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Prevalence of Posterior Subcapsular Cataracts in Volunteer Cytapheresis Donors

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Abstract

Background—Granulocyte donors routinely receive dexamethasone orally before donation. Steroids may increase the risk of posterior subcapsular cataract (PSC) formation.

Study design and methods—We recruited 100 granulocyte donors (≥ 4 granulocyte donations; any number of platelet donations) and 100 age-sex-matched platelet donors (0–3 granulocyte donations, any number of platelet donations) to examine the risk of PSC. PSC was assessed by a masked ophthalmologist and reading center lens photograph gradings, or medical record documentation of PSC as the reason for cataract extraction.

Results—Fourteen eyes of ten granulocyte donors and five eyes of four platelet donors had PSC (odds ratio (OR) = 2.82; 95% confidence interval [CI], 0.83–9.61; $p=0.10$). Risk of PSC increased with number of granulocyte donations: compared to 0–3 donations (4.0%), risk for 4–9, 10–19, and ≥ 20 donations was 8.6% (OR=2.25; 95% CI, 0.31–13.99; $p=0.30$); 9.5% (OR=2.53; 95% CI, 0.44–14.20; $p=0.21$); and 13.0% (OR=3.60; 95% CI, 0.48–22.81; $p=0.11$), respectively ($p=0.06$ for trend).

Conclusion—We did not demonstrate a statistically significant increased risk of PSC associated with granulocyte donation. However, although this makes a large risk unlikely, we cannot rule out a small to moderate risk and there is biologic plausibility that the steroid administration associated with granulocyte donation could be associated with PSC formation. Transfusion medicine professionals should advise granulocyte apheresis donors to maintain an appropriate frequency of eye examinations.

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Authorship Contributions

Janine A. Clayton: designed and performed research, collected, analyzed, and interpreted data, wrote the manuscript; Susan Vitale: designed research, analyzed and interpreted data, performed statistical analysis, wrote the manuscript; Jonghyeon Kim: analyzed and interpreted data, performed statistical analysis, wrote the manuscript; Cathy Conry-Cantilena: designed and performed research, collected, analyzed, and interpreted data; wrote the manuscript; Phyllis Byrne: performed research; collected data; George F. Reed: designed research, analyzed and interpreted data, performed statistical analysis, wrote the manuscript; Frederick Ferris, III: designed research, analyzed and interpreted data, wrote the manuscript; Susan F. Leitman: designed and performed research, collected, analyzed, and interpreted data, wrote the manuscript.

Keywords

granulocyte donation; apheresis; cataract; steroid; dexamethasone; posterior subcapsular cataract; blood donation

Introduction

Cataract is the leading cause of blindness worldwide and is a significant cause of visual impairment in the United States and industrialized nations. Several reports suggested that granulocyte donation may increase the risk of developing a specific type of cataract, posterior subcapsular cataract (PSC) ^{1,2}, due to the routine practice of stimulating the donor with oral steroids prior to donation. PSC involves the central posterior region of the lens often directly within the visual axis and causes glare, reduced vision in bright light such as when driving at night, and difficulties with near vision. Even relatively small PSC opacities may require cataract surgery. Age is the most important risk factor for cataract formation; however, there are many additional risk factors for the various types of cataract. The association of PSC with prolonged corticosteroid therapy, either topical or systemic, is well recognized. However, the relationship between dose, type of steroid, duration of therapy and development of cataracts is unclear. Other specific risk factors for PSC include ocular trauma, chronic uveitis, intraocular surgery, and alcohol use ^{3, 4, 5}.

The possibility that granulocyte donation may increase the risk of PSC development was suggested by Ghodsi and Straus ¹. In their case-control study, four of eleven neutrophil donors had PSC, compared with none of nine platelet donors. We sought to further assess this possible risk in a case-control study utilizing the relatively large group of granulocyte donors at the National Institutes of Health (NIH).

Materials and Methods

This study was approved by the National Eye Institute's Institutional Review Board and all participants gave written informed consent. All persons who had donated granulocytes at least 4 times in the previous 20 years, as documented in NIH Department of Transfusion Medicine (NIH DTM) records, were recruited to participate in this study. For each granulocyte donor, we identified a matched control "platelet donor" who had donated granulocytes less than four times (never, 1, 2, or 3 times), matching on age (± 5 years), sex, and total number of cytapheresis donations. The medical and ocular history of each participant was assessed by using a standardized questionnaire administered by the clinical coordinator, who did not reveal the donor type to the examining ophthalmologist so that she could remain masked. The questionnaire was designed to measure potential confounding risk factors for the development of PSC lens opacities, including ocular trauma, history of ocular surgery, uveitis, glaucoma, smoking status, alcohol consumption, diabetes, and for women only, use of hormone replacement with estrogen and/or progesterone.

Exposure to risk factors for PSC

Lifetime exposure to corticosteroid medications was assessed by a series of questions on route of administration (inhaled, oral, topical), duration of treatment (< 1 week, ≥ 1 week but < 1 year, or ≥ 1 year), and dosage. High steroid exposure was defined as any of the following: skin: at least weekly for ≥ 1 year (≥ 52 administrations); inhaled: at least daily for ≥ 1 year (≥ 365 administrations); oral: ≥ 3 methylprednisolone packs; nasal: at least daily for ≥ 1 month (≥ 30 administrations); injectable (other than peri- or intra-ocular): ≥ 5 times; or any topical ocular administration (eye drops or any peri- or intra-ocular injections). Participants who had no exposure to steroids by any route were classified as "no exposure".

Participants who were not classified as “no” or “high” exposure were classified as “moderate.” Sun exposure was assessed by estimating adult lifetime average annual ocular ultraviolet-B (UV-B) exposure. The exposure index was estimated from regional ambient UV-B, hours spent outdoors from April through September, time spent outdoors or in tropical latitudes, and use of ocular protection (brimmed hat, sunglasses, prescription spectacles), adapted from questionnaires developed for previous studies ^{6, 7}. Participants’ height and weight were measured and body mass index (BMI) was computed as (weight (kg))/(height (m))².

Assessment of PSC

A single cornea specialist (JAC), masked to the donation status of the participants, performed a complete dilated eye evaluation of both eyes of each participant, including slit-lamp examination of the anterior segment and fundus and grading of PSC using the Age-Related Eye Disease Study (AREDS) cataract grading scheme ⁸. AREDS grading of PSC is performed using four standard reference photographs. The grader judges where the degree of PSC opacity falls relative to the scale and assigns a digital grade ranging from 0.0 (no PSC) to 4.0 (PSC involving the entire central 5 mm of the lens).

A Neitz retro-illumination camera was used to take color photographs of the lenses of both eyes to detect PSC lens changes, using a standardized technique ⁸. The lens photographs were independently evaluated by two masked readers at the University of Wisconsin Photo Reading Center for the presence and severity of PSC lens opacities, using the Wisconsin System for classifying cataracts from photographs ⁹. PSC was graded within the central zone (5 mm), composed of the central subfield (2 mm) and the 8 inner subfields of the AREDS grid. The percent opacification in each subfield was determined and an overall weighted percentage of PSC within the central zone was calculated. The weighting factor was obtained for each subfield by dividing the area of the subfield by the total visible lens area in the central zone. The individual subfield percentages were combined to estimate an overall percentage of involvement within the central 5 mm of the lens. All lens photographs graded as questionable or definite PSC were reviewed by a senior grader ⁹ to arrive at a final photo grade.

For 7 participants (10 eyes) who had previous cataract surgery, the medical chart of the cataract surgeon was abstracted to determine the type of cataract present before surgery. For all subjects, PSC lens status was determined by percent opacification within the central 5 mm, as determined by the Reading Center and by clinical grading, or by documentation of PSC as the reason for cataract extraction.

Donors found to have PSC, along with a random sample of donors not found to have PSC, were re-examined approximately one year after baseline to confirm the presence and grade of PSC, using the same methods employed at baseline and with the clinical examiner masked to the baseline examination results. The final PSC grade was based on an adjudication of the PSC grades at the original and re-examination visits. Donors were allowed to continue granulocyte donation during this one-year interval.

Granulocyte collection

The NIH DTM limits granulocytopheresis and plateletpheresis donations to once per month. To increase circulating granulocyte counts and maximize the number of cells collected per procedure, granulocyte donors were given a single dose of 8 mg of dexamethasone to be taken by mouth 10–12 hours before donation. Since 1998, nearly all granulocyte donors also received granulocyte-colony-stimulating factor (G-CSF, filgrastim, Amgen, Thousand Oaks, CA) either 5 µg/kg or 480 µg subcutaneously 16–24 h prior to donation.

Granulocytapheresis procedures were performed on a CS3000 Plus continuous-flow apheresis device (Fenwal Inc., Lake Zurich, IL). Seven liters of blood were processed per procedure. Anticoagulation of the circuit was achieved by adding 30 mL of a 47% solution of trisodium citrate (Trictrasol, Cytasol, Braintree, MA) to 500 mL of a 6% hydroxyethyl starch (hetastarch) solution (Hespan, Dupont Pharma, Wilmington, DE). Hetastarch was used as a red cell sedimenting agent to increase the efficiency of granulocyte collection. The citrate/hetastarch mixture was added continuously at a 1:12 ratio with whole blood during the procedure. Thus, a 30-g dose of hetastarch was infused with each 7-liter procedure. Plateletpheresis was performed by similar methods, except that platelet donors did not receive dexamethasone, G-CSF, or hetastarch, the anticoagulant was acid citrate dextrose (ACD-A), and only five liters of blood were processed per procedure.

Statistical Methods

Analyses were conducted using SAS (version 9.1, SAS Institute, Cary, NC). Baseline characteristics and exposure levels between granulocyte donors and platelet donors were compared and tested by chi-squared tests, Fisher's exact test, or two-sample t-tests, depending on the attributes of the variable of interest. The primary outcome of interest was the presence of PSC in one or both eyes. Because of concerns related to adjusting for correlations between eyes of an individual when few events are observed, all analyses presented here are person-based. We used multivariable logistic regression to adjust for potential confounders of the relation between donor type and PSC. To evaluate the dose-response relationship, we used the Cochran-Armitage test for homogeneity to assess whether there was a linear trend in prevalence¹⁰. The type I error level was 0.05.

Results

Two hundred eligible donors agreed to participate in this study: 100 granulocyte donors (who had donated granulocytes 4 or more times) and 100 platelet donors (who had donated granulocytes less than four times (never (n=83) or 1–3 times (n=17)). Over 95% of the donors approached in both groups consented to participate. Granulocyte donors had made a mean of 14 prior granulocyte donations (median, 12; range 4–41); the mean length of time over which these donations occurred was 8.85 years (range, 0.9 to 16.1 years). Platelet and granulocyte donors were similar with respect to age, race, history of diabetes, BMI, weight, alcohol intake, smoking, exposure to steroid medications, total number of apheresis donations, UV-B exposure, and ocular risk factors (history of ocular trauma or surgery) (Table 1). Despite attempts to match cases and controls by sex, there was a statistically significant difference in gender distribution between the two donor groups, with proportionally more males in the granulocyte group (69%) than in the platelet group (54%) ($p = 0.04$).

Platelet and granulocyte donors did not differ with respect to corticosteroid medication history; they had similar frequency rates of steroid administration for each route (skin, inhaled, oral, injection, nasal, and ocular) (Table 2). Overall exposure to steroids, other than for granulocyte donation, did not differ significantly between the two donor groups: 54% of granulocyte donors and 61% of platelet donors ($p = 0.62$).

Among granulocyte donors, 14 eyes of 10 participants (7% of eyes; 10% of donors) had PSC (Table 3). Among platelet donors, five eyes of four participants (2.5% of eyes; 4% of donors) had PSC. The odds ratio (OR) of PSC in granulocyte donors relative to platelet donors was 2.67 (95% confidence interval [CI], 0.81–8.81, $p = 0.11$). Clinical and photographic lens evaluations performed one year after the baseline assessments revealed one new donor with a small PSC in one eye, but were mainly helpful in resolving discrepancies between clinical and Reading Center evaluations noted on the initial

evaluations. Two donors with PSC detected on initial evaluation underwent unilateral cataract extraction between the initial and follow-up evaluations. In total, 5 donors (7 eyes) underwent surgical PSC extraction, including 3 granulocyte donors (4 eyes) and 2 platelet donors (3 eyes).

We conducted univariate analyses of the association of personal and ocular factors with risk of PSC (Table 4). When we examined granulocyte donation as a continuous variable, rather than as granulocyte donors versus platelet donors, we found that for each additional granulocyte donation, there was an estimated increased risk of PSC of 5% (OR=1.05; 95% CI, 1.00–1.10; $p = 0.08$). Older age was statistically significantly associated with increased risk of PSC (OR for each additional year of age=1.11; 95% CI, 1.03–1.20; $p = 0.004$). There were additional associations in these unadjusted univariate analyses with strong trends, but these were not statistically significant. Alcohol intake ≥ 1.5 ounces/day and BMI ≥ 26 were both associated with a possible decreased risk of PSC (OR 0.50; 95% CI, 0.06–3.95; $p = 0.51$; and OR 0.47; 95% CI, 0.15–1.45; $p = 0.17$, respectively). However, weight as a continuous variable had no significant effect on PSC risk (OR 0.98 for each additional kg of weight; 95% CI, 0.95–1.02; $p = 0.27$). A history of ocular disease or surgery was associated with an apparent doubling of the risk of PSC (OR 2.26; 95% CI, 0.66–7.70; $p = 0.19$).

We next examined the association of PSC with donor type, adjusting for age and, in successive models, for each of the potentially confounding factors from Table 4 (a potentially confounding factor was defined as being associated in univariate analyses with an OR of ≥ 2.0 or ≤ 0.5 , or as being statistically significant). After adjusting for age, the OR for PSC in granulocyte donors relative to platelet donors was 2.82 (95% CI, 0.83–9.61; $p = 0.10$) (Model 1, Table 5). Adjustment for each of the other potential confounders (Models 2 through 4 in Table 5) did not substantially alter the ORs for donor type: ORs for granulocyte donation ranged from 2.82 – 2.89, with p -values ranging from 0.09 to 0.10. Because of the imbalance in sex between the donor groups, we also computed a model adjusting for age, donor type, and sex (Model 5, Table 5). The age- and sex-adjusted OR for PSC in granulocyte donors relative to platelet donors increased slightly but did not reach statistical significance (OR = 3.10; 95% CI, 0.89–10.73; $p = 0.08$).

We speculated that the cumulative number of granulocyte donations might be a more precise measurement of risk than donor group alone. We found no reports in the literature that provided useful guidelines for categorizing exposure; therefore, we selected categories that partitioned the granulocyte donor group into approximate thirds: 4–9 granulocyte donations (35 participants), 10–19 granulocyte donations (42 participants), and ≥ 20 granulocyte donations (23 participants). Compared with platelet donors (4/100 with PSC), the risk of PSC increased with increasing number of granulocyte donations. For 4–9 donations, the prevalence of PSC was 3/35, or 8.6% (OR = 2.25; 95% CI, 0.31–13.99; $p = 0.30$); for 10–19 donations, prevalence of PSC was 4/42, or 9.5% (OR = 2.53; 95% CI, 0.44–14.20; $p = 0.21$); and for ≥ 20 donations, prevalence of PSC was 3/23, or 13.0% (OR = 3.60; 95% CI, 0.48–22.81; $p = 0.11$), respectively. The test for linear trend of the risk of PSC with increasing number of granulocyte donations was borderline statistically significant ($p = 0.06$). Of the 17 platelet donors who had donated granulocytes one to three times in the past, 1 (5.9%) who had donated granulocytes on a single occasion had PSC, versus three of 83 (3.6%) who had never donated granulocytes ($p = 0.53$). The odds ratio for PSC in granulocyte donors (≥ 4 lifetime granulocyte donations) relative to the 83 platelet donors who had never donated granulocytes was 2.96 (95% CI, 0.72–17.24, $p = 0.09$).

Discussion

Our study did not demonstrate a statistically significant increased risk of PSC associated with granulocyte donation in healthy apheresis donors. However, we found a nearly threefold increase in the OR for risk when we examined the entire population of 100 granulocyte donors available to us for this case-control study. Exposure to steroids is a well-known risk factor for PSC, and indeed we found an increasing point estimate of PSC risk with higher exposure, especially in those with the highest number of granulocyte donations (≥ 20): for each additional granulocyte donation, there was an estimated increased risk of PSC of 5%. However, it was notable that even the least frequently exposed donors, with a total of four to nine granulocyte donations, had a possible increased PSC risk compared with platelet donors.

Our study was designed to have at least 80% power to detect a 12% difference in PSC prevalence between granulocyte and platelet donors. Among the assumptions underlying our sample size computation was an estimation of 2% prevalence of PSC in the platelet donor group and 14% prevalence of PSC in the granulocyte donor group, for an estimated odds ratio of approximately 8. In choosing our initial prevalence estimate, we sought information from studies that reported age-specific prevalence of PSC. The Blue Mountains Eye Study⁽¹¹⁾ reported that the prevalence of PSC was 2.7% in people under 55 and 3.8% in people aged 55–64. McCarty et al⁽¹²⁾ found that the prevalence of PSC in Australia was 1.9% (age 40–49), 2.5% (age 50–59) and 4.2% (age 60–69). An estimate of 2% prevalence in the PSC donors was chosen because 74% of our study population was less than age 60, and because we reasoned that blood donors might have healthier lifestyles, less exposure to PSC risk factors, and a lower prevalence of PSC than the general population. Since smaller sample sizes are required to detect larger odds ratios, our study was underpowered to declare statistically significant the odds ratio of 3.0 that we ultimately found. A total of 315 platelet donors and 315 granulocyte donors would have been required to achieve 80% power for the observed prevalences in our study.

Initial concerns regarding the effect of granulocyte donation on risk of PSC were raised by Ghodsi and Strauss¹ in a case-control study of apheresis donors. They found that 4/11 (36%) of granulocyte donors (defined as those who had donated granulocytes at least 15 times) and 0/9 platelet donors had PSC. This study was limited by possible selection bias (only 11/21 granulocyte donors and 9/28 platelet donors consented to participate) and the assessment of PSC by clinical examination only. In contrast to this relatively small study, we recruited 100 granulocyte donors and 100 platelet donors, with a greater than 95% participation rate, and assessed PSC using masked clinical gradings, masked photograph gradings, and a re-grading one year after the original examination to improve our assessment of PSC. Cumulative risk may also have been greater in the Ghodsi study in that their subjects had a larger number of granulocyte donations than our donors (mean prior donations 26 versus 14, respectively).

Burch et al² conducted a cross-sectional study with a similar design to evaluate the association between PSC and granulocyte donation. Their study used photographic assessment to identify PSC, with clinical examination of a randomly selected 2/3 of participants. Of 124 eligible granulocyte donors, 72% participated in the study; however, the occurrence of PSC was largely confined to a single center in which donors received the highest cumulative dose of steroids. They reported insignificant odds ratios of 1.5 to 1.6 for the association of PSC with all granulocyte donations, but the incidence of PSC was 9 of 52 (17.3%) in their highest-dose center, versus 4 of 52 (7.8%) of controls. Their data suggest, as in our study, that a large number of subjects is needed to definitively determine the risk of PSC. In contrast to their study, we did not exclude eyes which had undergone surgical

cataract removal; instead, we elected to identify the indication for cataract extraction from the patient's medical records. Donors who underwent surgical PSC extraction may have experienced the most clinically severe adverse ocular effects of steroid administration and excluding them from analysis may underestimate the incidence and the severity of the risk.

Although our study did not definitively demonstrate an increased risk of PSC with granulocyte donation, we believe it extends our knowledge on this question. We assessed the known confounders for PSC (exposure to steroids, alcohol usage, smoking, and sun exposure) in the most detailed fashion that was practicable in the donation setting; however, our analyses indicated that these variables did not substantially affect the risk of PSC. We assessed PSC using both clinical and photographic methods for all participants, and also conducted a year-later validation grade to improve the reliability of our outcome measure. We found the photographic assessment to be somewhat less sensitive than clinical grades, due to the ability of the clinical examiner to adjust the depth of focus through a range of values and identify PSC that may not have been apparent in the retro-illumination photographs, which were restricted to a single depth of focus. We believe that this is the most comprehensive assessment of PSC in blood donors to date.

Granulocyte transfusion is used as a lifesaving intervention for neutropenic patients. Since the granulocyte donation process requires additional discomfort and risks due to the administration of G-CSF and steroids, granulocyte donors tend to be particularly altruistic, even among highly altruistic apheresis donors as a whole. In the U.S. in 2006, nearly 6,000 individuals donated granulocytes¹³. To adequately inform these individuals of the potential risks of granulocyte donation, it is important to obtain as much information as possible on both the magnitude and the significance of the risk of PSC. Although PSC can be treated by conventional cataract extraction, the procedure is not risk free and even early PSC might be responsible for some level of visual disability^{14, 15, 16}. In addition, PSC can be rapidly progressive¹⁷ and are associated with a disproportionate percentage of cataract extractions, relative to their population frequency¹⁸.

Our study is potentially limited by several factors. Susceptibility to steroid effects may vary from subject to subject; however, our relatively high subject participation rate is an assurance that there was no selection bias. We allowed platelet donors who had donated granulocytes 1–3 times to be included in the study as part of the platelet donor control group, because we felt it was biologically implausible for such a low exposure to increase the risk of PSC, and because these subjects provided very close age, sex, and cytapheresis history matches with the granulocyte group. The single donor in this group found to have PSC had made only one lifetime granulocyte donation, making a causal relationship highly unlikely. When our analyses were repeated with these 17 individuals removed, our findings were similar. Despite our efforts to match by sex, we had a significantly higher percentage of females among the platelet than among the granulocyte donors. However, adjustment for gender did not substantially alter the OR of PSC in granulocyte donors relative to platelet donors.

In conclusion, although our case-control study did not demonstrate a statistically significant increased risk of PSC associated with granulocyte donation in healthy apheresis donors, the nearly threefold increase in risk that we observed, combined with the biological plausibility that donation-related steroid exposure is associated with PSC formation, suggest that the steroids given as part of the granulocyte donation process may increase the relative and the absolute risk of PSC formation. The low event rates in both groups in this study suggest that a larger study would be necessary to precisely define the extent of the increased risk. Transfusion medicine professionals should advise granulocyte apheresis donors to maintain an appropriate frequency of eye examinations. Donors found to have PSC should consider

discontinuing dexamethasone or other steroids as part of their preparative regimen for donation.

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References

1. Ghodsi Z, Strauss R. Cataracts in neutrophil donors stimulated with adrenal corticosteroids. *Transfusion*. 2001; 41:1464–8. [PubMed: 11778057]
2. Burch JW, Mair DC, Meny GM, Moroff G, Ching SS, Naidoff MA, Steuer ER, Loftus SA, Armstrong J, Clemons TE, Klein BE. The risk of posterior subcapsular cataracts in granulocyte donors. *Transfusion*. 2005; 45:1701–8. [PubMed: 16271093]
3. Hodge HG, Whitcher JP, Stariano W. Risk factors for age-related cataracts. *Epidemiol Rev*. 1995; 17:336–46.
4. Leske MC, Chylack LT, Wu S-Y. the Lens Opacities Case-Control Study Group. The Lens Opacities Case-Control Study. Risk factors for cataract. *Arch Ophthalmol*. 1991; 109:244–51. [PubMed: 1993036]
5. Miglior S, Marighi PE, Mussicco M, Balestreri C, Nicolosi A, Orzalesi N. Risk factors for cortical, nuclear, posterior subcapsular and mixed cataract: a case-control study. *Ophthalm Epidemiol*. 1994; 1:93–105.
6. Duncan DD, Munoz B, Bandeen-Roche K, West SK. the Salisbury Eye Evaluation Project Team. Assessment of ocular exposure to ultraviolet-B for population studies. *Photochem Photobiol*. 1997; 66:701–9. [PubMed: 9383994]
7. West SK, Duncan DD, Munoz B, Rubin GS, Fried LP, Bandeen-Roche K, Schein OD. Sunlight exposure and risk of lens opacities in a population-based study: the Salisbury Eye Evaluation project. *JAMA*. 1998; 280:714–8. [PubMed: 9728643]
8. Age-Related Eye Disease Study Research Group. The Age-Related Eye Disease Study (AREDS): design implications. AREDS report no. 1. *Controlled Clin Trials*. 1999; 20:573–600. [PubMed: 10588299]
9. Age-Related Eye Disease Study Research Group. The age-related eye disease study (AREDS) system for classifying cataracts from photographs: AREDS report no. 4. *Am J Ophthalmol*. 2001; 131:167–75. [PubMed: 11228291]
10. Corcoran CD, Ryan L, Mehta CR, Senchaudhuri P, Patel N, Molenberghs G. An exact trend test for correlated binary data. *Biometrics*. 2001; 57:941–8. [PubMed: 11550948]
11. Mitchell P, Cumming RG, Attebo K, Panchapakesan J. Prevalence of cataract in Australia. The Blue Mountains Eye Study *Ophthalmology*. 1997; 104:581–588.
12. McCarty CA, Mukesh BN, Fu CL, Taylor HR. The epidemiology of cataract in Australia. *Am J Ophthalmol*. 1999; 128:446–465. [PubMed: 10577586]
13. Whitaker, BI.; Green, J.; King, MR.; Lieberg, LL.; Mathew, SM.; Schlumpf, KS.; Schreiber, GB. The 2007 national blood collection and utilization survey report. American Association of Blood Banks; Bethesda, MD: United States Department of Health and Human Services;
14. Wu SY, Hennis A, Nemesure B, Leske MC. Barbados Eye Studies Group. Impact of glaucoma, lens opacities, and cataract surgery on visual functioning and related quality of life: the Barbados Eye Studies. *Invest Ophthalmol Vis Sci*. 2008; 49:1333–8. [PubMed: 18385046]
15. James ER. The etiology of steroid cataract. *J Ocular Pharmacol Therap*. 2007; 23:403–20.
16. Stifter E, Sacu S, Thaler A, Weghaupt H. Contrast acuity in cataracts of different morphology and association to self-reported visual function. *Invest Ophthalmol Vis Sci*. 2006; 47:5412–22. [PubMed: 17122131]

17. Leske MC, Chylack LT Jr, He Q, Wu SY, Schoenfeld E, Friend J, Wolfe J. Incidence and progression of cortical and posterior subcapsular opacities: the Longitudinal Study of Cataract. The LSC Group. *Ophthalmology*. 1997; 104:1987–93. [PubMed: 9400756]
18. Adamsons IA, Munoz B, Enger C, Taylor HR. Prevalence of lens opacities in surgical and general populations. *Arch Ophthalmol*. 1991; 109:993–7.

Table 1

Characteristics of platelet (n=100) and granulocyte donors (n=100).

Characteristic	Platelet donors	Granulocyte donors	p-value *
<i>Age (years)</i>			0.86
<50	32%	32%	
50–59	40%	44%	
60–69	23%	21%	
70+	5%	3%	
Sex			0.04
Female	46%	31%	
Race			0.25
Black	3%	0%	
White	97%	100%	
Diabetes			1.00
Yes	3%	2%	
Body mass index (kg/m²)			0.67
≥26	51%	55%	
Weight (kg)			0.19
Mean±SD	84.2±15.0	81.2±16.6	
Alcohol intake (average per day)[†]			0.83
≥1 ½ oz	14%	12%	
Smoking (cumulative pack-years)			0.52
≥ 10	24%	29%	
Exposure to steroid medication[‡]			0.39
None	39%	46%	
Moderate or high	61%	54%	
Number of granulocyte donations			
<4	100%	0%	N.A.
4 – 10	0%	41%	
11 – 19	0%	36%	
≥20	0%	23%	
Total apheresis donations, lifetime			0.76
Mean±SD	78.83±55.94	92.38±57.07	
Cumulative ocular sunlight exposure			1.00
High exposure	3%	4%	
Ocular risk factor index[§]			0.56
At least one ocular risk factor	14%	18%	

* Exact likelihood ratio test of homogeneity if categorical; 2-sample t-test if continuous

[†] Includes consumption of beer, wine, and/or liquor[‡] Derivation of risk level from steroid medication history. For skin, inhaled, oral, injected, and nasal, the risk level was based on the approximate total duration of steroid medication use.

§ History of any of the following: cataract, glaucoma, trauma, uveitis, or intraocular surgery (refractive, glaucoma, retinal laser, retinal detachment repair, or vitrectomy).

Table 2

Steroid medications in platelet and granulocyte donors.

Route of administration	Exposure level [*]	Platelet donors (n=100)	Granulocyte donors (n=100)	p-value [†]
Skin	None	83%	79%	0.69
	Moderate	12%	16%	
	High	5%	5%	
Inhaled	None	92%	91%	1.00
	Moderate	7%	7%	
	High	1%	2%	
Oral	None	99%	100%	1.00
	Moderate	1%	0%	
Injected	None	100%	100%	.
Nasal	None	77%	75%	0.68
	Moderate	16%	20%	
	High	7%	5%	
Ocular	None	97%	94%	0.50
	Yes	3%	6%	
Overall exposure to steroids	None	61%	54%	0.62
	Moderate	24%	29%	
	High	15%	17%	

* Derivation of risk level from steroid medication history. For skin, inhaled, oral, injected, and nasal, the risk level was based on the approximate total duration of steroid medication use.

[†] Exact likelihood ratio chi-squared test

Table 3

Prevalence of PSC in granulocyte and platelet donors

Donor status	Total # donors	Total # eyes	PSC in both eyes	PSC in one eye	Total # eyes with PSC	Total # donors with PSC in at least 1 eye	Proportion of eyes with PSC (%)	Proportion of donors with PSC (%)
Granulocyte*	100	200	4	6	14	10	14/200 (7 %)	10/100 (10%)
Platelet	100	200	1	3	5	4	5/200 (2.5%)	4/100 (4%)
							Odds ratio	2.67 (p=0.11)
							95% CI	0.81–8.81

* Number of granulocyte donations ≥ 4 .

Table 4

Univariate logistic regression for association of participant and ocular factors with PSC.

Variable	Reference group	Odds ratio *	Lower 95% CI	Upper 95% CI	P
Donor type	Platelet[‡]	2.67	0.81	8.81	0.11
Number of granulocyte donations	Per additional granulocyte donation	1.05	1.00	1.10	0.08
Age	Per year	1.11	1.03	1.20	0.004
Sex	Male	1.22	0.40	3.65	0.73
Alcohol intake	<1 ½ oz per day	0.50	0.06	3.95	0.51
Smoking	<10 pack-years	1.12	0.34	3.73	0.86
Body mass index	<26	0.47	0.15	1.45	0.17
Weight	Per kg	0.98	0.95	1.02	0.27
Use of steroid medication [‡]	None or moderate	1.48	0.39	5.62	0.57
Ocular risk factor index §	None	2.26	0.66	7.70	0.19

* An odds ratio >1 indicates that the potential risk factor (versus the reference category) has a higher risk of PSC lens opacity. For example, granulocyte donors have a higher risk of PSC lens opacity, compared with platelet donors (odds ratio = 2.67, i.e., 167% higher in granulocyte donors than in platelet donors), but this risk does not achieve statistical significance.

[‡] Number of granulocyte donations <4.

[‡] Derivation of risk level from steroid medication history. For skin, inhaled, oral, injected, and nasal, risk level was based on the approximate total duration of steroid medication use.

§ Any history of glaucoma, uveitis, ocular trauma, or ocular surgery (glaucoma surgery or retinal detachment repair).

Table 5

Multivariate logistic regression analysis for the association between PSC lens opacity and donor status.

Model number	Covariates included in model	Reference group	Odds ratio [*]	Lower 95% CI	Upper 95% CI	P
1	Age	Per year	1.115	1.035	1.201	0.004
	Donor type	Platelet [†]	2.822	0.829	9.608	0.097
2	Age	Per year	1.119	1.038	1.206	0.003
	Donor type	Platelet	2.870	0.837	9.840	0.094
	Alcohol intake	< 1.5 oz per day	0.364	0.042	3.113	0.356
3	Age	Per year	1.116	1.035	1.203	0.004
	Donor type	Platelet	2.887	0.838	9.942	0.093
	Body mass index	<26	0.438	0.135	1.420	0.169
4	Age	Per year	1.117	1.037	1.203	0.004
	Donor type	Platelet	2.855	0.830	9.827	0.096
	Ocular risk factor index [‡]	None	2.464	0.674	9.008	0.173
5	Age	Per year	1.121	1.039	1.209	0.003
	Donor type	Platelet	3.096	0.893	10.734	0.075
	Sex	Male	1.917	0.590	6.234	0.279

^{*} Adjusted for all other covariates in the model. An odds ratio >1 indicates that the potential risk factor (versus the reference category) has a higher risk of PSC lens opacity. For example, after adjusting for age, granulocyte donors have a higher risk of PSC lens opacity, compared with platelet donors (odds ratio = 2.822, i.e., 282.2% higher in granulocyte donors than in platelet donors), but this risk does not achieve statistical significance (p=0.097).

[†] Number of granulocyte donations <4.

[‡] Any history of glaucoma, uveitis, ocular trauma, or ocular surgery (glaucoma surgery or retinal detachment repair).