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Glaucoma

Glaucoma is a group of diseases that is one of the leading causes of blindness and visual impairment. What these diseases have in common is that they damage the eye’s optic nerve.

Damage to the optic nerve can initially cause blind spots at the outer edges of the field of vision, called the peripheral or side vision. Sometimes patients will complain of some eye discomfort. But the scary thing about glaucoma is often times the disease is asymptomatic. Damage to the optic nerve leads to vision loss, so early detection through screening is needed.

Patients and people should visit an eye care doctor every one to two years for a dilated eye exam. It’s important just not to focus on the eye pressure. You can have glaucoma with normal eye pressures. So the eye care doctor has to do a dilated eye exam and carefully look at the optic nerve for signs of glaucoma as well as assess the side vision or visual field in that patient.

Certain ethnic groups are at higher risk for glaucoma. African-Americans are particularly at higher risk for developing blindness from glaucoma, also patients who are 40-years or older, everyone over age 60. People with a family history of glaucoma also are at higher risk. Also, if you are either profoundly far-sighted or near-sighted you also may be at risk for developing glaucoma.

Early detection of glaucoma is especially important in helping older adults retain their vision and independence.

Glaucoma can be a challenging disease to manage. And the reason is it often times is quite insidious—it causes very slow vision loss that is very difficult to perceive especially in its early stages. And the therapies that we often times use sometimes have some side effects so it’s important for the patient to establish a very close relationship with their eye care provider so that they understand what the potential for their vision loss could be and they understand all the therapies that would help them keep their vision.

Source NIH
Stem Cells, Genetic Therapy Take Aim at Vision Loss

By Gina Shaw

The retina is an essential component of your vision: It's the layer of tissue in the back of your eye that senses light and sends images to your brain. Nearly 2 million people in the United States alone have severely impaired vision due to diseases of the retina, many of which are progressive and have few treatment options.

But what if you could generate your own new cornea or retina with just a few cells taken from your own skin? It sounds like science fiction, but recent advances in stem cell technology and ophthalmology make it something that could be happening at a leading hospital near you within the fairly near future.

In January, the results of the world's first human trial using embryonic stem cells to treat eye disease appeared in the Lancet. The trial, conducted by scientists at the Jules Stein Eye Institute at the University of California-Los Angeles and funded by California biotech firm Advanced Cell Technology, involved two female patients—a elderly woman with dry age-related macular degeneration, a leading cause of blindness in the United States, and a woman in her 50s with Stargardt disease. Both were considered blind.

Embryonic stem cells had been coaxed to grow into retinal pigment epithelium (RPE), a highly specialized tissue whose malfunction is at the heart of many eye diseases. After injections of 50,000 new RPE cells into their diseased eyes, both women were doing well and the cells had attached to the eyes' membranes as doctors had hoped, although it was still too soon to say how their vision would improve, if at all.

Someone who had been waiting for the results of the trial is Dr. Stephen Tsang, assistant professor of ophthalmology, pathology and cell biology at Columbia University Medical Center in New York. Creating patient-specific cell lines that can be used to treat eye disease is one of Tsang’s primary research goals.

Tsang has been doing research similar to Advanced Cell Technology and UCLA’s work, and he has also been able to coax embryonic stem cells to develop into RPE cells, or into corneal stem cells.

“The technology is most advanced with corneal stem cells,” he said. “For people who have had a bad alkaline burn to the cornea or another trauma, we will soon be able to take stem cells from the good eye and help generate a new cornea for the other eye.”

But what if the person's eye damage comes from a disease, such as diabetic retinopathy? If the disease is part of the patient’s own genetic code, transplanting new corneal or retinal cells with the patient’s existing genetic programming could just reintroduce the same disease.

In some cases, that would actually be fine. With a condition such as age-related macular degeneration (AMD), that might not even be so bad, says Dr. Lucian Del Priore, professor of clinical ophthalmology at Columbia and a noted researcher in the application of stem cell technology to eye disease. “Newly generated retinal cells should behave as if they are brand new, which should give the patient another 55 or so years before AMD sets in,” he explained.

Other diseases, however, aren't age-related. A condition called Leber’s congenital amaurosis, for example, is an inherited eye defect that appears early in life and causes severe loss of vision by childhood or late adolescence. “Transplanting newly generated cells with the exact same genetic defect would make very little difference,” said Del Priore.

To use cell-based therapy for patients with such diseases, ophthalmologists will need to correct the “mistake” in the original genetic code. The early results from the UCLA trial, showing that this process can be done safely, are a promising first step. Tsang soon hopes to apply to the U.S. Food and Drug Administration for a trial that would involve using human skin cells (rather than embryonic stem cells) to correct eye defects. “We would take stem cells from the skin of patients with the most severe macular degeneration, correct the genetic defect, and re-implant them,” he explains.

But even before stem cell therapies becomes ready for prime time, personalized medicine and genetics are
already being used to treat eye disease — allowing ophthalmologists to select the perfect drug for an individual patient, or to develop new drugs that target individual genetic mutations that cause eye disease.

“At Columbia, we’re generating patient-specific cell lines that allow us to test hundreds of new medications,” said Del Priore. “The ability to do this large-scale screening really lets us establish the efficacy of a drug across a wide range of patients.”

Many patients with eye disease already receive a personalized genetic “prescription.” When patients come to the Edward S. Harkness Eye Institute at Columbia with certain genetically linked eye diseases, like age-related macular degeneration, they are screened to see if they have one of the known genetic mutations involved with that condition.

“With AMD, for example, we now know of about 10 genes involved with susceptibility to that disease, and we know the variants in those genes that increase risk, so we can estimate the risk of certain patients for getting the disease and for disease progression,” said Rando Allikmets, research director of the Harkness Eye Institute.

In most cases, gene defect-specific medications for eye diseases aren’t yet available, but that, too, may soon be changing for many conditions.

For example, scientists screening hundreds of drug targets for a possible treatment for retinitis pigmentosa — a group of inherited eye diseases involving retinal degeneration — recently found that retinal cells with a specific type of degeneration survived longer in laboratory culture if the culture contained an anti-seizure medication called valproic acid. A small study in patients with retinitis pigmentosa then showed that their eye degeneration slowed down when they started taking valproic acid. Now, the treatment is being tested in a larger phase II clinical trial with about 90 patients, which is still recruiting.

Whether it’s stem cell therapy or new, patient-specific medications (or old medications used for new purposes), genetic and cellular technologies have the potential to slow down, improve or even reverse hundreds of thousands of cases of vision loss every year.
Diabetic Retinopathy

Definition

Diabetic retinopathy (DR) is a **Microangiopathy** of the retinal arterioles, capillaries and the venules, which occurs due to long standing systemic disease-diabetes mellitus (DM).

Prevalence and Incidence in India:

The prevalence of diabetic retinopathy in pts with Type 2 DM is much lesser as compared to Type 1 DM pts.

In young /juvenile Type 1 diabetics DR doesn’t occur up to 3-5 yrs of onset of systemic disease. Similar results have been seen for Type 2 diabetics; but the time and duration of diabetes have been difficult to determine precisely. In patients with DM diagnosed before 30 yrs of age incidence of DR is 50% at 10yrs and 90%after 30yrs. In a population based assessment of DR in an urban Indian population according to BJ0-99.

- 1.8% of people more then 30yrs had DR.
- 89.3% had mild-moderate NPDR out of which 12% had CSME and
- 1/3rd of those had visual acuity <6/12.
- 10.7% pts had PDR.

In one more study in an urban Indian population in Oct’96-June’97 Total of 2522 subjects were interviewed and examined,of these 124 had reported DM.

- (22.4%)28 were >30 yrs old had DR.
- (50%)14 had mild NPDR.
- (39.3%)11 had moderate NPDR.
- (7.1%)2 had severe NPDR.
- (3.6%)1 had PDR.
- Of the 28 subjects-4(14.3%) had CSME.

In one more study for assessment of prevalence of retinopathy in newly diagnosed diabetic pts in Southern India.

- 448 of newly diagnosed Type 2 DM pts.
- Of these 32 had DR.

**Conclusion:** Overall prevalence of retinopathy at diagnosis among clinic based South Indian pts. With Type 2 DM appears to be lower than that reported among Europeans.

Pathogenesis:

DR is a microangiopathy primarily affecting pre-capillary arterioles; capillaries and post capillary venules. Exhibits features of both microvascular occlusion and leakage. Occlusion leads to Retinal ischemia

Two consequences of retinal hypoxia due to ischemia

1. Arteriovenous shunts-associated with capillary drop outs called as Intraretinal Microvascular Abnormalities (IRMA).
2. Neovascularization-caused by growth factors (vasoformative substances) elaborated by hypoxic retinal tissue in an attempt to revascularize the hypoxic retina.VEGF (vascular endothelial growth factor) is recognized to be responsible.

Microvascular Occlusion

<table>
<thead>
<tr>
<th>Capillary changes</th>
<th>Haematological changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickening of basement membrane</td>
<td>Deformation of RBCs</td>
</tr>
<tr>
<td>Damage and proliferation of endothelial cells and aggregation</td>
<td>Increased rouleax formation</td>
</tr>
<tr>
<td>Loss of pericytes</td>
<td>Increased platelet stickiness</td>
</tr>
</tbody>
</table>
Leakage

Breakdown of Inner Blood Retinal Barrier (tight junctions between the endothelial cells) → leakage of plasma constituents into the retina.

This results in saccular outpouchings of the vessel wall → termed Microaneurysms.

These may leak or may become thrombosed.

Increased vascular permeability leads to h’rrages and edema.

Haemorrhages

- Superficial h’rrages (flame shaped) - present in the Nerve Fibre Layer (NFL).
- Deep h’rrages (dot and blot) - present in the Outer Plexiform Layer (Henle’s layer).

Diffuse retinal edema

Occurs due to extensive capillary dilatation and leakage.

Localized retinal edema

Caused by focal leakage.

Chronic localized edema leads to deposition of hard exudates at the junction of normal and edematous retina.

These are composed of lipoprotein and lipid filled macrophages.

Cotton wool spots – present in severe NPDR are due to focal infarcts of the NFL due to interruption of axoplasmic transport.

Risk factors:

Duration of diabetes:

More than the control of diabetes it’s the duration of diabetes, which has been found to be more important. More the duration more the chance of having DR.

Systemic Hypertension:

In addition to diabetes if hypertension is associated, it is seen to aggravate the onset and progression of retinopathy changes, more so if uncontrolled blood pressure levels.

Associated Diabetic Nephropathy:

Associated nephropathy or changes in the renal function tests is also found to affect the progression of retinopathy. Its also found that renal transplant could improve DR.

Pregnancy:

Pregnancy associated with systemic diabetes or gestational diabetes; also increases the progression of DR due to hormonal changes.

Fluctuating Levels of Sugars:

Fluctuating blood sugar levels are known to progress the time in which DR starts and also progress the DR changes.

Modifiable Factors like Smoking, Alcohol and Hyperlipidemia:

Smoking and Alcohol consumption increases the arteriosclerosis changes and increases sugar levels thus; progression of DR. Hyperlipidemia is also associated with progression of DR.

Certain benefits of intensive metabolic control

- Delays onset of DR; but doesn’t prevent it.
- Slows progression of nonproliferative DR.
- Decreases rate of conversion of NPDR to PDR.
- Decreases incidence of macular edema.
- Decreases need for photocoagulation.

Screening

<table>
<thead>
<tr>
<th>Eye examination schedule</th>
<th>Time of onset of DM</th>
<th>Recommended time for first visit</th>
<th>Routine minimum follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 yrs of age</td>
<td>5 yrs after onset</td>
<td>Yearly</td>
<td></td>
</tr>
<tr>
<td>Age 30yrs or older</td>
<td>At the time of diagnosis</td>
<td>Yearly</td>
<td></td>
</tr>
<tr>
<td>Before pregnancy</td>
<td>Before/soon after conception</td>
<td>At least every three months.</td>
<td></td>
</tr>
</tbody>
</table>
Classification:

There are many described classifications of DR but the routinely and most followed of them all is the Modified ETDRS (Early Treatment Diabetic Retinopathy Study classification).

**Modified ETDRS classification:**

**Non-Proliferative Diabetic Retinopathy**

A. Mild NPDR.
   Atleast one microaneurysm
   Definition not met for B,C,D,E,F.

B. Moderate NPDR.
   \( \geq \) Standard photograph no.2A, soft exudates, venous beading,
   IRMAs definitely present.
   Definition not met for C,D,E,F.

C. Severe NPDR.
   H’rrages /Microaneurysms \( \geq \) standard photograph no.2A in all four quadrants.
   Venous beading in 2 or more quadrants.
   IRMAs \( \geq \) standard photograph no.8A in atleast 1 quadrant.

D. Very Severe NPDR.
   Any two or more of C
   Definition not met for E,F

**Proliferative Diabetic Retinopathy:**

Composed of NVD or NVE or both, preretinal h’rrage or fibrous tissue proliferation.

E. Early PDR.
   New vessels
   Definition not met for F

F. High risk PDR.
   NVD \( \geq \) \( \frac{1}{3} \) – \( \frac{1}{2} \) disc area
   NVD and vitreous or preretinal h’rrage
   NVD \( \geq \) \( \frac{1}{2} \) disc area preretinal or vitreous h’rrage

**Clinically Significant Macular Edema:**

1. Thickening of the retina located \( < = \) 500 microns from the center of the macula; or
2. Hard exudates with thickening of the adjacent retina located \( < = \) 500 microns from the center of the macula; or
3. A zone of retinal thickening ,1 disc are or larger in size located \( < = \) 1 disc diameter from the center of the macula.

**Treatment options:**

Argon laser photocoagulation-done in patients with CSME or Diabetic Maculopathy.

**Focal treatment** is preferred

Spot size – 50 to 100µ.

Duration – 0.1 sec

Sufficient power to obtain moderate intensity burn
Grid treatment:
Used for areas of diffuse retinal edema more than 500 µ from center of fovea & 500µ from temporal margin of optic disc.
Spot size – 100 to 200µ
Duration 0.1 sec
After this treatment —70% of eyes achieve stable VA —15% show improvement —15% may subsequently deteriorate.
Pan retinal photocoagulation:
Done in pts with PDR with or without high risk characteristics

AIM:
Conversion of hypoxic retina to anoxic retina so that the oxygen demand decreases. Hence new vessels are not formed.
PRP helps in regression of new vessels & prevents complications like VH & TRD.
Spot size - 500µ with Goldman’s lens.
Duration – 0.05 sec - 0.1 sec.
Power – enough to produce gentle burn.
Initial treatment consists of 2000 – 3000 burns in a scatter pattern extending from posterior pole to peripheral retina in 1 or more sessions.

Advanced Diabetic eye disease:
VH & TRD may need Pars plana Vitrectomy with release of traction & FGE with EL with SO injection.

Diabetic Retinopathy Study (DRS):
Primary outcome measurement was severe visual loss (SVL), which is defined as VA of < 5/200 on 2 consecutive follow-ups 4 months apart

Outcome:
50% or > reduction in rates of SVL in eyes treated with PRP compared to untreated control eyes during follow up of up to 5 yrs.

Early Treatment Diabetic Retinopathy Study (ETDRS)
Study evaluating Photocoagulation & Aspirin treatment of diabetic pts with < high risk PDR in BE. Primary measurement of outcome was mild visual loss (MVL) which is drop in 3 or more lines of Snellen’s equivalent.

Outcome:
50% or > reduction in rates of MVL in laser treated eyes with CSME When NPDR becomes severe & reaches high-risk stage, Scatter PRP can be considered & should not be delayed. Aspirin did not alter rates of progression of DR nor had any influence on final visual outcome.

Diabetic Retinopathy Vitrectomy Study (DRVS)
Trial investigating role of vitrectomy in managing eyes with very severe PDR.

Outcome:
In Type I (IDDM) pts with severe VH benefit of early vitrectomy was clearly demonstrated but no such advantage was found in mixed or Type II (NIDDM) pts.

Diabetes Control & Complications Trial (DCCT)
Trial designed to study connection between metabolic control & retinal, renal & neurological complications in Type I (IDDM) pts.

Outcome:
Intensive insulin treatment can delay onset & slow the progression of DR in Type I pts.

REFERENCES
Retinal detachment often is a preventable cause of vision loss. There are three types of retinal detachments: exudative, tractional, and rhegmatogenous. The most common type is rhegmatogenous, which results from retinal breaks caused by vitreoretinal traction. Risk factors for retinal detachment include advancing age, previous cataract surgery, myopia, and trauma. Patients typically will present with symptoms such as light flashes, floaters, peripheral visual field loss, and blurred vision. Early intervention facilitates prevention of retinal detachment after formation of retinal breaks and improves visual outcomes of retinal detachment surgery. Patients with acute onset of flashes or floaters should be referred to an ophthalmologist.

Retinal detachment is relatively uncommon, affecting only one in 10,000 people per year, or approximately one in 300 patients in the course of a lifetime. Retinal detachment often is repaired with little or no vision loss; therefore, it is a much less significant cause of irreversible blindness than other retinal diseases, such as diabetic retinopathy and macular degeneration. Retinal detachment should be considered in the differential diagnosis of vision loss, however, because it is more prevalent in defined subpopulations and may require urgent surgical repair.

Pathogenesis of Retinal Detachment

The retina is a neurosensory tissue that lines the interior posterior two thirds of the eye (Figure 1, left). The central retina, or macula, and the centermost macula, or fovea, exhibit structural and cellular specializations for fine central acuity.

Retinal detachment results when physiologic and anatomic mechanisms of retinal attachment are overcome and the retina separates from the underlying retinal pigment epithelium (Figure 1, lower right). Retinal detachments are classified into three pathogenetic types (Table 1). A patient may present with one or more of these types.

Exudative (or serous) retinal detachment results from the accumulation of serous and/or hemorrhagic fluid in the subretinal space because of hydrostatic factors (e.g., severe acute hypertension), or inflammation (e.g., sarcoid uveitis), or neoplastic effusions. Exudative retinal detachment generally resolves with successful treatment of the underlying disease, and visual recovery is often excellent.

The second type of detachment, tractional retinal detachment, occurs via centripetal mechanical forces on the retina, usually mediated by fibrotic tissue resulting from previous hemorrhage, injury, surgery, infection, or inflammation. Correction of tractional retinal detachment requires disengaging scar tissue from the retinal surface. In patients with tractional retinal detachment, vision outcomes are often poor.

The third and most common type is rhegmatogenous retinal detachment. The key pathogenetic steps of rhegmatogenous retinal detachment are illustrated in Figure 2. The vitreous humor is a hydrated gel whose structure is maintained by a collagenous and mucopolysaccharide matrix (Figure 2a). As persons age, this macromolecular network begins to liquefy and collapse, the vitreous shrinks, and vitreo-retinal traction develops. Eventually, the vitreous partly separates from the retinal surface, which is known as posterior vitreous detachment (Figure 2b). Approximately one in four persons develops a posterior vitreous detachment between 61 and 70 years of age, and nearly two thirds have posterior vitreous detachment after 70 years of age. Posterior vitreous detachment is harmless by itself, though bothersome floaters (blood or retinal pigment epithelium cells) may develop and persist. However, in 10 to 15 percent of patients with symptomatic posterior vitreous detachment, a retinal flap tear or hole forms as the vitreous pulls away from the retina, especially in the periphery where the retina is thinner (Figure 2c).
(Left) Schematic diagram indicating several ocular structures. (Lower right) Cross-section through the posterior eye wall shows the retina in contact with the vitreous at its inner aspect. Photoreceptor cells in the outermost retina adhere to the retinal pigment epithelium, which appears as a darkly pigmented cellular monolayer above the vascular choroid. The sclera is the white outer coat of the eye that invests the optic nerve and is continuous with the dura. The plane of separation in retinal detachment is between the retina and the retinal pigment epithelium. Vision is lost because photoreceptor cells require contact with the retinal pigment epithelium and choroid for metabolic and vascular support.

Retinal tears may occur without symptoms, but often photopsia (luminous rays or light flashes in vision) is noted. Photopsia results from mechanical stimulation of the retina by vitreoretinal traction. When the retina tears, blood and retinal pigment epithelial cells may enter the vitreous cavity and are perceived as floaters (Figure 2c). Patients with symptomatic retinal tears are at high risk of progression to retinal detachment.

Rhegmatogenous detachment occurs when liquid vitreous enters the subretinal space through a retinal break and creates a plane of dissection between the retina and retinal pigment epithelium (Figure 2d). Over time, the area of detachment increases as more fluid passes through the retinal break. Symptoms depend on the location and extent of the detachment. For example, a small detachment in the inferior retina results in a small superior visual field defect, while a large temporal detachment causes extensive nasal field loss. When the macula detaches, central acuity is lost. If untreated, nearly all rhegmatogenous retinal detachments progress to involve the macula.

**Epidemiology of Retinal Detachment**

The role of the vitreous in the pathogenesis of retinal breaks and detachments clarifies the risk factors for retinal detachment (Table 2). Detachment is more likely with advancing age because molecular breakdown and shrinkage of the vitreous humor increases over time.4,6 Previous cataract surgery commonly is associated with retinal detachment.7 The detachment occurs because following the surgical removal of the lens during cataract surgery, vitreous hyaluronic acid may pass into the anterior chamber and escape through the trabecular meshwork. Shrinkage and detachment of the vitreous are accelerated, and increase the risk of development to retinal tears. Retinal detachment occurs in approximately 1 percent of patients in the weeks to years following cataract surgery.8

### TABLE 1

**Classification and Management of Retinal Detachment**

<table>
<thead>
<tr>
<th>Type</th>
<th>Etiology</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exudative (serous)</td>
<td>Inflammation (sarcoid uveitis), severe acute hypertension, neoplastic tumors</td>
<td>Treat underlying disease.</td>
</tr>
<tr>
<td>Tractional Fibrosis*</td>
<td>Surgical excision of fibrosis</td>
<td></td>
</tr>
<tr>
<td>Rhegmatogenous</td>
<td>Retinal tears†</td>
<td></td>
</tr>
</tbody>
</table>

*—Caused by previous retinal detachment, surgery, trauma, or proliferative retinopathy.  
†—See Figure 2.

Myopia, or nearsightedness, is another leading risk factor for retinal detachment.9 In most patients with moderate or severe myopia, the axial (anteroposterior) length of the eye is greater, resulting in an egg-shaped globe. As a consequence, centripetal vitreoretinal traction increases and posterior vitreous detachment may occur at a younger age than in persons without myopia.4 Also, in myopic eyes, the retina is thinner and more prone to tear or hole formation at the time of posterior vitreous detachment. Therefore, persons with myopia are at risk of retinal detachment even in early adulthood; acute symptoms of flashes and/or floaters in these patients warrant a thorough fundus examination. Focal areas of peripheral retinal thinning and vitreoretinal adhesion occur less often in those without myopia, and are associated with retinal detachment.10

### TABLE 2

**Risk Factors for Retinal Detachment**

<table>
<thead>
<tr>
<th>Common</th>
<th>Less Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aging</td>
<td>Congenital eye diseases</td>
</tr>
<tr>
<td>Cataract surgery</td>
<td>Diabetic retinopathy</td>
</tr>
<tr>
<td>Focal retinal atrophy*</td>
<td>Family history of detachment</td>
</tr>
<tr>
<td>Hereditary vitreoretinopathy</td>
<td></td>
</tr>
<tr>
<td>Myopia (axial)</td>
<td>Prematurity</td>
</tr>
<tr>
<td>Trauma</td>
<td>Uveitis</td>
</tr>
</tbody>
</table>

*—Atrophic retinal lesions are designated by descriptive terms such as “lattice” degeneration.

Pathogenesis of rhegmatogenous retinal detachment. (A) The vitreous gel evenly fills the vitreous cavity and
is adherent to the retinal surface. (B) With aging and other factors, the gel shrinks, exerts a centripetal traction force on the retina (arrows), and eventually separates from the retina, a condition known as posterior vitreous detachment; a fluid-filled space enlarges between the retracting gel and the retinal surface. (C) In susceptible persons, vitreoretinal traction and posterior vitreous detachment result in a retinal break, from which blood and retinal pigment epithelium cells may enter the vitreous cavity (floaters). (D) As liquid vitreous passes through the break (curved arrow), it dissects the retina from the underlying retinal pigment epithelium, resulting in retinal detachment.

Trauma precipitates retinal detachment for several reasons. At the moment of impact, rapid compression and decompression of the globe may generate sufficient vitreoretinal traction to produce retinal tears.11 Alternatively, retinal detachment may occur weeks, months, or even years after trauma because vitreous contraction is accelerated by inflammatory and blood-borne mediators that access the vitreous cavity at the time of injury.12 Despite these concerns, retinal detachment rarely follows head and periorcular trauma,13,14 and fundus examination is warranted only if visual symptoms or external or radiographic evidence of ocular injury are present.

Less common associations with rhegmatogenous retinal detachment include a family history of detachment, a history of congenital eye diseases (such as glaucoma or cataract), hereditary vitreopathies with abnormal vitreous gel and high myopia (such as Stickler’s syndrome), and previous retinopathy of prematurity (Table 2).

### Evaluation of Patients with Suspected Retinal Detachment

A careful history helps to distinguish retinal detachment from other conditions with similar symptoms (Table 3). Floaters caused by acute posterior vitreous detachment, especially in the presence of a retinal tear, occur more abruptly and dramatically than do the floaters that people experience for much of their lifetime. Floaters are described by patients as fine dots, veils, cobwebs, clouds, or strings. Similar floaters occur with other causes of intraocular bleeding, such as proliferative diabetic retinopathy, trauma, and ocular inflammation (uveitis).

Light flashes may precede migraine headaches, but these typically occur bilaterally (though often in one area of the visual field). Photopsia that is induced by eye movements may indicate optic neuritis. Light flashes also may occur with postural hypotension and vasovagal reactions; these are bilateral and often accompanied by temporary dimming of vision and lightheadedness.

Visual field loss caused by retinal detachment begins suddenly, usually in the periphery, and progresses toward the central visual axis over hours to weeks; patients may describe this as a dim “shadow” or “curtain.” Field loss caused by stroke or other central nervous system processes is always bilateral, stable, and homonymous, due to crossing of nasal retinal projections at the optic chiasm. Even in patients with severe field loss caused by cerebral disease, the macula is spared and central vision persists. Visual loss from a transient ischemic attack may be unilateral, but is episodic, not persistent or progressive as in cases of retinal detachment, and may be accompanied by other neurologic symptoms. Fixed field defects of variable size occur in patients with retinal vascular occlusion; these patients often have hypertension or other atherogenic diseases, lack acute flashes, floaters, or other risk factors for retinal detachment, and may exhibit flame hemorrhage or arteriolar plaques by ophthalmoscopy.

### TABLE 3

<table>
<thead>
<tr>
<th>Differential Diagnoses of Retinal Detachment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptom</strong></td>
</tr>
<tr>
<td>Photopsia</td>
</tr>
<tr>
<td>Floaters</td>
</tr>
<tr>
<td>Visual field loss</td>
</tr>
<tr>
<td>Blurred vision</td>
</tr>
</tbody>
</table>

PVD = posterior vitreous detachment; PDR = proliferative diabetic retinopathy; CVA = cerebrovascular accident; BRVO = branch retinal vein occlusion; BRAO = branch retinal artery occlusion.

In patients with optic nerve disorders, visual field loss is typically central or paracentral, pupillary reactions are diminished in the affected eye, and optic nerve head edema may be evident. Macular degeneration is the leading cause of painless sudden vision loss in older patients, but the scotoma is central and the peripheral field is intact. Common ocular signs and symptoms, such as pain, irritation, tearing, intermittent blurring, and conjunctival redness, are unrelated to retinal detachment.
Prompt referral and evaluation of patients who are suspected of having retinal tears are important because treatment of retinal tears is highly effective in preventing retinal detachment, and because progression of retinal detachment into the macula typically results in permanent visual loss. All patients with acute onset of flashes or floaters should be referred to an ophthalmologist (Table 4). If the patient has additional risk factors (e.g., myopia, previous cataract surgery, trauma, retinal detachment in the fellow eye, family history of detachment), suspicion of retinal detachment is heightened. If the patient exhibits acute visual field loss, whether subjective or demonstrable by confrontation, immediate referral is recommended. When the macula detaches, the potential to maintain normal vision is often lost. Thus, patients with extramacular detachment require more urgent management, even though they may present with excellent central visual acuity. These patients may benefit from direct referral to a retinal specialist to avoid the delay associated with additional examination by a general ophthalmologist or optometrist. In North America, most retinal detachment surgeries are performed by retinal specialists.

The direct (hand-held) ophthalmoscope is useful to detect an altered red reflex sometimes associated with retinal detachment. However, because its view is narrow, a normal examination with the direct ophthalmoscope cannot exclude a diagnosis of retinal detachment. Ophthalmologists use indirect examination techniques that greatly enhance visualization of the peripheral fundus. In cases where severe photophobia, periorbital edema, or opacity (e.g., cataract, intraocular blood) preclude ophthalmoscopy, ophthalmic ultrasonography is superior to magnetic resonance imaging and computed tomography for revealing occult retinal detachment (Figure 3).

**Treatment of Retinal Detachment**

Prevention is important in the treatment of retinal detachment. Protective eyewear is recommended for persons participating in contact sports, especially if they have moderate or severe myopia. Patients undergoing cataract surgery must be instructed about the importance of reporting symptoms of retinal tears and detachments. The greatest opportunity for prevention exists in the hours to weeks following posterior vitreous detachment and retinal tear formation, because there is often a variable interval between retinal break and detachment. Only 1 to 2 percent of patients with a posterior vitreous detachment have a retinal break. If vitreous hemorrhage is present (often manifested as more marked floaters and blurring), this risk increases to 70 percent. Symptomatic retinal breaks are surrounded with laser or cryo burns to create a chorioretinal scar that prevents fluid access into the subretinal space. This treatment is over 95 percent effective in preventing progression of a retinal tear to retinal detachment (Figures 4a and 4b).

Surgical correction of retinal detachment aims to relieve vitreoretinal traction, and close retinal tears and holes. Scleral buckling techniques achieve reattachment in over 90 percent of cases (Figure 4c). An alternative means to relieve vitreoretinal traction is to remove the vitreous humor. This approach, called posterior vitrectomy, is successful in 75 to 90 percent of patients. Less invasive procedures, such as pneumatic retinopexy, allow repair of selected detachments in a clinic or office setting.

If the central macula has not yet detached when the repair is achieved, visual acuity equal to preretinal detachment levels can be expected. However, if the central macula is detached at the time of repair, final visual recovery may vary from none to nearly complete, depending on the duration and degree of elevation of macular detachment and the patient’s age. Therefore, surgical repair is indicated more urgently in patients with preserved central acuity, less urgently in patients whose macula detached in the previous hours to days, and routinely in those whose macula has been detached for several days or weeks (Table 4). Within months, photoreceptors in a detached retina suffer severe and irreversible damage caused by the separation from the underlying choroidal vascular supply (Figure 1, lower right), and repair yields less visual improvement.

B-mode ocular ultrasound. This ultrasound reliably detects retinal detachment and is particularly useful in children and uncooperative patients, and when the view to the retina is obscured by periorbital edema, blood, cataract, or other opacities. (Top) Partly detached retina (white arrowhead) lies within an otherwise echolucent vitreous cavity. (Bottom) Detached retina (white arrowhead) caused by traction on the retinal surface by intravitreal fibrosis (white arrow) in a patient with diabetic retinopathy. (C = cornea; L = lens; V = vitreous cavity; S = sclera)

Retinal detachment surgery fails in 5 to 10 percent of patients because of the growth of scar tissue on the retinal surface in the weeks following repair. Sources of fibrosis include blood cells, fibrin, inflammatory cells associated with postoperative healing, and retinal astrocytes and retinal pigment epithelium cells that enter the vitreous cavity when a retinal tear forms. Fibrotic tissue may exert sufficient inward traction to cause redetachment.
This condition, known as proliferative vitreoretinopathy, is surgically corrected in 60 to 90 percent of patients, though visual acuity is often poor. Suppression of epiretinal fibrosis with antiproliferative agents is being intensively investigated, but remains elusive.

(A) U-shaped retinal tear with vitreous adherent to its anterior flap (above). (B) Post-treatment photo of a retinal tear surrounded by multiple laser-induced burns that strengthen retinal adhesion to underlying tissues. (C) In scleral buckling, a pliable silicone element is positioned beneath the rectus muscles and sutured to the sclera. The inward scleral indentation (buckling) brings the detached retina in closer apposition to the eye wall and reduces internal vitreo-retinal traction.

### TABLE 4
Guidelines for Referral to an Ophthalmologist

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute photopsias</td>
<td>Within one week</td>
</tr>
<tr>
<td>Acute floaters</td>
<td>Within one week, sooner</td>
</tr>
<tr>
<td>if the floaters worsen</td>
<td></td>
</tr>
<tr>
<td>Visual field loss</td>
<td>Emergent, within one day</td>
</tr>
<tr>
<td>day, if possible</td>
<td></td>
</tr>
<tr>
<td>Any of above, chronic</td>
<td>Routine, within one to two months</td>
</tr>
<tr>
<td>Acute blurring</td>
<td>Urgent, within one to three days</td>
</tr>
</tbody>
</table>

Therefore, surgical repair is indicated more urgently in patients with preserved central acuity, less urgently in patients whose macula detached in the previous hours to days, and routinely in those whose macula has been detached for several days or weeks. B

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Ocular Pressures Spike During Robotic Prostate Surgery, Raising Risk for Eye Damage

San Diego—Patients who undergo robot-assisted laparoscopy in the steep Trendelenburg position for radical prostatectomy experience significant increases in intraocular pressures throughout the majority of operative time, placing them at greater risk for visual disturbances and even visual loss, researchers have found.

As a result, patients with pre-existing eye disease should be counseled about the potential risks of such procedures and ophthalmic consultation should be considered, according to the investigators.

“Our initial concern was there wasn’t much research into robot-assisted laparoscopic procedures, even though the urology community has found a couple of patients who had visual disturbances after being in the steep Trendelenburg position,” said Lt. Cmdr. Eugenio Lujan, MD, assistant professor of anesthesiology and residency director at Naval Medical Center San Diego, who led the study. “What’s more, the patient population for this procedure has some definite co-morbidities associated with visual loss to begin with.”

The pilot study included 33 patients, of whom 17 (mean age, 56.7±11.9 years) underwent surgery in the steep Trendelenburg position on a da Vinci robot (Intuitive Surgical). The remaining patients underwent open and laparoscopic procedures and served as controls (mean age, 54.4±15.5 years). Each patient had an ophthalmologic examination before surgery and one month after the procedure. Anesthetic technique was controlled for all patients, as was intra-abdominal pressure during surgery.

As Dr. Lujan reported at the 2010 annual meeting of the American Society of Anesthesiologists (abstract A195), baseline intraocular pressures were similar in patients undergoing robotic or conventional surgery (14.6±3.4 vs. 15.2±5.3 mm Hg, respectively). After one hour, however, patients in the steep Trendelenburg position experienced a doubling of their mean intraocular pressure, which remained at or above that level for the rest of the case. This increase corresponded to a significant rise in intraocular pressure compared with controls at all time points from the 60-minute mark through the end of the case (P<0.017).

The investigators also found significant increases in intraocular pressures during the steep Trendelenburg position compared with either the open or the laparoscopic surgery controls considered separately. An hour after the conclusion of the procedure, pressures remained slightly elevated but not significantly different between the two groups of patients (19.9±6.3 mm Hg in the robot-assisted group vs. 18.6±4.2 mm Hg in controls; P=0.320), the researchers said.

“As you might expect, these results were concerning,” Dr. Lujan said. “These are patients at high risk for visual disturbances; now their intraoperative intraocular pressures are increasing to the point where we run the risk of injuring the optic nerve or even the retina.”

Six patients in the group undergoing robot-assisted laparoscopy experienced an increase in intraocular pressure of more than 45 mm Hg; one patient had an optic hemorrhage with significant visual loss.

Two questions remaining to be answered, Dr. Lujan said, are which groups of patients are at greater risk for developing increased intraocular pressure during these procedures, and what—if anything—can be done to prevent its occurrence.

“I think it’s too soon to tell if people should change their practice at this point,” he said. “I think the big thing we should consider is screening. If you have patients with glaucoma or other significant risk factors, they should be referred to ophthalmology prior to surgery.”

The results are similar to those reported in a 2009 study published in Anesthesia & Analgesia, by Ohio researchers who looked at intraocular pressure in 33 patients undergoing robot-assisted prostatectomy (2009;109:473-478). According to the authors, the length of surgery and end-tidal carbon dioxide “were the only significant variables predicting changes in [intraocular pressure] during stable and prolonged Trendelenburg positioning.” After adjusting for end-tidal carbon dioxide, the
researchers observed an increase in intraocular pressure of 0.05 mm Hg for every minute of surgery.

Charles Watson, MD, chairman of anesthesia at Bridgeport Hospital in Bridgeport, Conn., said the new findings contradict the long-held belief that ophthalmic circulation autoregulates perfusion in the Trendelenburg position. But they fit with data from his own institution, dating from 2004, showing that intraocular pressures in patients who spend one to two hours in the steep Trendelenburg position during laparoscopic surgery may increase more than fourfold, with subsequent, potentially dangerous decreases of ophthalmic perfusion pressure and a potential risk for ischemic optic neuropathy, unless pharmacologic and other interventions are performed.

“It is my impression that awareness of this risk in the United States has increased to the extent that several groups are measuring intraocular pressure during these procedures," added Dr. Watson, a member of the editorial board of Anesthesiology News. “The specific risk of eye injury during such procedures is discussed preoperatively with all patients scheduled for robot-assisted laparoscopic prostatectomy and other lengthy laparoscopic procedures performed in steep Trendelenburg position.”

Early screening more useful for those with moderate Visual Acuity Loss

Children identified with mild unilateral acuity loss during visual screening at the age of 3 to 5 years do not appear to benefit from glasses and patching, or from glasses alone. However, children with the poorest acuity at screening improve significantly with treatment.

Among the 177 children identified with mild to moderate unilateral acuity impairment, defined as 6/9 to 6/12 and 6/18 to 6/36, respectively, “the overall response to treatment was disappointing: an increase equivalent to one line on a Snellen chart,” report Clarke et al[BMJ 2003;327:1251-4].

The researchers randomly assigned 59 children to each of 3 study arms:

- Full treatment including glasses and patching if needed, including orthoptist assessments every 6 weeks;
- Glasses alone with no other treatment;
- No intervention for 52 weeks.

Overall, 98% of the study population had significant refractive error and of these, 72% had anisometropia.

“Children with moderate initial acuity loss,” the researchers write, “improved with full treatment from 6/18 or worse to a mean acuity close to 6/9, while those in the mild group were essentially unchanged.” This suggests that the benefit from 12 months of wearing glasses is limited and that the effect of patching conferred the most benefit.

Two weeks after the initial interventions ended, the children in the glasses only and no interventions group received treatment according to the study protocol for the full treatment group. Six months after the formal trial interventions ended the researchers conducted follow ups in the 154 children available for assessment and found no significant differences in acuity between the 3 initial treatment groups.

The finding that children with moderate acuity loss of 6/18 or worse showed a clear response to treatment supports the continued visual acuity screening for young children. However, because children with mild acuity loss received limited benefit from treatment, "We argue that children with 6/9 in only one eye should no longer constitute screen failures," the authors write, "and do not justify treatment, even with glasses."

Supplements help preserve Vision

A simple vitamin supplement could significantly reduce the number of people with vision loss from age-related macular degeneration, or ARMD, the number one cause of blindness among older people, finds a new study.

In a study, investigators from the Age-Related Eye Disease Research Group built on earlier study results which showed that a combination of the antioxidant vitamins C, E, and beta carotene, along with zinc oxide or zinc alone could slow down or prevent ARMD among those considered at high risk for the advanced form of the condition, by estimating the impact the supplements could have on the total population of people at risk for developing advanced ARMD[Archives of Ophthalmology, 2003;121:1621-1624].

First, they estimated about 8 million people 55 and older have early signs of ARMD and are at high risk of developing advanced disease and significant vision loss. About 1.3 million, they say, would go on to develop advanced ARMD without preventative treatment.

The investigators’ model suggests more than 300,000 of these people could avoid advanced ARMD over the next five years if they took the vitamin supplements
recommended by the earlier study.

They write, “Avoiding the development of advanced ARMD can have a major effect on the quality of life for an individual ... These data suggest that the recommendations of such a supplement for those individuals should have a major impact on them as well as on the public health.”

Retinal Arteriolar size linked to Amputation Risk in Diabetics

According to a new study findings, the risk of lower extremity amputations can be predicted by the presence of generalized or focal retinal arteriolar narrowing in patients with type 1 diabetes. This increased risk is independent of glycosylated hemoglobin levels and blood pressure.

Moss et al analyzed 20-year follow-up data for nearly 1000 subjects with diabetes onset before age 30 who required insulin [Arch Intern Med 2003;163:2505-2510].

The cohort had undergone baseline examinations between 1980 and 1982. Retinal vessel caliber was measured on digitized fundus photographs.

The 79 lower extremity amputations that occurred during the ensuing 20 years translated to a cumulative 20-year incidence of 9.9%. After adjusting for age and sex, the odds ratio for amputation was 2.73 for those in the lowest quartile of arteriolar/venular ratio compared with those in the upper three quartiles. The odds ratio for risk associated with focal narrowing was even higher at 3.48.

Multivariate analysis revealed that the odds ratios for focal and generalized narrowing and diabetic retinopathy remained elevated after adjusting for glycosylated hemoglobin levels, blood pressure, and history of foot ulcers.

It is likely that type 2 diabetes mellitus patients with microvascular retinal changes are probably also at increased risk for amputation.

Drug therapy for SLE may precipitate Cytomegalovirus Retinitis

Retinitis resulting from CMV infection is common in patients with cancer, organ transplant recipients taking immunosuppressives, and patients with acquired immunodeficiency syndrome although it is not commonly associated with rheumatic diseases.

However, according to a recent case report, azathioprine and low dose corticosteroid therapy in patients undergoing haemodialysis with systemic lupus erythematosus (SLE) and end-stage renal disease may increase the risk of cytomegalovirus (CMV) retinitis.

Shahnaz et al [Mayo Clin Proc 2003 Nov;78:11:1412-5] reported a case study of bilateral CMV retinitis that probably resulted from azathioprine therapy in a patient with SLE who was undergoing haemodialysis for end-stage renal disease (ESRD).

The 37-year old woman presented with floaters in her right eye, yet no other remarkable symptoms. She had been diagnosed with SLE 17 years earlier. Moreover, renal biopsy in previous years had revealed diffuse proliferative glomerulonephritis. The patient later developed hypertension and ESRD and required tri-weekly haemodialysis. Notably, the patient was negative for HIV and hepatitis B and C.

Concurrent medications included azathioprine (2mg/kg/day), low dose corticosteroid (0.167 mg/kg/day) and hydroxychloroquine (400 mg/day) among others in order to manage her lupus flares.

Upon funduscopic examination, inflammatory cells and cell aggregates were found in the vitreous, denoting vitritis. Haemorrhages and perivascular white exudates were also found in the right eye. Similar, but smaller signs were found in the left eye. Bilateral CMV retinitis was diagnosed at this time and the patients was hospitalized.

Laboratory analysis determined that the patient had leukopaenia and lymphopaenia, which likely resulted from azathioprine therapy. Both azathioprine and hydroxychloroquine were discontinued at this time and the prednisone dose was reduced. Treatment with ganciclovir was initiated after every haemodialysis session for 3 weeks at an intravenous dose of 1.25 mg/kg that was later reduced to 0.625 mg/kg for 6 months.

Lesion regression occurred at week 6 of therapy and clinical symptoms subsequently resolved.

“The CMV retinitis in this patient was associated with combined azathioprine and low-dose corticosteroid therapy for lupus flare,” which “may have important clinical implications because this drug combination is used routinely to treat active SLE.” Researchers write.

“The subtle presentation of vision-compromising CMV retinitis warrants a heightened index of suspicion for early detection,” they caution.
Duration and dose of Inhaled Steroids may increase risk of Cataract Risk

Currently, due to the usefulness of inhaled corticosteroids in bronchial asthma they are now often used as first-line therapy and apart from the largely preventable risk of colonization. Of the pharynx, they are considered very safe.

However, according to the results of a population-based case-control study higher dose and longer use of inhaled steroids increases the risk of cataracts. [Br J Ophthalmol. 2003;87:1247-1251]

Using the U.K.’s General Practice Research Database, the investigators identified 15,479 patients with cataract older than 40 years and 15,479 control patients without cataract matched for age, sex, medical practice, and observation period.

Among those with cataract, nearly 11.5% had been prescribed inhaled steroids compared with nearly 7.5% of controls. The risk of cataract increased in a dose-related fashion, with little or no apparent increased risk for those taking a daily dose less than 400 µg (adjusted odds ratio [OR], 0.99; 95% confidence interval [CI], 0.87 - 1.13), but with an increased risk of 69% for those taking doses greater than 1600 µg a day (adjusted OR, 1.69; 95% CI, 1.17 - 2.43). Risk of cataract also rose with increased duration of inhaled steroid use.

The authors emphasize the importance of being aware of this complication and using the lowest effective dose to prevent asthma symptoms.
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