A Roundtable Discussion on Dry Eye

INTRODUCTION

Dry Eye is a pervasive and ubiquitous disease or condition. Dry Eye syndrome affects more than 10 million people in the United States and is one of the leading reasons for patients to consult eye care practitioners. This number probably grossly underestimates the number suffering from the condition because it does not include the estimated 50% of symptomatic contact lens wearers and there are currently approximately 35 million contact lens wearers in North America. While most of these patients do not suffer from severe dry eye, the condition can be debilitating and affect vision of many sufferers. This discussion is also timely because of environmental changes that presumably affect eye health and dry eye has been identified as a very important area of research.

Desmond Fonn (moderator).

I would like to thank you all for attending. The purpose of this forum is to discuss the diagnosis and management of Dry Eye. We are here at the kind invitation of Alcon Canada and I would specifically like to thank Brian Beatty and David Bard for sponsoring this Roundtable discussion. I hope that the next two hours will be fruitfully spent discussing important clinical issues. Brian and I selected the topics for discussion knowing full well that the time restraints would be a serious limitation. I will attempt to control the discussion as moderator and with that let me begin by asking the first question.

Dr Desmond Fonn: Dr Caffery the current definition of dry eye is: "Dry eye is a disorder of the tear film due to tear deficiency or excessive
treatment in order to keep the interpalpebral ocular surface free of dryness. Does this definition still suffice and if not how should it be altered?

Dr. Barbara Caffery: Since the definition was published 10 years ago much has been learned about dry eye and the ocular surface. In 2005, the Dry Eye Workshop (DEWS) was established to re-evaluate the definition and determine whether it should be altered. Deliberations on this subject are continuing.

The first point that I want to make is that in health care there is more at work than a definition. A definition of a disease is important but so are the criteria for diagnosis and the classification criteria. It is important not to confuse these terms.

Let’s start by determining what a definition is. The Oxford dictionary states that a definition is “an exact description of the nature, scope or meaning of something”. It may be useful to look at the definitions of other diseases to help us get a feel for how the terms are used in health care. For example rheumatoid arthritis is defined as “a chronic and destructive form of joint inflammation caused by the body’s own immune system attacking the tissues”. Sjogren’s syndrome is “an autoimmune disorder in which immune cells attack and destroy the glands that produce tears and saliva”. Diabetes is “a metabolic disorder resulting from the body’s inability to make enough or properly use insulin”. Definitions then seem short and precise. Our present definition of dry eye disease seems rather long by comparison but perhaps that is necessary given the vagaries of dry eye disease.

Dr. F. Maroni: I think that the issue of inflammation requires our attention. Newer studies have come out that link the cornea, conjunctiva, lacrimal gland and lids as an integrated unit. There are hormonal and sensory issues that also apply to the breakdown in dry eye disease. Finally the idea of inflammation should be added to the definition because of the studies that show the use of low dose steroids can improve the condition.

Dr. T. Simpson: The problem I have with the current definition of dry eye is it states the disease is a tear disorder. I believe there can be clinical dry eye without a tear film disorder, for example in contact lens wear. Another example is dry eye following laser surgery. I think calling the disease an ocular surface disease may be more inclusive.

Dr. D. Latz: I have a problem with the latter part of the present definition in that it includes symptoms of ocular discomfort. I have many patients who don’t have symptoms and have signs of dry eyes.

Dr. L. Jones: On the other hand, there are a large number of patients who have symptoms but no signs. It would be wrong to leave out those patients just because our clinical testing is not sufficient to describe their condition. However, I would like the definition to be as short as possible.

Dr. G. Leinweber: I think that the definition needs to be short followed by a description with the details. The definition can be broad but the categories should be clearly described to make it easier for diagnosis.

Dr. Desmond Funn: Should contact lens induced dry eye be placed in the same category as general dry eye and if not how does it differ?

Dr Temperd Simpson: A flippant response would be they are the same but unfortunately this is not supported by direct and indirect data from a number of directions.

The first bit of evidence is epidemiological. There is a large body of information that has emerged over the last decade that suggests that the prevalence of dryness is approximately 20%. Table 1 provides examples from a variety of countries illustrating this. However, we and others have shown that the prevalence is as much as 2-4 times higher in contact lens wearers. The tear film in lens wearers and non-wearers is also fundamentally different. This was recently illustrated by Nichols et al who showed differences in the thinning rates of prelens and precorneal tear films. So, if tear film thinning and drying are related to symptoms, again we have a difference depending on whether a lens is or is not on the eye.

Another physiological difference stems from a current theory that there is an “integrated loop” containing the structural, sensory and secretory components of the ocular surface that all operate in concert to generate a wet comfortable, healthy ocular surface. This is
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<th>COUNTRY</th>
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<td>Sweden (Jacobson et al.)</td>
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<td>705</td>
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Disrupted in a variety of ways during contact lens wear (including the altering the tear film, the structure of the ocular surface and the sensory channels) that suggests it is unlikely that symptoms in those wearing and not wearing lenses would be similar.

Finally, the treatment of dry eye in lens wearers is so fundamentally different than that in non-lens wearers that it renders any argument about the similarity or dissimilarity irrelevant. In those patients whose symptoms of dryness are extreme, if they are lens wearers, simply removing the lenses is the basic treatment. This is done by millions of contact lens wearers each year and is one of the direct causes of contact lens discontinuation. Obviously non-lens related dry eye does not have as easily identifiable an etiology and therefore the therapy and prognosis is much more unclear.

So in closing, there are a number of converging lines of evidence that lens-related and non-lens related symptoms of dryness are not the same. Perhaps, however, because the basic treatment of each of these is so fundamentally different, any question about similarity is moot in any case.

**Dr Desmond Fonn:** Should ocular inflammation be included as part of the global definition of dry eye?

**Dr Lyndon Jones:** As far as the definition is concerned, the current definition was already long enough, but inflammation is obviously involved in many cases of dry eye. Inflammation should be included in the discussion, but that it may be better served by being included within the description of the disease and in the diagnostic tests performed.

Interestingly, it was pointed out that during the 1994 workshop paper on dry eye diagnosis and management, that there was almost no mention of inflammation, reflecting the changing view of the role of inflammation in dry eye. This is felt to be due to a number of reasons, the major one being that at that point in time the laboratory techniques available to investigate inflammatory biomarkers were poorly developed. A recent Medline literature search looking at the relationship between inflammation and dry eye reveals that over a hundred
peer-reviewed papers have been published on this topic. However, the first of these did not appear until late 1997 to early 1998, reflecting the relatively recent development of this area of research.

Historically, a big problem with analyzing tear samples is that most analytical techniques require large volumes of fluid for the analysis to be undertaken. This obviously poses a problem in tear film analysis of dry-eyed patients, who simply do not have large volumes of tears. The recent development of laboratory-based techniques such as flow cytometry and many other related technologies have allowed researchers to take very small samples of tear fluid (sometimes <1 microlitre) and provide a wealth of information on the biomarkers contained within this fluid sample.

While we acknowledge that dry eye and inflammation are linked, we do not know if the inflammation produces the dry eye state, or whether the dry eye problems result in an inflammatory cascade. It would appear that there is good evidence to support either model and both processes may occur, depending upon the type of dry eye that is present and the severity.

Dr Barbara Caffery: The body’s response to many forms of primary disease is an inflammatory reaction response to the primary anomaly. If you break your leg, the inflammation at that level is very high, but we don’t talk about the disease as an inflammatory disease. It’s a disease of broken bones that needs to be fixed. The inflammation itself may need to be treated, of course.

Dr Lyndon Jones: The management of inflammation and dry eye currently involves the use of a number of agents. One simple method involves the regular use of artificial tears to flush the toxic biomolecules, such as pro-inflammatory cytokines, from the ocular surface, thereby preventing them damaging the ocular surface. However, recently there has been a growth in the number of therapeutic agents specifically targeted towards reducing the inflammatory cascade. These include the release of agents aimed at reducing cytokine release and build-up (such as Allergan’s Restasis), along with other anti-inflammatory agents such as steroids.

Dr Nish Rajani: With the availability of Restasis and other agents such as Lotemax and Alrex - which are sitespecific, non-penetrating, very safe-to-use steroids - dry eye is being treated more and more as an inflammatory disease, and with great results”.

Dr Desmond Fonn: Can symptoms alone be diagnostic of dry eye?

Dr. Lucie Berthiaume: I have always taken the approach of concluding my examination by summarizing my findings with the patient and making sure to refer to their chief complaint. The chief complaint is most often identified during the patient’s history, but other complaints or symptoms, can also come up during the course of the exam. Many patients will present with statements such as “My eyes are dry” - easy enough. If your eyes are dry, then they must be dry, regardless of the clinical findings: no corneal or conjunctival staining, no poor tear meniscus and even no reduced BUT.

In a busy practice there are in my opinion, only a certain number of tests you can do to identify dry eye signs. If these tests are negative as they are in some cases, this does not exclude dry eye diagnosis. We can certainly spend more time with more in depth evaluation of patients presenting specifically with dry eye but I would question whether a Shrimer test should be performed on every patient who has symptoms of dry eye.

Other patients will report symptoms of dry eye but say such things as “My eyes burn”, “My eyes feel gritty”, “I need to blink more at times”. In these cases these patient do not think their eyes are dry, and it’s a surprise to tell them that what they are feeling and experiencing may be due to dry eye.

Dr. Leinweber: In our office we have a “Welcome Back” or “Welcome to Our Practice” questionnaire that asks about symptoms such as whether or not your eyes burn, do they water, do you get tearing you’re reading, do you find you have to blink a lot when you’re reading because your vision gets blurred? If we get a positive response to some of those questions, then a more detailed investigation will follow. Symptoms are so important in the diagnosis and treatment options.

Dr. Bitton: I think dry eye is significantly under diagnosed because most people do not present with their chief complaint being that their eyes are dry. Many patients are there for their annual exam, and it’s usually
a secondary complaint, or when prodded by questions that the dry eye symptoms will come out. I think at least one single question would be something like “Do you think you have dry eye”.

Dr. Caffery: When a patient comes in with symptoms and you see evidence of dry eye, I always make a point of explaining to the patient that dry eye is chronic and the need for treatment, will need to be ongoing. Often those patients return and won’t have followed up with the treatment plan. We therefore first need a product that makes it easy for the patients to comply.

Dr Desmond Fonn: Which tests are essential in the diagnosis of dry eye?

Dr Dagmar Lutze: I think the major test that is essential in the diagnosis of dry eye is a thorough biomicroscopy, including instillation of fluorescein. This will actually encompass a series of other tests. Biomicroscopy should include an investigation for lid disease; specifically, one should look for blepharitis and meibomian gland dysfunction. Although technically not diagnostic of dry eye, these conditions certainly exacerbate it.

Corneal integrity can be evaluated by fluorescein staining which is typically found in the lower third of the cornea in dry eye. One must be careful not to instill excess amounts of fluorescein, as this may mask subtle staining that may be associated with this disease. Excessive conjunctival staining can also be an indication of dry eye. Rose Bengal stain can be used to detect degenerated and dead cells on the anterior surface of the eye that will not stain with fluorescein. Lissamine green works similarly and is reported to be less irritating to the patient than rose bengal.

Tear breakup time can be performed during biomicroscopy to assess tear quality. A low tear breakup time may represent a deficiency in the mucin layer of the tear film, a contributing factor in dry eye. Fluorescein aids in the evaluation of the height of the tear meniscus. The tear meniscus should also be examined for the presence of excess debris or mucous that might be indicative of dry eye. Schirmer tear test is used to measure tear quantity; however, it is time-consuming and its interpretation may be influenced by the instillation of a topical anaesthetic prior to performing the test.

Dr Gerry Leinweber: Are there any tests that our staff are capable of doing?

Dr Barbara Caffery: My staff does Schirmer test. There’s a huge amount of literature on Schirmers testing and I consider it a very important part of diagnosing dry eye.

Dr Vidi Maroun: One test that hasn’t been brought up is collagen plugs. I’m not too sure why optometry has not been more proactive about using collagen plugs as a temporary plug. We are always keen on adding products to the eye, which again is changing the chemistry on the ocular surface, versus keeping that which is there and seeing if you can solve the problem. This test is not time-consuming and it can bring the patient back to the office ten days later.

Dr Leticia Bertheau: Another way you can deal with this, if there are no clinical signs, there are just symptoms, is to send them home with artificial tears, make sure they will comply and have them back maybe two or three weeks later to reassess their symptoms.

Dr Desmond Fonn: Tear break-up time (TBUT) is considered to be a useful test of tear film stability. Is this statement true and what is the best method of measuring tear break-up time?

Dr Eitty Bitton: Tear break-up time has had a long clinical and controversial history. The TBUT is considered a clinically reliable test of tear film stability, with some pitfalls. The TBUT has shown a great amount of variability in the literature, and certainly we see it in practice with our patients. Most of the variability has been attributed to the methodology: How much fluorescein is instilled? How is the TBUT being measured? Are the lids being held open? What size beam is being used to observe the cornea? All these factors contribute to the variability observed between visits. Furthermore, the magical 10-second cut-off has been challenged by work from Cho10,11 where ethnic differences were noted. Consequently care should be taken in applying the 10 sec cut-off to all of our patients since lid structure, environmental factors can contribute to a lower acceptable norm for those individuals. To limit the variability of the TBUT even further, Korb12 proposed a smaller fluorescein strip, called the Dry Eye Test (DET), which limits the amount of fluorescein instilled in the eye. Unfortunately the DET is no longer commercially available.
How should TBUT be measured? The fluorescein strip should be moistened using non-preserved saline, with the excess shaken off. The strip should then be applied gently to the inferior palpebral conjunctiva. Allow the patient to blink 2-3 times to spread the fluorescein evenly prior to assessment. To maximize viewing, the Cobalt filter should be in place along with the use of a yellow barrier filter (Wratten #12), now an integrated part of most modern slit lamps.

To properly observe the cornea during the TBUT, Cho suggested using a wide illumination beam. This may cause photophobia in some patients, hence lowering the intensity of light may render the patient more comfortable. To further enhance the reliability of the TBUT, Nichols suggests doing the test twice and taking an average. In conclusion, the TBUT is an easy test to perform and remains clinically useful if attention to methodology is taken.

**Dr. Lyndon Jones:** I think if people are taught how to perform the test, it will certainly increase the reliability. Do something simple, like cut the fluorescein strip in half and use as little non-preserved saline as possible. The difference that you observe when you use the Wratten 12 filter is phenomenal.

**Dr. Kerby Kelly:** What about the non-invasive tear break-up time (NIBUT) test?

**Dr. Trefford Simpson:** There are several ways of measuring TBUT without the use of fluorescein, hence NIBUT. We use a corneal topographical device which creates placido rings images on the cornea which seems to work well.

**Dr. Barbara Caffery:** My impression is that if I have a soft lens wearer take their lens off and the TBUT is going to be much lower than without having worn their lens. So how reliable do you think a lens-removed TBUT is?

**Dr. Lucie Berthiaume:** I think that’s an excellent question. It’s definitely been shown that the TBUT in CL wearers is shorter, and so, again, I’d advocate that it could be used as a good screening.

**Dr. Lyndon Jones:** People have actually looked at how long it takes you to re-establish a tear film after removing your soft lens, and it’s a minimum of 20 minutes.

**Dr. Barbara Caffery:** A quick comment. I think we have to use Lissamine green or Rose Bengal to evaluate staining of the conjunctiva.

Dr. Desmond Fonn: Do you think you’ve seen more staining with these 2 dyes than fluorescein and is that telling you something more about the condition?

Dr. Barbara Caffery: Yes, I think I see more disturbed cellular walls, or whatever it is that causes this dye to penetrate.

Dr. Desmond Fonn: What are the traditional methods of treating mild and moderate dry eye?

Dr. Nish Rajani: Treating mild to moderate ocular surface disease is relatively straightforward; patient compliance of our treatment regimens, well that’s a different story. I think that the greatest obstacle in treating dry eye syndrome successfully is proper patient education so that they will follow our treatment protocol.

There is a disconnect between the way optometrists and their patients perceive the extent of this problem: “Patients perceive their dry eye as much more severe than their practitioner,” according to Robin L. Chalmers, OD in a paper she presented to the American Academy of Optometry. In her study 19% said their symptoms were severe whereas the optometrists in the study said only 9% of the subjects displayed severe symptoms. Although it is generally not sight threatening, it does cause our patients significant discomfort and we must treat and educate our patients about ocular surface disease even though this is somewhat tedious.

Believe it or not, what we call “dry eye” is, in my opinion, part of the problem. William Shakespeare wrote: “What’s in a name? That which we call a rose by any other word would smell as sweet.” This may have been true in the Elizabethan era but I do not think the Bard of Avon’s famous verse is applicable to modern day “dry eye”.

I think that doctors and patients alike are overwhelmed with the diagnosis of “dry eye”. In addition to the fact that the name does not sound clinical it is also a misnomer in that it tends to suggest only an aqueous deficiency. Also, patients with “wet dry eye” are easily confused by this moniker. I like the term ocular surface disease better than dry eye syndrome. It sounds more morbid as it should make doctors and patients take it more seriously and hopefully there would be a concomitant increase in counseling and compliance.
Let's Shed a Tear for our “Dry Eye” Patients

Artificial tears, in addition to managing lid disease, remains the mainstay therapy for dry eye syndrome. For currently available ocular lubricant drops to be effective they must be used q 2-3 hrs; we often fail to adequately convey this to our patients and it is tedious for them to instill drops this often. As a result patients tend use their drops infrequently or often not at all. I do not think it is possible to over-emphasize the frequency of instillation.

Historically, we have essentially considered two things when dealing with artificial tear products: preservatives and viscosity agents. We now have several brands of artificial tears with excellent preservatives in that they don’t cause toxicity. The best known are: Tears Nauturale, GenTeal, Theratears and Refresh lines of products.

I tend to favor the higher viscosity artificial tears like Syntane, Tears Naturale Forte (Alcon) and Refresh Liquigel (Allergan). Most tend to blur vision for a few minutes. If patients are forewarned about this they tend to be more accepting of this treatment.

I tend to use punctal plugs less frequently than I did several years ago although they remain an excellent option for patients with low tear volume. In addition to increasing the residence time of naturally produced tears, they do the same for artificial tears supplementation. Artificial tears must still be used as otherwise we may create a cesspool of pro-inflammatory cytokines and other inflammatory mediators. This is the reason that I tend to utilize them less frequently.

Omega-3 fatty acid supplementation has become a cornerstone of ocular surface disease treatment in my practice in the past several years. “Evaporative dry eye” occurs in the presence of meibomian gland dysfunction and this tends to be pervasive. Oral doxycycline and omega-3 fatty acids enhance meibomian gland function and result in a more stable film.

David Star Jordan a physician and educator at Stanford University once stated: “Wisdom is knowing what to do next, skill is knowing how to do it, and virtue is doing it.” Optometrists have the wisdom and skill to treat ocular surface disease; however, we all could be a little more virtuous in this regard.

Dr. Barbara Caffery: I think that a healthy body is an important aspect in the management of dry eye disease.

My advice is don’t smoke, drink plenty of water during the day, eat fruits and vegetables and exercise.

Dr. Lucie Lesault: I think sleep patterns have a huge effect on people’s symptoms and, at times, clinical signs as well. Sleep deprivation and stress may be linked to dry eye.

Dr. Trefford Simpson: I would like to add an accurate refraction and a good pair of glasses to avoid eye strain.

Dr. Barbara Caffery: Perhaps patients are not very compliant because the products we recommend are available OTC. If tear supplements were prescription items it might change their attitude.

Dr. Desmond Fonn: How have the new treatments for mild/moderate dry eye performed?

Dr. Gerry Leinweber: In general, the new generation of products have performed well. I am pleased to see we have many more options for providing relief to patients with dry eye. The new treatments that include Syntane, are moving beyond simple lubricants to formulations that improve the quality of the tears over a longer period of time. Having non-preserved products is also a real benefit, as many patients are sensitive to preservatives, plus the single dose products are convenient.

Canada is a very big country. The climate in Alberta where I practice is very dry compared to other parts of Canada, and we can have very cold winters. I know that in speaking to practitioners across the country, the demands of our various local climates can greatly affect which products are of most benefit. In areas with more smog issues, a more frequent drop during the day seems to help, while in other areas, lid scrubs seem to be of more benefit. If there is a lot of conjunctival staining, the gels are of more benefit.

We have used NSAIDS but usually not for mild or moderate problems. I prefer to reserve these medications or steroids for more serious or stubborn problems but keeping the doses short. I would not consider Pulse Dosing as standard treatment for mild or moderate dry eye, but in stubborn cases, where a combination of first line treatments did not resolve the problem, then pulse dosing can be used.

There certainly is great logic in using the combination of lid scrubs bid to enhance natural tear production,
with drops or gels qid or prn and this is my preference when treating most moderate cases of dry eye. The next stage is to consider punctual occlusion to further enhance the benefits of therapy if this is not effective, and finally if still no relief, to consider TPA options.

Dr Desmond Fonn: What strategies do you use to treat contact lens related dryness and is this a major problem amongst your contact lens patients?

Dr Trevor Miranda: Lets tackle the second part of the question first. The short answer is yes. It contributes to increased numbers of contact lens dropouts and also to lower comfort and overall satisfaction amongst those patients that continue to wear their lenses.

The results above from Vistakon’s Attitude and Usage Study of Vision Corrected Consumers 2002, 49% cited the lenses not being comfortable. Dryness causes at least half of all contact lens related discomfort issues.

Dryness in the discussion of contact lens wear can be divided into pre-existing dry eye and contact lens induced dry eye (CLIDE). CLIDE is characterized by dryness and discomfort at the end of the wearing time; decreased wearing times; burning; lens intolerance; corneal and conjunctival staining and rapid TBUT. Dryness is a problem because we are fitting more presbyopic patients than ever before with multifocal contact lens options. Many patients want to wear their lenses longer or even on a continuous wear basis.

Strategies for treatment:
It is vital to determine the cause firstly. Is it the low production of tears as found by a Schirmer’s test or is it pre-existing lid disease? Just asking how your lenses feel is not enough. Here are some of the strategies I employ for treating dryness in my contact lens practice:

- Fit new low dehydration, high Dk/t lenses. I fit a lot of silicone hydrogel lenses whether or not the patient is considering overnight wear. This helps to reduce hypoxic effects on the cornea, which may contribute to symptoms of dryness. Simple and easy to follow instructions will help increase compliance. We recommend regular replacement schedules.

We often provide lubricating drops for patients when they are wearing contacts and Systane before and after contact lens wear. Dr Lutzi has found that drops containing sodium hyaluronate have provided patients with improved comfort and longer wearing times.

- We recommend sunwear over contacts to reduce external drying forces such as wind and sun.
- Recommend lid hygiene and lid scrubs for any lid disease.
- We try single use lenses either on a daily disposable or continuous wear basis to avoid solutions sensitivities and corneal inflammation that contribute to discomfort and dryness
- Decrease the wearing times.
- Reduce eye makeup that can cause irritation and local inflammation.
- Recommend oral omega 3 fatty acid intake. Patients who are deficient in omega 3 oils have meibomian glands with very thick secretion. Consequently people who are deficient in omega-3 oils end up with an evaporative tear loss and dry eye syndrome.
- Consider punctual occlusion for highly motivated contact lens patients as a last resort.
- Future strategies may include topical cyclosporin A to reduce local inflammation.

Dr Desmond Fonn: Do contact lens disinfecting systems contribute to dryness/discomfort symptoms and if so what strategies do you use to minimize/eliminate the symptoms?

Dr: Kerby Kelly: Historically, preservatives have caused some adverse effects to contact lens wearers and to the contact lens material itself.

We can remember the toxic or hypersensitivity reactions to thimerosal and benzalkonium chloride. Fortunately
**Fluorescein Angiography** Standard procedures for fluorescein angiography should be observed. Certain medical conditions (such as pregnancy or allergy to fluorescein) may make the injection of fluorescein eyes for a particular patient undetectable in the clinical situation. Approximately 1/2 50% of the fluorescein dye may be excreted in the urine, and may persist for a period of 12 to 24 hours. Most side effects are mild, such as temporary nausea or vomiting in a few patients and rash, hives, or wheezing of the respiratory tract. Effects on ability to drive and use machines Following Visudyne Therapy, patients may develop transient visual disturbances such as abnormal vision, vision decrease, or visual field defects that may interfere with their ability to drive or use machines. Patients should be advised not to drive or use machines such as typewriters that may be hazardous because of the possibility of a sudden and unexpected change in vision.

**Adverse Reactions** In randomized clinical trials in choroidal neovascularization, mainly in patients with age-related macular degeneration (AMD), the most frequently reported adverse events to VISUDYNE (verteporfin) are injection site reactions (including pain, edema, inflammation, erythema, redness, and, less commonly, hemorrhage and discoloration) and visual disturbances (including blurred vision, flashes of light, visual acuity and visual field defects such as gray or pink halos, dark halos, and black spots). These events occurred in approximately 10%-20% of the patients. The following is a list of side effects that occurred in at least 1/1000 of patients:

**Ocular Treatments:** Blurred vision, color abnormalities, conjunctivitis/mydriasis reaction, eye styes, eye irritation, severe vision decrease with or without subconjunctival or subepithelial hemorrhage.

**Stereoscopic Vision:** Any ocular reactions should be reported to either the patient or the patient's eye doctor as soon as possible. Generalized symptoms may include headache, malaise, nausea, vomiting, dizziness, rash, urticaria, pruritis, dyspnea, flushing and changes in blood pressure or heart rate.

**Adverse reactions recorded in treated eyes in patients with posterior uveitis or presumed ocular histoplasmosis were similar to those reported for fluorescein angiography.**

**SYMPTOMS AND TREATMENT OF OVERDOSE** Overdose of drug and/or light in the treated eye may result in phototoxic injury and may be irreversible. Treatment is not known to be beneficial. Any overdose may result in the prolongation of the period during which the patient remains photosensitive to bright light. In such cases, it is recommended to have the patient avoid bright sunlight and using protective eye glasses for a period of time.

**Drug Interactions** Visudyne (verteporfin) is not metabolized by the liver and does not appear to be excreted in the urine. However, Visudyne is a photosensitizing agent and should be used with caution in patients who are currently undergoing photodynamic therapy (PDT) with another photosensitizer.

**Carcinogenesis, Mutagenesis, Impairment of Fertility** No studies have been conducted to evaluate the carcinogenic potential of verteporfin. verteporfin was not mutagenic, and in the absence or presence of light, when studied in microbial mutagenicity tests, verteporfin did not induce gene rearrangement or reverse mutation in an in vitro mammalian system or in a mammalian cell transformation assay.

**Pharmacokinetics** Photosensitizing properties of PDT (C) in a test chamber has been reported to result in DNA damage including DNA strand breaks, alkali-labile sites, DNA reactivity, and DNA-protein cross linkages which result in chromosomal aberrations, sister chromatid exchanges (SCE). These photochemical changes may be induced by the action of verteporfin at the site of PDT. Verteporfin has been shown to increase the yield of sister chromatid exchanges in Chinese hamster lung (CHO) cells irradiated with visible light and in Chinese hamster lung fibroblasts irradiated with UV light. In addition, verteporfin has induced terminal deletions in man, and human cervical carcinoma cells, but not in normal cells. Verteporfin was not evaluated in these latter systems. It is not known how verteporfin and PDT agents tolerate each other.

**Seizures** Approximately 9% of the patients treated with VISUDYNE in the clinical efficacy trials were noted on the age of 65. A reduced treatment effect was seen with increasing age.

**PRESCRIBING INFORMATION** (September 2004)

**Verteporfin** Verteporfin for injection (September 2004)

**PHOTOTHERAPEUTIC AGENS FOR AGE-RELATED MACULAR DEGENERATION, PATHOLOGIC MYOPIC AND PRESSURED OCULAR HOSTILE CONDITIONS.** VISUDYNE (verteporfin) is a drug to be used in Visudyne Therapy. Visudyne Therapy is a two-stage process requiring administration of a systemic agent followed by injection of light (photodynamic therapy - PDT).

CAUTION: Verteporfin Therapy should only be used by physicians trained in the treatment of age-related macular degeneration and pathologic myopia using photodynamic therapy with verteporfin for injection and specified lasers. Following VISUDYNE injection, the photodynamic effect is permanent. It is possible that the patient may result in photophobia and blinding of the eye if exposed to bright or filtered bleached light. **INDICATIONS** VISUDYNE (Verteporfin) Therapy is indicated for the treatment of age-related macular degeneration, pathologic myopia and presumed ocular histoplasmosis in patients with predominantly classic subfoveal choroidal neovascularization.

**CONTRAINDICATIONS** VISUDYNE (verteporfin) is contraindicated for patients with photophobia or a known hypersensitivity to any component of this preparation, and in patients with severe hepatic impairment.

**WARNINGS** Following injection with VISUDYNE (verteporfin), care should be taken to avoid exposure of skin to direct sunlight or bright indoor light for 2 days. In the event of photophobia during injection or the injection area must be covered from direct sunlight. Following VISUDYNE injection, the patient’s visual acuity will decrease by 10% to 30% for 24 hours and the visual field will be decreased by 10% to 30% for 24 hours. If the patient’s visual acuity of 0.04 or greater (20/100 of visual acuity) before treatment is noted, until their vision completely returns to pre-treatment levels and the potential benefits and risks of treatment should be reviewed with the patient by the treating physician.

**Cautions** Should be exercised when Visudyne Therapy under general anesthesia is considered (See PRECAUTIONS). The use of a gauze or cloth over the patient’s eye should be avoided as it may result in photophobia and blinding of the eye if exposed to bright or filtered bleached light.

**Pregnancy AND TUBAL EFFECTS** There are no adequate and well-controlled studies in pregnant women. Verteporfin Therapy should only be used in pregnant women if clearly needed and the risk to the fetus is less than the possible benefit to the pregnant woman. Rare but fatal fetal deaths have occurred following maternal administration of approximately 40-fold the human dose of verteporfin (5 mg/kg) in rabbits. Studies in the rabbit have shown that verteporfin is teratogenic during the organogenesis period (approximately 100-fold the human dose of verteporfin in rabbits). A large number of rabbit fetuses have been evaluated in rabbits of 10 mg/kg for 1 month. Maternal Verteoporfin and its metabolite have been found in the breast milk of women after a 4 mg/kg. The verteportin breed milk levels were at 60% of the corresponding plasma levels. Verteoporfin was undetectable after 72 hours in the milk. The peak plasma levels of Verteoporfin and its metabolite are at peak plasma levels of approximately 1 to 6 hours after administration. The therapeutic benefit of verteporfin and its metabolite to neonates are unknown, either should be treated or removed postpartum. Taking into account the drug’s system of Verteoporfin in rabbits, women should be shown 90 weeks after Visudyne Therapy.

**Pediatric Use** Safety and effectiveness in pediatric patients have not been established.

**PRECAUTIONS** Changes in the visual function of VISUDYNE, especially if the affected area is in exposed to light, can cause severe pain, inflammation, swelling or discoloration at the injection site. The relief of pain may require analgesic treatment.

**Contraindications** The use of verteporfin (Verteporfin) should be avoided in patients with known photosensitivity reaction to verteporfin or any component of VISUDYNE (verteporfin).

**Pain** Pain in the arm or shoulder area should be reported before starting VISUDYNE infusion and the line should be closely monitored.

**Due to the possible high risk of use of some elderly patients, it is strongly recommended that the largest arm vein possible, preferably subclavian, be used for injection.**

**Small veins in the hand should be avoided.**

If extravasation occurs it should be injected into the arm to be the is under observation. The extravasation area must be thoroughly protected from direct light until the swelling and discoloration have faded in order to prevent the occurrence of a local burn which could be severe. Cool compress should be applied to the injection site (area of vision) for 48 hours or more may result in syncope and blinding of the eye if exposed to bright or filtered bleached light.

**Visudyne Therapy** should be considered carefully in patients with moderate hepatic impairment or History obligation since there is limited data available on the expected pharmacokinetics of verteporfin.

**Liver▌** Pain, vaso-occlusive reactions and hypersensitivity reactions, which can occur rare can be observed. Allergic reactions (urticaria, urticarial reactions, angioedema) and anaphylactic reactions are associated with general symptoms such as nausea, vomiting, edema, rash, fever, hypotension, tachycardia, and shortness.

**In case of clinical data related to the use of VISUDYNE for anthelminthic patients.** At least 15-50 hours done given by hepatic disease or severe renal function impairment, verteporfin should be avoided due to the potentially large amount of drug (verteporfin) when used in patients with severe hepatic impairment. The use of verteporfin in patients with severe hepatic impairment is not recommended.

**Hypersensitivity to verteporfin** has been observed in a patient with known history of severe reactions to verteporfin. Hypersensitivity reactions can be considered under treatment with verteporfin should be avoided. The patient may not be on the day of the treatment or the day before the treatment.

**Vaso-occlusive reactions** and hypersensitivity reactions, which can occur rare can be observed. Allergic reactions (urticaria, urticarial reactions, angioedema) and anaphylactic reactions are associated with general symptoms such as nausea, vomiting, edema, rash, fever, hypotension, tachycardia, and shortness.

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today's preservatives have a large molecular weight and size which precludes them from entering the matrix of hydrophilic lenses. These preservatives cause more damage to microbes making them as effective at lower concentrations. There are fewer solution problems, however, reactions still occur. The SiliconeHydrogels.org web site is a great resource of information on studies comparing the similarities and differences between conventional hydrogel and silicone hydrogel lenses. It appears that some solutions may not work as well with silicone hydrogels as conventional hydrogels but it is unclear whether symptoms are manifested.

Adverse reactions to older contact lens solutions were often easier to find and identify. There was more of a diffuse SPK apparent. With newer formulations there might only be slight dryness or perhaps mild discharge. Sometimes you'll see low-grade inflammation of the tarsal plate as well. So it is somewhat more difficult now to figure out if it's the solution that's causing the problem.

Apparently many contact lens wearers in the U.S. use generic brands that are not prescribed by the practitioner. Patients may often ignore our recommendations and purchase the cheapest alternative. Many of the generic brands change the formulation without notice to the consumer. It may make more sense to retail the solution ourselves to ensure patient compliance.

Most care systems now are advertised as no-rub and unfortunately often equated in the patient's mind as no care. Digital cleaning is an important step with the new silicone hydrogel materials especially as they may attract more lipid deposition. Another useful tip is to have the patient rinse the contact lens as it may actually get rid of about 90 percent of the contaminants.

Depending on the severity of the symptoms patients may try rewetting or rewetting/surfactant combination drops or perhaps graduate to preservative-free alternatives such as peroxide or ultraviolet disinfection systems. Another good tip is to simply have the patient rinse their lenses with a non-preserved saline before insertion. This may solve some of the initial stinging and burning often experienced first thing in the morning.

Dr. Eitty Button: I really want to reinforce the use of the Wraaten yellow barrier filter to make it easier to observe mild SPK changes as it may otherwise go undetected.

When things go wrong with contact lenses we, as practitioners, have a knee-jerk reaction to change the contact lens without considering the disinfecting system.

Dr. Gerald Leinweber: Interestingly for some people who have had solution sensitivities - "no solution" seems to be the answer for those people, and the other solution is extended wear, 30 days.

**REFERENCE LIST**

11. Cho P, Brown B. Review of the tear break-up time and a closer look at the tear break-up time of the Hong Kong Chinese. OVS 1993;70:30-38