



Follow up in Pediatric Pancreas Center<sup>2</sup> and with Primary Care



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# **TARGET POPULATION**

#### **Inclusion Criteria**

Patients greater than 6 months of age with diagnosis of acute pancreatitis: i.e. if 2 of 3 criteria are met:

- Abdominal pain
- Serum lipase or amylase greater than or equal to 3 times upper limit of normal
- Imaging findings consistent with pancreatitis

#### **Exclusion Criteria**

- Patients who develop acute pancreatitis during hospitalization for another cause.
- Patients less than 6 months old.



# **BACKGROUND | DEFINITIONS**

## **Definition**

Acute Pancreatitis: Condition diagnosed by meeting two of the following three elements: clinical symptoms such as abdominal pain, nausea/vomiting, or radiating back pain; serum levels of pancreatic amylase and/or lipase three times the upper limit of normal; and radiographic evidence of acute pancreatitis including pancreatic edema on ultrasound or computed tomography<sup>1</sup>.

### Background

Major considerations for management of acute pancreatitis are adequate fluid resuscitation, pain control, early enteral nutrition, evaluation for common etiologies, and monitoring/management of complications. Most cases of acute pancreatitis in children are mild, meaning little to no involvement of other organ systems, but there are some cases of severe pancreatitis which can lead to respiratory, renal, and circulatory compromise, as well as sequelae such as abdominal fluid collections and pancreatogenic diabetes type 3c.

Optimal management of pediatric pancreatitis is an area of ongoing research, but several paradigms of management have been found to be unnecessary or harmful, such as prolonged gut rest or avoidance of certain types of opioid medications<sup>2</sup>. Standardization of initial management using best available evidence is an important step to improve patient care.

## **INITIAL EVALUATION**

Once the diagnosis of acute pancreatitis has been made, next management steps should focus on:

### **Pain Control**

- Use a low threshold for using IV opioids (no data to support one type vs another) for severe pain including early initiation of patient controlled analgesia pump (PCA).
- Consider scheduled oral acetaminophen (unless patient meets criteria for IV acetaminophen) 15 mg/kg Q6 hours, max 1000 mg and ketorolac IV 0.5 mg/kg Q6 hours max 30mg for 48 hours.
- If mild pain and tolerating oral intake, can use sliding scale of acetaminophen, oxycodone, and IV morphine. NSAIDS can be considered as well.
- If pain is unable to be adequately controlled, recommend escalating pain control to PCA, and consulting acute pain service if pain is not controlled within 24 hours.

## Fluid Rehydration

Acute pancreatitis leads to intravascular hypovolemia via decreased intake, vomiting, and 3<sup>rd</sup> spacing of fluid. IV rehydration is critical for circulatory support, and may change disease course by decreasing pancreatic tissue ischemia. Optimal fluid type and amount are not known in pediatrics, but there is limited adult data that Lactated Ringers may be beneficial compared to normal saline if used early<sup>3</sup>. Volume goal is intravascular euvolemia, knowing that some 3<sup>rd</sup> spacing may occur. Recommendations for patients <u>outside of the ICU</u> are:

- Lactated Ringers preferred over normal saline for first 24-48 hours (unless patient with hyperkalemia or < 6 months old) bolus 20 ml/kg (max 1 L), repeat if necessary.</li>
- Fluids at 1.5X maintenance (max 150 mL/hr) and assess fluid status Q4H (HR, BP, urine output goal ≥ 1 mL/kg/hr, BUN/Cr daily or Q12 hours until normal). If this is inadequate, can repeat bolus or increase rate to 2X maintenance.
- Euvolemia: Provider has determined that the patient is at their ideal volume status (neither dehydrated, nor volume overloaded). The patient therefore requires intravenous fluids to *maintain* their ideal volume status rather than for repletion purposes
- Once euvolemia achieved, adjust fluid rate to maintain and account for enteral intake, and switch to D5 NS + 20 mEq KCl with total fluids at maintenance.



## Evaluate for etiologies which will guide initial management

Reasons to consider for pediatric pancreatitis:

- Choledocholithiasis and other obstructive processes
- Adbominal Trauma
- Medications (reference Figure 1: UptoDate List of Medications for Drug-Induced Acute Pancreatitis)
- Toxins, alcohol in particular
- Ductal anatomic abnormality
- Genetic
- Autoimmune
- Idiopathic

Pancreatitis caused by gallstones or pancreaticobiliary obstruction or pancreatic duct disruption will be managed differently than pancreatitis from other causes.

- Abdominal ultrasound is first line imaging test to assess for gallstones and biliary obstruction. If ultrasound was performed at an outside facility, it should be repeated at CHCO.
- If an outside CT or MRI was performed, these should be uploaded into EPIC <u>and over read</u> instead of a repeat ultrasound.
- Initial labs include CMP to monitor electrolytes, serum calcium, renal function, and assess for biliary obstruction, CBC for WBC, and triglycerides as a potential cause of pancreatitis

#### **Disposition depends on clinical status**

- For very mild pancreatitis (patients able to tolerate adequate oral intake and control symptoms with oral medications), home discharge from the ED with return precautions may be appropriate if the family is comfortable.
- Need for ICU is uncommon in pediatric pancreatitis, but can be considered if there are signs of multisystem dysfunction or clinical status is not suitable for the medical floor. Patients with severe pancreatitis can decompensate quickly. Respiratory compromise (progressive increased work of breathing, increasing oxygen requirement not accounted for by hypopnea from pain medication), persistent hypotension after 40 ml/kg (or 2 L) fluid resuscitation, or worsening clinical status (other than pain control) should prompt a discussion with the ICU team and the inpatient medical team for appropriate disposition.
- Patients with biliary obstruction/gallstone pancreatitis, or pancreatic duct disruption should be admitted to the surgical service.
- Typically, most patients with acute pancreatitis should be admitted to the Green Team if at Anschutz. Special considerations which may warrant admission to other teams are: Kaiser insurance (should discuss with Kaiser attending), active multi-system disease (discuss with GI fellow green vs. general medical team), or current malignancy (discuss with oncology). If the patient is at a satellite campus with inpatient services, there should be a discussion with the inpatient team if the patient is clinically appropriate for admission at that site, or if transfer to Anschutz campus is necessary.



Class Ia	Class Ib	Class II	Class III	Class IV
a-methyldopa	All-trans-retinoic acid	Acetaminophen	Alendronate	Adrenocorticotrophic
zodisalicylate	Amiodarone	Chlorothiazide	Atorvastatin	hormone
Bezafibrate	Azathioprine	Clozapine	Carbamazepine	Ampicillin
Cannabis	Clomiphene	Didanosine	Captopril	Bendroflumethiazide
Carbimazole	Dexamethasone	Erythromycin	Ceftriaxone	Benazepril
Codeine	Ifosfamide	Estrogen	Chlorthalidone	Betamethasone
Cytosine	Lamivudine	L-asparaginase	Cimetidine	Capecitabine
rabinoside	Losartan	Pegaspargase	Clarithromycin	Cisplatin
Dapsone	Lynestrenol/methoxyethinylestradiol	Propofol	Cyclosporin	Colchicine
nalapril	6-mercaptopurine	Tamoxifen	Gold	Cyclophosphamide
urosemide	Meglumine		Hydrochlorothiazide	Cyproheptadine
soniazid	Methimazole		Indomethacin	Danazol
lesalamine	Nelfinavir		Interferon/ribavirin	Diazoxide
letronidazole	Norethindronate/mestranol		Irbesartan	Diclofenac
entamidine	Omeprazole		Isotretinoin	Diphenoxylate
Pravastatin	Premarin		Ketorolac	Doxorubicin
Procainamide	Trimethoprimsulfamethazole		Lisinopril	Ethacrynic acid
vritonol			Metolazone	Famciclovir
Simvastatin			Metformin	Finasteride
tibogluconate			Minocycline	5-fluorouracil
Sulfamethoxazole			Mirtazanine	Fluvastatin
Culindas			Naprovop	Gemfibrozil
otraguelina			Daditaxel	Interleukin-2
etracycline			Pacificaxei	Ketoprofen
alproic acid			Ponatinio	Lovastatin
			Prednisone	Mefenamic acid
			Predhisoione	Nitrofurantoin
				Octreotide
				Oxyphenbutazone
				Penicillin
				Phenophthalein
				Propoxyphene
				Ramipril
				Ranitidine
				Rifampin
				Risperidone
				Ritonavir
				Roxithromycin
				Rosuvastatin
				Sertraline
				Strychnine
				Tacrolimus
				Vigabatrin/Jamotricing
				Vigabacini/ianocrigini
				Vincibulie
roduced with permi iew. Clin Gastroento	ssion from: Badalov N, Baradarian R, Kad erol Hepatol 2007; 5:648. Copyright © 20	irawel I, et al. Drug-Ir 007 Elsevier.	nduced Acute Pancreatit	is: An Evidence-Based

Figure 1: UpToDate List of Medications for Drug-Induced Acute Pancreatitis<sup>14</sup>



# CLINICAL MANAGEMENT

## **Management During Admission**

#### **General Management**

- If there is a suspected pancreatic duct disruption, consider surgical consult.
- Cross-sectional imaging can be considered for clinical worsening such as new worsening pain unrelated to
  eating, new fevers, new hypotension, or new anemia (Abdominal MRI/MRCP preferred if stable and no sedation
  required, CT with IV contrast otherwise).
- Routine use of antibiotics has not been found to be beneficial, but can be considered on a case-by-case basis for high suspicion of infected fluid collections or infected necrotic pancreatic tissue.

#### **ICU Management**

- ICU management is primarily on case-by-case basis by ICU team with GI consultation.
- Enteral nutrition compared to parenteral nutrition has been shown to improve outcomes in multiple prospective, randomized adult studies in patients with severe acute pancreatitis (patients with necrotizing pancreatitis and/or needing ICU-level care). Studies have shown early enteral nutrition to have lower mortality<sup>4</sup>, lower overall<sup>5</sup> and septic complications<sup>4-6</sup> as well as lower cost<sup>6</sup> and improved inflammatory markers<sup>7</sup> in patients with severe acute pancreatitis. The benefits have been confirmed in meta-analyses as well<sup>8</sup>. Unless patient condition prohibits (needing pressors, unable to attain enteral access), early enteral nutrition should be strongly considered.

#### Surgical team management of gallstone pancreatitis

- Fluid management with goal of intravascular euvolemia
- Adequate pain control (see initial management), consult acute pain service if pain not controlled in 24 hours
- GI consult if Endoscopic Retrograde Cholangiopancreatography (ERCP) is needed or other questions. Patients
  may need additional imaging to assess for choledocholithiasis prior to ERCP (such as a patient with mild LFT
  elevation or biliary dilation without definite choledocholithiasis seen on other imaging). This is typically MRCP or
  endoscopic ultrasound. ERCP is only available at Anschutz campus. If ERCP is needed, transfer will be
  required from satellite campuses.
- Cholecystectomy prior to discharge to decrease risk of recurrent biliary pancreatitis<sup>9,10</sup>

#### **Medical team management**

- Pain control (see initial management). If pain not adequately controlled within 24 hours, consult acute pain service.
- Regular diet, no role for routine fat-restricted diet or prolonged NPO. Allowing children with mild pancreatitis to advance their diets as tolerated has been associated with shorter hospitalizations without increased complications<sup>11</sup>.
- IV lactated ringers at 1.5X maintenance until euvolemia achieved, then can transition to standard IV fluids (D5 NS with 20 mEq KCl) for total fluids at 1X maintenance, accounting for oral intake.
- Monitor fluid status closely (strict Is and Os, HR, BP, UOP greater than or equal to 1 mL/kg/hr).
  - Renal function panel (RFP) daily or Q12 H until patient is tolerating fluid needs enterally.
- Complete etiologic workup (family or prior history of pancreatitis, trauma, medication/substance exposures). UpToDate has a useful summary table with medications to consider and strength of evidence for associations with acute pancreatitis. Obtain a Hereditary Pancreatitis panel if family history of pancreatitis or 2 or more episodes of pancreatitis with complete resolution of symptoms and/or normal lipase between episodes.
- Consider DVT prophylaxis as patients often have limited mobility during acute pancreatitis and it is an inflammatory state. Refer to <u>Venous Thromboembolism (VTE) Prevention</u> clinical pathway.

#### **Discharge Readiness**

## CLINICAL PATHWAY



- Tolerating adequate oral intake.
- Pain has resolved or well controlled by oral medications.

### Follow Up

There is up to a 42% rate of repeat hospitalization for children discharged after acute pancreatitis<sup>12</sup>.

- Children with uncomplicated / mild acute pancreatitis who do not require admission can follow up through primary care office in 2-4 days. If GI follow up is desired, this can be arranged by PCP office.
- Inpatients admitted with acute pancreatitis should have follow up with primary care office within 1-2 weeks to monitor symptoms and ensure adequate hydration.
- Inpatients admitted with acute pancreatitis should also have follow up in the Pediatric Pancreas Center approximately 1 month after discharge
- Exceptions:
  - Patients outside of Denver-metro-area (reviewed case-by-case basis; could follow up with general GI provider in Colorado Springs).
  - Primary oncology / bone marrow transplant.
  - Uncomplicated Gallstone (biliary) pancreatitis s/p cholecystectomy does not require routine GI follow up.
  - o If sooner access in GI is required than can be accommodated in pancreas center, then GI clinic is reasonable.

# LABORATORY STUDIES | IMAGING

#### Imaging

- Abdominal ultrasound is first line imaging test to assess for gallstones and biliary obstruction. If ultrasound was performed at an outside facility, it should be repeated at CHCO.
- If an outside CT or MRI was performed, these should be uploaded into EPIC and over read instead of an ultrasound.
- Cross-sectional imaging can be considered for clinical worsening such as new worsening pain unrelated to eating, new fevers, new hypotension, or new anemia (Abdominal MRI/MRCP preferred if stable and no sedation required, CT with IV contrast otherwise).
- Patients may need additional imaging to assess for choledocholithiasis prior to ERCP (such as a patient with mild LFT elevation or biliary dilation without definite choledocholithiasis seen on other imaging). This is typically MRCP or endoscopic ultrasound.

#### Labs

- For diagnosis: serum lipase or amylase (lipase generally more reliable)
- Initial labs include CMP to monitor electrolytes, serum calcium, renal function, and assess for biliary obstruction, CBC for WBC, and triglycerides as a potential cause of pancreatitis
- Monitoring labs:
  - o Daily Renal Function Panel while receiving IV fluids.
- Obtain a Hereditary Pancreatitis panel if family history of pancreatitis or 2 or more episodes of pancreatitis with complete resolution of symptoms and/or normal lipase between episodes.

# **THERAPEUTICS**

## **Antibiotics**

 Routine use of antibiotics has not been found to be beneficial in multiple adult studies, but can be considered on a case-by-case basis for high suspicion of infected fluid collections or infected necrotic pancreatic tissue. Consult GI before administering any antibiotics.

## Pain Control

- Low threshold for using IV opioids (no data to support one type vs another) for severe pain including early initiation of patient controlled analgesia pump (PCA).
- Consider scheduled oral acetaminophen (unless patient meets criteria for IV acetaminophen) 15 mg/kg Q6 hours, max 1000 mg and ketorolac IV 0.5 mg/kg Q6 hours max 30mg for 48 hours.
- If mild pain and tolerating oral intake, can use sliding scale of acetaminophen, oxycodone, and IV morphine. NSAIDS can be considered as well.
- If pain is unable to be adequately controlled, recommend escalating pain control to PCA, and consulting acute pain service if pain is not controlled within 24 hours.

## **Fluid Management**

- Lactated Ringers preferred over normal saline **for first 24-48 hours** (unless patient with hyperkalemia or less than 6 months old) bolus 20 ml/kg (max 1 L), repeat if necessary for initial resuscitation.
- Fluids at 1.5X maintenance (max 150 mL/hr) and assess fluid status Q4H (HR, BP, urine output goal greater than or equal to 1 mL/kg/hr, BUN/Cr daily or Q12 hours until normal). If this is inadequate, can repeat bolus or increase rate to 2X maintenance (max 200 mL/hr).
- Once euvolemia achieved, adjust fluid rate to maintain and account for enteral intake, and after 24-48 hours can switch to D5 NS with 20 mEq KCI with total fluids at maintenance.

#### **Nutrition**

- Regular diet, no role for routine fat-restricted diet or prolonged NPO. Allowing children with mild pancreatitis to advance their diets as tolerated has been associated with shorter hospitalizations without increased complications<sup>11</sup>.
- Enteral nutrition compared to parenteral nutrition has been shown to improve outcomes in multiple prospective, randomized adult studies in patients with severe acute pancreatitis (patients with necrotizing pancreatitis and/or needing ICU-level care). Studies have shown early enteral nutrition to have lower mortality<sup>4</sup>, lower overall<sup>5</sup> and septic complications<sup>4-6</sup> as well as lower cost<sup>6</sup> and improved inflammatory markers<sup>7</sup> in patients with severe acute pancreatitis. The benefits have been confirmed in meta-analyses as well<sup>8</sup>. Unless patient condition prohibits (needing pressors, unable to attain enteral access), early enteral nutrition should be strongly considered.

# **PARENT | CAREGIVER EDUCATION**

#### **Discharge Instructions**

Activity as tolerated. No need to restrict exercise or contact sports except in some cases of pancreatitis from trauma to the pancreas.

#### **Regular Diet**

Typically dietary fat restriction is not necessary. In some cases, children may feel abdominal pain and/or nausea if they eat high fat foods. In these cases, a low fat diet may help control symptoms.

#### Second-hand Smoke

Cigarette smoking is known to contribute to pancreatitis in adults. In children, second-hand smoke has been associated with more episodes of pancreatitis<sup>13</sup>. If there are members of the family who smoke, we recommend cutting back or quitting to help your child's pancreas. You can discuss ways to do this with your primary care physician or contact the Colorado quitline at <u>www.coquitline.org</u> or 1-800-QUIT-NOW.



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Clinical Pathway and Measures Review Committee - August 22, 2019

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Pharmacy & Therapeutics Committee – August 1, 2019

#### **REVIEW | REVISION SCHEDULE**

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