INVASIVE DIAGNOSTIC TECHNIQUES FOR UVEITIS AND SIMULATING CONDITIONS*

BY *James J. Augsburger,* MD

INTRODUCTION

MANY PATIENTS WITH UVEITIS HAVE SUCH CHARACTERISTIC OCULAR SIGNS and symptoms, associated systemic disorders, and laboratory abnormalities that the correct diagnosis can be established beyond reasonable doubt without any invasive studies on the eye. Many other patients with uveitis have mild, self-limited disease, readily controllable disease, or both that does not warrant aggressive invasive testing. In contrast, some patients with uveitis have atypical ophthalmic and/or systemic features or do not respond to conventional anti-inflammatory therapies. Such patients may be candidates for invasive diagnostic techniques.

The principal goals of invasive diagnostic techniques in uveitis are (1) identification of etiologic agents of infection, if present, and (2) exclusion of neoplastic infiltration simulating uveitis. A secondary goal of some diagnostic procedures (especially diagnostic vitrectomy) is clearing of the optical media to provide visual improvement.

In the remainder of this paper, I would like to describe and illustrate specific invasive intraocular techniques I have employed in the evaluation of selected patients with uveitis or a simulating condition over the past 10 years. I will emphasize indications, instrumentation, techniques, results, limitations, and complications of the various invasive diagnostic procedures.

SPECIFIC INVASIVE TECHNIQUES

AQUEOUS ASPIRATION

Aspiration of aqueous from the anterior chamber can be used to assess the

*From the Oncology Unit, Retina Service, Wills Eye Hospital, Department of Ophthalmology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania.

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nature of cells suspended in the fluid and to evaluate iris nodules. The instrumentation I generally employ for aqueous aspiration consists of a 27 gauge hollow-lumen needle attached to a tuberculin syringe. In most cases, I perform aqueous aspiration under local anesthesia. When local anesthesia is used, I usually administer mepivacaine hydrochloride 2% or a similar anesthetic in the form of a retrobulbar injection. For children and uncooperative adults, general anesthesia is required. I have done a number of aqueous taps at the slit lamp, but I have performed the majority of the aqueous aspirations with the patients supine with the aid of loupes or an operating microscope. Because of the anatomy of the face, I generally approach the anterior chamber from the temporal side. I fixate the globe by grasping the conjunctiva with forceps at the limbus adjacent to my intended limbal puncture. I direct my needle tip through the cornea and into the anterior chamber using steady pressure and a rotating movement of the syringe between my fingers (Fig 1). I direct the needle obliquely toward the periphery of the iris rather than toward the pupil. Once the tip of the needle has entered the anterior chamber, I slowly advance the needle to the appropriate position (adjacent to or within the

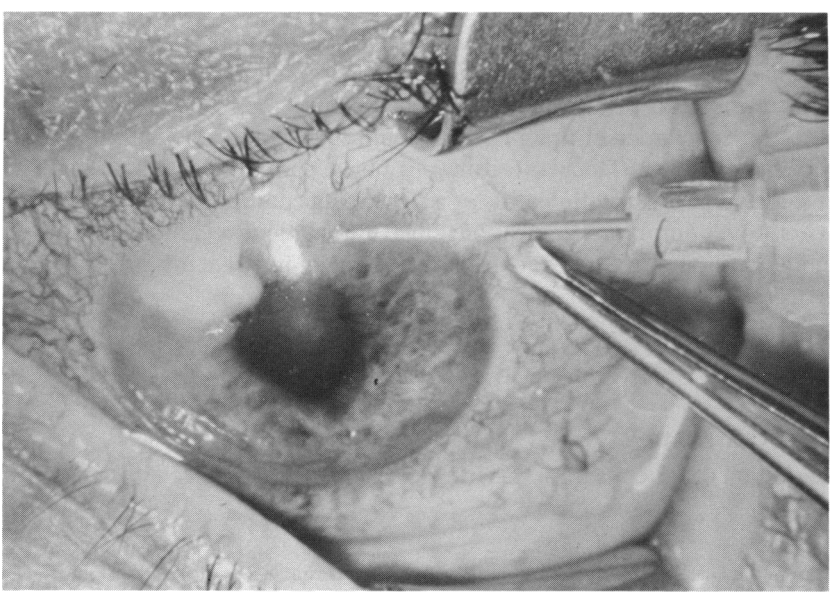

FIGURE 1
Aqueous aspiration using 27 gauge needle. Conjunctiva is being grasped with forceps next to puncture site.

mass of anterior chamber cells). At this time, I release my forceps grasp and use my free hand to slowly aspirate aqueous. I generally withdraw no more than 0.2 ml of aqueous, after which I slowly withdraw the needle. Care must be taken to avoid hitting the lens or incarcerating the iris. While I am withdrawing the needle, I regrasp the conjunctiva adjacent to the puncture site to stabilize the globe. Immediately after withdrawal of the needle, I instill an antibiotic ointment on the surface of the eye and apply a pressure patch.

Processing of the specimen consists of direct inoculation of culture plates and media, preparation of two glass slides with small droplets of the aspirate for immediate fixation and staining to look for bacteria and fungi, and submission of the remainder of the aspirate to pathology for cytologic processing and study. After the aspirate has been processed, I remove the pressure patch to make sure that the anterior has reformed. Once reformation of the anterior chamber has been confirmed, patching is no longer required.

Potential complications of aqueous aspiration using the technique I have described include hyphema, traumatic cataract, iris incarceration, and vitreous incarceration (in aphakic eyes). In my experience, hyphema is the most common complication but is usually minimal in extent and self-limited. All of the blood usually resolves within about 6 to 12 hours in most patients. To date, I have not encountered any instances of traumatic cataract, iris incarceration, or vitreous incarceration. Should one of the latter complications occur, one could attempt to reposit the incarcerated iris or vitreous by external manipulation of the eye. An alternative approach might be to use YAG laser techniques to cut the incarcerated tissues free.

The nature of the cellular reaction (acute inflammatory, chronic inflammatory, or neoplastic) can usually be ascertained by review of gram stained and Giemsa stained slides of the thinly spread fluid. The gram stain will usually disclose bacteria, if present, and give some indication as to the category of the microorganism. Fungal stains can be employed if a fungus is suspected. A diagnosis of malignant infiltration is usually based on review of membrane filter preparations prepared from the major portion of the aspirated fluid.[1-3]

VITREOUS ASPIRATION

Aspiration of liquid vitreous is indicated in suspected endophthalmitis (exogenous or endogenous) and neoplastic intravitreal infiltration (lymphomatous and leukemic). When I perform vitreous aspiration, I usually employ a larger caliber needle than that used for aqueous aspiration. The

needle I use most commonly is a 21 gauge hollow-lumen needle, but I have used needles as large as 18 gauge and as small as 30 gauge for this procedure. Unlike the situation with aqueous aspiration, in which I attach the aspirating syringe directly to the needle, I employ a sterile connector tubing between the hub of the needle and the tip of the aspirating syringe. I do so to allow me to position the tip of the needle accurately without having to be concerned that some slight movements in the aspirating device will induce significant movement in the needle tip inside the eye. I usually choose either a 5 ml or 10 ml sterile plastic syringe as my aspirating device.

I generally perform a vitreous aspiration by first making a small conjunctival incision in the pars plana region in the selected quadrant of the eye and dissecting the subconjunctival connective tissues down to bare sclera. I then make a partial thickness scleral incision concentric with the limbus at approximately 3.5 mm from the limbus. I generally place a prepuncture suture of 8-0 or 9-0 monofilament nylon across the lamellar scleral incision to enable me to close the wound immediately upon withdrawal of my biopsy needle. In most cases, I attempt to observe the placement of my needle tip with indirect ophthalmoscopy (Fig 2). I puncture the remaining layers of the eyewall in the lamellar scleral incision with the biopsy needle and pass the needle tip into the mid-vitreous. If the view is satisfactory for my visualization of the needle tip, I will generally move the tip posteriorly to a position just in front of the optic disc. If the vitreous is very cloudy or opaque and my needle tip cannot be visualized, I will instead attempt to direct my needle tip to approximately the mid or mid-posterior vitreous level. Once my needle is in place, I will direct my assistant to *slowly* aspirate with the attached syringe. I ask my assistant to continue to maintain the suction in the line at a moderate level, and I visualize the tubing to see if vitreous material is appearing. If after a few seconds no vitreous aspirate appears in the tubing, I will ask my assistant to release the suction. I will then reposition the needle tip slightly and repeat the procedure. Once I have aspirated a small amount of vitreous (usually no more than 0.5 ml), I will have the assistant release the suction force on the syringe. I will then withdraw the needle. I will immediately close the sclerotomy by tying the preplaced suture. I will usually also close the conjunctival incision with a 6-0 or 7-0 absorbable suture. I instill an antibiotic ointment and apply a pressure patch to the eye.

Processing of the aspirated vitreous follows the guidelines mentioned under processing of the aqueous aspirate.[1-3] The principal potential complications of a vitreous aspiration include intravitreal bleeding, vitreous

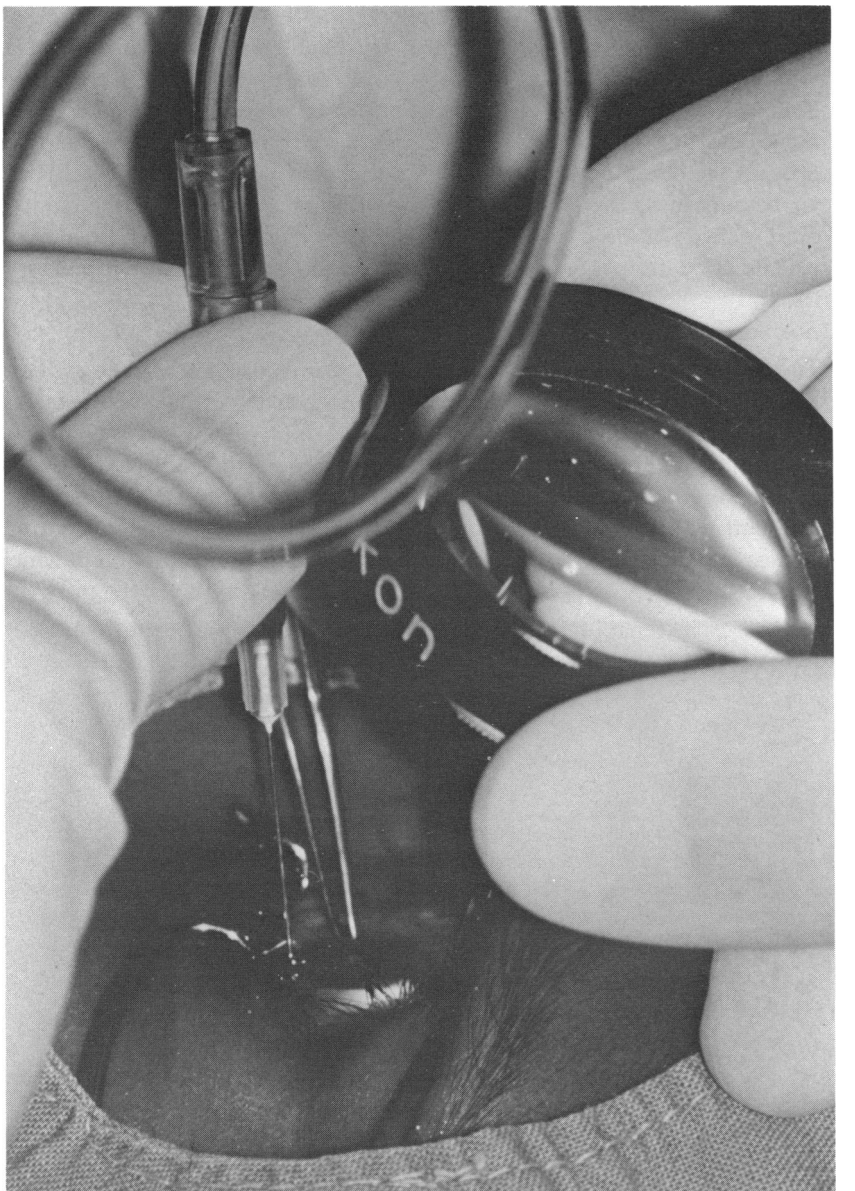

FIGURE 2
Vitreous aspiration using 25 gauge needle via the pars plana. Needle tip position is being monitored by indirect ophthalmoscopy. Note vitreous aspirate in connector tubing.

incarceration into the sclerotomy, and retinal hole formation and retinal detachment. In my experience to date, I have yet to encounter intravitreal bleeding following diagnostic vitreous aspiration. Similarly, I have not encountered iatrogenic retinal breaks or secondary retinal detachment following diagnostic vitreous aspiration. In eyes with very cloudy or opaque vitreous, I have generally performed a diagnostic "wash out" vitrectomy immediately following the vitreous aspiration; consequently, most of the gelatinous vitreous will be removed and any retinal breaks will usually be detected and managed appropriately during that procedure.

DIAGNOSTIC VITRECTOMY

The indications for diagnostic vitrectomy are virtually the same as those listed under vitreous aspiration above. Posterior vitrectomy is, of course, not only diagnostic but also therapeutic in eyes with extensive vitreous clouding, infectious endophthalmitis, and neoplastic infiltrations.[4,5]

Instrumentation for diagnostic vitrectomy consists of a vitreous suction-cutting instrument with some infusion system. For diagnostic vitrectomies in which the vitreous is not extremely hazy or opaque but in which

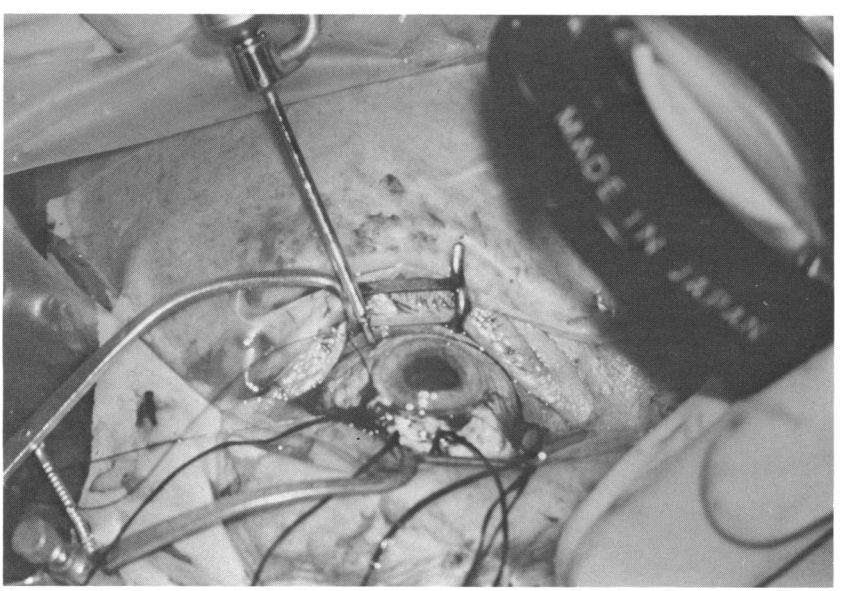

FIGURE 3
Diagnostic posterior vitrectomy performed using single port technique. Note infusion sleeve over vitrectomy tip.

a fungal abscess or neoplastic infiltration is suspected, I generally perform a diagnostic vitrectomy using a single port technique (Fig 3). In this technique, I use an infusion sleeve over the vitrectomy tip. I introduce the vitrectomy tip and infusion sleeve into the vitreous chamber via a single sclerotomy in the pars plana region. I monitor the tip of the vitrectomy instrument with indirect ophthalmoscopy during this single port technique. I aspirate the cloudy vitreous but make no attempt to perform membrane peeling or other delicate maneuvers. At the conclusion of the vitreous "wash out," I close the sclerotomy site with 9-0 monofilament nylon mattress suture.

In suspected infectious endophthalmitis or in other eyes with extremely cloudy vitreous, I generally have had one of my vitreoretinal colleagues perform a complete therapeutic vitrectomy using a standard two instrument approach with separate pars plana region infusion. This approach allows the surgeon to perform a much more complete vitrectomy and also to perform any other manipulations that might be felt necessary for maintenance of retinal attachment. Of course, the positioning of the instrument tips in such a posterior vitrectomy is routinely monitored using the operating microscope and an appropriate contact lens system for posterior fundus viewing.

Regardless of whether the single port or multiple ports approach is used, my colleagues and I have frequently employed a set-up which enables us to obtain relatively undiluted vitreous for initial microbiologic processing. We put a 3-way stopcock in the aspiration line. At the start of the posterior vitrectomy, we set the stopcock to direct the vitreous fluid to an aspirating syringe. We employ manual suction with this syringe to aspirate relatively undiluted vitreous. Once we have aspirated a small amount of the liquid vitreous into the syringe, we will redirect flow through the stopcock to allow the remainder of the specimen to be collected in the sterile cassette. While the posterior vitrectomy is continuing, one of my assistants performs the initial processing of the specimen for gram and Giemsa staining and inoculation of culture media. The diluted vitreous aspirate that is contained in the sterile cassette at the end of the procedure is then submitted to pathology for membrane filter processing and cytologic study. If the specimen is processed promptly at the beginning of the case, the results of the gram stain will usually be known by the end of the procedure. Based on the gram stain findings, the surgeon can select what he or she feels is the most appropriate antibiotic regimen. He or she may choose to give intravitreal as well as periocular antibiotics at the conclusion of the procedure.

The potential complications of diagnostic vitrectomy are identical to those of posterior vitrectomies in general.[6]

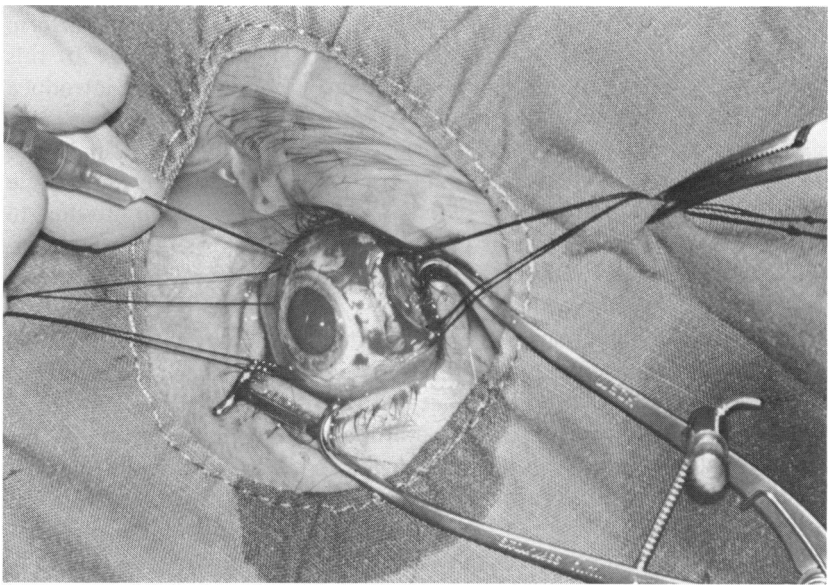

FIGURE 4
Diagnostic fine-needle aspiration biopsy of choroidal lesion using 25 gauge needle via pars plana. Note that globe is stabilized with muscle traction sutures.

FINE-NEEDLE ASPIRATION BIOPSY OF RETINAL OR CHOROIDAL LESIONS

Some eyes containing a granulomatous appearing lesion or a suspected neoplastic lesion (metastatic carcinoma or lymphomatous or leukemic infiltration) of the retina or choroid can be approached by fine-needle aspiration biopsy techniques.[7] Indications for such an approach to solid posterior segment lesions have been described in detail.[7,8] Instrumentation and techniques have also been described.[7,8]

In general, I employ a 25 gauge hollow-lumen needle attached via a connector tubing to an aspirating 10 ml syringe for fine needle aspiration biopsy (Fig 4). The technique can be performed under either local or general anesthesia. In either case, secure fixation of the globe is required. I generally puncture the eyewall with the tip of the biopsy needle in the pars plana region in a lamellar scleral incision. In most cases, I direct the tip of the biopsy needle across the vitreous and into the lesion of interest under indirect ophthalmoscopic visualization. If the lesion is more than 3 mm thick, I generally use a straight needle and impale the lesion directly. If the lesion is less than 3 mm thick (and I have approached lesions as thin

as 1 mm or less), I generally employ a specially bent needle. In this technique, I use a straight hemostat to bend the shaft of the needle at about 3 mm from its tip to an angle of approximately 80 to 90 degrees. I generally make the bend so that the bevel and lumen of the needle face the needle's hub. Penetrating the eye wall and passing the tip of this needle across the vitreous is a bit more dangerous and difficult than passage of a straight needle. However, with enough experience, it can be done with relative ease. I generally approach the lesion of interest from one of its margins, and I manipulate the needle so that its tip slides into the lesion of interest from the side. Once the tip of the needle is embedded within the lesion of interest, the surgical assistant is instructed to aspirate briskly to the 10 ml mark on the aspirating syringe and then immediately release. I reposition the tip of the needle several times, and each time I have the assistant repeat the aspiration sequence. Generally, there is so little material aspirated via this method that no fluid or other material appears in the hub of the needle or tubing. Withdrawal of the needle tip from the lesion of interest is the most delicate step, which requires a great deal of manual dexterity. Once the needle tip has been carefully withdrawn from the lesion and the tip can be seen in the vitreous, the needle is withdrawn from the eye. The sclerotomy is closed as for a posterior vitrectomy.

The aspirate obtained by such a technique is generally contained within the aspirating needle. If a bacterial or fungal infection is strongly suspected, a small drop of this material may be inoculated directly onto appropriate culture media. However, most of the material is generally flushed into a syringe with balanced salt solution, and this suspension is then transferred to the pathology laboratory for cytologic processing using the membrane filter technique.[1-3] Several filters can be prepared, and different stains can be used depending on the suspected diagnosis.

My colleagues and I have been able to identify a specific agent responsible for the clinical lesion in several cases to date using fine-needle aspiration biopsy techniques. One patient was a cardiac transplant recipient who developed a white, hemorrhagic inflammatory chorioretinal lesion which proved to be a *Nocardia asteroides* granuloma.[9] This lesion responded promptly and completely to appropriate antibiotic therapy. Another patient with a chorioretinal lesion and limited overlying vitreous cellular haze was confirmed by fine-needle aspiration biopsy to be a *Cryptococcus neoformans* abscess.[10]

The principal potential complications of fine-needle aspiration biopsy of a retinal or choroidal lesion include subretinal, intraretinal and preretinal bleeding and retinal detachment.[7,8] In spite of the fact that the retina is

punctured in the technique I have described, I have yet to see an iatrogenic retinal detachment following this technique. I do not perform photocoagulation around the puncture site in the retina or a posterior vitrectomy in these cases. Almost all cases develop a small amount of preretinal and subretinal hemorrhage,[8] but only a few of the diagnostic fine-needle aspiration biopsies which I have personally performed have been associated with more than minor intraocular bleeding. One patient in whom fine-needle aspiration biopsy was performed for diagnosis of a focal retinitis following cardiac transplantation has subsequently developed a subretinal neovascular membrane related to the retinal puncture site.

CONTROLLED ASPIRATION OF SUBRETINAL FLUID

Occasional patients develop a retinal detachment which is believed to be inflammatory or neoplastic in nature. In some of these eyes, the vitreous and aqueous are relatively clear. Such eyes may be appropriately evaluated by controlled aspiration of the subretinal fluid.

Sternberg and co-workers[11] have described a method for posterior aspiration of subretinal fluid using a specially designed scleral depressor through which a small caliber aspirating cannula can be advanced via the sclera into the subretinal space. This technique has been reported to be an effective diagnostic technique in certain cases of metastatic carcinoma to the choroid. An alternative technique which I have employed in patients with an extensive exudative retinal detachment due to suspected metastatic carcinoma to the choroid or following episcleral plaque radiation therapy is a procedure initially described by McLeod.[12] In this technique (Fig 5), a 19 gauge to 21 gauge long hollow-lumen needle is bent in two positions: first, it is bent at approximately mid-shaft to an angle of approximately 100 degrees. Second, it is bent near the distal end (approximately 5 mm from the tip) to approximately 80 degrees (an acute angle) relative to the shaft. The hub of the needle is then connected to a 10 ml aspirating syringe. As described by McLeod,[12] the plunger is left in place to aspirate fluid during the procedure. By my modification, the plunger is removed so that fluid can be withdrawn slowly by the force exerted by fluid injection into the eye via a sclerotomy or anterior chamber infusion needle. Prior to the introduction of the aspirating needle, the infusion line should be established. Once the infusion line is in place, the tip of the aspirating needle can be passed along the mall of the eye posterior to the equator. By pulling up on the syringe slowly, one can generally see the site of indentation of the sclera posteriorly by examining the fundus with indirect ophthalmoscopy. Once the position of the needle indentation posteriorly is found to be satisfactory, the surgeon draws the

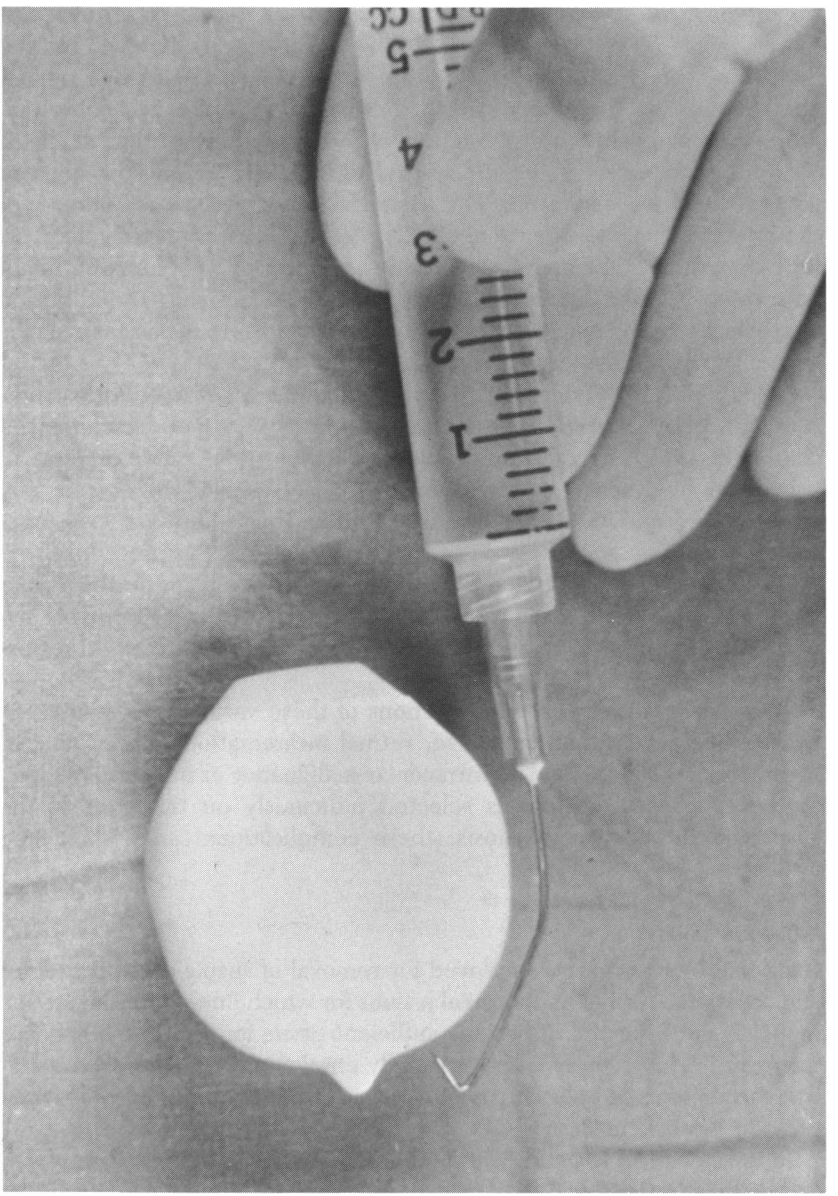

FIGURE 5
Illustration of appropriately bent 20 gauge needle and attached syringe (alongside a model eye) as used for controlled aspiration of subretinal fluid.

tip of the needle into the subretinal space by means of a quick upthrusting motion on the syringe. In viewing the fundus, one will see the flash of the needle tip as it enters the subretinal space. At this time, I open the infusion line to increase the intraocular pressure. The subretinal fluid is slowly pushed into the lumen of the aspirating needle and chamber of the attached syringe. By controlling the rate of infusion, one can control the rate of aspiration. Once the retina gets very close to the tip of the aspirating needle, the tip of the needle can be withdrawn by depressing the syringe. Obviously, closure of the posterior puncture site is not performed in this technique. Consequently, this approach would not be appropriate for any eye in which an active primary intraocular malignancy or a suspected infectious endophthalmitis is present.

In eyes with a suspected intraocular inflammatory or neoplastic condition with both vitreous clouding and a secondary retinal detachment, a combined pars plana vitrectomy approach with intraoperative drainage of subretinal fluid via a retinotomy can be performed. Of course, any iatrogenic retinotomy must be closed either by a fluid-gas exchange, scleral buckling, or another approach at the end of the procedure.

Processing of the aspirated subretinal fluid is according to the guidelines indicated above. In most cases, the cytologic filters will provide the most reliable information about the cellular composition of the subretinal fluid.[1-3]

The principal potential complications of these various procedures appear to be subretinal hemorrhage, retinal incarceration, retinal detachment, and exteriorizing of an intraocular malignancy or infection. As long as the type of procedure is selected judiciously on the basis of the suspected intraocular diagnosis, these complications can probably be avoided.

INCISIONAL BIOPSY

Incisional biopsy can be employed for removal of suspicious iris nodules and occasional retinal or choroidal lesions for which fine-needle aspiration biopsy is not expected to provide sufficient tissue for diagnosis. Standard microsurgical instrumentation is usually employed. A diathermy apparatus, carbon dioxide laser, or contact laser is usually required in addition to provide local hemostasis.

In the case of an iris nodule or nodules suspected of being inflammatory versus neoplastic, a standard iridectomy via the limbus can usually be performed. The iris tissue can usually be made to prolapse through the lips of the limbal incision, and a small peripheral iridectomy can usually be taken and processed by standard histologic methods. If the lesion of

interest involves a large sector of the iris, a sector iridectomy may be required. In the hands of experienced surgeons, diagnostic iridectomy is likely to be a safe and effective procedure for determining the nature of an iris lesion.

In contrast to iridectomy, chorioretinal incisional biopsy for a retinal or choroidal lesion is an infrequently performed diagnostic intervention.[13-15] It is most likely to be suggested in patients with bilateral ocular involvement who have already failed to respond to what was believed to be conventional therapeutic intervention for their suspected disorder. In this technique, the site of intended biopsy must be localized by indirect ophthalmoscopy with scleral depression. A lamellar or full thickness scleral window can then be cut directly overlying the intended biopsy site. Generally, the actual chorioretinal incision rarely needs to be larger than about 3 mm in size; however, the lamellar scleral flap that one would create might be considerably larger than this to provide some protection to the biopsy site at the time of closure.[13] Once the site has been prepared, heavy diathermy or laser coagulation are generally delivered to the margins of the planned resection. The surgical incision is then completed through the underlying choroid and retina with a sharp blade and

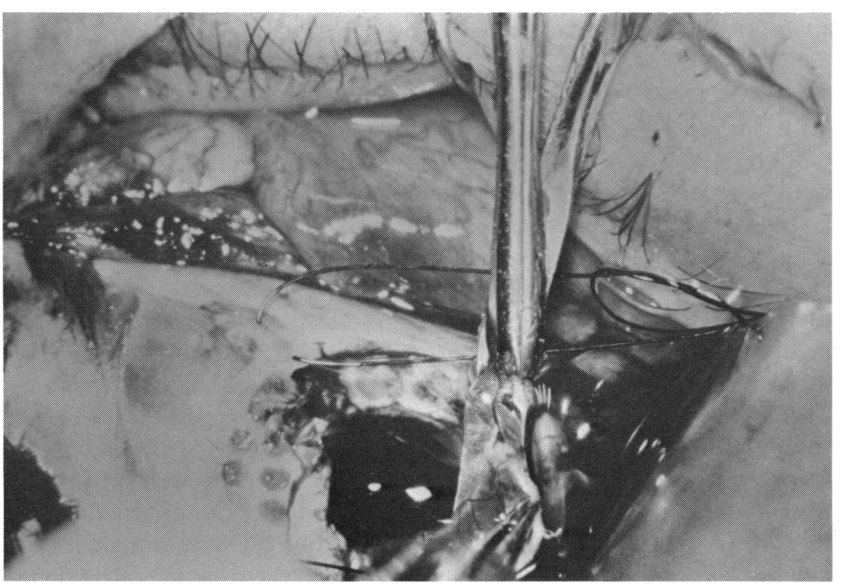

FIGURE 6
Diagnostic chorioretinal biopsy beneath a lamellar scleral flap (courtesy of David H. Fischer, MD).

microscissors (Fig 6). The surgical specimen is excised as a single piece and submitted to pathology for light microscopy, microbiologic studies, and possibly even electron microscopy. A small amount of vitreous occasionally prolapse at the site, so a vitrectomy instrument should be available for removing vitreous from the wound margins. The scleral window must be closed, and I generally use 8-0 monofilament nylon sutures for this step. I have generally elected to perform scleral buckling immediately over the resection site using a small radial sponge to prevent late retinal detachment.

The principal potential complications of such an intervention are major intraocular bleeding, retinal detachment, and retinal incarceration. In spite of the expected severity of intraocular bleeding, the use of diathermy or the carbon dioxide laser, particularly if coupled with relative hypotensive anesthesia, usually keeps bleeding to a minimum.[13,15] My colleagues and I have had several cases in which the pathologic and microbiologic findings altered our therapeutic approach substantially and resulted in a satisfactory patient outcome. The most dramatic case of this type was in a patient with AIDS and an atypical pattern of acute retinal necrosis unresponsive to antiviral therapy. Chorioretinal biopsy showed *Toxoplasma gondii* as the etiologic agent and enabled us to institute an appropriate antibiotic regimen.

DIAGNOSTIC ENUCLEATION

Although one usually does not consider enucleation to be a diagnostic procedure, there are some instances in which this intervention could be considered both diagnostic and therapeutic. The principal indications for diagnostic enucleation in suspected uveitis or simulating conditions include a blind painful eye with inflammatory features, a blind eye in a bilateral condition where the second eye is progressing on a downhill course and in which the diagnosis is not established, and possibly phthisis bulbi secondary to a presumed intraocular inflammatory condition. The surgeon should work closely with the ophthalmic pathologist, who may wish to be present in the operating room to begin processing the ocular tissues. A scleral window can usually be cut in the enucleated globe immediately following the eye's removal, and specimens of intraocular tissues can be inoculated onto appropriate media for bacterial and fungal cultures (if indicated) prior to immersion of the globe in formaldehyde. The remainder of the globe can be processed according to conventional histopathologic techniques and studied by light microscopy.

The principal potential complications of diagnostic enucleation are globe rupture or incision during the procedure, which could release

organisms and inflammatory or neoplastic cells into the orbit.

We have had several instances in which diagnostic enucleation was effective in identifying the underlying pathology that was not recognized by noninvasive methods. In one patient, cryptococcosis was diagnosed.[16] In another, nocardiosis in association with Wegener's granulomatosis was determined.

COMMENTS ON INVASIVE DIAGNOSTIC TECHNIQUES

Just because an invasive diagnostic technique can be performed on a patient with uveitis or a simulating condition does not mean that it should be. The risks of these procedures can be substantial, as I have attempted to indicate in the preceding sections of this paper. The pros and cons of such invasive techniques must be weighed carefully and discussed in great detail with the patient and family members. The worse the visual potential of the eye and the greater the risk of an infiltrative malignancy, however, the more appropriate an invasive diagnostic approach appears to be.

Except for diagnostic aqueous aspiration and possibly vitreous aspiration, most of the techniques I have described are not appropriately employed by general ophthalmologists. However, all ophthalmologists should be aware of the availability of alternative invasive diagnostic techniques for patients who might benefit from their use. The true indications for several of these techniques, such as monitored posterior transscleral drainage of subretinal fluid and eye wall biopsy, are likely to remain extremely limited.

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DISCUSSION

DR STEPHEN J. RYAN Doctor Augsburger has described a series of techniques, including aqueous aspiration, vitreous aspiration, diagnostic vitrectomy, fine-needle biopsy of the retina and choroid, aspiration of subretinal fluid, incisional biopsy, and diagnostic enucleation.

The key questions in this discussion concern the risk/benefit ratio for the individual patient and the number of times the outcome/results of these invasive diagnostic techniques have influenced or, more importantly, changed the management of a patient. It would be helpful to know the number of cases in which these seven techniques have been employed and, specifically, how they have influenced the therapeutic decision, and what follow-up is available. Perhaps the most important question is in relation to outcome. In what percentage of the cases did the biopsy influence or change the contemplated treatment?

In all cases, the potential side effects of an invasive procedure for diagnostic purposes must be weighed against the advantages of a specific treatment that will result for the individual patient.

The great majority of cases can be diagnosed by an individual ophthalmologist or retinal specialist or by a panel of consultants. It is only in exceptional cases that these invasive diagnostic techniques would be considered. The therapeutic options for the individual patient must be considered and, specifically, the influence of the biopsy results must be carefully evaluated before performing such an invasive procedure.

Aqueous Aspiration: This is a technique that involves relatively low risk, and which also has a relatively low yield. Paracentesis and aspiration have been performed for many years, and distinguished ophthalmologists such as Amsler and Verrey have reported on thousands of such cases (*Ophthalmologica* 1943; 105:144-150).

For aqueous aspiration, culture plates and media must be available, and, as in most of the techniques described by Doctor Augsburger, cytopathology and, specifically, the cytopathologist are often more important than is the ophthalmolo-

gist carrying out the procedure. Regarding potential infection, one is always well advised to go where the most prominent focus of infection is, and, in most cases, this is the vitreous.

Vitreous Aspiration: This procedure, which entails considerable preparation, is directed to aspiration of liquid vitreous. Since this is done using sterile techniques, and considering the significant amount of preparation, it is the usual practice of the surgeons at the Doheny Eye Institute to carry out a diagnostic vitrectomy rather than simply a vitreous aspiration. At Doheny, the main indications for vitreous aspiration rather than vitrectomy relate to medical contraindications to surgery or to logistics such as problems in scheduling an operating room. The very great majority of our cases undergo a vitrectomy.

Diagnostic Vitrectomy: We perform a standard vitrectomy with three incisions; ie, sclerotomies, through the pars plana. We do not activate the infusions so as to avoid diluting the specimen. Rather, with indentation of the globe with a cotton-tipped applicator, we compensate for the volume that is removed from the eye, thereby maintaining normal intraocular pressure and avoiding collapse of the globe. Only after the specimen has been obtained do we activate the infusion through the infusion canula.

We favor the diagnostic vitrectomy because it provides us more control and options at the time of surgery. Our goal is to obtain the optimum specimen for multiple purposes, and a secondary goal is often to clear the media. With this procedure, we can pursue adjunct goals as needed.

Doctor Augsburger described several patients to illustrate the different applications of these techniques. We describe a 66-year-old woman who had floaters and good visual acuity and a normal computed tomography scan. The clinical diagnosis was large cell lymphoma, but we needed tissue confirmation to justify radiotherapy, and we therefore performed a diagnostic vitrectomy. Large cells typical of large cell lymphoma and B cells were identified, and the patient was appropriately treated with radiation.

Fine Needle Biopsy of the Retina and Choroid: Doctor Augsburger has significant experience in this regard and has previously reported the value and indications for fine needle biopsy (*Trans Am Ophthalmol Soc* 1988; 86:499-560). Others, such as Jakobiec, have also reported their experience. We do not have much experience in fine needle biopsy, and have found this technique to be controversial. We recognize our bias in that a large number of patients with metastatic disease are referred to us from the Norris Cancer Center, which is located adjacent to the Doheny Eye Institute, but, in such patients, the primary tumor has been diagnosed previously, and thus the patient does not require primary diagnosis. Doctor Augsburger has pointed out the value of this technique in obtaining tissue. When the differential diagnosis is small melanoma, we prefer to follow such small melanomas. We have performed biopsy when necessary to confirm diagnosis for treatment by oncologists, but we do not have experience with fine needle biopsy. Doctor Augsburger does have considerable experience with the technique of fine needle biopsy and does not report significant complications.

Aspiration of Subretinal Fluid: There are some unusual cases, in which the aspiration of subretinal fluid can be utilized to identify or to culture organisms, such as toxoplasmosis.

Incisional Biopsy: This technique is reasonable for some tumors of the iris, and for the retina and choroid a full-thickness biopsy can be considered. The decision of using an internal approach versus an external approach must be made with consideration of potential complications.

Doctor Friedman presented a paper on toxoplasmosis at this meeting of the American Ophthalmological Society immediately prior to the paper of Doctor Augsburger. We therefore present a patient who had a positive VDRL and a positive MHATP and who was known to have AIDS. He was treated with penicillin. It is noteworthy that he did not have any significant titers for cytomegalovirus, herpes simplex, herpes zoster, or toxoplasmosis. At that time, some 5 years ago, we were not as familiar with the fact that patients with toxoplasmosis and AIDS can have few significant cells in the vitreous, and thus did not have a high suspicion of toxoplasmosis. However, when the patient did not respond to treatment for syphilis, we carried out a full-thickness biopsy. Toxoplasma organisms were identified and the patient was appropriately treated for toxoplasmosis.

Diagnostic Enucleation: Indications for this ultimate surgical procedure relate to bilateral inflammatory conditions. These are unusual, but there are rare cases in which a diagnostic enucleation can be of benefit.

In summary, invasive diagnostic techniques have limited indications, and we must always consider the potential complications. We cannot over-emphasize that the cytopathologist is as important as the surgeon in interpreting these specimens, and this must be kept in mind when deciding to biopsy. Pars plana vitrectomy for diagnosis is by far the most common technique when an invasive procedure for biopsy is considered.

We emphasize that in the majority of cases, the diagnosis can be made by the individual ophthalmologist or retinal specialist or by a panel of consultants. There are those exceptional cases, however, but we must always consider the therapeutic options and, most importantly, how the biopsy will influence therapy. The percentage of cases in which a biopsy influences or changes contemplated therapy remains the central issue in considering these diagnostic biopsies.

DR JAMES J. AUGSBURGER. Thank you, Doctor Ryan, for your pertinent comments. Your emphasis on the limited indications for many of the procedures I have mentioned is certainly appropriate. I endorse your preference for diagnostic vitrectomy over needle aspiration of vitreous in most cases in which a vitreous specimen is indicated. I disagree with you slightly about the indications for fine-needle aspiration biopsy of suspected infectious or neoplastic fundus lesions, but I readily admit that the long-term risk-benefit ratio of such an invasive diagnostic approach has not been established. Since my paper was intended to be a review of currently available invasive diagnostic techniques and not a summary of my personal experience with the various procedures, I do not have tabulations of the number of times I have performed each procedure.

I thank the Program Committee of the American Ophthalmological Society for permitting me to present this paper and respond to Doctor Ryan's comments.