

Aug 23, 2023

ISG
P.O. Box 5000
Daphne, AL 36526

Re: Jane Doe

Dear Dr. Tim Chen:

This letter constitutes further medical verification that Ms. Doe has the following conditions secondary to a MVA on 12/29/2022 as well as the scientific evidence supporting the use of the therapies that have benefited Ms. Doe.

TBI with post-concussive syndrome
Memory loss
Sound and light sensitivity
Mood changes
Brain fog and mental fatigue
Whiplash- of thoraco-lumbo spine
Lumbago with lumbar disc degeneration
Cervicalgia

Ms. Doe has pursued multiple therapies including acupuncture, chiropractic and medical management with limited benefits. I have recommended appropriately that receive hyperbaric oxygen therapy per protocol (40 treatments at 1.5 ATA), intranasal PRP and PBSCs x 1 treatment for her brain, and injectional treatment with PRP x 1 treatment for her neck and back.

Ms. Doe has followed through with a majority of these therapies, including hyperbaric oxygen therapy, with substantial clinical improvements. However, it is apparent that Mr. Chen has failed in his understanding of the benefits of these procedures for Ms. Doe. Mr. Chen has also failed to read and understand the multitude of scientific studies supporting these treatments for traumatic brain injury, including hyperbaric medicine. In a claims letter with Mr. Chen's commentary, he fails to provide any journal based, peer-reviewed literature that supports his erroneous assertion that hyperbaric medicine as well as platelet-rich plasma injections or intranasal infusions have no benefit for traumatic brain injury patients.

In contrast to Mr. Chen's failed rationale and clinical knowledge, hyperbaric oxygen therapy (HBOT), when used for concussion and traumatic brain injury has significant, proven benefits and is medical necessary for Ms. Doe. Benefits are directly related to HBOT include:

- Increases tissue oxygenation in the brain

- Slows and reverses hypoxic induced apoptosis
- Restores blood supply to the compromised region of the brain
- Generates new capillary networks (neovascularization)
- Aids other regenerative therapies, such as PRP and stem cell therapies

Many studies show the effectiveness of HBOT in improving brain function and quality of life in mild traumatic brain injury (mTBI) patients suffering chronic neurocognitive impairments. The common conclusion is that HBOT can induce neuroplasticity, leading to repair of chronically impaired brain functions and improved quality of life in mTBI patients with prolonged post-concussion syndrome (PCS) at late chronic stage. Studies also reveal that HBOT can reduce cognitive impairment related to memory performance and connectivity using functional MRI.

The science behind HBOT for TBI patients is vast.^[4] It has been shown that breathing 100% oxygen at increased atmospheric pressures allows the body to absorb about 10-15 times its normal supply of oxygen. This “high dose” oxygen, stimulates the growth of neuronal tissue, bone and blood vessels, reduces inflammation, and mobilizes stem cells.

See the following references to support these benefits of HBOT for post-concussion symptoms in mild-moderate traumatic brain injury patients.

Boussi-Gross, R., Golan, H., Fishlev, G., Bechor, Y., Volkov, O., et al. (2013) [Hyperbaric Oxygen Therapy Can Improve Post Concussion Syndrome Years after Mild Traumatic Brain Injury – Randomized Prospective Trial](#). *PLoS ONE* 8(11): e79995. doi: 10.1371/journal.pone.0079995.

Cifu, D. X., Hart, B. B., West, S. L., Walker, W., & Carne, W. (2014). [The effect of hyperbaric oxygen on persistent postconcussion symptoms](#). *The Journal of head trauma rehabilitation*, 29(1), 11-20.

Harch, P. G. (2022). [Systematic review and dosage analysis: hyperbaric oxygen therapy efficacy in mild traumatic brain injury persistent postconcussion syndrome](#). *Frontiers in neurology*, 160.

Harch, P. G., Andrews, S. R., Rowe, C. J., Lischka, J. R., Townsend, M. H., Yu, Q., & Mercante, D. E. (2020). [Hyperbaric oxygen therapy for mild traumatic brain injury persistent postconcussion syndrome: a randomized controlled trial](#). *Medical gas research*, 10(1), 8.

Intranasal PRP and PBSCs also have significant benefits for patients with traumatic brain injury as well. See references here <https://tbitherapy.com/tbi-protocol-references/> as well as the following references.

Platelet rich plasma (PRP) is rich in numerous growth factors associated with repair processes after injury in the central nervous system, which consists of the brain and spinal cord. One [study](#) investigated the ability of PRP to promote the growth of nerve tissue and to determine which growth factors were responsible for this growth. The study suggested that the addition of PRP promotes axonal nerve growth, particularly through mechanisms associated with growth factors known as IGF-1 (insulin-like growth factor 1) and VEGF (vascular endothelial growth factor).

To help patients with brain injuries, doctors have developed a combination of plasma and platelet-rich insulin. To avoid this risk, doctors prescribe the mixed drug through the nasal cavity so that it passes through the sevenfold cribriform plate in the brain. This is where PRP falls into the brain, spinal fluid and brain to regenerate nerve damage.

PRP and PBSCs (Peripheral blood stem cells) treatments for brain injury cause different functions in the brain and central nervous system:

- Brain collagen regeneration, a type of protein that strengthens and builds.
- Reduce the amount of amyloid protein, which leads to memory loss.
- Stimulate the formation of new blood vessels.
- Reduce inflammation in the brain, affecting its function.
- Specifically target and activate stem cells to promote regeneration and differentiation.

See also the following references.

Horcajo, C. B., Castillo, M. Z., & Crespo, J. V. (2018). [Platelet-rich plasma-derived scaffolds increase the benefit of delayed mesenchymal stromal cell therapy after severe traumatic brain injury.](#) *Cytotherapy*, 20(3), 314-321

[Platelet Rich Plasma \(PRP\) for brain injuries](#), retrieved from prpmed.de January 12th, 2023.

Akeda, K., Imanishi, T., Ohishi, K., Masuda, K., Uchida, A., Sakakibara, T., Kasai, Y., Sudo, A. (2012). [Intradiscal Injection of Autologous Platelet-Rich-Plasma for the Treatment of Lumbar Disc Degeneration.](#) Department of Orthopaedic Surgery and Spinal Surgery and Medical Engineering.

<https://patents.google.com/patent/US10130657B2/en>

Intranasally delivered insulin has also shown effectiveness for the treatment of post-concussion syndrome in TBI patients.

Using the intranasal (IN) delivery method to target insulin to the central nervous system (CNS) originally developed by Frey, Born and coworkers demonstrated that cerebrospinal fluid insulin levels significantly increased after treatment of normal adults with insulin, with no change in blood levels of insulin. In normal adults, IN treatment with insulin for 8 weeks improved memory (delayed recall of words) and mood at doses that did not alter blood levels of insulin or glucose.

The sum of insulin's effects on the brain include the following:

- improves brain ATP production
- decreases CSF cortisol
- improves neuronal viability in the hippocampus
- increases the expression of anti-inflammatory microglia
- reduces beta-amyloid and tau protein deposition

References to intranasal insulin can be found here:

Reed, J. R. (2017). [Intranasal insulin in treating cortical and hippocampal injury after moderate TBI](#). Uniformed Services University.

Frey, W. H. (2013). [Intranasal insulin to treat and protect against posttraumatic stress disorder](#). The Journal of nervous and mental disease, 201(7), 638-639.

Brabazon, F. P., Khayrullina, G. I., Frey, W. H., & Byrnes, K. R. (2014, June). [INTRANASAL INSULIN TREATMENT OF TRAUMATIC BRAIN INJURY](#). In JOURNAL OF NEUROTRAUMA (Vol. 31, No. 12, pp. A106-A106). 140 HUGUENOT STREET, 3RD FL, NEW ROCHELLE, NY 10801 USA: MARY ANN LIEBERT, INC.

For an overview of these references and the protocols used in the 21st century to treat the post-concussive syndrome due to TBI, see <https://tbitherapy.com/wp-content/uploads/2022/12/Theoretical-Framework.pdf>

Please call our office if you have any questions.

Kind regards,

John C. Hughes, D.O.