Biologic Intervention is Warranted

By David Smith, MD and Matt Torrington, MD

The National Institute on Drug Abuse has championed the medical model of substance dependence: Addiction is a Brain Disease. The American Society of Addiction Medicine stresses that this illness has biologic, psychological and social elements and needs corresponding biologic, psychological and social treatment interventions. If this model is to be embraced in the United States, scientific and medical inquiry should follow the approach used with other chronic, relapsing and potentially fatal illnesses.

The Prometa treatment protocol for the treatment of alcoholism and psychostimulant addiction is based on a clinically derived theory from Spain and involves multiple FDA-approved medications administered in a unique combination with nutritional support and psychosocial interventions. The Prometa Protocol embraces "best practices" in addiction medicine treatment by emphasizing the need for biologic, psychological and social interventions. Thus far clinical results for patients suffering from alcohol, cocaine and methamphetamine dependence have been overwhelmingly positive.

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For patients who have relapsed following multiple episodes of traditional treatment and for those with severe psychostimulant addiction, for which there is no approved pharmacotherapy, the benefit of the treatment has been especially striking.

How does Prometa work? The hypothesized mechanism of action of the biologic aspect of the Prometa treatment is focused on the GABA A alpha subunit. Preclinical data suggests that prolonged exposure to alcohol and psychostimulants can cause changes in GABA A alpha subunits. Specifically, these subunits change from "functional" GABA A alpha 1 subunits to "dysfunctional" GABA A alpha 4 subunits.

Preclinical data has illustrated the ability of the protocol to reverse this change in the GABA receptors. Clearly the dysfunction of the GABA system to inhibit limbic desire to continue to use drugs is at the heart of the problem in substance dependence. Although the restoration of GABAergic function does not explain the dramatic reduction or elimination of limbically mediated craving for alcohol, cocaine and methamphetamine that patients report, it is what we understand thus far.

How is this being studied? Hal Urshel presented an open label controlled study of Prometa for the treatment of methamphetamine dependence at the annual College on Problems of Drug Dependence meeting in June. His high quality study illustrated safety in the outpatient model, high adherence to the protocol and a dramatic reduction in methamphetamine use confirmed by urine drug screening, in a trial conducted without a specific drug abuse counseling element. Randomized double blind clinical trials, funded by unrestricted grants are currently underway. A multicenter randomized double blind clinical trial of Prometa for the treatment of methamphetamine dependence is being conducted by **Walter Ling, MD** at UCLA and a randomized double blind clinical trial of Prometa for the treatment of alcohol dependence is being conducted by **Raymond Anton, MD** at the University of South Carolina. Moreover at Cedars Sinai in Los Angeles, CA, **Jeff Wilkins, MD** is comparing the efficacy of Prometa to that of acamprosate and long acting depot naltrexone. In addition to these studies there are pilot projects looking into the benefit of adding the Prometa treatment protocol to existing psychosocial models in the criminal justice system. Pilot studies in Geary Indiana drug court and in Pierce County, Washington, were so overwhelmingly positive that both programs adopted the Prometa protocol.

Clearly, more study of this biologic intervention is warranted. We are only on the surface of completely understanding how and why this intervention is so helpful to our patients. Unfortunately, the real message of the Prometa treatment protocols has been lost in the current debate. We cannot change the fact that market forces influence every aspect of the field of medicine. We can not change the fact that many of the treatments we use today (i.e. residential treatment, nutraceuticals, etc.) are not yet evidence based. We can however, continue to do what we can to help those who suffer so much.

As data continues to accumulate, more and more patients hopefully will gain access to biologic interventions with such robust effects on craving.

For the sake of our patients, we hope we can move the debate in the addiction field beyond ideologies about market forces to a patient-centric, scientific level. ▪

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Editor's note: Drs. Smith and Torrington are investors in Hythiam and have opened a new medical practice that operates an outpatient facility in Los Angeles managed by Hythiam.