



## GRAVES' DISEASE & THYROID FOUNDATION

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# Eye Changes With Graves' – Continuing Concepts

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**(Note: See last page for Figures)**

The exact cause and pathophysiology of the soft tissue changes in the eyelids and orbit in Graves' disease continue to remain unknown. The management of these changes, particularly in the acute stage, presents a very frustrating problem to the doctor and the patient. This area is filled with controversy as illustrated by the recent example of our First Lady's problems in the management of her acute changes with Graves' disease. Her situation, even though somewhat distorted by the media, represents the dilemmas and frustrations which the physician encounters when faced with a patient with acute progressive changes of the eyes with Graves' disease.

There are no major breakthroughs in the management of these patients – so why is this a subject of a bulletin? Even though there are no “breakthroughs,” there

still have been some refinements in management techniques and recognition that there are more dimensions than previously thought in the modes of treatment available to the patient. These techniques may offer our patients better treatment with a better end result of this condition.

### Natural History

The natural course of the active phase of Graves' disease (soft tissue, eyelid and orbital changes) that occur run a course of activity of about six months to a year. Whatever eye changes have occurred may then stabilize (Rundel's curve). In some cases, as edema subsides, some improvement may occur. The actual pathologic process is still felt to be an immune attack on extraocular muscle tissue within the orbit and fibroblasts contained therein. A great deal of scarring is produced, and also the fibroblasts under attack release great quantities of glycosaminoglycans, which is

very hydrophilic causing water to be absorbed producing severe orbital edema. The natural course of these changes can vary from patient to patient. The course may be improved with use of anti-inflammatory measures, or made worse by treating the thyroid gland (radioactive iodine; surgery). This is not to say that the thyroid gland should not be treated, but that it is a well known phenomenon that the eye changes can accelerate following this treatment. Improvement of the eye changes may be seen when the inflammation abates (presumably changes that are due to edema and not fibrosis). After the inflammatory phase (“hot phase”) subsides, residual changes of increased tissue and scarring will remain, and the Graves' patient will then be in the inactive phase (“cold phase”).

### Treatment of the Active Inflammatory Phase – “Hot Phase”

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Every effort to suppress inflammation and reduce edema is made during this period. Because of a constantly changing situation, one should avoid surgery in the “hot phase.” Vision should be monitored, because in extreme cases, orbital pressure will increase to the point that the optic nerve becomes compressed. The first sign of reduced vision before actual acuity is lost is color desaturation. Other supportive treatment can be used such as head elevation, topical lubricants and other remedy type treatments. In extremely mild cases of inflammatory changes, one may elect to do nothing; however, if progressive changes do occur, the physician is compelled to intervene with some mode of treatment to reduce inflammation or try to prevent irreversible changes that may affect ocular health and function.

### **Systemic Steroids**

For many years, high dose cortisone has been the first line of defense against the orbital inflammation in Graves’ disease, and the standard approach has been to treat the patient with immuno-suppressive doses (usually greater than 100mg Prednisone equivalent per day) for two weeks. If there

has not been a “significant” response within two weeks, then the steroids have been discontinued. Sergot et.al. have identified immunologic subgroups of Graves’ patients and have categorized them into “Responders” and Non-responders” depending on certain populations of t-lymphocytes in the peripheral blood. Clinical experience has shown that some patients respond quite dramatically to steroids; some do not respond at all, and others somewhere inbetween. A trial of the systemic steroids is certainly indicated with acute progressive changes in Graves’ disease.

Guy and Rubin have felt that in patients who have not been particularly responsive to steroids, the “immuno-suppressive level” has simply not been reached. They have hospitalized patients with the most severe changes of visual loss and treated them very intensively for three or four days with extremely high doses of methyl-prednisolone in a pulse type manner with three to five mg per kg and have effected very dramatic responses in vision. Some of the patients did have recurrence of visual loss, and went on to other modes of treatment, however. It is an avenue that should be considered in some patients.

Also, in the area of steroids, it has been shown recently by Bartelena et.al. that the worsening of Graves’ orbitopathy eye changes that are so commonly seen when the patient is treated with radioactive iodine can be lessened dramatically with the use of cortico-steroids during the treatment period. This was published in the *New England Journal of Medicine* in 1989. The complications of steroids are well known, and the patient should be so informed when undergoing this therapy.

### **Radiotherapy**

It is a well-known fact that the acute inflammatory orbital changes in Graves’ disease can be suppressed, and in some cases, an almost prophylactic type effect can be obtained with the use of high voltage orbital radiotherapy. However, this is an area of great controversy because of the dosage needed and possible side effects. Very smart people at the Mayo Clinic are in disagreement with its use, whereas others around the country, such as Kriss at Stanford, have promoted it successfully for years. It is of interest to note that it is the therapy which our First Lady received for her progressive inflammatory orbital changes caused by Graves’ disease.

The techniques were originally outlined by Kriss and consist of delivery of divided dosages of 2000 RADS (2000 gry) super-voltage radiotherapy. The linear accelerator is preferred because of its highly focused effect with fewer side effects due to less scattering. There are many series in the literature showing an extremely beneficial effect in patients with compressive neuropathy, and even more recently papers show a beneficial effect in acutely inflamed orbits that are not a risk for visual loss, but are critical to avoiding ocular complications. The dose of 2000 RADS is below the dose that produces radiation retinopathy in normal eyes. It is felt that the dose that will produce radiation retinopathy in normal eyes is 3000 RADS, and 5000 RADS for radiation optic neuropathy. It is also felt that patients who have ischemic disease, particularly diabetics, probably have a much lower threshold for retinopathy, and the radiation technique is contraindicated in these patients.

### **Orbital Decompression**

A surgical enlargement of the bony socket to relieve compressive changes affecting the optic nerve has been used for years

successfully. It still may be needed in certain patients who are not responsive to steroids or radiotherapy or for other reasons, but it is a formidable procedure with risk when successful from the standpoint of restoring vision. It does introduce other problems of strabismus and lid malposition that need further surgery. This is particularly true if the decompression is performed when the orbit is "hot" with a lot of orbital edema. It should be considered a last resort treatment mode for patients who have severely threatened visual loss that cannot be treated by these other modes of treatment.

### **Treatment of Graves' Disease in the Inactive or "Cold" Phase (Residual Changes)**

When the inflammatory process has stabilized and the orbital edema has subsided, the Graves' patient may be left with exophthalmus, lid retraction and double vision. Exposure problems, as well as disfigurement, may be present. Since the patient has become stable and since no more inflammatory changes (presumably) will occur, surgery is indicated to rehabilitate the patient with Graves' disease. It is to be emphasized that in this phase, one should not use

antiinflammatory agents, because the inflammation is gone and the treatment does no good. Surgical rehabilitation is the indicated treatment in this phase of the disease. One may ask how does the physician know when the changes are stable. The answer is that one does not know for certain, because there is no chemical test or blood test that can be measured to indicate that the immune process is finished. The substance causing the eye changes is not known, but it is known that it is not the thyroid hormone. Eye changes occur in the face of hypo, hyper, or euthyroidism. Possibilities for the source of the substance affecting the eye are:

- sub fragments of TSH (disproved),
- shared antigenicity of the eye tissue and thyroid gland for an unknown antibody (not proven),
- "leaking" thyroid gland, thyroglobulin-immune complexes travel to orbital tissue (strong case, but not proven).

The evaluation of activity of eye changes is based on clinical signs. Six months of stabilized eye changes during which the patient has a stabilized treated thyroid status if felt to be enough time to consider them stable It is felt by me (but certainly not

proven) that after treatment of their hyperthyroidism, patients who do have a significant amount of residual thyroid gland tissue left may develop additional changes even after this period.

The changes that occur usually fall into three areas with regards to surgical procedures: exophthalmus, eyelid retraction with herniated tissue, and double vision.

In most cases, the double vision is either treated with eyeglass prisms or strabismus surgery, which is best performed by the strabismus surgeons.

When confronted with the stable Graves' patient with very prominent eyes and corneal exposure, the initial decision that is made regarding surgical rehabilitation is whether just the eyelid surgery alone can accomplish the desired effect. It is possible to improve almost every patient with eyelid surgery alone; however, some patients with quite severe exophthalmus can never reach the best rehabilitative state without undergoing an orbital decompression.

## Orbital Decompression Technique

It is felt that the most effective and safest method of enlarging the bony socket for patients who have prominent eyes is the *antral* (removal of the floor of the orbit) - *ethmoidal* (removal of the medial wall of the orbit) type of orbital decompression. In some severe or asymmetric cases, the lateral orbital wall can also be expanded. The best surgical approach for the decompression is trans-lid with a canthotomy, eversion of the lower lid, and exposure of the floor and ethmoids through this fornix excision. This approach is shown in Figures 1 and 2. This approach also allows the surgeon to remove the fat pads in the lower lids to enhance the effect. Good retroplacement of the globe can be obtained from this approach, and the side effects are very few. Varying degrees of retroplacement of the globe are obtained depending on how "stiff" the orbital tissue is.

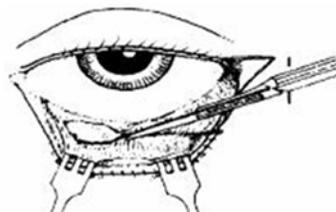


Figure 1

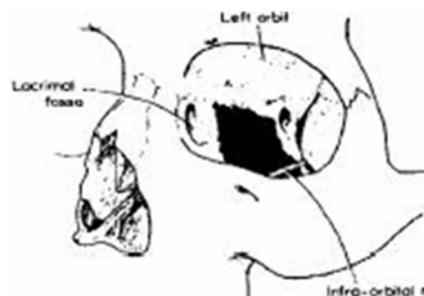


Figure 2

The most complete rehabilitation is really a two-step procedure with orbital decompression followed by eyelid surgery. After the orbital decompression, the eye settles backward and downward, which improves the lower lid; but because of the stiffness of the upper lid, there is still lagophthalmus with retraction of the upper lid. In the large majority of cases after decompression, patients will need additional upper lid surgery, which can be performed on an outpatient basis.

Figure 3 and Figure 4 show a person before and after orbital decompression who will need additional upper lid surgery. Figure 5 and Figure 6 show a person before and after orbital decompression followed by additional upper lid surgery (the "two step" sequence).

In patients who have mild amounts of exophthalmos and mainly lid retraction, only eyelid surgery is needed. This is accomplished by recession

of the scarred retractor muscles. At the same time, most of the patients require some trimming of the excessive fatty tissue skin. Figure 7 and Figure 8 show a person before and after eyelid surgery alone. In this person, the “prominence” of the eyes was due to eyelid retraction; not much exophthalmos was present.

**References for Additional Reading:**

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decompression followed by additional upper lid surgery (the “two step” sequence).



Figure 3



Figure 4



Figure 5



Figure 6



Figure 7



Figure 8