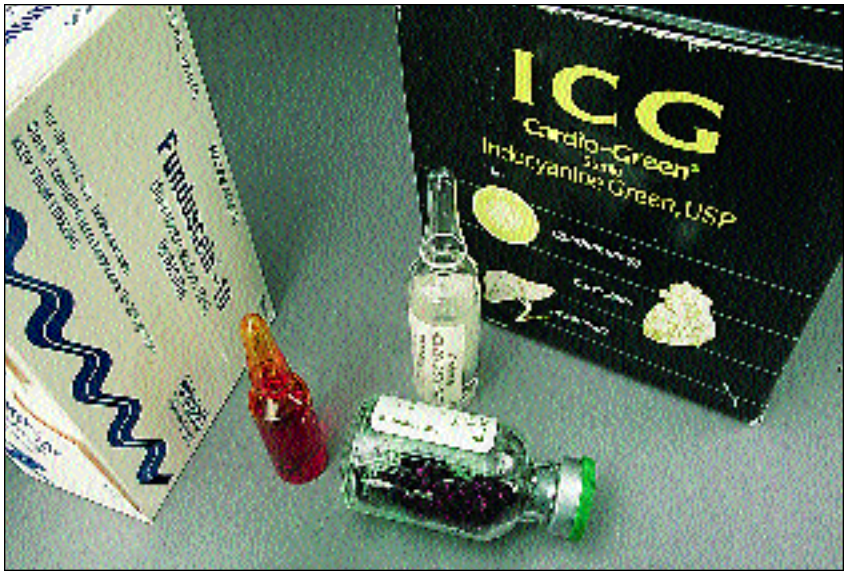

FIGURE 4-3
Types of ocular angiographic dyes. Vials of fluorescein sodium and indocyanine green dye as prepared by the manufacturers. The fluorescein sodium is ready for use, but the indocyanine green must be combined with the accompanying saline solution before injection. Both dyes have fluorescent properties.

removed, as in a child's "glow-in-the-dark" toy. Fluorescein sodium and indocyanine green both have fluorescent properties, and their emissions can be recorded on photographic film or electronic sensors. Excitation is supplied by light from the flash tube passing through excitation filters.

In a normal eye, no tissues obscure the view of the posterior pole vascular system. Because of the unique anatomy of the eye, light from the camera can be directed through the transparent cornea, through the pupil and lens, to shine directly on the retina. The light then travels back along the same pathway to the camera's film plane. The dye can be injected into the bloodstream via any vein and travels along the venous system to the heart, flows through the cardiopulmonary circuit, then up the carotid arteries, to the ophthalmic arteries, where some will circulate through the choroid and some will course through the central retinal artery to the retina.

Dyes Used in Ocular Angiography

Fluorescein sodium and indocyanine green (ICG) are the primary dyes used to perform ocular angiography (Figure 4-3). They do not have similar chemical configurations and are not of the same chemical "families." While they both have fluorescent properties, fluorescein sodium has much stronger fluorescence abilities. ICG contains a small amount of sodium iodide, but it is not radio-opaque and is used in ocular angiography because of its fluorescent properties.

Interestingly, while the retina and choroid of the eye are intimately associated, their circulatory characteristics are very different, as are methods for performing angiography of each. It is not surprising, then, that the dyes used to accomplish these studies are very different as well. Because of these differences, this chapter discusses each of these dyes individually.

Before describing the unique characteristics of these dyes and clearing up some misconceptions, it is valuable to explain some basics about biological stains.

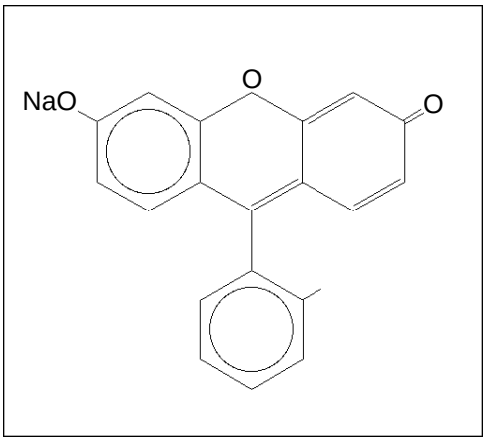

FIGURE 4-4
Molecular diagram of fluorescein sodium.

Biological dyes are colored substances used to help reveal the gross and microscopic structure and nature of plant and animal tissue.[8] Manufacturers of dyes give them two classifications: natural and synthetic. Natural dyes are mineral or plant products. Because of their natural impurities, which cannot be controlled, they are decreasing in use because they cannot be certified for use in drugs and cosmetics. Synthetic dyes are manufactured dyes produced through chemical reactions. The first synthetic dyes were derived from aniline, a derivative of coal tar. Synthetic dyes used in drugs, cosmetics, and food are assigned identifying food, drugs, and cosmetics (F, D, & C) and color index (CI) numbers by the Federal Color Standards Directory.

The color of a dye is determined by its chemical configuration in combination with its *chromophore*. Chromophores are carbon rings with double bonds involving carbon, oxygen, and nitrogen that are associated with color. Dye groups based on their color are classified by similar chemical structure. Chromophores alone do not dictate color, as identical chromophores can be found in all the colors of the rainbow.[9]

Fluorescein Sodium (Resorcinolphthalein Sodium)

Fluorescein sodium ($C_2OH_{10}Na_2O_5$) (Figure 4-4), or resorcinophthalein sodium, is the biological dye used to perform retinal angiography. In drug supply catalogs, it is called uranin or uranine yellow. It is the disodium salt of the biological dye fluorescein ($C_2OH_{12}O_5$), also called eosin.

There are some misconceptions associated with the dye fluorescein (eosin), including the mislabeling of retinal angiography. Fluorescein is *not* the dye used in retinal angiography. We use the salt fluorescein sodium.

According to its chemical structure, fluorescein is in the xanthene dye group. There are three classes of xanthene dyes: fluorenes, rhodols, and fluorones. Fluorones (hydroxyxanthenes) are called the fluorescein derivatives as fluorescein has the simplest chemical structure of the group. Other members of the fluorone group used in medicine are rose bengal and mercurochrome.[10]

Fluorescein was first synthesized by Adolf Baeyer in 1871 as a derivative of the dye gallein.[11] It produced a bright yellow color and was intended for use in dying wool and silk. As fluorescein is *insoluble in* water, benzene, chloroform, and ether, Baeyer used hot alcohol to make the textile dye.

Table 4-3. Intravenous Injection Supplies for Fluorescein Angiography

Arm board	To stabilize patient's arm and hand
Tape	For securing needle at injection site
Alcohol swabs	To cleanse the skin around the injection site
3 x 3 gauze pads	To apply to the injection site after the needle is removed or to protect a site that is already prepared
Tourniquet	To restrict venous flow causing veins to become more prominent; a blood pressure cuff may be used instead
Gloves	An OSHArequirement whenever there is potential exposure to blood
Syringe and filter needle/filter straw	To extract fluorescein sodium from vial or ampule
Butterfly infusion set of 21- or 23-gauge needle	To inject fluorescein sodium into vein 3" or 12" tubing connects the needle to the syringe and allows greater flexibility when positioning needle tubing Less intimidating to patient than a rigid needle/syringe unit
Stopcock	For injecting more than one substance (i.e., fluorescein sodium and indocyanine green or fluorescein sodium and saline)
Sharps container	For proper disposal of needle and syringe; always observe universal precautions
Adhesive bandage	To cover the venipuncture site
Portable lined receptacle	Should a patient become nauseated
Emergency kit	Minimal: oxygen, CPR equipment, antihistamine, smelling salts Ideal: standard crash cart with above and full complement of injection supplies and emergency medications

plans, employee education, and exposure-incident follow-up. The act also mandates that employees follow strict protocols and methods of compliance for "universal precautions," which include proper hand-washing, proper use and disposal of needles, appropriate use and disposal of gloves and other protective equipment, proper sterile technique, and other precautions in the workplace. Each health care facility, whether a major medical center or private physician's office, must have written procedures for carrying out the OSHAmandates regarding blood-borne pathogens. You should check with your clinic or office manager to get a copy of those procedures and guidelines and then follow them to protect yourself, your coworkers, and your patients.

Injection techniques can vary greatly among facilities, as can the brands and designs of the equipment used. Specific supplies should be dictated by the individual facility, following established IV protocols and procedures. If the facility does not have an existing IV protocol, as may be the case in private offices, state nursing associations or the hospital or surgical center where your ophthalmologist is affiliated can help you obtain copies of IV protocols. In most cases, supplies are chosen by the trained professional performing the injection. In any case, patient safety and comfort should be the first priority in choosing supplies. Table 4-3 lists the supplies needed to perform an efficient, safe IV injection. In thinking through the procedure step-by-step, you can understand the need for each of these items.

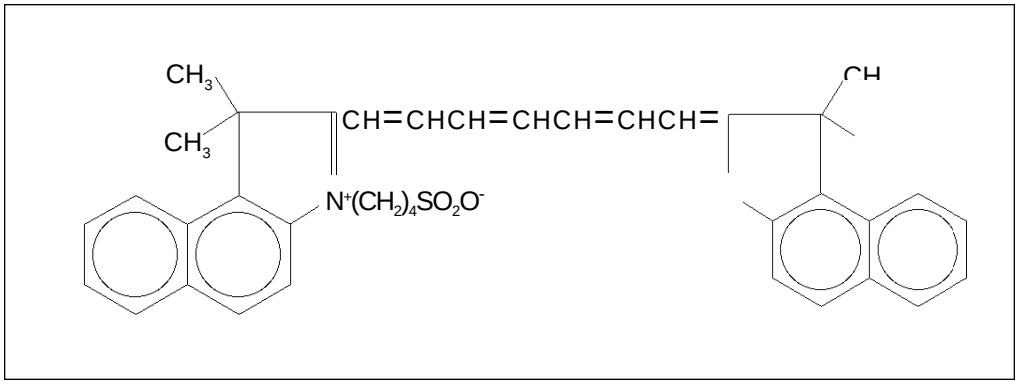

FIGURE 4-12
Amolecular diagram of indocyanine green.

SPECIAL CONSIDERATIONS

Patients who require special caution during intravenous injections include elderly patients with senile skin changes (thin skin due to loss of collagen and adipose tissue), patients with impaired circulation such as diabetics, patients with blood abnormalities, patients with impaired or absent lymphatic systems such as mastectomy patients, and patients who are dehydrated or underweight. (An intravenous injection nightmare would be an anorexic, diabetic teenage girl.)

Fluorescein sodium angiography is contraindicated in patients who are pregnant and in juvenile asthmatics and should be used with caution in patients with a previous history of severe adverse reactions to the dye and patients who have a recent history of chest pain or cardiac irregularities. It is not contraindicated in nursing mothers, although the dye has been found in mother's milk, nor is it contraindicated in patients on hemodialysis or in renal failure.

There have been reports of patients developing skin photosensitivity resulting in increased risk of sunburn after injection of fluorescein sodium. This may be a photoallergic reaction enhanced by sunlight.[36] It does not appear to be a common reaction.

Effect of Fluorescein Sodium on Laboratory Tests

Bloom studied the effect of fluorescein sodium with certain serum laboratory tests.[32] Serum and urine samples were checked. No interference was found in the urine samples, but of 27 serum analyte tests, six were affected by the presence of fluorescein sodium in the blood. Those tests affected by fluorescein sodium were levels of creatinine, cortisol, digoxin, quinidine, thyroxine, and total protein. The interference may persist for as long as 24 hours after injection. These tests can be performed on various analytical systems, and not all tests on all systems were affected.

To avoid false test results, when you orient your patients before fluorescein sodium angiography, they should be informed that the dye may affect some test results. If they are scheduled for tests within 24 hours of the angiogram, either they should have their blood drawn before the injection of the dye or you should give them a list of which tests by which analytical system are affected. They can then take the list to the laboratory where alternatives may be found.

Indocyanine Green

ICG ($C_{43}H_{47}N_2NaO_6S_2$) is a tricarbocyanine dye used to perform choroidal angiography (Figure 4-12). According to its chemical struc-