

Understanding Cataract Risk in Aerospace Flight Crew And Review of Mechanisms of Cataract Formation

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Abstract

Induction of cataracts by occupational exposure in flight crew has been an important topic of interest in aerospace medicine in the past five years, in association with numerous reports of flight-associated disease incidences. Due to numerous confounding variables, it has been difficult to determine if there is increased cataract risk directly caused by interaction with the flight environment, specifically associated with added radiation exposure during flight. Military aviator records from the United States Air Force (USAF) and Navy (USN) and US astronauts at the National Aeronautics and Space Administration (NASA) /Lyndon B. Johnson Space Center (JSC) were evaluated for the presence, location and age of diagnosis of cataracts. Military aviators were found to have a statistically significant younger average age of onset of their cataracts compared with astronauts, however the incidence density of cataracts was found to be statistically higher in astronauts than in military aviators. USAF and USN aviator's cataracts were most commonly located in the posterior subcapsular region of the lens while astronauts' cataracts were most likely to originate generally in the cortical zone. A prospective clinical trial which controls for confounding variables in examination technique, cataract classification, diet, exposure, and pharmacological intervention is needed to determine what percentage of the risk for cataracts are due to radiation, and how to best develop countermeasures to protect flight crews from radiation bioeffects in the future.

Introduction

In the past five years, an increased scrutiny of the occupational health risks of flight crews has been observed, and the evaluation of ocular health risks has been no exception. Cataracts, if found in the visual axis can produce diminution in visual acuity, and are disqualifying for pilots. However they are usually only slowly progressive and can be detected with routine screening, usually before significant visual acuity loss. They can be surgically excised and the affected lens artificially replaced, making them usually a source of healthcare cost and morbidity in the United States, but not mortality in the flight crew population. Cataracts surgery is the most frequently reimbursed procedure by Medicare, and accounts for 12% of Medicare budget. 1.18 million lens implanted /year in the U.S. Studies of the incidence and prevalence of cataracts in the U.S. is summarized in Table 1.

[Table 1 here]

However worldwide, cataracts are a major cause of blindness. There is an increased incidence of cataracts in equatorial(45)and high altitude locations, presumably associated with increased UV exposure. (21, 28, 75, 94, 121, 122, 126, 128, 136, 138-140, 142, 153, 155) The risk of cataracts has many associated risk factors including age(104, 108, 127), diabetes, nutrition(137), genetic factors, cigarette smoking, drug use (30, 43, 103, 125), e.g. psoralen(61, 62, 141), steroids and alcohol, obesity, occupational exposures (117, 151, 152), e.g. welding(37), elevated temperatures (95, 134) or radiofrequency energy(31, 68-71, 87, 88, 102), including microwaves(32, 33, 54-57, 66, 89, 112, 120), ultraviolet (UV)(2, 5, 6, 8, 47, 96) and ionizing radiation exposure. (14, 40, 48-50, 52, 53, 64, 65, 76, 77, 82-84, 92, 109, 110, 133, 143-150). Research to date seems to indicate that multiple mechanisms may cause the lens to degenerate (29, 30) thereby making assignment of causative blame to the principle risk factors which may account for an increased rate of cataract formation in flight crew, a rather complex task.(125) Nevertheless, since 2000, there have been multiple reports of increased rates of cataract formation in specific flight populations, e.g. airline pilots (86, 97-99) and astronauts (23, 24, 100), however a comparison of the aerospace-induced cataract risk across flight populations has not previously been reported. Understanding the correlation of the degree of occupational environmental exposure and the subsequent rate and severity of biological outcome is essential to quantifying the risk to flight crews for carrying out their missions(34, 35).

Several etiologies for the increased rate of cataracts in astronauts and pilots have been discussed, however since there are potentially a number of confounders, pinpointing the precise causative agent is difficult and most likely multi-factorial. A key question still unanswered, is how much did the spaceflight-specific radiation exposure contribute to the cataracts rate and degree of formation? The methodology for the clinical detection of cataracts has also varied over the years and amongst different screening examination facilities, thereby rendering the validity of the comparisons questionable. The objectives of the current evaluation are 1) to compare the cataract formation rate across several flight and non-flight groups, to determine if any light can be shed on the etiologic factors contributing to this organ-specific disease, and 2) to review the pathogenic mechanisms

for cataract formation, in order to suggest candidates for countermeasure development for prevention of ocular diseases in flight crews.

Methods

A retrospective review of US Air Force, Navy, FAA and NASA flight crew databases was conducted to determine the incidence of cataract formation in the relevant flight populations. The information in the databases was verified by reviewing individual aviator records within each of the databases, to ensure accurate characterization of each cataract occurrence was correctly cataloged.

Description of Examination procedures for ocular examinations:

NASA: A complete ocular history and medical history was accomplished with particular emphasis on the exclusion items of active ocular disease, dilating drug sensitivity, pseudophakia, glaucoma, diabetes, use of history of use of steroids, visually significant corneal opacities or visually significant retinal/ocular pathology.

Bilateral ocular examinations were conducted annually to include standard visual acuity, color and depth perception evaluations. Intraocular pressure was measured by applanation tonometry. Gross evaluation of adnexal tissues was evaluated; to include lids, lashes, extraocular muscle function and pupillary function (size, symmetry and light response), All anterior segment tissues were evaluated by slit lamp methods to include lashes, lids, conjunctiva, cornea, iris, lens and media. Closeable angles were ruled out.

Refraction was derived by standard optometric methodologies utilizing monitor derived eye charts positioned and calibrated at a 6 meter test distance. Upon completion of the manifest refraction (non-cycloplegic) the measurement of best correctable LogMAR visual acuity was documented via Precision Vision ETDRS back-illuminated charts at 4 meters. The acuity was measured while viewing through the refractor with the derived best correction. Each eye was tested independently and both high and low contrast acuities were recorded.

Proparicaine 0.5% was utilized for the measurement of intra-ocular pressure by applanation (Goldmann). Pupillary responses were evaluated, and if normal, pupils were dilated with a combination of tropicamide 1% and neosynephrine 2.5%. Dilation allowed evaluation of the posterior segment tissues to include lens, vitreous, retina, optic nerve and associated vasculature. The lens was evaluated in great detail utilizing both subjective and objective methodologies. Subjective methods involved estimating nuclear color and opacity, area of cortical and posterior sub-capsular using the LOCS III (Lens Opacities Classification System – Version III) point system. Objective methods involved imaging the lens using a Nidek EAS1000 digital camera to capture both Scheimflug slit and retroilluminated images of each eye. The retroilluminated images were captured at two repeated anterior and posterior lens points of reference.

Each subject was requested to fill out a detailed standardized food frequency survey and smoking questionnaire annually. A standardized questionnaire regarding life-style issues such as the amount of time spent in the sun, time spent in water activities, flight

activities and locations lived for the past thirty years was administered during the first year visit only.

DOD- USAF/USN The majority of testing points and methods are the same as NASA with some significant and notable exceptions.

1. Test Distance: Testing in DOD facilities may vary in test distance in that some facilities may have 6 meter testing lanes while others are much shorter but utilize mirrors to create the 6 meter test distance.
2. Pupil Dilation: Dilation may not be accomplished each year as it is at the discretion of the examining doctor.
3. Detail of lens evaluation accomplished at NASA is far more detailed than is standard in DOD facilities. DOD facilities will evaluate lens opacities as present or absent, or possibly use a grading system, which is generally a 0 to 4 method and not standardized from facility to facility or doctor to doctor.

Data collection and Statistical methods:

Standard epidemiological methods were applied to cataract case logging and determination of follow-up for each case as well as for the entire cohort. For 206 subjects with recorded cataracts before age 65 yrs. (27 astronauts, 144 AF, 35 Navy), a Cox proportional hazards model was used to compare the distributions of age at cataract diagnosis, adjusting for time since beginning of service and age at entry. As long as the diagnosis was made before age 65 yrs., subjects were included in this analysis even if they had retired from astronaut or military service. Since this analysis was made only on recorded cases of cataracts, no censoring was involved and by definition, all three groups had 100% cataract cases by age 65. After fitting the model, the method of Grambsch and Therneau was used to see if the proportional hazards assumption was reasonable. Differences between astronauts and the military groups are reflected in estimates of hazard ratios for AF and Navy relative to astronauts.

Results

[Figure 1 here]

Figure 1 shows a graph of prevalence of cataracts comparing 4 populations: U.S. males general populace, commercial airline pilots, and previously flown astronauts who received low dose or high dose space radiation, influenced by duration, altitude and destination of the mission. (Dose rate is generally higher for missions beyond low earth orbit (LEO), although high altitude and high inclination LEO missions can also see higher dose rates due to interaction with trapped particulate radiation within the Van Allen belts). This data would suggest that space radiation is an independent and stronger risk factor than either commercial flight altitude and polar aviation route radiation, or surface UV. However most of the early spaceflight crews during Mercury, Gemini, Apollo, Skylab and Apollo-Soyuz, who are now of likely cataract age, came from a military aviation background. So it seems that the military aviator cohort is the most relevant for comparisons that would confirm if space radiation is the likely causative factor in the increased prevalence of cataracts in space crewmembers. There are several

reasons for this assertion: 1) the prior occupational exposures are similar, 2) the physical, educational, and medical screening selection processes are similar, and 3) the annual examinations are conducted in a similar standardized manner, as seen in the methods description. The latter factor is in contrast to the comparisons the authors made earlier to the LSAH control population. (24)

Review of the Department of Defense aircrew ocular health information, from USAF and USN aircrew health records revealed 13,560,303 person-years of cumulative follow-up. This is compared with 5086 person-years of follow-up obtained from review of NASA astronauts and matched controls.

The prevalence of cataracts in astronauts by age is shown in Figure 2. When grouped together, the shape of the curve does not look dissimilar to what would be expected in an aging predominantly male population, and from what was previously reported in Table 1.

[Figure 2 here]

Figure 3 depicts the cumulative prevalence of cataract cases according to age amongst the analogous flight groups. Inspection of this data reveals an earlier age of onset of cataracts in the military aviator populations compared to astronauts, especially astronauts with higher grade cataracts. It should be noted here that follow-up data for USN aviators was not complete beyond age 65 and is therefore not shown in this graph.

[Figure 3 here]

The finding of earlier age of onset for cataracts in USAF and USN aviators compared to astronauts is reinforced in figure 4 which shows the average age of onset of cataract per eye, including those that developed cataracts in both eyes. Since follow-up was not complete in the USN aviators, the means were not compared statistically with the other groups, although the trend would suggest at earlier age of onset in that cohort as well.

[Figure 4 here]

The most telling information in comparing these 3 cohorts may come from evaluating incidence density of cataracts, as shown in figure 5. The total number of cataracts in astronauts is almost an order of magnitude greater incidence density than in military aviators, especially those occurring in both eyes. Even the number of grade 3 and 4 cataracts has a higher incidence density than total cataracts in aviators.

[Figure 5 here]

Finally, figure 6 shows the incidence of cataracts by anatomic location, comparing the 3 groups. Prior studies have found that UV and other sources of ionizing radiation-induced cataracts are commonly found in the subcapsular location.(11, 13, 16, 17, 19, 22, 26, 27, 42, 75, 124) The most common anatomic location for military aviator cataracts in this study was in the posterior subcapsular location, as is commonly observed in ionizing radiation induction, however the astronaut cataracts were mostly found in the lens cortical region, as previously reported.(24)

[Figure 6 here]

The Grambsch and Therneau test showed no significant departure from the proportional hazards assumption ($P = 0.63$). Estimates of hazard ratios (AF/astronauts and Navy/astronauts) were 2.6 (1.5, 4.8) and 4.1 (2.1, 8.0) respectively, where numbers in parentheses are 95% confidence limits. In other words, AF and Navy pilots had significantly higher hazards than astronauts ($P < 0.005$, $P < 0.001$, respectively), thus given that they had a cataract, the distribution of age of occurrence for the military pilots tended to be shifted significantly towards younger ages than for astronauts, even after adjusting for age of entry and time since beginning of service. Within the two military groups, Navy pilots had a significantly higher hazard ($P = 0.018$), hence an earlier adjusted age distribution at cataract diagnosis than did Air Force pilots.

[Figure 7 here]

Discussion

Pathophysiology of Cataracts Formation:

The formation of cataract in the ocular lens is a complex, multi-factorial, and incompletely understood set of processes. (123) Cataracts may form due to genetic and other dietary and disease-associated factors, which are independent of the environmental exposures of the individual. (12) Yet it is the environmental exposure risk associated with the flight crew occupation that is under scrutiny in this study. Possible mechanisms for observed changes in the lens associated with external factors can be classified into the following categories: biophysical(59, 115, 116), biochemical(8, 15, 59, 60, 106, 127), physiological(5, 115, 116), and cellular(25, 36, 79, 81, 106, 114, 118, 123, 143).

- Some important biophysical considerations include: 90% of UV which hits lens is UVA (315-400 nm), tryptophan absorbs 95% of photon energy absorbed by amino acids in the lens, tryptophan + UV produces 3-HKG (hydroxykynurenine) and other products, 3-HKG- attaches to proteins and turns from clear to brown in color (46, 78, 118).
- Some key biochemical considerations related to lenticular cataracts, are tied to potential oxidative injury with aging: defense enzymes' G-3-PD, G-6-PD, aldolase, enolase, and PG kinase activity decrease with age. Aging is associated with decreased antioxidant concentration which leads to increased vulnerability to oxidative damage, and lipid peroxidation, e.g. decreased glutathione, ascorbate, Aging is also associated with decreased protein solubility and number of soluble proteins (protein denaturation by free radicals), increased disulfide bonds in proteins, oxidation of protein thiols, and changes in membrane permeability, all of which can lead to dehydration of the lenticular cells (osmotic change) especially with radiation exposure. In addition, formation of crystallins, which are high molecular weight aggregates that accumulate with aging, along with degraded polypeptides and amino acid changes e.g., loss of sulfhydryl groups,

deamination of glutamine and asparagine, are commonly observed with typical senile cataracts.

Typical physiological changes observed in the lens over time include: loss of gap junction proteins(15, 20, 22 kDa) with age, loss of cellular membrane potential, increased intracellular sodium concentration (25 mEq/l to 40 mEq/l), as well as changes in Na⁺, K⁺-ATPase activity, secondary to loss of the γ -isoform of ATPase with advancing age.

Changes in lenticular cells depend on the mechanism and location of the cataract process. Anterior subcapsular cataracts most commonly associated with UV light exposure, show lenticular metaplasia, i.e. the cells become spindle-shaped, (myofibroblast-like) in the central lens epithelium. Posterior subcapsular cataracts, which are commonly associated with ionizing radiation and also with UV, show germinal epithelium dysplasia and posterior migration along suture lines.(38, 154) Whereas nuclear cataracts, most commonly associated with aging (senile) show few cellular changes, as it seems the light scatter is produced by high molecular weight proteins in the cytoplasm. (135)

The observations regarding radiation induction of cataracts are not uniform, mainly due to the differences in cellular and biophysical and biochemical effects of various forms of radiation. There is not a universal bioeffect and cellular response across the spectrum of electromagnetic and particulate radiation energy. Prior common thinking on radiation-induced cataracts was posterior subcapsular (11, 13, 26) as the most common location, however they had potential to progress to full cortical, and even nuclear (mixed) cataracts with time(16, 19, 27, 42, 75, 103, 124, 126).

Energy deposition from cosmic, gamma rays, and neutrons causes ionization of lens constituents (mainly water) producing free radicals (primarily hydroxyl radicals) which can easily react and alter function of DNA and cell membranes.(83, 91, 98, 101) Cells with higher mitotic rate, such as the lens equatorial fibers, are differentially affected by these processes.

Typically a 9-12 month latent period from time of exposure to onset of lenticular opacity has been observed. The radiation-induced cataract has been typified by multiple vacuoles, feathery appearance, and even web-like fringes. Glare is a common initial complaint from patients with PSC cataracts.

Although it was the first clinical study to quantify cataracts in astronauts in association with their specific spaceflight radiation exposures(24), there were some issues with the authors previous study in trying to determine if the incidence of cataracts was higher than would be expected in the aging cohort evaluated. These issues include:

- Inequality in screening examination between the LSAH controls and astronauts, in that the controls typically had indirect, non-dilated ophthalmoscopy and no slit lamp examination vs. direct dilated ophthalmoscopy and slit-lamp in the astronaut exams.
- The influence of non-space flight radiation- UV, blue light exposure during high altitude flights; LASER, toxin (e.g. metals, anticholinesterases, antimalarials) exposure was not controlled in the astronauts

- The influence of space-acquired UV and blue light, independent of the cosmic and trapped particulate radiation, determined by the number of spacewalks (EVA-extravehicular activity) time spent with spacesuit visor up, amount of time looking through space windows with sun in the field of view, etc. was not controlled in astronauts.
- There was a lack of photographic documentation for post-hoc review of categorization/stage of cataracts, Instead there was subjective assignment of each diagnosed cataract by a single examiner, resulting in a clinical grading.
- Other risk factors for cataracts were not controlled in either group.

Although the data was highly suggestive of a dose-dependent increase in cataracts in the astronauts relative to age-matched controls, it is still difficult to attribute the risk specifically to the spaceflight radiation exposure, without controlling for the confounders.

In striving to answer the question, does spaceflight radiation produce an independent risk of cataracts in astronauts, we compared the incidence of astronaut cataracts to a population with a background similar to the typical astronaut between 1962 and 1985 – the military aviator. That comparison reveals some important findings: 1) astronauts do not acquire lenticular opacities at a younger age versus their military aviator counterparts, 2) the incidence density of cataracts is much higher in astronauts than in military aviators, 3) the location of cataracts in astronauts is not typical of either what is observed in aviators or what is commonly associated with ionizing radiation exposure.

Perhaps the first two findings can be explained by the fact that while the aviation flight exposure to radiation is common to both groups and occurs relatively early in their career, the exposure to space radiation usually occurs later in the astronaut career. However, given the above fact, the latency from age of exposure, as cited in Cucinotta et al(24), to the age of diagnosis, is longer than would be commonly observed with radiation-induction. This finding may be due to the reduced rate and total dose of exposure than is typically given during research studies on radiation bioeffects. However, the location of the cataracts in astronauts may be the most difficult to explain, if our current mechanistic understanding is correct.(38, 39, 46, 47) Perhaps space radiation, both cosmic and trapped particulate, produce cataract-like changes in the lens via a different mechanism than does ultraviolet, gamma and other ionizing radiation sources. Clearly the location of cataracts in the lens cortex in astronauts is not typical of the nuclear cataracts seen with aging alone.

What is needed:

A prospective study is underway, being led by one of the nation's experts in the field, Dr. Leo Chylack. This study may go a long way to determining if astronauts are truly at increased risk associated with their occupational exposures, although the numbers of individuals with significant space radiation exposure is quite small and the numerous confounders discussed above will still be at play. The study by Chylack, et al employs lenticular imaging with photographic records that will allow independent assessment of the classification/grade of the cataract in both astronauts and controls thereby eliminating the bias in grading of opacities, potentially affecting the earlier reported results.

Since the majority of cataracts detected in astronauts did not result in visual axis impairment thereby limiting the usefulness of acuity as an outcomes measure, the current prospective study would benefit from a more sensitive means of detecting cataract formation prior to the development of clinical sequelae. This would facilitate reducing the length of follow-up required to determine if a statistical and clinical difference exists between the study groups. Such a device has been recently developed at the NASA, John Glen Research Center, under a NASA-NEI interagency agreement and employs a dynamic light scattering device. It appears to be the most sensitive method of detecting early lens abnormalities, currently available for clinical use (3).

For future space missions, taking astronauts again beyond low earth orbit (LEO) and onto other planetary bodies within the solar system, an effective countermeasure to reduce the risk of biological effects in the crew needs to be developed. Countermeasures for exploration spaceflight should protect not only ocular tissue (18, 73, 119, 129, 132): such as the cornea, lens, retina, but also other tissues vulnerable to ionizing radiation-induced direct cellular injury and secondary oxidative damage. Understanding the mechanism of the cataract formation in space radiation-induced forms of the disease, may be pivotal in producing an effective countermeasure.(9, 129) Recent studies suggest that agents which limit the propagation of peroxidation and the interaction of reactive oxygen species(72) with cellular organelles (1, 107) and membranes(44, 73, 93, 131) may protect the lens(105) and retina(85, 90, 111) from damage. (4, 7, 10, 41, 74, 103, 105, 113, 125, 129, 137) Measuring the state of oxidative damage in the 2 study groups may improve characterization of the contributing factors. While understanding the role of spaceflight shielding(20, 67, 130), dietary and pharmacological interventions which may augment the inherent cellular repair mechanisms; (80) are likely to be helpful in developing an effective defense for exploration-class spaceflight.

Tables and Figures

Tables

Table 1: U.S. study data on cataracts prevalence and incidence- (51, 58, 63)

Framingham	n=2477	
Age group	% with lens changes (opacities prevalence)	% with visually significant cataracts
52-64	42	5
65-74	73	18
75-85	91	46
NHANES	n=10,000	
65-74	60	18
	5-year Incidence	
55	10	
60	16	
65	23	
70	31	
75	37	

Table 2: Incidence; Incidence Density and Age at Diagnosis for military pilots and astronauts

	Number of Cases (Number of Individuals)			Number of Person-years (Time of Observation)	Incidence Density /100 Person-years	Average Age at Diagnosis		
	Right Eye Only	Left Eye Only	Both Eyes	Both Eyes	Both Eyes	Right Eye	Left Eye	Both Eyes
Astronaut Corps	51	51	102 (54)	5,103 (1971 - June 2003)	1.999	61.2	60.8	61.0
Astronaut Corps (Grades 3 & 4 only)	4	4	8 (5)	5,103 (1971 - June 2003)	0.1568	65.8	68.5	67.1
U.S. Air Force Aviators	133	137	270 (179)	1,356,303 (1955 - 2000)*	0.0199	44.1	44.7	44.4
U.S. Navy Aviators	20	29	49 (37)	446,130 (1973 - 1999)	0.0110	41.0	39.5	40.1

(*The year 1999 was used twice to serve as a proxy for year 2000, which was not included in the data provided by the USAF. The difference in incidence density for 1955-1999 as compared with 1955-2000 with the year 1999 used twice as a proxy is less than 0.001cases/100 person years.)

Figures

Figure 1

Prevalence of cataracts as a function of age in astronauts, pilots and healthy U.S. males.

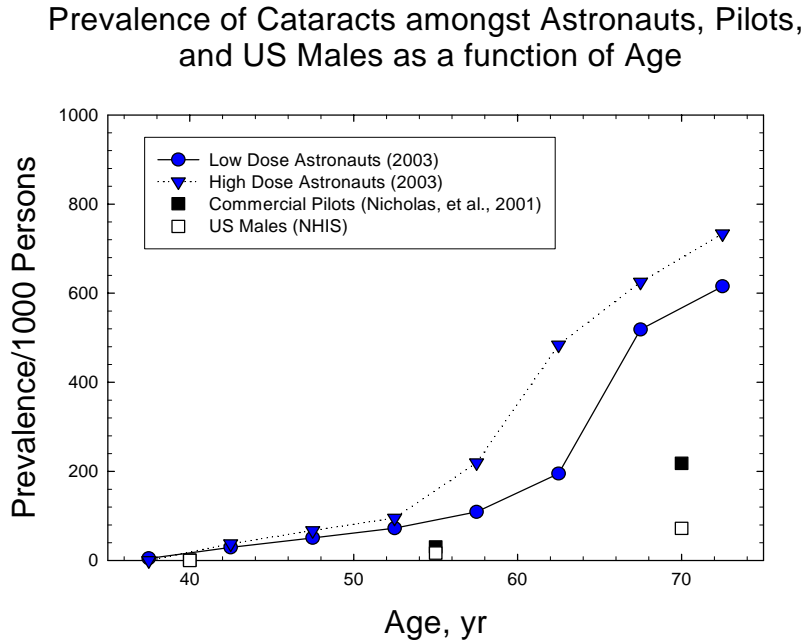


Figure 2

Cataract prevalence by age in U.S. astronauts

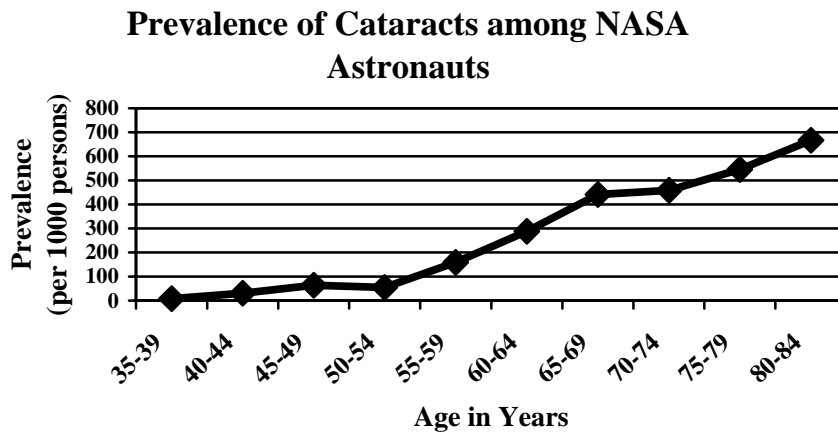


Figure 3: Cumulative Prevalence of Cataract Cases by Age Category among Analogous Populations: Astronaut Corps, Air Force Aviators, Naval Aviators

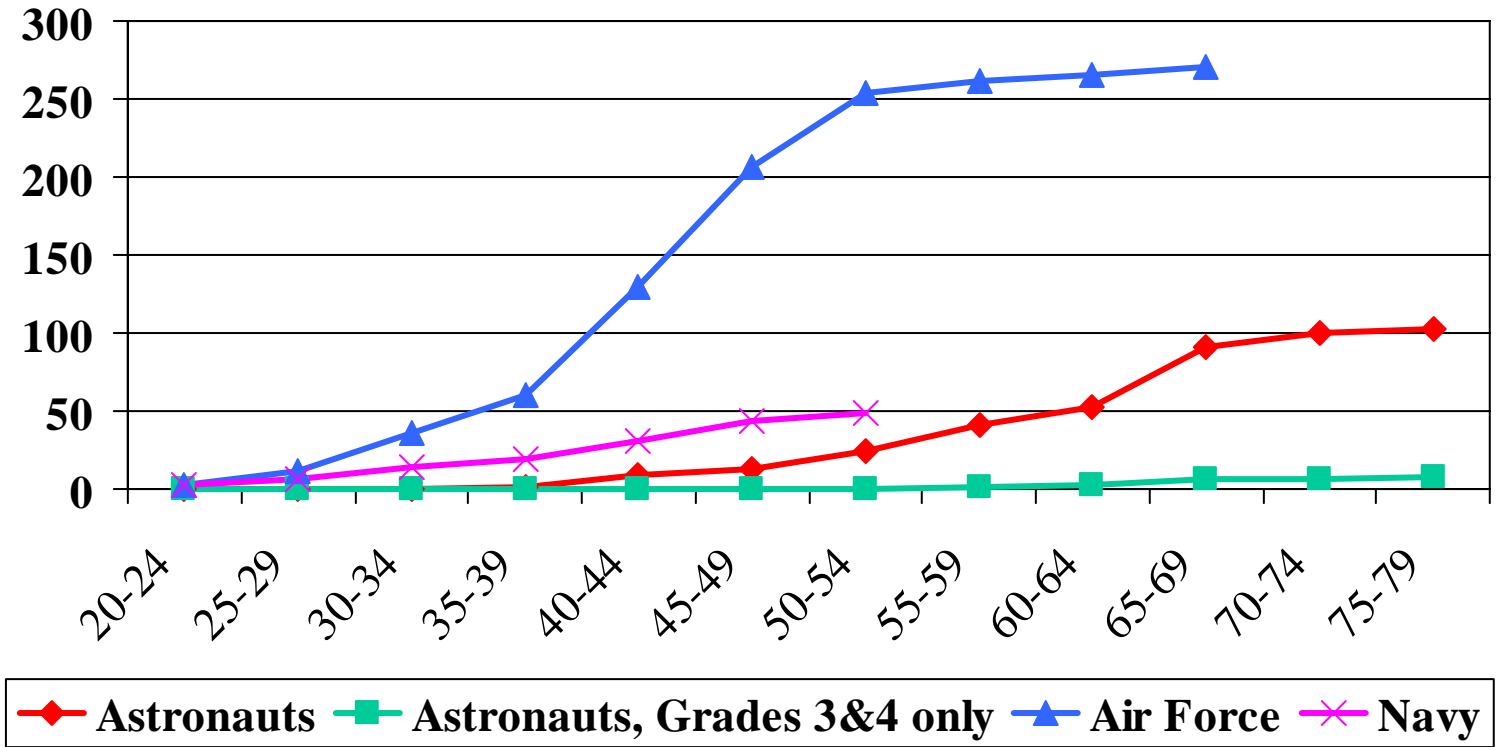


Figure 4; Average Age at Diagnosis of Cataracts among Analogous Populations:
Astronaut Corps, Air Force Aviators, Naval Aviators

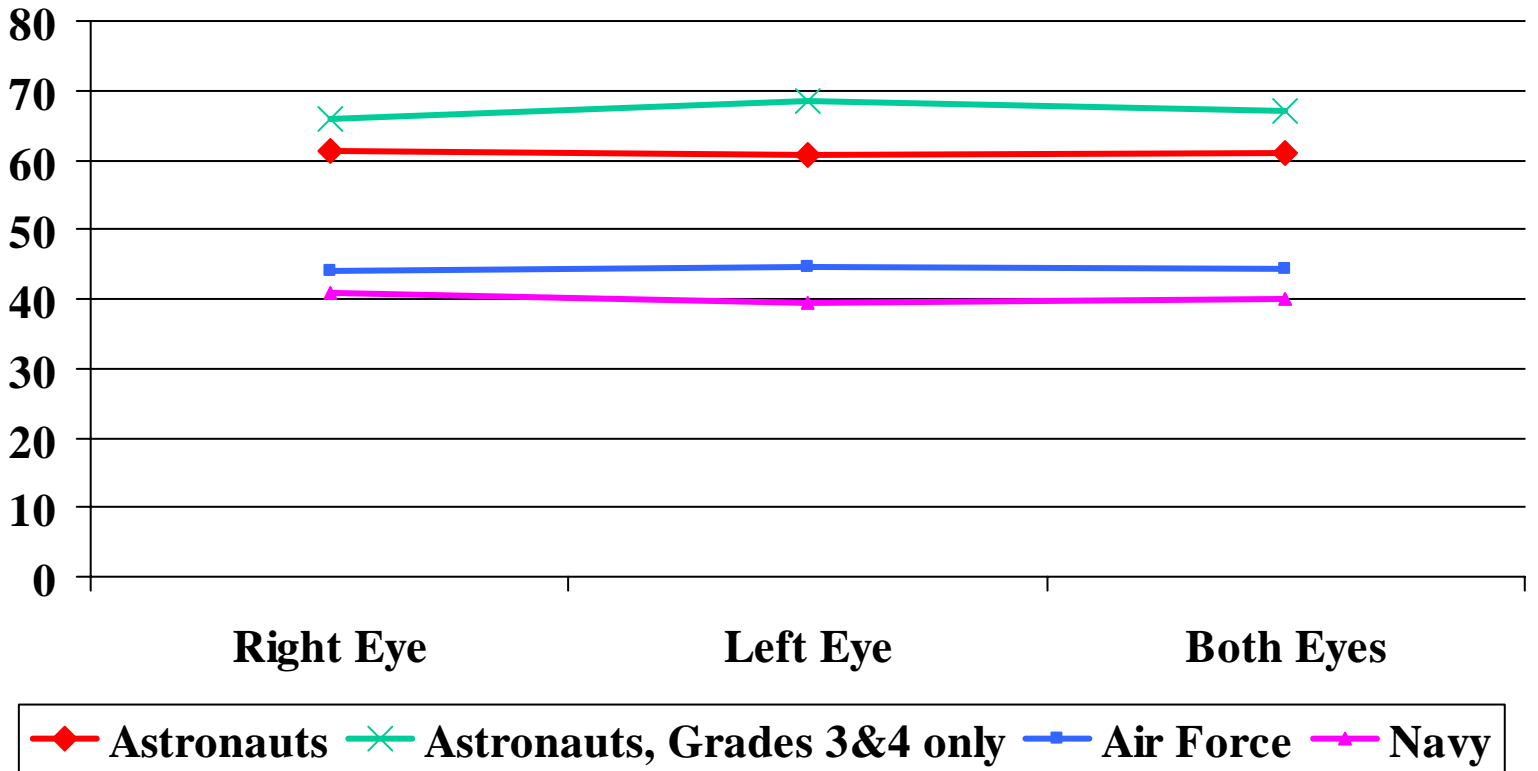
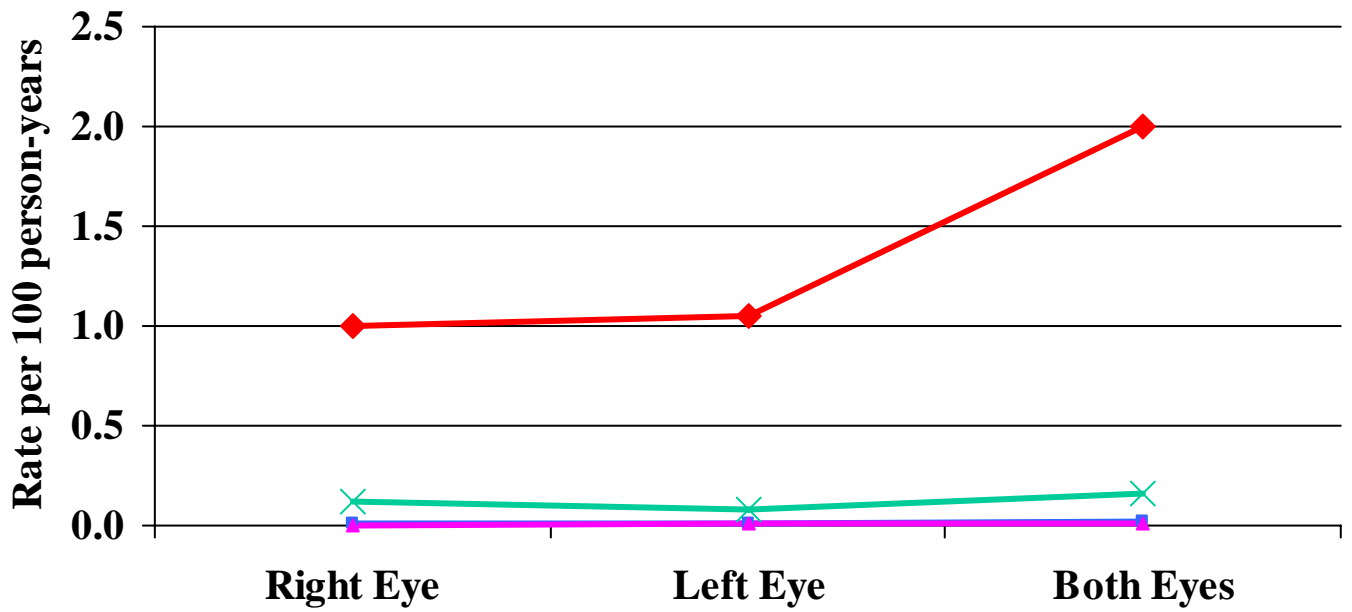
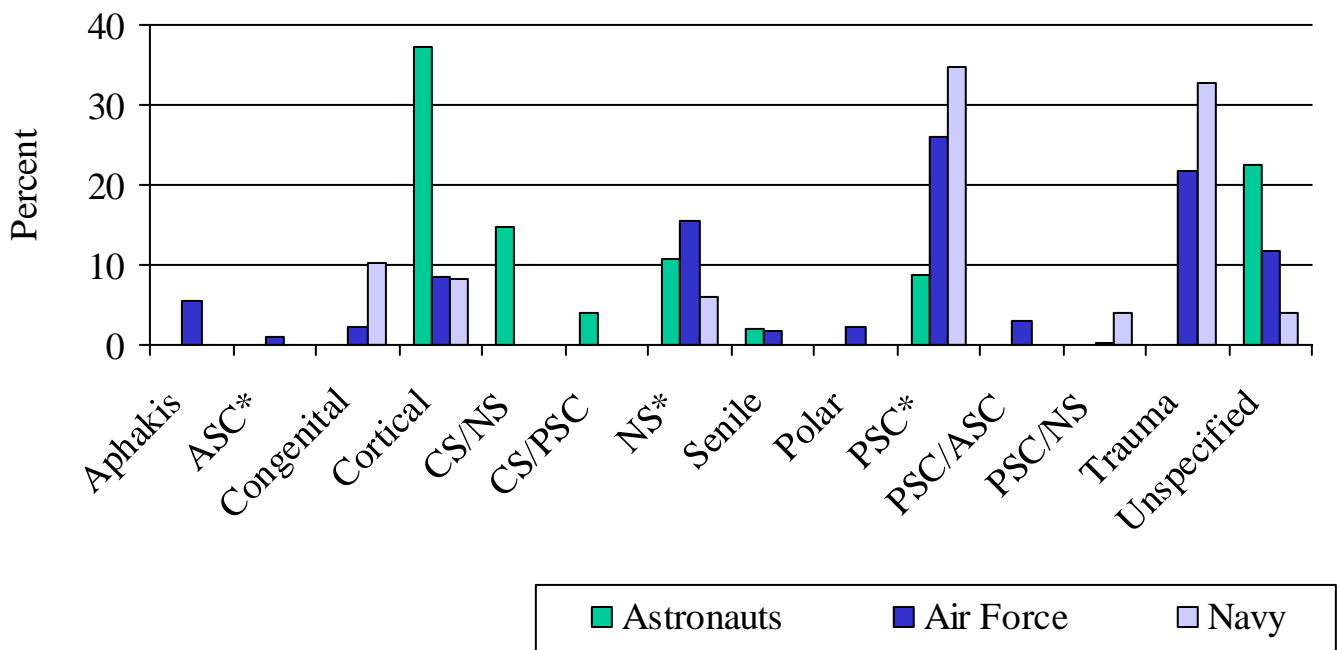


Figure 5: Incidence Density of Cataract Cases among Analogous Populations: Astronaut Corps, Air Force Aviators, Naval Aviators



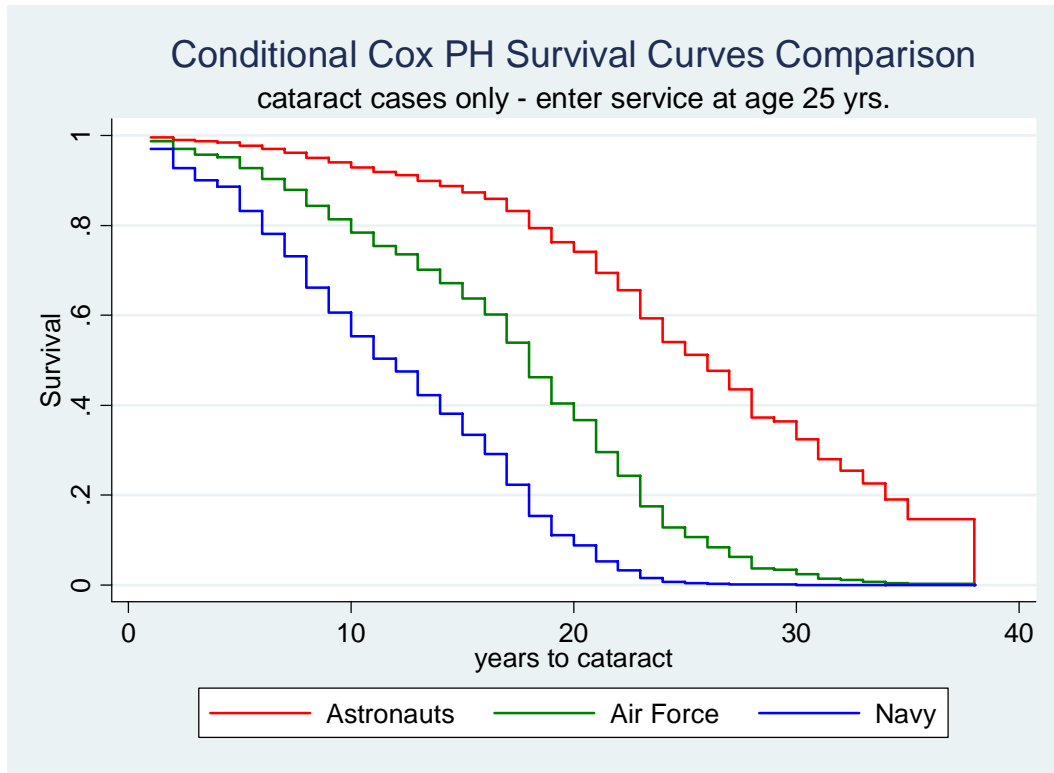
—◆— Astronauts —×— Astronauts, Grades 3&4 only —■— Air Force —▲— Navy

Figure 6: Ratio of Cataract Cases by anatomic location among Analogous Populations: Astronaut Corps, Air Force Aviators, Naval Aviators



* ASC = Anterior Subcapsular Cataract
 NS = Nuclear Sclerosis
 PSC = Posterior Subcapsular Cataract

Figure 7: Cox Porportional Hazards comparison of cataract cases in DOD pilots to astronauts, by years since entry into occupation.



References

1. Afaq F, Adhami VM, Mukhtar H. Photochemoprevention of ultraviolet B signaling and photocarcinogenesis. *Mutat Res* 2005;571(1-2):153-73.
2. Anduze AL. Ultraviolet radiation and cataract development in the U.S. Virgin Islands. *J Cataract Refract Surg* 1993;19(2):298-300.
3. Ansari RR, Clark, J.I., King, J.F., and Seeberger, T. Early detection of cataracts and response to therapy with non-invasive static and dynamic light scattering. *Proc. SPIE* 2003;4951:168-75.
4. Anwar MM, Moustafa MA. The effect of melatonin on eye lens of rats exposed to ultraviolet radiation. *Comp Biochem Physiol C Toxicol Pharmacol* 2001;129(1):57-63.
5. Ayala MN, Michael R, Soderberg PG. In vivo cataract after repeated exposure to ultraviolet radiation. *Exp Eye Res* 2000;70(4):451-6.
6. Ayala MN, Michael R, Soderberg PG. Influence of exposure time for UV radiation-induced cataract. *Invest Ophthalmol Vis Sci* 2000;41(11):3539-43.
7. Ayala MN, Soderberg PG. Reversal of reciprocity failure for UVR-induced cataract with vitamin E. *Ophthalmic Res* 2005;37(3):150-5.
8. Balasubramanian D. Ultraviolet radiation and cataract. *J Ocul Pharmacol Ther* 2000;16(3):285-97.
9. Bantseev V, Bhardwaj R, Rathbun W, et al. Antioxidants and cataract: (cataract induction in space environment and application to terrestrial aging cataract). *Biochem Mol Biol Int* 1997;42(6):1189-97.
10. Bardak Y, Ozerturk Y, Ozguner F, et al. Effect of melatonin against oxidative stress in ultraviolet-B exposed rat lens. *Curr Eye Res* 2000;20(3):225-30.
11. Baum J, Pitts DG. Posterior subcapsular cataract following intense ultraviolet radiation exposure: a case report. *Eye* 1997;11 (Pt 5):661-2.
12. Belkacemi Y, Touboul E, Meric JB, et al. [Radiation-induced cataract: physiopathologic, radiobiologic and clinical aspects]. *Cancer Radiother* 2001;5(4):397-412.
13. Bochow TW, West SK, Azar A, et al. Ultraviolet light exposure and risk of posterior subcapsular cataracts. *Arch Ophthalmol* 1989;107(3):369-72.
14. Bonney CH, Hunter DM, Conley GE, Hardy KA. Heavy-ion-induced cataractogenesis. *Aviat Space Environ Med* 1977;48(8):731-3.
15. Borkman RF. Cataracts and photochemical damage in the lens. *Ciba Found Symp* 1984;106:88-109.
16. Brown NA, Shun-Shin GA, Lewis P, et al. Relationship of cataract to radiation sensitivity. *Br J Ophthalmol* 1989;73(12):955-9.
17. Choshi K, Takaku I, Mishima H, et al. Ophthalmologic changes related to radiation exposure and age in adult health study sample, Hiroshima and Nagasaki. *Radiat Res* 1983;96(3):560-79.
18. Clark JI, Livesey JC, Steele JE. Delay or inhibition of rat lens opacification using pantethine and WR-77913. *Exp Eye Res* 1996;62(1):75-84.

19. Collman GW, Shore DL, Shy CM, et al. Sunlight and other risk factors for cataracts: an epidemiologic study. *Am J Public Health* 1988;78(11):1459-62.
20. Cousin AJ, Lawdahl RB, Chakraborty DP, Koehler RE. The case for radioprotective eyewear/facewear. Practical implications and suggestions. *Invest Radiol* 1987;22(8):688-92.
21. Cruickshanks KJ. Sunlight exposure and risk of lens opacities in a population-based study. *Arch Ophthalmol* 1998;116(12):1666.
22. Cruickshanks KJ, Klein BE, Klein R. Ultraviolet light exposure and lens opacities: the Beaver Dam Eye Study. *Am J Public Health* 1992;82(12):1658-62.
23. Cucinotta F, Manuel, K, Jones, J.A., et al. Erratum. *Radiat Res* 2001;156(6):811.
24. Cucinotta F, Manuel, K, Jones, J.A., et al. Space radiation and cataracts in astronauts. *Radiat Res* 2001;156(5 (Pt 1)):460-6.
25. Dairou J, Malecaze F, Dupret JM, Rodrigues-Lima F. The xenobiotic-metabolizing enzymes arylamine N-acetyltransferases in human lens epithelial cells: inactivation by cellular oxidants and UVB-induced oxidative stress. *Mol Pharmacol* 2005;67(4):1299-306.
26. Delcourt C, Carriere I, Ponton-Sanchez A, et al. Light exposure and the risk of cortical, nuclear, and posterior subcapsular cataracts: the Pathologies Oculaires Liees a l'Age (POLA) study. *Arch Ophthalmol* 2000;118(3):385-92.
27. Dolin PJ. Assessment of epidemiological evidence that exposure to solar ultraviolet radiation causes cataract. *Doc Ophthalmol* 1994;88(3-4):327-37.
28. Dolin PJ. Ultraviolet radiation and cataract: a review of the epidemiological evidence. *Br J Ophthalmol* 1994;78(6):478-82.
29. Dong X, Soderberg PG, Ayala M, Lofgren S. The effect of exposure time on maximum acceptable dose for avoidance of ultraviolet radiation-induced cataract. *Ophthalmic Res* 2005;37(4):197-201.
30. Durovic B, Spasic-Jokic V. [Occupational exposure to ionizing radiation and the occurrence of cataract]. *Vojnosanit Pregl* 2004;61(4):387-90.
31. Elder JA. Ocular effects of radiofrequency energy. *Bioelectromagnetics* 2003;Suppl 6:S148-61.
32. Foster MR, Ferri ES, Hagan GJ. Dosimetric study of microwave cataractogenesis. *Bioelectromagnetics* 1986;7(2):129-40.
33. Frey AH. Data analysis reveals significant microwave-induced eye damage in humans. *J Microw Power Electromagn Energy* 1985;20(1):53-5.
34. Fry RJ. Deterministic effects. *Health Phys* 2001;80(4):338-43.
35. Fry RJ. Radiations in space: risk estimates. *Radiat Prot Dosimetry* 2002;100(1-4):475-7.
36. Giblin FJ, Leverenz VR, Padgaonkar VA, et al. UVA light in vivo reaches the nucleus of the guinea pig lens and produces deleterious, oxidative effects. *Exp Eye Res* 2002;75(4):445-58.
37. Hanke C, Karsten H. [Cataract in welders. Contribution of occupational exposure, references for recognition as an occupational disease and presentation of preventive measures]. *Z Gesamte Hyg* 1990;36(2):110-3.
38. Hayashi LC, Hayashi S, Yamaoka K, et al. Ultraviolet B exposure and type of lens opacity in ophthalmic patients in Japan. *Sci Total Environ* 2003;302(1-3):53-62.

39. Hayashi LC, Tamiya N, Yano E. Correlation between UVB irradiation and the proportion of cataract--an epidemiological study based on a nationwide patient survey in Japan. *Ind Health* 1998;36(4):354-60.
40. Hayes BP, Fisher RF. Influence of a prolonged period of low-dosage x-rays on the optic and ultrastructural appearances of cataract of the human lens. *Br J Ophthalmol* 1979;63(7):457-64.
41. Hodge WG, Whitcher JP, Satariano W. Risk factors for age-related cataracts. *Epidemiol Rev* 1995;17(2):336-46.
42. Hu H. Effects of ultraviolet radiation. *Med Clin North Am* 1990;74(2):509-14.
43. Jacobson BS. Cataracts in retired actinide-exposed radiation workers. *Radiat Prot Dosimetry* 2005;113(1):123-5.
44. Jacques PFC, L. T., Jr. Epidemiologic evidence of a role for the antioxidant vitamins and carotenoids in cataract prevention. *Am J Clin Nutr* 1991;53:352S-5S.
45. Javitt JC, Taylor HR. Cataract and latitude. *Doc Ophthalmol* 1994;88(3-4):307-25.
46. Jose JG. Posterior cataract induction by UV-B radiation in albino mice. *Exp Eye Res* 1986;42(1):11-20.
47. Jose JG, Ainsworth EJ. Cataract production in mice by heavy charged argon, neon, and carbon particles. *Radiat Res* 1983;94(3):513-28.
48. Junk AK, Egner P, Gottloeber P, et al. [Long-term radiation damage to the skin and eye after combined beta- and gamma- radiation exposure during the reactor accident in Chernobyl]. *Klin Monatsbl Augenheilkd* 1999;215(6):355-60.
49. Kabachenko AN, Fedorenko BS. [Cataractogenic effect of protons with energies of 25 and 50 MeV]. *Kosm Biol Aviakosm Med* 1977;11(4):59-62.
50. Kabachenko AN, Fedorenko BS. [Lens opacity in mice exposed to helium ions with energy of 4 GeV/nuclon and gamma-irradiation with Co-60]. *Kosm Biol Aviakosm Med* 1985;19(1):56-8.
51. Kahn HA LH, Ganley JP, Kini MM, Colton T, Nickerson RS, Dawber TR.. . The Framingham Eye Study. I. Outline and major prevalence findings. *Am J Epidemiol* 1977; July 106(1):17-32.
52. Kirk JH, Casey HW, Traynor JE. Summary of latent effects in long term survivors of whole body irradiations in primates. *Life Sci Space Res* 1972;10:165-73.
53. Klein BE, Klein RE, Moss SE. Exposure to diagnostic x-rays and incident age-related eye disease. *Ophthalmic Epidemiol* 2000;7(1):61-5.
54. Kojima M, Okuno T, Miyakoshi M, et al. Environmental temperature and cataract progression in experimental rat cataract models. *Dev Ophthalmol* 2002;35:125-34.
55. Kramar P, Harris C, Guy AW. Thermal cataract formation in rabbits. *Bioelectromagnetics* 1987;8(4):397-406.
56. Kurz GH, Einaugler RB. Cataract secondary to microwave radiation. *Am J Ophthalmol* 1968;66(5):866-9.
57. Langley RK, Mortimer CB, McCulloch C. The experimental production of cataracts by exposure to heat and light. *Arch Ophthalmol* 1960;63:473-88.
58. Leibowitz HM KD, Maunder LR, et al. . The Framingham Eye Study monograph: An ophthalmological and epidemiological study of cataract, glaucoma, diabetic retinopathy, macular degeneration, and visual acuity in a general population of 2631 adults: 1973-1975. *Surv Ophthalmol* 1980;24:335-610.

59. Lerman S. Chemical and physical properties of the normal and aging lens: spectroscopic (UV, fluorescence, phosphorescence, and NMR) analyses. *Am J Optom Physiol Opt* 1987;64(1):11-22.
60. Lerman S. An experimental and clinical evaluation of lens transparency and aging. *J Gerontol* 1983;38(3):293-301.
61. Lerman S. Ocular phototoxicity and psoralen plus ultraviolet radiation (320-400 nm) therapy: an experimental and clinical evaluation. *J Natl Cancer Inst* 1982;69(1):287-302.
62. Lerman S. Potential ocular complications of psoralen-UV-A therapy. *Derm Beruf Umwelt* 1980;28(1):5-7.
63. Leske MC, Wu, S. Y., Hyman, L., Sperduto, R., Underwood, B., Chylack, L. T., Milton, R. C., Srivastava, S. & Ansari, N. Biochemical factors in the lens opacities. Case-control study. The Lens Opacities Case-Control Study Group. *Arch Ophthalmol* 1995;113:1113-9.
64. Lett JT, Cox AB, Lee AC. Cataractogenic potential of ionizing radiations in animal models that simulate man. *Adv Space Res* 1986;6(11):295-303.
65. Lett JT, Lee AC, Cox AB. Late cataractogenesis in rhesus monkeys irradiated with protons and radiogenic cataract in other species. *Radiat Res* 1991;126(2):147-56.
66. Lipman RM, Tripathi BJ, Tripathi RC. Cataracts induced by microwave and ionizing radiation. *Surv Ophthalmol* 1988;33(3):200-10.
67. Littleton JT, Durizch ML, Perry N. Radiation protection of the lens for patients and users. *Radiology* 1978;129(3):795-8.
68. Lydahl E. Infrared radiation and cataract. *Acta Ophthalmol Suppl* 1984;166:1-63.
69. Lydahl E, Glansholm A. Infrared radiation and cataract. III. Differences between the two eyes of glass workers. *Acta Ophthalmol (Copenh)* 1985;63(1):39-44.
70. Lydahl E, Philipson B. Infrared radiation and cataract II. Epidemiologic investigation of glass workers. *Acta Ophthalmol (Copenh)* 1984;62(6):976-92.
71. Lydahl E, Philipson B. Infrared radiation and cataract. I. Epidemiologic investigation of iron- and steel-workers. *Acta Ophthalmol (Copenh)* 1984;62(6):961-75.
72. Machlin LJ, Bendich A. Free radical tissue damage: protective role of antioxidant nutrients. *Faseb J* 1987;1(6):441-5.
73. Mayer UM, Muller Y, Bluthner K. [Vitamins C and E protect cultures of bovine lens epithelium from the damaging effects of blue light (430 nm) and UVA light (300-400 nm)]. *Klin Monatsbl Augenheilkd* 2001;218(2):116-20.
74. McCarty CA, Taylor HR. Recent developments in vision research: light damage in cataract. *Invest Ophthalmol Vis Sci* 1996;37(9):1720-3.
75. McCarty CA, Taylor HR. A review of the epidemiologic evidence linking ultraviolet radiation and cataracts. *Dev Ophthalmol* 2002;35:21-31.
76. Medvedovsky C, Worgul BV. Neutron effects on the lens. *Radiat Res* 1991;128(1 Suppl):S103-10.
77. Medvedovsky C, Worgul BV, Huang Y, et al. The influence of dose, dose-rate and particle fragmentation on cataract induction by energetic iron ions. *Adv Space Res* 1994;14(10):475-82.
78. Meyer LM, Soderberg P, Dong X, Wegener A. UVR-B induced cataract development in C57 mice. *Exp Eye Res* 2005;81(4):389-94.

79. Michael R. Development and repair of cataract induced by ultraviolet radiation. *Ophthalmic Res* 2000;32 Suppl 1:ii-iii; 1-44.
80. Michael R, Soderberg PG, Chen E. Long-term development of lens opacities after exposure to ultraviolet radiation at 300 nm. *Ophthalmic Res* 1996;28(4):209-18.
81. Michael R, Vrensen GF, van Marle J, et al. Repair in the rat lens after threshold ultraviolet radiation injury. *Invest Ophthalmol Vis Sci* 2000;41(1):204-12.
82. Miller RW. Delayed effects of external radiation exposure: a brief history. *Radiat Res* 1995;144(2):160-9.
83. Minamoto A, Taniguchi H, Yoshitani N, et al. Cataract in atomic bomb survivors. *Int J Radiat Biol* 2004;80(5):339-45.
84. Nakashima E, Neriishi K, Minamoto A. A reanalysis of atomic-bomb cataract data, 2000-2002: a threshold analysis. *Health Phys* 2006;90(2):154-60.
85. National Eye Institute N. Age-Related Eye Disease Study Group. "A randomized placebo-controlled, clinical trial of high dose supplementation with vitamins C, and E, beta carotene, and zinc for age-related macular degeneration and vision loss AREDS report No. 8,". *Arch Ophthalmol*. 2001;119:1417-36.
86. Nicholas JS BG, Lackland DT, Tessier GS, Mohr LC Jr, Hoel DG. Health Among commercial airline pilots. *Aviation, Space, and Environmental Medicine* 2001;72(9):821-6.
87. Odland LT. Observations on microwave hazards to USAF personnel. *J Occup Med* 1972;14(7):544-7.
88. Odland LT. Radio-frequency energy: a hazard to workers? *IMS Ind Med Surg* 1973;42(7):23-6.
89. Okuno T. Thermal effect of visible light and infra-red radiation (i.r.-A, i.r.-B and i.r.-C) on the eye: a study of infra-red cataract based on a model. *Ann Occup Hyg* 1994;38(4):351-9.
90. Olmedilla B, Granado, F., Blanco, I. & Vaquero, M. Lutein, but not alpha-tocopherol, supplementation improves visual function in patients with age-related cataracts: a 2-y double-blind, placebo-controlled pilot study. *Nutrition* 2003;19:21-4.
91. Otake M, Finch SC, Choshi K, et al. Radiation-related ophthalmological changes and aging among Hiroshima and Nagasaki A-bomb survivors: a reanalysis. *Radiat Res* 1992;131(3):315-24.
92. Otake M, Schull WJ. A review of forty-five years study of Hiroshima and Nagasaki atomic bomb survivors. Radiation cataract. *J Radiat Res (Tokyo)* 1991;32 Suppl:283-93.
93. Pastor-Valero M. Antioxidant micronutrients and cataract: a review of epidemiological evidence. *Gac Sanit* 2002;16(Suppl 2):29-40.
94. Perkins ES. The association between pinguecula, sunlight and cataract. *Ophthalmic Res* 1985;17(6):325-30.
95. Pitts DG, Cullen AP. Determination of infrared radiation levels for acute ocular cataractogenesis. *Albrecht Von Graefes Arch Klin Exp Ophthalmol* 1981;217(4):285-97.
96. Pitts DG, Cullen AP, Hacker PD. Ocular effects of near ultraviolet radiation: literature review. *Am J Optom Physiol Opt* 1977;54(8):542-9.
97. Rafnsson V. Cosmic Radiation Increases the Risk of Nuclear Cataract in Airline Pilot. *Arch Ophthalmol* 2005;123(August).

98. Rafnsson V, Olafsdottir E, Hrafnkelsson J, et al. Cosmic radiation increases the risk of nuclear cataract in airline pilots: a population-based case-control study. *Arch Ophthalmol* 2005;123(8):1102-5.
99. Rafnsson VD, Manuel. Airline Pilots have sky-high risk of cataracts. 2005.
100. Rastegar N, Eckart P, Mertz M. Radiation-induced cataract in astronauts and cosmonauts. *Graefes Arch Clin Exp Ophthalmol* 2002;240(7):543-7.
101. Rini FJ, Worgul BV, Merriam GR, Jr. Scanning electron microscopic analysis of radiation cataracts in rat lenses. I. X-radiation cataractogenesis as a function of dose. *Ophthalmic Res* 1983;15(3):146-59.
102. Roberts NJ, Jr., Michaelson SM. Epidemiological studies of human exposures to radiofrequency radiation. A critical review. *Int Arch Occup Environ Health* 1985;56(3):169-78.
103. Robman L, Taylor H. External factors in the development of cataract. *Eye* 2005;19(10):1074-82.
104. Rosmini F, Stazi MA, Milton RC, et al. A dose-response effect between a sunlight index and age-related cataracts. Italian-American Cataract Study Group. *Ann Epidemiol* 1994;4(4):266-70.
105. Ross WM, Creighton MO, Inch WR, Trevithick JR. Radiation cataract formation diminished by vitamin E in rat lenses in vitro. *Exp Eye Res* 1983;36(5):645-53.
106. Ross WM, Creighton MO, Trevithick JR. Radiation cataractogenesis induced by neutron or gamma irradiation in the rat lens is reduced by vitamin E. *Scanning Microsc* 1990;4(3):641-9; discussion 9-50.
107. Ruther W, Jacobi KW, Kovacs G, et al. [Chemical radiation protection of rabbit eyes following exposure to 60Co gamma rays]. *Klin Monatsbl Augenheilkd* 1969;154(2):232-8.
108. Sasaki K, Kojima M, Sakamoto Y, et al. A current UV-B-related cataract epidemiology study in Japan. *Dev Ophthalmol* 1997;27:32-41.
109. Schull WJ. Late radiation responses in man: current evaluation from results from Hiroshima and Nagasaki. *Adv Space Res* 1983;3(8):231-9.
110. Schull WJ. The somatic effects of exposure to atomic radiation: the Japanese experience, 1947-1997. *Proc Natl Acad Sci U S A* 1998;95(10):5437-41.
111. Seddon JM, Ajani, U.A., Sperduto, R.D., Hiller, R., Blair, N., Burton, T.C., Farber, M.D., Gragoudas, E.S., Haller, J., Miller, D.T., Yannuzzi, L.A. and Willet, W. Dietary carotenoids, vitamin A, C, and E. and advanced age-related macular degeneration. *J. Am. Med. Assoc.* 1994;272:1413-20.
112. Shacklett DE, Tredici TJ, Epstein DL. Evaluation of possible microwave-induced lens changes in the United States Air Force. *Aviat Space Environ Med* 1975;46(11):1403-6.
113. Shichi H. Cataract formation and prevention. *Expert Opin Investig Drugs* 2004;13(6):691-701.
114. Shubik VM, Kvasova MD. [Immunological studies on cataracts under conditions of exposure to low-dose radiation]. *Vestn Oftalmol* 1996;112(4):21-3.
115. Sliney DH. Epidemiological studies of sunlight and cataract: the critical factor of ultraviolet exposure geometry. *Ophthalmic Epidemiol* 1994;1(2):107-19.
116. Sliney DH. UV radiation ocular exposure dosimetry. *Doc Ophthalmol* 1994;88(3-4):243-54.

117. Sliney DH, Vorpahl KW, Winburn DC. Environmental health hazards from high-powered, infrared, laser devices. *Arch Environ Health* 1975;30(4):174-9.
118. Soderberg PG. Acute cataract in the rat after exposure to radiation in the 300 nm wavelength region. A study of the macro-, micro- and ultrastructure. *Acta Ophthalmol (Copenh)* 1988;66(2):141-52.
119. Spector A, Wang GM, Wang RR, et al. The prevention of cataract caused by oxidative stress in cultured rat lenses. I. H₂O₂ and photochemically induced cataract. *Curr Eye Res* 1993;12(2):163-79.
120. Stewart-DeHaan PJ, Creighton MO, Larsen LE, et al. In vitro studies of microwave-induced cataract: reciprocity between exposure duration and dose rate for pulsed microwaves. *Exp Eye Res* 1985;40(1):1-13.
121. Strzhizhovskii AD. [Natural ultraviolet radiation as a human risk factor (review)]. *Radiats Biol Radioecol* 1996;36(2):299-309.
122. Strzhizhovskii AD. [Ultraviolet radiation as a risk factor on the Earth and outer space]. *Aviakosm Ekolog Med* 1998;32(1):4-13.
123. Tao F, Powers-Risius P, Alpen EL, et al. Radiation effects on late cytopathological parameters in the murine lens relative to particle fluence. *Adv Space Res* 1994;14(10):483-91.
124. Taylor HR. The biological effects of UV-B on the eye. *Photochem Photobiol* 1989;50(4):489-92.
125. Taylor HR. Epidemiology of age-related cataract. *Eye* 1999;13 (Pt 3b):445-8.
126. Taylor HR. Ocular effects of UV-B exposure. *Doc Ophthalmol* 1994;88(3-4):285-93.
127. Taylor HR. Ultraviolet radiation and the eye: an epidemiologic study. *Trans Am Ophthalmol Soc* 1989;87:802-53.
128. Taylor HR, West SK, Rosenthal FS, et al. Effect of ultraviolet radiation on cataract formation. *N Engl J Med* 1988;319(22):1429-33.
129. Turner ND, Braby LA, Ford J, Lupton JR. Opportunities for nutritional amelioration of radiation-induced cellular damage. *Nutrition* 2002;18(10):904-12.
130. van Kuijk FJ. Effects of ultraviolet light on the eye: role of protective glasses. *Environ Health Perspect* 1991;96:177-84.
131. Varma SD, Richards RD. Ascorbic acid and the eye lens. *Ophthalmic Res* 1988;20(3):164-73.
132. Varma SD, Srivastava VK, Richards RD. Photoperoxidation in lens and cataract formation: preventive role of superoxide dismutase, catalase and vitamin C. *Ophthalmic Res* 1982;14(3):167-75.
133. Voelz GL. Eye-survey study of nuclear-reactor workers. *J Occup Med* 1967;9(6):286-92.
134. Vos JJ, van Norren D. Thermal cataract, from furnaces to lasers. *Clin Exp Optom* 2004;87(6):372-6.
135. Vrensen GF. UV-B and early cortical and nuclear changes in the human lens. *Doc Ophthalmol* 1994;88(3-4):255-61.
136. West S. Ocular ultraviolet B exposure and lens opacities: a review. *J Epidemiol* 1999;9(6 Suppl):S97-101.
137. West SK. Daylight, diet, and age-related cataract. *Optom Vis Sci* 1993;70(11):869-72.

138. West SK, Duncan DD, Munoz B, et al. Sunlight exposure and risk of lens opacities in a population-based study: the Salisbury Eye Evaluation project. *Jama* 1998;280(8):714-8.
139. West SK, Longstreth JD, Munoz BE, et al. Model of risk of cortical cataract in the US population with exposure to increased ultraviolet radiation due to stratospheric ozone depletion. *Am J Epidemiol* 2005;162(11):1080-8.
140. West SK, Rosenthal FS, Bressler NM, et al. Exposure to sunlight and other risk factors for age-related macular degeneration. *Arch Ophthalmol* 1989;107(6):875-9.
141. Wolff K. Side-effects of psoralen photochemotherapy (PUVA). *Br J Dermatol* 1990;122 Suppl 36:117-25.
142. Wolff SP. Cataract and UV radiation. *Doc Ophthalmol* 1994;88(3-4):201-4.
143. Worgul BV. Accelerated heavy particles and the lens. V. Theoretical basis of cataract enhancement by dose fractionation. *Ophthalmic Res* 1988;20(3):143-8.
144. Worgul BV, Brenner DJ, Medvedovsky C, et al. Accelerated heavy particles and the lens. VII: The cataractogenic potential of 450 MeV/amu iron ions. *Invest Ophthalmol Vis Sci* 1993;34(1):184-93.
145. Worgul BV, Kundiev Y, Likhtarev I, et al. Use of subjective and nonsubjective methodologies to evaluate lens radiation damage in exposed populations--an overview. *Radiat Environ Biophys* 1996;35(3):137-44.
146. Worgul BV, Medvedovsky C, Huang Y, et al. Quantitative assessment of the cataractogenic potential of very low doses of neutrons. *Radiat Res* 1996;145(3):343-9.
147. Worgul BV, Medvedovsky C, Powers-Risius P, Alpen E. Accelerated heavy ions and the lens. IV. Biomicroscopic and cytopathological analyses of the lenses of mice irradiated with 600 MeV/amu ⁵⁶Fe ions. *Radiat Res* 1989;120(2):280-93.
148. Worgul BV, Merriam GR, Jr., Medvedovsky C, Brenner DJ. Accelerated heavy particles and the lens. III. Cataract enhancement by dose fractionation. *Radiat Res* 1989;118(1):93-100.
149. Worgul BV, Smilenov L, Brenner DJ, et al. Mice heterozygous for the ATM gene are more sensitive to both X-ray and heavy ion exposure than are wildtypes. *Adv Space Res* 2005;35(2):254-9.
150. Yang VC, Ainsworth EJ. A histological study on the cataractogenic effects of heavy charged particles. *Proc Natl Sci Counc Repub China B* 1987;11(1):18-28.
151. Zaret MM, Snyder WZ. Cataracts and avionic radiations. *Br J Ophthalmol* 1977;61(6):380-4.
152. Zaret MM, Snyder WZ, Birenbaum L. Cataract after exposure to non-ionizing radiant energy. *Br J Ophthalmol* 1976;60(9):632-7.
153. Zigman S. Environmental near-UV radiation and cataracts. *Optom Vis Sci* 1995;72(12):899-901.
154. Zintz C, Beebe DC. Morphological and cell volume changes in the rat lens during the formation of radiation cataracts. *Exp Eye Res* 1986;42(1):43-54.
155. Zuclich JA. Ultraviolet-induced photochemical damage in ocular tissues. *Health Phys* 1989;56(5):671-82.