

Paraquat, Parkinson's Disease, and Agnotology

E. Ray Dorsey, MD,^{1*}  and Amit Ray, PhD²

¹Department of Neurology and Center for Health + Technology, University of Rochester Medical Center, Rochester, New York, USA

²Department of English, Rochester Institute of Technology, Rochester, New York, USA

“History’s what people are trying to hide from you, not what they’re trying to show you. You search for it in the same way you sift through a landfill: for evidence of what people want to bury.”

—Hilary Mantel, historical novelist

Nearly 60 years ago, a chemical company found that skin exposure to very high doses of its weedkiller paraquat caused “weakness and incoordination” in rabbits. Large amounts of the herbicide, which is used on corn, cotton, and vineyards,¹ caused some mice and rats in its labs to develop a stiff gait or tremors. A decade later, an autopsy of a farm worker exposed to paraquat showed “degenerative change” in the “cells of the substantia nigra,” a pathological hallmark of Parkinson’s disease.^{2,3}

Rather than remove this dangerous chemical from the market or develop a safer alternative, the company doubled down on its “blockbuster” product and sought to expand its use. Along the way, the company appeared to use techniques to underestimate the toxic effects of the chemical, hide the results of its own research from regulatory authorities, and discredit the research of an academic investigator and prevent her from serving on a U.S. Environmental Protection

Agency (EPA) advisory panel. These are just some of the findings (Table 1) that the British newspaper the *Guardian* recently uncovered after examining the company’s internal records.²

The company’s alleged efforts seem to have worked brilliantly. Despite numerous animal^{3,4} and epidemiological studies^{5–7} linking the environmental toxicant to Parkinson’s disease, paraquat’s use in the United States from 2013 to 2018 more than doubled.⁸ As pesticides can contaminate drinking water and pollute the air, their harmful effects are not limited to farmers but extend (at least) to other rural residents who also have a higher risk of developing Parkinson’s disease.⁹ Because of its health risks, over 30 countries—including China—have banned paraquat. Yet in 2021 the EPA reauthorized its use even though its own website says, “One Sip Can Kill.”¹⁰

Agnotology, the Deliberate Production of Ignorance

The actions that the manufacturer of paraquat has been accused of taking are just the latest example of agnotology.^{2,11} Agnotology, coined by the linguist Iain Boal in 1992, is the deliberate production of ignorance often for commercial gain. The doubt can be created by inaccurate or misleading scientific data, disinformation, document destruction, and secrecy and suppression. As opposed to the ignorance that a child may have as a “native state” that can be filled with education, the ignorance induced by agnotology is “made, maintained, and manipulated.”¹¹

According to the historian Robert Proctor, the classic example of this ignorance creation is the tobacco industry’s long campaign (“Doubt is our product”) to mask the health risks of smoking.¹¹ The industry simultaneously feigned its own ignorance, affirmed the absence of definitive proof, and created doubt within the public at large. The result was millions of avoidable deaths, enormous economic costs borne by individuals and societies, and immeasurable personal suffering.

The makers of paraquat apparently have done the same. Knowledge of the toxic effects of paraquat is

© 2023 The Authors. *Movement Disorders* published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Key Words: environment, paraquat, Parkinson’s disease, pesticides, public health

***Correspondence to:** Dr. E. Ray Dorsey, Department of Neurology and Center for Health + Technology, University of Rochester Medical Center, 265 Crittenden Boulevard, CU420694, Rochester, NY 14642, USA; E-mail: ray.dorsey@chet.rochester.edu

Relevant conflicts of interest/financial disclosures: E.R.D. was an unpaid advisor to the Center for Biological Diversity in its legal challenge of EPA’s paraquat re-registration.

Received: 25 January 2023; **Revised:** 9 February 2023; **Accepted:** 16 February 2023

Published online in Wiley Online Library ([wileyonlinelibrary.com](https://www.wileyonlinelibrary.com)). DOI: 10.1002/mds.29371

TABLE 1 Select findings from the Guardian report on the manufacturer's actions on its weedkiller paraquat, 1955–1985²

Year	Event
1955	Company identifies paraquat as a potent weedkiller
1962	Company introduces paraquat (brand name Gramoxone) into the United Kingdom and later the United States.
1964	Company finds skin exposure to paraquat in rabbits in very high doses causes “weakness and incoordination”
1966	Company scientists find that some rats and mice given large doses of paraquat display a stiff gait or tremors
1968	Poisoning deaths and suicides due to paraquat start to increase
1974	State regulators express concerns about workers “who might inadvertently lick small quantities of paraquat residue off lips, or inhale paraquat mist”; rumors circulate that some in the EPA are in favor of banning paraquat
1975	Meeting between chemical companies reports that long-term spraying could injure the central nervous system
1976	Autopsy of farmworker shows “degenerative changes” in the “cells of substantia nigra”
1985	Company memo reports scientific article showing “extraordinarily high correlation of .967 was found between levels of pesticide use and Parkinson’s cases.” Memo warns that paraquat could become a huge legal liability like asbestos and says, “Parkinson’s can go on for decades”

Abbreviation: EPA, U.S. Environmental Protection Agency.

alleged to have been hidden for decades, and a credible academic researcher appears to have been prevented from highlighting the weedkiller's true risks. All the while, the manufacturer continues to maintain that paraquat does not cause Parkinson's disease.² Actions like these should be recognized for what they are: attacks on science, attacks on scientists, and attacks on the health of the public.

Attacks on Science and a Scientist

The goal of science is to advance knowledge. The purpose of agnotology is to obscure it.

According to the *Guardian*, in 2009 the makers of paraquat were trying to determine if “the scientific community [will] conclude from the laboratory and epidemiological data that paraquat exposure is a *causal factor* [their emphasis] in Parkinson's Disease or parkinsonism.” It appears that this is a conclusion the company did not want us Parkinson's researchers to make.²

This report and the company's own findings now indicate that we know what one cause of Parkinson's disease is—paraquat. With this conclusion, paraquat should be banned, and the search for other causative factors in the environment should accelerate.

The attack on a Parkinson's researcher also should not go unanswered. Dr. Deborah Cory-Slechta is a highly regarded neurotoxicologist who with her colleagues in 1999 found that in mice “systemically absorbed paraquat crosses the blood-brain barrier to cause destruction of dopamine neurons in the substantia nigra, consequent reduction of dopaminergic innervation of the striatum and a neurobehavioral syndrome similar” to that produced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine.¹² Two decades later in 2021, she and her fellow researchers demonstrated that inhaled paraquat concentrates in the olfactory bulb and enters all regions of the brain that were examined while bypassing the blood-brain barrier.¹³

To prevent her service on an EPA advisory panel on pesticides in 2005, the manufacturer, according to the *Guardian*, asked an industry lobbying group to “disparage Cory-Slechta's work in communications to the EPA.” Because the company was apparently concerned that such comments could later be used against it, it decided on secrecy and did not want the public or the EPA to know of its efforts. Internal emails within the company are alleged to have said that “for many, many of our projects it would be a real disaster” to have Dr. Cory-Slechta on the scientific advisory panel and suggested to the lobbying firm that the EPA be told that her scientific conclusions were “in reality, speculation” and her statements “overly dogmatic.” A regulatory expert at the lobbying firm also evidently communicated the company's concerns to the EPA, omitted that the concerns actually came from paraquat's manufacturer, and did so outside of the public docket. Ultimately, the EPA did not choose Dr. Cory-Slechta for the advisory panel but instead selected a scientist supported by the lobbying firm.²

These attacks on a scientist and science are not limited to the Parkinson's community but extend to investigators studying the effects of other pesticides, air pollution, and greenhouse gases.^{11,14} Without a response, companies will only be more emboldened in their future efforts to discredit researchers conducting work that may be contrary to their narrow, commercial interests.

Finally, agnotology is an attack on the public health. Today, possibly because of the spread of environmental toxicants like paraquat, Parkinson's disease is the world's fastest-growing brain disease.¹⁵ From 1990 to 2016 the number of people with the disease more than doubled globally, far more than can be explained by aging alone.¹⁵ Absent change, Parkinson's disease is poised to double again in the coming generation.¹⁶ In

the United States, the incidence is likely increasing¹⁷ and may be 50% more than previously estimated.¹⁸ According to the Global Burden of Disease study, the three countries with the highest rates of Parkinson's disease in the world are Canada, the United States, and Argentina.¹⁵ Until 2022 when the manufacturer of paraquat voluntarily discontinued its use in Canada,¹⁹ all three allowed the spraying of the toxic weedkiller.²

The Costs of Agnotology

Agnotology is harmful and carries immense human, societal, and scientific costs. Unknown numbers of farmers and possibly many millions of rural residents globally have been exposed to paraquat, which has likely helped fuel the increase in Parkinson's disease in these communities. The resulting untold death, disability, and suffering for more than 50 years were, if the *Guardian* reporting is accurate, preventable.

Human suffering should not be subservient to one corporation and the revenue of its \$400 million product.² By comparison, Medicare (the U.S. federal health insurance program for older adults) alone spends about \$25 billion annually caring for over 1 million Americans with the disease.²⁰ The indirect costs of caregiving and disability increase the economic burden of Parkinson's disease in the United States to over \$50 billion,²⁰ more than 100 times what the chemical company reaps in global sales from a 60-year-old pesticide. This is essentially subsidizing corporate profit with human life. The result makes no economic sense and is ethically repugnant. The subsidy must end.

Agnotology also affects the conduct of science itself. Scientific inquiry is selective.¹¹ Some questions are asked, whereas others are left uninvestigated or underinvestigated. This has happened in Parkinson's disease. Since the company is believed to have begun hiding the risks of its own chemical, studies analyzing the genetics of Parkinson's disease, which has a low heritability,²¹ outnumber environmental studies by a factor of six.²² As Proctor writes, “[Knowledge] switched onto one track cannot always return to areas passed over; we don't always have the opportunity to correct old errors. Research lost is not just research delayed; it can also be forever marked or never recovered.”¹¹

Remedies for Agnotology

There are several antidotes to the doubt that chemical manufacturers have generated. First, wrongdoers must be punished. The truth about paraquat was revealed only as a result of lawsuits against the manufacturer by large numbers of people who have alleged they developed Parkinson's disease as a result of exposure to the chemical.² In addition to personal injury litigation,

regulatory agencies and governments must bring civil or criminal actions against those who harm the public's health. Second, the burden of proof of safety must shift to manufacturers.²³ This “precautionary principle” would mirror what is required of drug manufacturers who must demonstrate both the efficacy and safety *before* medications are approved for use. Third, the control of many regulatory agencies by the interests they regulate (“regulatory capture”) must end.²⁴ According to the *Guardian*, one of the EPA officials who signed off on the EPA's review of paraquat in 2019 belonged to a “powerful Washington-based lobbying organization that represents the pesticide industry.”²

Finally, we must investigate whether other inhaled toxicants, such as pesticides, industrial solvents (eg, trichloroethylene^{25,26}), and ambient air pollution,²⁷ are fueling the growth of Parkinson's disease. Such research might generate explanations for a wide range of conditions beyond Parkinson's disease, including other neurological (eg, amyotrophic lateral sclerosis and Alzheimer's disease) and medical (eg, autoimmune diseases and cancer) conditions. If a chemical company is able to hide a pesticide's risk of Parkinson's disease, we must ask what other businesses are doing about the environmental pollutants that they manufacture or sell.

The battle over paraquat, Parkinson's disease, and agnotology is not over. In response to a recent lawsuit, the U.S. Department of Justice has ordered the EPA to reevaluate its decision to permit the continued use of the deadly weedkiller.² Until then, paraquat continues to be sprayed on farms across America and globally and, along with it, the possible seeds of future cases of Parkinson's disease. ■

Data Availability Statement

All data cited in the paper are publicly available from the sources referenced.

References

1. Estimated Annual Agricultural Pesticide Use: Paraquat. United States Geological Survey [cited 2022 Dec 19]. Available from: water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2018&map=PARAQUAT&chilo=L.
2. Gillam C, Uteuova A. Secret files suggest chemical giant feared weedkiller's link to Parkinson's disease. *The Guardian* 2022; [cited 2022 Dec 19]. Available from: <https://www.theguardian.com/us-news/2022/oct/20/syngenta-weedkiller-pesticide-parkinsons-disease-paraquat-documents>.
3. McCormack AL, Thiruchelvam M, Manning-Bog AB, Thiffault C, Langston JW, Cory-Slechta DA, Di Monte DA. Environmental risk factors and Parkinson's disease: selective degeneration of Nigral dopaminergic neurons caused by the herbicide Paraquat. *Neurobiol Dis* 2002;10(2):119–127. <https://doi.org/10.1006/nbdi.2002.0507>
4. Richardson JR, Quan Y, Sherer TB, Greenamyre JT, Miller GW. Paraquat neurotoxicity is distinct from that of MPTP and rotenone. *Toxicol Sci* 2005;88(1):193–201. <https://doi.org/10.1093/toxsci/kf304>

5. Tanner CM, Kamel F, Ross GW, et al. Rotenone, Paraquat, and Parkinson's disease. *Environ Health Perspect* 2011;119(6):866–872. <https://doi.org/10.1289/ehp.1002839>
6. Costello S, Cockburn M, Bronstein J, Zhang X, Ritz B. Parkinson's disease and residential exposure to Maneb and Paraquat from agricultural applications in the Central Valley of California. *Am J Epidemiol* 2009;169(8):919–926. <https://doi.org/10.1093/aje/kwp006>.
7. Paul KC, Cockburn M, Gong Y, Bronstein J, Ritz B. Agricultural paraquat dichloride use and Parkinson's disease in California Central Valley. medRxiv 2022:2022.12.28.22284022. <https://doi.org/10.1101/2022.12.28.22284022>
8. Estimated Annual Agricultural Pesticide Use, 2018. United States Geological Survey [cited 2022 Nov 2]. Available from: water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2018&map=PARAQUAT&chilo=L.
9. Hubble JP, Cao T, Hassanein RES, Neuberger JS, Roller WC. Risk factors for Parkinson's disease. *Neurology* 1993;43(9):1693. <https://doi.org/10.1212/wnl.43.9.1693>.
10. Paraquat Dichloride: One Sip Can Kill. United States Environmental Protection Agency. 17 Oct 2022 [cited 2022 Nov 2]. Available from: epa.gov/pesticide-worker-safety/paraquat-dichloride-one-sip-can-kill.
11. Schiebinger L, Proctor RN. *Agnology: The Making and Unmaking of Ignorance*. 1st ed. Stanford: Stanford University Press; 2008:312.
12. Brooks AI, Chadwick CA, Gelbard HA, Cory-Slechta DA, Federoff HJ. Paraquat elicited neurobehavioral syndrome caused by dopaminergic neuron loss. *Brain Res* 1999;823(1–2):1–10. [https://doi.org/10.1016/S0006-8993\(98\)01192-5](https://doi.org/10.1016/S0006-8993(98)01192-5) PubMed PMID: 10095006
13. Anderson T, Merrill AK, Eckard ML, et al. Paraquat inhalation, a translationally relevant route of exposure: disposition to the brain and male-specific olfactory impairment in mice. *Toxicol Sci* 2021; 180(1):175–185. <https://doi.org/10.1093/toxsci/kfaa183>
14. Attacks on Science. Union of Concerned Scientists [cited 2022 Dec 19]. Available from: ucsusa.org/resources/attacks-on-science.
15. Dorsey ER, Elbaz A, Nichols E, et al. Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol* 2018; 17(11):939–953. [https://doi.org/10.1016/S1474-4422\(18\)30295-3](https://doi.org/10.1016/S1474-4422(18)30295-3)
16. Dorsey ER, Bloem BR. The Parkinson pandemic—a call to action. *JAMA Neurol* 2018;75(1):9–10. <https://doi.org/10.1001/jamaneurol.2017.3299>
17. Savica R, Grossardt BR, Bower JH, Ahlskog JE, Rocca WA. Time trends in the incidence of Parkinson disease. *JAMA Neurol* 2016; 73(8):981–989. <https://doi.org/10.1001/jamaneurol.2016.0947>
18. Willis AW, Roberts E, Beck JC, et al. Incidence of Parkinson disease in North America. *NPJ Parkinsons Dis* 2022;8(1):170. <https://doi.org/10.1038/s41531-022-00410-y>
19. The relationship between pesticides and Parkinson's. Parkinson Canada [cited 2022 Dec 19]. Available from: parkinson.ca/about-parkinsons/pesticides/.
20. Yang W, Hamilton JL, Kopil C, et al. Current and projected future economic burden of Parkinson's disease in the U.S. *npj Parkinson's Dis* 2020;6(1):15. <https://doi.org/10.1038/s41531-020-0117-1>
21. van Dongen J, Slagboom PE, Draisma HHM, Martin NG, Boomsma DI. The continuing value of twin studies in the omics era. *Nat Rev Genet* 2012;13(9):640–653. <https://doi.org/10.1038/nrg3243>
22. De Miranda BR, Goldman SM, Miller GW, Greenamyre JT, Dorsey ER. Preventing Parkinson's disease: an environmental agenda. *J Parkinsons Dis* 2022;12(1):45–68. <https://doi.org/10.3233/jpd-212922>
23. Kriebel D, Tickner J, Epstein P, et al. The precautionary principle in environmental science. *Environ Health Perspect* 2001;109(9):871–876. <https://doi.org/10.1289/ehp.011109871>
24. Carpenter D, Moss DA. *Preventing Regulatory Capture: Special Interest Influence and how to Limit it*. Cambridge: Cambridge University Press; 2013.
25. Gash DM, Rutland K, Hudson NL, et al. Trichloroethylene: parkinsonism and complex 1 mitochondrial neurotoxicity. *Ann Neurol* 2008;63(2):184–192. <https://doi.org/10.1002/ana.21288>
26. De Miranda BR, Greenamyre JT. Trichloroethylene, a ubiquitous environmental contaminant in the risk for Parkinson's disease. *Environ Sci Process Impacts* 2020;22(3):543–554. <https://doi.org/10.1039/C9EM00578A>
27. Palacios N. Air pollution and Parkinson's disease – evidence and future directions. *Rev Environ Health* 2017;32(4):303–313. <https://doi.org/10.1515/reveh-2017-0009>

SGML and CITI Use Only DO NOT PRINT

Author Roles

E.R.D. and A.R. developed the manuscript. E.R.D. drafted the paper, and A.R. reviewed and edited it. Both authors read and approved the manuscript.

Full financial disclosures for the previous 12 months

E.R.D. was an unpaid advisor to the Center for Biological Diversity in its legal challenge of EPA's paraquat re-registration. E.R.D. has received honoraria for speaking at the American Academy of Neurology; the American Neurological Association; Excellus BlueCross BlueShield; the International Parkinson's and Movement Disorders Society; the National Multiple Sclerosis Society; Northwestern University; Physicians Education Resource, LLC; PRIME Education, LLC; Stanford University; Texas Neurological Society; and Weill Cornell. E.R.D. received compensation for consulting services from Abbott; AbbVie; Acadia; Acorda; Bial-Biotech Investments, Inc.; Biogen; Boehringer Ingelheim; California Pacific Medical Center; Caraway Therapeutics; CuraSen Therapeutics; Denali Therapeutics; Eli Lilly; Genentech/Roche; Grand Rounds; Huntington Study Group; Informa Pharma Consulting; Karger Publications; LifeSciences Consultants; MCM Education; Mediflix; Medopad; MedRhythms; Merck; The Michael J. Fox Foundation; NACCME; Neurocrine; NeuroDerm; NIH; Novartis; Origent Data Sciences; Otsuka; Physician's Education Resource; Praxis; PRIME Education; Roach, Brown, McCarthy & Gruber; Sanofi; Seminal Healthcare; Spark; Springer Healthcare; Sunovion Pharma; Theravance; Voyager; and WebMD. E.R.D. received research support from Biogen, Biosensics, Burroughs Wellcome Fund, CuraSen, Greater Rochester Health Foundation, Huntington Study Group, The Michael J. Fox Foundation, National Institutes of Health, Patient-Centered Outcomes Research Institute, Pfizer, PhotoPharmics, Safra Foundation, and Wave Life Sciences; E.R.D. provided editorial services for Karger Publications; E.R.D. has stock in Included Health and Mediflix and ownership interests in SemCap. A.R. has no disclosures.