Chronic Pain
post-acute sequelae of COVID-19

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Bateman Horne Center 2022

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THE COVID-19 PANDEMIC AND ITS CONSEQUENCES FOR CHRONIC PAIN: A NARRATIVE REVIEW (Sept 2022)

The COVID-19 pandemic has increased the prevalence of chronic pain and headache.

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Shanthanna H, Nelson AM, Kissoon N, Narouze S. The COVID-19 pandemic and its consequences for chronic pain: a narrative review. Anaesthesia. 2022 Sep;77(9):1039-1050. doi: 10.1111/anae.15801. Epub 2022 Jul 18. PMID: 35848380; PMCID: PMC9350079.

Table 1

Key findings on pain and headache associated with COVID-19.

1. **Acute SARS-CoV-2** infection can present with pain, commonly as *myalgia, joint pains and headache*.
2. **New-onset chronic pain after SARS-CoV-2 infection** is *one of the five common features of long COVID*. Its prevalence decreases over time and symptoms can fluctuate.
3. **Common pain conditions** with long COVID include myalgia, fatigue, joint pains and post-intensive care syndrome-like syndrome.

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Table 1 (continued)

Key findings on pain and headache associated with COVID-19.

4. **Risk factors** for developing chronic pain include the following: the need for intensive care, high BMI, female sex, myalgia at hospital admission, loneliness and a perception of increased isolation.

5. **Possible mechanisms** for pain include sympathetic overactivity, dysregulation of neural activity similar to chronic fatigue syndrome and inflammatory-immune mediators.

6. **Headache** as a presenting symptom predicts a milder course, but delayed onset along with other neurological symptoms warrants evaluation for secondary causes.

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Figure 1.
Possible mechanisms of pain and associated symptoms with COVID-19.

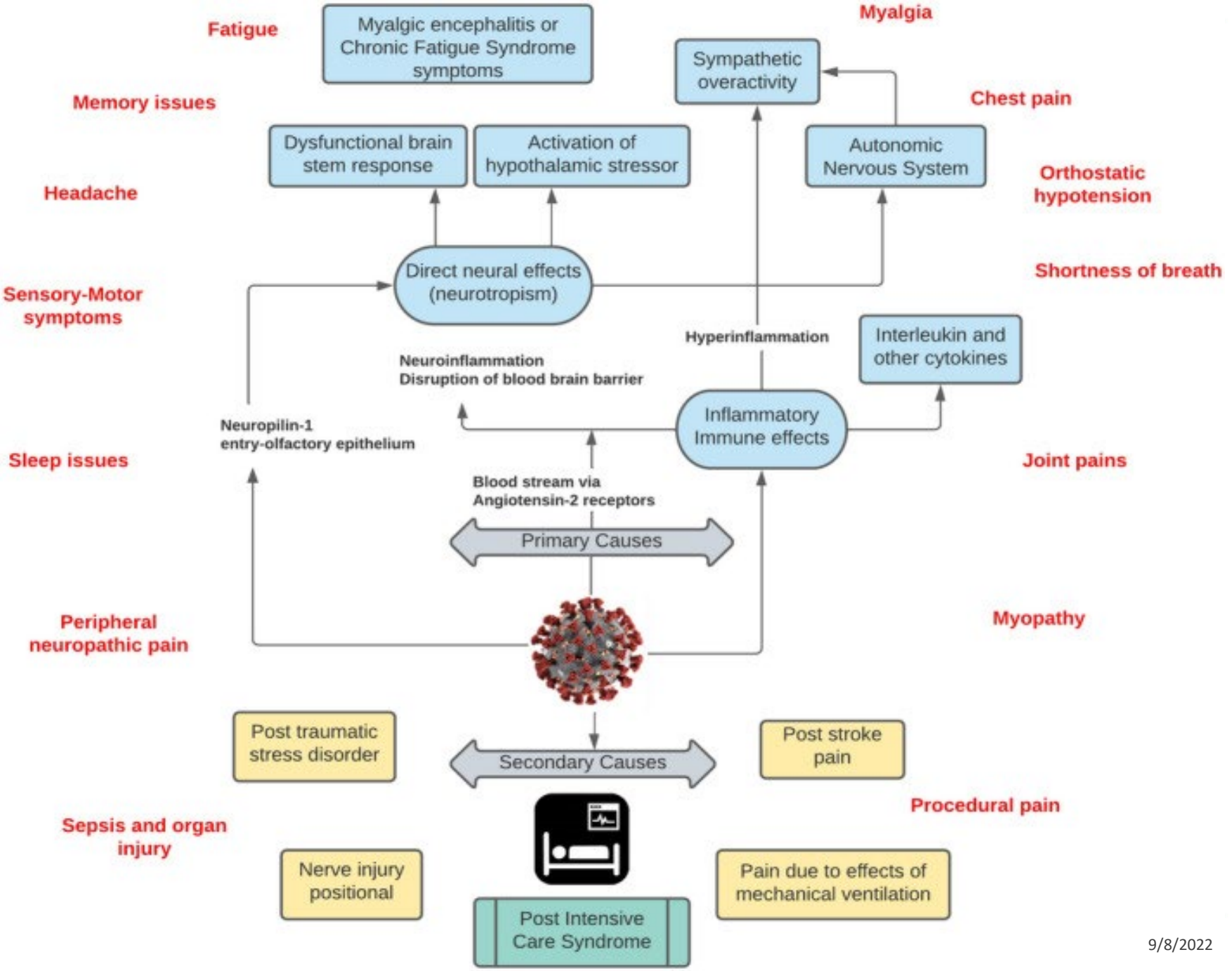

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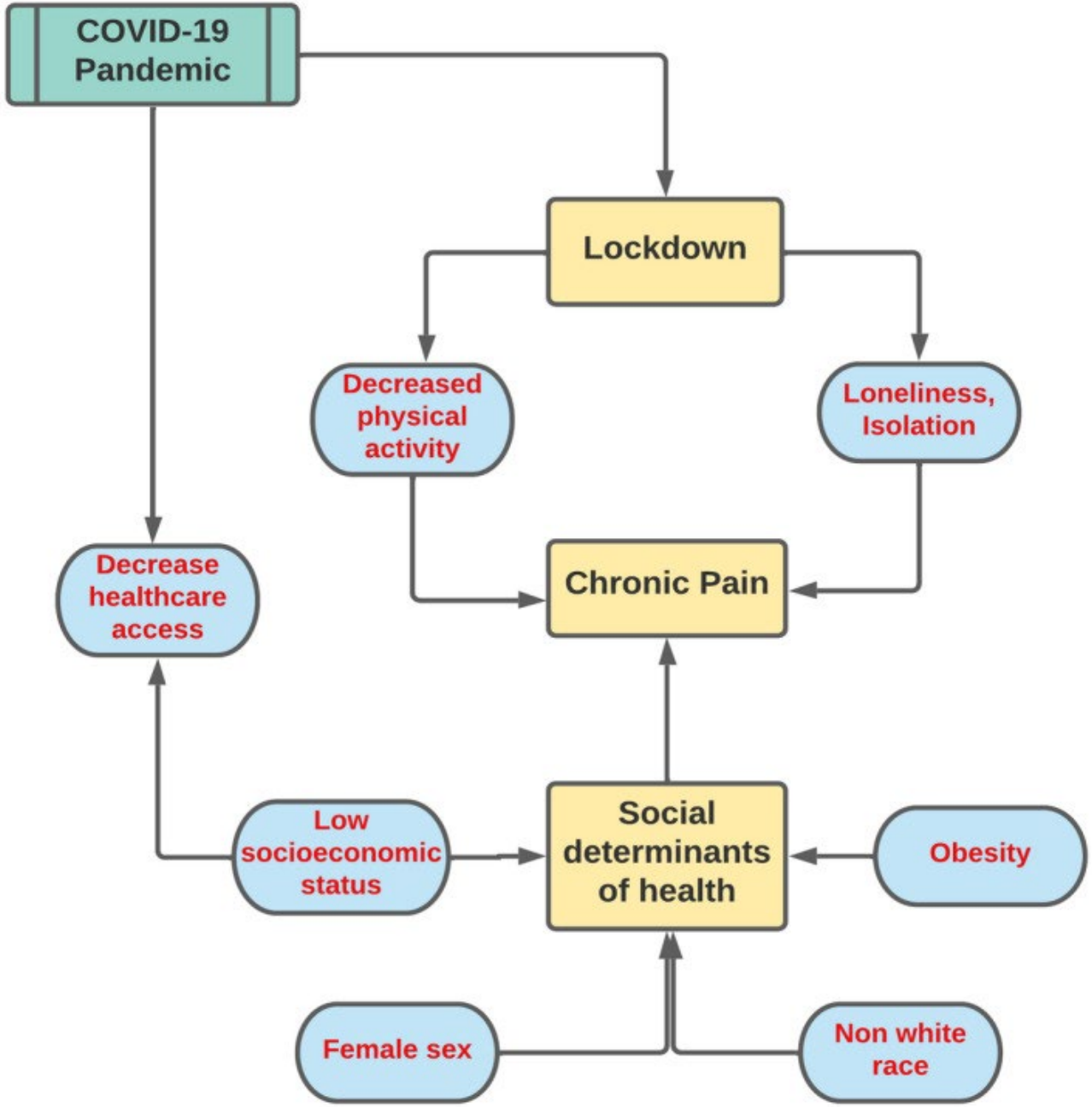
Figure 2. Factors influencing symptom burden during the COVID-19 pandemic on *existing* chronic pain patients.



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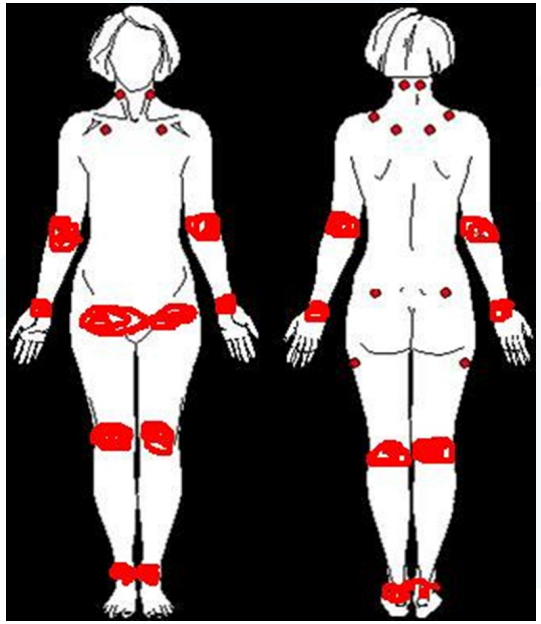
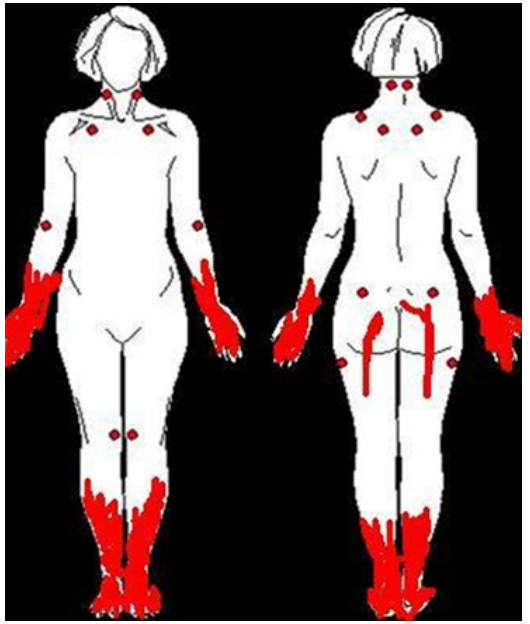
CHRONIC PAIN AND CHRONIC WIDESPREAD PAIN

- **Pain** has many causes, types, treatments
- **Chronic pain** usually responds to treatment but may be difficult to cure
- **Pain specialists** and **physiatrists** can help with many aspects of pain management

PAIN DIAGRAMS:
A PICTURE WORTH 1000 WORDS





ASSESS AND TREAT PAIN BY TYPE

- Osteoarthritis and musculoskeletal pain
- Inflammatory conditions (CTD, injuries, gout)
- Spine---cervical and lumbar DJD/DDD: a combination of OA/DJD and nerve pain with muscle spasm
- Neuropathies: peripheral and other…
- Hyperalgesia, generalized pain amplification (FM, ME/CFS)
- IBS, interstitial cystitis, pelvic pain---mostly hyperalgesia
- Headaches, tension or chronic daily headaches
- Migraine headaches: a vascular phenomenon with hyperalgesia

OSTEOARTHRITIS AND INFLAMMATION

- Light exercise and range of motion
- Anti-inflammatories (NSAIDS and COXII)
  - ibuprofen, naproxen, diclofenac absorbed topically
  - meloxicam
  - celecoxib *should be* *easiest on the stomach*
- Corticosteroids---short term use safer than long term use
  - prednisone, methylprednisolone, etc Oral or injectable
- Immune suppressing and targeted agents for inflammatory arthritis
  - Numerous drugs through rheumatologist

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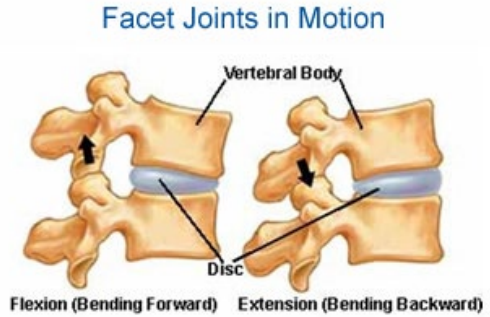
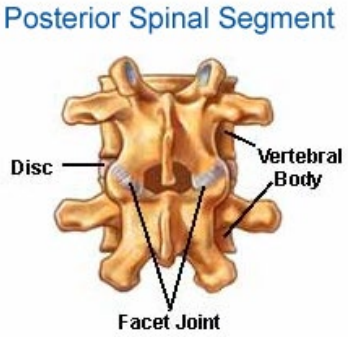
CERVICAL, THORACIC OR LUMBAR SPINE DISEASE





- Facet arthritis—multiple small joints
- Lateral foraminal narrowing (stenosis)
- Central canal narrowing (stenosis)
- Mild nerve compression→ muscle spasm and pain
- Moderate to severe nerve compression→ loss of sensation, reflex, motor
- All aspects of spine disease pain can be worsened by the pain amplification of FM
- May be amenable to physical therapy, pain relieving procedures, or surgery

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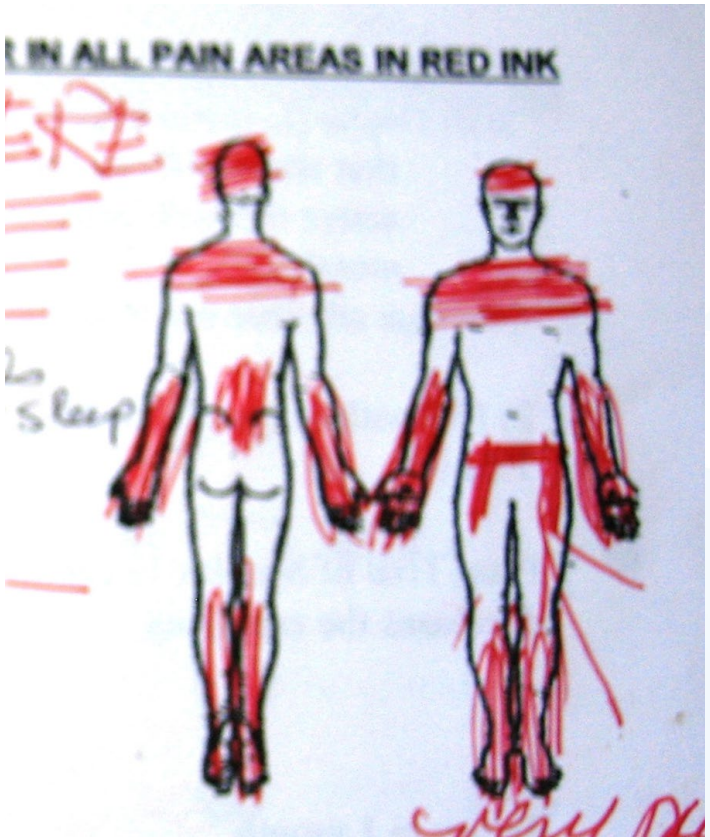
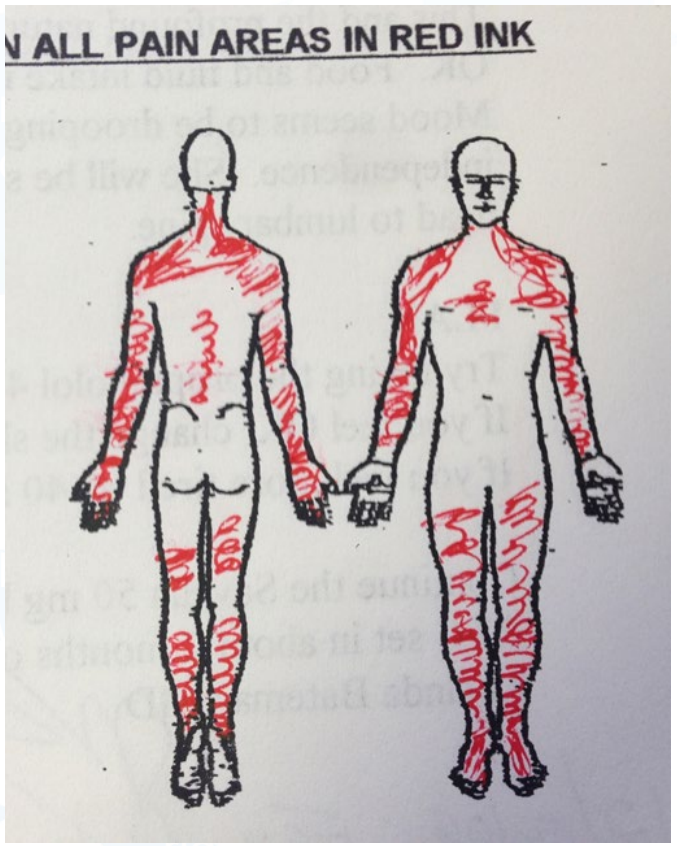

IN ALL PAIN AREAS IN RED INK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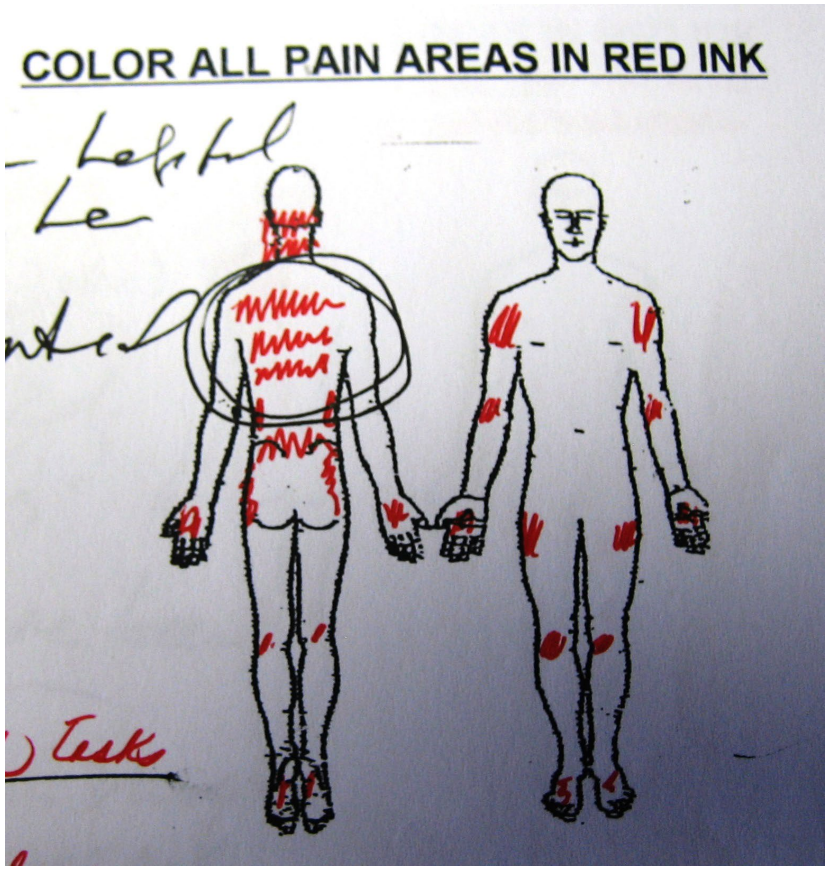
COLOR ALL PAIN AREAS IN RED INK

FM AND HYPERALGESIA RESPOND TO:

- Improved sleep
- Relaxation, meditation, emotional calm, mental distraction
- Physical activity in the right amount:
  - not too little (being sedentary)
  - not too much (low impact--not intense--exercise)
- Massage, acupuncture, other manual methods
- Warm baths and other relaxation techniques

FM PAIN RESPONDS TO DRUGS THAT MODULATE THE CENTRAL NERVOUS SYSTEM

- **FDA approved** drugs for FM
  - Anticonvulsants: **pregabalin**
  - SNRI: **duloxetine** and **milnacipran** (Savella)
- **Non-FDA approved** drugs used for FM used "off label" with varying FDA indications
  - Anticonvulsants: **gabapentin, topiramate, zonisamide** (no weight gain)…
  - SNRI: levomilnacipran (Fetzima), venlafaxine, desvenlafaxine
  - Low dose TCA: **amitriptyline, doxepin,** nortriptyline, etc.
  - Muscle relaxants: **cyclobenzaprine,** tizanidine, methocarbamol, baclofen…
  - tramadol, buprenorphine variants, opioids as a last resort. FDA approved for pain.
  - **LDN** (low dose naltrexone) and **CBD** may have anti-neuroinflammatory effects

Topical agents can also be helpful (CBD, lidocaine, diclofenac, gabapentin, compounded combos, etc.)

LDN (LOW DOSE NALTREXONE)– OFF LABEL USE

- naltrexone hydrochloride is an opioid receptor antagonist, FDA approved for treatment of alcohol and opioid dependence (50 mg)
- In very low doses (1 to 4.5 mg) LDN may:
  - paradoxically **decrease** pain amplification due an increase in the release of endogenous opioids with transient opioid receptor blockade
  - **calm microglial cell activation** in the CNS (anti-inflammatory or neuroinflammatory agent)

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Low-dose naltrexone for the treatment of fibromyalgia: findings of a small, randomized, double-blind, placebo-controlled, counterbalanced, crossover trial assessing daily pain levels. Younger J1, Noor N, McCue R, Mackey S. Arthritis Rheum. 2013 Feb;65(2):529-38. doi: 10.1002/art.37734

The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain. Younger J, Parkitny L, McLain D. Clin Rheumatol. 2014 Apr;33(4):451-9. doi: 10.1007/s10067-014-2517-2. Epub 2014 Feb 15. **Review.**

LOW DOSE NALTREXONE (LDN) --- OFF LABEL USE

- LDN *works gradually* to reduce pain. Observe at least 3 months to determine efficacy. Most generally take LDN at bedtime.
- Naltrexone is a generic drug, but only in 50 mg form, so must be compounded ($$) or mixed into an oral elixir and refrigerated (dissolve 50 mg tab in 50 ml distilled water to make 1 mg/1 ml elixir).
- LDN can sometimes disrupt sleep, but this usually resolves. Some people start at a lower dose (1-2 mg) and work up gradually to minimize start-up side effects.
- LDN cannot be used in combination with opioids (hydrocodone, oxycodone, tramadol) because LDN **inhibits** the opioid receptors and opioids **stimulate** the receptors.
- Stop LDN in advance of elective surgery or other situations where short acting opioids might be needed. Inform all medical personnel about taking LDN. In an emergency situation requiring opioids, it may take a higher dose to control pain if LDN has not been stopped in advance.

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Covered in a future ECHO lecture!