

Pesticides implicated in Parkinson's? Government, researchers and foundations know it, but, the public is not fully apprised of this association.

With various organizations consistently fundraising for research, the public should be demanding that they provide education and prevention as part of their fundraising efforts.

We feel that the public has a right to be protected from this debilitating disease and the pesticide association, therefore, we have created this condensed summary of research and funding that confirms this association.

In May 2008, the National Neurotechnology Initiative Act, was introduced by bi-partisan members of Congress and the Senate to allocate 200 million dollars to battle brain related illnesses. It is estimated that 1 in 3 Americans are living with a brain related illness, injury or disease. [1]

Although the average age of diagnosed onset for Parkinson's disease is in the early 60s, approximately 10% of the 1.5 million people with the disease are thought to be below the age of 40. [2]

The National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health (NIH):

- ❖ announced today that it will award three new grants totaling \$21.25 million over a five-year period to study how environmental factors contribute to the cause, prevention and treatment of Parkinson's disease and other related disorders.
- ❖ "Given the growing body of literature that is identifying environmental stressors such as pesticides as risk factors for Parkinson's disease, it is more important than ever that we bring clinical and basic scientists together to clarify the causes of this disease," said Cindy Lawler, Ph.D., program administrator at NIEHS.
- ❖ Marie-Françoise Chesselet, M.D., Ph.D., University of California, Los Angeles
The researchers at UCLA have previously shown associations between high levels of exposure to specific environmental pesticides and Parkinson's disease
- ❖ Their work is expected to shed light on the pathological processes involved in sporadic Parkinson's disease, the most frequent form of the disorder, and could have public health implications for precautions in the use of some pesticides. [3]

More Evidence for Parkinson's Disease and Pesticide Link:

- ❖ A large epidemiologic study shows that individuals reporting regular exposure to pesticides had a 70 percent higher incidence of Parkinson's disease than those reporting no exposure.
- ❖ The study, funded by NIEHS and conducted by researchers at the Harvard School of Public Health, is the first large scale prospective study to examine the possible links between chronic pesticide exposure and Parkinson's disease.
- ❖ The current study included more than 143,000 subjects; 7,800 reported exposure to pesticides.
- ❖ No increased risk for Parkinson's disease was found from other occupational hazards including exposure to other chemicals or solvents.
- ❖ Research utilizing twins has established that genetics probably plays a minor role in Parkinson's disease and thus has made environmental exposures the focus of much interest.
- ❖ A compound known as MPTP, a byproduct of the production of a heroinlike illicit drug and structurally similar to the herbicide paraquat, causes death of neurons in the substantia nigra, the part of the brain affected by Parkinson's disease.
- ❖ For that reason pesticides and herbicides exposures are considered likely to cause or contribute to the development of Parkinson's disease. [4]

Government orders an inquiry into pesticide links to Parkinson's Disease

- ❖ Professor David Coggon, the professor of occupational and environmental medicine at the Medical Research Council, said his committee wanted to commission a team of expert epidemiologists. "If we were confident that there was nothing in it at all, we wouldn't be paying taxpayers' money to carry out a review. It's about being responsible about these things and looking if it's appropriate," he said. "If new evidence suggests there might be a problem we have to look at it."
- ❖ He said that overall, the results "support the idea" that exposure to pesticides increases the chance of getting Parkinson's. His study came out in November 2000.
- ❖ However, a far more damning one was published earlier that year by a team at Stanford University in California who had studied more than 1,000 people, half of whom had Parkinson's.
- ❖ They found that those who had been frequently exposed to pesticides were twice as likely to develop the disease. [5]

Emory Awarded \$6 Million to Study Causes of Parkinson's

- ❖ Parkinson's disease has been linked to pesticide exposure, mitochondrial damage and altered storage of the neurotransmitter dopamine. [6]

Parkinson's Disease: Environment Plays a Larger Role than Genetics in Swedish Twins

- ❖ The cause of Parkinson's disease is considered to involve both genetic and environmental factors as well as interactions between these-the so called, gene-environment interaction.
- ❖ Mutations in several genes have been linked to Parkinson's disease. Although they are important for understanding the mechanism and process of the disease, they do not appear to explain most late-onset Parkinson's cases.
- ❖ Of the 382 pairs of twins, 7 pairs were found in which both had evidence of Parkinson's disease.
- ❖ These data agree with other twin studies that determined that "genetic effects are of little importance in Parkinson's disease."
- ❖ The results of almost no genetic influence for Parkinson's are quite notable in this study, given the considerably higher heritability estimates reported for other disorders such as Alzheimer's disease, asthma, and Type I diabetes.
- ❖ In other words, specific genes may increase the risk of Parkinson's disease only in individuals exposed to a certain risk factor.
- ❖ This study's results suggest that if genetic effects are important, they are only expressed once sufficient environmental factors are present.
- ❖ As Dr. Ken Olden, Director, NIEHS has said, "Genes load the gun. The environment pulls the trigger." [7]

Pesticide-Parkinson link explored

- ❖ The initiative has given new impetus to the field. William Langston, founder and CEO of the Parkinson's Institute, says, "What the NIEHS is saying [with the latest initiative] is that the research is far enough along to become proactive." NIEHS estimates that it will provide \$12 million in funding for PD research in 2002, a doubling of its FY2001 support.
- ❖ A number of large population studies suggest that people with jobs that expose them to pesticides have a higher risk of developing PD, a neurodegenerative illness marked by the death of the brain cells that produce and release dopamine.
- ❖ However, "there has not been a specific class of pesticides or specific pesticide linked to PD," says Harvey Checkoway, an epidemiologist at the University of Washington. "There is no smoking gun."
- ❖ This "gun" is what several projects that will receive funding are trying to find. UCLA epidemiologist, Beate Ritz, is conducting "the largest prospective study, looking at both occupational and residential exposure."
- ❖ The work will take advantage of the fact that California law requires that all agricultural application of pesticides are reported, thereby providing a detailed record of what people have used and where. [8]

Center for Gene-Environment Studies in Parkinson's Disease-Grant from NIEHS

- ❖ The UCLA-CGEP will explore mechanisms by which genetic and environmental influences combine to increase the risk for Parkinson's disease (PD) in susceptible individuals through interplay between neurotoxic pesticides and biologic mechanisms regulating the neurotransmitter dopamine in brain cells.
- ❖ There is extensive evidence that pesticides, a suspected risk factor for Parkinson's Disease, interact with multiple mechanisms that regulate the intra- and extracellular levels of the dopamine, which itself is a powerful oxidant that can be highly toxic to cells.
- ❖ Critical factors in this interaction of dopamine homeostasis and pesticides may be oxidative stress and the function of the proteasome, an organelle involved in protein degradation in cells.
- ❖ Both dopamine and pesticides can produce oxidative stress; pesticides can directly affect dopamine transporters, thus causing alterations in dopamine homeostasis, and possibly interfere with proteasomal function. [9]

Association of Pesticide Exposure with Neurologic Dysfunction and Disease

- ❖ An extensive literature suggests that pesticide exposure may increase risk of Parkinson disease
- ❖ Recent studies with more detailed exposure assessment have generally found an association of pesticide exposure with Parkinson disease, with 1.5- to 7-fold increases in risk.
- ❖ Case-control studies found increased risk associated with possession of a pesticide use license cumulative pesticide exposure based on complete occupational histories, or occupational or other pesticide use
- ❖ A cross-sectional study found an association of parkinsonism with exposure to any pesticide, although not with specific pesticides or pesticide classes, and an ecologic study found that Parkinson disease mortality was higher in California counties where pesticides were used than in counties where they were not
- ❖ Two cohort studies with detailed exposure information confirmed these findings: Risk was related to years of plantation work and to self-reported pesticide exposure in men enrolled in the Honolulu Heart Program cohort, and occupational exposure to pesticides assessed with a job-exposure matrix was strongly associated with Parkinson disease risk (5.6-fold increase in risk) in an older cohort living in a vineyard-growing region of France
- ❖ Most studies of pesticide exposure and Parkinson disease risk have been unable to implicate specific pesticides. Several studies found increased risk associated with exposure to either insecticides or herbicides, and one study indicated that risk was elevated by exposure to organochlorines, OPs, or carbamates
- ❖ Several studies have implicated the herbicide paraquat, which produces selective degeneration of neurons involved in Parkinson disease
- ❖ Case reports have described Parkinson disease in individuals exposed to Ops, to herbicides including glyphosate, paraquat, and diquat; and to fungicides including maneb and other dithiocarbamates
- ❖ Higher concentrations of organochlorines, particularly dieldrin, have been found in postmortem brains of Parkinson disease patients compared to patients with other neurologic diseases tests
- ❖ There is also evidence suggesting that other types of pesticides, including organochlorines, carbamates, fungicides, and fumigants, are neurotoxic.
- ❖ No study has evaluated the association of herbicides with symptom prevalence or neurobehavioral performance, but these chemicals have been implicated as risk factors for Parkinson disease.
- ❖ Although it is important to identify classes of pesticides and even specific chemicals associated with neurotoxicity, it is also important to recognize that most workers are exposed to complex mixtures of pesticides, which may contribute synergistically to neurotoxicity.
- ❖ In conclusion, there is mounting evidence that chronic moderate pesticide exposure is

neurotoxic and increases risk of Parkinson disease. [10]

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