

# Understanding Pesticide Toxicity

**NIEHS-funded research on genetic factors that affect individual sensitivity to pesticide exposure paves the way for policy changes.**

Exposure to a group of pesticides called organophosphates can contribute to neurodevelopmental problems, among other health challenges.<sup>32</sup> Since 1989, the National Institute of Environmental Health Sciences (NIEHS) has supported research into the role of a gene called PON1, which helps protect people from the harmful effects of organophosphate exposure.

Organophosphates disrupt communication between nerve cells. The PON1 protein plays a protective role in humans by detoxifying certain organophosphates before they can damage the nervous system.

Some people are more sensitive to organophosphates than other people. Over time, investigators have learned that sensitivity depends on how much PON1 protein a person produces, and how effective the protein is at breaking down organophosphates.<sup>10-11</sup>

In 2018, a team of researchers funded partly by NIEHS recommended policy reforms to minimize people’s exposure to the pesticide chlorpyrifos, an organophosphate.<sup>32</sup> Three years later, the U.S. Environmental Protection Agency (EPA) banned the use of chlorpyrifos on all food sold in the country.<sup>33</sup>

“Our work on PON1 helped inform the EPA decision,” said longtime NIEHS grantee Clement Furlong, Ph.D., who, with collaborator Lucio Costa, Ph.D., has studied PON1 for decades.



*Agricultural workers in California. (Photo courtesy of Kim Harley)*

*“The quantity and effectiveness of the PON1 protein determine your resistance to certain pesticides.”*

*– Clement Furlong, Ph.D.  
University of Washington*

## Marking Milestones



### Understanding Sensitivity

Researchers found that PON1 protein concentrations in the blood and protein activity — how effective the protein is at breaking down organophosphates — both influence a person’s sensitivity to certain organophosphates.<sup>10-11</sup>



### Identifying Vulnerable Groups

Studies suggested that fetuses and infants are more susceptible than adults to the toxic effects of organophosphate exposure.<sup>13-16</sup>



### Sharing Results

Investigators with CHAMACOS have given more than 1,000 presentations, and educated more than 30,000 partners and community members, about their research on pesticides and other chemicals.<sup>9</sup>



### Reducing Exposures

Researchers proposed an action plan to reduce organophosphate pesticide exposure for consideration by governments, public health and medical institutions and organizations, and agricultural entities.<sup>32</sup>



### Informing Policy

In 2021, the EPA banned use of chlorpyrifos on food sold in the United States.<sup>33</sup>

## Then and Now

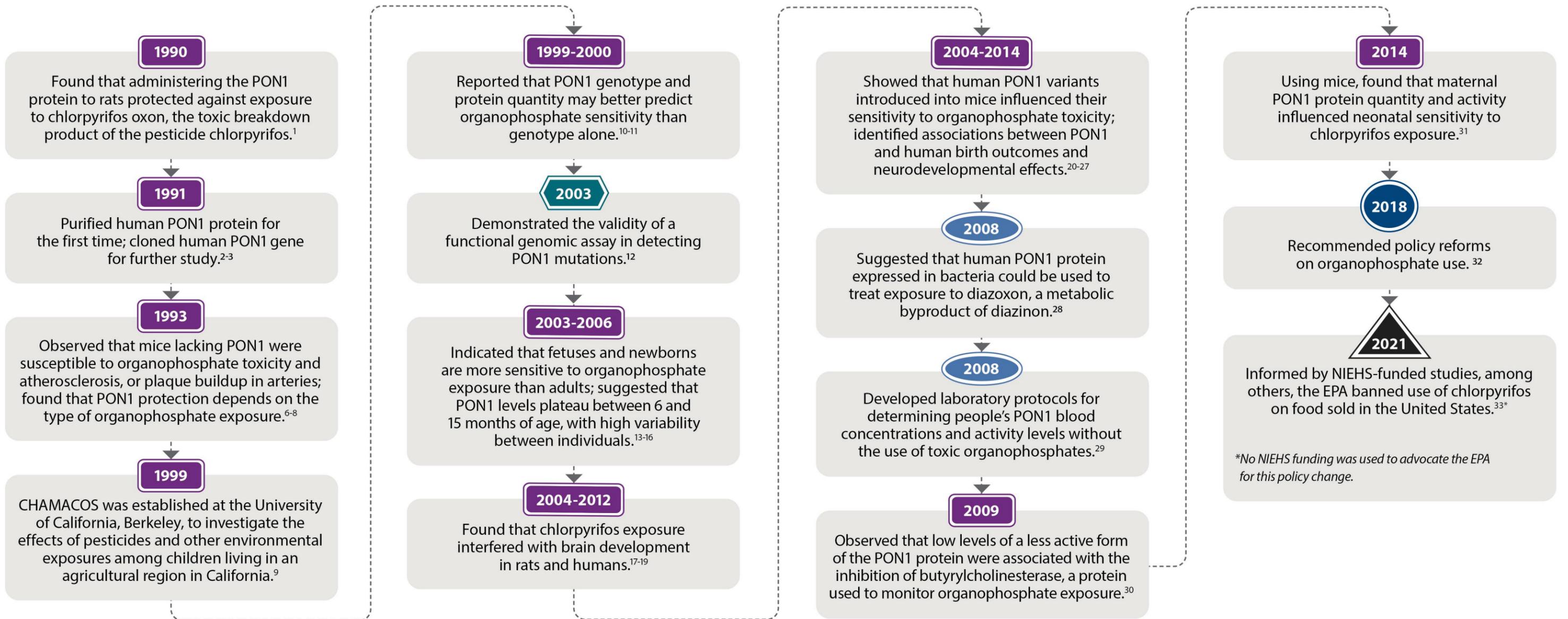
### Then

- Investigators initially thought PON1 provided protection against the pesticide parathion.<sup>8</sup>
- Researchers described common genetic variations in PON1 that affect how protective the gene is against organophosphate toxicity.<sup>4</sup>
- Studies indicated that fetuses and infants are more sensitive than adults to organophosphate exposure.<sup>13-16</sup>
- Researchers found associations between PON1 and human birth outcomes and neurodevelopmental effects.<sup>21-27</sup>

### Now

- Research showed that PON1 is not protective against parathion. Rather, it targets toxic breakdown products of the pesticides chlorpyrifos and diazinon.<sup>8</sup>
- Investigators reported that PON1 protein quantity and protein activity influence a person’s sensitivity to the chemicals.<sup>5,10-11</sup>
- Research suggested that maternal PON1 protein quantity and activity might affect fetal sensitivity to organophosphates.<sup>31</sup>
- The EPA banned the use of chlorpyrifos on food sold in the United States.<sup>33</sup>

# PON1 and Pesticides



## Addressing Exposures in a Farming Community

A long-term project based at the University of California, Berkeley, has investigated the risk that organophosphate exposure poses to certain populations. Established in 1999 and funded partly by NIEHS, the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) follows more than 800 children in a Latino farmworker community in the Salinas Valley, with the aim of characterizing chemical exposures and associated health effects.<sup>9</sup>

This project has also investigated the role of PON1. In one study, CHAMACOS researchers found that infants with lower levels of less active PON1 protein were born earlier and had smaller head measurements than infants with higher levels of more active PON1 protein.<sup>25</sup> In related work, investigators found an association between PON1 levels and activity and children's cognitive performance and, to a lesser extent, measures of muscle coordination.<sup>23,27</sup>



Participants in the CHAMACOS Study.  
(Photo courtesy of the CHAMACOS Study)



Members of the CHAMACOS Youth Council — a group of high school students from Salinas, California, that works with the CHAMACOS team on environmental justice projects — collaborated with artist José Ortiz to create a mural illustrating how they can protect themselves from pesticide exposure. (Photo courtesy of Hijos del Sol Productions and the CHAMACOS Study)

## Research Challenges and Solutions

**Challenge:** Researchers needed to sequence PON1 to study its role.

**Solution:** They used genetic material from rabbits to ultimately isolate the human PON1 gene. Rabbit PON1 and human PON1 showed striking similarities, suggesting that the protein may serve the same metabolic role across species.<sup>3</sup>

**Challenge:** Investigators wanted to examine the PON1 protein in a living organism.

**Solution:** They deleted the PON1 gene in mice, replacing it with human PON1 DNA. After exposing the mice to different organophosphates, they found that

PON1 played an important role in breaking down toxic metabolic byproducts of the pesticides diazinon and chlorpyrifos.<sup>8</sup>

**Challenge:** Few human studies had investigated connections between the PON1 protein and other proteins affected by organophosphate exposure.

**Solution:** Working with agricultural pesticide handlers, researchers found that low PON1 quantity and activity were linked with interference of a protein called butyrylcholinesterase, which is used to monitor organophosphate exposure.<sup>30</sup>



A farmworker in a Salinas Valley strawberry field. (Photo courtesy of the CHAMACOS study)

For references, supplementary information, and more on the impact of NIEHS research, please visit <https://niehs.nih.gov/research/programs/translational/examples>.