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Arcadia Case Study

PT-702

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**Retrospective Case Analysis of a Patient Experiencing Musculoskeletal Lower Back Pain
and Shoulder Pain Who Later Developed Non-musculoskeletal Abdominal Pain**

26

27

Abstract

28

29 **Background and Purpose**

30 A young woman with a history of chronic intermittent low back pain is referred to physical
31 therapy by her orthopedic surgeon. During the course of her physical therapy treatment she
32 develops abdominal pain and is referred by the physical therapist to an internal medicine
33 specialist.

34 **Case Description**

35 The patient was a 34 year old woman who reported a 5 year history of intermittent lower back
36 pain. The physical therapy examination revealed findings suggestive of lumbar segmental
37 instability. Her plain films were negative for pathology. She was taking prescription ibuprofen
38 tablets (400mg) twice daily. The patient's systems review was negative for pathology or
39 pregnancy. Approximately 3 weeks into her physical therapy treatment regimen she complained
40 of right upper quadrant abdominal and right trapezius pain. The physical therapist re-examined
41 the patient and determined the abdominal symptoms were most likely visceral in origin, and the
42 patient was referred to internal medicine specialist. Blood tests and an abdominal diagnostic
43 ultrasound, confirmed a diagnosis of drug-induced hepatitis and hepatic cyst as a result of the
44 ibuprofen use.

45 **Outcomes**

46 The patient was immediately taken off the ibuprofen and was cleared to resume physical therapy.
47 This intervention resulted in the abolition of the patient's right upper quadrant abdominal and
48 trapezius pain within 2 weeks of discontinuing the ibuprofen. The patient's lower back pain
49 significantly improved over the course of physical therapy which enabled her to resume a normal
50 activity level.

51 **Discussion**

52 Physical therapists may have an important role in identifying non-musculoskeletal disorders
53 utilizing a differential diagnosis process. Recognizing visceral signs and symptoms is imperative
54 and should be an important part of the physical therapist examination. Appropriate medical
55 referral is necessary to provide proper diagnosis and intervention of visceral disorders.

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57

58 **Background and Purpose**

59
60 Physical therapy practice is progressing toward an autonomous role in the health care system
61 ¹⁻³. Physical therapists must possess differential diagnostic skills to enable appropriate clinical
62 decision making. During an initial evaluation or subsequent re-evaluation the physical therapist
63 must recognize the signs and symptoms of both musculoskeletal and nonmusculoskeletal causes
64 of pain and dysfunction. Jette et al. demonstrated that physical therapists with an orthopedic
65 specialization were almost twice as likely to make correct decisions for critical medical and
66 musculoskeletal conditions in a direct-access environment ⁴. Davenport et al. stated that physical
67 therapists can act as intermediaries for revising diagnoses by recognizing that certain features of
68 the history and physical examination that are unresponsive to physical therapy intervention, and
69 that referral to an appropriate specialist is necessary for additional testing and treatment ⁵.

70 Physical therapists use a diagnostic process to gain enough certainty that initiating physical
71 therapy treatment will not delay a patient's access to more appropriate health services ⁵.

72 Visceral structures of the abdominopelvic cavity may refer pain to particular areas of the body
73 that can mimic musculoskeletal pain. The physical therapist must continually screen for medical
74 conditions throughout the treatment process in order to identify potential nonmusculoskeletal
75 conditions that require physician referral. The site of the visceral pain corresponds to
76 dermatomes from which the diseased organ receives its innervations ⁶. Visceral disease of the
77 abdomen and pelvis is more likely to refer pain to the back, whereas intrathoracic disease refers
78 pain to the shoulder(s) ⁶. Visceral pain rarely occurs without associated signs and symptoms.
79 Careful questioning of the patient will usually elicit a systemic pattern of the symptoms.

80 Visceral pain is not well localized because innervation of the viscera is multisegmental with few

81 nerve endings. Back and shoulder range of motion is usually full and painless in the presence of
82 visceral pain⁶. Table 1, describes the typical differentiation of systemic and musculoskeletal
83 pain. Figure 1, demonstrates visceral referred pain sites for several organ systems. Table 2,
84 describes signs and symptoms of systemic related back pain.

85 Drug- induced hepatitis also known as non-viral hepatitis is a condition that can mimic
86 musculoskeletal pain or coexist with a true musculoskeletal pathology that is amenable to
87 physical therapy treatment. This type of hepatitis is a form of liver inflammation that occurs
88 secondary to exposure to certain drugs from which most people recover without serious
89 complications⁶. Drug-induced hepatitis causes liver alterations with liver responses dependent
90 on the chemical nature of the hepatotoxin or the genetic makeup of the person. Several non-
91 steroidal anti-inflammatory (NSAID) agents have been documented to cause hepatic injury in
92 over-the-counter (OTC) and prescription doses⁶⁻⁹. Approximately 10% of the total reported
93 drug-induced hepatotoxicity is related to NSAID consumption⁷.

94 Ibuprofen is one of the NSAID medications that has been shown to cause drug-induced hepatitis
95⁷⁻⁹. Studies indicate ibuprofen's potential to create toxicity and cause liver injury⁷⁻¹². Since the
96 introduction of ibuprofen in 1969, this drug has become one of the most prescribed drugs for
97 musculoskeletal pain throughout the world⁸. Doses of this medication range from 400mg/day
98 (analgesic dose) to 2400mg/day (anti-inflammatory dose) the latter is associated with higher GI
99 adverse events⁸. The pharmacokinetic properties of ibuprofen, especially the short plasma half-
100 life of elimination (t_{1/2} is 2-3 hours) and lack of development of pathologically related
101 metabolites support the view that it has a low toxic potential^{7,8}.

102 Clinical signs and symptoms of drug induced hepatitis may include: sense of fullness of the
103 abdomen, right upper quadrant (RUQ) abdominal pain and tenderness, right shoulder pain,
104 fatigue/malaise, nausea/vomiting, jaundice, dark urine, clay-colored stools, abdominal pain not
105 relieved by position change or rest ⁶. Figure 2, shows the common sites for referred pain from
106 the liver and gallbladder.

107 The most common medical tests used to confirm the diagnosis of hepatotoxic disease are blood
108 tests for liver function, diagnostic ultrasound, and CT scan ^{2,13}. The treatment of this disorder is
109 to cease the NSAID medication, and resolution of symptoms usually occurs within 4 weeks of
110 cessation ^{7,8}. Although rare, adverse hepatotoxicity from the use of ibuprofen can and does
111 occur. The purpose of this case study is to describe the clinical reasoning process associated with
112 a patient referred to physical therapy for low back and shoulder pain who later developed a drug-
113 induced hepatitis and liver cyst from prescription ibuprofen.

114

115 **Patient History and Review of Systems**

116 **Patient Description**

117 The patient was a 34 year old female who worked as a marketing representative for a local theme
118 park. She complained of a 5 year history of intermittent low back pain (LBP). She reported the
119 initial injury while lifting boxes of home furnishings during a move to a new house. She
120 described her LBP as localized and sharp, with intermittent “catching”. She denied any
121 neurologic or radicular signs or symptoms. The patient was seen by her family physician at that
122 time (5 years ago) who prescribed a pain medication and muscle relaxer. She was seen by a

123 physical therapist in another city and received passive modalities and stretching for
124 approximately 6-8 weeks. She reports the pain resolved slowly over a 6 to 9 month time period.
125 She went on to report at least 5 episodes of LBP since the initial back injury each lasting 2-
126 12weeks.

127 The patient described a recent onset of LBP along with intermittent right shoulder pain 2 months
128 prior to initiating physical therapy. She reported initiating an exercise class that involved
129 repetitive bending and overhead barbell lifting as the probable cause of her symptoms. She
130 described the pain as localized and made worse by bending, lifting, and prolonged sitting or
131 standing. The patient was seen by her family physician approximately 4 weeks after the onset of
132 her symptoms. Plain films of her LB and pelvis were performed which were reported as
133 negative by the patient. She was given ibuprofen 800mg/day prescription and instructed to see
134 an orthopedic specialist because of this ongoing history of LBP. Approximately 6 weeks after
135 the onset of her symptoms she was seen by an orthopedic specialist. Another set of plain films
136 were taken of her lumbar spine, pelvis and hips. The new films were interpreted as negative as
137 well, and she was instructed to continue the ibuprofen and referred for physical therapy. She was
138 diagnosed with a lumbar sprain/strain and right shoulder impingement syndrome.

139 The patient was seen for a physical therapy evaluation approximately 2 months after the most
140 recent exacerbation of her LBP. The patient had stopped her exercise program and continued to
141 use the prescribed ibuprofen, reporting on some days taking twice the normal dosage because of
142 increased LBP. Upon reviewing her health history forms, she was a non-smoker and reported no
143 significant medical history. She reported no gynecological issues, bowel or bladder issues, and
144 was not pregnant. She listed pharmaceutical use including an oral contraceptive and occasionally

145 a multi-vitamin. Her height was 1.65 m and her weight was 61kg which corresponded to a BMI
146 of 22 kg/m² which is in the normal healthy range for females. Based on the information gathered
147 during the interview and systems review the patient's signs and symptoms were determined to be
148 musculoskeletal in nature. Her complaints followed a typical pattern of musculoskeletal
149 impairment that was manageable by physical therapy.

150

151 **Examination**

152

153 The patient was experiencing LBP described as 7 out of 10 pain on the numeric pain rating scale
154 (NPRS) and minor right shoulder and upper trapezius pain rated at 3 out of 10 on the NPRS.

155 Stratford and Spadoni¹⁴ reported the NPRS as a reliable assessment for documenting pain
156 intensity (ICC's .64 to .86). Standing posture was observed in the frontal and sagittal planes.

157 The patient had an accentuated lumbar lordosis and thoracic kyphosis as well as a forward head
158 posture described by McGee¹⁵. She ambulated independently, but was guarded with transferring
159 sit-to-stand and supine-to-sit.

160 **Spinal exam:** Standing trunk active range of motion (AROM) was assessed, as described by
161 Boissonnault². AROM revealed 20% limitation and increased pain with flexion and extension
162 as well as right trunk rotation. Repeated movement testing of her trunk revealed aberrant motion
163 and complaint of "catching" upon returning to an upright stance from the forward flexed
164 position. Hip AROM was recorded as within normal limits (WNL). Sacroiliac assessment
165 consisting of 5 provocative tests described by Laslett¹⁷ was negative. A cervical and thoracic

166 spine screen involving AROM, quadrant testing and vertebral posterior to anterior spring testing
167 were negative for symptom reproduction or loss of motion. Rib springing was negative and full
168 inhalation and exhalation did not appear difficult or reproduce symptoms. Spinal vertebral
169 posterior to anterior spring testing as described by McGee¹⁵ of the lumbar spinal segments
170 reproduced her LBP at the lower lumbar levels and were assessed as hypermobile at 2 of the 5
171 lumbar segments. She was tender to palpation over the lumbar paravertebral muscles especially
172 along the right side of her lumbar spine. There was no palpable “step off” which may have
173 indicated a spondylitic lesion¹⁵. The patient reported increased LBP with extension and side
174 bending quadrant testing of the trunk^{15,16}. Lastly, she had a positive lower trunk instability test
175 as described by Hicks¹⁹. This resulted in a significant reduction in symptoms with manual
176 stabilization of the patient’s lumbar spine during prone bilateral leg extension.

177 **Neuromuscular testing included:** Manual muscle testing (MMT), reflex testing, and sensory
178 testing as described by McGee¹⁵ and Hoppenfield¹⁶. Deep tendon reflexes for the upper and
179 lower extremities were WNL. Sensory assessment of light touch along all extremity dermatomes
180 was unremarkable. The MMT of the extremities revealed strength of 5/5 for all major muscle
181 groups except right shoulder external rotation with her arm at her side, and left hip flexion, left
182 hip abduction and left hip internal rotation that were each assessed as 4/5. The patient reported
183 minor increase in right shoulder pain and LB pain with muscle testing across these joints. The
184 supine straight leg raise was negative and measured as 95 degrees on the left and 100 degrees on
185 the right.

186 **Shoulder exam:** Shoulder AROM was tested in a seated position as described by McGee¹⁵, and
187 was WNL without complaints of increased symptoms. Right shoulder impingement testing

188 using the Neer and Hawkins tests described by McGee¹⁵ increased her right shoulder pain along
189 with tenderness over the rotator cuff tendon attachment on the head of the humerus. The shoulder
190 impingement tests have a sensitivity ranging from 75 to 92.1 and specificity ranging from 25 to
191 47.5 as reported by Cook¹⁸.

192 Following the physical examination the therapist was convinced the patient's condition was of a
193 musculoskeletal origin and a plan for physical therapy intervention was initiated. The patient's
194 low back signs and symptoms correlated with a clinical prediction rule (CPR) for lumbar
195 instability treatable with stabilization exercise²⁰. This CPR developed by Hicks et al.²⁰ included
196 4 variables; age < 40 years, average straight leg raise > 91 degrees, aberrant movement present,
197 and a positive prone instability test²⁰. The presence of at least 3 of these variables resulted in a
198 specificity of 0.86 (95% CI; 0.71-0.94) and a positive likelihood ratio of 4.0 (95% CI; 1.6-10.0).
199 In light of this patient meeting all 4 criteria for the CPR, a course of lumbar stabilization exercise
200 was planned and implemented for this patient.

201

202 **Intervention**

203

204 The original plan of care was to treat the patient for 2 times a week for 4 weeks to address the
205 musculoskeletal impairments. Spinal stabilization exercises have been shown to be effective in
206 the treatment of patients with acute and chronic LBP^{21,22}. This type of exercise as well as more
207 functional global pushing, pulling and squat/lunge type exercises described by Porterfield and
208 DeRosa²³ were implemented immediately and progressed over the next 2-3 weeks of treatment.
209 The patient also initiated shoulder girdle exercises for rotator cuff and scapular strength and

210 stabilization similar to those described by Tate et al.²⁴. Biomechanical counseling, postural
211 awareness and body mechanics training were also implemented.
212 Approximately 3 weeks after initiating treatment the patient reported a significant change in her
213 symptoms. She was now experiencing new pain in the area of her right upper trapezius and
214 right upper quadrant abdominal area under her right rib cage. The treating physical therapist
215 decided a re-evaluation was warranted in light of the new symptoms.

216

217 **Re-evaluation**

218

219 The interview was based on differential diagnostic procedures described by Boissonault². The
220 patient was interviewed regarding the sudden onset of her new symptoms and she described a
221 constant, dull ache pain in her right upper abdominal quadrant and right upper trapezius, as well
222 as a feeling of fullness under her right rib cage. The pain was unaffected by postural or
223 positional changes and woke her at night when she would lie in a prone position. A review of
224 systems revealed a “slight” increase in abdominal pain after eating “fast food”. She reported no
225 increase in her symptoms when eating other types of food or drink and denied any nausea or
226 vomiting. She reported no other bowel or bladder symptoms and stated she was not pregnant or
227 experiencing any gynecological pain or dysfunction. The patient reported no signs or symptoms
228 of an infection (fever, chills, malaise). She was not experiencing any neurologic signs with loss
229 of sensory or motor function. The patient denied any recent history of trauma or event that may
230 have a direct cause and effect relationship to this new pain. Lastly, she was questioned about her
231 medication use and she reported, prescription oral contraceptive, an OTC multi-vitamin, and
232 prescription ibuprofen. By the time of the re-evaluation she had been taking the ibuprofen for

233 approximately 7 weeks. Based on the information from this interview, the signs and symptoms
234 did not correlate with a musculoskeletal impairment. The differential diagnostic process
235 concluded a probable non-musculoskeletal origin of the patient's pain. Other medical conditions
236 (Figure 3) would need to be ruled out as potential causes of the patient's new symptoms.

237
238 The physical examination included a re-assessment of the patient's neck, trunk and rib cage
239 mobility and bilateral upper and lower quarter screen which were performed on the initial
240 evaluation^{2,15}. The patient's trunk mobility had improved and had only a minor complaint of
241 "catching" in the lumbar spine upon extending from the flexed position. She had full mobility of
242 her neck, thoracic spine, and both shoulders in all planes. Cervical and thoracic vertebral
243 segmental posterior to anterior spring testing was negative for any symptom reproduction.
244 Vertebral spring testing over the lumbar spine still reproduced her localized LBP, but reported as
245 diminished compared to her initial examination. She continued to have tenderness over the right
246 rotator cuff tendon attachment site on the humeral head. Manual muscle testing for external
247 rotation of the right shoulder elicited some discomfort at the rotator cuff attachment site on the
248 humerus. Hawkins impingement testing of the right shoulder caused minor discomfort at the
249 rotator cuff attachment site only. The lower quarter screen revealed full pain-free range of
250 motion of bilateral hips, knees, and ankles. Her neurologic scan demonstrated normal reflexes
251 for upper and lower extremities and no sensory changes along any extremity dermatome or over
252 the abdomen. She had no bruising or skin changes over her abdominal area or rib cage.
253 Palpation over the inguinal lymph nodes was unremarkable. The patient's abdominal symptoms
254 were reproduced with palpation over the superior border of the right upper abdominal quadrant.
255 Bioassault² describes placing the therapist's left hand under the patients back, around the T10-

256 T11 region on the right side of the patient, then lift gently. The fingers of the therapist's right
257 hand apply a moderate pressure slightly cephalically and posteriorly. The patient is asked to
258 hold a deep breath; the therapist may note the liver edge as it moves down into the therapists
259 fingers ². This maneuver reproduced the patient's pain in the right upper quadrant and right
260 upper trapezius area. The data collected during the physical exam suggested the patients
261 abdominal and right upper trapezius pain was likely originating from the abdominal viscera, in
262 particular, the liver. The patient was instructed to contact her orthopedic physician and seek a
263 referral to an internal medicine specialist.

264 The patient was seen by an internal medicine specialist approximately 1 week after the physical
265 therapist re-evaluation. She had blood tests ordered that were suggestive of a liver disorder. A
266 diagnostic ultrasound was performed in the physician's office which revealed an "inflamed liver"
267 and a liver cyst. The physician diagnosed the patient with a drug induced hepatitis resulting
268 from the use of the prescription ibuprofen. She was instructed to immediately discontinue the
269 ibuprofen and was cleared to resume physical therapy.

270

271 **Outcome**

272

273 The patient returned to physical therapy 3 days after her visit to the internist and resumed her
274 course of physical therapy. The abdominal and right upper trapezius pain were monitored and
275 within 12-14 days after discontinuing the ibuprofen, she had complete abolition of her abdominal
276 and right upper trapezius pain. Approximately 8 weeks after initiating physical therapy
277 treatment, the patient reported an 86% reduction in her LBP which was reported as an
278 intermittent 1/10 on the NPRS. Her shoulder impingement pain had completely resolved, and

279 she reported no recurrence of her abdominal and upper trapezius pain. She was able to sleep
280 without interruption and returned to full unrestricted activity and was discharged from physical
281 therapy.

282

283 **Discussion**

284

285 The patient in this case study presented with signs and symptoms of a musculoskeletal and non-
286 musculoskeletal condition coexisting during the course of her physical therapy treatment. This
287 case analysis emphasizes the importance of using a differential diagnostic approach to
288 hypothesize the potential systemic dysfunction, and the referral to an appropriate medical
289 specialist. Visceral disorders frequently refer pain to the spine and extremities that may be
290 difficult to differentiate from musculoskeletal dysfunction ². A thorough physical therapy
291 interview and examination are necessary to identify a potential disease process not appropriate
292 for physical therapy intervention.

293

294 The risk of serious gastrointestinal, renal, and hepatic toxicity due to OTC and prescription
295 ibuprofen is well documented ^{7,8,25-27}. Nonsteroidal anti-inflammatory drugs are among the most
296 common drugs associated with drug induced liver injury, with an estimated incidence of 3 to 23
297 per 100,000 patient years ¹². The incidences of death, liver failure, vanishing bile duct
298 syndrome, hepatocellular, and cholestatic liver damage have been reported as a result of
299 ibuprofen toxicity ⁷. Data also suggests ibuprofen produces liver reactions with concomitant use
300 of certain antibiotics, anti-hypertensive, and statin drugs ⁸. The physical therapist needs to be
301 aware of the potential for these types of reactions because of the widespread use of ibuprofen.

302 Searching the literature for possible interactions between ibuprofen and oral contraceptives
303 revealed no evidence of adverse interaction between these pharmaceuticals and several articles
304 describe a synergistic effect in controlling dysmenorrhea^{28,29}.

305

306 In this case study recognizing the signs and symptoms of a potential coexisting visceral
307 pathology led to a medical referral for further testing and treatment. Vigilant re-examination
308 throughout the physical therapy treatment is important to monitor for possible systemic
309 conditions. The patient in this case study did not complain of several common signs and
310 symptoms associated with hepatobiliary or gallbladder disease. She denied having a history of
311 nausea, vomiting, fatigue, ascites, or jaundice⁶. Given the cluster of other signs and symptoms
312 such as, pain matching the common pattern of referral for liver and gallbladder pathology,
313 constant ache pain unaffected by postural change or movement, a reported feeling of fullness
314 under the right rib cage, night pain, a “slight” increase in symptoms associated with ingestion of
315 “fatty food”, and reproduction of abdominal and right upper trapezius pain with palpation of the
316 liver, the treating therapist suspected a visceral origin of pain co-existing with her LBP and right
317 shoulder dysfunction. The physician’s examination included blood tests and a diagnostic
318 ultrasound, both of which are standard procedures for diagnosing liver pathology. A definitive
319 diagnosis of drug induced liver injury is based largely on exclusion and the gold standard is
320 expert opinion³⁰. The abolition of abdominal symptoms following discontinuation of ibuprofen
321 left no doubt as to the cause of the patient’s abdominal pain.

322 The strength and stabilization intervention for both the trunk and shoulder girdle musculature
323 demonstrated excellent results and are in line with those described by Hicks²⁰, Tate²⁴ and
324 McClure³¹. Hicks et al. reported a positive likelihood ratio of 4.0 for successful outcome with

325 utilizing a stabilization exercise program with LBP patients²⁰. McClure and Tate described a
326 positive impact on physical impairments and functional limitations with an exercise program
327 combined with education on patients diagnosed with shoulder impingement syndrome^{24,31}. The
328 results obtained in this case study correlated well with the outcomes of these particular studies.

329

330 This case study emphasizes that the physical therapist may be the first practitioner to recognize
331 visceral pathology. A thorough examination and screening for musculoskeletal and visceral
332 impairments, along with a process of differential diagnosis will hasten proper intervention, for
333 physical therapy patients.

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348 **REFERENCES**

349

350 1. APTA. Guide to Physical Therapy Practice. Second Edition. Phys Ther. 2001; 81: 9-
351 746.

352 2. Boissonnault W. Primary Care for the Physical Therapist: Examination and triage. St.
353 Louis, MO: WB Saunders Co; 2005.

354 3. Donato EB, DuVall RE, Godges JJ, Zimmerman GJ, Greathouse DG. Practice analysis:
355 defining the clinical practice of primary contact physical therapy. J Orthop Sports Phys
356 Ther. 2004; 34: 284-304.

357 4. Jette DU, Ardleigh K, Chandler K, McShea L. Decision-making ability of physical
358 therapists: physical therapy intervention or medical referral. Phys Ther. 2006; 86: 1619-
359 1629.

360 5. Davenport TE, Kulig K, Resnik C. Diagnosing pathology to decide the appropriateness of
361 physical therapy: Whats our role? J Orthop Sports Phys Ther. 2006; 36(1):1-2.

362 6. Goodman C, Snyder T. Differential Diagnosis in Physical Therapy. 3rd ed. Philadelphia,
363 PA: WB Saunders Co; 2000.

364 7. Bessone F. non-steroidal anti-inflammatory drugs: what is the actual risk of liver
365 damage? World J Gastroenterol. 2010; 16 (45): 5651-5661.

366 8. Rainsford KD. Ibuprofen: pharmacology, efficacy and safety. Inflammopharmacology.
367 2009; 17: 275-342.

368 9. Mayoral W, Lewis JH, Zimmerman H. Drug-induced liver disease. Curr Opin
369 Gastroenterol. 1999; 15 (3): 208-16.

- 370 10. Rostom A, Goldkind L, Laine L. Non-steroidal anti-inflammatory drugs and hepatic
371 toxicity: a systematic review of randomized controlled trials in arthritis patients. *Clin*
372 *Gastroenterol Hepatol.* 2005; 3 (5): 489-98.
- 373 11. O'Connor N, Dargan PI, Jones AL. Hepatocellular damage from non-steroidal anti-
374 inflammatory drugs. *QJM.* 2003; 96 (11): 787-91.
- 375 12. Aithal GP, Day CP. Non-steroidal anti-inflammatory drug-induced hepatotoxicity. *Clin*
376 *Liver Dis.* 2007; 3: 763-75.
- 377 13. McKinnis L. *Fundamentals of Musculoskeletal Imaging*, 3rd Ed. FA Davis, Philadelphia,
378 PA. 2010.
- 379 14. Stratford PW, Spadoni GF. The reliability, consistency, and clinical application of a
380 numeric pain rating scale. *Physiotherapy Canada.* 2001; 51 (2): 88-91.
- 381 15. Magee DJ. *Orthopedic Physical Assessment*, 4th Ed. Saunders, Philadelphia, PA. 2002.
- 382 16. Hoppenfeld S. *Physical Examination of the Spine and Extremities.* Appleton-Century-
383 Crofts, Nowalk, Connecticut. 1976.
- 384 17. Laslett M, Aprill CN, McDonald B, Young SB. Diagnosis of sacroiliac pain: validity of
385 individual provocation tests and composites of tests. *Man Ther.* 2005; 10 (3): 207-218.
- 386 18. Cook CE. *Orthopedic Physical Examination Tests: An Evidence-Based Approach.*
387 Pearson Education Inc. Upper Saddle River, NJ. 2008.
- 388 19. Hicks GE, Fritz JM, Delitto A, Mishock J. Interrater reliability of clinical examination
389 measures for identification of a lumbar segmental instability. *Arch Phys Med Rehabil.*
390 2003; 84: 1858-64.

- 391 20. Hicks GE, Fritz JM, Delitto A, McGill SM. Preliminary development of a clinical
392 prediction rule for determining which patients with low back pain will respond to a
393 stabilization exercise program. *Arch Phys Med Rehabil.* 2005; 86: 1753-1762.
- 394 21. O'Sullivan PB, Phytly GD, Twomey LT, Allison GT. Evaluation of specific stabilizing
395 exercise in the treatment of chronic low back pain with radiologic diagnosis of
396 spondylolysis or spondylolisthesis. *Spine.* 1997; 22; 2959-2967.
- 397 22. Hides JA, Richardson CA, Jull GA. Multifidus muscle recovery is not automatic after
398 resolution of acute, first-episode low back pain. *Spine.* 1996; 21: 2763-2769.
- 399 23. Porterfield JA, DeRosa C. *Mechanical Low Back Pain: Perspectives in Functional*
400 *Anatomy.* W.B. Saunders, Philadelphia, PA. 1998.
- 401 24. Tate AR, McClure PW, Young IA, Salvatori R, Michener LA. Comprehensive
402 impairment-based exercise and manual therapy intervention for patients with subacromial
403 impingement syndrome: a case series. *J Orthop Sports Phys Ther.* 2010; 40 (8): 474-493.
- 404 25. Moore N. Forty years of ibuprofen use. *Int J Clin Pract Suppl.* 2003; 135: 28-31.
- 405 26. Lewis JD, Kimmel SE, Localio AR, Metz DC, Farrar JT, Nessel L, Brensinger C,
406 McGibney K, Strom BL. Risk of serious upper gastrointestinal toxicity with OTC
407 nonaspirin non-steroidal anti-inflammatory drugs. *Gastroenterology.* 2005; 129 (6):
408 1865-74.
- 409 27. Fendrick AM, Greenberg BP. A review of the benefits and risk of non-steroidal anti-
410 inflammatory drugs in the management of mild-to-moderate osteoarthritis. *Osteopath*
411 *Med Prim Care.* 2009; 3: 1-9.

- 412 28. Chan WY, Dawood MY, Fuchs F. Prostaglandins in primary dysmenorrhea. Comparison
413 of prophylactic and nonprophylactic treatment with ibuprofen and use of oral
414 contraceptives. *Am J Med.* 1981; 70 (3): 535-41.
- 415 29. Knights KM, McLean CF, Tonkin AL, Miners JO. Lack of effect of gender and oral
416 contraceptive steroids on the pharmacokinetics of ibuprofen in humans. *Br J Clin
417 Pharmacol.* 1995; 40 (2): 153-6.
- 418 30. Hayashi PH. Causality assessment in drug-induced liver injury. *Semin Liver Dis.* 2009;
419 29: 348-356.
- 420 31. McClure PW, Bralcker J, Neff N, Williams G, Karduna A. Shoulder function and 3-
421 dimensional kinematics in people with shoulder impingement syndrome before and after
422 a 6-week exercise program. *Phys Ther.* 2004; 84:832-8.
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432 **Table 1. Systemic vs. Musculoskeletal Pain** ⁶.

433 **Differentiation of Systemic and Musculoskeletal Pain**

Systemic

Disturbs sleep

Deep aching or throbbing

Reduced with pressure

Constant or waves of pain and spasm

Is not aggravated by mechanical stress

Associated with:

Jaundice, migratory arthralgias, skin rash, fatigue, weight loss,

low-grade fever, generalized weakness, cyclic and progressive symptoms,

history of infection

Musculoskeletal

Generally lessens at night

Sharp or superficial ache

Usually decreases with cessation of activity

Usually continuous or intermittent

Is aggravated by mechanical stress

Usually associated with nothing specific

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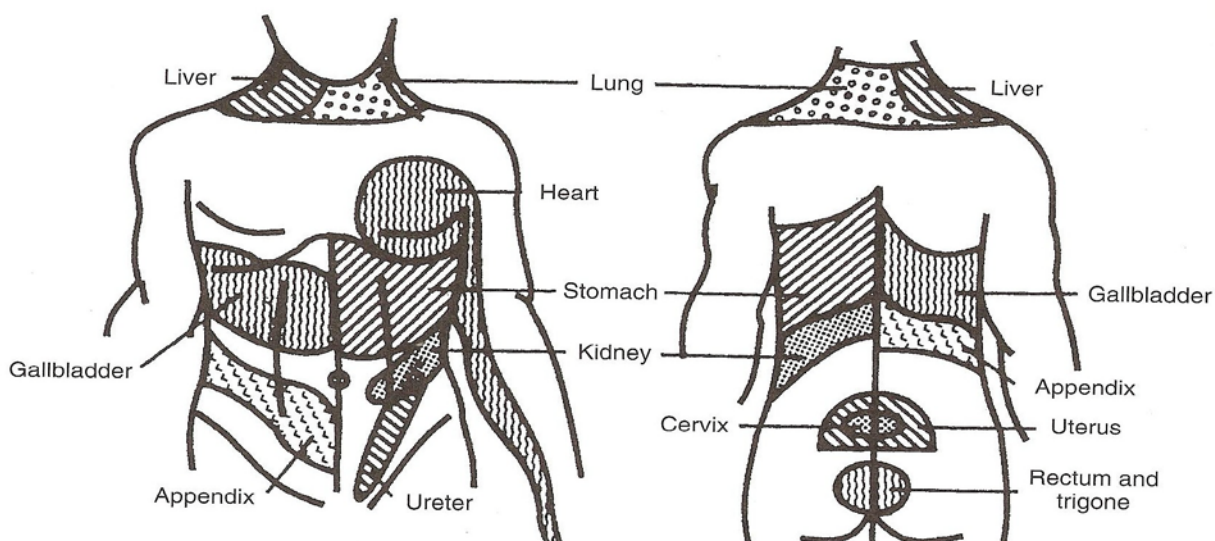
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439 **Table 2. Signs and symptoms of systemic back pain ⁶.****CLUES SUGGESTING SYSTEMIC BACK PAIN**

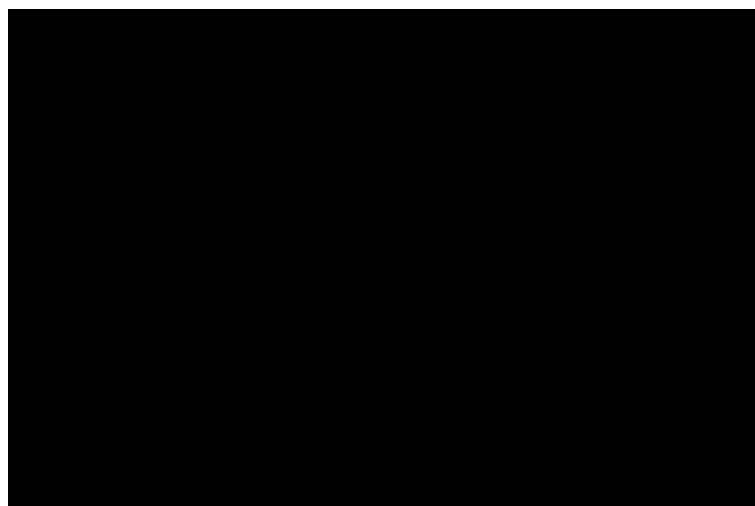
- Age over 45 years
- Nocturnal back pain
- Back pain that causes writhing, prompts the client to move about, or curl up in the sitting position
- Back pain with constitutional symptoms: nausea, fatigue, vomiting, diarrhea, fever
- Back pain that is insidious in onset and progression
- Previous history of cancer
- Back and abdominal pain at the same level (may occur simultaneously or alternately)
- Sacral pain in the absence of history of trauma or overuse
- Elevated body temperature, night sweats, febrile chills
- Back pain that is unrelieved by recumbency
- Back pain that does not vary with exertion or activity
- Severe, persistent back pain with full and painless movement of the spine
- Severe back and lower extremity weakness without pain
- Back pain associated with meals (increase or decrease in symptoms)

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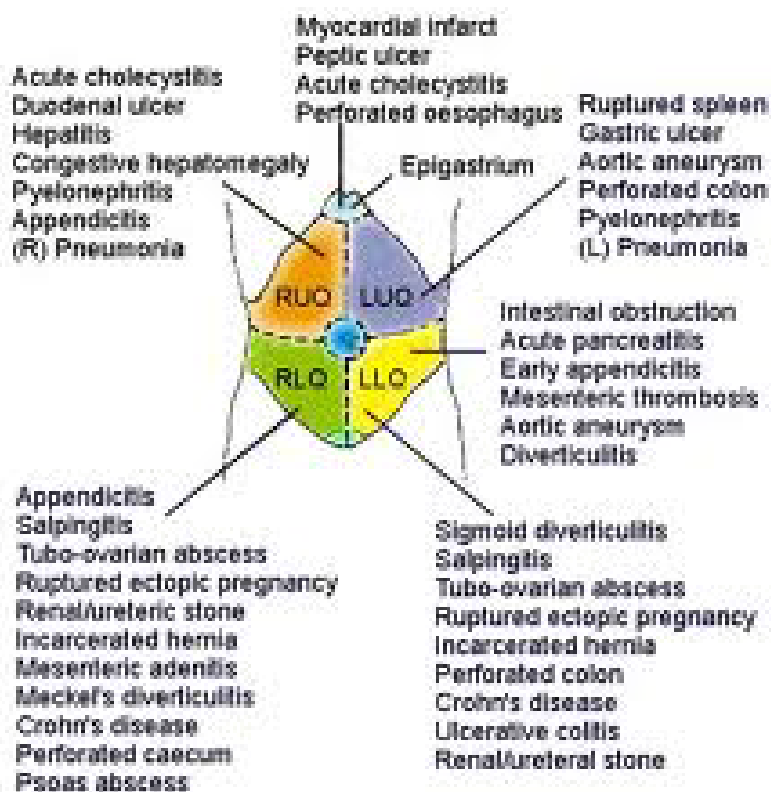
441 **Figure 1. Chart demonstrating typical visceral referred pain sites ².**

442

443 **Figure 2. Common sites for referred pain from the liver/gallbladder ⁶**



444
445 **Figure 3. Conditions associated with pain in various abdominal quadrants (Google Images)**



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