GULF WAR ILLNESS

The Effects of a Low Glutamate Dietary Intervention on Anxiety and PTSD in Veterans with Gulf War Illness (FS15-08-19).

Brandley E[1], Kirkland A[1], Sarlo G[1], VanMeter J[2], Baraniuk J[3], Holton K[1].

Curr Dev Nutr. **2019 Jun 13**;3(Suppl 1). pii: nzz031.FS15-08-19. doi: 10.1093/cdn/nzz031.FS15-08-19. PMCID: PMC6576215. PMID: 31224991.

Objectives: Glutamate is an amino acid and also serves as the most ubiquitous neurotransmitter in the human body. Previous work has shown that dysregulated glutamatergic neurotransmission is implicated in the etiology of anxiety disorders.

Objective: To examine the effect of a low glutamate dietary intervention on anxiety and Posttraumatic Stress Disorder (PTSD) in veterans with Gulf War Illness (GWI).

Methods: Forty veterans with GWI are being recruited for a randomized-controlled clinical trial testing the effects of a low glutamate diet on neurological symptoms. After consent, subjects complete baseline measures, then subjects are randomized to the low-glutamate diet or a wait-listed control group. For the active intervention phase, they follow a 1-month low glutamate diet and then are re-tested prior to entering a double-blind, placebo-controlled crossover challenge with monosodium glutamate (MSG) or placebo, to test for return of symptoms. Preliminary data are presented here for changes observed on the Generalized Anxiety Disorder 7-item (GAD-7) scale and the PTSD Checklist (PCL-C) after one month on the diet in subjects recruited to date. Pre-post diet scores were compared for anxiety and PTSD using a Wilcoxon Signed Rank test in SAS.

Results: Seventeen veterans (M = 15; F = 2) with GWI have been recruited to date (mean age = 50 ± 4 yrs). Preliminary analyses demonstrate that after one month on the diet, significant improvements were noted for anxiety (score reduced from a median (IQ range) of 9 (13) to 5 (10), p = 0.01) and for PTSD (median (IQ) score reduced from 58 (33) to 43 (28), p = 0.04).

Conclusions: This study suggests that consuming a low glutamate diet may improve anxiety and PTSD in veterans suffering from Gulf War Illness. More research is needed to further explore the role of dietary glutamate in anxiety disorders.

Funding Sources: U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD 21702-5014 is the awarding and administering acquisition office. This work was supported by the Office of the Assistant Secretary of Defense for Health Affairs, through the Gulf War Illness Research Program under Award No. W81XWH-17-1-0457. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.

CHRONIC FATIGUE SYNDROME

No Updates this Week for Chronic Fatigue Syndrome.

HEADACHE and MIGRAINE

Early efficacy and late gain in chronic and high-frequency episodic migraine with OnabotulinumtoxinA.

Alpuente A[1,2], Gallardo VJ[2], Torres-Ferrús M[1,2], Álvarez-Sabin J[1], Pozo-Rosich P[1,2].

Eur J Neurol. **2019 Jun 20**. doi: 10.1111/ene.14028. PMID: 31220392. [Epub ahead of print]

BACKGROUND: To analyze the clinical characteristics of a long-term follow-up of patients with chronic and high frequency episodic migraine in treatment with OnabotulinumtoxinA.

METHODS: We included patients diagnosed with high-frequency episodic migraine (HFEM) or chronic migraine (CM) according to ICHD-3beta. A comparative analysis was carried out at each study timepoint identifying outcome measures according to initial diagnosis and treatment duration.

RESULTS: 578 patients were recruited and after 24 months outcome data was collected from 100 patients: 84.0% CM and 16.0% HFEM. After 24 months, headache frequency was significantly reduced by 10.5 days from baseline, 64.0% reported a ≥50% reduction in pain intensity and 70.0% of patients had ≥50% reduction in analgesic use. When comparing baseline diagnoses, at month 6, CM presented higher mean reduction in frequency (CM-44.3%±32.6 vs. HFEM-34.6%±24.8) and analgesic use (CM-53.6±35.4% vs. HFEM-39.3±33.2%). At month 12, the mean reduction in frequency was similar in CM and HFEM (CM-44.7±33.4% vs. HFEM-41.2±28.2%). Improvement in pain intensity, analgesic use and MIDAS were proportional in both diagnoses.

CONCLUSIONS: OnabotulinumtoxinA efficacy is significant at 6 months in frequency and analgesic intake, and remains stable during follow-up; while the intensity of pain decreases in a stepwise manner at each timepoint of the analysis. The improvement in CM and HFEM is proportional and significant after one year of treatment.

A ketogenic diet normalizes interictal cortical but not subcortical responsivity in migraineurs.

Di Lorenzo C[1], Coppola G[2], Bracaglia M[2], Di Lenola D[2], Sirianni G[3], Rossi P[4], Di Lorenzo G[5], Parisi V[6], Serrao M[2], Cervenka MC[7], Pierelli F[2,8].

BMC Neurol. **2019 Jun 22**;19(1):136. doi: 10.1186/s12883-019-1351-1. PMID: 31228957.

BACKGROUND: A short ketogenic diet (KD) treatment can prevent migraine attacks and correct excessive cortical response. Here, we aim to prove if the KD-related changes of cortical excitability are primarily due to cerebral cortex activity or are modulated by the brainstem.

METHODS: Through the stimulation of the right supraorbital division of the trigeminal nerve, we concurrently interictally recorded the nociceptive blink reflex (nBR) and the pain-related evoked potentials (PREP) in 18 migraineurs patients without aura before and after 1-month on KD, while in metabolic ketosis. nBR and PREP reflect distinct brain structures activation: the brainstem and the cerebral cortex respectively. We estimated nBR R2 component area-under-the-curve as well as PREP amplitude habituation as the slope pof the linear regression between the 1st and the 2nd block of 5 averaged responses.

RESULTS: Following 1-month on KD, the mean number of attacks and headache duration reduced significantly. Moreover, KD significantly normalized the interictal PREP habituation (pre: + 1.8, post: - 9.1, p = 0.012), while nBR deficit of habituation did not change.

CONCLUSIONS: The positive clinical effects we observed in a population of migraineurs by a 1-month KD treatment coexists with a normalization at the cortical level, not in the brainstem, of the typical interictal deficit of habituation. These findings suggest that the cerebral cortex may be the primary site of KD-related modulation.

TRIAL REGISTRATION: ClinicalTrials.gov NCT03775252 (retrospectively registered, December 09, 2018).

HEADACHE and MIGRAINE (Continued)

Advances in genetics of migraine.

Sutherland HG[1], Albury CL[1], Griffiths LR[2].

J Headache Pain. **2019 Jun 21**;20(1):72. doi: 10.1186/s10194-019-1017-9. PMID: 31226929.

BACKGROUND: Migraine is a complex neurovascular disorder with a strong genetic component. There are rare monogenic forms of migraine, as well as more common polygenic forms; research into the genes involved in both types has provided insights into the many contributing genetic factors. This review summarises advances that have been made in the knowledge and understanding of the genes and genetic variations implicated in migraine etiology.

FINDINGS: Migraine is characterised into two main types, migraine without aura (MO) and migraine with aura (MA). Hemiplegic migraine is a rare monogenic MA subtype caused by mutations in three main genes - CACNA1A, ATP1A2 and SCN1A - which encode ion channel and transport proteins. Functional studies in cellular and animal models show that, in general, mutations result in impaired glutamatergic neurotransmission and cortical hyperexcitability, which make the brain more susceptible to cortical spreading depression, a phenomenon thought to coincide with aura symptoms. Variants in other genes encoding ion channels and solute carriers, or with roles in regulating neurotransmitters at neuronal synapses, or in vascular function, can also cause monogenic migraine, hemiplegic migraine and related disorders with overlapping symptoms. Next-generation sequencing will accelerate the finding of new potentially causal variants and genes, with high-throughput bioinformatics analysis methods and functional analysis pipelines important in prioritising, confirming and understanding the mechanisms of disease-causing variants. With respect to common migraine forms, large genome-wide association studies (GWAS) have greatly expanded our knowledge of the genes involved, emphasizing the role of both neuronal and vascular pathways. Dissecting the genetic architecture of migraine leads to greater understanding of what underpins relationships between subtypes and comorbid disorders, and may have utility in diagnosis or tailoring treatments. Further work is required to identify causal polymorphisms and the mechanism of their effect, and studies of gene expression and epigenetic factors will help bridge the genetics with migraine pathophysiology.

CONCLUSIONS: The complexity of migraine disorders is mirrored by their genetic complexity. A comprehensive knowledge of the genetic factors underpinning migraine will lead to improved understanding of molecular mechanisms and pathogenesis, to enable better diagnosis and treatments for migraine sufferers.

CHRONIC PAIN

Effects of yoga on chronic neck pain: a systematic review and meta-analysis.

Cramer H[1], Klose P[1], Brinkhaus B[2], Michalsen A[2,3], Dobos G[1].

Clin Rehabil. **2017 Nov**;31(11):1457-1465. doi: 10.1177/0269215517698735. PMID: 29050510. Epub 2017 Mar 9.

[Note: Delayed posting in PubMed—Not previously listed in RAC Research Alerts.]

OBJECTIVE: The aim of this review was to systematically assess and meta-analyze the effectiveness of yoga in relieving chronic neck pain.

METHODS: PubMed/MEDLINE, the Cochrane Library, Scopus, and IndMED were screened through January 2017 for randomized controlled trials assessing neck pain intensity and/or neck pain-related disability in chronic neck pain patients. Secondary outcome measures included quality of life, mood, and safety. Risk of bias was assessed using the Cochrane tool.

RESULTS: Three studies on 188 patients with chronic non-specific neck pain comparing yoga to usual care were included. Two studies had overall low risk of bias; and one had high or unclear risk of bias for several domains. Evidence for short-term effects was found for neck pain intensity (standardized mean difference (SMD) = -1.28; 95% confidence interval (CI) = -1.18, -0.75; $P < 0.001$), neck pain-related disability (SMD = -0.97; 95% CI = -1.44, -0.50; $P < 0.001$), quality of life (SMD = 0.57; 95% CI = 0.17, 0.197; $P = 0.005$), and mood (SMD = -1.02; 95% CI = -1.38, -0.65; $P < 0.001$). Effects were robust against potential methodological bias and did not differ between different intervention subgroups. In the two studies that included safety data, no serious adverse events occurred.

CONCLUSION: Yoga has short-term effects on chronic neck pain, its related disability, quality of life, and mood suggesting that yoga might be a good treatment option.

CHRONIC PAIN (Continued)

A Systematic Review of Radiofrequency Treatment of the Ankle for the Management of Chronic Foot and Ankle Pain.

Orhurhu V[1], Urits I[1], Orman S[2], Viswanath O[3,4,5], Abd-Elsayed A[6].

Curr Pain Headache Rep. **2019 Jan 19**;23(1):4. doi: 10.1007/s11916-019-0745-5. PMID: 30661127.

BACKGROUND: Chronic pain of the lower extremity remains challenging to manage. Radiofrequency treatment applies heat to nerve fibers with the goal of mitigating chronic pain conditions. The clinical efficacy has not yet been adequately established for pathologies of the ankle and foot. In this review paper, we report the use and efficacy of radiofrequency treatment applied to foot and ankle pain.

RECENT FINDINGS: PubMed and the Cochrane Controlled Trials Register were searched (final search 30 March 2018) using the MeSH terms "radiofrequency ablation," "neurolysis," "radiofrequency therapy," "pain syndrome," "analgesia," "plantar heel pain," "plantar fascitis," and "chronic pain" in the English literature. Of the 23 papers screened, 18 were further investigated for relevance. Our final search methodology yielded 15 studies that investigated the use of radiofrequency treatment at the ankle. Of these 15 studies, there were three randomized control trials, four prospective studies, three retrospective studies, and five case reports. The quality of selected publications was assessed using the Cochrane risk of bias instrument. The evidence from our studies suggests that radiofrequency treatment can be used safely for the management foot and ankle pain. The technique (continuous vs pulsatile), temperature, location of treatment, and duration of administration need more thorough evaluation. Randomized control trials are needed to establish the efficacy and safety profile of radiofrequency ablation and its long-term benefits in patients with chronic pain of the foot and ankle.

CONCLUSION: The evidence from our studies suggests that radiofrequency treatment can be used safely for the management foot and ankle pain. The technique (continuous vs pulsatile), temperature, location of treatment, and duration of administration need more thorough evaluation. Randomized control trials are needed to establish the efficacy and safety profile of radiofrequency ablation and its long-term benefits in patients with chronic pain of the foot and ankle.

IRRITABLE BOWEL SYNDROME

Increasing the Dose and/or Repeating Faecal Microbiota Transplantation (FMT) Increases the Response in Patients with Irritable Bowel Syndrome (IBS).

El-Salhy M[1,2,3], Hausken T[4,5], Hatlebakk JG[6,7].

Nutrients. **2019 Jun 24**;11(6). pii: E1415. doi: 10.3390/nu11061415. PMCID: PMC6628324. PMID: 31238507.

BACKGROUND: Faecal microbiome transplantation (FMT) appears to be an effective method for treating irritable bowel syndrome (IBS) patients. However, it is not clear if a high transplant dose and/or repeating FMT are/is needed to ensure a response. The present study was undertaken to clarify this matter.

METHODS: Ten IBS patients who did not respond to a 30-g transplant subsequently received a 60-g transplant into the duodenum via a gastroscope. The patients provided faecal samples before and 1 month after FMT. They completed five questionnaires measuring symptoms, fatigue and quality of life at baseline and then at 2 weeks, 1 month and 3 months after FMT. The dysbiosis index (DI) was measured using the GA-map Dysbiosis Test®.

RESULTS: Seven patients (70%) responded to the 60-g transplant, with significant clinical improvements in the abdominal symptoms, fatigue and quality of life in 57%, 80% and 67% of these patients. The 60-g transplant also reduced the DI.

CONCLUSION: FMT is an effective treatment for IBS. A high-dose transplant and/or repeated FMT increase the response rate and the intensity of the effects of FMT.

OTHER RESEARCH OF INTEREST

The associations between deployment experiences, PTSD, and alcohol use among male and female veterans.

Banducci AN[1], McCaughey VK[2], Gradus JL[3], Street AE[4].

Addict Behav. **2019 Jun 24**;98:106032. doi: 10.1016/j.addbeh.2019.106032. PMID: 31336265. [Epub ahead of print]

OVERVIEW: Alcohol use is common following traumatic military deployment experiences. What is less clear is why, and for whom, particular deployment experiences lead to alcohol use.

METHOD: The current study explored associations between deployment stressors (Warfare, Military Sexual Trauma, and Concerns about Life and Family Disruptions-"Life Disruptions"), PTSD (PCL-5), and alcohol use (CAGE) post-deployment, stratified by gender among 2344 male and female veterans (1137 men; Mage = 35). Conditional process analyses examined the indirect effect of traumatic deployment experiences on alcohol use, via PTSD symptom severity, with Life Disruptions as a moderator.

RESULTS: More severe Warfare and military sexual trauma (MST) were associated with greater PTSD symptom severity, which was associated with higher problematic alcohol use. PTSD symptom severity accounted for the associations between trauma type (i.e., MST or Warfare) and alcohol use. Among women, but not men, Life Disruptions moderated the associations between trauma type (i.e., MST, Warfare) and PTSD symptom severity, such that elevated Life Disruptions amplified the associations between trauma type and PTSD symptom severity. Moderated mediation was significant for MST among women, indicating that the strength of the indirect effect (MST ➔ PTSD ➔ problematic alcohol use) was moderated by Life Disruptions; problematic alcohol use was highest for women with greater PTSD symptom severity following exposure to more severe Life Disruptions and MST (Est. = 0.0007, SE = 0.0001, CI = 0.0002 to 0.0013).

CONCLUSIONS: Taken together, alcohol use following potentially traumatic deployment experiences can be understood by considering PTSD symptom severity, gender, and Life Disruptions.

Aspirin for Primary Prevention of Cardiovascular Events.

Abdelaziz HK[1], Saad M[2], Pothineni NVK[3], Megaly M[4], Potluri R[5], Saleh M[6], Kon DLC[7], Roberts DH[7], Bhatt DL[8], Aronow HD[9], Abbott JD[10], Mehta JL[11].

J Am Coll Cardiol. **2019 Jun 18**;73(23):2915-2929. doi: 10.1016/j.jacc.2019.03.501.

BACKGROUND: The efficacy and safety of aspirin for primary prevention of cardiovascular disease (CVD) remain debatable.

OBJECTIVES: The purpose of this study was to examine the clinical outcomes with aspirin for primary prevention of CVD after the recent publication of large trials adding >45,000 individuals to the published data.

METHODS: Randomized controlled trials comparing clinical outcomes with aspirin versus control for primary prevention with follow-up duration of ≥1 year were included. Efficacy outcomes included all-cause death, cardiovascular (CV) death, myocardial infarction (MI), stroke, transient ischemic attack (TIA), and major adverse cardiovascular events. Safety outcomes included major bleeding, intracranial bleeding, fatal bleeding, and major gastrointestinal (GI) bleeding. Random effects DerSimonian-Laird risk ratios (RRs) for outcomes were calculated.

RESULTS: A total of 15 randomized controlled trials including 165,502 participants (aspirin n = 83,529, control n = 81,973) were available for analysis. Compared with control, aspirin was associated with similar all-cause death (RR: 0.97; 95% confidence interval [CI]: 0.93 to 1.01), CV death (RR: 0.93; 95% CI: 0.86 to 1.00), and non-CV death (RR: 0.98; 95% CI: 0.92 to 1.05), but a lower risk of nonfatal MI (RR: 0.82; 95% CI: 0.72 to 0.94), TIA (RR: 0.79; 95% CI: 0.71 to 0.89), and ischemic stroke (RR: 0.87; 95% CI: 0.79 to 0.95). Aspirin was associated with a higher risk of major bleeding (RR: 1.5; 95% CI: 1.33 to 1.69), intracranial bleeding (RR: 1.32; 95% CI: 1.12 to 1.55), and major GI bleeding (RR: 1.52; 95% CI: 1.34 to 1.73), with similar rates of fatal bleeding (RR: 1.09; 95% CI: 0.78 to 1.55) compared with the control subjects. Total cancer and cancer-related deaths were similar in both groups within the follow-up period of the study.

CONCLUSIONS: Aspirin for primary prevention reduces nonfatal ischemic events but significantly increases nonfatal bleeding events.

OTHER RESEARCH OF INTEREST (Continued)

Efficacy of Esketamine Nasal Spray Plus Oral Antidepressant Treatment for Relapse Prevention in Patients With Treatment-Resistant Depression: A Randomized Clinical Trial.

Daly EJ[1], Trivedi MH[2], Janik A[3], Li H[1], Zhang Y[4], Li X[5], Lane R[6], Lim P[6], Duca AR[1], Hough D[1], Thase ME[7], Zajecka J[8], Winokur A[9,10], Divacka I[11], Fagiolini A[12], Cubala WJ[13], Bitter I[14], Blier P[15], Shelton RC[16], Molero P[17], Manji H[1], Drevets WC[3], Singh JB[3].

JAMA Psychiatry. **2019 Jun 5**. doi: 10.1001/jamapsychiatry.2019.1189. PMCID: PMC6551577. PMID: 31166571. [Epub ahead of print]

Importance: Controlled studies have shown short-term efficacy of esketamine for treatment-resistant depression (TRD), but long-term effects remain to be established.

Objective: To assess the efficacy of esketamine nasal spray plus an oral antidepressant compared with an oral antidepressant plus placebo nasal spray in delaying relapse of depressive symptoms in patients with TRD in stable remission after an induction and optimization course of esketamine nasal spray plus an oral antidepressant.

Design, Setting, and Participants: In this phase 3, multicenter, double-blind, randomized withdrawal study conducted from October 6, 2015, to February 15, 2018, at outpatient referral centers, 705 adults with prospectively confirmed TRD were enrolled; 455 entered the optimization phase and were treated with esketamine nasal spray (56 or 84 mg) plus an oral antidepressant. After 16 weeks of esketamine treatment, 297 who achieved stable remission or stable response entered the randomized withdrawal phase.

Interventions: Patients who achieved stable remission and those who achieved stable response (without remission) were randomized 1:1 to continue esketamine nasal spray or discontinue esketamine treatment and switch to placebo nasal spray, with oral antidepressant treatment continued in each group.

Main Outcomes and Measures: Time to relapse was examined in patients who achieved stable remission, as assessed using a weighted combination log-rank test.

Results: Among the 297 adults (mean age [SD], 46.3 [11.13] years; 197 [66.3%] female) who entered the randomized maintenance phase, 176 achieved stable remission; 24 (26.7%) in the esketamine and antidepressant group and 39 (45.3%) in the antidepressant and placebo group experienced relapse (log-rank P = .003, number needed to treat [NNT], 6). Among the 121 who achieved stable response, 16 (25.8%) in the esketamine and antidepressant group and 34 (57.6%) in the antidepressant and placebo group experienced relapse (log-rank P < .001, NNT, 4). Esketamine and antidepressant treatment decreased the risk of relapse by 51% (hazard ratio [HR], 0.49; 95% CI, 0.29-0.84) among patients who achieved stable remission and 70% (HR, 0.30; 95% CI, 0.16-0.55) among those who achieved stable response compared with antidepressant and placebo treatment. The most common adverse events reported for esketamine-treated patients after randomization were transient dysgeusia, vertigo, dissociation, somnolence, and dizziness (incidence, 20.4%-27.0%), each reported in fewer patients (<7%) treated with an antidepressant and placebo.

Conclusions and Relevance: For patients with TRD who experienced remission or response after esketamine treatment, continuation of esketamine nasal spray in addition to oral antidepressant treatment resulted in clinically meaningful superiority in delaying relapse compared with antidepressant plus placebo.

Trial Registration: ClinicalTrials.gov identifier: NCT02493868.

OTHER RESEARCH OF INTEREST (Continued)

Altered microbiome composition in individuals with fibromyalgia.

Minerbi A[1], Gonzalez E[2,3], Brereton NJB[4], Anjarkouchian A[5], Dewar K[3,6], Fitzcharles MA[1,7], Chevalier S[5,8,9], Shir Y[1].

Pain. **2019 Jun 18**. doi: 10.1097/j.pain.0000000000001640. PMID: 31219947. [Epub ahead of print]

Fibromyalgia (FM) is a prevalent syndrome, characterised by chronic widespread pain, fatigue and impaired sleep, that is challenging to diagnose and difficult to treat. The microbiomes of 77 women with FM and that of 79 control participants were compared using 16S rRNA gene amplification and whole genome sequencing. When comparing FM patients to unrelated controls using differential abundance analysis, significant differences were revealed in several bacterial taxa. Variance in the composition of the microbiomes was explained by FM-related variables more than by any other innate or environmental variable and correlated with clinical indices of FM. In line with observed alteration in butyrate metabolising species, targeted serum metabolite analysis verified differences in the serum levels of butyrate and propionate in FM patients. Using machine learning algorithms, the microbiome composition alone allowed for the classification of patients and controls (ROC AUC 87.8%). To the best of our knowledge, this is the first demonstration of gut microbiome alteration in non-visceral pain. This observation paves the way for further studies, elucidating the pathophysiology of FM, developing diagnostic aids and possibly allowing for new treatment modalities to be explored.

Nonorgan manifestations of sarcoidosis.

Tavee J[1,2], Culver D[3].

Curr Opin Pulm Med. **2019 Jun 18**. doi: 10.1097/MCP.0000000000000597. PMID: 31219834. [Epub ahead of print]

PURPOSE OF REVIEW: The current review discusses the diagnosis and management of nonorgan-related symptoms that commonly arise in the setting of systemic sarcoidosis. Fatigue, small fiber neuropathy (SFN) and neuropsychological symptoms are highlighted.

RECENT FINDINGS: The debilitating effects of chronic nonorgan-based symptoms in sarcoidosis have led to recent studies focusing on incidence rates, contributing factors and potential therapeutic strategies. In a web-based survey of over 1000 sarcoidosis patients, the most common symptom was fatigue, which was reported by over 90% of participants, whereas memory loss and concentration problems were reported in 50%. SFN was also common, and may be diagnosed with tools such as skin biopsy measurement of intraepidermal nerve fibers and corneal confocal microscopy. In a recent cohort study of SFN patients, serologic evaluation demonstrated other contributing causes such as diabetes and vitamin B12 deficiency, which warrant-specific treatment. Finally, physical inactivity in patients with sarcoidosis correlated with lower quality-of-life (QOL) scores and possibly fatigue. Multidisciplinary programs that include physical therapy, patient education and psychological support were found to improve fatigue and mood disorders.

SUMMARY: Recognition of nonorgan-related symptoms and their impact on patient QOL is essential to optimal treatment of the sarcoidosis patient.

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