There are certain rules of etiquette you should follow when performing PRP laser. For example, never say you’re “Killing, Burning, Zapping, or Liquidating” the retina …

In fact, there’s one of our doctors performing PRP right now … notice his professional demeanor and impeccable dress.

No, Mr. Bond … I don’t expect you to talk. I expect you to DIE! Hahahaha!

So … did you see the 007 marathon on TV last night?
The retina can be intimidating as it’s not easy to visualize the posterior pole and there is a bunch of pathology back there. There are many things I could cover in this chapter, but I’ve decided to keep things simple and only discuss a few topics like diabetic retinopathy and retinal detachments. Other disease processes that involve the retina will be covered in other chapters.

**Diabetic Retinopathy**

Diabetes is a common disease and many affected patients have vision problems. In fact, diabetics are twenty times more likely to go blind than the general population. **Diabetic retinopathy** is the term used to describe the retinal damage causing this visual loss. Diabetics have a high prevalence of retinopathy, and one out of every five patients with newly diagnosed diabetes will also show signs of retinopathy on exam.

**Mechanism of Vessel Breakdown**

How are the eyes affected? Basically, diabetes is a disease of blood vessels. With large amounts of glucose coursing through the circulatory system, a **glycosylation reaction** occurs between sugar and the proteins that make up blood vessel walls. Over time, this reaction promotes denatures the collagen protein within the walls, creating capillary thickening and eventually, wall breakdown.

While this process occurs throughout the entire body, the microvasculature of certain organs, such as the kidneys and eyes, are more susceptible to damage. Along these lines, a good predictor of microvasculature damage in the diabetic eye is prior evidence of renal microvasculature disease as measured by proteinurea, elevated BUN, and creatinine.

Because vessel damage accumulates over time, the most accurate predictor of retinopathy is duration of diabetes. After 10 years, more than half of patients will show signs of retinopathy, and after 15 years this number increases to nearly 90%. The relative control of glucose during this time is also important, and studies have shown that patients who
maintain lower hemoglobin A1C levels have delayed onset and slower progression of eye disease.

**Two Types of Retinopathy**
It is useful to divide patients into two categories of retinopathy, as these categories define treatment:

A. Nonproliferative diabetic retinopathy (NPDR)
Most patients (95%) have NPDR. This is the earliest stage of retinopathy and it progresses slowly. Because so many diabetic patients have NPDR, this stage is commonly described as “background retinopathy.” The earliest signs of retinal damage arise from capillary wall breakdown, seen on the fundus exam as vessel microaneurysms. Injured capillaries can leak fluid into the retina and the aneurysms themselves can burst, forming “dot-and-blot hemorrhages.”

Dot-blot hemorrhages look small and round because they occur in the deep, longitudinally-oriented cell layers of the retina. This contrasts with the “flame hemorrhages” of hypertension that occur within the superficial ganglion nerve layer, and thus spread horizontally.
With worsening retinopathy and vessel damage, the retina begins to show early signs of ischemia. **Cotton-wool spots**, also seen with hypertension and venous stasis, are gray spots with soft edges that indicate ischemia/infarction of the superficial retinal nerve fibers. As vessel damage progresses, you can also see beading of the larger retinal veins and other vascular anomalies.

### B. Proliferative Retinopathy
With ongoing injury to the retinal vasculature, eventually the vessels occlude entirely, shutting down all blood supply to areas of the retina. In response, the ischemic retina sends out chemicals that stimulate growth of new vessels. This new vessel growth is called **neovascularization**, and is the defining characteristic of proliferative retinopathy. Far fewer patients have proliferative retinopathy, which is fortunate as this stage can advance rapidly with half of these patients going blind within five years if left untreated. The mechanism and complications of neovascularization merit study, so let’s take a closer look.

### The Mechanism of Neovascularization
With complete vessel occlusion, parts of the retina become starved for nourishment. The ischemic retina responds by releasing angiogenic molecules like VEGF to promote new vessel growth. These new blood vessels serve to bypass the clogged arteries in order to resupply the starved retina.
A collateral blood supply seems like a great idea, but unfortunately there is a problem. The newly formed vessels are abnormal in both appearance and function. The new vessels are friable and prone to leaking. They also grow in the wrong place, spreading and growing along the surface of the retina. They can even grow off the retina, sprouting up into the vitreous jelly. The vitreous is mostly water, but it also contains a lattice framework of proteins that the new vessels can adhere to. With vitreous movement or contraction, these new connections pull on the retina and the traction can cause a retinal detachment. Since the new blood vessels are also weak, any vitreous traction can break the vessels and create sudden hemorrhaging with subsequent vision loss as the eye fills with blood. Finally, the new vessels can regress and scar down, creating massive traction on the retina underneath.

Neovascularization isn’t just limited to the retina, but can also occur on the iris itself. NVI (neovascularization of the iris) is an ominous sign, as the new vessels can cover the trabecular meshwork and create a sudden neovascular glaucoma.

**Macular Edema**

Despite the neovascularization phenomenon and its potential for detachments and hemorrhage, the most common cause of blindness in diabetic patients is from macular edema. This occurs when diffuse capillary and microaneurysm leakage at the macula causes the macular retina to swell with fluid.
Macular edema occurs in about 10% of patients with diabetic retinopathy and is more common with severe retinopathy. On exam the macula looks mildly elevated, and you can see past evidence of edema in the form of yellow-colored "hard exudates." These exudates are fatty lipids that are left behind after past macular swelling subsides, similar to a dirt ring in a bathtub.

**Treatment of DR (diabetic retinopathy)**

Preventative medicine with tighter control of glucose is the ideal treatment, but for worsening symptoms, surgical treatment may be necessary. The two main surgeries are laser treatment and vitrectomy.

**Laser Treatment**

In cases of macular edema, an argon laser can be used to seal off leaking vessels and microaneurysm in the retina by burning them. If the leakage or microaneurysm is small and well-defined, it can be selectively sealed off. With larger areas of leaking capillaries, such as diffuse macular edema, the laser can lay down a “grid photocoagulation” pattern over the entire area.

With advanced retinopathy and neovascularization, a different approach is taken. Instead of individually targeting vessels, **PRP (pan-retinal photocoagulation)** is performed. With PRP, the ophthalmologist burns thousands of spots around the peripheral retina. This destroys the ischemic retina, decreasing the
angiogenic stimulus, and commonly leads to regression and even the complete disappearance of the neovascular vessels. This treatment may seem drastic, but it has proven to be effective. Naturally, there are side effects, with peripheral vision loss and decreased night vision (from the loss of peripheral rod photoreceptors), but this is acceptable if the central vision is saved. I’ve never seen anyone actually complain of decreased vision, but it’s possible and should be stressed during consent.

**Vitrectomy**
A vitrectomy may be needed and is often done in conjunction with other surgeries. This surgery involves removing the vitreous humor from the eye and replacing it with saline. This allows removal of hemorrhaged blood, inflammatory cells, and other debris that may obscure the visual axis. While removing the vitreous, the surgeon also removes any fine strands of vitreous attached to the retina in order to relieve traction that might have, or will, cause a detachment.

**Conclusion**
As you can see, diabetic retinopathy is a big problem and very common as a large percentage of our patients have diabetes. Retinal vessel damage leads to edema, and vessel occlusion stimulates neovascularization that can lead to trouble. Fortunately, better glucose control and surgical treatments have significantly decreased the incidence of visual loss in these patients.

**Retinal Detachments**
A retinal detachment is an abnormal separation between the sensory retina and the underlying RPE and choroid plexus. If you remember from the anatomy chapter, the outer third (the part furthest from the inner vitreous) of the retina gets its nourishment primarily from the underlying choroids vascular bed. With a detachment, the photoreceptor layer separates from the choroid, and without this blood supply becomes ischemic. The macular retina is especially susceptible to this damage. The prognosis for patients with retinal detachments depends upon the quickness of treatment and whether the central retina is involved; patients with detachments that involve the macula have much worse outcomes.

**Risk Factors and Epidemiology**
Up to six percent of the general population have retinal breaks of some kind, though most of these are benign atrophic holes. The actual incidence of retinal detachment is only 1 in every 10,000 people. Relative risk is equal between men and women, with higher rates in those of Jewish descent and decreased risk in black populations.
When looking at patients who already have retinal detachments, you begin to see some interesting trends. Many of these patients are myopic (near-sighted). Myopic eyes are physically larger and longer than normal eyes and have thinner retinas at the periphery. This thin retina is more likely to break, forming small holes and tears that may progress to a detachment.

Up to 35 percent of patients with retinal detachments develop them after another eye surgery – typically a cataract extraction. Finally, traumatic sports such as boxing, football, and bungee-jumping predispose younger people to forming detachments.

The Three Types of Detachment
Retinal detachments generally occur by three different mechanisms.

1. The most common detachment is the **rhegmatogenous retinal detachment**. This is an actual tear in the retina, with a full-thickness break through the retinal sensory layers. These tears can occur from trauma, surgery, or extend from preexisting retinal holes. Fluid from the vitreous chamber flows through the tear and collects in the sub-retinal space. Eventually, the retina tears away, peeling off the underlying RPE and choroid. Without treatment, a rhegmatogenous detachment can spread and eventually involve the entire retina.

2. The second type of detachment is from **traction** on the retina. This is when the retina is pulled from its base. This can occur from vitreous pulling, or from diseases like diabetic retinopathy where neovascular membranes on the retinal surface contract and tug on the retina with great force.

3. A less common mechanism for detachment is from **hemorrhagic** or **exudative retinal detachment**. This occurs when blood or fluid builds up under the retina, slowly pushing the retina upwards. This occurs with dysfunction of the RPE or choroid plexus and can be caused by ocular tumors, inflammatory diseases, or congenital abnormalities that create a breakdown of the blood-retina barrier.
Symptoms
With detachment, patients often report seeing flashes of light and floaters. Flashing lights, or photopsias, are often seen when a detachment first occurs. Photoreceptors are normally triggered by light, but severe mechanical disturbance can stimulate them as well. These flashes look like a camera or lighting flash in the peripheral vision.

Floaters look like dark specks that obscure vision, and patients say they look like a swarm of flies. They are created by objects (blood cells or pigment) floating in the vitreous fluid that cast shadows on the retina. While the presence of a few floaters is normal, the sudden appearance of hundreds of floaters may indicate a vitreous hemorrhage.

A more ominous symptom that is sometimes described is seeing a “dark curtain” that obscures peripheral vision. Most detachments start in the peripheral retina, and as they progress create a dark “shade” across the visual field. Fortunately, this is rare, but the combination of flashing lights and floaters should be considered a retinal detachment until proven otherwise.

Findings
The definitive way to diagnose a retinal detachment is to actually see it with the indirect ophthalmoscope. If the tear is large enough, it will be obvious as the floating retina contains blood vessels and undulates with eye movement. Suspended pigment particles...
may be seen floating in the anterior vitreous (Shafer's sign) that is described as “tobacco dust,” and is pathognomonic for a retinal tear.

An ultrasound of the eye may be helpful, especially when the tear is not obvious or when the retina can’t be visualized because of hemorrhage or cataracts. An ultrasound can also pick up other pathology such as tumors that might cause an exudative detachment.

This illustration shows an ultrasound of a patient with a complete retinal detachment. The retina looks like a letter V in this picture, because it is still attached at two places – the optic disk and at the peripheral ora seratta. Choroidal effusions can give a similar appearance, but I won’t talk about them because it would just be confusing at this point.

Treatment Options
The treatment for retinal detachment varies. The primary treatment for the majority of retinal tears and traction detachments is surgical. How fast a patient needs surgery depends upon whether the central macula has detached or not. If the macula has detached, the vision is pretty much toast, so it may be ok to wait a few days before going to surgery. If the macula is still on, then you want to make sure it STAYS on, so you go to surgery sooner.

If the retina has a tear or hole that hasn’t yet detached, the tear can be "pegged down" by welding down the surrounding retina with a laser. The retina can also be scarred down by freezing it into place with a cryoprobe applied from the outside of the eye.

Scleral buckling is the traditional surgical procedure, and involves encircling the eye with a silicone band that squeezes the eye like a belt. The buckle indents the eye and pushes the RPE into contact with the retina, allowing it to heal into place. Because of the orbital anatomy, scleral buckles are most useful for anterior breaks at the equator because you can't really buckle the back of the eye.

Over the past few decades, pneumatic retinopexy has become quite popular. In this procedure, after repairing the retinal tear the surgeon injects a bubble of gas or silicon oil into the globe which acts to push (or tamponade) the retina into position until it heals. There are many different types of gas that we use, but they all eventually absorb back into the body. The disadvantage to this procedure is that patients have to keep their head down for several weeks to keep the bubble in place. This is very taxing
and patients tend to look quite disheveled at their post-op appointments. An oil bubble doesn't require this head positioning, but does require a return to the OR to remove the oil.

If the detachment is severe and complicated, a **vitrectomy** may need to be done. The vitreous fluid is removed, and the retina is manually floated back into position. With access to the inner globe, scar tissue and any other causes of traction, such as the neovascular membranes, can be removed.

**Rubber Band Theory**

When treating a retinal detachment, a good way to think about traction is the “rubber band” theory. Thus, there is almost always some tension inside the eye that is keeping the retina from laying flat like a rubber band. There are two ways to relieve this tension: you can perform a vitrectomy and “cut” the band, or you can perform an encircling buckle procedure to shorten the band.

**RD Summary**

Retinal detachments were once universally blinding, but with modern surgical techniques, sight can now be saved. If you suspect a retinal detachment in your patients, send them to an ophthalmologist right away as their prognosis depends upon the speed in seeking treatment.

**ARMD**

ARMD stands for Age Related Macular Degeneration and is a common retinal finding in older patients. ARMD is actually the leading cause of blindness in the elderly, at least in developed countries like the USA.

These patients develop extracellular breakdown deposits called “drusen” that form deep in Bruch’s membrane. Bruch’s membrane is the thin layer that separates the RPE/Retina from the underlying choroidal blood supply. This blockage keeps nutrition from percolating up from the choroid to the retina, and conversely blocks photoreceptor waste products from draining down into the choroidal bed.

On exam you see localized retinal atrophy and pigmentary changes in the macula that correlate with poor central vision. The visual loss occurs slowly, however, and takes many years to progress.
Neovascular “wet” ARMD

If a break occurs in Bruch’s membrane, vessels can grow up out of the deep choroidal circulation directly up into the retina! This is dangerous, as this neovascularization can bleed, create edema, and rapidly destroy vision.

Treating this macular neovascularization is tricky - we would love to burn it away with a laser, but those bad blood vessels are often right at the fovea, and you don’t want to burn away central vision! Instead, we can use a few other techniques with variable success:

**PDT (photodynamic therapy):** With PDT, you inject a special chemical into the blood that reacts to specific wavelengths of light. Once the chemical floats within the retinal blood vessels, we then focus light of that desired wavelength directly at the fovea to coagulate the blood vessels without destroying the retina around it. Sounds good in theory, but it sometimes doesn’t work well so this technique is not always used.

**Injection:** You can also inject anti-VEGF drugs like Avastin or Lucentis into the eye to stop angiogenesis. These anti-neovascular drugs also decrease vessel wall leakage and can help with other causes of macular edema.

**Monitoring progression**

Early, dry ARMD is very common and requires no treatment (other than possibly antioxidant vitamins), but we want to monitor these patients for
progression to wet-ARMD. Patients can monitor themselves with an Amsler grid -- a sheet of straight lines they can look at weekly for new metamorphopsia (distorted lines that might indicate macular edema).

**Risk Factors?**
So who gets ARMD? This disease occurs most often in elderly Caucasians with a positive family history for the condition. It’s almost always bilateral. Disease progression is also highly associated with smoking.

1. **What is diabetic retinopathy, and by what mechanism does it occur?**
   This is retinal bleeding, edema, ischemia, and ultimately neovascularization caused by diabetic damage to the retinal blood vessels.

2. **What are the retinal signs of diabetic retinopathy. How do they compare to, say, hypertensive retinopathy.**
   With diabetic retinopathy you typically see a lot of dot-blot hemorrhages, cotton-wool spots, and hard exudates. Hypertension usually has more flame hemorrhages and vascular changes such as arterial-venous nicking and copper/silver wiring.

3. **How are angiogenic molecules involved with diabetic retinas?**
   VEGF production by areas of ischemic retina leads to neovascularization. These new vessels are harmful as they can cause traction, bleeding, detachments, etc.
4. How do we categorize diabetic retinopathy?
As either NPDR (nonproliferative diabetic retinopathy) or PDR (proliferative diabetic retinopathy) depending upon the presence of neovascularization.

5. What are some mechanisms in diabetic retinopathy that might lead to decreased vision? What causes the majority of vision loss in diabetic patients?
There are several mechanisms for potential vision loss in these patients, including:
- Macular edema (probably the leading cause of vision loss)
- Vitreous hemorrhage
- Retinal detachment

6. How do we treat advanced diabetic retinopathy?
Proliferative diabetic retinopathy is treated with PRP (pan retinal photocoagulation). By ablating the peripheral ischemic retina with a laser, we decrease VEGF production and thus decrease neovascularization.

7. A 35 year old man with bad type-1 diabetes presents with a pressure of 65. His anterior chamber is deep but you find neovascularization everywhere - in the retina and on the iris. What do you think is causing the pressure rise, and how do you treat it?
The pressure is up because of neovascularization of the iris angle with blood vessels clogging up the trabecular drain. You treat neovascularization by PRP lasering the peripheral retina to decrease VEGF production. NVA (neovascularization of the angle) is hard to manage and this patient will probably require a surgical drainage procedure in the near future.

8. Describe the three types of retinal detachment?
These include rhegmatogenous detachments, tractional detachments, and exudative detachments.

9. What are the symptoms of a retinal tear or detachment?
Flashes and floaters are the classic signs. With a large detachment your patient may also notice an area of “dark curtain” or “blurry spot” in their peripheral vision.
10. What is a PVD?
This is a posterior vitreous detachment - with aging the vitreous jelly liquefies and contracts. A sudden contraction can cause new floaters. This event is usually harmless, but you should search carefully for retinal tears.

11. An elderly patient presents with a brief episode of flashing and now has a single floater that moves with eye movement. A thorough retina exam reveals no detachment or tear, but you observe a small vitreous opacity floating over the optic disk. What has happened?
This again sounds like a PVD. The floater is a Weis ring, a piece of optic disk debris that has pulled off with the vitreous detachment. PVDs are common and usually harmless, though patients should have a thorough exam for retinal tears and be taught the symptoms of retinal detachment.

12. A patient presents late at night with a large rhegmatogenous retinal detachment. The central fovea is also detached. How soon do you need to go to surgery?
If the macula is off, then the macular photoreceptors are already damaged and it may be ok (this is the retina surgeon’s call) to schedule repair later when your surgeon is well-rested and you’ve got your best operating team. However, if the macula is still ON, you want to intervene sooner to make sure the macula STAYS on.

13. What kind of surgeries can we perform to relieve retinal detachments?
You can perform a vitrectomy to clean out the inside of the eye and relieve retinal traction. While in there you can also reappose the retina. You can also perform a scleral buckle or a pneumatic retinopexy.

14. What is Schafer’s Sign?
This is when you see retinal pigment particles floating in the anterior vitreous chamber behind the lens. This slit-lamp sign increases your suspicion for a tear or detachment.

15. What’s the difference between dry and wet age-related macular degeneration?
Dry ARMD is when you have drusen and macular RPE atrophy. Wet ARMD implies choroidal neovascularization that has grown up through Bruch’s membrane and bleed into the retina. “Wet” essentially means “bloody” in this instance.
16. What kind of travel restrictions would you tell a patient who has a pneumatic retinopexy?

You don’t want these patients to fly. A decrease in ambient pressure causes gases to expand. If this happens in the eye it could explode! Your patients should also avoid SCUBA diving for similar reasons, as the change in gas volume over the changing atmospheric pressure will cause extreme pain and possible damage.

You swallowed the SCUBA tank again, didn’t you?