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S13-00096: Investigation of the Role of Steroids in Enhancing Voice Therapy Outcomes
RESEARCH PROTOCOL (version 6.19.13)

SPECIFIC AIMS

The recently-published clinical practice guidelines (CPG) for hoarseness (1) pointed out several significant deficiencies in the laryngology literature. **One of the more confounding statements in the document was related to the paucity of evidence for the use of steroids for the treatment of patients with complaints of hoarseness, regardless of etiology.** Specifically, the document only suggests a role for steroids in the context of 'allergic laryngitis' in vocal performers. To address this comment, we recently surveyed the greater otolaryngology community in an attempt to describe current practice patterns with regard to the use of steroids for voice disorders (manuscript in revision). The results of this survey confirmed our hypothesis: steroid use is, in fact, quite common among otolaryngologists for a variety of diagnoses underlying voice complaints. Admittedly, these types of surveys are fraught with confounds, but frankly, **this mismatch between the literature and clinical practice presents an opportunity to address this rather large research gap in the study of this very commonly used drug class, one that would benefit from comparative effectiveness research.**

Our anectdotal experience suggests that steroids are effective in improving voice in patients related to the presence of benign vocal fold lesions. Specifically, we commonly use steroids to reduce edema surrounding benign lesions yielding short-term improvement in vocal quality. We also noticed that some patients will have sustained improvement in voice in the long-term following a short course of oral steroids. We hypothesize that these outcomes may be due to a reduction of laryngeal inflammation and phonatory pressures required due to improved glottal closure as well as reduced vocal fold mass, thereby improving the overall laryngeal biomechanics and providing an ideal starting point for behavioral voice therapy.

The current proposal seeks to prospectively and systematically address these phenomena. Typically, patients diagnosed with benign vocal fold lesions are referred for voice therapy for treatment of such lesions that are deemed to be non-surgical cases. Voice therapy has shown benefit for the treatment of a variety of such lesions.(2-10) For the current study, we propose to introduce oral steroids as a variable prior to the initiation of voice therapy. **We hypothesize that subjects in the steroid treatment group will have an enhanced voice therapy experience as evidenced by more rapid improvement, the necessity for fewer voice therapy sessions, and a more global voice improvement when compared to the non-steroid treatment group.**

Specific Aim #1. To determine the effectiveness of a short course of oral steroids prior to the initiation of behavioral voice therapy in patients with benign, phonotraumatic vocal fold lesions.

We hypothesize that a short course of oral steroids with resultant diminished vocal fold edema will increase the efficacy of voice therapy for patients with benign, phonotraumatic lesions. Specifically, we hypothesize that the improved inflammatory profile of the vocal folds will allow for contemporary voice therapy techniques to optimize vocal efficiency with an increased likelihood for long-term translation to everyday scenarios. To address this hypothesis, we seek to perform a prospective, randomized trial to compare objective, subjective, and patient-based outcome measures between two cohorts: patients with benign vocal fold lesions that are assigned to voice therapy that will receive oral steroids immediately prior to the initiation of voice therapy and those who receive no steroids prior to therapy.

Data obtained under the auspices of this mechanism will not only address a significant deficiency in the clinical practice guidelines, but also alter the course of treatment for many patients, potentially yielding a paradigm for optimal patient care.

(a) Significance

Glucocorticoids were first used in the 1940's to treat severe rheumatoid arthritis.(11) The discovery of this class of drugs irreversibly changed the treatment of inflammatory disorders and led to the award of a Nobel prize. Since the initial discovery, steroids have found their way into everyday clinical use for a variety of different disorders. In Otolaryngology, steroids are used in the treatment of facial nerve disorders, chronic sinusitis, and airway disorders, among others.(12-18) Although used commonly for the treatment of voice disorders (unpublished data, manuscript in revision), very little evidence exists for their use.

The clinical practice guidelines (CPG) for hoarseness (1), cites that the only evidence for steroid efficacy in treating vocal fold disease was for allergic laryngitis and for rheumatologic disorders.(19-22) However, in reviewing the citations, it is evident that the "evidence" for use in allergic laryngitis is just expert opinion. Since the publication of the CPG, one publication has reviewed the use of oral steroids in the treatment of patients with vocal fold polyps. In the study, the authors noted that 70.6% patients treated with oral corticosteroids had either complete resolution or shrinkage of vocal fold polyps. However, the retrospective nature of the study and the lack of controls make it difficult to make any definitive conclusions with regards to the true effects of these drugs on vocal fold polyps.

Intralesional steroids have been studied to a greater degree.(23-28) The rationale for their use is based on the high local concentration of drug at the site of injection. In a prospective, multicenter study, Woo, et. al. demonstrated improvement in almost 85% of benign vocal fold lesion cases (Reinke's edema, vocal polyp, nodule, and scarring). In a similar study, Hsu, et. al. found a 91% positive response rate with complete remission in 59% in vocal fold polyp cases treated with intralesional steroid injection.(24) In another prospective study, injected steroids were found to resolve or improve vocal fold nodules in 93% of cases by 4 weeks after treatment.(25) **These studies point to the fact that steroids do have a positive effect on vocal fold pathology, at least when delivered in high doses.**

In our practice and in those at other voice centers, steroids (oral and intralesional) have a wide application in a variety of vocal fold lesions. We have used these drugs orally for the acute treatment of inflammatory conditions of the vocal folds, such as viral laryngitis and vocal fold hemorrhage. We have also used them in an oral form in various other circumstances, including perioperative management of benign vocal fold lesions and for acute and chronic treatment of benign vocal fold lesions. Anecdotally, we have seen value in the use of these drugs orally taken for these indications, though we cannot point to any significant literature base that supports their use. **This is a critical research gap that needs to be addressed.**

(b) Innovation

The current study is innovative, as it will be the first of its kind—one that will prospectively study the efficacy of oral steroids for the treatment of benign vocal fold lesions in a controlled manner. As mentioned above, this is of importance, as these drugs are being used routinely in practice without any evidence base in the literature. Such a study is long overdue.

The current proposal employs a controlled, prospective, randomized, blinded study design. There are many confounding variables in the treatment of vocal fold lesions. For those treated non-surgically, the patients are typically prescribed voice therapy, which includes a range of behavioral modifications and motor learning techniques, along with vocal hygiene measures and education. Since it would be unethical to withhold voice therapy for many of these patients, we chose instead to include it in the study design, as described below.

The current proposal is also innovative in that it will collect several different outcome measures, including objective, subjective, and patient-based outcome measure. The study will allow for quantification of lesion size before and after oral steroid treatment, expert rating of stroboscopy,

subjective rating of vocal quality, and patient rating of voice handicap (Voice Handicap Index-10 or VHI-10 (**see attached questionnaire**)).

In addition, the study will also investigate the potential added advantage of the use of steroids in patients undergoing voice therapy. We hypothesize that oral steroids will lead to a reduction in lesion size, which will substantially aid in the delivery and incorporation of voice therapy techniques, since the reduced lesion size will likely improve glottal closure and reduce vocal fold mass, thereby improving the overall laryngeal biomechanics and providing an ideal starting point for behavioral voice therapy.

(c) Approach

Subjects and Protocol

The specific aim of this project is to determine the effectiveness of a short course of oral steroids prior to the initiation of behavioral voice therapy in patients with benign, phonotraumatic vocal fold lesions. As mentioned above, the study is designed to be prospective, randomized, and controlled. The study group will be recruited from our patient population. Our Center serves the population of the greater metropolitan New York area and has a high volume of patients that present with benign, phonotraumatic vocal fold lesions. Subjects that are non-surgical candidates that are assigned to receive voice therapy at our institution by a single voice therapist (Gherson) will be eligible for the study. Potential subjects will be identified by the PI or research staff and will be enrolled right after their clinical visit if they agree to the study protocol and do not meet the exclusion criteria (**Figure 1**). Recruitment will be done solely from the PI's clinical practice. The PI (Amin), research coordinator (Achlatis) or the co-Investigators (Gherson, Branski) will be obtaining written consent after their clinical visit. Participants will be provided a copy of the completed consent form. Subjects are free not to participate in the study and their decision will not alter the quality of medical treatment that they will be receiving.

At the time of enrollment, the study coordinator will open a pre-sealed envelope that will assign a subject to either receive oral steroids or placebo prior to the initiation of voice therapy. There will be twenty envelopes each that will read either "steroid" or "placebo". Replacement envelopes will be added if/when subjects drop out from the study.

According to their assignment, subjects will then be dispensed pills and counseled on proper dosing and potential side effects. Subjects assigned to the "steroid" arm will be prescribed two 20 mg prednisone doses per day (40 mg total), taken together in the morning for four days. This dose was chosen as it is the most common dose used in our practice and is within the lower part of the starting range recommended for this drug for the treatment of other inflammatory conditions of the airway, including asthma. A four-day treatment regimen has demonstrated efficacy in our experience, while reducing the risk of side effects.

The therapist (Gherson), the scientist that will be conducting the evaluation (Branski) and other individuals involved in collection and analysis of data will be blinded as to whether the subject received drug. The prescribing physician (also the PI) will not be blinded, as this would interfere with routine clinical care of the subject. The research assistant (Achlatis) will also be non-blinded, as he will be in charge of the randomization and tracking process. Neither of these two individuals will be directly involved in providing or directing therapy, nor will be involved in collection or analysis of the data.

Prior to the initiation of therapy, subjects will be asked to return for an "interval evaluation", which is a research visit. During this evaluation, subjects will undergo videostroboscopy and voice evaluation by one of the co-investigators (Branski). Measures to be collected are described in the following section. Subjects will be reimbursed $75 for the time and expense involved in returning for this research evaluation, which is considered outside of routine clinical care. The charges for this visit will also be paid by the research account for the same reason.

Subjects will then enter the voice therapy part of the protocol. They will receive an initial evaluation, which is part of routine clinical care. This evaluation will be used to determine the best mode of therapy to pursue. Subjects will receive the form of therapy that specifically meets their needs. The therapist will then keep records of the subject's progress, including a timeline of progress. Subjects will be asked to maintain a regular schedule with the therapist, as this is ideal and will allow for better tracking of time to improvement. During therapy, subjects will be asked to fill out VHI-10 forms on a bi-weekly basis. These forms will be collected for study purposes.

At the completion of therapy, subjects will follow-up with the treating physician (Amin) for a routine follow-up clinical visit. During this visit, routine videostroboscopy and voice evaluation by the co-investigator (Branski) will take place. The general experimental design is summarized in **Figure 2**.

Dependent Variables and Data Collection (Figure 3)

1. **Voice Handicap Index (VHI)-10**. The primary dependent variable is difference in VHI-10 scores from baseline (pre-treatment). The VHI-10 is a standardized and validated instrument that measures patient perception of their voice disorder.(29) It is administered routinely as a component of clinical care at the NYU Voice Center. Completed forms are scanned into the patient's electronic medical record for easy access and longitudinal comparison. For this study, VHI-10 data will be collected during the initial, interval, and final evaluations.
2. **Video-Perceptual Analysis.** Videostroboscopic clips will be collected during clinical visits to the NYU Voice Center per normal protocol. Briefly, following application (spray) of topical oxymetazoline and 4% lidocaine, a flexible endoscope will be passed through the nasal cavity and into the pharynx. Subjects will be asked to perform a variety of vocal tasks, including sustained phonation, rapid phonation, sniffing, and counting. Each exam will be recorded as is routine in our practice. There will be a total of three videos collected from each subjects (initial, interval, and final). The images/video obtained will be used for two separate analyses, as described below. For the expert analysis of the videostroboscopy, the clips will be edited in a manner that allows for de-identification and shortening of the clips to demonstrate the most salient parts of the video, including clear imaging of the pathology and at least 5 seconds of continuous mucosal wave. The edited clips will then be sent to 6 expert reviewers (otolaryngologists with a strong laryngology background) for review. The clips will be paired as follows: initial with interval and interval with final. The videos will be presented in random order, followed by a rating form. On the rating form, the reviewers will be asked to rate change in both mucosal wave and glottal closure on a relative 3-point scale (worse, same, better), as described in our previous work.(30) The reviewers will then be asked to return the rating forms, so the data can be collated. Twenty (20) percent of the samples will be repeated randomly for both the expert reviewer and lesion measurement analyses to assess intra-rater reliability. Data will also be subjected to analysis of inter-rater agreement.

   The second analysis will be to measure lesion size. This method has been previously described by our group.(30) Briefly, still images of the glottis will be obtained from the video such that the vocal folds are captured in an open position (at least 40 degrees at the anterior commissure). Image J software (NIH) will then be used to outline the lesion and measure the length of the ipsilateral vocal fold (as shown in **Figure 4**). The ratio of these will be used as the adjusted size variable. Measurements will be done bilaterally when appropriate.
3. **Audio-perceptual Analysis.** Auditory perceptual analysis will be performed based on the protocol recently developed as a component of the Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V). Subjects are asked to repeat pre-determined sentences into a microphone. The stimulus sentences are collected as a component of routine clinical care at the NYU Voice Center and archived permanently via the Computerized Speech Laboratory (KayPentax, Montvale, NJ). These digitized files will then be culled, edited, and presented in random fashion to three expert listeners (speech pathologists with particular expertise in voice who are uninvolved in the current experiment). The standardized CAPE-V forms will be employed using

the visual analog scale. Data will be collected via measurement of the hatch mark on the 100mm line for each variable. Twenty (20) percent of the samples will be repeated randomly to assess intra-rater reliability. Data will also be subjected to analysis inter-rater agreement as well as the overall change from pre-therapy to the two treatment arms.

4. **Aerodynamic Analysis of Voice.** Aerodynamic analysis of voice will be employed to quantify vocal efficiency (i.e., acoustic output as a function of the pulmonary pressure required to sustain phonation). These measurements are collected as a component of routine patient care at the NYU Voice Center using the Phonatory Airflow System (KayPentax, Montvale, NJ). Essentially, patients are instructed on the appropriate positioning and placement of the mask to ensure no air leakage. Patients are then instructed to produce five productions of /pa/ at their most comfortable pitch and loudness at a rate of approximately 1.5 syllables per second. This protocol is followed at least twice to ensure compliance. The middle three productions will then be subjected to analyses, specifically the variables of average phonatory pressure and dB output will be obtained. This protocol has been described extensively in the literature.(31)

Data Analysis.

In general, data analysis will consist of comparisons of the above collected outcome variables measures from initial to interval evaluations and from interval to final evaluations. Where applicable, we will also conduct comparisons between initial and final evaluations.

Research Versus Non-Research Procedures.

Subjects enrolled in the study will be asked to take either steroid or placebo as described above. Although oral steroids are used regularly in the management of benign vocal fold lesions, in this study we randomize the subjects that will receive steroids versus placebo. This is therefore considered a specific research procedure.

Subjects enrolled in the study will also undergo the data collection procedures described in the section above entitled “Dependent Variables and Data Collection” a total of three times. The initial set of procedures will be performed on the initial visit as a part of the routine clinical care for which the subject is visiting the NYU Voice Center. Similarly, the final study visit is considered part of routine clinical care and the procedures performed will not be performed specifically for research purposes. The procedures performed on the second or interval visit will be considered “research procedures”, since they are being performed outside of routine clinical care. Subjects will be reimbursed for their time and expense in participating in the interval visit and their visit costs will be covered by the study account for this visit as described above. A specific explanation of the procedures that will occur during each visit is provided below (each visit has the same set of procedures):

The patient will complete the Voice Handicap Index (VHI)-10 upon arrival to the clinic. An Audio-perceptual Analysis and an Aerodynamic Analysis of Voice will be performed in the voice lab the speech pathologist (Branski or Gherson). Finally, the patient will be brought to the examination room, where a history and physical examination will be performed, followed by videostroboscopy.

Investigational Drug Use.

As mentioned, subjects will be randomized to receive prednisone or placebo. Prednisone is a drug product lawfully marketed in the U.S. The investigation is not intended to be reported to the FDA as a well-controlled study in support of a new indication for use and is not intended to be used to support any other significant change in the labeling for the drug. The investigation is not intended to support a significant change in the advertising for the product. The route, dose and indication of the medication will be as per FDA approval. The investigation is conducted in compliance with the requirements for IRB review set forth in 21 CFR Part 56 and with the requirements for informed consent set forth in 21 CFR

Part 50. The investigation is conducted in compliance with 21 CFR 312.7 (regarding promotion and charging for investigational drugs).

Risks/Benefits of Research Procedures.

The procedures involving some level of risk that will be involved in this study are listed in below, along with a description of the potential risks and benefits.

Videolaryngoscopy – As mentioned above, this procedure involves the use of topical nasal sprays and passage of an endoscope. The use of oxymetazoline and lidocaine nasal sprays involves a small risk of self-limited nasal bleeding and an extremely low risk of an allergic reaction. The benefit of their use is that they minimize the discomfort of the endoscope. The risks of the endoscope include minor nasal discomfort, self-limited nasal bleeding, and gagging. Vasovagal reactions do occur, but are extremely rare. There is no particular benefit to the use of the endoscope, except to help guide diagnosis and therapy clinically.

Steroids – As mentioned above, half of the subjects in the study will receive oral prednisone (**see attached product information**). There is an extremely low risk of an anaphylactic reaction to prednisone. Other potential risks of long-term use of steroids include the following: sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalemic alkalosis, hypertension, muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, tendon rupture, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathologic fracture of long bones, peptic ulcer with possible perforation and hemorrhage, pancreatitis, abdominal distention, ulcerative esophagitis, impaired wound healing, thin fragile skin, petechiae, ecchymoses, facial erythema, increased sweating, may suppress reactions to skin tests, convulsions, increased intracranial pressure with papilledema, vertigo, headache, menstrual irregularities, development of cushingoid state, secondary adrenocortical and pituitary unresponsiveness, decreased carbohydrate tolerance, increased requirements for insulin or oral hypoglycemic agents in diabetics, posterior subcapsular cataracts, increased intraocular pressure, glaucoma, exophthalmos, and negative nitrogen balance due to protein catabolism. The exclusion criteria, relative low dosage and short duration of the intake of prednisone that is used in this project will minimize possible risks.

The potential benefit of taking prednisone includes possible improved outcome with reference to faster healing time of the benign vocal fold lesion.

Provisions to Protect Privacy of Data and Confidentiality of Subjects.

Subjects will be recruited after their initial clinical visit if they meet the inclusion criteria. Subjects will be approached in the exam room immediately after completion of their visit and the study will be explained by the PI, research coordinator, or co-investigators confidentially.

All written consent forms and other study-related documents will be kept in a single folder located in a locked cabinet within the NYU Voice Center. Digital files related to the project, including collected data and the randomization key will be kept on a password-protected computer of the research coordinator. The final data spreadsheet will be kept on a separate computer within the clinic, where only the personnel involved in this study will have access. The videos from the laryngoscopic exams will be also kept on a password-protected computer that is located in the examination room of the clinic.

Sample Size and Statistical Considerations.

The sample size was based on assumptions related to the primary dependent variable (ΔVHI). Based on a cursory review of our current outcomes, we assumed a ΔVHI of 10 (SD=7) for the placebo plus voice therapy group and a ΔVHI of 14 (SD=7) for the steroid plus voice therapy cohort. Using these assumptions with an alpha error level of 0.05 and a power of 80%, a sample size of 20 in each group

was determined to be adequate to demonstrate a statistical difference between the groups. To ensure adequate enrollment, approximately 60 subjects will be screened, assuming a 33% screen failure rate. The proposed sample size is certainly feasible during the award period given the clinical caseload at the NYU Voice Center. The breakdown of the population characteristics for the proposed study group is listed below and is based on the demographics of the PI's practice.

Total Planned Enrollment: 40

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	5	5	10
Not Hispanic or Latino	15	15	30
Ethnic Category Total of All Subjects*	20	20	40
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	2	2	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	4	8
White	14	14	34
Racial Categories: Total of All Subjects*	20	20	40

Each data will be analyzed separately and presented descriptively as a mean and standard deviation. Furthermore, each variable will be subjected to independent two-tailed t-tests to determine statistically-significant differences between the two experimental arms. Given the diversity of outcomes and the fact that they are largely independent, there does not appear to be the need to perform a Bonferroni adjustment to avoid Type I error. However, the data will be scrupulously analyzed and if evidence of Type I error is observed, such an adjustment will be made.

Timeline.

It is anticipated that the project will take approximately 12 months to complete. We estimate that recruitment and treatment will take place in 11 months and that there will be a 1-month period of data analysis.

Research Staff.

The following are the research staff for this study and their roles:

Milan Amin, MD, Director, NYU Voice Center, Associate Professor, Dept. of Otolaryngology – will perform videostroboscopy and he has expertise in the diagnosis and management of vocal pathology.

Ryan Branski, PhD, Assistant Professor, Dept. of Otolaryngology – will collect voice recordings and aerodynamic measures and has expertise in voice evaluation and conducting voice research.

Shirley Gherson, MA, CCC-SLP, Rusk Institute of Rehabilitation – will provide voice therapy. She is a voice pathologist and specialist in the rehabilitaion of the injured voice.

Efstratios Achlatis MD, NYU Voice Center – will be the study coordinator. He is a research associate and has expertise in conducting voice related research.

Facilities.

The research will be conducted at the clinical offices of Dr. Amin (PI), located at 345 East 37th Street, Suite 306, New York, NY 10016 and at Rusk Rehabilitation Outpatients Services, ACC- 240E 38th street, 17th floor, New York, NY 10016. The offices have the necessary equipment, personnel, and computer hardware/software for conducting the study.

Limitations.

We acknowledge that there are certain limitations to this study. The study sample size is relatively small, although sample size calculations determine that we should be able to demonstrate a significant change if one exists, our results would certainly be more robust with a larger cohort. In this regard, we are limited by budget constraints, since the study is relatively expensive to run. The other major limitation of the study is that we are not differentiating between lesion types. We feel that this is quite difficult to do in reality, since vocal fold lesions, even within a type, are quite variable. Of course, we could theoretically conduct a post-hoc analysis of lesion type as a variable, but our cohort size is likely too small for this.

Future Directions.

In the future, we will need to address the limitations by opening up a multicenter, prospective trial of oral steroids for benign phonotraumatic vocal fold lesions. In this larger trial, it will be possible to differentiate effects of steroids on different lesion types. In addition, it may be possible to investigate dose and formulation effects of different steroids.

This project is a small part of a larger research program examining the role of glucocorticoids for clinical use for laryngeal lesions. In addition to studying the use of oral steroids, we will also study the effects of intralesional steroids for a variety of vocal fold lesions types, including vocal fold fibrosis, which remains a major clinical problem.

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Figure 1

Inclusion Criteria	Exclusion Criteria
Age 18-80 Males and Females	Use of any glucocorticoids (oral, inhaled, or intravenous) within 3 months of the initial evaluation
Presence of phonotraumatic lesion deemed to be etiologic for the complaint of dysphonia	Known allergy or hypersensitivity to oral steroids
Voice therapy deemed to be the primary (or at least initial) treatment to address the dysphonia	Active infection
Willingness to be an active participant in voice therapy	Diabetes Mellitus
	Prior history of radiation to the neck
	Recent myocardial infarction
	Recent gastrointestinal surgery with bowel anastamosis (3 months)
	Active peptic ulcer
	Pregnancy
	Severe depression or history of psycosis
	History of recent laryngeal surgery (within 12 months)

Figure 1. Inclusion and exclusion criteria for the proposed trial.

Figure 2

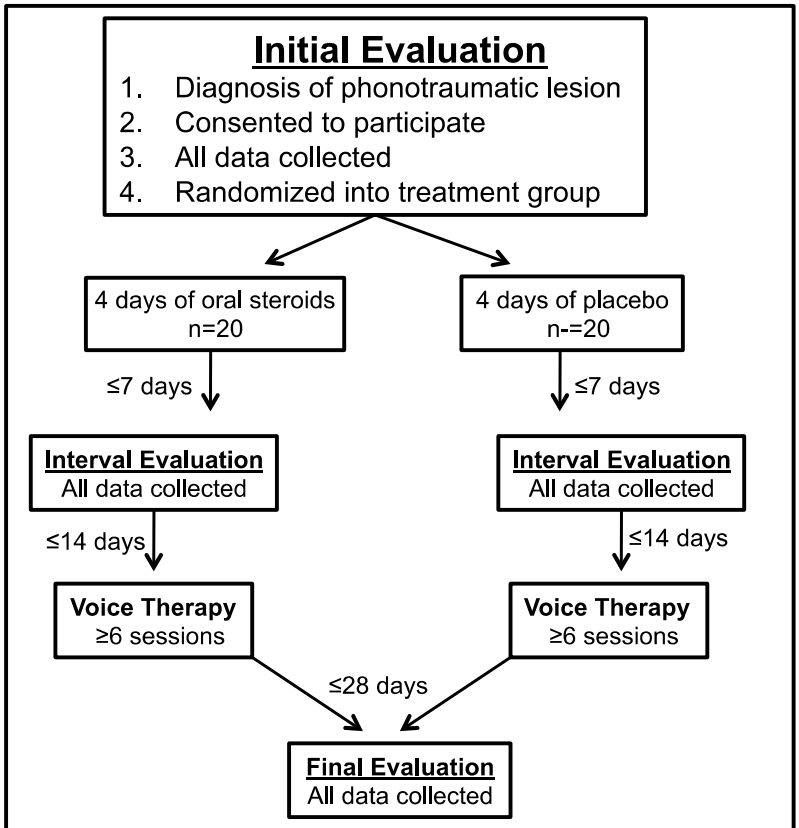

Figure 2. General experimental paradigm for the proposed trial. Briefly, patients will be randomized into either treatment arm following an initial evaluation. Subjects will undergo an Interval Evaluation within 7 days of completing a course of oral steroids or placebo and then must initiate voice therapy with 14 days. Subjects will then undergo a Final Evaluation within 4 weeks of completing therapy.

Figure 3

Dependent Variable	Brief Description
VHI (primary dependent variable)	The change in VHI-10 scores from pre-treatment to following treatment
Video-Perceptual Analysis	Analysis of stroboscopic parameters by expert raters as well as quantification of lesion size
Audio-Perceptual Analysis	The CAPE-V stimuli will be analyzed using a visual analog scale with expert listeners
Aerodynamic Voice Analysis	Collection of acoustic output (dB) and pulmonary pressure (cmH2O) during /pa/

Figure 3. Dependent variables to be analyzed in the current proposal.

Figure 4

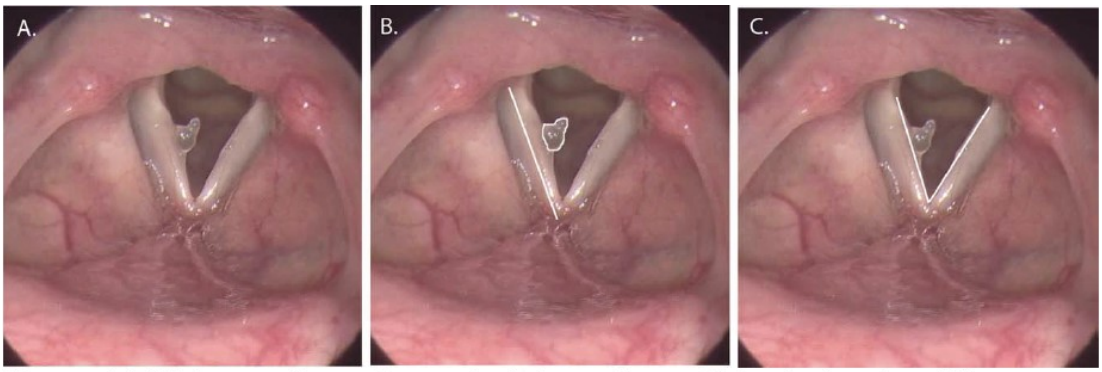

Figure 4: This image shows the methodology of quantifying lesion size. (A) Representative image of right vocal fold polyp. (B) Lesion area and vocal fold length to be measured. (C) Angle of anterior commissure to be measured.

NYU Voice CENTER

Name_____ Date_____

I would rate my degree of talkativeness as the following: (circle response)

1	2	3	4	5	6	7
Quiet Listener			Average Talker			Extremely Talkative

FOR STAFF USE
1- TALK ____
2- VHI-10 ____
3- RSI ____
4- SVHI-10 ____

VHI-10 Instructions: These are statements that many people have used to describe their voices and the effects of their voices on their lives. Circle the response that indicates how frequently you have the same experience.

My voice makes it difficult for people to hear me.	0	1	2	3	4
People have difficulty understanding me in a noisy room.	0	1	2	3	4
My voice difficulties restrict personal and social life.	0	1	2	3	4
I feel left out of conversations because of my voice.	0	1	2	3	4
My voice problem causes me to lose income.	0	1	2	3	4
I feel as though I have to strain to produce voice.	0	1	2	3	4
The clarity of my voice is unpredictable.	0	1	2	3	4
My voice problem upsets me.	0	1	2	3	4
My voice makes me feel handicapped.	0	1	2	3	4
People ask “What’s wrong with your voice?”	0	1	2	3	4

0 = Never
1 = Almost never
2 = Sometimes
3 = Almost always
4 = Always

Please check that you have answered all the questions.

RSI Instructions: These are statements that many people have used to describe their voices and the effects of their voices on their lives. Circle the response that indicates how frequently you have the same experience.

Within the last **MONTH,** how did the following problems affect you?

0 = No problem . . . . . 5 = Severe problem

Hoarseness or a problem with your voice	0	1	2	3	4	5
Clearing your throat	0	1	2	3	4	5
Excess throat mucous	0	1	2	3	4	5
Difficulty swallowing food, liquids or pills	0	1	2	3	4	5
Coughing after eating or after lying down	0	1	2	3	4	5
Breathing difficulties or choking episodes	0	1	2	3	4	5
Troublesome or annoying cough	0	1	2	3	4	5
Sensations of something sticking in your throat or a lump in your throat	0	1	2	3	4	5
Heartburn, chest pain, indigestion, or stomach acid coming up	0	1	2	3	4	5

Please check that you have answered all the questions.

IF YOU ARE A SINGER, PLEASE COMPLETE THE BACK OF THE PAGE.

Singers Only:

I sing the following kind of music (circle all that apply)	country	classical	choral	pop	rock
	gospel	jazz	other _____		

Singing is (circle one) primary source of income secondary source of income not source of income

How would you categorize your singing ? (circle) professional entertainment teacher/instructor music/singing student amateur choir/singing group

Singing Voice Handicap Index-10

These are statements that many people have used to describe their singing and the effects of their singing on their lives. **Circle** the response that indicates how frequently you have the same experience in the **last 4 weeks**.

	Never	Almost Never	Sometimes	Almost Always	Always
1) It takes a lot of effort to sing.	0	1	2	3	4
2) I am unsure of what will come out when I sing.	0	1	2	3	4
3) My voice "gives out" on me while I am singing.	0	1	2	3	4
4) My singing voice upsets me.	0	1	2	3	4
5) I have no confidence in my singing voice.	0	1	2	3	4
6) I have trouble making my voice do what I want it to.	0	1	2	3	4
7) I have to "push it" to produce my voice when singing.	0	1	2	3	4
8) My singing voice tires easily.	0	1	2	3	4
9) I feel something is missing in my life because of my inability to sing.	0	1	2	3	4
10) I am unable to use my "high voice."	0	1	2	3	4

DELTASONE - prednisone tablet
Pharmacia and Upjohn and Company

DESCRIPTION

DELTASONE Tablets contain prednisone which is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Prednisone is a white to practically white, odorless, crystalline powder. It is very slightly soluble in water; slightly soluble in alcohol, in chloroform, in dioxane, and in methanol.
The chemical name for prednisone is pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy- and its molecular weight is 358.43.
The structural formula is represented below:

DELTASONE Tablets are available in 5 strengths: 2.5 mg, 5 mg, 10 mg, 20 mg and 50 mg. Inactive ingredients: **2.5 mg**—Calcium Stearate, Corn Starch, Erythrosine Sodium, Lactose, Mineral Oil, Sorbic Acid and Sucrose. **5 mg**—Calcium Stearate, Corn Starch, Lactose, Mineral Oil, Sorbic Acid and Sucrose. **10 mg**—Calcium Stearate, Corn Starch, Lactose, Sorbic Acid and Sucrose. **20 mg**—Calcium Stearate, Corn Starch, FD&C Yellow No. 6, Lactose, Sorbic Acid and Sucrose. **50 mg**—Corn Starch, Lactose, Magnesium Stearate, Sorbic Acid, Sucrose, and Talc.

ACTIONS

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.
Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS

DELTASONE Tablets are indicated in the following conditions:

1. **Endocrine Disorders**
   Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance)
   Congenital adrenal hyperplasia
   Hypercalcemia associated with cancer
   Nonsuppurative thyroiditis

2. **Rheumatic Disorders**
   As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:
   Psoriatic arthritis
   Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy)
   Ankylosing spondylitis
   Acute and subacute bursitis
   Acute nonspecific tenosynovitis
   Acute gouty arthritis
   Post-traumatic osteoarthritis
   Synovitis of osteoarthritis
   Epicondylitis

3. **Collagen Diseases**
   During an exacerbation or as maintenance therapy in selected cases of:
   Systemic lupus erythematosus
   Systemic dermatomyositis (polymyositis)
   Acute rheumatic carditis

4. **Dermatologic Diseases**
   Pemphigus
   Bullous dermatitis herpetiformis
   Severe erythema multiforme (Stevens-Johnson syndrome)
   Exfoliative dermatitis
   Mycosis fungoides
   Severe psoriasis
   Severe seborrheic dermatitis

5. **Allergic States**
   Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment:
   Seasonal or perennial allergic rhinitis
   Bronchial asthma
   Contact dermatitis
   Atopic dermatitis
   Serum sickness
   Drug hypersensitivity reactions

6. **Ophthalmic Diseases**
   Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:
   Allergic corneal marginal ulcers
   Herpes zoster ophthalmicus
   Anterior segment inflammation
   Diffuse posterior uveitis and choroiditis
   Sympathetic ophthalmia
   Allergic conjunctivitis
   Keratitis
   Chorioretinitis
   Optic neuritis
   Iritis and iridocyclitis

7. **Respiratory Diseases**
   Symptomatic sarcoidosis
   Loeffler's syndrome not manageable by other means
   Berylliosis
   Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy
   Aspiration pneumonitis

8. **Hematologic Disorders**
   Idiopathic thrombocytopenic purpura in adults
   Secondary thrombocytopenia in adults
   Acquired (autoimmune) hemolytic anemia
   Erythroblastopenia (RBC anemia)
   Congenital (erythroid) hypoplastic anemia

9. **Neoplastic Diseases**
   For palliative management of:
   Leukemias and lymphomas in adults
   Acute leukemia of childhood

10. **Edematous States**
    To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus

11. **Gastrointestinal Diseases**
    To tide the patient over a critical period of the disease in:
    Ulcerative colitis
    Regional enteritis

12. **Nervous System**
    Acute exacerbations of multiple sclerosis

13. **Miscellaneous**
    Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy
    Trichinosis with neurologic or myocardial involvement

CONTRAINDICATIONS

Systemic fungal infections and known hypersensitivity to components.

WARNINGS

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated.

Corticosteroids may mask some signs of infection, and new infections may appear during their use. Infections with any pathogen including viral, bacterial, fungal, protozoan or helminthic infections, in any location of the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity, or neutrophil function.[1]

These infections may be mild, but can be severe and at times fatal. With increasing doses of corticosteroids, the rate of occurrence of infectious complications increases.[2] There may be decreased resistance and inability to localize infection when corticosteroids are used.

Prolonged use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Usage in pregnancy

Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers or women of child-bearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy, should be carefully observed for signs of hypoadrenalism.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered to patients receiving immunosuppressive doses of corticosteroids; however, the response to such vaccines may be diminished. Indicated immunization procedures may be undertaken in patients receiving nonimmunosuppressive doses of corticosteroids.

The use of DELTASONE Tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate anti-tuberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chicken pox develops, treatment with antiviral agents may be considered. Similarly, corticosteroids should be used with great care in patients with known or suspected Strongyloides (threadworm) infestation. In such patients, corticosteroid-induced immunosuppression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

PRECAUTIONS

General Precautions

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis.
Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.
Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission.
Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that corticosteroids affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (See DOSAGE AND ADMINISTRATION.)
Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.
Convulsions have been reported with concurrent use of methylprednisolone and cyclosporin. Since concurrent use of these agents results in a mutual inhibition of metabolism, it is possible that adverse events associated with the individual use of either drug may be more apt to occur.

Drug Interactions
The pharmacokinetic interactions listed below are potentially clinically important. Drugs that induce hepatic enzymes such as phenobarbital, phenytoin and rifampin may increase the clearance of corticosteroids and may require increases in corticosteroid dose to achieve the desired response. Drugs such as troleandomycin and ketoconazole may inhibit the metabolism of corticosteroids and thus decrease their clearance. Therefore, the dose of corticosteroid should be titrated to avoid steroid toxicity. Corticosteroids may increase the clearance of chronic high dose aspirin. This could lead to decreased salicylate serum levels or increase the risk of salicylate toxicity when corticosteroid is withdrawn. Aspirin should be used cautiously in conjunction with corticosteroids in patients suffering from hypoprothrombinemia. The effect of corticosteroids on oral anticoagulants is variable. There are reports of enhanced as well as diminished effects of anticoagulants when given concurrently with corticosteroids. Therefore, coagulation indices should be monitored to maintain the desired anticoagulant effect.

Information for the Patient
Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chicken pox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

ADVERSE REACTIONS
Fluid and Electrolyte Disturbances
- Sodium retention
- Fluid retention
- Congestive heart failure in susceptible patients
- Potassium loss

Hypokalemic alkalosis
Hypertension
Musculoskeletal
Muscle weakness
Steroid myopathy
- Loss of muscle mass
- Osteoporosis
- Tendon rupture, particularly of the Achilles tendon
- Vertebral compression fractures
- Aseptic necrosis of femoral and humeral heads

Pathologic fracture of long bones
Gastrointestinal
- Peptic ulcer with possible perforation and hemorrhage
- Pancreatitis
- Abdominal distention
- Ulcerative esophagitis

Increases in alanine transaminase (ALT, SGPT), aspartate transaminase (AST, SGOT) and alkaline phosphatase have been observed following corticosteroid treatment. These changes are usually small, not associated with any clinical syndrome and are reversible upon discontinuation.
Dermatologic
- Impaired wound healing
- Thin fragile skin

Petechiae and ecchymoses
Facial erythema
Increased sweating
May suppress reactions to skin tests

Metabolic

Negative nitrogen balance due to protein catabolism

Neurological

Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment
Convulsions
Vertigo
Headache

Endocrine

Menstrual irregularities
Development of Cushingoid state
Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness
Suppression of growth in children
Decreased carbohydrate tolerance
Manifestations of latent diabetes mellitus
Increased requirements for insulin or oral hypoglycemic agents in diabetics

Ophthalmic

Posterior subcapsular cataracts
Increased intraocular pressure
Glaucoma
Exophthalmos

Additional Reactions

Urticaria and other allergic, anaphylactic or hypersensitivity reactions

DOSAGE AND ADMINISTRATION

The initial dosage of DELTASONE Tablets may vary from 5 mg to 60 mg of prednisone per day depending on the specific disease entity being treated. In situations of less severity lower doses will generally suffice while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, DELTASONE should be discontinued and the patient transferred to other appropriate therapy. **IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT.** After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of DELTASONE for a period of time consistent with the patient's condition. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

Multiple Sclerosis

In the treatment of acute exacerbations of multiple sclerosis daily doses of 200 mg of prednisolone for a week followed by 80 mg every other day for 1 month have been shown to be effective. (Dosage range is the same for prednisone and prednisolone.)

ADT® (Alternate Day Therapy)

ADT is a corticosteroid dosing regimen in which twice the usual daily dose of corticoid is administered every other morning. The purpose of this mode of therapy is to provide the patient requiring long-term pharmacologic dose treatment with the beneficial effects of corticoids while minimizing certain undesirable effects, including pituitary-adrenal suppression, the Cushingoid state, corticoid withdrawal symptoms, and growth suppression in children.

The rationale for this treatment schedule is based on two major premises: (a) the anti-inflammatory or therapeutic effect of corticoids persists longer than their physical presence and metabolic effects and (b) administration of the corticosteroid every other morning allows for re-establishment of more nearly normal hypothalamic-pituitary-adrenal (HPA) activity on the off-steroid day.

A brief review of the HPA physiology may be helpful in understanding this rationale. Acting primarily through the hypothalamus a fall in free cortisol stimulates the pituitary gland to produce increasing amounts of corticotropin (ACTH) while a rise in free cortisol inhibits ACTH secretion. Normally the HPA system is characterized by diurnal (circadian) rhythm. Serum levels of ACTH rise from a low point about 10 pm to a peak level about 6 am. Increasing levels of ACTH stimulate adrenocortical activity resulting in a rise in

plasma cortisol with maximal levels occurring between 2 am and 8 am. This rise in cortisol dampens ACTH production and in turn adrenocortical activity. There is a gradual fall in plasma corticoids during the day with lowest levels occurring about midnight.
The diurnal rhythm of the HPA axis is lost in Cushing's disease, a syndrome of adrenocortical hyperfunction characterized by obesity with centripetal fat distribution, thinning of the skin with easy bruisability, muscle wasting with weakness, hypertension, latent diabetes, osteoporosis, electrolyte imbalance, etc. The same clinical findings of hyperadrenocorticism may be noted during long-term pharmacologic dose corticoid therapy administered in conventional daily divided doses. It would appear, then, that a disturbance in the diurnal cycle with maintenance of elevated corticoid values during the night may play a significant role in the development of undesirable corticoid effects. Escape from these constantly elevated plasma levels for even short periods of time may be instrumental in protecting against undesirable pharmacologic effects.
During conventional pharmacologic dose corticosteroid therapy, ACTH production is inhibited with subsequent suppression of cortisol production by the adrenal cortex. Recovery time for normal HPA activity is variable depending upon the dose and duration of treatment. During this time the patient is vulnerable to any stressful situation. Although it has been shown that there is considerably less adrenal suppression following a single morning dose of prednisolone (10 mg) as opposed to a quarter of that dose administered every 6 hours, there is evidence that some suppressive effect on adrenal activity may be carried over into the following day when pharmacologic doses are used. Further, it has been shown that a single dose of certain corticosteroids will produce adrenocortical suppression for two or more days. Other corticoids, including methylprednisolone, hydrocortisone, prednisone, and prednisolone, are considered to be short acting (producing adrenocortical suppression for 1¼ to 1½ days following a single dose) and thus are recommended for alternate day therapy.
The following should be kept in mind when considering alternate day therapy:
1) Basic principles and indications for corticosteroid therapy should apply. The benefits of ADT should not encourage the indiscriminate use of steroids.
2) ADT is a therapeutic technique primarily designed for patients in whom long-term pharmacologic corticoid therapy is anticipated.
3) In less severe disease processes in which corticoid therapy is indicated, it may be possible to initiate treatment with ADT.
More severe disease states usually will require daily divided high dose therapy for initial control of the disease process. The initial suppressive dose level should be continued until satisfactory clinical response is obtained, usually four to ten days in the case of many allergic and collagen diseases. It is important to keep the period of initial suppressive dose as brief as possible particularly when subsequent use of alternate day therapy is intended.
Once control has been established, two courses are available: (a) change to ADT and then gradually reduce the amount of corticoid given every other day **or** (b) following control of the disease process reduce the daily dose of corticoid to the lowest effective level as rapidly as possible and then change over to an alternate day schedule. Theoretically, course (a) may be preferable.
4) Because of the advantages of ADT, it may be desirable to try patients on this form of therapy who have been on daily corticoids for long periods of time (eg, patients with rheumatoid arthritis). Since these patients may already have a suppressed HPA axis, establishing them on ADT may be difficult and not always successful. However, it is recommended that regular attempts be made to change them over. It may be helpful to triple or even quadruple the daily maintenance dose and administer this every other day rather than just doubling the daily dose if difficulty is encountered. Once the patient is again controlled, an attempt should be made to reduce this dose to a minimum.
5) As indicated above, certain corticosteroids, because of their prolonged suppressive effect on adrenal activity, are not recommended for alternate day therapy (eg, dexamethasone and betamethasone).
6) The maximal activity of the adrenal cortex is between 2 am and 8 am, and it is minimal between 4 pm and midnight. Exogenous corticosteroids suppress adrenocortical activity the least, when given at the time of maximal activity (am).
7) In using ADT it is important, as in all therapeutic situations to individualize and tailor the therapy to each patient. Complete control of symptoms will not be possible in all patients. An explanation of the benefits of ADT will help the patient to understand and tolerate the possible flare-up in symptoms which may occur in the latter part of the off-steroid day. Other symptomatic therapy may be added or increased at this time if needed.
8) In the event of an acute flare-up of the disease process, it may be necessary to return to a full suppressive daily divided corticoid dose for control. Once control is again established alternate day therapy may be re-instituted.
9) Although many of the undesirable features of corticosteroid therapy can be minimized by ADT, as in any therapeutic situation, the physician must carefully weigh the benefit-risk ratio for each patient in whom corticoid therapy is being considered.

HOW SUPPLIED
DELTASONE Tablets are available in the following strengths and package sizes:
2.5 mg (pink, round, scored, imprinted DELTASONE
2.5) Bottles of 100 NDC 0009-0032-01
5 mg (white, round, scored, imprinted DELTASONE
5) Bottles of 100 NDC 0009-0045-01
Bottles of 500 NDC 0009-0045-02
Bottles of 1000 NDC 0009-0045-16
10 mg (white, round, scored, imprinted DELTASONE
10) Bottles of 100 NDC 0009-0193-01
Bottles of 500 NDC 0009-0193-02

20 mg (peach, round, scored, imprinted DELTASONE 20)
Bottles of 100 NDC 0009-0165-01
Bottles of 500 NDC 0009-0165-02
50 mg (white, round, scored, imprinted DELTASONE 50)
Bottles of 100 NDC 0009-0388-01
Store at controlled room temperature 20° to 25°C (68° to 77°F) [see USP].

REFERENCES

1 Fekety R. Infections associated with corticosteroids and immunosuppressive therapy. In: Gorbach SL, Bartlett JG, Blacklow NR, eds. *Infectious Diseases*. Philadelphia: WBSaunders Company 1992:1050–1.

2 Stuck AE, Minder CE, Frey FJ. Risk of infectious complications in patients taking glucocorticoids. *Rev Infect Dis* 1989:11(6):954–63.

Rx only

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