

Chronic Pain in Noonan Syndrome

Noonan Syndrome Family Conference

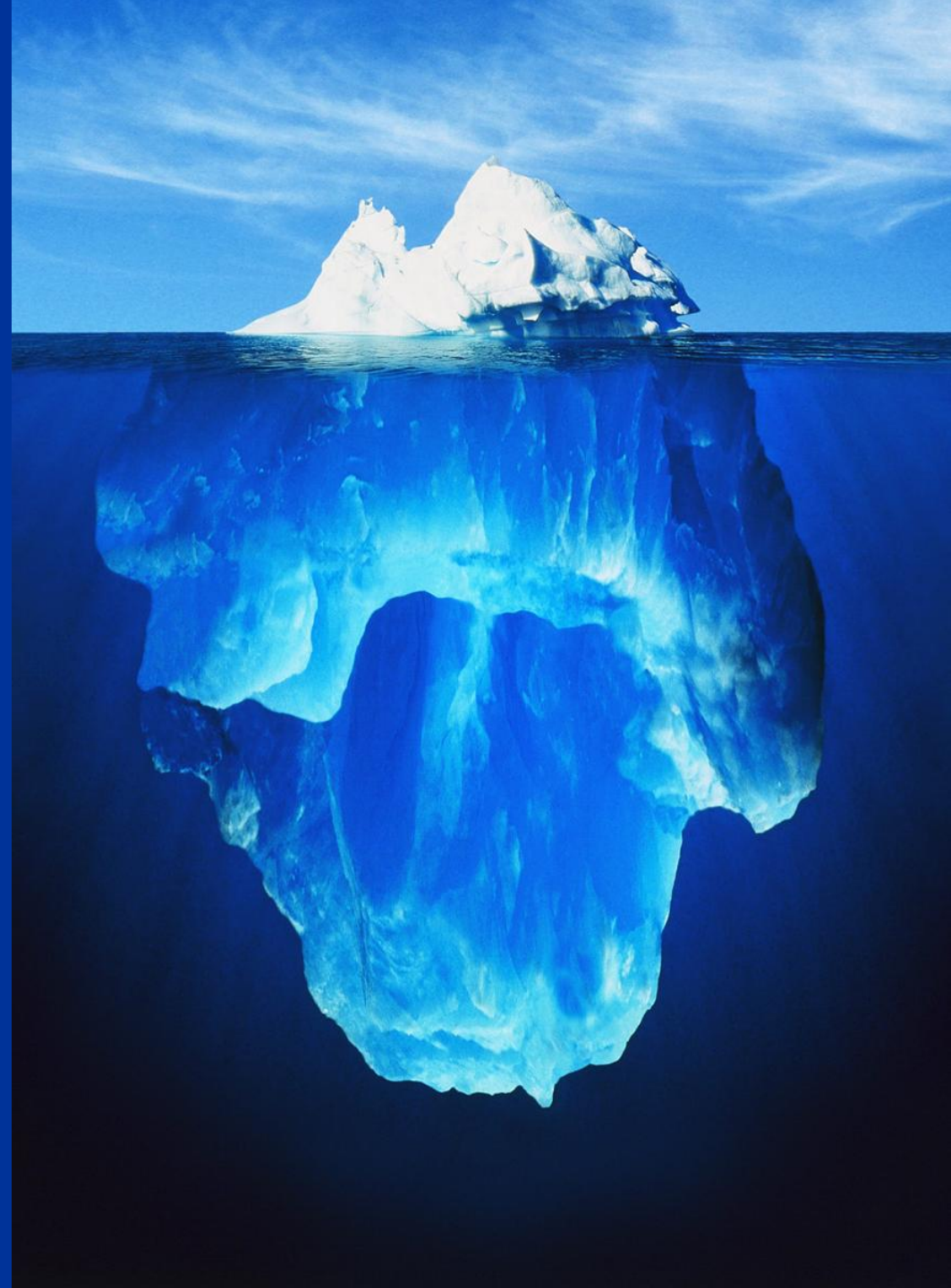
July 30, 2026

Amy E. Roberts, MD
Co-Director, Center for Cardiovascular Genetics
Boston Children's Hospital



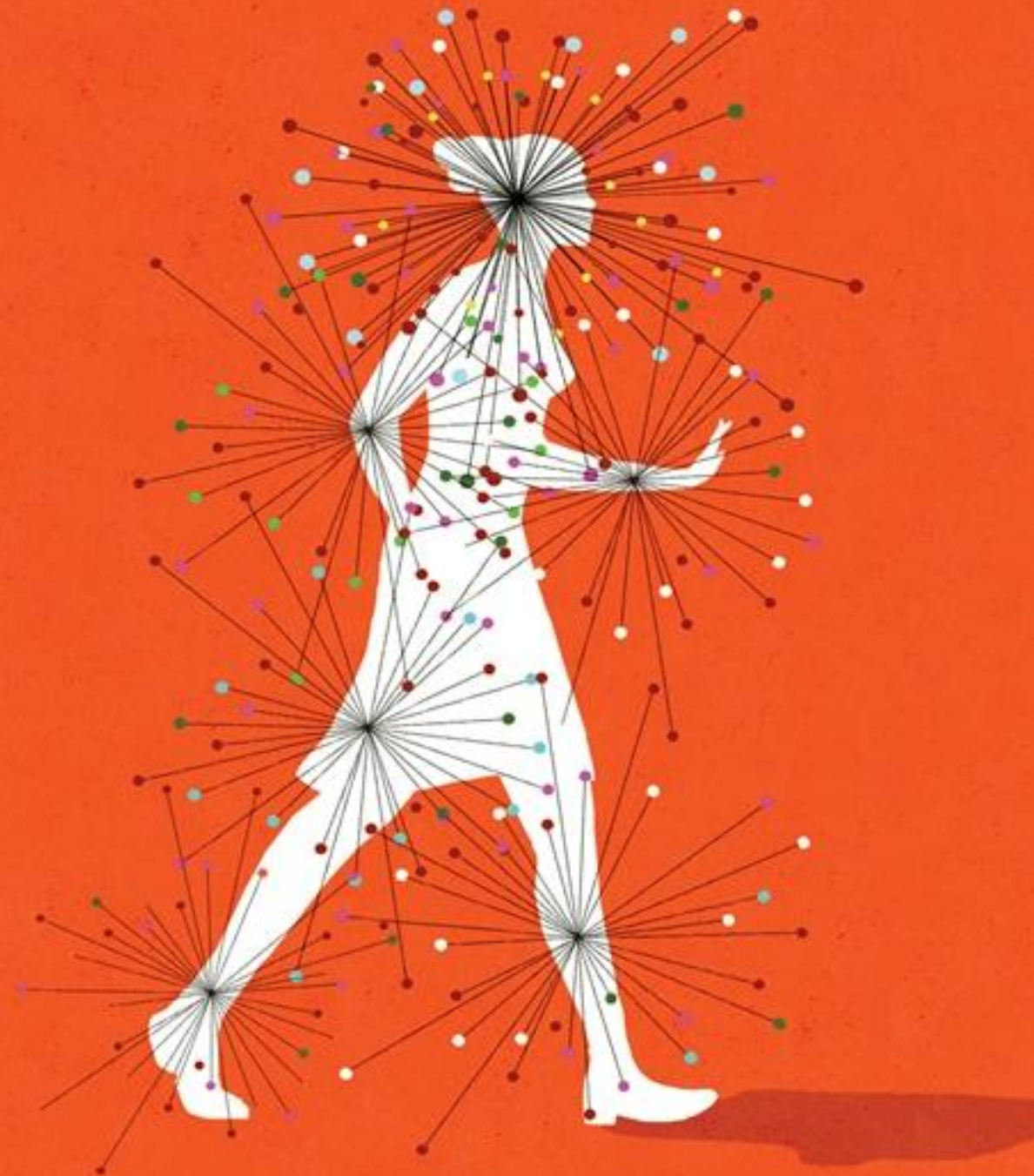
Why this matters

1. Common
2. Under-recognized
3. Function-limiting
4. Often multifactorial



How common is pain?

1. 50 to 62 percent in surveys
2. Up to 89 percent in focus groups
3. All ages affected
4. Often worse with age



Common pain patterns

1. Belly pain
2. Joint pain
3. Back pain
4. Muscle pain
5. Extremities

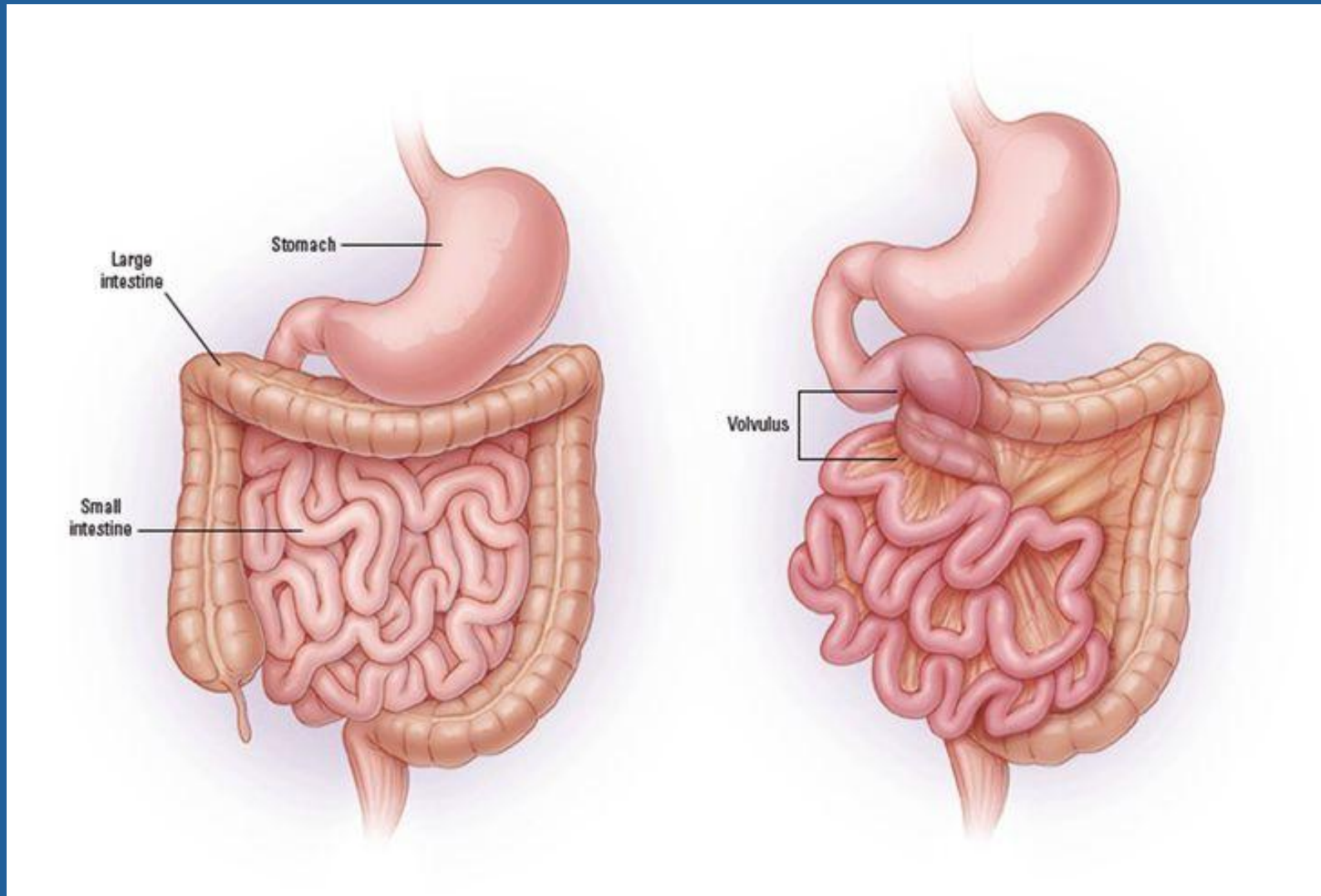


Abdominal “Belly” Pain

- Malrotation
- GERD
- Constipation
- Intestinal lymphangiectasia
- Functional abdominal pain



MALROTATION & VOLVULUS

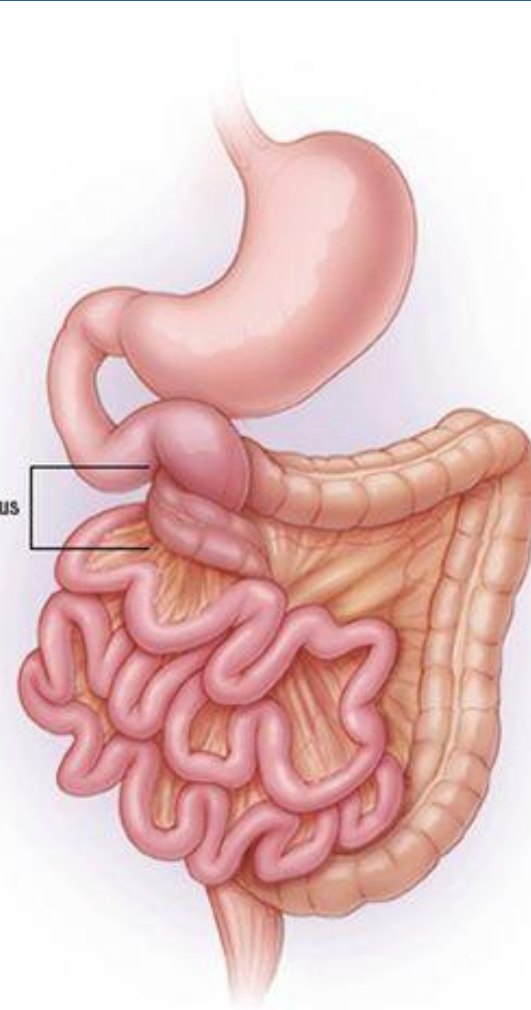


MALROTATION & VOLVULUS

SYMPTOMS

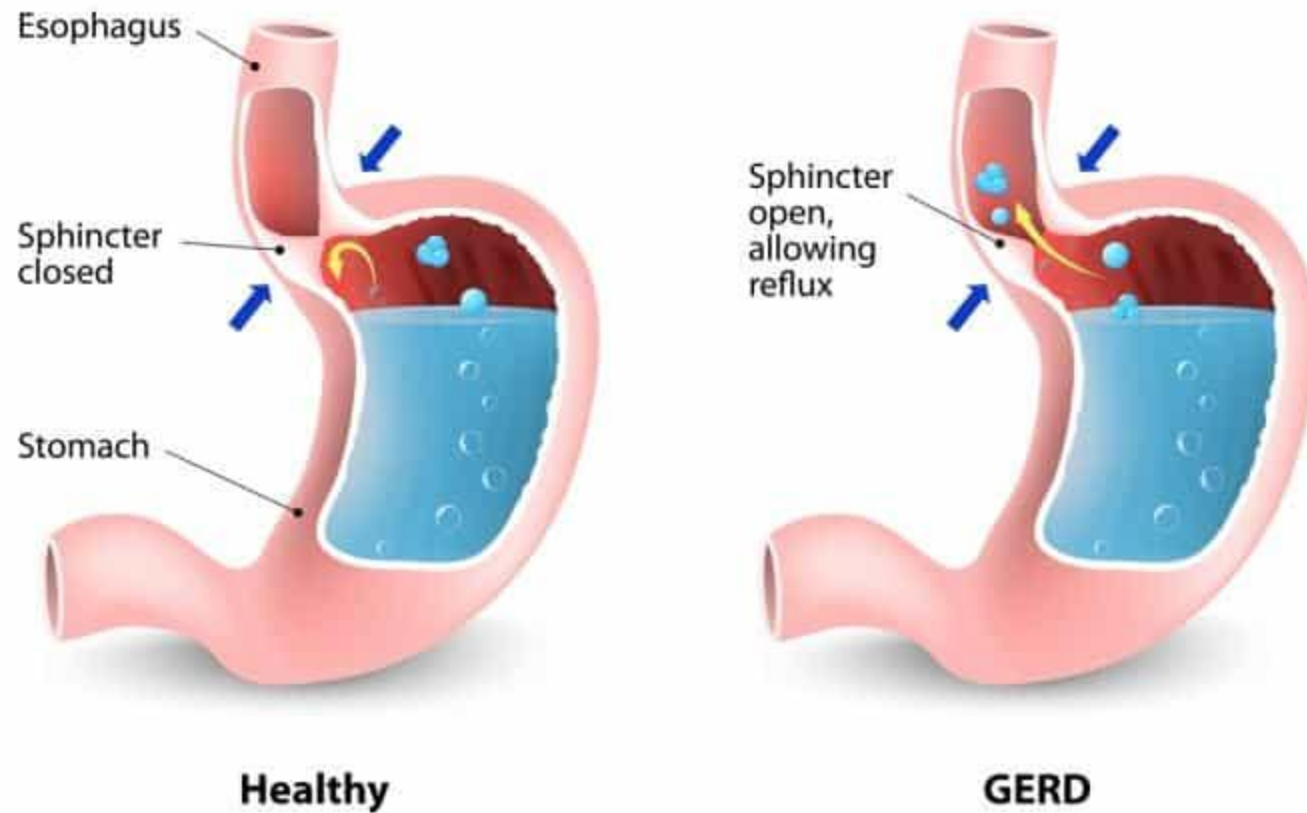
Vomiting (bile)
Abdominal pain
Diarrhea, Constipation
Blood in stool
Poor weight gain

Volvulus



GERD

Gastroesophageal reflux disease



- Bad breath or an acidic taste in the mouth
- Chronic dry cough, wheezing, or hoarseness
- Trouble or pain when swallowing

GERD

Gastroesophageal reflux disease

SYMPTOMS (Older children/Teens)

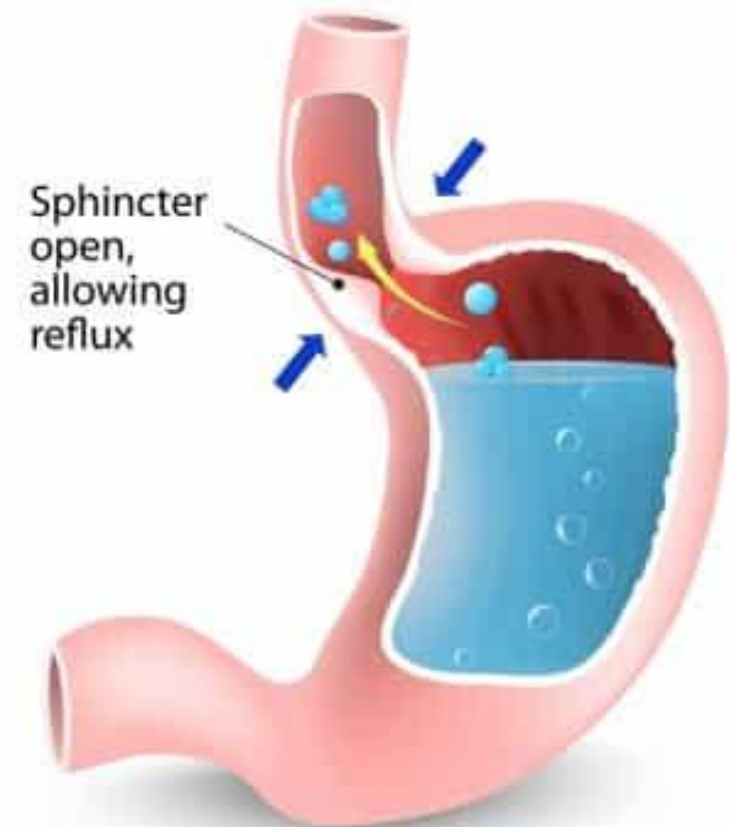
Heartburn/burning in chest

Nausea, upper abdominal pain

Acidic taste

Chronic dry cough, wheezing,
hoarseness

Trouble or pain with swallowing



GERD

CONSTIPATION

- BABIES AND TODDLERS vs SCHOOL AGE
- DO NOT UNDERESTIMATE
 - Abdominal pain, vomiting
 - Decreased appetite
 - Urinary incontinence
 - Painful defecation -> withholding -> worsening constipation

Milk of magnesia

Lactulose

Mineral oil,

Polyethylene glycol (PEG) (MiraLAX)

INTESTINAL LYMPHANGIECTASIA

- Leakage of lymphatic fluid into the bowel
- Often also have lower extremity swelling
- RARE
- Signs/Symptoms:
 - Diarrhea
 - Distended abdomen
 - Abdominal pain
 - Low albumin (protein)
 - Low immunoglobulins (antibodies)
 - Low calcium
 - Low blood counts

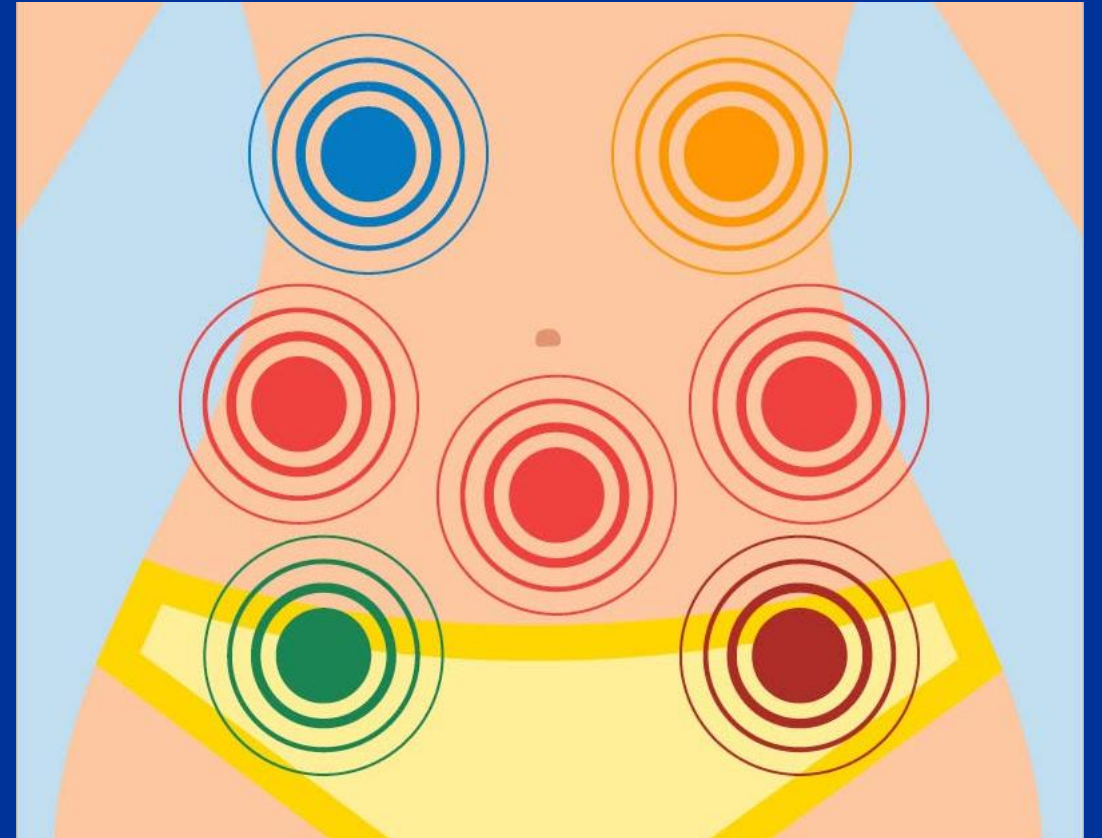
Functional Abdominal Pain

Chronic or recurrent abdominal pain without evidence of an underlying structural, biochemical, or inflammatory cause

At least three episodes of pain over three months severe enough to interfere with daily activities

Diagnosis of exclusion

REALLY COMMON!



Functional Abdominal Pain Disorders (FAPDs)

The Rome IV criteria divide FAPDs into four subtypes:

- **Functional dyspepsia** — bothersome after meal fullness, early fullness, or stomach pain/burning not associated with defecation; ≥4 days/month for ≥2 months
- **Irritable bowel syndrome** (IBS) — abdominal pain ≥4 days/month associated with changes in stool frequency or form; pain does not resolve with resolution of constipation alone; criteria met for ≥3 months
- **Abdominal migraine** — paroxysmal episodes of intense central/midline pain lasting ≥1 hour, separated by weeks to months of normal health, associated with ≥2 of: loss of appetite, nausea, vomiting, headache, light sensitivity, pallor; ≥2 episodes in 12 months
- **Functional abdominal pain** — not otherwise specified (FAP-NOS) — episodic or continuous abdominal pain ≥4 times/month for ≥2 months that *does not meet criteria for the other three subtypes*

Functional Abdominal Pain Disorders (FAPDs)

Causes

Visceral hypersensitivity and dysregulation of the microbiota-gut-brain axis

Contributing factors:

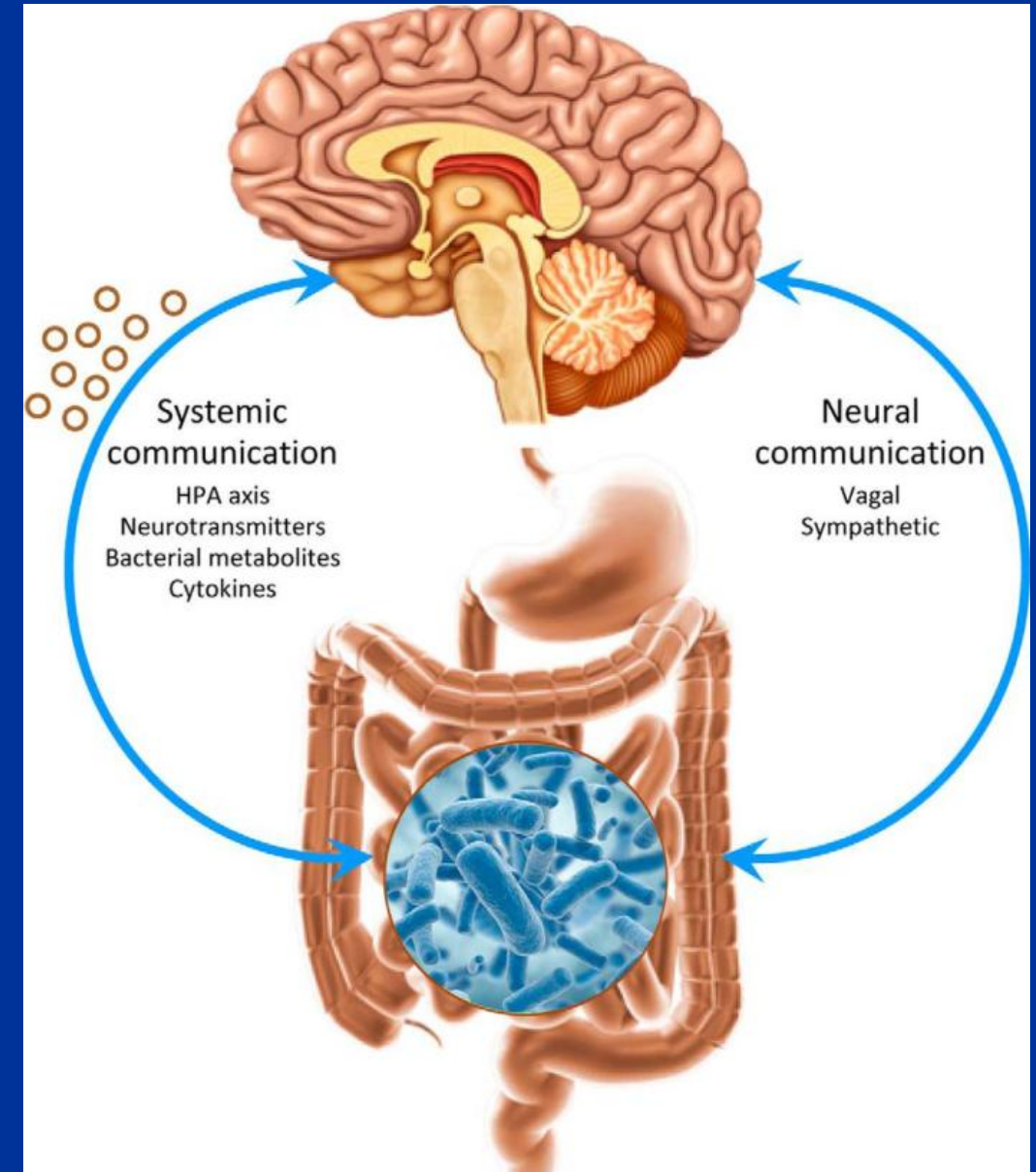
Intestinal inflammation

Altered motility

Gut microbiota changes

Psychological factors (anxiety, stress)

Central sensitization, and altered brain connectivity



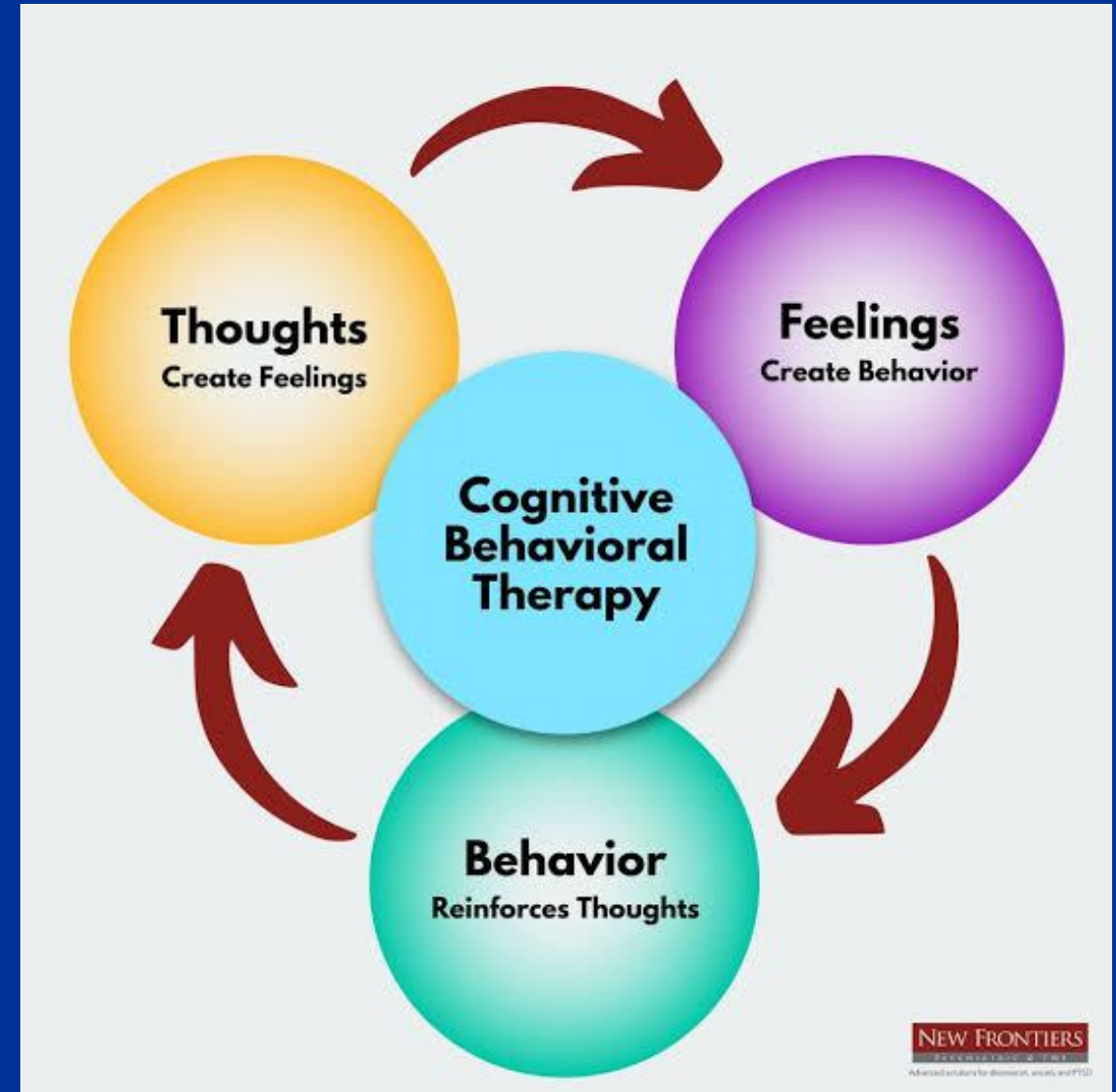
Functional Abdominal Pain Disorders (FAPDs) Management

GOAL is improve quality of life and reducing disability not complete pain resolution

First-line: Education, reassurance, and simple dietary/behavioral advice

Psychological therapies (strongest evidence):
Cognitive behavioral therapy (CBT) and gut-directed hypnotherapy

Limited evidence: probiotics, peppermint oil, mebeverine, neurostimulation (percutaneous electrical nerve field stimulation)



“GI Considerations in Noonan Syndrome”

Dr. El-Chammas

9am, Friday

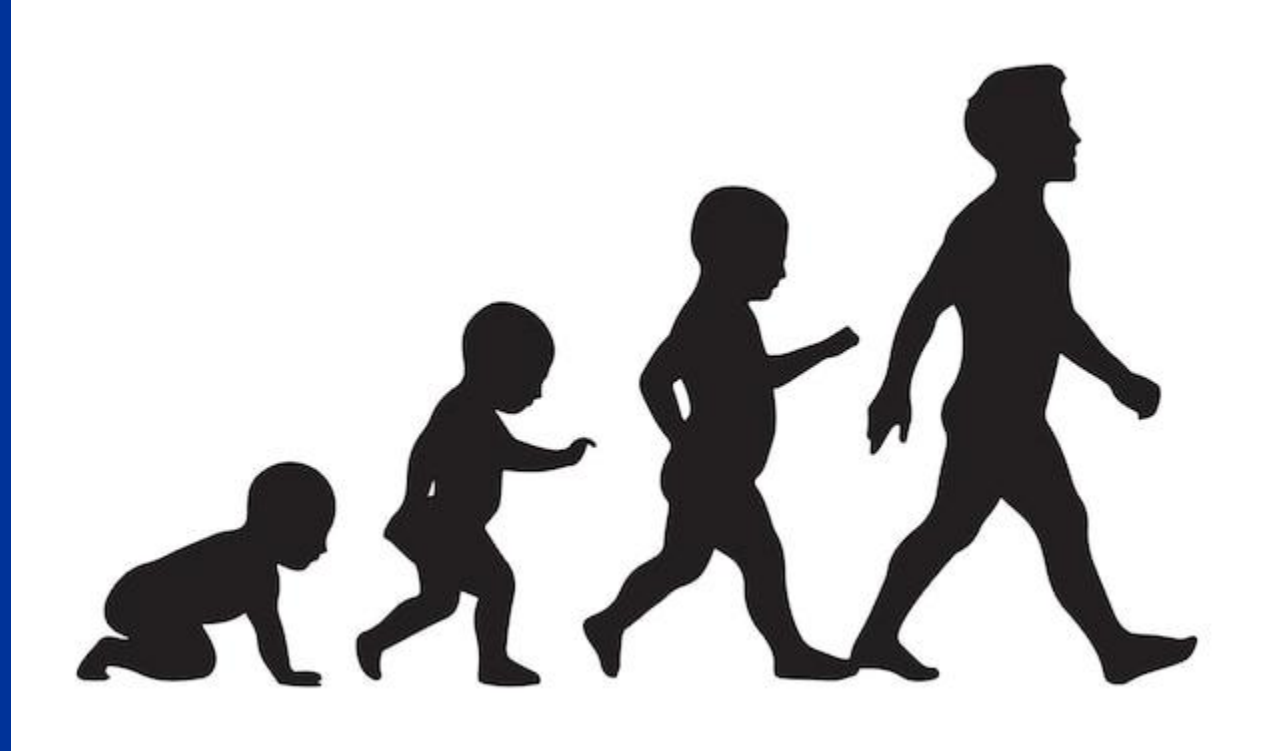
Common pain patterns

1. Belly pain
2. Joint pain
3. Back pain
4. Muscle pain
5. Extremities



Age-related pattern

1. Children and adults affected
2. Muscle pain may start early
3. Back pain often starts later
4. Pain burden may increase over time



Pain is multifactorial

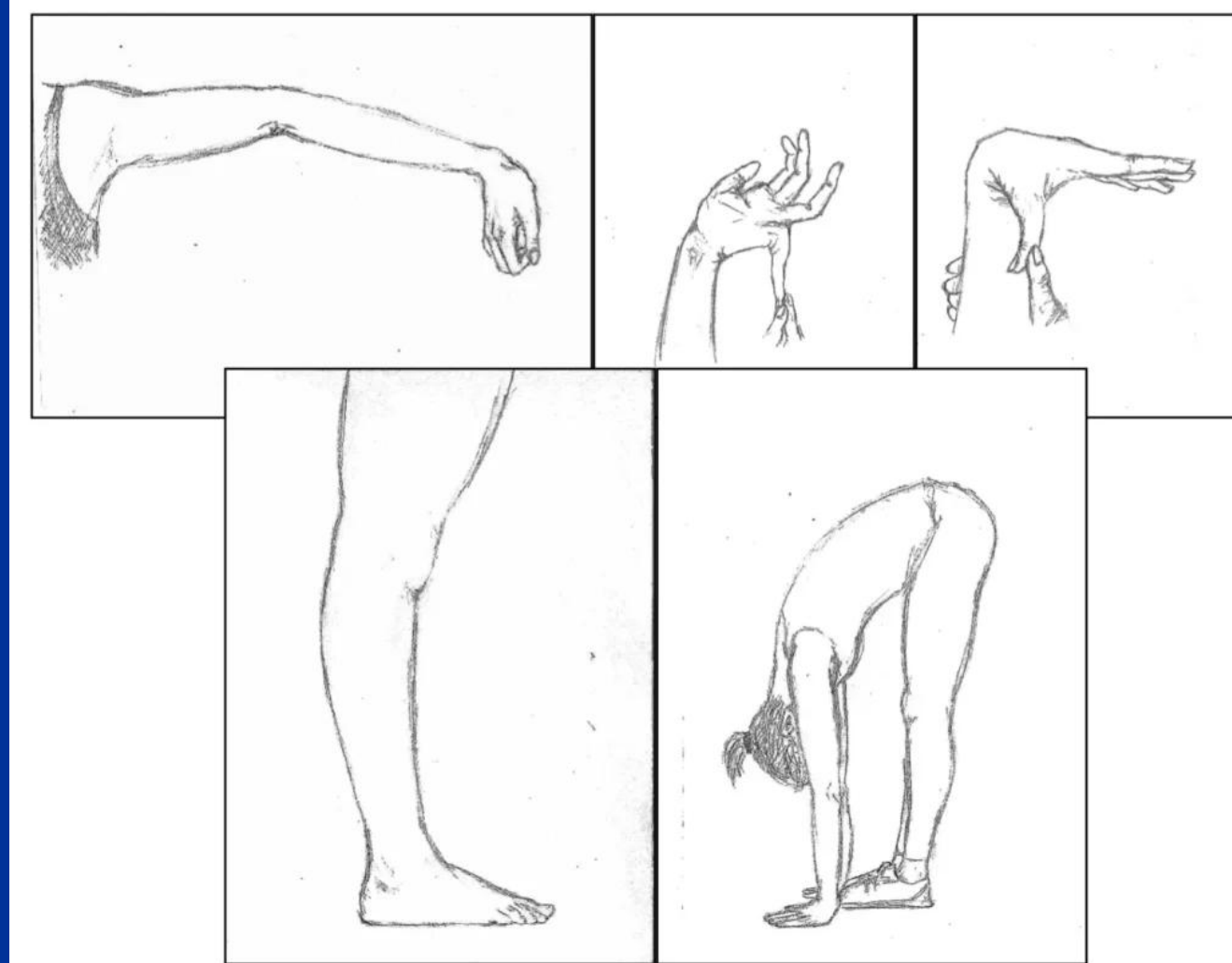
1. Musculoskeletal
2. Neuropathic
3. Inflammatory or autoimmune
4. Environmental modifiers

Nerve Pain vs Muscle Pain



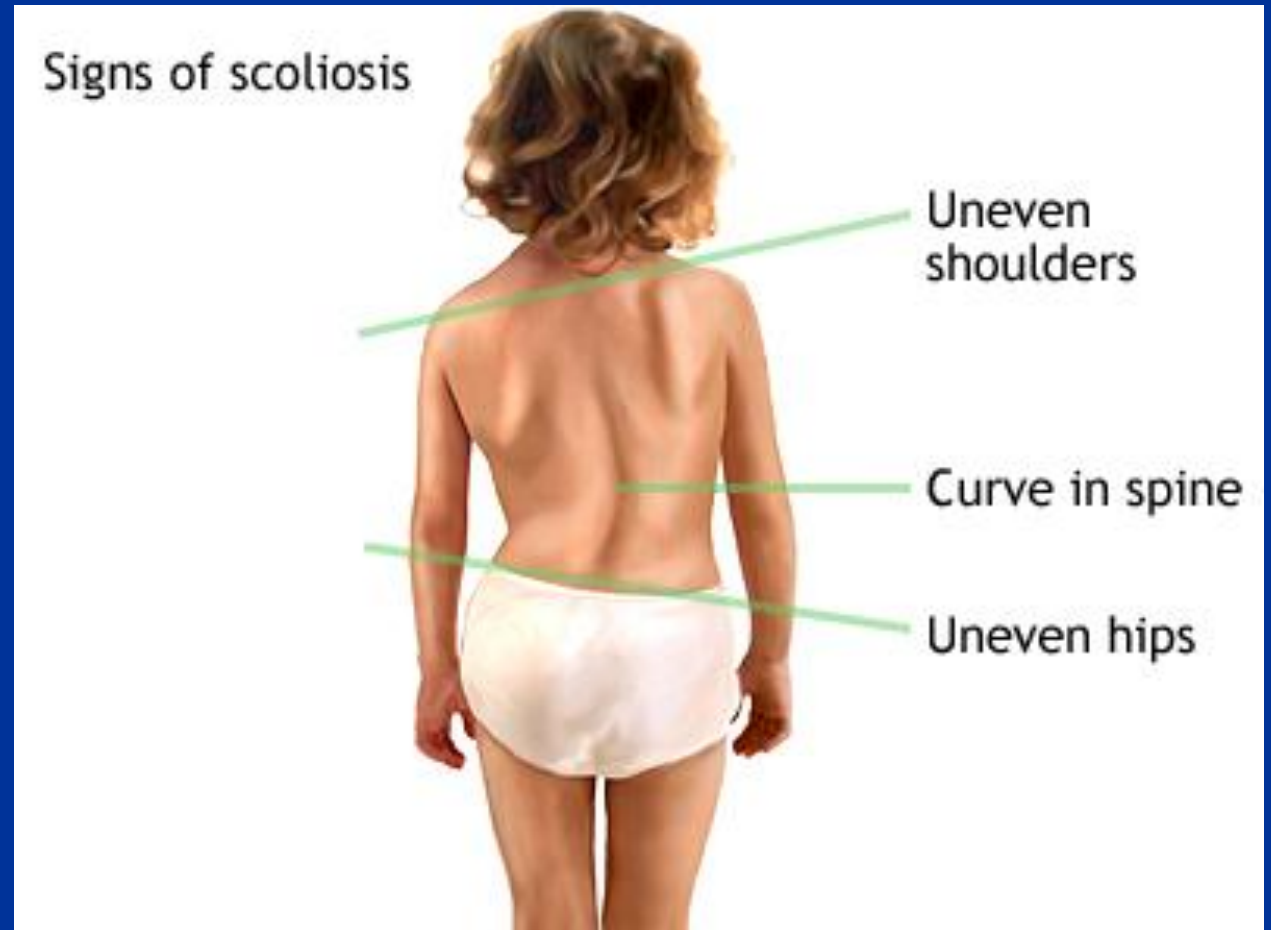
Musculoskeletal contributors

1. Joint hypermobility



Musculoskeletal contributors

1. Joint hypermobility
2. Scoliosis



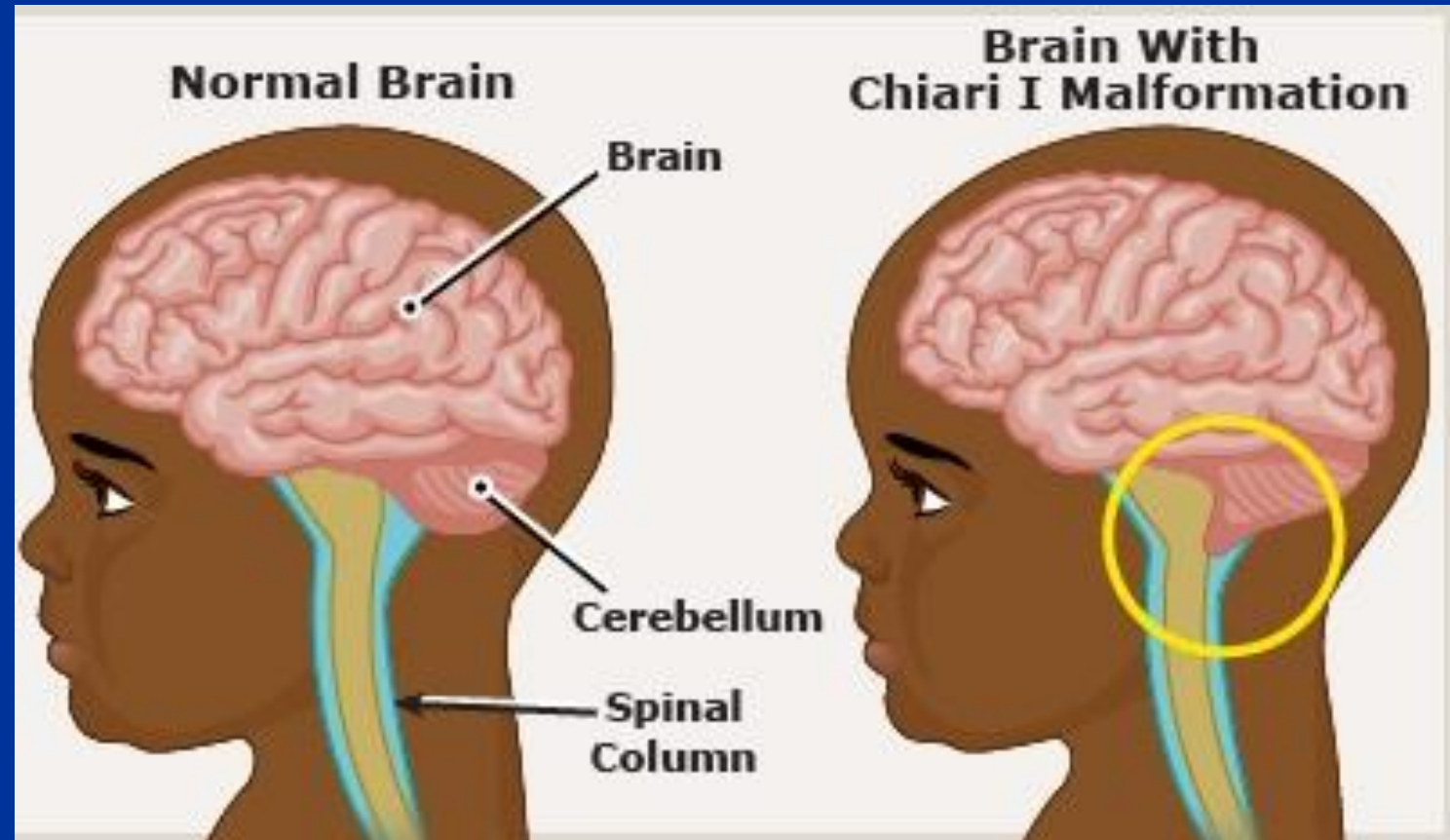
Musculoskeletal contributors

1. Joint hypermobility
2. Scoliosis
3. Joint stiffness



Musculoskeletal contributors

1. Joint hypermobility
2. Scoliosis
3. Joint stiffness
4. Cervical spine disease



“Understanding the Connection:
Noonan Syndrome, Chiari Malformation, and Tethered Cord”

Dr. Klinge

Friday, 1:45 PM

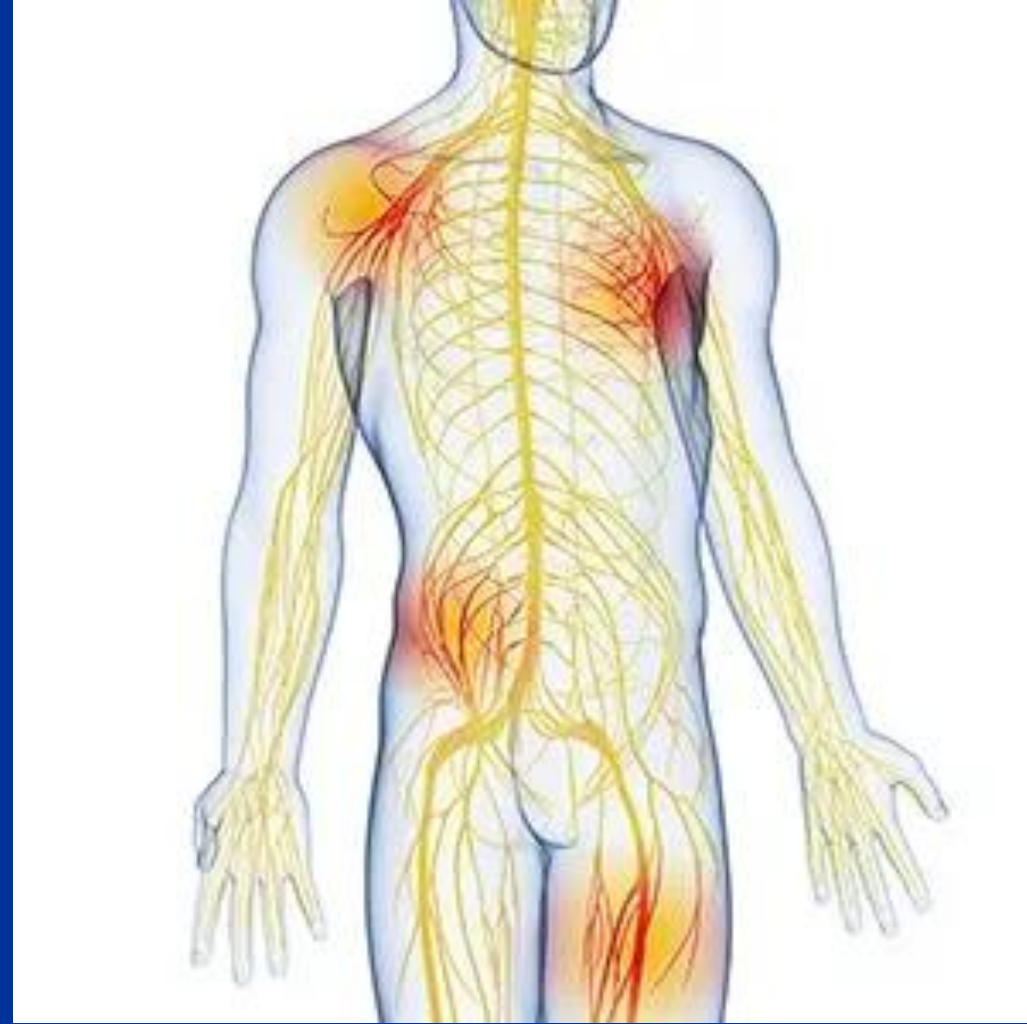
Nerve based pain

Burning

Paresthesias (pins and needles)

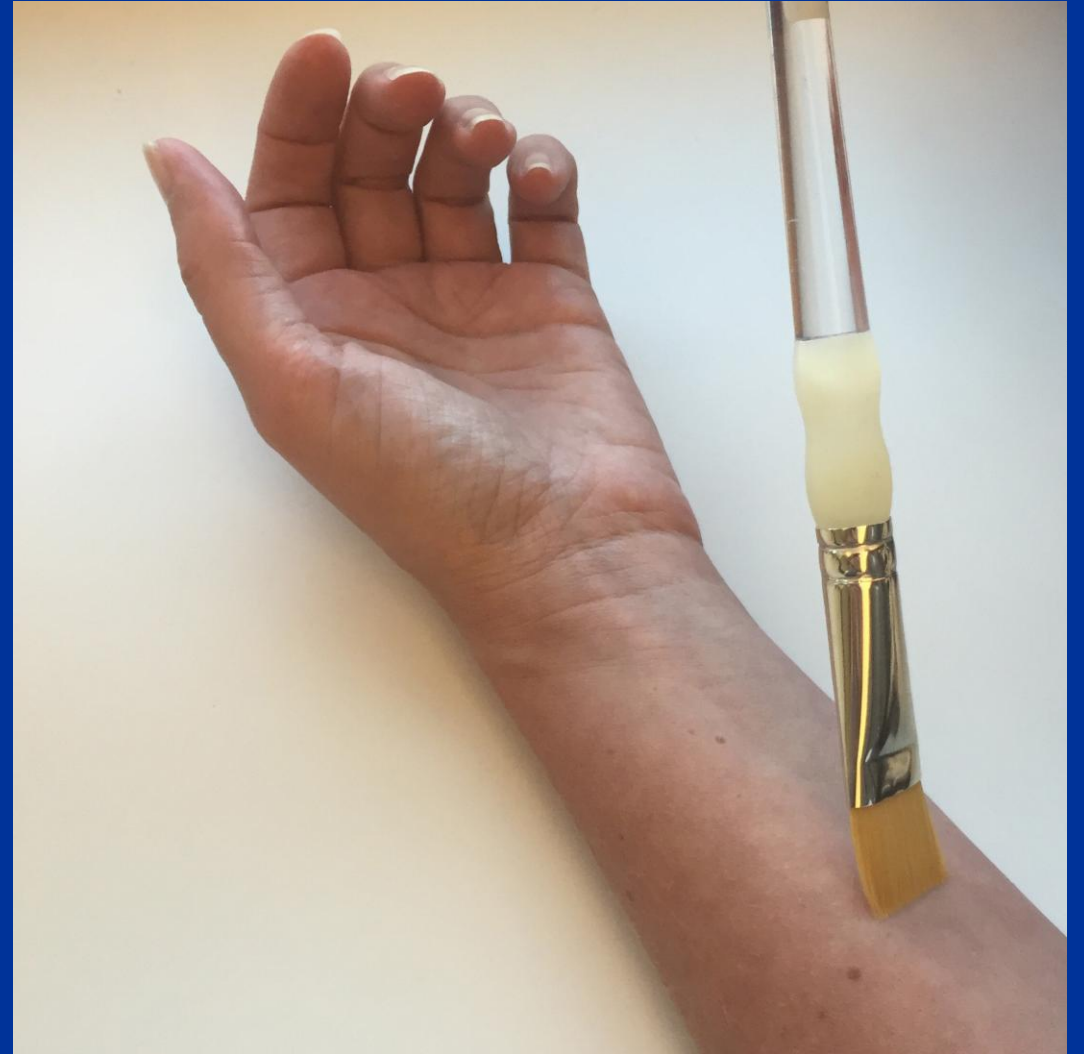
Numbness

Tingling



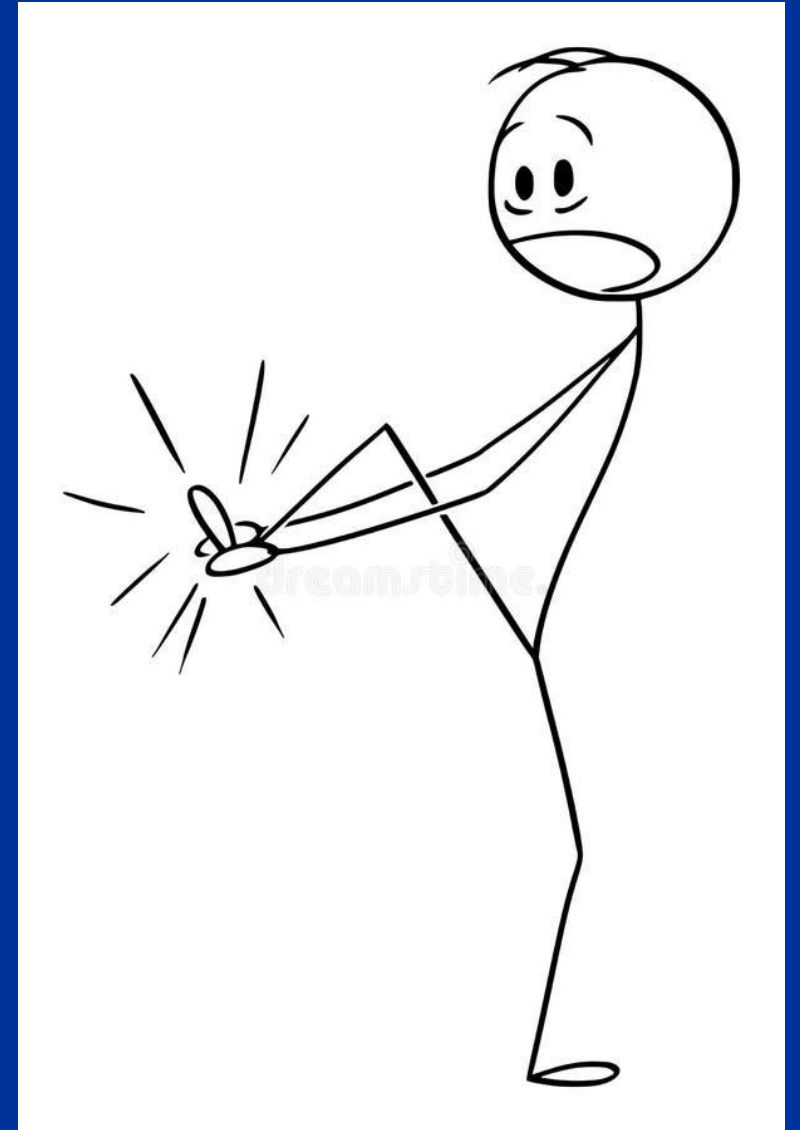
Neuropathic contributors

1. Allodynia: pain response to nonpainful stimulus (light touch, gentle breeze)



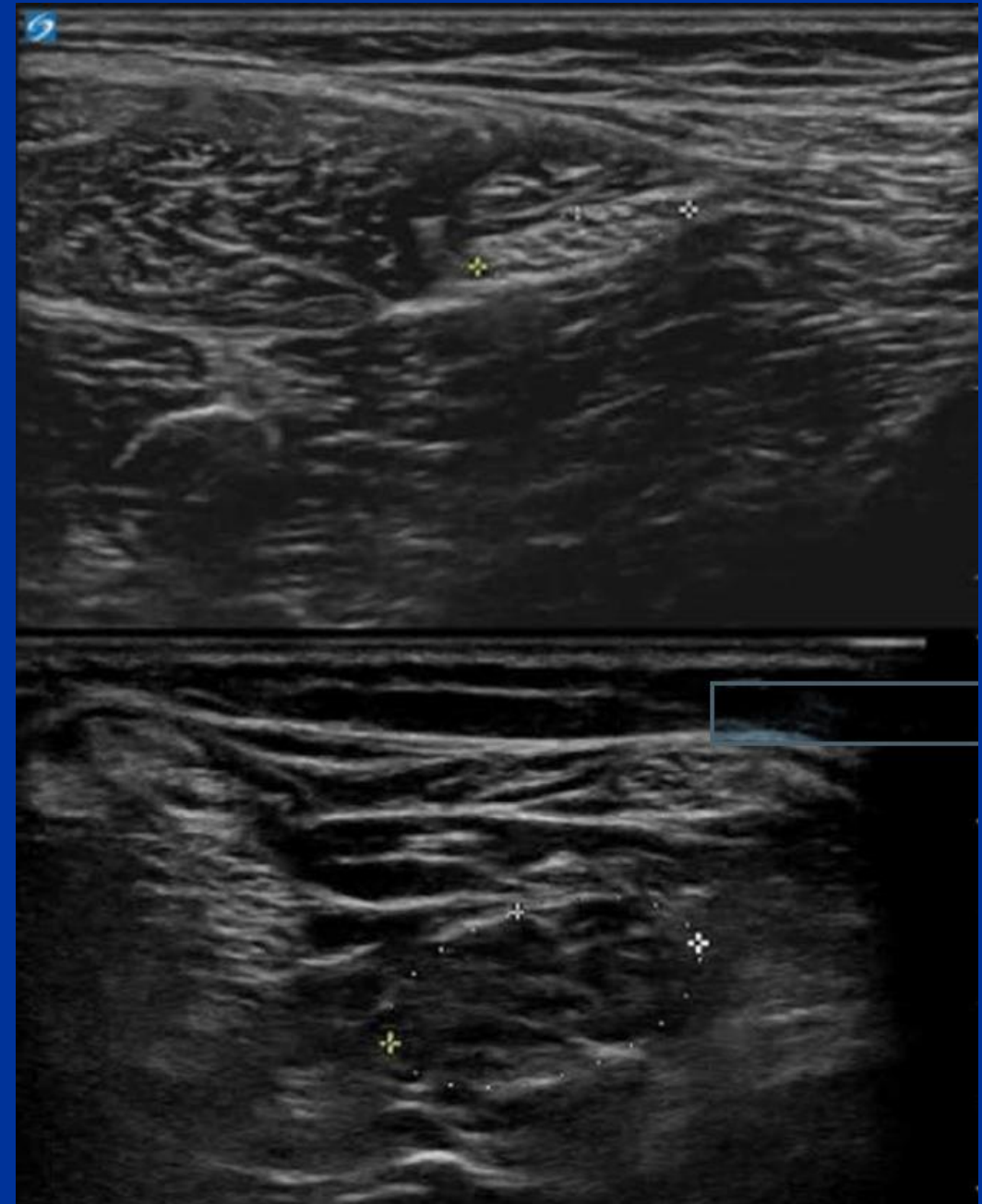
Neuropathic contributors

1. Allodynia (pain response to nonpainful stimulus)
2. Hyperalgesia: something that typically causes mild discomfort triggers an exaggerated or intensely painful response



Neuropathic contributors

1. Allodynia (pain response to nonpainful stimulus)
2. Hyperalgesia (mildly painful stimulus causes intense pain response)
3. **Peripheral nerve enlargement**



Contributors to musculoskeletal pain

Autoimmune disease

Juvenile Arthritis

Joint pain

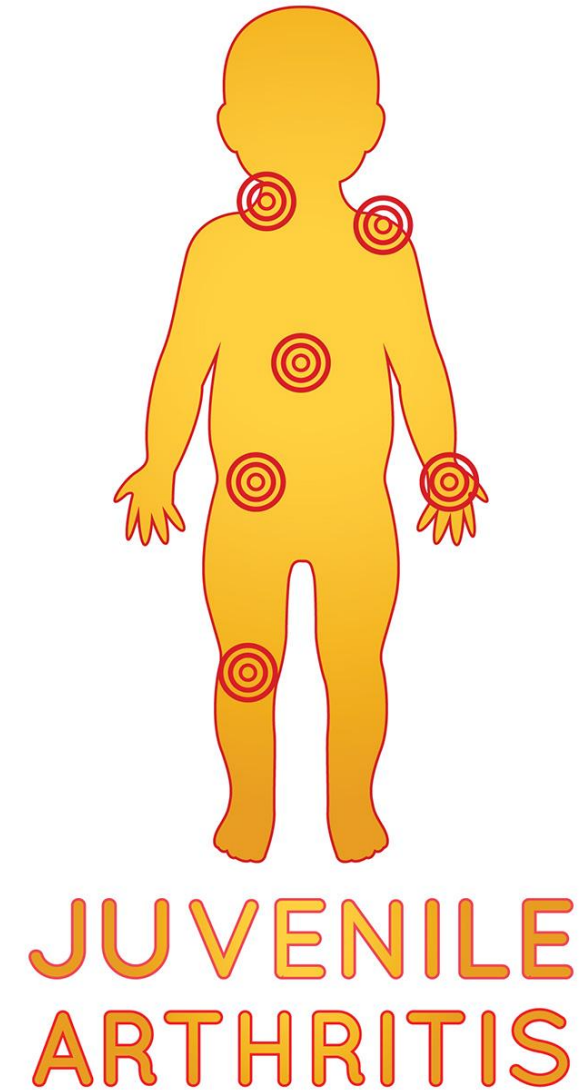
Change in mobility

Fever, tiredness

Chronic eye inflammation

Diagnosis: Rheumatologist, specialized blood tests and exam findings

Treatment: medication



Contributors to musculoskeletal pain

1. Autoimmune disease
2. Lymphedema
 - ~13% of children 1-18 years
 - ~30% of adults



“The Milky Way: Lymphatic Involvement in Noonan Syndrome”

Dr. Gelb

2:30 PM, Friday

Contributors to musculoskeletal pain

1. Autoimmune disease
2. Lymphedema
3. Giant cell lesions/PVNS

Joint pain

Joint swelling

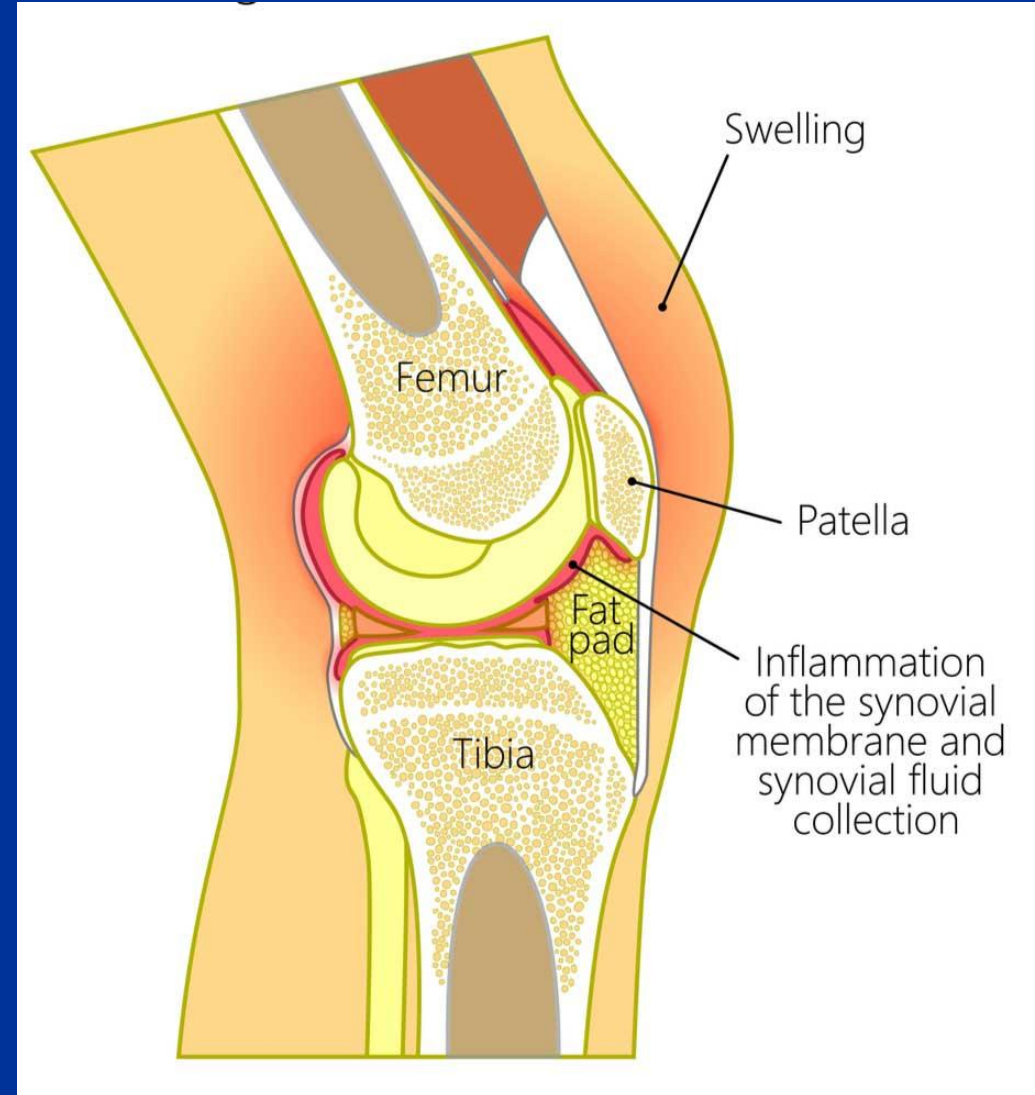
Decreased range of motion of the involved joint

Locking, catching, or giving way of the joint

NO fever, morning stiffness, fatigue
(a RARE association with NS)

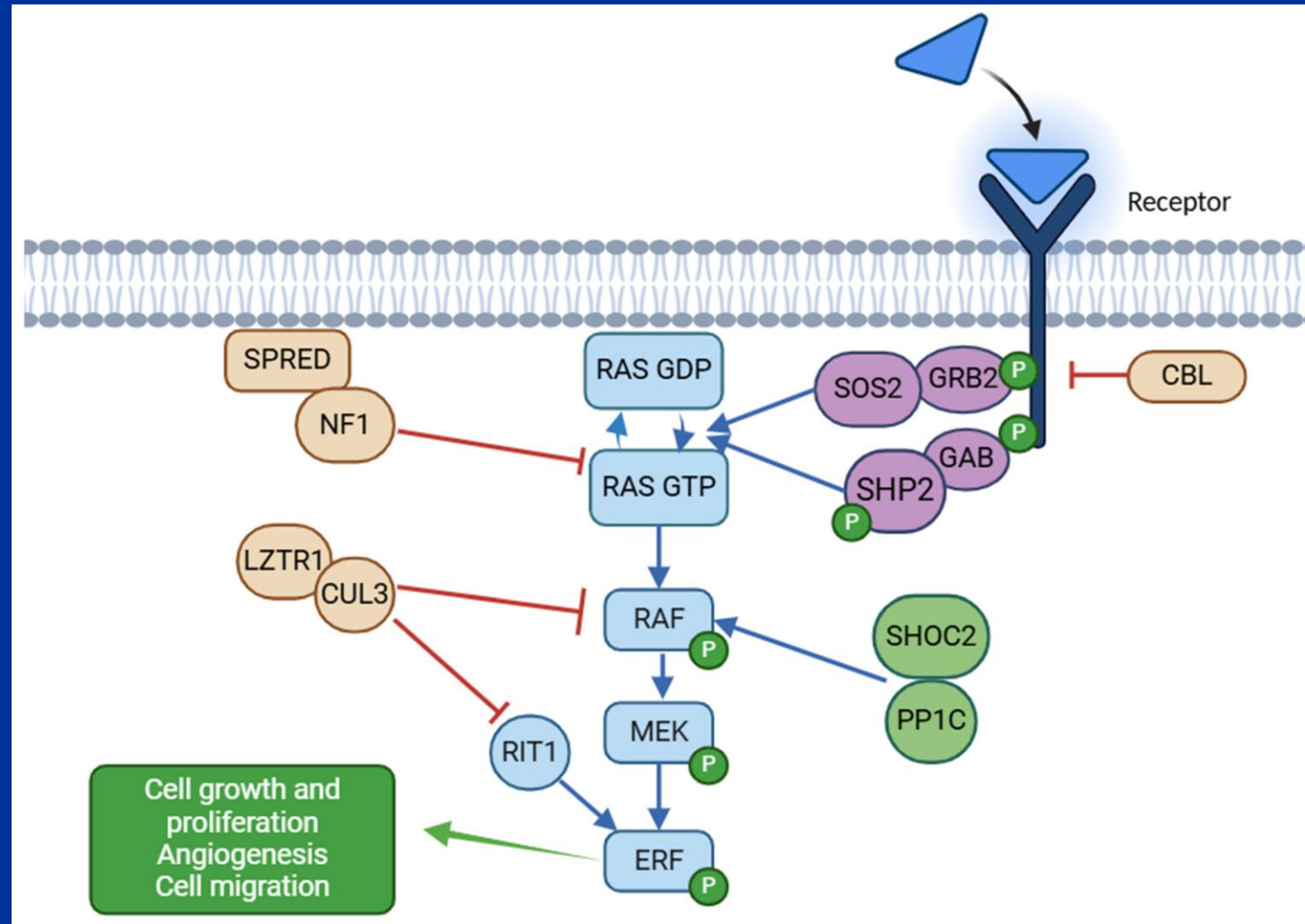
Diagnosis: ortho/rheumatology

Treatment: primarily surgical



Contributors to musculoskeletal pain

1. Autoimmune disease
2. Lymphedema
3. Giant cell lesions
4. Some genotype associations with chronic pain?



Evaluating pain: muscle pain versus nerve pain

 Muscle Pain	 Nerve Pain
• Dull, aching, or sore • Feels tight, stiff, or heavy • Usually stays local or slightly spreads • Tender to touch or stretch • Worsens with overuse or poor posture ✓ Trigger points may refer pain ✗ No neurological signs	• Sharp, burning, or shooting • Feels electric or zappy •  Often radiates down a limb • May come with numbness, tingling, or weakness • Worsens with positions like sitting or bending ✓ Positive neural tension tests (SLR, ULTT, etc.) ✓ May have weakness, numbness, or reflex changes ✓ May have weakness, numbness, or reflex changes

Helpful tests

1. Wong-Baker or similar scale



Helpful tests

1. Wong-Baker or similar scale
2. PainDETECT

painDETECT™ PAIN QUESTIONNAIRE

Date: Patient: Last name: First name:

How would you assess your pain now, at this moment?
0 1 2 3 4 5 6 7 8 9 10
none max.

How strong was the strongest pain during the past 4 weeks?
0 1 2 3 4 5 6 7 8 9 10
none max.

How strong was the pain during the past 4 weeks on average?
0 1 2 3 4 5 6 7 8 9 10
none max.

Mark the picture that best describes the course of your pain:

	Persistent pain with slight fluctuations	☐
	Persistent pain with pain attacks	☐
	Pain attacks without pain between them	☐
	Pain attacks with pain between them	☐

Please mark your main area of pain

Does your pain radiate to other regions of your body? yes ☐ no ☐

If yes, please draw the direction in which the pain radiates.

Do you suffer from a burning sensation (e.g., stinging nettles) in the marked areas?
never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Do you have a tingling or prickling sensation in the area of your pain (like crawling ants or electrical tingling)?
never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Is light touching (clothing, a blanket) in this area painful?
never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Do you have sudden pain attacks in the area of your pain, like electric shocks?
never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Is cold or heat (bath water) in this area occasionally painful?
never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Do you suffer from a sensation of numbness in the areas that you marked?
never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Does slight pressure in this area, e.g., with a finger, trigger pain?
never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

(To be filled out by the physician)

never	hardly noticed	slightly	moderately	strongly	very strongly
☐ x 0 = 0	☐ x 1 =	☐ x 2 =	☐ x 3 =	☐ x 4 =	☐ x 5 =

Total score out of 35

PainDETECT

Do you suffer from a <u>burning sensation</u> (e.g., stinging nettles) in the marked areas?					
never ☐	hardly noticed ☐	slightly ☐	moderately ☐	strongly ☐	very strongly ☐
Do you have a <u>tingling or prickling sensation</u> in the area of your pain (like crawling ants or electrical tingling)?					
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Does slight pressure in this area, e.g., with a finger, trigger pain?					
never ☐	hardly noticed ☐	slightly ☐	moderately ☐	strongly ☐	very strongly ☐

Helpful evaluations

1. Wong-Baker or similar scale
2. PainDETECT
3. High-resolution nerve ultrasound, MRI or EMG when needed



Management principles

1. Multimodal approach



Management principles

1. Multimodal approach
2. Match treatment to pain type



Management principles

1. Multimodal approach
2. Match treatment to pain type

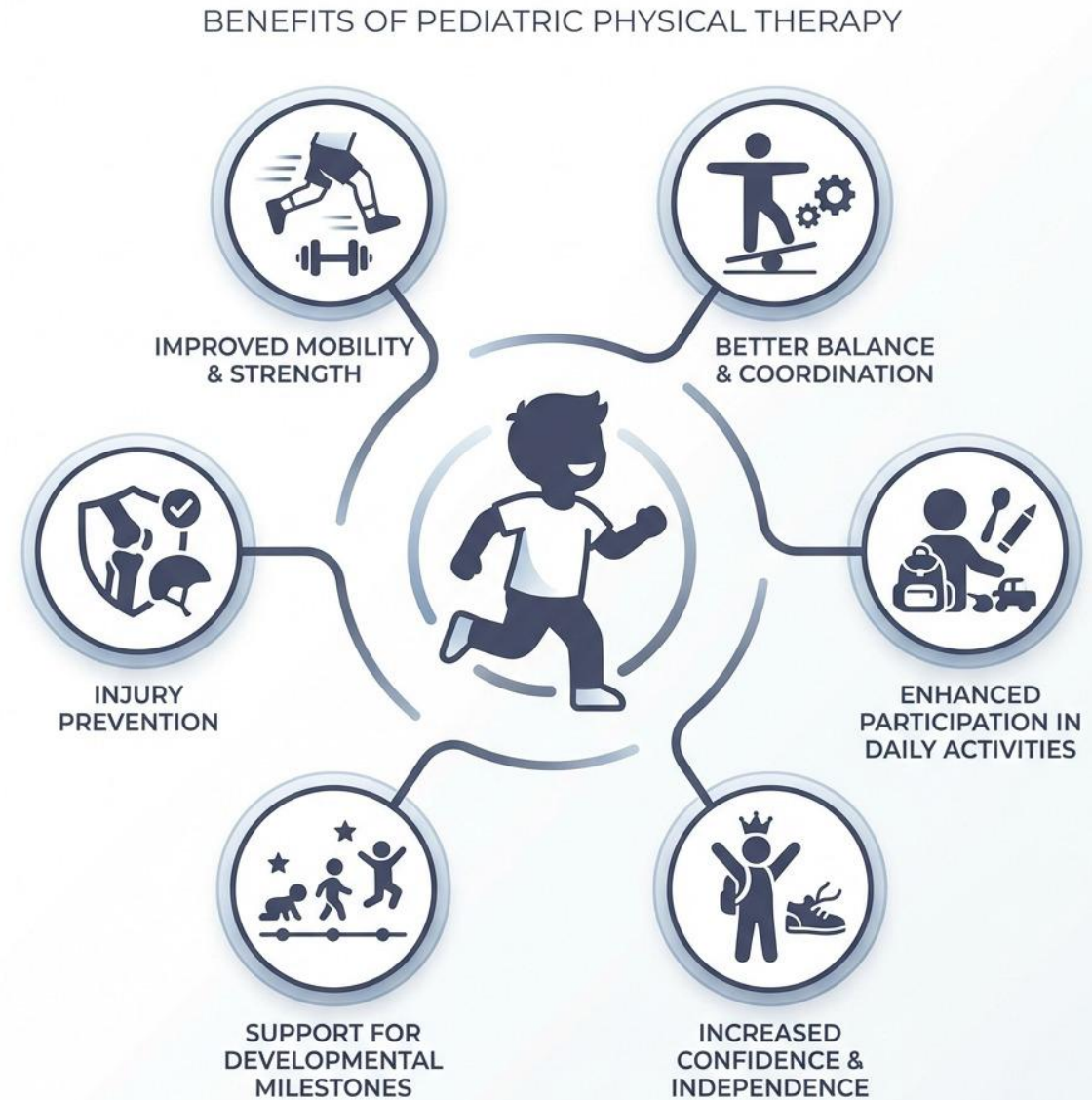
Primary Care
or
Geneticist



- Physical Therapist
- Occupational Therapist
- Neurologist/ Neurosurgeon
- Orthopedist
- Rheumatologist
- Pain Specialist
- Physical Medicine & Rehab (PM&R)

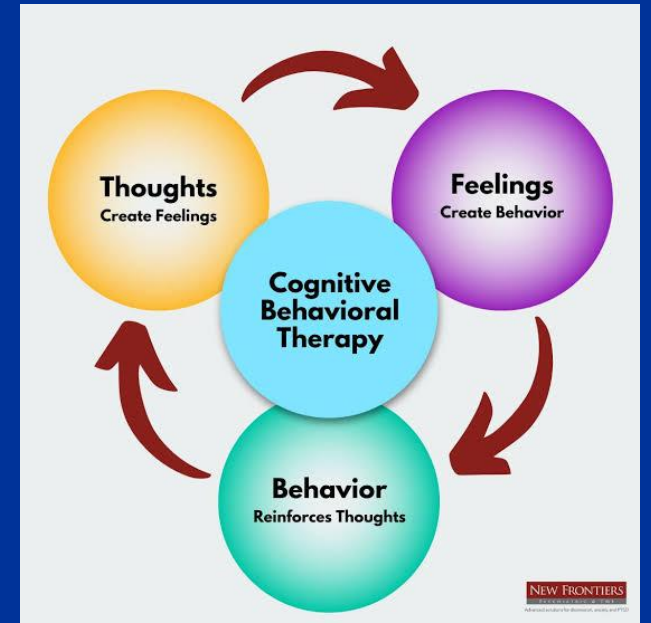
Management principles

1. Multimodal approach
2. Match treatment to pain type
3. Start with rehabilitation



Non-pharmacologic care

1. Physical therapy
2. Joint stabilization
3. Low-impact exercise
4. CBT and caregiver education



Pharmacologic options

1. Gabapentin for neuropathic pain
2. NSAIDs for muscle or joint pain
 *Use caution with bleeding risk
3. Other neuropathic agents

Neurologist
PM&R
Pain Specialist
(Cardiologist)

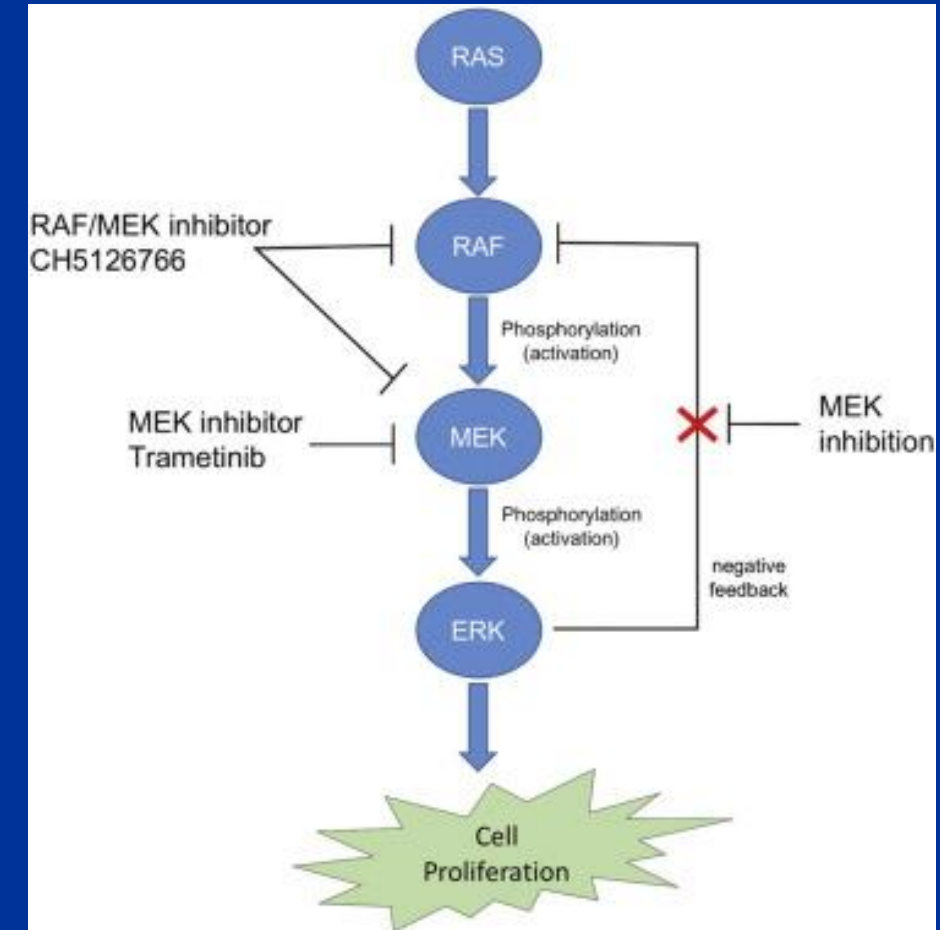


When to see a subspecialist

1. *Progressive* neurologic symptoms
2. Severe scoliosis or Chiari
3. Refractory pain
4. Concern for neuropathy

Emerging direction

1. MEK inhibitors
2. Pathway-targeted strategy
3. Possible effect on pain and nerve hypertrophy
4. Evidence still limited



Take-home points

1. Pain in Noonan syndrome is common
2. Think mixed mechanisms
3. Seen across the lifespan
4. Neuropathic pain should be considered
5. Needs a lot more research



References

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