EYES, EARS, NOSE, THROAT AND TEETH

It's well known that glutathione is important for the normal functioning of the eye. Some of the earliest studies with GSH focused on its role in preventing cataracts, and GSH is relatively well known among ophthalmologists. Specialists in ear, nose and throat (ENT) and in dentistry have only recently become aware of the role of glutathione in the diseases they treat. Given the critical roles of GSH as the body's most important naturally occurring antioxidant, its ability to detoxify substances encountered in the environment and its immune-sustaining abilities, glutathione research is now finally picking up in these fields as well.

OPHTHALMOLOGY CATARACTS

Cataract is a clouding (opacification) that takes place in the lens of the eye. It is the leading cause of morbidity and functional impairment among the elderly and leads to more than one million operations per year in the United States.

The lens of the eye is composed of deceptively simple tissue. This completely transparent part of the eye has the job of focusing light on the retina, which it does by changing shape to adjust its focal length. Scientists believe that any damage to the lens, no matter how small, contributes to opacification. This usually results from physical injury, repeated exposure to ionizing radiation (such as sunlight) or any of a host of different illnesses. Over time the damage accumulates and the lens begins to cloud.

Oxidative stress plays a role in the aging of the lens, so antioxidants are an important defense against cataracts. The researcher M.A. Babizhaev in Russia measured the breakdown products of lipid peroxidation as cataracts developed. He found that as the cataract worsened, oxidative stress increased. An Italian team at the University of Bari went a step further and demonstrated that in people with cataracts the loss of GSH paralleled the increase in oxidative breakdown products.

It is known that cataract in humans usually shows significant, extensive oxidation of lens proteins. With this in mind, researchers experimented on cataracts by stimulating them with various chemicals. They showed that cataract formation could be delayed or prevented by elevated GSH levels. Clearly, the key defense in the lens against oxidation is glutathione.

The legendary GSH expert, Alton Meister and a team at Cornell University in New York, used the drug BSO to deplete glutathione levels in the eyes of laboratory animals. The animals subsequently developed cataracts. Meister's team was then able to prevent cataract formation by reestablishing glutathione levels with GSH-monoester and suggested that this strategy may be effective in delaying cataract formation.

Diabetics are more prone to cataract than non-diabetics. E. Altomare's team in Italy measured glutathione status in the lenses of four groups of patients: diabetics with and

without cataracts and non-diabetics with and without cataracts. As expected, both cataract groups showed impaired glutathione defenses, but the diabetic groups fared worse in all cases.

CASE STUDY

Edgar loved to paint. Now retired, he could pursue this hobby fulltime if he so pleased. Over the previous few years, his wife had commented that the color in his landscapes was too loud. At first he did not believe he had changed his techniques, but a side-by-side comparison with earlier works proved him wrong. Still, he felt the colors in previous paintings were "weak". A routine check revealed cataracts. One eye required surgery, the other was "not yet ripe". After surgery he eventually recovered excellent vision, but post-operative complications left him hesitant about having the same treatment on the other eye. His wife did some homework, learning about glutathione and cataracts. She started him on Immunocal. One year later, his ophthalmologist was baffled by the unusual observation that the cataract was less dense.

MACULAR DEGENERATION

Macular degeneration is a progressive loss of sight due to breakdown of the macula – the portion of the retina responsible for fine vision. Age-related macular degeneration (ARMD) is a leading cause of visual loss in people over 65. Although susceptibility to this disease may be predominantly genetic, contributing factors such as smoking and atherosclerosis can make it worse. This disease is thought to result from the cumulative damage of free radicals primarily released by exposure to ultraviolet (UV) sunlight, but other sources of oxidative stress may play a role.

Because elderly people generally have low GSH levels, they are predisposed to oxidative damage. Researchers have shown that low GSH levels go along with poor eye health in ARMD patients compared to normal control groups. Experiments have been conducted to test glutathione's antioxidant function in the whole body and in the eyes of patients suffering from macular degeneration. S.M. Cohen and his team at the University of California (Davis) found significantly altered GSH activity in blood samples of macular degeneration patients. It appears that high GSH levels correspond to healthy eyes and suggests a possible role for GSH in the protection against or delay of this disease.

GLAUCOMA

Glaucoma is a serious condition in which fluid pressure within the eye rises. A certain amount of pressure is necessary to maintain the shape of the eyeball. Too much pressure compresses and obstructs the small blood vessels within the eye. This damages the surrounding areas, most importantly the optic nerve. Glaucoma is one of the leading causes of visual loss.

It becomes more common as we age, runs in certain families, and is often seen in conjunction with diabetes, hypertension (high blood pressure) and severe myopia

(nearsightedness). Traditional therapy aims to relieve the pressure in the eye either surgically or with drugs.

The Russians A.I. Bunin, A.A. Filina and V.P. Erichev measured GSH levels in the eyes of hundreds of patients undergoing surgery for all sorts of reasons. The lowest GSH levels were found among cataracts patients and in patients with open angle glaucoma. They noticed this fall even at the earliest stages of the disease and suggested that reestablished glutathione levels would help prevent or delay this process, and used the nutritional supplement lipoic acid to do so.

A Harvard University group investigated different GSH-related compounds to increase the outflow of fluid from the eye and reduce pressure within it. In combination with the topical form of ethacrynic acid (a diuretic) they found that cysteine, glutathione and N-acetylcysteine all benefited eye pressure and even lessened the side effects of the drug.

EAR, NOSE & THROAT

GLUTATHIONE IN THE UPPER RESPIRATORY TRACT

The nose, mouth and throat make up the upper respiratory tract. All the food we eat, fluids we drink and air we breathe pass through it. The importance of GSH in the lower respiratory tract (lungs) is well known. Since the upper tract is our front-line contact with the external environment, it seems fitting that glutathione would protect us here against xenobiotics (infections and toxins).

The respiratory tract is lined with a fluid made up of a complicated mixture of biochemicals and cells of the immune system, called the respiratory tract lining fluid (RTLF). Glutathione is the main antioxidant in this fluid and provides our initial defense against inhaled toxins. Institutions like the Inhalation and Toxicology Research Institute in Albuquerque, New Mexico started researching the role of antioxidant enzyme activities in RTLF in the early 1990's. More recent work at the University of California (Davis) elaborates further on the role of antioxidants in this fluid.

This research project is only one of several focusing on the importance of glutathione in the respiratory tract lining fluids, where it protects us from xenobiotics and infection. In severe or prolonged illnesses, these GSH levels may become depleted and enable the disease to progress and cause further complications. Furthermore, N.S. Krishna and his team at the University of Kentucky showed that this glutathione defense system weakens with aging, and more quickly in men than women.

B. Testa and M. Mesolella from the Institute of Otolaryngology, University of Naples, used a GSH nasal aerosol spray in their studies. Statistics from the experiments show that this treatment significantly improved nasal obstruction, rhinorrhea (runny nose) and ear fullness. The lining of the nose is one of few human tissues that readily absorb glutathione. Most other tissue can only use the glutathione it manufactures for itself from GSH precursors.

SINUSITIS

Infection or inflammation of the sinus cavities in the bones of the face is one of the most common reasons people go to the doctor. As many as 50 million Americans are affected each year. The most common causes of sinusitis include bacterial or viral infection, allergies and impaired mucus flow. Most treatments are designed to either destroy the infection or improve drainage of mucus from the sinuses. The sinus cavities are near the front of the head, behind the forehead, nose region and cheeks.

Physicians have long used the drug NAC for the treatment of disorders involving thickened lung secretions (cystic fibrosis, chronic bronchitis). It is now being used for upper airway problems such as sinusitis. NAC breaks down mucus and raises glutathione levels at the same time. American, French, Italian, Korean and Scandinavian research teams have all studied the efficacy of NAC and other antioxidants in the treatment of sinusitis.

The Amsterdam group led by G.J. Westerveld showed the glutathione levels fall during chronic sinusitis. They concluded that this drop is part of a generally decreased antioxidant defense, which subsequently worsens the disorder.

EAR INFECTION

Infection of the middle ear is an extremely common cause of illness, especially among children. It is caused mostly by a combination of fluid buildup in the middle ear and infection. The triggering event often is a viral infection, but the site is commonly superinfected (one infection on top of another) by bacteria. Treatment for many years was with antibiotics, but doctors are increasingly reluctant to over-prescribe these drugs nowadays, especially for ear infection. Decongestants can help drain fluid from the middle ear, through the Eustachian canal and into the throat.

More and more evidence shows that free radicals play a large part in the development of inflammation leading to middle-ear infections. Studies examining GSH levels in these tissues show that they fluctuate according to how infected or inflamed the site is. Scientists have examined the effects of both ways of raising glutathione levels – topical and ingested, and have found both to be effective ways to address oxidative stress in these tissues.

Patients with middle-ear infections are sometimes treated by placing tubes through the eardrum to drain accumulated fluid and prevent subsequent infection. This does the job but has its downside. In response to this intrusion by a foreign object the body sets up an inflammatory process. The procedure also encourages a high oxygen state in the middle ear. Both of these factors lead to free radical and oxyradicals formation, causing changes in the cells lining the middle ear that lead to scarring and fibrosis. T. Ovesen and his team of ENT researchers at the Aarhus University in Denmark instilled liquid NAC through these small tubes. The drug reduced inflammation and prevented the long-term scarring that normally follows this condition.

DEAFNESS AND HEARING LOSS

Almost 30 million North Americans experience sufficient hearing loss to interfere with their ability to converse. This is almost one person in ten. One percent of our population cannot hear at all and is considered deaf. Almost a third of individuals over the age of 65 have some form of hearing loss and this figure increases with age.

There are many causes of impaired hearing, all of which broadly fit into two categories: conductive hearing loss caused by a mechanical problem in the middle ear or external ear canal and sensorineural hearing loss, a problem of the inner ear or auditory nerve. In the latter category the problem may be sensory – in the cochlea, the essential organ of hearing – or neural – affecting the auditory nerve itself. Causes of hearing loss include physical trauma, exposure to repeated loud noise, infection, tumors and malignancies, obstruction of the ear canal, genetic defects, toxins and drugs, various neurological diseases and the aging process in general.

NOISE EXPOSURE

Exposure to noise accounts for about one third of all hearing loss cases. It's particularly unfortunate because most cases are avoidable. All it takes is appropriate caution. Teenagers often enjoy and are fed damaging levels of noise. Preventive aids such as earplugs can help. So can turning down the volume.

People working in noisy environments and those with noisy hobbies all risk their hearing. Most of us have experienced that buzzing, ringing or hissing in our ears after leaving a concert or construction site. Hearing is sometimes diminished temporarily. This can last minutes or days and is generally followed by a return to normal. This is a 'temporary threshold shift' and is caused by injury to the sensitive hair cells in the cochlea – the spiral shaped organ in the middle ear. Severe, repeated or prolonged exposure to excessive noise can destroy these neurological hair cells and lead to permanent hearing damage.

Interestingly enough, the cochlea can be trained to withstand greater noise levels and suffer less damage. This is known as 'sound conditioning' or 'toughening'. Priming the ear to low level noise before the higher levels seems to protect from hearing loss. Researchers at the Albert Einstein College of Medicine in New York examined the biochemical changes found in sound conditioning. They saw that certain enzymes which raise GSH levels or keep glutathione in a reduced (non-oxidized) state were stimulated by low noise exposure. This suggests that whatever protects or increases the glutathione system in the cochlea also protects against noise-induced hearing loss.

Other studies in the area of glutathione and noise exposure lend support to this model. A team at the Kresge Hearing Research Institute at the University of Michigan chemically depleted glutathione levels using the drug BSO, with the result that noise-induced hearing loss was more profound. The same team went on to raise GSH levels with OTC, with the result that hearing loss was minimized.

Dr. Denis McBride, from the Office of Naval Research in Arlington, Virginia, found that delivering antioxidants directly to the cochlea through a small tube could prevent permanent damage following noise exposure. This treatment must be delivered within six hours of exposure. Other researcher suggest that workers with prolonged noise exposure would gain long-term benefits from elevated glutathione levels.

HEARING LOSS INDUCED BY DRUGS OR TOXINS

Exposure to all sorts of pharmaceutical chemicals may lead to sensorineural hearing loss. They include high doses of aspirin, several different antibiotics, a number of diuretics (high blood pressure medication), quinine, and several chemotherapy agents.

One of these chemotherapy drugs is cisplatin. It is a common cancer treatment that can also damage auditory neurons (hearing nerve cells). Researchers have shown that this damage is caused by free radicals in the tissue. Studies lowering GSH levels show increased damage, those raising GSH decreased the damage. It seems that raising glutathione levels could protect patients from both the hearing and the kidney damage that may result from this treatment.

Similar studies have been conducted in relation to aminoglycoside antibiotics (gentamycin, kanamycin, amikacin, others) and loop diuretics (lasix, furosemide, ethacrynic acid, others). Research teams from the USA (University of Michigan, Southern Illinois University), Japan (Hiroshima General Hospital), and Germany (Universitats HNO) all found that substances used to raise glutathione activity have a protective effect against the hearing loss than can be provoked by these drugs. Dr. C.P. Maruzi from the Houston Medical Center even suggests that deafness following acute meningitis may be caused by free radicals in the inflamed tissue, and that antioxidants preventing lipid peroxidation in the auditory nerve would protect the patient.

DENTISTRY

A fact little known by doctors but common knowledge to dentists is that dental and periodontal (gum) disease is the most common illness in America. Even more importantly, periodontal disease has recently been linked to more serious systemic diseases that may be encouraged by poor oral hygiene. Robert Genco, editor-in-chief of the Journal of Periodontology has said, “It seems clear that gum disease, far from being just a oral health problem, actually represents a significant health risk to millions of people.”

It goes beyond unsightly smiles and bad breath. The infections and toxins harbored in the mouth have been linked with heart disease, stroke, bacteremia, prosthetic device infection, diabetes, pulmonary disease, impairment of fetal growth and other systemic disease. Dr. Charles Mayo, founder of the Mayo Clinic is purported to have said, “preventive dentistry can extend your life expectancy 10 years.”

One of the most impressive of all studies is the Veteran Administration's Normative Aging Study in Boston. They followed the medical history of over one thousand outwardly healthy men, starting in the 1960's. Those who started out with any sign of gum disease suffered about twice the death rate – mostly from cardiovascular disease – than those with healthy gums. At a recent conference on the subject, Dr. Raul Garcia, one of the researchers, stated, "Gum disease kills. Floss or die!"

Many links have been made between the infective and inflammatory processes of periodontitis and the generation of free radicals. Research is required to see whether elevated glutathione levels will combat the formation of free radicals and bolster the immune system's defenses. Immunotec Research has developed a toothpaste with glutathione precursors. Direct application to these tissues may combat the disease.

CONCLUSION

Scientists studying the eye have long recognized the critical importance of glutathione as an ocular antioxidant. Practical applications are now available for the prevention and treatment of disorders like cataract and macular degeneration.

GSH has a triple role in the upper respiratory tract. Its ability to suppress free radical formation, detoxify environmental xenobiotics and reinforce the immune system gives us a tool against airway irritation from pollution, sinusitis, otitis and other infections and inflammations of our ears, nose and throat. Having long utilized NAC in pulmonary disease, the medical profession is now pursuing its use in ear nose and throat diseases. An interesting clinical application of elevated GSH is the treatment and prevention of noise-induced hearing loss as well as that caused by certain ototoxic drugs.

The importance of dentistry in total health care is only recently being fully acknowledged. Periodontal disease has been identified as a risk factor for heart disease, stroke and other systemic disease. Enhanced glutathione levels should be part of a good oral hygiene program.

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