Photic sneeze reflex in nephropathic cystinosis*  

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Abstract  
Photic induced sneeze is a reflex that occurs in certain individuals after exposure to bright light. Cystinosis is an autosomal recessive inborn error of metabolism in which non-protein cystine accumulates within lysosomes. The pathognomonic ocular manifestation of cystinosis is corneal crystal deposition. We observed photic induced sneezes during ophthalmoscopic examination in five of 19 patients with nephropathic cystinosis (26%). We report on this observation and discuss possible pathophysiological mechanisms for photic induced sneezing in cystinosis.

Sneezing in response to bright light is a peculiar phenomenon that may occur in otherwise normal people. It most commonly occurs as a subject walks outside into bright sunlight; on occasion it happens during ophthalmoscopy and rarely with slit-lamp illumination. While numerous investigators have commented on this unique reflex, its physiological mechanism has not been clearly defined.

Cystinosis is an autosomal recessive metabolic disorder in which non-protein cystine accumulates in most body organs. The cystine accumulates within the lysosomes of cells owing to a defect in lysosomal cystine transport. Cystinosis is divided into two major clinical groups, nephropathic and benign. Systemic complications of the former include the renal Fanconi syndrome with rickets and growth retardation, and glomerular failure necessitating renal transplantation by an average age of 10 years. All phenotypes of cystinosis are associated with oculomotor abnormalities. The pathognomonic ocular manifestation of cystinosis is the presence of distinctive iridescent crystals within the conjunctiva and cornea. Histologically the crystals are birefringent, intracellular, and of varying morphology.

Crystals have also been seen in the iris, ciliary body, choroid, retinal pigment epithelium, sclera, episclera, extracellular muscles, and optic nerve sheath. A pigmented retinopathy characteristically affecting the periphery has been described in the nephropathic form of the disease, though not observed in the benign form. Although cystine crystals may be deposited in the choroid plexus and on rare occasion are seen within brain parenchyma, patients with cystinosis have been thought to be neurologically normal. Recent work has suggested that these patients do have neurological dysfunction. While cystinosis affects many ocular structures, the only complaints of patients are, generally, photophobia and glare.

In the course of our on-going study of the neuro-ophthalmological manifestations of nephropathic cystinosis we observed photic induced sneeze in a disproportionate number of these patients. We report on this observation, and relate its occurrence in cystinosis to a possible underlying pathophysiology.

Patients and methods  
We examined 19 patients with the infantile-onset form of nephropathic cystinosis. All had photophobia, though none had excessive lacrimation or obvious nasal allergies. All patients had normal visual acuity with normal colour vision (pseudoisochromatic plates). Their pupillary responses were normal, without evidence of afferent pupillary defect. No sectoral abnormality of iris innervation was noted, and accommodation was normal for age. Corneal reflexes were clinically normal in all the patients, and trigeminal function was intact. On four of the 19 we performed electrophysiological blink reflex studies, with transcutaneous stimulation of the supraorbital nerve and surface recording of the orbicularis oculi motor action potential. In all patients so studied a normal afferent limb to the blink reflex was demonstrated.

All of the cystinosis patients had extensive crystal deposition in the conjunctiva and cornea. Ophthalmoscopy revealed all patients to have depigmentation of the peripheral retina, with a patchy, mottled appearance to each fundus from the mid equator to the ora serrata. Optic nerves were of normal colour, contour, and capillarity. No defect of nerve fibre layer could be detected.

Results  
During the course of slit-lamp biomicroscopy two of the 19 patients had a photic induced sneeze, and during indirect ophthalmoscopy three more patients had one. Thus five of 19 (26%) nephropathic cystinosis patients showed this reflex. The sneeze occurred at the beginning of the exposure of the retina to light and did not persist with continued exposure. Pupillary evaluation with a hand held muscle light before slit-lamp examination and indirect ophthalmoscopy did not precipitate a photic sneeze in any patient. Of 100 control patients prospectively examined in the same manner none sneezed in
response to the light of the indirect ophthalmoscope or slit-lamp.

Discussion
Collie et al characterised the photic induced sneeze as an uncontrollable paroxysm of sneezing provoked in a reflex fashion by the sudden exposure of a dark-adapted subject to intensely bright light. The reported incidence of the photic sneeze reflex is surprisingly high. Peroutka and Peroutka reported it to be present in nine of 25 neurologists (36%), though their data were derived from questionnaires. Everett reported a history of photic sneeze in 68 of 414 persons (16.4%) surveyed. He found a higher incidence in Caucasians than blacks, and in those who had noted the reflex in family members, and he concluded that heredity was a factor in predisposing to photic sneeze. In a study of four families Collie et al found a distribution consistent with an autosomal dominant inheritance pattern for the trait, with a high degree of penetrance.

The usual source of stimulation in susceptible people is sunlight, though artificial light may also precipitate a sneeze. Sedan described the reflex in patients exposed to such varying stimuli as the indirect ophthalmoscope, photographic flash, and ultraviolet light. Although generally harmless, photic induced sneezing has been reported to cause conduction deafness, media-stinorhitis, and cerebral haemorrhage. Moreover, the photic sneeze reflex may be more than just a curiosity to those whose work requires exposure to flashes of illumination.

The sneeze reflex is a neurophysiological response to the light of the indirect ophthalmoscope or slit-lamp. The activity of the Edinger-Westphal nucleus, a part of the parasympathetic nervous system, is responsible for the sneeze reflex. The reflex is elicited by light falling on the retina, which stimulates the Edinger-Westphal nucleus. The parasympathetic fibres from the Edinger-Westphal nucleus and the trigeminal afferent fibres from the cornea pass through the ciliary ganglion, where they may participate in ephaptic transmission.

Parasympathetic generalisation may contribute to photic sneeze. Stimuli which excite primarily one branch of the parasympathetic nervous system tend to activate other branches. Light falling on the retina stimulates pupillary contraction, subserved by parasympathetic fibres of the oculomotor nerve. The parasympathetic activity of miosis may produce congestion of and secretion from the nasal mucosa (mediated through the seventh nerve and the sphenopalatine ganglion), factors which are recognised to initiate sneezing.

In summation, the photic induced sneeze is a reflex which seems to involve diverse neuroanatomical substrates including the optic, oculomotor, and trigeminal nerves, autonomic pathways, and central brainstem structures. Its remarkable prevalence in a nephropathic cystinosis population offers an opportunity for further study of its underlying pathophysiological mechanisms.