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Looking Backward: Long-Term Lead Exposure and Risk of Glaucoma

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Despite its status as the leading cause of irreversible blindness, the etiology of glaucoma remains shrouded in mystery. Researchers have identified several genetic risk factors for glaucoma, but environmental contributors remain almost completely unknown. A study in *Environmental Health Perspectives* suggests that long-term lead exposure may be a risk factor for primary open-angle glaucoma (POAG), the most common form of this disease.[1]

This is one of the first times scientists have been able to identify an environmental risk factor for glaucoma, says lead author Sung Kyun Park, an environmental health scientist at the University of Michigan. "There is no cure for glaucoma, which is why prevention is so important," Park says.

One thing researchers do know about glaucoma is that more than half of all cases are caused by too much fluid (aqueous humor) in the eye, which increases intraocular pressure.[2] Over time, this pressure can damage the optic nerve. If the damage is not halted or repaired, blindness can result. Unlike cataracts, glaucoma-related blindness cannot be reversed, and it accounts for 8% of all global cases of blindness.[3] POAG is generally a disease of middle-aged and older adults, with one study estimating that 93% of cases occur in people 55 years of age and older.[4]

An earlier study by another team found markers of oxidative stress in the aqueous humor of people with POAG. Oxidative stress can directly damage the optic nerve as well as interfere with the ability of the eye to drain excess aqueous humor.[5]

Park knew that chronic lead exposure is one common cause of oxidative stress.[6] But blood tests measure only recent lead exposure; to determine the effects of lead on glaucoma, Park and his colleagues would need a measurement that could assess decades' worth of exposures. Bone lead levels would give him the data he needed.

Part of what makes lead so dangerous is that it deposits in bone, where it has a half-life of many decades. Far from being an inert substance, bone is constantly built up and broken down, a process that can release stored lead back into the bloodstream.

K X-ray fluorescence (KXRF) is used to measure bone lead levels. KXRF readings of lead in hard outer bone (or cortical bone) reflect cumulative lifetime lead exposure, whereas levels in spongy inner bone (or trabecular bone) indicate the amount of bioavailable lead in the body.[7] The tibia and patella are often used as representatives of cortical and trabecular bone, respectively.

A new study suggests that higher exposures to lead over a lifetime may increase the risk of primary open-angle glaucoma, the most common type of glaucoma. Image: © iStockphoto/Nastasic.

The VA Normative Aging Study, which recruited 2,280 healthy men in 1963 and has followed them ever since, conducted both ocular exams and KXRF measurements. However, the study participants were not randomly selected from the population as a whole, and the lengthy follow-up period meant that the men with the highest lead levels may have died before they developed glaucoma, biasing the sample in favor of healthier individuals. Park and his colleagues used inverse probability weighting to account for this selection bias.

From a subset of 634 men with both KXRF and ophthalmologic data, the researchers identified 44 new cases of POAG, for an incidence of 74 cases per 10,000 person-years. After inverse probability weighting, Park and his colleagues estimated that the risk of POAG was about five times higher with a 10-fold increase in patella lead and about three times higher with a 10-fold increase in tibia lead. The authors conclude that cumulative lead exposure may be a risk factor for POAG.

"There's almost no work on lead and the aging visual system," says Kim Dietrich, a professor of environmental health at the University of Cincinnati who was not involved in the study. "It's a major challenge to capture early exposure history. Park took good advantage of the well-conducted Normative Aging Study."

The findings will need to be confirmed in a larger study as well as in populations that include women (unlike the VA Normative Aging Study). In the future, Park also hopes his lab and others will continue investigating links between environmental metal exposures and other diseases of aging. He says, "Much of the work in environmental health focuses on children and early-life exposures, but we need to know more about these effects later in life."

Carrie Arnold is a freelance science writer living in Virginia. Her work has appeared in *Scientific American*, *Discover*, *New Scientist*, *Smithsonian*, and more.

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