Managing Persistent Abdominal Pain: Three Case Studies

ASPMN 21st National Conference
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3:30 – 4:30 p.m.
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Springfield, IL

Objectives

• Identify at least two etiologies for persistent abdominal pain

• List at least one option for treating pain based on current evidence for each of the following:
  – Abdominal migraine with cyclic vomiting
  – Idiopathic abdominal pain
  – Chronic Pelvic Pain

Memorial Medical Center
526 bed academic teaching hospital
Memorial Health System
Springfield, IL
Magnet status in 2006

SpineWorks Pain Center
Medical Director
Ferdinand Salvacion, MD
Persistent Abdominal Pain: Neurophysiology

- Abdominal Pain
  - Chronic (persistent)
  - Intermittent or constant
  - Location difficult to pinpoint
  - Known underlying etiology
  - Idiopathic or functional disorder

- Symptoms – vary based on disorder
  - Cramping, colicky, non-specific deep, sharp, tender, nauseating, radiating, stretching, tugging, spasm, lancinating, heavy, fullness, aching
  - Rarely burning, tingling, itching or crawling

Pain Pathways and Processes

Persistent Abdominal Pain: Neurophysiology

Nociceptive visceral pain

1. **Anatomical** basis of nociception – spinal, vagal pathways, enteric nervous system
2. **Molecular** basis of nociception – peripheral and central signalling and sensitisation
3. **Modulatory** influences on nociception – descending neural, autonomic, hypothalamo-pituitary axis
Persistent Abdominal Pain: Neurophysiology

Anatomy of the gut
Two extrinsic innervations:

- **Vagal** afferent nerve fibers (lesser role)
- **Spinal visceral** afferent nerve fibers
  - Splanchnic
  - Pelvic

Nerve endings in all layers of the gut wall
Majority of axons are unmyelinated (C fibers)
Persistent Abdominal Pain: Neurophysiology

Anatomy: Spinal visceral afferents
- 3 groups of spinal mechanosensitive afferents
  - **Tonic** – respond linearly with rising wall tension starting at low thresholds (sensation such as fullness)
  - **Phasic** (high threshold) – respond only to noxious intensities of organ distention; also chemosensitive and respond to inflammatory mediators and mediate response to ischemia
  - **Silent** – develop mechanosensitivity AFTER exposure to inflammatory mediators

Persistent Abdominal Pain: Neurophysiology

Anatomy: Vagal role in nociception
- 50,000 vagal afferents (98% unmyelinated) supply the GI tract
- Senses non-noxious stimuli (satiety, nausea, fullness)
- Two main roles:
  - **chemosensitivity** to intraluminal chemicals and osmotic stimuli
  - mediation of unpleasant sensations such as nausea, vomiting

Persistent Abdominal Pain: Neurophysiology

Anatomy: Pelvic nerve fibers
- Innervate the lower colon and rectum independently of splanchnic neurons
- 1/3 are afferents both A delta and C fiber types
- Pass through the pelvic plexuses and nerves to segments S2-4
- Respond similarly to vagal endings, more mechanosensitive than nociceptive
Persistent Abdominal Pain: Neurophysiology

Molecular Basis of Nociception
Generator potentials produced by opening voltage-gated sodium channels in response to a depolarizing stimulus

Transduction of noxious stimuli – newly identified transducers TRPV, role in GI chemo, thermo, and mechano-nociception

Visceral Hypersensitivity Mechanisms
1. Sensitization of afferent nerves (peripheral sensitization)
2. Sensitization of spinal dorsal horn neurons (central sensitization)
3. Altered descending excitatory or inhibitory influences
4. Misinterpretation of non-noxious sensation as noxious due to cognitive and emotional biasing
Persistent Abdominal Pain: Neurophysiology

Molecular Level: **Peripheral Sensitization**

- **Prolonged stimulus** (i.e. injury or inflammation) leads to a change, permitting nociceptor firing at lower thresholds required for an acute noxious event...leads to **primary hyperalgesia**
- **Increased nociceptor excitability** – bradykinin, histamine, SHT, prostaglandin, proteases, cytokines
- **Reduced thresholds of cation channels**

Persistent Abdominal Pain: Neurophysiology

Molecular Level: **Central Sensitization**

- Repetitive firing of action potentials from the periphery leads to amplified responses to both noxious (hyperalgesia) and innocuous (allodynia) stimuli
- **Recruitment of adjacent spinal neurons leads to hypersensitivity of previously silent nociceptors**
- Effects changes at the dorsal horn and CNS
Persistent Abdominal Pain: Neurophysiology

Modulation

CNS receives input from visceral afferents affecting pituitary, neuroendocrine, and autonomic responses

Responses may be altered (modulated) via descending spinal pathways, autonomic system, and hypothalamic pituitary axis

Persistent Abdominal Disorders

- Inflammatory bowel disease
- Motility (GI neuromuscular) disorders
- Chronic hepatobiliary disorders
- Gynecological and pelvic disorders
- Adhesions and nerve entrapment
- Urologic disorders
- Functional disorders
Abdominal Migraine

• **Definition** - Sudden, paroxysmal episodes of abdominal pain followed by intense periumbilical pain (Rome III diagnostic criteria)
  - Typically no headache with abdominal symptoms
  - Pain lasts for hours to days
  - Associated with flushing, pallor, anorexia, nausea, vomiting, photophobia, headache (2 or more symptoms)
  - Pain interferes with normal activities
  - More prevalent in females
  - Onset between ages 7 and 12 years, but often overlooked until teen or early adult years
  - Family history of cephalic migraines 90%

Cyclic Vomiting Syndrome

• **Definition** – episodic, functional disorder of nausea and vomiting, with or without abdominal pain (Rome III criteria)
  - Sudden onset lasting hours or days (< 1 week)
  - Absence of N/V between the episodes
  - Three or more discrete episodes in the prior year
  - No metabolic, GI or CNS contributing disorders
  - Supportive criteria: personal or family history of migraine headaches

4 Phases of CVS:
1. **Interepisodic** – essentially symptom free
2. **Prodromal** – nausea, lethargy, anorexia, pallor; forceful vomiting may cause hematemesis; abdominal pain in 58% of adults during this phase
3. **Vomiting** – incapacitating, mean duration 41 hours with median # of 11 episodes; behaviors characteristically intolerant in being kept waiting for relief
4. **Recovery** – nausea and anticipatory anxiety may persist; sleep resumes; refeeding begins
Cyclic Vomiting Syndrome

Associated factors:
- **Personality traits** — competitive, perfectionistic, high achieving, strong-willed, moralistic; may become irritable and intolerant
- **Anxiety** — due to the burden of the illness, relationship stressors, financial impact, anticipation of the next episode
- **Physical changes** — tachycardia, elevated BP, diaphoresis, some loose stools, low-grade fever, neutrophilia without bandemia, mental clouding

Pareek et al. (2007). Am J of Gastroenterology, 102(12); 2832-2840.

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Cyclic Vomiting Syndrome

- **Triggers for CVS**
  - Infection 41% (i.e., sinusitis, URI, UTI)
  - Psychological stress 34% (eustress or distress)
  - Physical stress 18% (heavy exercise, inadequate sleep, pregnancy)
  - Diet 26% (chocolate, cheese, monosodium glutamate)
  - Motion sickness 9%
  - Onset of menses 13%

Pareek et al. (2007). Am J of Gastroenterology, 102(12); 2832-2840.

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Functional Abdominal Disorders

- IgE-mediated diet-induced allergy
- Gut mucosal immune responses increase CNS arousal, neuropeptides and transmitters released
- Dysregulation of the GI system


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Case Study #1: Abdominal Migraine/CVS

24 y/o black female admitted with intractable mid-right upper abdominal pain and nausea and vomiting.

- Hospitalized for 6 days at the time of pain consultation.
- Multiple diagnostic tests were inconclusive for underlying pathology.
- Was on a PCA pump with hydromorphone, approximately 40 mg used in 24 hours.
- Appeared frantic, hair unkempt, moaning and rolling in bed.

Case Study: Abdominal Migraine/CVS

Past Medical History

Childhood – asthma, atrial septal defect, irritable bowel syndrome diagnosed at age 12

Adult
- Gastroenteritis
- Pancreatic divisum
- Ovarian cysts
- Anxiety/depression
- Chronic UTI
- Gastropareis
- Chronic pancreatitis
- Biliary papillary stenosis
- Biliary HTN

Adult (cont'd)
- Clostridium difficile colitis
- Hyperlipidemia
- Chronic leukocytosis
- Atypical migraine with photophobia diagnosed in 2010
- Coproporphyrin I and III +
**Case Study: Abdominal Migraine/CVS**

**Past Surgical History**

<table>
<thead>
<tr>
<th>Year</th>
<th>Major Surgeries</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>Laproscopic cholecystectomy, Colonoscopy (tubular adenoma)</td>
</tr>
<tr>
<td>2008</td>
<td>ERCP, bilateral pancreatic duct stenting, biliary sphincterotomy, dorsal pancreatic sphincterotomy</td>
</tr>
<tr>
<td>2009</td>
<td>Pancreatectomy with islet cell transplant, splenectomy</td>
</tr>
<tr>
<td>2010</td>
<td>Adhesiolysis of abdomen, hernia repair, ileocolic anatomosis repair, insertion of J-tube and removal, partial colectomy, perihepatic abscess with IR drains X 3</td>
</tr>
</tbody>
</table>

**Family and Social History:**

Works as phlebotomist at hospital and local correctional center, married 2 years, no children, 2 dogs, attending 4 year college, never used tobacco, no alcohol, no history of substance abuse; attends church regularly

Father died age 42 MVA; mother age 46 has SLE; 2 siblings healthy; grandparents history of colon cancer and diverticulosis

**Physical Exam:** Tenderness in periumbilical area

**Objective findings:** Physical Exam unremarkable
- Temp 99.9, HR 118, BP 126/98, resp 18/min., O2Sat 98%
- H/H 12.2 & 28; WBC 16K, Absolute neuts 11.1, lymphs 4.3, band 0, Plts 313K
- CMP and LFTs normal except LD 251
- Ht 5’6” Wt 125 lbs

**Current medications:** Dilaudid PCA, pancrealipase, mirtazepine, phenergan, odanestrn creon, docusate sodium, metoclopramide, Lexvin SL

**Past medications:** Oxycontin, fentanyl patch, GoLytely, erythromycin, lactulose, Nexium, aceta-minophen, MiraLax, enemas, amitriptyline

**Allergies:** amoxicillin, demerol, metoclopramide
Case Study: Abdominal Migraine/CVS

Additional History:
- 2009 – 24 emergency department visits
- 2010 – 21 emergency department visits – only 6 after August OP pain clinic visit
- 2011 – 8 emergency department visits from Jan-Aug

Diagnostic tests since age 12:
- 42 abdominal Xrays
- 36 CT scans abdomen/body/pelvis
- 4 D Gastrogrfin studies
- 4 Nuclear Med: gastric emptying, Hida/CCK
- 3 MRI of the body
- Lab work-up included porphyria

Case Study #1: Hospital Visits

Pain Clinic Visits 2010

Care coordinated with PCP managing N/V, in conjunction with pain
- Set behavioral and prevention goals
- Referral to Motility Specialist ST. Louis
- Healthcare psychological counseling for anxiety and coping
- Coordinated continuum of care with ED, hospitalist, PCP, psychology, pain

Brenda Eden, MS, APN, ACNS-BC
**Case Study: Abdominal Migraine/CVS**

**Treatment Plan Considerations** (see handout)

- **Interepisodic Phase**
  - Recognize and reduce precipitating factors
  - Tricyclic antidepressant (amitriptyline, nortriptyline) or beta-blocker (propranolol)
  - Anti-migraine prevention (topiramate, PRN nasal triptan*)
  - Anti-anxiety agent (benzodiazepine)

*Conflicting evidence in pediatric and adult studies.

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**Case Study: Abdominal Migraine/CVS**

- **Prodromal Phase** (route of medications based on ability to tolerate po)
  - Abortive therapy with nasal triptan* (sumatriptan)
  - Prevent dehydration
  - Antiemetics (odansetron, phenergan)
  - Antihistamine (diphenhydramine, cyproheptadine)
  - Anti-anxiety medications (lorazepam)
  - Bowel regimen – address GI dysmotility
  - Sleep and rest

*Conflicting evidence in pediatric and adult studies.

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**Case Study: Abdominal Migraine/CVS**

- **Vomiting Stage**
  - Contact PCP prior to considering ED visit
  - Laboratory studies if indicated
  - Hydration – IV fluids
  - Repeat nasal triptan X1
  - Continue anti-emetics and antihistamine
  - Opioid therapy for pain (IV hydromorphone)
  - Benzodiazepine intravenously

*Conflicting evidence in pediatric and adult studies.

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- **Recovery Phase** – introduce oral foods as tolerated
Case Study: Idiopathic Abdominal Pain

48 y/o Caucasian female admitted with intractable nausea and vomiting and abdominal pain. Multiple past admissions with hospitalist oversight.

- Presents with periumbilical pain, often associated with chest tightness, initiating 3-4 days prior to ED visit. Rocking and fetal position improve comfort. Vomiting starts and occurs 8-10 X daily, ending with hematemesis. Some daily diarrhea stools, normal for patient since cholecystectomy.
- Recent increased stress with work. Father diagnosed with cancer. No changes in daily habits. Recently completed antibiotics for UTI.
- Consultation requested for both psychiatric and pain evaluations, never previously done.

Case Study: Idiopathic Abdominal Pain

Childhood
- Chronic migraine headache

Adult
- Migraine HA
- Mild LDDD and CDDD
- Nephrolithiasis with focal pyelonephritis (2005)
- Syncope
- Irritable Bowel Syndrome
- Diverticulosis
- Colitis - pseudomembranous
- Gastroesophageal reflux disease
- Fibrocystic breast disease
- Mod-severe gastroparesis

Adult (con’d)
- Chronic biliary duct dilation
- Ovarian polycystic disease
- Frequent UTI
- Erosive gastritis and duodenitis
- Shingles
- Chronic allergic rhinitis
- Colostidium difficile colitis
- Hypercholesterolemia
- Situational anxiety
- Left pneumothorax
- ANA titer +
- Coproporphyrin I and III +

Case Study: Idiopathic Abdominal Pain

Past Surgical History

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<tr>
<th>Year</th>
<th>Major Surgeries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to 2007</td>
<td>Carpal tunnel release, knee arthroscopy, vaginal hysterectomy, elective bilateral mastectomy</td>
</tr>
<tr>
<td>2007</td>
<td>MRCP, laparoscopic cholecystectomy, removal of adnexal mass, right oopherectomy, colonoscopy X2, EGD X2</td>
</tr>
<tr>
<td>2008-09</td>
<td>Multiple colonoscopies and EGDs, multiple PICC line insertions</td>
</tr>
<tr>
<td>2010</td>
<td>Liver biopsy, infusaport insertion</td>
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</table>
**Case Study: Idiopathic Abdominal Pain**

**Family and Social History:**
Married, first husband deceased, 2 adult children from 1st marriage and 3 step-children, works full-time for the state as a supervisor, no history of tobacco or substance abuse, rare alcohol use.

Parents history positive for coronary artery disease, father deceased MI, rheumatoid arthritis, IBS, migraine HA (both). Grandmother positive for Crohn disease. No history of cancer.

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**Objective findings:** Temp 98, BP 146/82, Resp 18/min., O2Sat 100% on room air;  Ht 5’5” Wt. 140lbs Alk Phos 153, Amylase 120; all other labs WNL; Physical Exam unremarkable

**Current Medications:** Tigan, phenergan, MiraLax, hydrocodone 5/325, odansetron, compazine, docusate, diphenhydramine – All PRN

**Home Medications:** Butabital, hydrocodone 5/325 Nexium, Oxycontin 10 mg b.i.d., MiraLax phenergan, lorazepam

**Allergies:** Demerol, erythromycin, toradol, tramadol

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**Additional History:**
2005-2011 61 emergency department visits

**Diagnostic tests past 6 years:**
52 chest and abdominal Xrays
30 CT scans abdomen/chest/pelvis
1 D Gastrografin studies
3 Nuclear Med: gastric emptying, Hida/CCK
3 MRI of the body
Case Study #2: Hospital Visits

### Case Study: Idiopathic Abdominal Pain

**Treatment** – protocol for CVS and Abdominal Migraine

**Primary Care Physician:**
- Allegra D, Nexium 40 mg daily, Zofran 8 mg SL bid, polyethylene glycol q hs, alprazolam 0.5mg tid prn, phenergan 25 mg q 4hours prn, amitriptyline 10mg q hs, citalopram 20mg daily, fentanyl patch 25 mcg/hr q 72hrs

**Pain Clinic:**
- Imitrex nasal spray prn, Fiornal bid prn, oxycodone IR 15 mg 1-2 po qid prn.

Case Study #3: Chronic Pelvic Pain

39 y/o Caucasian female presents to the OP pain clinic with a 16 year history of severe vulvar pain and chronic abdominal and pelvic pain. The pain started with sexual intercourse with her husband when first married.

She had undergone laser therapy for precancerous lesions of the vulva that worsened her pain.

The constant pain is in the lower pelvic region, with severe episodes of pain in the clitoris and labia regions. Reports burning sensation with full bladder & urination.
Case Study #3: Chronic Pelvic Pain

An exacerbation of the pain occurred 3 years prior during pregnancy with erythema in the vulvar region. Since that time the pain has become unremitting and aggravated by any type of stress. The pain causes nausea.

- burning, raw, sharp, shooting, and
- ranging in intensity from 3-7 on 0-10 scale
- standing, medications, physical therapy improves the pain
- Full bladder, sexual intercourse and menses aggravate the pain

Case Study: Chronic Pelvic Pain

Past Medical History:
- Psychiatric therapy for depression, abuse?
- Previous treatment at Pain Clinic in Chicago
- Migraine headaches
- Recurrent bronchitis, hx of pneumonia

Past Surgical History:
- Laser of vulva
- Perineorrhaphy
- Tonsillectomy
- Wisdom teeth extraction
- Cystoscopy (no inflammation)

Allergies: Sulfa and amoxicillin

Family and Social History:
Worked as financial executive, lost job due to corporate downsizing; currently working at home; married with a 3 y/old child; no history of tobacco use or substance abuse, occasional alcohol; low oxalate diet.

Current Medications: 
Klonopin, doxepin, multiple vitamins including magnesium oxide, topical estrogen, MetroGel

Past Medications: Hydroxyzine, methadone, steroids, topical creams
**Case Study: Chronic Pelvic Pain**

**Chronic pelvic pain syndromes**

<table>
<thead>
<tr>
<th>Treatment - Evidence Grade of Recommendation A, B, or C</th>
</tr>
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<tbody>
<tr>
<td>Bladder Pain syndrome/Interstitial cystitis</td>
</tr>
<tr>
<td>Analgesics, hydroxyzine, amitriptyline; pentosan polysulphate sodium, Intravesical instillation, TUR/laser, nerve block, SNS, PT; psychotherapy, bladder distention; botox; duloxetine; cyclosporin A; gabapentin; guided imagery; biofeedback; TENS</td>
</tr>
</tbody>
</table>

| Vulvar Pain Syndrome • Generalized Vulvar Pain • Localized Vulvar Pain • Vestibular Syndrome |
| Tricyclic antidepressant; alpha 2 ligand (gabapentin, Lyrica); local anesthetics; topical estradiol; SSNRIs (duloxetine, venlafaxine); biofeedback with pelvic floor therapy; psychotherapy; opioid analgesics |

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**Case Study: Chronic Pelvic Pain**

**Medical Treatment in Review:**

**Interventional therapy:** caudal epidural steroid injections, caudal injections with bupivacaine, superior hypogastric plexus block, SNS trial, SI joint Synvisc

**Opioid medications:** oxycodin 10-30 mg bid, fentanyl patch 12-25 mcg/hr q 72 hrs, oxycodone 5-15 mg for breakthrough pain, Norco 10/325 prn, Demerol PRN prior to irrigations, Actiq 400-600 mcg q 4 hrs

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**Case Study: Chronic Pelvic Pain**

**Medical Treatment in Review:**

**Adjuvant medications:** gabapentin up to 1600 mg/day, Lyrica 75mg bid, Klonopin, doxepin, duloxetine, metoclopramide, odansetron, scopolamine patch, Provigil, Nuvigil, Ritalin, Macrobid, pentosan polysulfate

**Alternative:** magnesium oxide chondroitin, biofeedback, physical therapy

**Other:** Bladder irrigations with local anesthetic and bicarbonate
DISCUSSION

Neurophysiology – Abdominal Pain
Medication Management
Continuum of Care Coordination
Chronic Pelvic Pain

References available in handouts

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References available in handouts
Cyclic Vomiting Syndrome/Abdominal Migraines
Pain Management Recommendations
SpineWorks Pain Center
12-31-10

4 phases:

**Interepisodic** (pain free)

**Prodromal** (Symptoms of lethargy, anorexia, pallor, nausea, pain begin but able to take oral meds)

**Vomiting** (Intense pain, persistant nausea, vomiting, retching)

**Recovery** (Nausea subsides, appetite recovers, pain resolved)

Plan for Treatment:

1. Recognize precipitating factors and limit them as possible. These include infection, sleep deprivation, exercise, conflicts, emotional stress, anxiety, menses, certain foods, and allergies. Note: Delay in gastric emptying correlates with abdominal migraine prodromal phase (Boyle et al.) Keep a diary of episodes.

2. Prophylaxis and Treatment:

   a. **Interepisodic Phase** – Use of tricyclic antidepressant (Amitriptyline, Nortriptyline) daily, triptan (Imitrex) nasal spray as needed, anti-anxiety agents, such as lorazepam, as needed.

   b. **Prodromal Phase**
      i. Take oral/transmucosal pain medication, such as Dilaudid or Actiq
      ii. Use abortive migraine medication – Imitrex Nasal spray
      iii. Take antiemetic (Zofran or Phenergan) along with 50 mg Benadryl
      iv. Rest/sleep in quiet, dark environment
      v. Repeat medications as needed; add anti-anxiety medication (lorazepam) if needed

   c. **Vomiting Phase**
      i. Unrelieved vomiting and pain after 2-3 days, contact primary care physician for evaluation
      ii. Perform laboratory and diagnostic studies as determined by assessment; include CBC, CMP, Urine analysis, plus CT scan only if indicated
      iii. Treat infections and dehydration as possible out-patient; may need to be sent to the ED for IV infusion; contact Pain Clinic if pain is uncontrolled.
      iv. Emergency Department – evaluation determined by physician. Consider 1 liter of IV fluids, Benadryl 50 mg IV, Dilaudid 1mg IV, Zofran or phenergan IV, IV Ativan

   d. **Recovery Phase** – Introduce oral foods as able to tolerate.

3. Primary Care/GI Follow-up - Keep regular appointments to evaluate recurrent episodes

Molecular events in visceral nociception

Transduction of the nociceptor generator potential

Central sensitisation

Further peripheral sensitisation

Transcriptional changes mediated by PK / MAPK / Erk, e.g. increased Na and transducer channel expression

Peripheral sensitisation

Fig. 3. Molecular basis of peripheral visceral nociceptive signalling before (1 and 2) and after (3–5) sensitisation. The main as-yet proven steps in this process are schematically demonstrated (see text for details).