



Information Sheet: Study of Thymectomy for Treatment of Myasthenia Gravis

You are being asked to participate in a study of thymectomy for the treatment of myasthenia gravis. Your first reaction may be “why?” Thymectomy has been used in the treatment of MG for nearly 50 years. At first patients and some doctors may be surprised that such a study is being performed. Many MG experts, including those doctors involved in this trial, think that thymectomy increases the chance of remission. However, treatment has changed since thymectomy first became an accepted therapy for MG, and many of the studies of thymectomy do not clearly determine whether surgery or other medical treatments, like prednisone, helped the patient most.

Physicians and patients are now more demanding in the proof that they require in making a decision about health care. In 2000, a report from the American Academy of Neurology authored by Drs. Gary Gronseth and Richard Barohn reviewed studies of thymectomy for myasthenia gravis and found “All currently published studies have serious methodological flaws that prevent definitive conclusions regarding the benefit of thymectomy.” Gronseth and Barohn recommended a prospective, randomized trial be done. In the experience of the investigators in this study, patients also demand to know detailed information about the chance of remission after receiving thymectomy or whether medications alone are just as good. We do our best in answering these questions but cannot supply precise answers because of the problems described.

Appreciating the need for a study, Drs. John Newsom-Davis from Oxford University in England, Gil Wolfe from the University of Texas Southwestern Medical School, Henry J. Kaminski from Case Western Reserve University, Alfred Jaretzki from Columbia University, and Gary Cutter from the University of Alabama at Birmingham have organized more than 70 investigators from six continents into a collaborative trial of thymectomy for treatment of generalized MG. The study has been funded by the National Institutes of Neurological Disorders and Stroke (NINDS). Starting in 2003 these investigators worked together to refine the study's design to meet the strict demands of NINDS for patient safety and scientific rigour. Funding was awarded in 2005. Recruitment to the study began in July 2006, and is continuing.

The basic design of the study is for patients with generalized MG to be randomized to receive prednisone under strict set guidelines OR thymectomy and prednisone with the same prednisone treatment plan. The most important, and often the most difficult aspect for some patients to understand, is “randomizing.” This means, “you have an equal chance of either undergoing the surgery or not having surgery, similar to a flip of a coin.” A patient needs to understand that to participate in this study they must accept that they may, or may not have, a thymectomy. Why does this need to be done? As we all know, each MG patient is unique, and the investigators need to make sure that the differences among patients are equally represented (to the best possible extent) in those who receive a thymectomy and those who do not. The best way to do this is “randomization”. If patients (or doctors) were to choose whether to undergo the thymectomy, it is possible that a “bias” would develop. It is possible that all the patients



that chose to have a thymectomy might have certain other characteristics (higher acetylcholine receptor antibody levels, be younger, or some other trait that cannot be identified) that make it less likely that they would benefit from the surgery. If that occurs, the results of the study would again be confusing or wrong!

You also need to be sure that you are willing to be monitored by the study for 3 years. During the 3 years of the study, the patients are monitored by specific examinations of their muscle strength, their prednisone dose, and development of adverse effects (any medical problems they have during the study). To avoid physician bias, the patient is asked NEVER to tell the study examiner to reveal if they have had a thymectomy or not (the neurologist at each study center will know so you always receive the safest medical treatment during the study). The study is long so patients need to be willing to be monitored for 3 years. If their treating neurologist or the patient feels that the patient is doing poorly in the study, other drugs can be added or they can stop participation in the study at any time.

Everyone receives the accepted treatment of prednisone. For the study to be effective a single operative procedure must be employed. The thymectomy procedure to be used is the extended transsternal approach. This has been selected because it is recommended as the procedure of choice at most major medical centers and predictably removes most or all of the thymus. Whether other thymectomy techniques produce similar results will have to be determined by similar rigorous studies in the future. The study does NOT allow any other type of thymectomy. The study cannot take a chance of more confusion in understanding MG treatment by allowing a surgeon or patient to choose the surgical method to be used

If you agree to participate in this study, you must be willing to have a thymectomy. The thymectomy procedure is an extended transsternal procedure and involves cutting through your breastbone. You will have a scar that extends from below your neck to the bottom of your breastbone. The investigators think that this procedure removes the greatest amount of thymus. As with any surgery, there are risks of complications and these are described in the consent form for this study. Also, if you are selected to undergo a thymectomy, the surgeon will further describe possible complications. If you are absolutely unwilling to undergo the surgery, you should not participate. If you feel that you want to have a thymectomy, you should not participate in this study, because you may be chosen NOT to have the surgery.

Patients will be at least 18 but less than 60 years of age and have generalized MG (patients with pure ocular myasthenia are not to be studied) and are seropositive (have antibodies against the acetylcholine receptor in the blood). Patients with a thymoma are not to be studied because all experts agree that these patients should have the thymoma removed. The goal of the study is to determine whether after 3 years of treatment patients receiving a thymectomy have received lower doses of prednisone, have fewer side effects, and are just as strong or stronger than patients not having the thymectomy.

You may wonder why cyclosporine or mycophenolate are not being studied, or why older patients or those with ocular MG are excluded. It is important to understand



that not all answers can be reached with one study. If too many questions are asked, none will be answered. The reason that so many centers are needed is that large numbers of patients have to be studied to have clear understanding of the result, because again the many differences among patients must be “equaled out”.

The study will take about 5 years to be completed. When it is completed we believe that the MG community will have a long-awaited definitive answer as to whether the generalized MG patient does better with a thymectomy than standard medical therapy alone.