CHAPTER 23

COLOR VISION

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Color vision is the ability to discriminate a light stimulus as a function of its wavelength. Various sensory and cognitive processes combine to result in the sense of color. The cooperative physical effects of light and object, the physiologic reaction of the visual organ to light, and the psychologic context of color perception together produce the picture of our surroundings, thus influencing our relationship and attitude toward our environment. This chapter focuses specifically on the reaction of the retina to light stimulus. The details of physical events outside of the body known as *optical physics,* theories of color, and the higher-order processing of the visual signal in the brain to produce visual experience are beyond the scope of this chapter.

COLOR AND LIGHT

Electromagnetic energy is wavelengths between approximately 380 and 760 nm and causes photoreactions on the human retina, which leads to the experience of vision. Although the perceptions caused by light waves cannot be directly measured, optical physics describes the origin of colors as a breaking down of light into its spectral constituents.[1] A *prism,* a transparent solid body with a triangular cross section, causes white, or neutral, light to be refracted so that it is divided into the spectrum of rainbow colors. Short-wavelength visible light causes the sensation of violet, and in an uneven transition, the colors blue, blue-green, green, yellow-green, yellow, orange, and red are perceived. For example, red does not noticeably change in perception from approximately 680 nm onward. *Monochromatic light* is colored light of a single wavelength. The remixing of all colors of light created by a prism, for example with a convex lens, will create the sensation of white. The sensation of white can also be created from the monochromatic light rays from the short-, middle-, and long-wavelength zones of the spectrum. For example, mixing blue (435 nm), green (545 nm), and red (700 nm) light produces white. These three light rays can also be combined to create any other color by changing the relative intensities of the individual components. Thus violet-blue, green, and red are called the *additive primary colors.*

The light rays from the mixing of any two thirds of the spectrum cause the sensations of yellow, magenta-red, and cyan-blue. These three colors are the so-called subtractive primary colors. Magenta-red, the mixing of rays of the short- and long-wavelength ends of the spectrum, does not itself exist in the natural spectrum. Any two colors are called *complementary colors* if their additive mixing forms white. Therefore it follows that blending any one additive primary color with the corresponding subtractive primary color forms the whole spectrum. The mixing of color pigments or dyes is an example of subtractive color mixing. The mixing of a cyan-blue dye and a yellow dye produces green. The cyan-blue dye absorbs, or subtracts, the long-wavelength part of the spectrum; the yellow dye absorbs the short-wavelength part. Because both dyes reflect the middle-wavelength light, green color is appreciated.

Color mixing (subtractive, additive, or proportional mixing of pairs of the six primary colors) produces the nearly limitless range of color hues that can be perceived. In addition to additive or subtractive mixing, color can be produced through the scatter of white light. One example is the deep blue–colored sky that is apparent at midday in the summer when the air is clean and dry. The sun's rays pass vertically through the earth's atmosphere

and the longer wavelengths are scattered. However, at sunrise and sunset the sun's rays fall on an acute angle and their pathlength is longer, giving rise to intense red color depending on prevailing atmospheric conditions. Finally, color can result from interference on thin films. Color perception changes with slight changes in the thickness of a film or with the angle of vision. The mother-of-pearl color of soap bubbles or the feathers of iridescent birds are examples of so-called interference colors.

The human eye differentiates colors according to the color itself (its wavelength), the brightness, and the saturation. Therefore a systematic organization of all colors would be possible only in the three-dimensional system. There is no perceptual basis for a hierarchy of colors, but color wheels generally are used to organize and group chromatic colors according to their appearance.

The existence of color is at some level a topic that is equally relevant to philosophy and science. Throughout recorded history, great philosophers and scientists have written on theories of color and color sense and have provided a rich literature on the subject. Isaac Newton (1642-1727) carried out experiments with a prism that transformed the science of color from the study of objects to the study of light. Johann Wolfgang von Goethe (1749-1832) wrote extensively on the experience of color. Thomas Young (1773-1829) proposed a theory of color vision based on three receptors in the retina that are sensitive to different spectral regions. David Brewster (1781-1868) introduced the term *color blindness,* which was formerly known as *daltonism,* after John Dalton (1766-1844), who described in detail his own inability to distinguish red. The genetic basis of Dalton's color blindness was recently determined, by polymerase chain reaction analysis of DNA extracted from his preserved postmortem eye, to be deuteranopia (see following discussion).[5] Arthur Schopenhauer (1788-1860) expanded on the work of Goethe and Immanuel Kant (1724-1804). Joseph Antoine Ferdinand Plateau (1801-1883) studied afterimages and color mixing and proposed the Talbot-Plateau law of color intensity perception. Hermann Ludwig Ferdinand von Helmholtz (1821-1894) extended Young's hypothesis, henceforth called the *Young-Helmholtz hypothesis,* and devised spectral absorption curves for three visual photoreceptors. Herman Rudolf Aubert (1826-1892) was one of the key contributors to physiologic optics in addition to measuring absolute visual sensitivity and light and dark adaptation. He demonstrated that color perception was largely restricted to the foveal region and depended on context in other parts of the retina. James Clerk Maxwell (1831-1879) was largely responsible for making the study of color vision a quantitative science. He devised methods to study additive and subtractive color mixing and color-defective subjects and developed many of the classifications that are still used today.

BIOCHEMISTRY OF COLOR VISION

All human visual pigments share a common chromophore, which is chemically related to vitamin A_1. The 11-*cis*-structural isomer of the aldehyde of vitamin A_1 reacts with an opsin protein to form a photoreceptor-pigment complex. The rod and cone cell pigments are all complexes of the same chromophore with different, but related, opsin proteins. Interestingly, the genes encoding the opsin proteins are members of a superfamily of related receptors called *G protein–coupled receptors.* These receptors are involved in different sensory and intercellular signaling pathways across a wide range of organisms. The receptors are integral membrane proteins that all share a common structural motif—seven-transmembrane segments—and they all communicate with cellular biochemical signal-transducer proteins in the cellular cytoplasm called *heterotrimeric G proteins.* In the case of rod and cone cells, the G proteins are called *transducins.* Specific forms of transducins are found in rods and cones, although the three cone cell types share a common form of transducin.

The unique properties of the chromophore in its opsin-bound state contribute to the key physiologic properties of vision, including color vision. Spectral tuning at a molecular level is related to the so-called opsin-shift. The *opsin-shift* refers to the change in the absorption of the chromophore when it becomes bound to a particular opsin. The magnitude of the opsin-shift varies with each particular visual pigment.

In the biochemical amplification cascade of the photoreceptor cells of the vertebrate visual system, the capture of a photon causes irreversible photochemical isomerization of the chromophore in the visual pigment. A series of protein conformational changes ensues, and the active pigment becomes a catalyst that converts transducin into its active form. Active transducin modulates cyclic guanosine monophosphate (GMP) phosphodiesterase, cGMP levels drop, and plasma membrane–cation conductance through a cGMP-gated membrane

channel protein decreases. The resulting hyperpolarization of the photoreceptor cell causes synaptic modulation, and downstream retinal signal processing can occur. Thus the basic elements of the biochemical transduction cascade are pigment, G protein, phosphodiesterase, and channel. However, numerous other regulatory proteins participate in various modulations of the signal, including signal turn-off, dark adaptation, and light adaptation.

Much of the biochemistry of visual signal transduction has been elucidated through the study of rod cells. One of the most salient and striking results of biophysical studies is that through coupled amplification cycles, the absorption of a single photon by the photopigment in a rod cell, rhodopsin, prevents approximately 10^7 ions from crossing the plasma membrane. However, despite their histologic and physiologic differences, the gains of transduction in rods and cones appear to be similar. Whereas rods are specialized for sensitivity, cone physiology is specialized for rapid temporal response, rapid recovery after exposure to intense light, and nonsaturable function over a wide range of luminosity.

The electrophysiology of cone photoreceptors and their associated retinal circuitry in the primate and human retinas are of considerable interest. One key component for future study is to elucidate the mechanism of photopic desensitization with background illumination. For example, because the magnitude of desensitization cannot be accounted for by the observed reduction of cone photocurrent or voltage, adaptation might somehow affect cone cell synaptic signaling.

Photoreceptor Cells and the Concept of Trichromacy

The retina can be thought of as the point of contact between radiated energy, light, and the human nervous system. In the initial step of color perception, light must be converted into a neurochemical signal by photoreceptor cells. As detailed in other chapters of this text, the photoreceptor cell layer is the innermost layer of the retinal neuronal cells. The two main classes of photoreceptor cells are rods and cones. Rod cells primarily mediate scotopic (dim-light) vision. Rods differentiate light intensity with a maximum response at approximately 510 nm. Cone photoreceptor cells are responsible for photopic (bright-light) color vision. Cones are significantly less sensitive than rods, but they can mediate differentiation of colors. Humans can distinguish two monochromatic light rays as close as approximately 2 nm apart, giving an effective color palette of up to 300 distinct spectral colors. The human retinal fovea contains a high density of cones but essentially no rods.

The part of the electromagnetic spectrum that makes up the sensory visible spectrum varies among organisms and species. For example, insects generally possess ultraviolet perception but lack long-wavelength sensitivity. The mammalian retina is actually highly evolved for scotopic vision as opposed to color vision. Among land mammals, only humans and old-world primates possess true trichromatic vision. Relatively recent gene duplication and unequal homologous recombination most likely produced the potential for trichromatic color vision in humans and certain nonhuman primates. The topics of ecology and evolution of visual pigment sensitivity are of considerable interest but are not discussed further here.

The most salient feature of normal human color vision is that it is trichromatic. Trichromacy results from the physiology of the retina—it is not a physical property of light. The three physiologic detection systems are the three classes of photoreceptor cells—each class containing a different photoreceptor pigment molecule—those being blue or short (S)-sensitive, green or middle (M)-sensitive, and red or long (L)-sensitive cones.[2,9] The three human cone types represent the three additive primary colors: blue, green, and red. Each pigment has a distinct absorption spectrum where absorbance is plotted as a function of the wavelength (λ) of incident light (see Color Plate 12). The peaks of absorbance vary for the three cone cell pigments, but their absorbance spectra overlap considerably so that a combination of one, two, or three cone types reacts more or less strongly to a given light stimulus.

A key fact is that the response of a particular cone cell is the same no matter what the energy is of the photon that it captures. Only the efficiency of photon capture varies with photon energy, and the dynamic output relates only to the rate of photon capture. For example, in the simplest case of a retina with only three individual cone cells, one of each class, chromatic lights would be perceived to be identical if they produce the same absorptions in all three cells, and different if they did not. Thus trichromatic vision is the result of three independent comparisons of rates of photon absorption by the three cone types.

Luminosity curves can be constructed as a function of wavelength for both scotopic and photopic vision. The entire visible spectrum ranges from ap-

proximately 400 to 700 nm. However, the peak of the photopic curve (555 nm) is red-shifted relative to that of the scotopic curve (505 nm). The scotopic curve essentially represents the photosensitivity of a single pigment, rhodopsin, whereas the photopic curve is a composite (essentially a weighted average of overlapping cone sensitivities). The boundaries of color sensitivity as projected on the retina depend on the distribution of the cone types, which are not uniform (see Color Plate 13). Of course, because the distribution of cone types varies, the photopic luminosity curve varies depending on the experimental conditions.

Signal Processing in the Retina

In development, the retina arises from an evagination of neural tube to form the optic vesicle, which subsequently invaginates to form the optic cup. The optic cup thus consists of two juxtaposed layers: The inner layer differentiates into the neural retina (rods, cones, bipolar cells, ganglion cells, horizontal cells, amacrine cells, glial cells) and the outer layer differentiates into the pigment epithelium. The neural retina is extensively laminated, but three main layers are easily appreciated. The deepest layer contains the photoreceptors. The inner nuclear layer (in the middle) contains perikarya of bipolar cells and interneurons (horizontal and amacrine cells) and glial cell nuclei. The most superficial layer is the ganglion cell layer, containing cell bodies of ganglion cells whose axons form the optic nerve.

These three layers are relatively easy to identify because they contain mainly cell bodies and are separated by thin neuropil layers: the outer plexiform layer between photoreceptors and inner nuclear layer and the inner plexiform layer between the inner nuclear and ganglion cell layers. The proportion, distribution, and patterning of rods and cones over the retina vary among species. In humans, cones are concentrated in the central retina. The unique biochemistry and ultrastructural anatomy of photoreceptor cells accounts for their unusual physiology: They are neurons that do not generate all-or-none action potentials. Rather, light causes a graded response, a membrane hyperpolarization that is detected by ganglion cells that do produce action potentials. The most simplified linear axis of retinal signaling is photoreceptor cell to bipolar cell to ganglion cell.

In addition to the response of threshold of an individual photoreceptor cell to light, the phenomena of convergence and divergence are functionally important neural mechanisms for determining acuity and spectral sensitivity. *Convergence,* or pooling, refers to the projection of multiple photoreceptor cells on a lesser number of bipolar cells. *Divergence* refers to the projection of a single photoreceptor cell on multiple cells in the next layer. For example, one cone may form functional synapses to three bipolar cells. One key difference between rod and cone systems is their respective degrees of convergence. Foveal cone cells tend to have so-called private-line communication—no divergence. In the retinal periphery, the photoreceptor cells, including mostly rods but also some cones, greatly outnumber the ganglion cells. Convergence is the rule in the periphery; the result is high sensitivity but low acuity.

The amacrine and horizontal cells are interneurons that permit lateral interactions within the retina. Although amacrine and horizontal cells are separate and distinct cell types, it should be noted that a wide range of distinctly different morphologic cell types exists in the primate interneuron layer. For example, there may be 20 to 50 types of amacrine cells, and the physiology of only a few of these cell types has been studied in any detail. A presentation of the precise topographic organization of the retina, the central visual pathways, and the subcortical and cortical visual center is beyond the intended scope of this chapter.

An understanding of the connections between retinal physiology and peripheral mechanisms in general and the associated central mechanisms to color perception is incomplete in any case. Color perception does, of course, require photon absorption by the three classes of receptors with different spectral responses. The chemical results of the photon capture are then transmitted to so-called opponent processes. A great deal is known about the process of proton absorption and subsequent signaling in the retina. Significant signal processing related to color perception occurs in the neuronal cell layers of the retina, and the peripheral mechanisms underlying color perception, in contrast with the central mechanisms, are generally well understood. Although a number of significant questions remain to be answered, psychophysical studies have provided a well-defined framework. Retinal neurons respond reliably to chromatic stimuli. Neurons of a particular class tend to behave reproducibly, and if not linearly, they at least display straightforward nonlinearities. However, understanding color perception requires the study of higher-order color mechanisms, primarily through psychophysical experiments.

The Young-Helmholtz theory of color vision emphasizes trichromacy and was essentially confirmed by the discovery of three cone photoreceptor systems as described previously. Historically, however, another theory was proposed to describe the process of color perception. Karl Hering (1834-1918) developed the opponent theory of color vision based on the hypothetical existence of three oppositional color pigment pairs.[4] These oppositional pairs are now known not to exist, but Hering's theory was correct in the sense that the signals from the three cone types are combined, not at the pigment level as he had suggested, but at the level of neurons to produce opposing pairs of red-green, blue-yellow, and black-white. Later work confirmed the role of opposing excitatory and inhibitory interactions in color perception.

Hering's proposals concerning opponent processes arose from relatively simple observations, but more recently, detailed definitions of a variety of concepts have advanced the study of second-stage mechanisms of color perception (i.e., mechanisms subsequent to activation of the cone cell biochemical signal-transduction pathway). The concepts relevant to second-stage mechanisms include definitions of color space useful for both psychophysical and electrophysiologic experiments and the identification of neural mechanisms that essentially transform in some way the retinal image (e.g., edge enhancement, spectral differencing, contrast induction, adaptation to steady background or temporally varying illumination, interference of motion and three-dimensional shape, perceptual constancy). If the most important task of visual perception is to segregate different objects from each other and from background, it follows that any visual process that enhances the perception of a difference between two contiguous fields will be beneficial. In this regard, color cues provide useful information in the perception of both shape and motion.

Opponent processes refer to apparently antagonistic responses within the retina that can be best understood by considering the concepts of neuronal excitation and inhibition. In the retina, opposing positive excitatory and negative inhibitory effects are organized in a clear, concentric spatial format. Kuffler[7] first mapped the organization of receptive fields in the retina in 1953.[7] In the retina the receptive field of a single ganglion cell can be defined by mapping the area of a stimulus that affects its rate of discharge in electrophysiologic recordings. A typical ganglion cell responds to an achromatic (dark-light) stimulus of its receptive field according to a pattern termed *center-surround.* The examples of two particular center-surround neurons (ON-center and OFF-center) demonstrate the concept of balanced antagonistic mechanisms in the retina. Ambient light produces a background rate of discharge. In ON-center neurons, a tiny spot of white light focused at the center of the receptive field produces a burst of discharge. When the center stimulus is terminated, a transient decrease in the rate of background discharge is observed. This temporal pattern of discharge is called an *ON-response.* If the light is focused as a discrete annulus surrounding a dark center of the field, the background discharge is inhibited. When the ring-shaped surround stimulus is terminated, a burst of discharge is noted. This temporal pattern of discharge is called an *OFF-response.* In OFF-center neurons, stimulation of the receptive field center causes an OFF-response and stimulation of the surround causes an ON-response. For achromatic stimuli the sizes of receptive field centers vary. Receptive field centers may be approximately 2 minutes of arc in the fovea and 2 degrees in the periphery. The size of the surround region is similar (approximately 2 degrees) throughout the retina.

For color vision, these opponent processes are also significant because antagonistic color responses are found at each level of the visual pathway, including the retina. In animals with high proportions of cone photoreceptors, center-surround mechanisms generally exhibit spectral sensitivities. For example, the center mechanism, which may be "ON" or "OFF," might display the spectral sensitivity curve of M-wavelength–sensing cones. The surround mechanism, which is antagonistic to the center mechanism, might display an L-wavelength–sensing cone sensitivity. Such receptive fields are classified according to whether they are ON-center or OFF-center and whether the center and surround show a spectral sensitivity approximating M-, L-, or S-wavelength–sensing cones. Less common are fields with center and surround mechanisms with the same, or similar, spectral sensitivities. Rarely, a receptive field shows no evidence of center-surround organization: A stimulus by light of one wavelength anywhere in the field causes an ON response, whereas a stimulus by light of a different wavelength produces an OFF response. In general, the range of color opponency displayed by M- and L-wavelength–sensing cones is greater than that of S-wavelength–sensing cones. Color Plate 14 represents schematically how the three cone systems might contribute to three types of receptive field neurons.

Several additional phenomena occur at the level of the retina and influence color perception, including optical mixing of small surfaces. For example, a color photographic print consists of three layers of color in a so-called gray screen of small dots of yellow, magenta-red, and cyan-blue. All other colors are created at the level of the retina through optical mixing. Black is created where all three dots overlap, and gray is created when the proportion and distribution of the three-color dots is equal. Subtractive mixing of overlapping transparent color dots in the retina creates violet-blue, green, and red. Optical mixing is also exploited in glowing television or computer screens that consist of points of blue, green, and red light that mix to form a gray background. As the intensities of the points change, all other colors are created.

Another example of optical mixing is easily demonstrated by using a colored disc on a spinning top, often called *Maxwell's disc* after James Clerk Maxwell. If the disc is colored half red and half blue, the perceived color of the spinning disc resembles magenta, a color that is not present on the object at all. The spinning disc stimulates red and blue sectors of the same point of the retina in rapid succession.

Color sensation can be caused by colored light rays and also by the activity of cone cells, principally by the phenomenon known as *negative afterimage*, in which an unchanging (adapted) image impressed on the retina moves when the eyes move and refocus. Afterimages can influence color perception, but generally not consciously.

Discussions of color adaptation and the influence of the appearance of color by its surroundings, or so-called simultaneous alternating effects of colors, are beyond the scope of this chapter.[8] However, the key point to be made is that the appearance of a color depends on its relationship to its surroundings.

MOLECULAR GENETICS OF COLOR VISION

Because human trichromatic color vision requires three classes of pigments with overlapping relative spectral sensitivities, but not necessarily any one particular pigment color, it is common to refer to the photopigment classes as short (S)-, middle (M)-, and long (L)-wavelength sensitive, rather than blue, green, and red sensitive. The molecular genetics of human color vision is complex because one of three distinct genes has to be expressed in a particular cone cell that is otherwise identical to its neighboring cones. The complexity arises in part because of M- and L-sensitive genes, which are approximately 98% identical, are juxtaposed on the X chromosome. Individual X chromosomes contain variable numbers of M- and L-sensitive genes arranged linearly in a tandem repeat array. Gene rearrangements including duplication and recombination have caused a great deal of variability in these gene arrays in the human population.

Recent advances in molecular biology have allowed remarkable parallel advances in understanding the molecular basis for color perception, especially at the level of the photoreceptor molecules.[5] However, variations in red-green color perception vary widely even within a particular broad genetic classification. The most reasonable hypothesis that links genotype to clinical phenotype may be the so-called spectral proximity hypothesis, which states that red-green color discrimination is a function of the difference between the wavelengths of maximal absorption of the M- and L-sensitive pigments. A normal separation of approximately 30 nm (approximately 560 nm versus 530 nm) might be optimal.

COLOR VISION DEFECTS AND COLOR VISION TESTING

Red-green color vision deficiency may result from the loss of an M- or L-wavelength gene, called *deuteranopia* and *protanopia*, respectively.[10,11,14] Loss of the S-sensitive wavelength gene would result in *tritanopia*. Inherited color vision defects that affect one pigment class are not generally associated with other visual dysfunction. However, severe loss of visual acuity may be associated with the absence of multiple cone types, as in various incomplete or complete achromatopias.[3]

A short discussion of inherited defects in red-green, or X-linked, color perception is relevant because up to 10% of males in the United States are affected. The most severely affected individuals are called *dichromats* because the sensitivity of one cone type is absent—L-sensing cones in protanopes and M-sensing cones in deuteranopes. The cones' sensitivities are absent because the corresponding pigment gene has been deleted from the X chromosome. Although anomalous trichromacy produces a milder form of color vision defect, which is still based on the presence of three spectral classes of functional cone cells, the underlying molecular genetics is much more complicated. In the case of *protanomaly* the presence of an L-wavelength–

sensitive pigment with an anomalous absorption spectrum, the normal L-wavelength–sensing gene is absent but its function is partially replaced by the presence of a second M-wavelength–sensing gene with a shift in its spectral peak relative to the normal M-sensing gene. The presence of anomalous M-wavelength–sensing pigment genes can be explained in terms of the mechanism of genetic rearrangements and the observation that a high degree of genetic polymorphism exists within both the M- and L-wavelength–sensing genes in humans.

Deuteranomaly, which is the most common type of color vision defect, may affect 1 in 20 males and 3 in 1000 females in the United States. In analogy with protanomaly, three functional cone classes exist—normal S- and L-wavelength–sensing cones and a spectrally anomalous second L-wavelength pigment. What are the consequences of a defect in red-green color perception, if any? Dichromacy and severe anomalous trichromacy result in significant perceptual disabilities. The normal visual perception of more than 100 different fully saturated hues may be reduced to one or two. Many of the activities of daily life are based on color images and color cues designed on a presumption of universal capacity for trichromatic color vision. Thus early diagnosis of color vision defects might allow for early modifications in educational and other activities.

Patients with severe cases of protanopia or deuteranopia confuse red and green, and those with tritanopia confuse yellow and blue or orange and violet. A variety of methods to screen for color defects, particularly protan and deutan defects, have been devised.[1,13] These include pseudoisochromatic color confusion charts (e.g., Dvorine, Ishihara, Stilling, Neitz), hue arrangement tasks (e.g., Farnsworth-Munsell 100-hue test, Farnsworth Panel D15, Lanthony Desaturated D-15), and lantern detection tests (e.g., Edridge-Green, Holmes-Wright). Despite the variety of testing methods available, or perhaps partly because of it, diagnostic testing for detecting color vision defects is not straightforward. Any test should ideally distinguish between patients with normal and abnormal color vision, between protan and deutan defects, and between congenital and acquired defects. In addition, tests should be easy to administer and should not require significant active cooperation on the part of the patient. The most widely used diagnostic tool is the Ishihara test, a collection of printed pseudoisochromatic plates. The Ishihara test is one of the best screening tests available, but it is not ideal because it is difficult to standardize and insensitive. Many patients with normal color vision make errors, and the test cannot reliably characterize a defect as protan versus deutan. Furthermore, the test cannot distinguish mild from severe defects or congenital from acquired defects. Color vision defects identified by a variety of screening tests, including the Ishihara test, generally require additional genetic and psychophysical testing by an experienced practitioner.

Precise follow-up testing is usually carried out using an instrument called an *anomaloscope* (Nagel Type I anomaloscope) to characterize so-called Rayleigh matches.[1] In a Rayleigh matching experiment the subject is simply asked to match a primary light that is spectral yellow (589 nm) to a mixture of primary light comprised of spectral red (679 nm) and spectral green (544 nm). The two variables are the intensity of the primary yellow light and the relative intensities of red and green lights that make up the mix. The rods and S-sensitive cones are excluded by limiting the viewing field to approximately 2 degrees of the fovea. The Rayleigh match is the intersection on a plot of the yellow intensity and the green–red mix ratio, and most normal trichromats choose a unique match reproducibly. Patients with defects may choose a match outside of the normal range, or they may allow more than one matching green–red ratio, depending on the type of defect. In summary, the precise phenotypes of color vision defects broadly called *protanopia* and *deuteranopia* are complex and variable, as are the underlying genotypes.

Disease or exposure to drugs or toxins also can affect color perception. Acquired disturbances of color vision are highly variable, and the clinical nomenclature tends to be somewhat confusing. Although the term *dyschromatopsia* refers to any disturbance of color perception, it is more commonly used in connection with acquired rather than congenital defects. *Chromatopsia*, which refers to the perception of color into a normally white or achromatic scene, is a particularly important symptom of many types of acquired defects. For example, xanthopsia is associated with the use of cardiac glycosides, and cyanopsia has been associated with the use of sildenafil citrate. Both of these adverse drug effects probably occur at the level of the retina. Dyschromatopsia is often a sensitive early symptom or diagnostic sign of an associated disease such as macular degeneration, glaucoma, or diabetic retinopathy. As such, color vision testing may be appropriate as a single noninvasive diagnostic screening test for a variety of disorders.

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