Protocols Relating to Carnitine

- **What is Carnitine?**
    - is a carrier molecule in the transport of long-chain fatty acids across the inner mitochondrial membrane. Carnitine is a naturally occurring substance required in mammalian energy metabolism.
    - Carnitine has been shown to facilitate long-chain fatty acid entry into cellular mitochondria, thereby delivering substrate for oxidation and subsequent energy production.
    - Fatty acids are utilized as an energy substrate in all tissues except the brain. In skeletal and cardiac muscle, fatty acids are the main substrate for energy production.
    - Because it increases adenosine triphosphate (ATP) generation and cellular oxidative respiratory processes, L-carnitine is often given with an antioxidant such as alpha-lipoic acid.
    - Carnitine is a derivative of Lysine- our body produces carnitine from lysine
- **What is Carnitine used for?**
    - Carnitine support various health conditions, including heart and circulatory issues,
    - Recently, it has gained prominence for its potential benefits in promoting weight loss and improving overall well-being.
        - Acetyl-L-carnitine infusion acutely ameliorated insulin sensitivity in type 2 diabetics with insulin resistance.
        - L-carnitine supplementation could improve BMI, but further research is needed for body composition and inflammation measured by CRP.
    - Carnitine can be used to enhance athletic performance.
    - Support renal insufficiency- Patients undergoing maintenance hemodialysis (HD), usually present with plasma carnitine insufficiency, due to accumulation of metabolic intermediates combined with impaired carnitine biosynthesis, reduced protein intake and increased removal via HD. **NOTE: This is outside of the Hydreight scope of practice.**
    - Male infertility- Overall, evidence supports that L-Carnitine can positively impact male fertility, even at a relatively low dose of 2 g/day. This supplementation enhances sperm parameters, regulates hormone levels, reduces ROS levels, and subsequently improves fertility rates.
    - Diabetes- L-Carnitine significantly lowers Fasting Plasma Glucose but increases fasting triglyceride in type II diabetic patients- so be aware
    - Other conditions Carnitine can improve or support are:
        - Cachexia
        - Dysthymic disorder (depression)

        - Migraine prophylaxis
        - Muscle Cramps
        - Peripheral Neuropathy
            - Carnitine may help reduce the severity of chemotherapy-induced peripheral neuropathy.
            - Carnitine may benefit the treatment of peripheral neuropathies associated with diabetes or caused by antiretroviral therapy.
    - Carnitine is also approved for the treatment of carnitine deficiencies secondary to inherited diseases,
        - such as propionyl-CoA carboxylase deficiency and
        - medium chain acyl-CoA dehydrogenase deficiency, and
        - in patients with end-stage renal disease undergoing hemodialysis
            - Hydreight does not treat deficiencies, this patient population will need to be supported by their nephrologist/medical team

- **What are Contraindications to getting Carnitine?**
    - **History of Seizures or with preexisting seizure activity:** In patients with preexisting seizure activity, an increase in seizure frequency and/or severity has been reported
    - **Pregnancy** (there is no safety data for use of Carnitine in pregnant clients); client must attest they are not pregnant to receive Carnitine infusion(intravenous "IV")/intramuscular injection ("IM"); if client is not absolutely positive she is not pregnant, then postponement and a client's self-administered pregnancy test is recommended prior to beginning any course of Carnitine IV/IM
    - **Breastfeeding** (there is no safety data for use of Carnitine in clients who are regularly engaged in breastfeeding a child); client must attest they are not breastfeeding to receive CarnitineIV/IM
    - **Renal Insufficiency:** chronic administration of high doses of oral levocarnitine in patients with severely compromised renal function or in ESRD patients on dialysis may result in accumulation of the potentially toxic metabolites, trimethylamine (TMA) and trimethylamine-N-oxide (TMAO), since these metabolites are normally excreted in the urine.
    - **Drug Interactions:** Warfarin
- **Important Requirements for Administrators of Carnitine**
    - Training- Watch the Carnitine Webinar
    - Review the Carnitine Protocol
    - Complete the Carnitine comprehension Quiz within the app

        - The Quiz may need to be reviewed and completed every 6-12 months

Carnitine Patient Specific RX 503A (Vendor is State Dependent)

- **Important Pre-Appointment Requirements for Carnitine:**
    - Client request Carnitine
        - They should complete Carnitine intake form and consent by booking through the app
        - Reminder: pregnancy, breastfeeding mothers, Patients with history of or current, preexisting seizure conditions are contraindicated
            - Chronic renal insufficiency must be evaluated every time by medical provider, as chronic administration of levocarnitine may result in the accumulation of toxic metabolites.

    - Once Carnitine intake form and consent are completed by client- they will schedule their patient consultation through the app
    - Once consult is complete the prescriber sends the prescription to the pharmacy for fulfillment.
    - Carnitine Patient Specific Prescription usually arrives to location -
        - Carnitine that is patient specific will be shipped to the patient themselves. UNLESS- you are approved by Hydreight Medical team
        - If you have a brick and mortar, and are approved, then Carnitine will be shipped to the administering partner, under the patient's name. This Carnitine is ONLY to be used for the patient whose name is on the label.
            - It is a felony to use/share a prescription on/with someone else.
        - Storage: Reminder you need to have safe storage for Carnitine, which is refrigerated once reconstituted. These vials have patient specific, PHI (protected health information), on them.
            - A locked refrigerator with a temperature log should be maintained
                - Any temperature excursion outside of labeled requirements should result in a call to the pharmacy who manufactured the product for next steps or disposal.
        - Follow up patient consults will be required for continuation of Carnitine every 3 months

    - Client may schedule once you have confirmation that prescription is sent and being shipped or once your location has received prescription. Please keep in mind if you schedule a client before the prescription has arrived, you do run the risk of the prescription not arriving on time.

Carnitine Office Use allowed-503B Olympia (all states except AL, CA, MS)

- After intake and approval by the medical provider proceed below
  - Once Carnitine intake form and consent are completed by client- they will schedule their patient consultation through the app

- **Important Pre-Infusion/IM Requirements for Carnitine IV/IM**
  - Verify completion of intake forms, Carnitine pre-screening, telehealth appointment, Informed Consent and any other applicable agreement, consent or other client document.
  - Review Carnitine IV/IM procedure, risks/dangers, adverse reactions, side effects or complications with client prior to initial Carnitine IV/IM.
  - Review Emergency Protocol with client prior to initial Carnitine IV/IM
  - Remind client of mandatory 15 minute post-infusion monitoring period (for initial and repeat Carnitine IV/IM).
  - Follow up patient consults will be required for continuation of Carnitine every 3 months

- **Important Drip Requirements for Carnitine IV:**
  - Carnitine must be combined in a minimum of 500mL normal saline or lactated ringers bag. (label vial with BUD, beyond use date, for 28 days).
  - Carnitine has a high osmolarity and under this protocol is to be given on its own as a separate administration.
    - Keep in mind if a client wants carnitine, the max volume of fluids is 1000ml.
      - Advise running carnitine in 500ml and any other regular drip in a 500ml as not to exceed the 1000ml limit.
        - Medical consult must occur for approval above 1000ml.
        - Contact the medical team for all further inquiries specific to your business.

- **Carnitine Infusion Protocol:**
  - Obtain Vital Signs
    - HR, BP, O2 Sats,Pulse, Temp
  - Starting dose for Carnitine is 500mg
      - BE MINDFUL and PAY ATTENTION to them as you titrate up.
    - Drip rate- should not initially exceed 5ml/min. After initiating, may increase as tolerated.

- Clients are slowly titrated up in 250-500mg increments- this is based on client tolerance of infusion.
- Monitor patient during and for 15 minutes after infusion
- Max dose to be given per infusion is 2000 mg
- Max weekly Carnitine dosing is 2000mg (be mindful of the 1000ml fluid volume limit)
    - Unless getting IM shots then take into account IM shots for Max weekly dosing of 4000mg
- Max monthly Carnitine dosing is 8,000 mg. (four 2000 mg on separate days)
    - Unless getting IM shots, then take into account IM shots for Max monthly dosing of 8000mg
- Infusions and IM shots should be at least 2 if not 3-4 days apart

- **Carnitine IM Protocol:**
    - Please label vial with BUD for 28 days.
        - Starting dose will be determined with consult. Somewhere between 250-500mg
        - The patient should then be increased by 250mg increments- this is based on client tolerance of injections
        - Max IM dose of 1000mg
        - Max weekly IM dose of 2000mg.
        - Total weekly dose max of 2000mg (this includes IV and IM)
            - Take into account total weekly dose if getting a Carnitine IM and infusion
        - Infusions and IM shots can be on the same day but must not exceed maximum dosing and be cautious while titrating
        - ***For the IM shot monitor the patient for 15-20 minutes post injection. ***

- **MAX Dosing Titration schedules**
    - Max dose to be given per infusion is 2000 mg
    - Max weekly Carnitine dosing is 2000mg
        - Unless getting IM shots then take into account IM shots for Max weekly dosing of 2000mg
    - Max monthly Carnitine dosing is 8,000 mg. (Four 2000 mg on separate days, at least 5 days apart)
        - Unless getting IM shots, then take into account IM shots for Max monthly dosing of 8000mg

- **If doing both IV and IM Carnitine dosing for a client:**
    - Take EXTRA PRECAUTION with your totals and titrating
        - Example titration
            - Week 1- 500mg IV, 250mg IM
            - Week 2-750mg IV, 250mg IM
            - Week 3-750mg IV, 500mg IM
            - Week 4-1000mg IV, 500mg IM
            - Week 5- 1000mg IV, 750mg IM
            - Week 6- 1250mg IV, 750mg IM (this is the max 2000mg)
            - Week 7-1500mg IV, 500mg OR 1000mg IV, 1000mg IM
            - Week 8-1750mg, 250mg
            - Week 9-2000mg IV
        - Example once tolerates 100mg IM and 250mg IV
            - Alternates 2000mg IV on weeks 1,3 and 1000mg IM twice weekly on weeks 2,4

- **Mandatory Post-Infusion/IM Monitoring Period:** Monitor and document the client's vital signs for a minimum of 15 minutes after the first infusion/IM injection ends, or any subsequent infusion/IM injection where the dose has been increased.
    - For routine infusions/IM Injections after the initial infusion/IM injection, need only monitor and document the client's vital signs for a minimum of 15 minutes after the treatment.
    - Clients should be advised of the applicable minimum monitoring period and that it is required for client safety (and, if they are driving from their appointment, others' safety).
    - If a client leaves the monitoring protocol before expiration of the required time, their early departure notwithstanding the minimum monitoring period should be noted.
- **Emergency Protocol**
    - Client to proceed, or if necessary client to be sent, to the emergency room at a local hospital; OR
    - Client to proceed, or if necessary client to be sent, to local urgent care center; OR
    - Client to call, or if necessary call on behalf of client, 9-1-1 emergency telephone number; OR
    - Client to call, client's regular, independent physician or other qualified healthcare provider
    - See Post-Emergency Protocol Below also.
- **Adverse Reactions, Complications and Side Effects of Carnitine Infusion/IM:**

- Clients and clinicians should be prepared to follow the Emergency Protocol – and see a doctor IMMEDIATELY – if the Carnitine IV/IM client experiences any one or more of the below adverse reactions, side effects or complications during, immediately after or within 12-hours after completing an Carnitine IV/IM.
  - If any of these occur during the infusion, stop the infusion, and enact Emergency Protocol. Commence monitoring period and monitor and document client's vital signs. Contact your medical director after commencing Emergency Protocol.
  - If any of these occur during the monitoring period after the infusion/IM injection, enact Emergency Protocol. Continue monitoring and documenting client's vital signs. Contact your medical director after commencing Emergency Protocol.
  - If any of these occur after the monitoring period and within 12 hours after the infusion/IM injection then the client should enact and enact Emergency Protocol. Client should contact business partner or associate who administered Carnitine IV/IM Injection as provided below in "Post-Emergency Protocol".
- Adverse Reactions, Side Effects or Complications for Emergency Protocol

Some Potential Adverse Reactions, Side Effects or Complications to Carnitine		
Headaches	Diarrhea	Pharyngitis
Malaise	Hyper and Hypotension	Cough increase
Chest Heaviness	Difficulty Breathing*	Dizziness
Vomiting	Shortness of Breath	Nausea

*Denotes possible anaphylactic reaction. Enact Emergency Protocol

Some General IV Infusion Side Effects or Complications		
Infusion-Site Effects*	Headache	Nausea/Upset Stomach
Indigestion/Heartburn	Mild Diarrhea	Joint Pain
Vein Inflammation	Lightheadedness	Increased Thirst
Dizziness	Chills	Severe Fatigue
Infection	Fever	Shakes

* Infusion-site effects may include, without limitation, temporary pain, burning, bruising, blood, cellulitis or discoloration at the site of infusion.

- **Post-Emergency Protocol** – After the Emergency Protocol,
  - Client to service provider, and service provider will prepare and complete an incident report by phone to be submitted on the app under specific client profile.

- If the client does not complete a report, business partner or associate partner then will coordinate completion of relevant portions of the report with its Medical Director without client input.
- Final incident report shall be submitted directly to the medical director email, and thru the app.

- **Tips**
  - You may have inquiries for up to 1000mg. There is not currently data supporting doses greater than 500mg. Please educate the patient for safety purposes you are happy to incrementally increase them to the appropriate dose for their body within the prescribers instructions on THEIR specific vial.

Additional Resources

Links to studies

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020182s015lbl.pdf

https://pubmed.ncbi.nlm.nih.gov/19620516/

https://pubmed.ncbi.nlm.nih.gov/15591003/

https://pubmed.ncbi.nlm.nih.gov/32397485/

https://pubmed.ncbi.nlm.nih.gov/15741989/

https://pubmed.ncbi.nlm.nih.gov/33596883/

https://pubmed.ncbi.nlm.nih.gov/37762736/#:~:text=Overall%2C%20evidence%20supports%20that%20L,and%20subsequently%20improves%20fertility%20rates.

https://ods.od.nih.gov/factsheets/carnitine-HealthProfessional/

https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=cf801cc4-775e-433d-9d32-e5d9a98981d3#i4i_dosage_admin_id_1cba78be-61fb-4cf6-920a-c00c82a4aad4

https://www.drugs.com/npp/l-carnitine.html

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