allowed these herbicides to be applied to their skin, and then clearance from the body was evaluated. The material on lymphoma is nearly identical to that in the above monograph, as is the final opinion. International Agency for Research on Cancer (World Health Organization).

Ibrahim, M.A., Bond, G.G., Burke, Cole, P., Dost, F.N., Enterline, P.E., Gough, M., Greenberg, R.S., Halperin, W.E., McConnell, E., Munro, I.C., Swenberg, J.A., Zahm, S.H., & Graham, J.D. Weight of the evidence on the human carcinogenicity of 2,4-D. *Environmental Health Perspectives* 96: 213–222 (1991).

This group examined the published research on 2,4-D (a phenoxy herbicide) and cancer. They reviewed issues and controversies, case-control studies (in which each person with cancer is compared with one or more people who do not have cancer), and cohort studies (in which a group of people sharing some characteristic or circumstance are studied for their incidence of cancer compared to those not exposed). They found that, generally, evidence for a cause-effect relationship between 2,4-D and cancer was weak, but that some studies which focused on non-Hodgkin's lymphoma tended to show a stronger link. Eleven of the thirteen scientists concluded that 2,4-D is a possible carcinogen. Various universities; National Cancer Institute; Dow Chemical Co.; Office of Technology Assessment; NIOSH. Panel funded through the National Wheat Growers Foundation by a grant from the Industry Task Force II on 2,4-D Research Data; meetings were held at an American Chemical Society facility.

James, W.H. Further evidence that pesticides or herbicides cause non-Hodgkins lymphoma. *Journal of the National Cancer Institute* 83(19): 1420–1 (Oct. 2, 1991).

James poses this question: are alterations in sex hormones in men exposed to certain pesticides

related to findings concerning the altered ratio of male/female offspring born to men with non-Hodgkin's lymphoma (more female children)? He notes that at least one pesticide (1,2-dibromo-3-chloropropane/DBCP) has been shown to cause high gonadotropin levels and sterility in exposed males. He suggests that both the sex hormone alterations and the lymphoma could be caused by the pesticide exposures. (DBCP, a soil fumigant for killing worms that harm crops, was formerly used on tomatoes and grapes, especially in California, but in 1979 the U.S. EPA banned all uses except for pineapples in Hawaii.) University College of London.

Johnson, E.S. Association between soft tissue sarcomas, malignant lymphomas, and phenoxy herbicides/chlorophenols: evidence from occupational cohort studies. *Fundamental and Applied Toxicology* 14(2): 219–234 (Feb., 1990).

Johnson reviews many studies and, believing that workers in pesticide manufacturing plants experience higher exposure levels than do those who spray pesticides, compares these two groups of studies (pesticide factory workers vs. pesticide appliers). He finds no convincing evidence that the presumed higher exposures produce a higher incidence of lymphoma than do lower exposures, but remarks that the factory cohorts are small and the latency periods too short. He notes that all groups studied had multiple exposures to many potential carcinogens. He believes the evidence of a pesticide/lymphoma link is weak. National Institute of Enviromental Health Sciences, Epidemiology Branch, North Carolina.

Levin, P.H. and Hoover, R. The emerging epidemic of non-Hodgkin's lymphoma: current knowledge regarding etiological factors. *Cancer Epidemiolgy, Biomarkers, and Prevention* 1: 515–517 (1992).

This is a report of a National Institutes of Health conference on research directions and findings concerning the rapid increase in incidence of non-Hodgkin's lymphoma. By the time of the conference (1991), non-Hodgkin's lymphoma had become the sixth most common malignancy for both men and women in the U.S. A variety of theories and research results were presented and discussed, including studies on viruses, pesticide exposures, HIV, immune diseases, the typing of lymphomas, relation of cell type to possible cause, genetic factors, etc. This technical report is an overview of research directions and scientific thought on non-Hodgkin's lymphoma. National Cancer Institute.

Longo, D.L. [Untitled] Comments on Palackdharry. *Oncology* 8(8): 73–77 (August, 1994).

Longo agrees with the Palackdharry article linking pesticides and lymphoma, and adds comments from his own perspective. He regards "chronic exposure to man-made chemicals designed to control the environment" as a major cause of the increase in non-Hodgkin's lymphoma. He discusses the particular vulnerability of lymphocytes to chemicals as well as the effects of HIV infection, aging, medical treatments (including chemotherapy for other cancers), viruses, and autoimmune disorders, noting, "It appears that either too much or too little immune reactivity is bad for you." Longo mentions the work of Scherr, et al. (1992) in which certain occupations such as the agricultural, forestry, and fishing industries were associated with increased incidence of lymphoma. After briefly reviewing the research concerning possible causes and the ways in which lymphoma develops within cells, he points out that more knowledge is needed about all the various causes of non-Hodgkin's lymphoma, especially in view of the recent increase in incidence. National Cancer Institute.

Markovitz, A. and Crosby, W.H. Chemical carcinogenesis. A soil fumigant, 1,3-dichloropropene, as possible cause of hematologic malignancies. *Archives of Internal Medicine* 144(7): 1409–1411 (1984).

This is an unusual case report. In April, 1973, nine firemen who cleaned up a truck spill of 1,3-dichloropropene (a pesticide used to kill worms in soil) were treated for toxic symptoms. Of the nine firemen, two became ill in October, 1979. Both were found to have developed histiocytic non-Hodgkin's lymphoma. Both died in early 1980. In a third case, a farmer was exposed to 1,3-dichloropropene for 30 days (it leaked onto him continually from a broken hose on his equipment). He developed acute myelomonocytic leukemia. A year later, when he again applied the same chemical to his fields and was again exposed, the leukemia became very agressive and he died. The authors note that a case report of this kind can only serve as an alert. UCLASchool of Medicine and Medical Corps; Walter Reed Army Institute of Resarch.

Morrison, H.I.; Wilkins, K.; Semenciw, R.; Mao, Y.; Wigle, D. Herbicides and cancer. *Journal of the National Cancer Institute* 84(24): 1866–1874 (Dec. 16, 1992).

This well-organized review of the studies on herbicides and cancer includes tables that show the types of studies done, locations, dates, and types of cancers studied. There is a discussion of study design and the ways it influences results. The authors note that "the most convincing evidence that herbicides may be human carcinogens arises from studies of non-Hodgkin's lymphoma" and "there is reasonable evidence to suggest that phenoxy herbicide exposure results in an increased risk of developing non-Hodgkin's lymphoma." Bureau of Chronic Disease Epidemiology, Health and Welfare Canada.

Palackdharry, C.S. The epidemiology of non-Hodgkin's lymphoma: why the increased incidence? *Oncology* 8(8): 67–78 (August, 1994).

In light of the dramatic increase in incidence of non-Hodgkin's lymphoma in the U.S. (called an "epidemic" by some observers), Palackdharry provides an overview of the literature to date and discusses possible causes of lymphoma. Concerning pesticides, the author notes the varying results obtained by researchers studying occupationally-exposed populations, and also the high level of pesticide use among private homeowners. She discusses the hypothesis that chemical exposures may predispose to non-Hodgkin's lymphoma by weakening the immune system. Medical College of Ohio.

Roberts, H.J. Effects of pentachlorophenol exposure. *Lancet* 349(9069): 1917 (June 28, 1997).

Roberts points out that pentachlorophenol (PCP) exposure, which is very widespread because PCP is used to treat wood, has been associated with Hodgkin's and non-Hodgkin's lymphoma as well as many other serious health problems. [PCP is a manmade chemical used as a wood preservative, preventing growth of bacteria and fungi which cause wood to rot. People may be exposed to PCP by touching or working with wood in construction projects, breathing contaminated air at wood treatment facilities or lumber mills, breathing contaminated air near work sites or waste sites, drinking contaminated water near waste sites, etc.] Palm Beach Institute for Medical Research Inc., Florida.

Smith, A.H., and Bates, M.N. Epidemiological studies of cancer and pesticide exposure. *American Chemical Society* (414): 207–22 (1989).

After conducting an overview of the scientific literature on pesticides and cancer—not just lymphoma—the authors conclude that only arsenic-containing pesticides appear to pose a risk. They consider fairly low ORs and varying results in various studies to be signs of failure to detect any causal relationship. Also, the authors consider immediate toxic effects of chemicals, such as skin rashes, to be significant signs of potential carcinogenicity, and the lack of such

effects to indicate safety. Univ. of Calif, Berkeley.

Weisenburger, D.D. Epidemiology of non-Hodgkin's lymphoma: recent findings regarding an emerging epidemic. *Fifth International Conference on Malignant Lymphoma*, Lugano, Switzerland, 1993 (p. 29 of the proceedings).

This report offers a brief but thorough overview of risk factors which have been found to be associated with non-Hodgkin's lymphoma in epidemiological studies. As regards pesticides, the author reviews the various studies and concludes that pesticides may play a significant role in the recent increase in incidence of non-Hodgkin's lymphoma. University of Nebraska Medical Center.

Youness, E., Ahearn, M.J., & Drewinko, B. Simultaneous occurrence of non-Hodgkin's lymphoma and spontaneous acute granulocytic leukemia. *American Journal of Clinical Pathology* 70(3): 415–420 (Sept., 1978).

This is a report of a single case of non-Hodgkin's lymphoma and acute granulocytic leukemia occurring simultaneously in the same person—which is very rare. The patient had been chronically exposed to an insecticide (type unknown), and the authors conjecture that this exposure may have been a causative factor. University of Texas System Cancer Center, Houston.

Zahm, S.H. Geographical variation in lymphoma incidence. *British Journal of Cancer* 57(4):443 (1988).

This is a brief letter in response to a report by Barnes et al., in which a greater incidence of non-Hodgkin's lymphoma, but not Hodgkin's lymphoma, was found in rural areas of Yorkshire, England, than in urban areas. She points out that the difference, also found in the U.S., may be due to greater pesticide exposures in rural areas. National Cancer Institute.

Zahm, S.H., and Blair, A. (1992). Pesticides and non-Hodgkin's lymphoma. *Cancer Research* 52(19): 5485s–5488s (October 1, 1992).

This concise, but information-packed article provides an excellent overview of the research findings to date. Zahm and Blair review the many studies, methods, and results, and summarize the findings, their meaning, reasons for discrepancies in results, and recommendations for future research (i.e., better evaluation of pesticide exposures in study populations). Noting that the incidence of NHL rose over 50% in the fifteen years preceding 1992, they conclude that 2,4-D in particular may well have been a factor in this increase, since studies in which length of time of exposure was considered show increasing risk of non-Hodgkin's lymphoma with increasing time of exposure, even though less specific studies have shown mixed results. National Cancer Institute.

Zahm, S.H. Epidemiologic research on Vietnam veterans. Difficulties and lessons learned. *Annals of Epidemiology* 5(5): 414–416 (Sept., 1995).

Zahm's article is a preface to two epidemiological studies of Vietnam veterans, Watanabe et al. and Dalager et al. She says that record-keeping on the 9 million members of the armed services during the Vietnam era was not done in a way that makes good epidemiological research possible. No well-organized military records exist concerning either the pesticide exposures or the Vietnam service of individuals; researchers would have to comb through all the records separately to discover which persons served in Vietnam. The lesson learned is that military records should be kept in a way that allows systematic retrieval of information. National Cancer Institute.

Zahm, S.H., & Ward, M.H. Pesticides and childhood cancer. *Environmental Health Perspectives* 106 (Supp. 3): 893–908 (June, 1998).

This overview of the scientific literature concerning children, pesticides, and cancer gives information on the scope and nature of children's exposures to pesticides. Children are frequently exposed to pesticides in their homes, and are more vulnerable than adults to their effects. The authors summarize the results of eight studies of non-Hodgkin's lymphoma. In several of these, the incidence of non-Hodgkin's lymphoma was greater when the time or amount of exposure to pesticides was greater. This dose-response effect may indicate a causative relationship. In one study, children whose mothers used household insecticides daily showed 5.2 times the risk of non-Hodgkin's lymphoma as children whose mothers did not use them. Children whose mothers used these insecticides 1 or 2 times a week had 2.2 times the risk of children whose mothers used them less than once a week. However, many of the studies were small and/or reported cancers without distinguishing among types of cancer. The authors state that much more investigation of the relationship between pesticides and childhood cancer is needed. National Cancer Institute.

Dog Studies: Pesticides and Lymphoma

Hayes, H.M.; Tarone, R.E.; & Cantor, K.P. On the association between canine malignant lymphoma and opportunity for exposure to 2,4-dichlorophenoxyacetic acid. *Environmental Research* 70(2): 119–125 (Aug., 1995).

In 1991, the authors published the results of a case-control study of lymphoma in dogs in relation to their exposure to 2,4-D, a chemical herbicide frequently used in lawn and garden care as a weed killer. They had found a small but significant increase in incidence and also a dose-response effect . The present report is a detailed analysis of the data in response to critical objections by industry-sponsored reviewers. Critics complained that there could have been "recall bias" (greater tendency to remember using pesticides) among the owners of dogs with cancer. However, Hayes et al. had used separate control groups: dogs with cancers other than lymphoma, and dogs without cancer. There was no significant difference between the two control groups, showing that recall bias regarding cancer in general was not an issue. In this report, data showing the geographic location of cases and controls, use of pesticides other than 2,4-D, multiple pesticide use, and owner application vs. application of the pesticides by a lawn care company or professional landscaper were all included. The authors conclude that there is no evidence of inappropriate bias in their work, and that while no one epidemiological study can prove causation, "until additional studies are undertaken…the higher risk we found in dogs…would, at the very least, argue for prudence in the pursuit of a perfect lawn." National Cancer Institute.

Sternberg, S.S. Canine malignant lymphoma and 2,4-dichlorophenoxyacetic acid herbicides. *Journal of the National Cancer Institute* 84(4): 271 (Feb. 19, 1992).

In response to Hayes' 1991 findings, Sternberg wrote a letter expressing doubt whether the increased incidence of lymphoma in dogs could be attributed to 2,4-D, since blood levels of 2,4-D in the dogs had not been measured and it was not even known to what extent, if any, dogs absorb 2,4-D from lawn environments. He said that dogs are more likely to lick their backsides than their paws, making ingestion of lawn-care products unlikely. Memorial Sloan-Kettering Cancer Center.

Reynolds, P.M.; Reif, J.S.; Ramsdell, H.S.; Tessari, J.D. Canine exposure to herbicide-treated lawns and urinary excretion of 2,4-dichlorophenoxyacetic acid. *Cancer Epidemiol Biomarkers Prev* 3(3): 233–237 (Apr.–May 1994).

To determine whether dogs absorb 2,4-D and excrete it through their urine after their owners have applied lawn herbicides (weed killers), the authors tested the urine of 44 dogs which had recently been exposed to herbicides on their home lawns and 15 dogs which had not. Findings showed a clear correlation between recent application of lawn herbicides and the presence of 2,4-D in the dogs' urine. Some dogs whose owners had not recently applied herbicides had small amounts of 2,4-D in the urine, indicating that they might have been exposed to the chemical at parks or by contact with pesticides applied to neighbors' yards. These findings appear to support those of Hayes et al. concerning canine lymphoma and to contradict the Sternberg letter. College of Veterinary Medicine, Colorado State University.

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