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In This Issue…

Editorial Board

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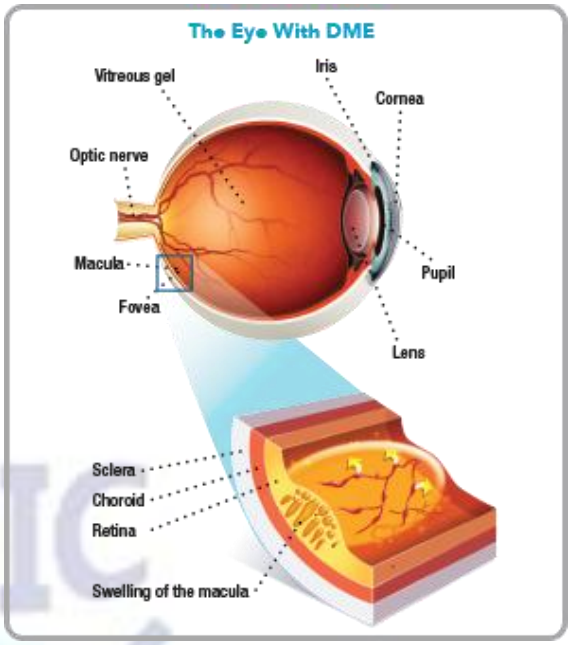
Macular Edema in Diabetes

Background:

Macular edema in diabetes, defined as retinal thickening within 2 disc diameters of the center of the macula, results from retinal microvascular changes that compromise blood-retinal barrier, causing leakage of plasma constituents into the surrounding retina and consequently, retinal edema.



Pathophysiology:

Focal edema is associated with hard exudate rings caused by leakage from microaneurysms. Diffuse edema is caused by leakage from microaneurysms, retinal capillaries and arterioles.

Epidemiology:

Diabetes is the leading cause of new blindness in the United States, with clinically significant macular edema (**CSME**) contributing greatly to this vision loss.

Signs and symptoms:

The following findings indicate the presence of clinically significant macular edema (**CSME**),

- Retinal thickening within 500 µm of the center of the fovea .
- Hard, yellow exudates within 500 µm of the center of the fovea with adjacent retinal thickening .
- At least 1 disc area of retinal thickening, any part of which is within 1 disc diameter of center of fovea.

Diagnosis:

Diabetic macular edema (**DME**) is diagnosed by funduscopic examination. The following studies can also be performed, to provide information for treatment and follow-up:

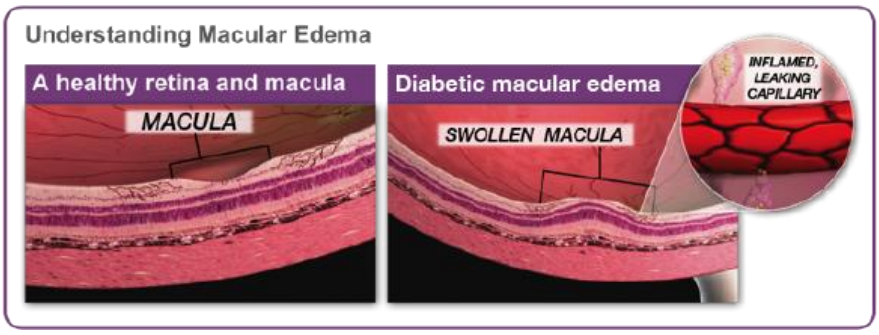
- Optical coherence tomography (**OCT**): Captures reflected light from retinal structures to create a cross-sectional image of the retina, which is comparable to histologic sections as seen with a light microscope; it can demonstrate 3 basic structural changes of the retina from diabetic macular edema: retinal swelling, cystoid edema, and serous retinal detachment.
- Fluorescein angiography: Distinguishes and localizes areas of focal versus diffuse leakage, thereby guiding the placement of laser photocoagulation.
- Color stereo fundus photographs: Can be used to evaluate long-term changes in the retina.

Visual acuity should also be measured. Although it does not aid in the diagnosis of **CSME**—initially, at least, patients may have a visual acuity of 20/20. It is an important parameter in following the progression of macular edema.

Laboratory studies

- Protein levels: Proteinuria is a good marker for the development of diabetic retinopathy; thus, patients with diabetic nephropathy should be observed more closely.
- Lipid and triglyceride levels: Elevated triglyceride and lipid levels increase the risk of retinopathy, while normalization of lipid levels reduces retinal leakage and deposition of exudates.

Complications:



Adverse effects and complications of laser use are related mostly to either misdirected light or excessive energy, both of which are generally preventable with operator familiarity with standard treatment parameters.

Sub-retinal fibrosis is a vision-threatening condition, which occurred in 2% of eyes with diabetic macular edema.Sub-retinal fibrosis is an elevated mound or flat sheet of grey or white tissue deep to the retina at or near the center of the macula. On fluorescein angiography, this lesion is hyper-fluorescent in the capillary phase with persistence into the late phase and diffusion of dye. Sub-retinal fibrosis is associated most strongly with very severe hard exudates. It is also associated with a poor lipid profile. Prognosis for patients with this complication is poor; sub-retinal fibrosis is generally refractive to focal laser therapy.

Residual massive foveal hard exudates may remain after the resolution of diabetic macular edema and may be associated with profound and irreversible vision loss. In one study, aspiration of hard exudates following a small retinotomy and serous neurosensory detachment resulted in an increase of visual acuity in 5 of 7 patients.

Treatment and management:

Approach Considerations:

As with all complications of diabetes, successful management of macular edema requires good control of the diabetes itself.

The early treatment diabetic retinopathy study was the first study to provide a treatment paradigm in this disease using laser therapy to reduce moderate vision loss in patients with clinically significant macular edema by approximately 50%.Although prevention of vision loss is important, visual improvement would be preferable.

Over the past few years, research has started to focus on the use to anti–vascular endothelial growth factor therapy to treat **DME**. As new and promising treatment options emerge and prospective data begin to mount, it is becoming clearer that anti-**VEGF** therapy will play an increasing role in the treatment of **DME**.

A variety of intravitreal medications are currently available. Pars planavitrectomy may also be beneficial.Medical treatment should focus on optimizing glycemic and hypertensive control and lowering lipid levels. Optimal control of diabetes, blood pressure, and lipids has been shown to positively impact diabetic retinopathy.These issues are best managed by primary care physicians and internists.

Intravitreal Treatment:

(A) Intravitreal corticosteroids

Intravitreal triamcinolone acetonide (IVTA) has been shown to significantly reduce macular edema and to improve visual acuity, particularly when the macular edema is pronounced. Action is maximal at 1 week, lasting 3-6 months.Patients should be counseled about the risk (30-40%) of increased intraocular pressure, which usually can be medically controlled. In July 2014, the FDA approved dexamethasone intravitreal implant for diabetic macular edema in patients who are pseudophakic or are phakic and scheduled for cataract surgery. This indication was expanded to include the general DME patient population in September 2014.

Fluocinolone acetonide is a long-acting fluocinolone intravitreal implant was approved by the FDA in September 2014 for the treatment of diabetic macular edema in patients who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure.

(B) Intravitreal anti-VEGF agents

Currently available anti-VEGF agents include pegaptanib sodium, ranibizumab, aflibercept, and bevacizumab. Bevacizumab is not commercially available as an intravitreal injection.

Pegaptanib sodium is a pegylated aptamer directed against the VEGF-Aisoform. It was the first FDA-approved ophthalmologic anti-VEGF agent for the treatment of choroidal neovascularization from age-related macular degeneration. Ranibizumab is a recombinant humanized antibody fragment that is active against all isoforms of VEGF-A. Intravitreal ranibizumab is FDA approved for the treatment of exudative ARMD.

Laser treatment:

Laser photocoagulation is a well-proven therapy to reduce the risk of vision loss from diabetic macular edema. Treatments include the following:

- Focal treatment: Addresses leaking microaneurysms
- Grid pattern photocoagulation: Used for diffuse leakage

Future Therapies:

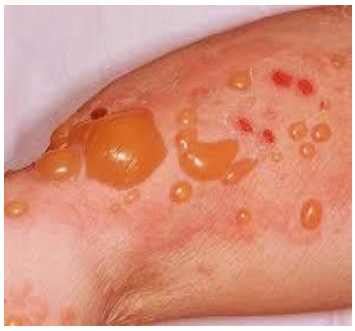
VEGF Trap-Eye is a soluble **VEGF** receptor fusion protein that binds all forms of **VEGF-A** and related placental growth factor (**PGF**). When administered as a single 4 mg intravitreal injection in a phase 1 study, a marked decrease in central retinal thickness and mean macular volume was noted.

Retisert,a steroid implant (**fluocinoloneacetonide**), was evaluated in patients with diabetic macular edema with good results, but its adverse effect profile wasacause for concern (90% of patients developed cataracts, and 40% required glaucoma surgery within 3 y).

Source: http://emedicine.medscape.com/article/1224138-treatment#d13

Terminology

Bullous pemphigoid



Bullous pemphigoid is an uncommon skin disease characterized by tense blisters on the surface of the skin such as the lower abdomen, upper thighs or armpitsand the inner lining tissue of the mouth, nasal passages, or conjunctivae of the eyes (mucous membrane tissue) can be involved. The condition is caused by antibodies and inflammation abnormally accumulating in a particular layer of the skin or mucous membranes. This layer of tissue is called the "basement membrane." These antibodies (immunoglobulins) bind to proteins in the basement membrane called hemidesmosomal BP antigens and this attracts cells of inflammation. The mucous membrane disease is also referred to separately as mucous membrane pemphigoid.
A majority of those affected by bullous pemphigoid are 50 years of age or older. While the cause is unknown, it is felt by some that an aging immune system may become activated in certain individuals with a genetic predisposition to it.

Source: http://www.medicinenet.com/bullous_pemphigoid/article.htm

Complementary Medicine

FructusZizyphi

Order:Rosales
Family:Rhamnaceae(Buckthorn Family)
Genus:Ziziphus
Species:Ziziphus jujuba.
Botanical Source:Dry fruit of Ziziphus jujuba Mill.
Botanical Names:Zyzyphus jujube,Zyzyphus ziziphus.
Common names: Fructus Jujube fruit,Chinese Date.

Description:

Black date is a spiny, deciduous shrub or a small tree jujube having palmate veined leaves spiny stipules small yellowish flowers and dark red fruit. The fleshy edible drupe of this tree also called Chinese date.

Nutritional Values and constituents:

The desiccated fruit has been analyzed for nutritional qualities; per 100 grams, it has:
Calories: About 350 cal.
Minerals: Potassium: 1050 mg, Phosphorus: 168 mg, Calcium: 130 mg Sodium: 12 mg Iron: 3.5 mg.
Vitamins: Vitamin C: 300 mg, Vitamin A: 125 mg, Niacin: 2.8 mg, Riboflavin: 0.2 mg, Thiamine: 0.1 mg.
Fruit without water is 84% sugar, which explains its very sweet taste.In a serving of 10 grams of desiccated fruit the only significant nutrients for a modern diet would be 3.6~3.7 grams of protein and 30 mg of vitamin C.
Fruit contains triterpenes betulinic acid,aiphitolic acid, betulonic acid, oleanonic acid, maslinic acid, oleanolic acid and ursolic acid together with a number of isomeric β-coumaric acid esters of aiphitolic and maslinic acid. Two alkaloids named zizyphusine and daechucyclopeptide were also isolated from the fruit.

Medicinal actions and uses:

Medicinal uses supported by clinical data:Rare; although one uncontrolled human study has suggested that FructusZizyphi may be of some benefit for the treatment of insomnia.
Uses described in pharmacopoeias and well established documents: To promote weight gain, improve muscular strength, and as an immune-stimulant to increase physical stamina. Treatment of insomnia due to irritability and restlessness.
Uses described in traditional medicine:As an antipyretic, diuretic, emmenagogue, expectorant, sedative and tonic. Treatment of asthma, bronchitis, diabetes, eye diseases, inflamatory skin conditions, liver disorders, scabies, ulcers and wounds

Safety and Toxicity:

No known drug interactions with jujube or any reports of toxicity from excessive jujube consumption. However it should not be used by patients who are suffering from abdominal cramps and bloating excessive phlegm or intestinal parasites.

Indications and Dosage:

Jujube is used as a nutrient and tonic.It is also used as a prophylactic against liver disease and stress ulcers and gives some precautions and adverse reactions.No health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages.

Sources: WHO monographs on selected medicinal plants.VOL. 3.,2007, pp 359-366.
http://www.mdidea.com/products/new/new030.html

Test Your Knowledge

1. Oneyear old child has been admitted to emergency with suspicious of atropine overdose as there are:

A) Abdominal cramps.
B) Increased gastric secretion.
C) Increased cardiac rate.
D) Papillary constriction.
E) Increased urinary frequency.

2. Why indomethacinis preferred over colchicine for acute attack of gout?

A) Less likely to cause gastrointestinal bleeding.
B) Less likely to cause diarrehea.
C) Less likely to cause acute renal failuar.
D) More likely to reduce inflammation.
E) More likely to prevent further acute attacks.

3. Myopia:

A)Results in light rays being focused behind the retina.
B)Can be corrected by using concave lenses for spectacles orcontact lenses.
C)Occurs when the person cannot clearly see an object that ismore than 1 meter from the eye

4. Patients should be advised to avoid direct sunlight when taking:
A) Gliclazide
B) Clarithromycin
C) Amiodarone

WHO Pharmaceuticals Newsletter

WHO Recommends against International Control of Ketamine

December 2015 – For the fourth time since 2006, the World Health Organization (**WHO**) today recommended that ketamine should not be placed under international control after review of the latest evidence by the **WHO** Expert Committee on Drug Dependence. The Committee concluded that ketamine abuse does not pose a global public health threat, while controlling it could limit access to only anaesthetic and pain killer available in large areas of developing world.

"The medical benefits of ketamine far outweigh potential harm from recreational use," said Marie-PauleKieny, Assistant-Director General for Health Systems and Innovation at **WHO**. "Controlling ketamine internationally could limit access to essential and emergency surgery, which would constitute a public health crisis in countries where no affordable alternatives exist."

Ketamine is an anaesthetic used in surgical and diagnostic procedures, it is often the only anaesthetic agent available in most developing countries and is also used for pain management. Ketamine has a good safety profile and is easy to use, especially in under-resourced health systems and emergency settings where clinical conditions and medical equipment are generally not available. In recent years ketamine has also been used recreationally, which has prompted moves to control the substance under international law. On each of these occasions (2006, 2012, 2014 and this year)**WHO** Committee has recommended against scheduling. This and other recommendations of the Expert Committee will be conveyed to the Commission on Narcotic Drugs for its final decisions in March 2016.

"We have found that placing substances under international control can often limit access to them for medical purposes," said Kees De Joncheere, **WHO** Director for Essential Medicines and Health Products. "Morphine is a case in point: even though it is inexpensive and one of the best substances available for pain management, in most countries availability and use are limited due to excessive regulation."

Source: http://www.who.int/medicines/access/controlled-substances/recommends_against_ick/en/

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional healthteam as well as from others. Here's one of the enquiries received at the center:

Enquiry received from:Ph. Sara Ahmed, Pediatric hospital Assiut,University.
Enquiry: What is the toxic dose of camphor oil for children?
Summary of the answer: Camphor is**possibly unsafe**for children when applied to the skin. Health professionals should be aware of camphor toxicity in young children and warn the parents about its potential danger. Children tend to be more sensitive to the side effects. Camphor is definitely **unsafe** when taken by mouth. Seizures and death can occur if these products are swallowed. Keep camphor-containing products away from children.

Toxic effects appear after the ingestion of 0.5-1 g of pure camphor for Children.

For Infants: 70 mg/kg of pure camphor is toxic.

FDA News

FDA approves first drug to treat hallucinations and delusions associated with Parkinson's disease

April 29, 2016

The U.S. Food and Drug Administration (FDA) approved Nuplazid (pimavanserin) tablets, the first drug approved to treat hallucinations and delusions associated with psychosis experienced by some people with Parkinson's disease.


New Parkinson's Drug Nuplazid Seeks 2015 FDA approval

Hallucinations or delusions can occur in as many as 50 percent of patients with Parkinson's disease at some time during the course of their illness. People who experience them see or hear things that are not there (hallucinations) and/or have false beliefs (delusions). The hallucinations and delusions experienced with Parkinson's disease are serious symptoms, and can lead to thinking and emotions that are so impaired that the people experiencing them may not relate to loved ones well or take appropriate care of themselves.

An estimated about 370,000Egyptians are diagnosed with Parkinson's disease. The neurological disorder typically occurs in people over age 60, when cells in the brain that produce dopamine become impaired or die. Dopamine helps transmit signals between the areas of the brain that produce smooth, purposeful movement -- like eating, writing and shaving. Early symptoms of the disease are subtle and

occur gradually. In some people Parkinson's disease progresses more quickly than in others. As the disease progresses, the shaking, or tremor, which affects the majority of people with Parkinson's disease, may begin to interfere with daily activities. Other symptoms may include depression and other emotional changes; hallucinations and delusions; difficulty in swallowing, chewing, and speaking; urinary problems or constipation; skin problems; and sleep disruptions.

The effectiveness of Nuplazid was shown decreasing the frequency and/or severity of hallucinations and delusions without worsening the primary motor symptoms of Parkinson's disease.As with other atypical antipsychotic drugs, Nuplazid has a Boxed Warning alerting health care professionals about an increased risk of death associated with the use of these drugs to treat older people with dementia-related psychosis. No drug in this class is approved to treat patients with dementia-related psychosis.In clinical trials, the most common side effects reported by participants taking Nuplazid were: swelling, usually of the ankles, legs, and feet due to the accumulation of excessive fluid in the tissue (peripheral edema); nausea; and abnormal state of mind (confused state).
Nuplazid is marketed by Acadia Pharmaceuticals Inc. of San Diego, California.

Source: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm498442.htm
http://www.rightdiagnosis.com/p/parkinsons_disease/stats-country.htm#extrapwarning

Answers:

1. (C) Most of the side effects of atropineare directly related to its antimuscarinic action. Dryness of the mouth, blurred vision, photophobia and tachycardia commonly occur with chronic administration of therapeutic doses.

2. (B) It is well known that colchicine in the treatment doses may cause strong diarrhea while indomethacin is not. indomethacin as one of NSAIDS competitively inhibits the cyclooxygenaseisoenzymes COX-1 and COX-2 by blocking arachidonate binding, thereby preventing conversion of arachidonic acid to prostaglandin G2, a first step in rapid, early inflammatory responses.

3. (B, C) Myopia is an ophthalmic condition resulting in parallel rays being focused in front of the retina. It may be caused by an elongation of the eyeball or by anerror of refraction. The condition is also called nearsightedness or shortsightedness as affected individuals cannot clearly see objects that are more than a meter from the eye. Concave lenses for spectacles or contact lenses are usedto correct the error.

4. (C) Some drugs may cause phototoxic or photoallergic reactions if the patient is exposed to ultraviolet light. When patients taking amiodarone (for arrhythmias) are exposed to direct sunlight or to sun lamps, photosensitivity may occur owing to a phototoxic reaction. A skin reaction may occur and this may continue for some weeks after treatment when amiodarone is stopped. Patients using amiodarone should be advised to use total sunblock preparations, to wear protective clothing and to avoid exposure to sun.