

Figure 12.26
Cataracts Classified by Location

The lens is shown from the front and as a vertical slice through the lens poles. The nucleus is enclosed by a dashed line and regions of opacity are shaded. Cortical cataracts may be peripheral, as in an equatorial cataract (a), or central, as in an anterior cortical cataract (b). Nuclear cataracts (c) are central, as are posterior subcapsular cataracts (d). All but equatorial cataracts affect visual acuity.

Cataracts, most of which are age-related, take different forms and can affect any part of the lens

Cataracts—opacities in the lens—occur at all ages from birth through adulthood. Congenital and juvenile-onset cataracts are not common, however; the vast majority of cataracts appear after the age of 50. The incidence of cataract is so strongly associated with advancing age that almost everyone over the age of 70 has some degree of transparency loss in the lens. Worldwide, cataracts account for almost half the cases of blindness, and they know no boundaries; all people—regardless of race, sex, national origin, or socioeconomic status—are potentially at risk.

Cataracts differ in optical density, shape, color, size, and location, creating difficulties in how we think about them because it is not always clear which of these differences are important in terms of the cataract's etiology. This discussion uses the simplest subdivision that seems meaningful—a coarse subdivision by location: Cataracts are cortical, nuclear, or posterior subcapsular.

Most age-related cataracts are **cortical cataracts**, in which the initial opacity is confined to the outer lens shells. A cortical cataract can be peripheral in the lens, which makes it an equatorial cataract (Figure 12.26a) or located more centrally near either the anterior (Figure 12.26b) or the posterior pole. The second most prevalent group consists of **nuclear cataracts**, in which the opacity first appears in the center of the lens (Figure 12.26c). A third, less common group consists of **posterior subcapsular cataracts** (Figure 12.26d), which lie in the outermost layers of the cortex at the posterior pole. The prevalence of cortical and nuclear cataracts in the population varies with age. Cortical cataracts are more common up to about age 65; nuclear cataracts dominate thereafter.

Cataracts absorb and scatter more light than do normal regions of the lens, thereby producing more light spread and less contrast in the retinal image. The result is reduced visual acuity, and acuity loss is related to the density and extent of the opacity. Small equatorial cataracts are the only sort to leave acuity unaffected; because they are peripheral, light entering through the normal, undilated pupil does not encounter the cataract. Any other cataract does affect acuity, however; nuclear and posterior subcapsular cataracts are the major offenders. In time, any cataract may expand to involve the entire lens, reducing vision to just the perception of light. Cataract surgery is discussed in Box 12.1.

Because cataracts are so common and affect so many people, efforts to understand how they form and to delineate the underlying causal factors have generated an enormous, often confusing body of literature. For example, a recent review of epidemiological studies listed six major categories of risk factors for cataracts, repeated here in the order given: social and personal factors, ultraviolet radiation, diabetes, diarrhea, antioxidants, and drugs. The social and personal factors included education, gender, smoking, alcohol, and hypertension. (A risk factor, incidentally, is not necessarily something that *causes* cataract,

although a risk factor may turn out to be a causal factor. Risk factors increase the likelihood of cataract by enhancing the effects of causal factors.)

Epidemiological studies are difficult, as demonstrated by the silly conclusion that incidence of cataract is inversely related to educational level. The common-sense explanation is that people with little education more often end up in outdoor jobs; that is, the real issue is occupational exposure to sunlight—not education. Statisticians know this, of course, and they use methods designed to factor out such extraneous variables. But the fact that education level keeps popping up as a factor in cataractogenesis is probably a sign that the statistical models are inappropriate for the data sets.

Problems of this sort are unavoidable. Trying to remove the influence of the dominant variable is difficult, perhaps impossible, and it may be difficult to measure the dominant variable in any meaningful way. In this case, the dominant variable is likely to be sunlight, something to which we are all exposed in varying degrees and something for which the degree of exposure is difficult to specify.

All the major and minor risk factors notwithstanding, the argument has been made that most cataracts in adults are due to the cumulative effects of exposure to sunlight, specifically to the ultraviolet component of solar radiation.* In this view, cataracts are exaggerations of normal transparency loss, where the exaggeration has come about by greater-than-normal exposure to sunlight or by other factors giving normal exposure a greater-than-normal impact.

As mentioned earlier, absorption of high-energy photons can not only break chemical bonds directly but also break them indirectly by increasing normal rates of oxidation or by producing heat through reradiation. All of these effects alter protein structure, causing the native monomeric or dimeric forms to link together as large, insoluble aggregates. These insoluble aggregates reduce the normal regularity of protein packing in the lens cells and thus reduce transparency. Nuclear and cortical cataracts appear to form by this process of protein alteration from UV absorption; the main difference between them being the longer time period required for the effects to accumulate in the nucleus.

Posterior subcapsular cataracts differ from the others in their mechanism of formation. Nuclear and cortical cataracts are alterations occurring within normal lens fibers, but posterior subcapsular cataracts contain abnormal cells. Interference with lens cell production at the equator produces lens fibers that do not elongate properly, and they migrate to the posterior pole, where their irregular structure creates an opacity. But while this process differs from the opacification in nuclear and cortical cataracts, the causal agent appears to be the same. Here, however, absorption of UV light interferes with epithelial cell differentiation and protein synthesis rather than with the protein structure in mature cells. (One piece of related evidence is the unusually high incidence of posterior subcapsular cataracts among survivors of the atomic bomb blasts at Hiroshima and Nagasaki. Atomic radiation interferes with cellular DNA more readily than ultraviolet radiation does.)

The lens normally changes with age, not only in gross features of size and weight but also at the level of molecular structure. Much of this normal senescence may be related to ultraviolet radiation exposure, and it is not unreasonable to think of cataractogenesis as an acceleration or exaggeration of normal lens aging. Or to put it another way, we will all have some degree of lens transparency loss if we live long enough; those of us who have had the highest expo-

*Much of this discussion is derived from *Age-Related Cataract* by R. W. Young (1991). The author, who is a basic scientist, draws a clean line through a messy clinical problem, but the book is rarely cited; the specialists may feel that he doesn't understand the nuances and complexities of their subject. I found it the best thing I read on the subject, but I'm not really a clinician either. Among other things, Young pioneered the use of radiolabeled amino acids to study cellular regeneration and renewal processes in the eye, including the lens, and was the first to demonstrate shedding and renewal of the photoreceptor outer segment (see Chapter 13).

Chapter 7). Some elderly cataract patients may find these requirements difficult to meet.

Because spectacle and contact lens corrections of aphakia are so often unsatisfactory, most extracapsular lens extractions are combined with insertion of a plastic or silicone intraocular lens. Intraocular lenses are made in several different designs—for insertion in the anterior chamber or, more routinely, for insertion in the posterior chamber in roughly the same position as the natural lens. Figure 2a shows one of the posterior chamber lenses. The lens is about 6 mm in diameter and has two springy arms that hold the lens in position (Figure 2b). The lens arms press outward against the ciliary body just anterior to the ciliary processes; this pressure and support from the intact posterior capsule keep the intraocular lens stable and centered with respect to the pupil and the visual axis.

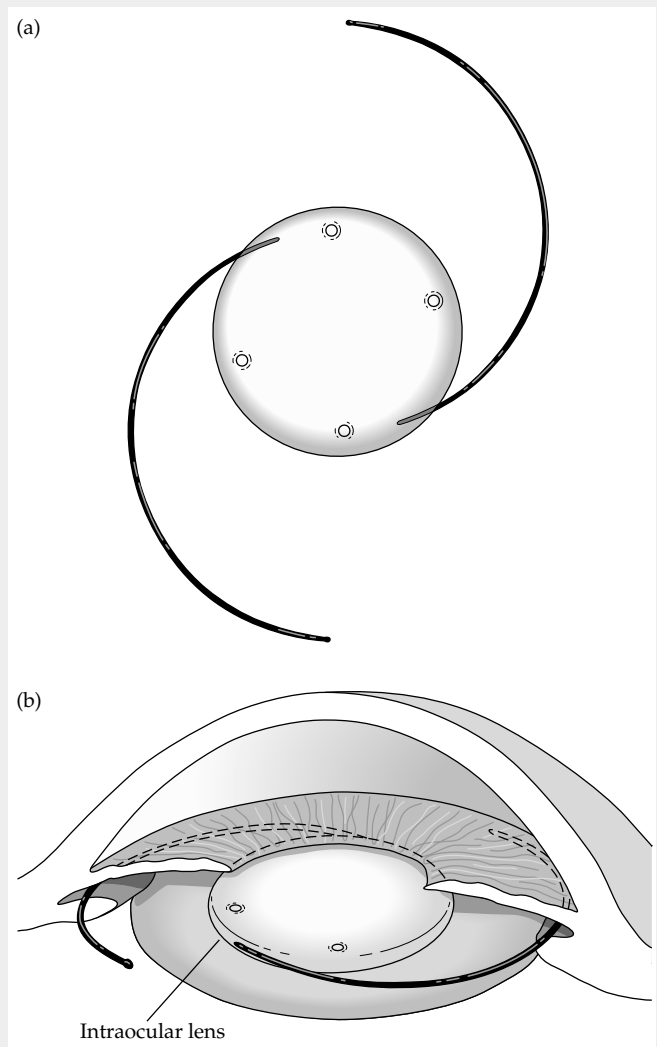
In a recent variation, intraocular lenses have been made of flexible silicone. They can be rolled up as a small tube, thereby requiring only a very small incision for their insertion, after which the lens opens up inside the eye to its original shape. (A rigid lens requires an incision slightly larger than the lens diameter.) Although there have been some questions about the stability and optical quality of the flexible lenses, the small incisions make for less traumatic surgery and they do not require sutures for closure (cyanoacrylate glue—“crazy glue”—is often used instead of sutures).

Penetrating the eye for any reason risks complications of various kinds—bleeding into the anterior chamber or vitreous, inflammatory reactions, abnormal tissue adhesions, and so on—and cataract surgery is not immune to these sequelae. Nor is the technique as simple as it has been outlined here. But current success rates, without complications, are very high, and the surgery—usually done on an outpatient basis—is fast; in 20 minutes or so, an eye that is functionally blind from cataract can be restored to normality.

Figure 2

An Intraocular Lens

(a) There are different designs of intraocular lenses, but most have some form of springy arms attached to the lens to hold it firmly in place. The small holes in the lens allow it to be hooked and maneuvered. For a posterior chamber lens, the arms press against the ciliary body just behind the root of the iris (b). (After Jaffe and Horwitz 1992.)



sure to ultraviolet radiation will have more and earlier transparency loss, as will those who have been exposed to other accelerants of biochemical aging.

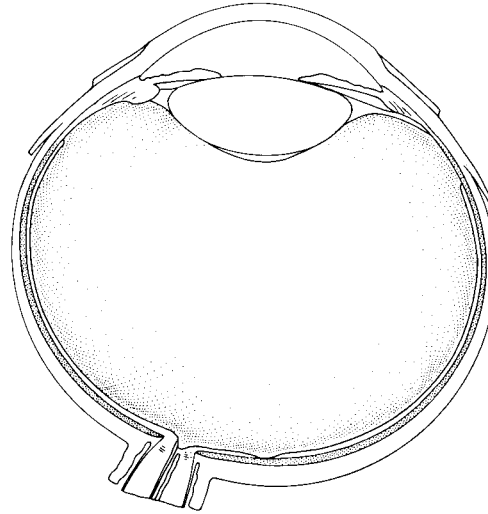
This is where other risk factors come into play. Trauma increases the risk of cataract formation, as do some metallic salts (e.g., cobalt and selenium), some ocular drugs (particularly cholinesterase inhibitors), and some systemic drugs (corticosteroids and chlorpromazine). Smokers may be more subject to nuclear cataracts, and heavy alcohol consumption may increase the risk for all types of cataract. Abnormal blood sugar levels increase the risk of cataract, and diabetics have been said to be at higher risk, but the evidence for increased prevalence of cataracts among controlled diabetics is contradictory.

Because of the numerous risk factors that may bear on the problem, cataract is often described as “a multifactorial disease,” thereby implying that it’s all very complicated and mysterious, and perhaps it is. But this description may obscure rather than illuminate the dominant factor, which is ultraviolet exposure, its contribution to normal senescence, and its cumulative impact on lens biochemistry.

Figure 12.27

The Vitreous

The vitreous is shaded in this cross section through the eye. It occupies about 80% of the eye's total volume and is therefore the largest component of the eye.



Total ocular volume \approx 6.5 ml:

Anterior chamber }
Posterior chamber } \approx 10%
Lens }

Vitreous \approx 80%

Other tissues \approx 10%

Although some loss of lens transparency is an inevitable fact of life, transparency loss to the point of cataract formation may be preventable. Like the production of basal and squamous cell carcinomas in the skin, the effect of sunlight in cataractogenesis is cumulative; preventative measures must begin early and be practiced routinely. UV-blocking sunglasses are an obvious part of a solution.* As a global public health issue, however, the problem is making sunglasses acceptable and accessible to populations at high risk.