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Retinitis Pigmentosa

and

Education Issues

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Retinitis pigmentosa (R.P.) is a group of diseases which affects an estimated 100,000 Americans and 1.5 million worldwide (Berson, 1996. Retinitis Pigmentosa foundation as cited by Scarangella, n.d.). R.P. is an inherited condition which results in the degeneration of the photoreceptor cells found in the retina. The symptoms include photophobia (light sensitivity), a reduction in visual acuity, night blindness, and a gradual reduction in the visual field (Rundquist, 2005). Persons with R.P. also have “greater deficits in contrast sensitivity” (Alexander, Barnes, & Fishman, 2003; Alexander, Barnes, Fishman, Pokorny, & Smith, 2003).

The visual acuity of persons with retinitis pigmentosa ranges from 20/20 to no light perception and acuity is generally affected significantly only in the latter stages of the disease (Rundquist, 2004). According to Sacks & Silberman (1998) the various eye diseases in R.P. category also include “numerous diseases grouped together which damage the retina in this way but manifest different characteristics” (p.18). These various diseases include: “Usher’s syndrome, Leber’s congenital amaurosis, Laurence-Moon-Biedl syndrome, and Bassen-Kornsweig syndrome” (Levack, 1999. p 18). Other low incidence syndromes that manifest some of the symptoms of R.P. include Best disease, gyrate-atrophy, choroideremia, and Stargardt disease (The Foundation Fighting Blindness, n.d.).

The first documentation of retinitis pigmentosa recorded in a medical publication was in 1855 by John Hecken-Lively. The diagnosis of this disease was made possible by the invention of the ophthalmoscope that had been invented just a few years earlier by Hermann von Helmholtz. F. C. Bonders (1818-1889) is credited with first diagnosing the disease utilizing von Helmholtz’s device (The Foundation of the American Academy of Ophthalmology, n.d.; Scarangella, n.d.). The condition’s name comes from the appearance of the brown pigment in the lower half of the eye (University of Iowa, n.d.).

The earliest symptom of retinitis pigmentosa is a decline in one's night vision, followed by a gradual reduction in peripheral vision. In addition to the visual diagnosis made with an ophthalmoscope by observing a change in the pigment of the eye, retinitis pigmentosa is also diagnosed by an electroretinogram (ERG). An ERG can determine retinal function by measuring retinal response to light using electrodes (Berson, 1996; EyeMblink.com, n.d.; Scarangella, n.d.). A sure and certain diagnosis of the condition is based on an ERG. Other eye diseases may manifest similar observable pigment changes and degeneration of the visual field (Stonely, n.d.).

To determine the extent of peripheral vision loss, examiners may rely on several tests to measure the field of vision: Perimetry tests determine if there are blind spots in the 180 degree field of view (University of Iowa, n.d); the Tangent screen "a computerized test that tests the central 25-35 degrees of the visual field (Scarangella, n.d.); and the Amsler Grid which determines if there is any field of vision loss in the macular area (Prevent Blindness America, n.d.).

Although the progression of retinitis pigmentosa can vary greatly with each individual, the gradual degeneration of the photoreceptor cells is a common element with all forms of the disease. With the majority of forms of R.P. the rod cells are affected first. The degeneration of the rod cells results in a decrease in vision under low light conditions, with one of the early symptoms being night blindness. The progression of the disease results in the further degeneration of rod cells resulting in the loss of peripheral vision. As the disease progresses the cone cells begin to deteriorate affecting the central field of vision (The Foundation Fighting Blindness, n.d.; Scarangella, n.d.).

Some forms of retinitis pigmentosa may initially affect the central field of vision. Also referred to as cone-rod dystrophy, the resulting loss of vision from degeneration of the cone cells

is not correctable with lenses. Another consequence of cone-cell dystrophy is the reduction in color perception. As the disease progresses, there is a loss of peripheral vision associated with the degeneration of rod cells (The Foundation Fighting Blindness, n.d.; Scarangella, n.d.).

Retinitis pigmentosa is an inherited condition. Jay has listed three different ways in which R.P. can be transmitted genetically: autosomal dominant, autosomal recessive, and X-linked (Berson, 1996; Ray, 2005). Only one mutated gene is responsible for R.P. that is autosomal dominant. This type of retinitis pigmentosa affects men and women equally. It has been estimated that autosomal forms of the disease account for approximately 15-25% of R.P. cases (Stonely, n.d.). Although statistically there is a one in two chance of a child inheriting this form from a parent with the autosomal condition, there are families in which the condition seems to only exist for two generations or “skip” a generation (Ray, 2005).

Autosomal recessive retinitis pigmentosa also affects men and women in equal numbers, however for this type of R.P. to be passed on, both parents must contribute an abnormal gene for their child to have the condition. There are three possible genetic outcomes when both parents are autosomal recessive: a child with R.P. having received the gene from both parents, a child that is a carrier having received the gene from either parent, and a child with receiving normal genes from both parents. Types of R.P. that are autosomal recessive in nature also include Usher’s syndrome, Leber’s congenital amaurosis, Laurence-Moon-Biedl syndrome, and Basson-Kornsweig syndrome (Levack, 1999; Ray, 2005). It has been estimated that of the forms of R.P. transmitted genetically, autosomal recessive forms account for 50-84% of the cases when other disorders are not present (Scarangella, n.d.). In contrast, Stonely estimated that of the individuals affected with R.P., 5-20% are autosomal types (Stonely, n.d.).

The transmission of X-linked retinitis pigmentosa affects primarily men. The abnormal gene responsible for this type of R.P. occurs on the X chromosome. Men have one X and one Y chromosome and women possess two identical X chromosomes. A man with X-linked R.P. will pass on the defective gene on his X chromosome to his daughters but not to his sons. The daughters will be carriers of the condition, with a fifty percent chance of passing the gene on to their children, assuming that their husbands do not have retinitis pigmentosa (Jay, 2005; Scarangella, n.d.; The Foundation Fighting Blindness, n.d.). According to Jay (2005), female carriers of X-link R.P. may show some signs of the condition. Although mild changes have been observed in the retinas of X-linked carriers, they “do not experience serious vision loss” (The Foundation Fighting Blindness, n.d.).

Harvard scientists were able to identify mutations in the peripheran gene of some R.P. patients in 1991. Through a technique known as denaturing gradient gel to the isolated gene, the researchers were able to eventually discover “20 R.P. families with peripheran mutations. (University of Iowa, n.d.). L. Brilliant reported that approximately 60% to 80% of the cases are autosomal recessive in nature (as cited by Rundquist, 2004). Rundquist also states that “there have been some reported cases with no known family history” (Rundquist, 2004. p. 718). Research involving 25 Paskistani families suggested that the gene which causes autosomal recessive R.P., known as RP1, “can result in recessive as well as dominant retinitis pigmentosa” (Riazudden, et al., 2005).

There are several areas of concern when considering the educational needs of a student with retinitis pigmentosa. Often the visual acuity will fall within the range of sighted peers, however there are psychological factors that should be taken into consideration. Retinitis pigmentosa slowly and gradually results in the deterioration of the peripheral vision. Due to the

genetic nature of R.P., students with the condition often have witnessed the loss of vision by another family member. One can only guess at the psychological burden imposed by retinitis pigmentosa when a child or young adult knows that they will very likely become legally blind one day, following the same path as a sibling, parent, or grandparent.

Chiappetta (n.d.) reported that there is a higher incidence of depression among individuals that suffer from low vision. People with retinitis pigmentation are often diagnosed later in life and have difficulty accepting the loss of independence. In a survey of individuals with moderate to severe vision loss conducted by Chiappetta, the participants identified giving up driving as “the most difficult aspect of their adjustment *to retinitis pigmentosa...*”

(Chiappetta, n.d.). The second major concern of respondents was a fear of losing all of their sight (Chiappetta, n.d.). Adolescents suffering from the loss of peripheral vision and night blindness may be faced with issues that set them apart from their sighted peers. Wolffe (2000) reported that children with visual impairments “are confronted with unique issues, including the inability to obtain a driver’s license...” (as cited by Griffin-Shirley & Nes, 2005. p. 277).

Other researchers (Tuttle and Tuttle, 2004; and Warren, 1994) have reported that children with visually impairments “may have more difficulty developing positive self-esteem” (as cited by Griffin-Shirley & Nes, 2005. p. 277). Scarangella (n.d.) stated that “People with R.P. who have had sight and then lose it, have a much greater difficulty in developing a stable self-concept than do people who were born blind.”

The typical adaptations for R.P. focus on “High illumination with no glare, absorptive lenses, infra-red viewing devices, prism glasses to increase visual fields, closed circuit television for maximum contrast” (Levack, 1999. p. 145). Educational considerations usually include the following:

Physical activities and mobility may be restricted by low light situations such as bad weather and night time. Teach organized search patterns using a grid pattern to aid the student in locating objects or visual targets. Students may need to be seated farther away to increase their visual field. Precautions should be taken to prevent retinal detachment (Levack, 1999 p. 145).

Individuals with R.P. often receive mobility training in the use of a cane, electronic aids and low vision devices. Learning about public transportation is also a component of O&M training (Scarangella, n.d.). When O&M training should begin is difficult to determine, but that the need exists is emphasized by the fact that sometimes R.P. can result in blindness as early as age 30, and the “majority are legally blind by age 60, with a central visual field diameter of less than 20 degrees” (Berson, 1996, p. 4526).

Although there is at present no cure for this progressive disease) nutritional approaches and gene therapy may hold promise (Chapatti, n.d.; Smith, 2004; The Foundation Fighting Blindness, n.d.; Smith, 2004). Many researchers believe that such factors as stress, environment, diet, and metabolism may be related to the rate of progression of the disease. (Retina Foundation of the Southwest, n.d.). Berson, Grant, and others have reported that some nutritional approaches may slow the progression of retinitis pigmentosa (as cited by Smith, 2004; Berson, 1996). In a randomized controlled study, the progression of retinal deterioration was slower among the patients taking 15,000 international units of vitamin A (Berson, 1996). The Linus Pauling Institute has stated that research suggests “that patients with common forms of retinitis pigmentosa may benefit from long term vitamin A supplementation” (Oregon State University, n.d.).

The results of Berson's study however have been questioned by others including Bird and Marshall of the British Retinitis Pigmentosa Society (Bird & Marshall, 1999). Bird and Marshall allege that Berson's claims are unsupportable and that "no significant effects were seen as a result of taking either vitamin *A* or *E* in terms of the size of the visual field' and that "no improvement was made in any visual function" (Bird and Marshall, 1999, p. 1).

Other approaches center on the genetic aspects of the disease. Many of the genes that are associated with R.P. have been mapped. Research in the 1990s led to the discovery of the position of two of the genes that are responsible for R.P. There have been more than 30 genes linked to R.P. (Chopra, 2000; Duke University Medical Center, 2000). The British Retinitis Pigmentation Society reports that gene therapy offers an opportunity to replace defective genes in cells that are affected. J. Bennett successfully replaced defective genes in mice with retinal degeneration. The death of photoreceptor cells was delayed (Nature Medicine, 1996 as cited by British Retinitis Pigmentosa Society, n.d.). However, Smith (2004) noted that "specific genetic defects have been found in a relatively small number of retinal degenerative diseases, which thereby limits the potential application of gene therapy for those few patients with a known mutation" (p.755).

There has also been research utilizing neural stem cell transplants as a possible treatment for retinitis pigmentosa. This approach however has been troubled by cell rejection and the "political and ethical controversies related to the use of embryonic stem cells" (Smith, 2004). Research involving the use of bone marrow derived stem cells has offered promise in preventing central vision loss. In a study involving mice with retinal degeneration, researchers discovered that stem cells derived from bone marrow minimized rejection and prevented the loss of central vision cones (Smith, 2004).

Many researchers believe that recent discoveries of the gene mutations are the key to the design of effective gene therapy and pharmaceutical treatment of retinitis pigmentosa. To continue making progress towards an effective treatment of R.P., Chader (n.d.) has suggested that the following steps be taken: a). careful clinical evaluation; b). genotyping of individual R.P. patients to identify mutations; c). continuation of animal studies which center on R.P. at a genetic and cellular level; and d). government approval and subsequent development of human clinical trials of possible therapies and treatments (Chader, n.d.).

References

- Alexander, K., Barnes, C. S., and Fishman, G.A. (2003). Deficits in temporal integration for contrast processing in retinitis pigmentosa [Electronic version]. *Investigative Ophthalmology and Visual Science*. 44, 3163-3169.
- Alexander, K., Barnes, C. S., Fishman, G.A., Porkorny, J., and Smith, V.C. (2003). Spatial frequency characteristics in retinitis pigmentosa [Abstract] [Electronic version]. *Journal of Vision*. 3 (12), 56a.
- Berson, E. L. (May, 1996). Retinitis pigmentosa: Unfolding the mystery [Electronic version]. *Proceedings of the National Academy of Science*. 93, 4526-4528.
- Bird, A. and Marshall, J. (1999). Statement from the BRPS on vitamin a. British Retinitis Pigmentosa Society. Retrieved September 9, 2005 from http://www.brps.org.uk/White/W_Articles2.html
- Chader, G. J. (n.d.). Medical therapy of the retina: Turning the corner from laboratory work to human clinical trials. British Retinitis Pigmentosa Society. Retrieved September 9, 2005 from http://www.brps.org.uk/White/W_Articles_2.html
- Chiappetta, A. (n.d.). How those with retinal eye disease cope with the challenges of everyday life. Retrieved September 3, 2005 from: <http://www.jwen.com/rp/articles/living-p.html>
- Chopra, P. (2005). Conserving cones to save daylight [Electronic version]. *News In Science*.
- Duke University Medical Center. (October 16, 2000). *Duke eye researchers describe cascade of events that may lead to retinal degeneration*. Retrieved September 3, 2005 from <http://www.jwen.com/rp/articles/dukeresearch-p.html>

EyeMDlink.com (n.d.). Electroretinogram. Retrieved September 25, 2005 from:

<http://www.eyemdlink.com/Test.asp?TestID=12>

Griffin-Shirley, N. and Nes, S. L. (2005). Self-esteem and empathy in sighted and visually impaired adolescents [Electronic version]. *Journal of Visual Impairment and Blindness*, 99, (5), 276-285.

Jay, M. R. (July 2005). Genetics and retinitis pigmentosa. British Retinitis Pigmentosa Society. Retrieved September 9, 2005 from http://www.brps.org.uk/White/W_Genetics.html

Levack, N. (December, 1999). *Low vision: A resource guide with adaptations for students with visual impairments*. Austin: Texas School for the Blind and Visually Impaired.

Ophir-Cohen, M., Ashkenazy, E., Cohen, A., and Tirosh, E. (August, 2005). Emotional status and development in children who are visually impaired [Electronic version]. *Journal of Visual Impairment & Blindness*, 99 (8), 478- 485.

Prevent Blindness America (n.d.). Amsler grid. Retrieved September 25, 2005 from: http://www.preventblindness.org/eye_tests/amd_test.html

Retina Foundation of the Southwest. (Fall, 2004). Results of x-linked rp nutrition research study announced. *Insight* [Electronic version].

Riazuddin, S. A., Zulfiqar, F., Zhang, Q., Sergeev, Y. V., Qazi, Z. A., Husnain, T. et al. (2005). Autosomal recessive retinitis pigmentosa is associated with mutations in *rp1* in three consanguineous Pakistani families [Electronic version]. *The Association for Research in Vision and Ophthalmology*, 46, 2264-2270.

- Rundquist, J. (2004). Low vision rehabilitation of retinitis pigmentosa [Electronic version].
Journal of Visual Impairment & Blindness, 98 (11), 718-724.
- Sacks, S. Z. & Silberman, R. K. (Eds.). (1998). *Educating students who have visual impairments with other disabilities*. Baltimore: Paul H. Brookes Publishing Co,
- Scarangella, C. (n.d.). *The history of retinitis pigmentosa*. Retrieved August 3, 2005 from
<http://www.jwen.com/rp/articles/hist-p.html>
- Smith, L. E. (2004) Bone marrow-derived stem cells preserve cone vision in retinitis pigmentosa [Electronic version]. *Journal of Clinical Investigation*. 114. 755-757
- Stonely, D. E. (n.d.). Retinitis pigmentosa. Caremark. Retrieved September 25, 2005 from
http://www.caremark.com/wps/portal/_s.155/5522/.cmd/ad/.pm/-/.c/1703/.Ce/5535/.p/3711/_s155/5522?PC_3711_docid=CMS-2-MM001166
- The Foundation of the American Academy of Ophthalmology. (n.d.) *The Ophthalmoscope and Hermann von Helmholtz*. Retrieved September 5, 2005 from <http://www.Eyecareamerica.org/eyecare/museum/exhibits/online/ophthalmoscope.cfm>
- The Foundation Fighting Blindness. (n.d.). *What is retinitis pigmentosa?* Retrieved September 3, 2005 from: <http://www.blindness.org/content.asp?id=45>
- The Linus Pauling Institute Oregon State University. (n.d.) Retinitis pigmentosa. Retrieved September 22, 2005 from <http://lpi.oregonstate.edu/infocenter/vitamins/vitaminA/>
- University of Iowa. Department of Ophthalmology and Visual Sciences. (n.d.). *Retinitis pigmentosa*. Retrieved September 3, 2005 from: <http://www.opth.uiowa.edu/RP.html>

University of Iowa, Department of Ophthalmology and Visual Sciences. (n.d.). Perimetry.

Retrieved September 25, 2005 from <http://webeye.ophth.uiowa.edu/dept/service/perimetry/index.htm>