NEW YORK SOCIETY FOR GASTROENTEROLOGY & ENDOSCOPY
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Preventing post ERCP pancreatitis: What to do and how to do it

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December 12, 2024

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Disclosure

Consultant for:

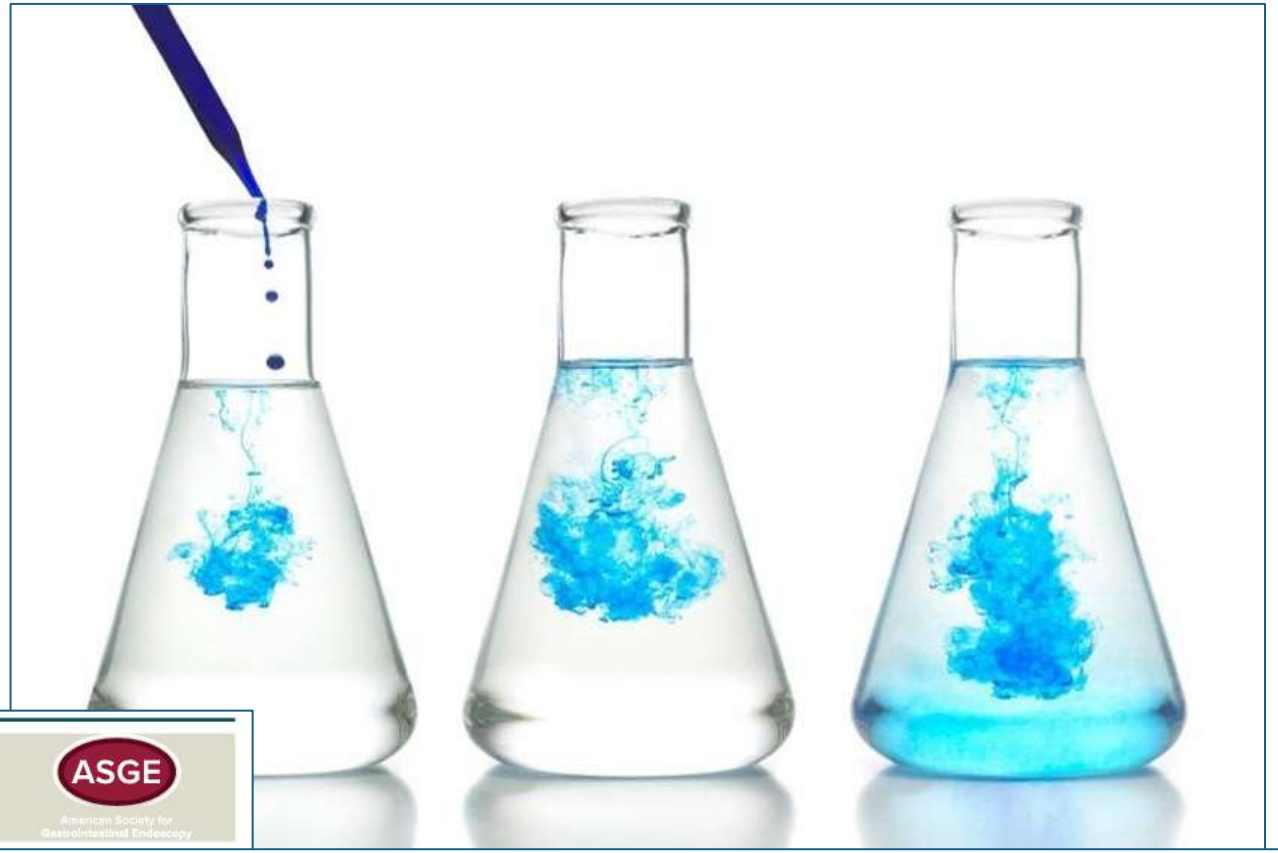
Cook

Steris

Interscope

Objectives

- Review risk factors for post-ERCP pancreatitis
- Updates on post-ERCP pancreatitis prevention/mitigation strategies
- Future directions



Communication from the ASGE Standards of Practice Committee

GUIDELINE

ASGE

American Society for Gastrointest
post-ERCP pancreatitis preventio
recommendations

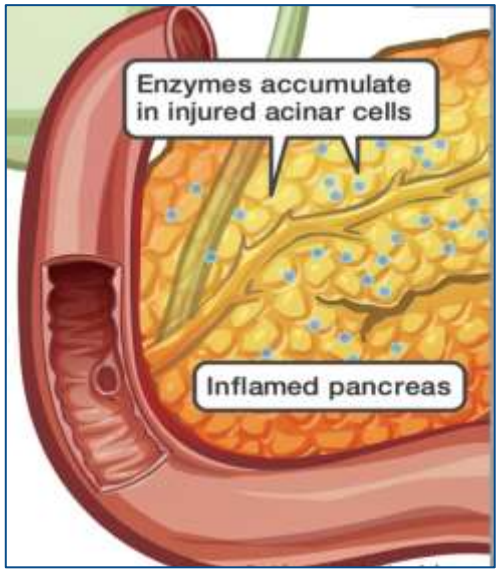
Prepared by: ASGE STANDARDS OF PRACTICE C

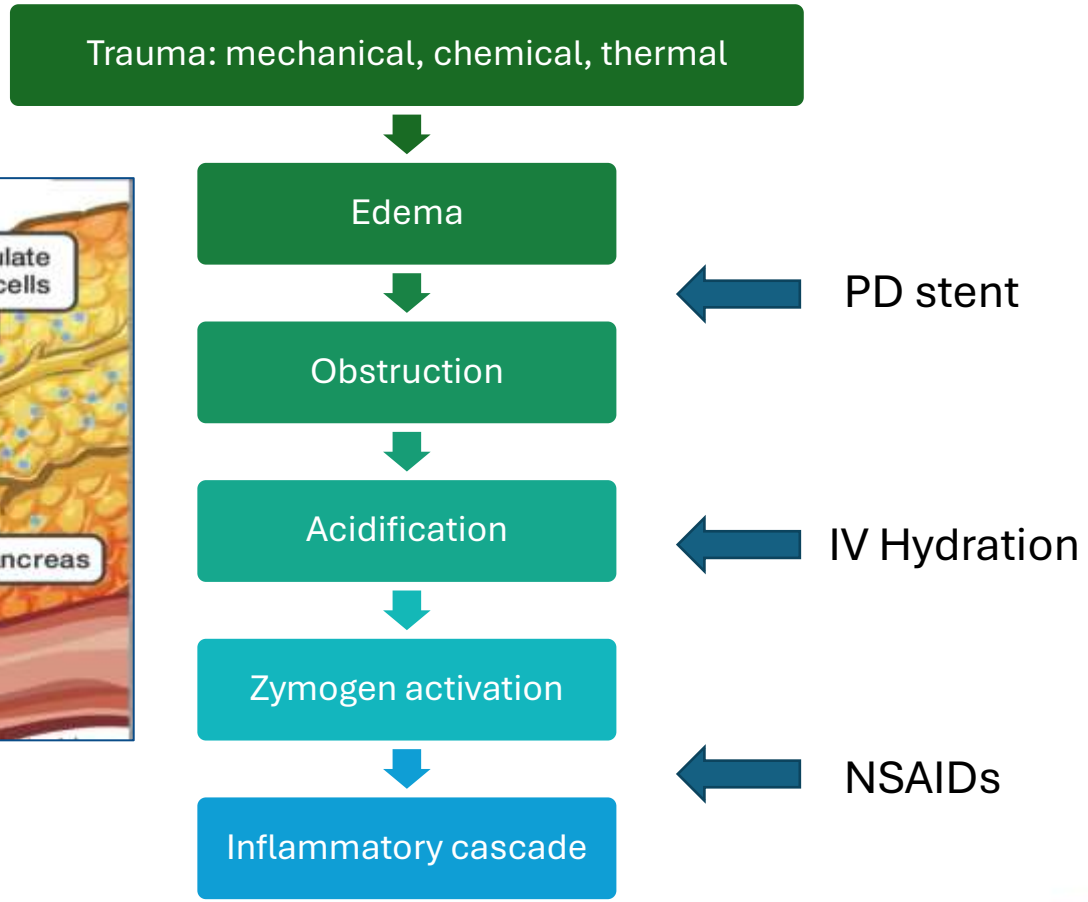
American College of Gastroenterology Guidelines: Management of Acute Pancreatitis

Scott Tenner, MD, MPH, JD, FACG[1], Santhi Swaroop Vege, MD, MACG[2], Sunil G. Sheth, MD[3], Bryan Sauer, MD, MSci, FACG[4], Allison Yang, MD, MPH[5], Darwin L. Conwell, MD, MSc, FACG[6], Rena H. Yadlapati, MD, MHS, FACG[7] and Timothy B. Gardner, MD, FACG[8]

Post ERCP Pancreatitis (PEP)

- Most common adverse event of ERCP
- Incidence 2%–15%
- Mortality <1%
- About 5% of patients who develop PEP go onto a severe course





Chandrasekhara et al. GIE 2017, Kochar et al. GIE 2015, Luo et al. Lancet 2016, Marta et al. Panc 2021, https://patient.gastro.org/pancreatitis/

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PEP Risk Factors

Patient related

- **Prior history of PEP**
- **Previous recurrent pancreatitis**
- **Female**
- Nondilated CBD
- Normal bilirubin
- Younger age (<35yo)

Procedure

- **Trauma associated with prolonged cannulation attempts (> 10 min)**
- **“Difficult” cannulation (“5-5-1” rule)**
- **Repeated pancreatic guidewire passage (>1)**
- **Pancreatic injection**
- Biliary balloon dilation of intact sphincter
- Ampullectomy
- Pancreatic sphincterotomy
- Precut sphincterotomy
- SEMS (nondilated PD)?

Cotton et al. JAMA 2014, El Nakeeb et al. World J Gastro 2016, ESGE guidelines 2016

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What Can We Do to Prevent/Mitigate PEP?

- Pre-procedural
- Rectal indomethacin 100mg

- Procedural
- Plus prophylactic pancreatic duct stent
- ERCP technique
- IV hydration

Multi-targeted preventive therapy

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Rectal Indomethacin

- Dampen pancreatitis inflammatory cascade by inhibiting prostaglandin synthesis and phospholipase A2 activity
- Single 100 mg dose of indomethacin reduces the incidence of PEP by ~ 50%[1]
- Administered ≥30 min before or during[2]
- NNT = 13 patients to prevent PEP in high risk patients[3]
- Contraindications:
  - NSAID allergy
  - Acute PUD
  - Renal insufficiency (creatinine level >1.4 mg/dL)
  - Pregnant woman ≥ 30 weeks
- For whom?

[1]Buxbaum et al. GIE 2023, [2]Luo et al. Lancet 2016, [3]Elmunzer et al. NEJM 2012

Guidelines

ESGE 2020	ASGE 2023	ACG 2024

Prophylaxis

1 ESGE recommends routine rectal administration of 100 mg of diclofenac or indomethacin immediately before endoscopic retrograde cholangiopancreatography (ERCP) in all patients without contraindications to nonsteroidal anti-inflammatory drug administration.

Strong recommendation, moderate quality evidence.

Recommendation 1: Among unselected patients undergoing ERCP, the ASGE recommends periprocedural rectal NSAIDs be given to prevent PEP (*strong recommendation/moderate quality of evidence*).

Preventing PEP

6. We recommend rectal indomethacin to prevent PEP in individuals considered to be at high risk of post-ERCP pancreatitis	Strong recommendation, moderate quality of evidence
7. We suggest placement of a pancreatic duct stent in patients at high risk for PEP who are receiving rectal indomethacin	Conditional recommendation, low quality of evidence

Cost of rectal indomethacin has skyrocketed from $2 in 2005 to $723.81 in 2023

Median hospital charge of $1,867.34!

Dumonceau Endoscopy 2020, Buxbaum GIE 2023, Tenner AJG 2024, Levenick Gastro 2016, Feder *JAMA Net Open* 2024, Thiruvengadam Clin Gastr Hep 2022

ERCP Best Practice Techniques

- ✓Patient selection and indication - avoid diagnostic ERCP
- ✓Wire-guided cannulation rather than contrast-guided approach
  - 15 RCTs- 50% reduction in the rate of PEP
- ✓Avoid PD- forceful or repeated wire advancement
- ✓Placement of prophylactic PD stents
- ✓”Difficult cannulation” situations, move quickly onto plan B strategy
  - Double guidewire
  - Needle-knife fistulotomy
  - Precut sphincterotomy over PD stent

Buxbuam et al. GIE 2023, Tang et al. Med 2018, Sundaralingam et al. Clin Gastro Hep 2015, Mariani et al. Endoscopy 2016

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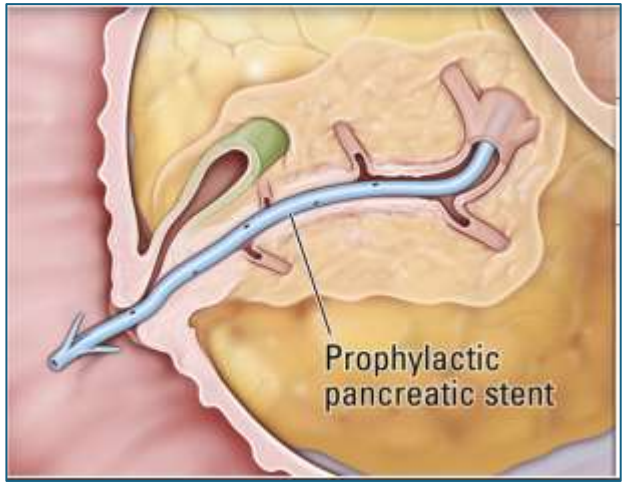
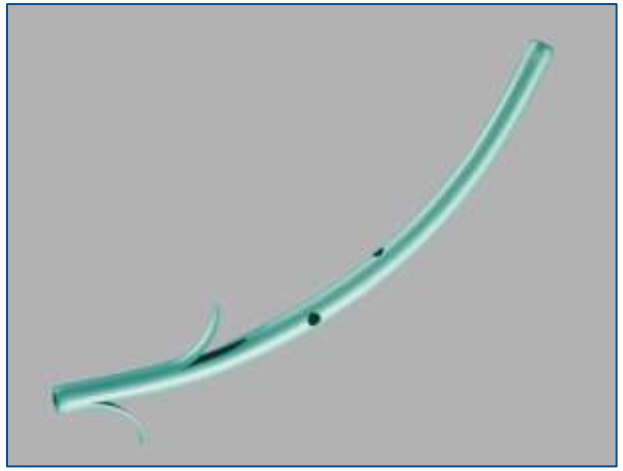
Prophylactic PD Stents

- In high risk patients where PD is repeatedly or deeply accessed or inadvertently opacified
- Reduces risk of PEP by 65%[1]
- NNT= 8[2]
- ONLY intervention that reduces both moderate and severe PEP
- 5Fr > 3Fr stent without internal flange[3]
- AXR to confirm spontaneous passage within ~ 2 weeks
- Spontaneous passage in > 90%[4]
- Otherwise, EGD to remove stent





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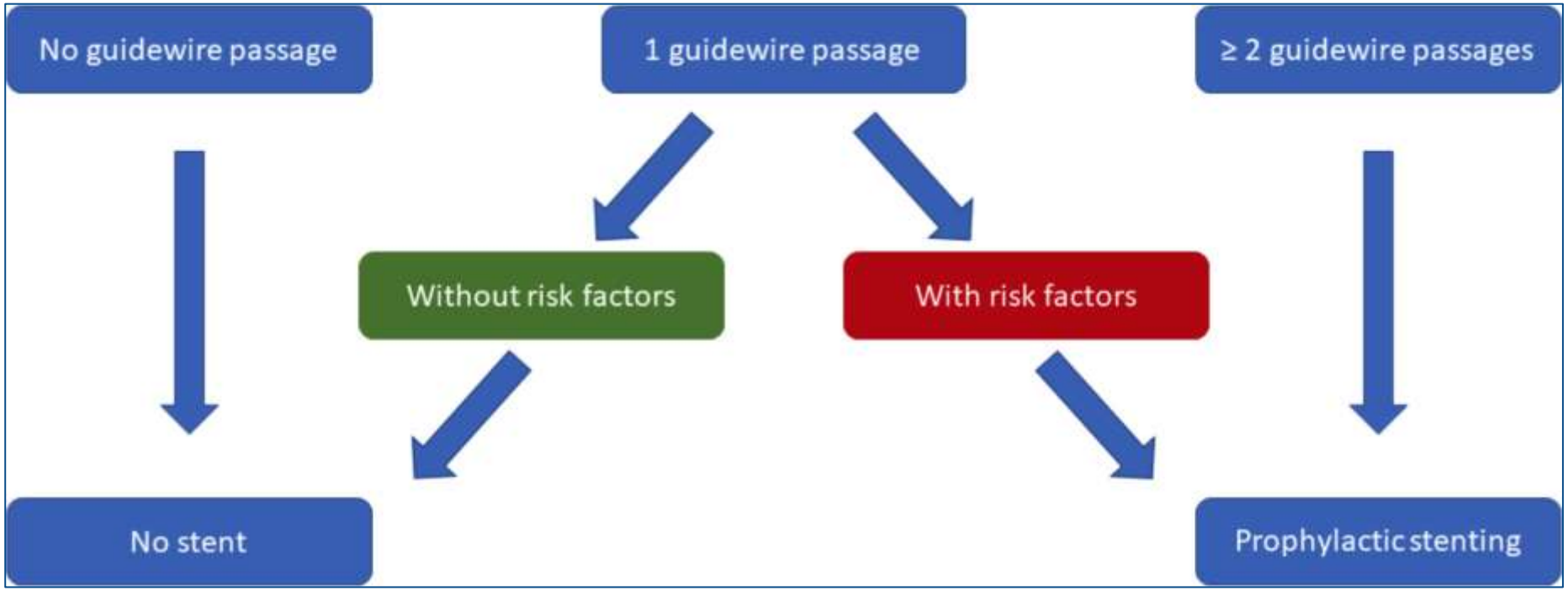
[1]Deviere,*Gastrointest Endosc Clin N Am 2011,* [2]*Choudhary GIE 2011,* [3]Afghani, Endoscopy 2014, *ESGE guidelines 2014*

Prophylactic PD Stents



- **BUT… in the real world, prophylactic PD stents are used in ~50% of high-risk cases, despite compelling evidence of their efficacy**

Conrad et al. Front Gastroenterol *2023,* Ashat *et al. Clin Endo 2023,* Issak et al. Endosc Int Open 2021, Smith et al. *Am J Gastro 2020,* Avila et al. *GIE 2020*

PD Stent + Indomethacin Better

- RCT non-inferiority study of 1950 patients across 20 centers
- In high risk patients
  - >80% were difficult cannulation
- 32% higher risk in the rectal indomethacin alone vs. indomethacin + stent of developing PEP
- Fewer cases of severe post-ERCP pancreatitis and death
- Most benefit seen in the highest risk patients
- NNT = 7 to prevent 1 case of PEP in the highest risk (score ≥ 3)

Elmunzer et al. Lancet 2024

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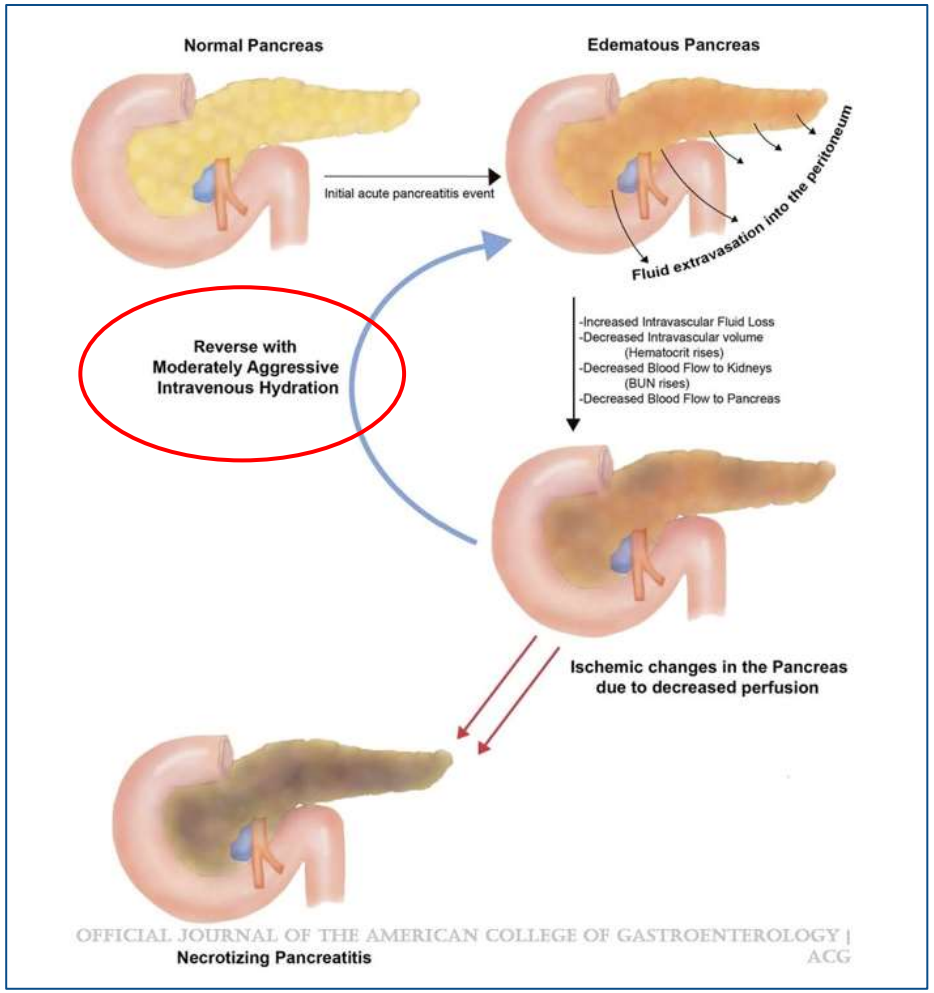
IV Hydration: Rationale



- **Decreased perfusion of the pancreas** from third space losses and microangiopathic effects
- **Intravenous hydration can promote blood flow** preventing pancreatic cellular death and the ongoing release of pancreatic enzymes activating the numerous cascades characteristic of pancreatic sepsis and necrosis

ACG guidelines 2024

Aggressive Hydration

In unselected patients undergoing ERCP, the ASGE suggests aggressive periprocedural and postprocedural intravenous hydration to prevent PEP pancreatitis (Conditional recommendation/Moderate quality of evidence).

- Based on 12 RCTs:
- 56% reduction in rate of PEP compared to standard hydration
- No difference in the risk of volume overload between the 2 groups
- NNT = 17 patients treated with AH to prevent 1 episode of PEP

Buxbaum et al. GIE 2023, Radadiya et al. Pancreatology 2019

Closer Look at the Details

- Lactated Ringer's solution
- Rate
  - ✓Aggressive = 20 mL/kg bolus and 3 mL/kg/h for 8 hours post procedure[1]
  - ✓Standard = no bolus, 3 mL/kg/h

Total ~3L vs. 1.5L (70 kgs patient)

- Timing: Early >> rapid[2]
- WATERFALL study for acute pancreatitis:
  - IV hydration strategy tailored to volume status[3]
  - ✓10 ml/kg bolus in patients with hypovolemia or no bolus in euvolemia, followed by 1.5 ml/kg/hour over 72 hours
  - ✓Fluid overload 20.5% in aggressive vs. 6.3% in moderate (p= 0.004)

Total 8.3 vs. 6.6L given!

- FLUYT study- aggressive LR hydration + NSAIDs was not superior to NSAIDs alone in mod/high risk, but did show a trend toward less severe PEP[4]

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[1]Buxbaum et al. GIE 2014, [2]Kumari et al. BMC Gastro 2024, [3]de-Madaria et al. NEJM 2022, [4]Sperna Weiland et al. Lancet Gastro Hep 2021

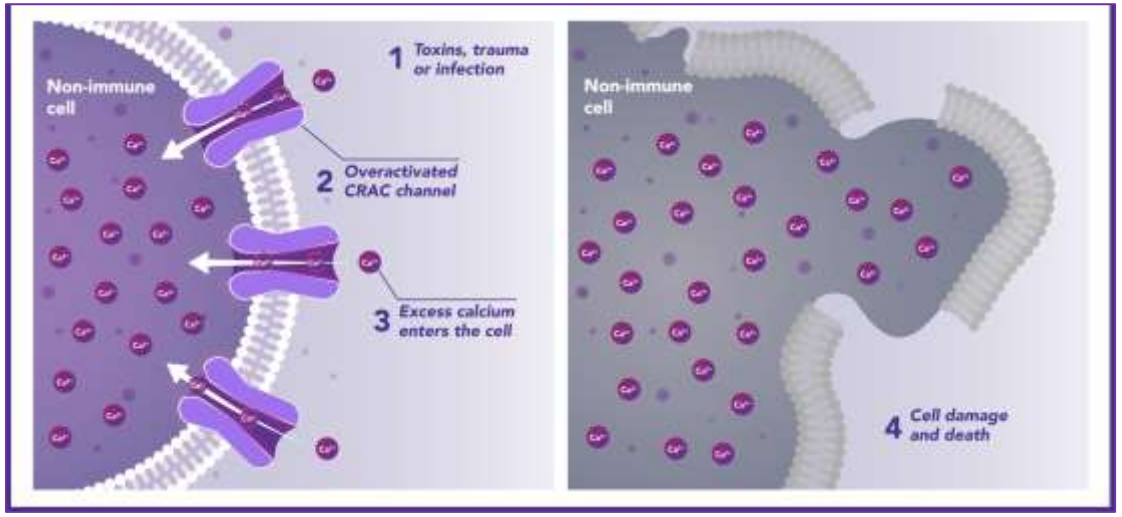
Future Directions

- Can we further identify clinical characteristics associated with increased PEP risk such as race, BMI, etc?
- PEP predictors to help tailor therapy
- Should outpatient and inpatient PEP be managed the same?
- Call to action for drug price regulations
- Room for improvement overall, as rate of PEP and associated mortality has not decreased despite guidelines

Mutneja et al. Endoscopy 2021

New Therapies on the Horizon?

- Novel calcium release-activated calcium (CRAC) channel inhibitor
- In the setting of acute pancreatitis + SIRS
- Targets multiple inflammatory pathways:
  - End organ
  - Pancreatic acinar and ductal cells
  - Pro-inflammatory mediators
  - Cytokines
  - Macrophages
  - Neutrophils
- Daily IV infusion over 4 hours x 3 days



Gerasimenko et al. J Physiol 2022, Sutton et al. ACG late breaking abstract 2024

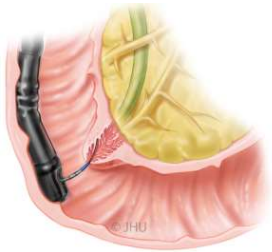
CARPO trial- Phase IIB

- International, double-blinded, randomised, placebo-controlled study designed to determine the dose-response and efficacy of CRAC
  - 216 patients with acute pancreatitis and ≥ 2 SIRS
- Results-
  - ✓Faster time to **solid food tolerance** vs. placebo
    - 43.6% relative reduction (2.1 day improvement) in median
  - ✓No new onset **severe respiratory failure** vs. 4/47 (8.5%) placebo (p=0.0027)
  - ✓Lower rate of new onset **necrotizing pancreatitis** at 30 days (30%) vs. placebo (37%)
  - ✓No patient with **> 21 day LOH**

Sutton et al. ACG late breaking abstract 2024

Summary

- PEP is the Achilles heel of ERCP
- Multi-targeted mitigation strategies include:
  - ✓Pre-procedure- rectal indomethacin
  - ✓Peri-procedure- wire cannulation, PD stents
  - ✓Post-procedure- IV lactated Ringer's
- Potential medical treatments are on the horizon
- Despite data, strategies are under-utilized ➡ call for action!



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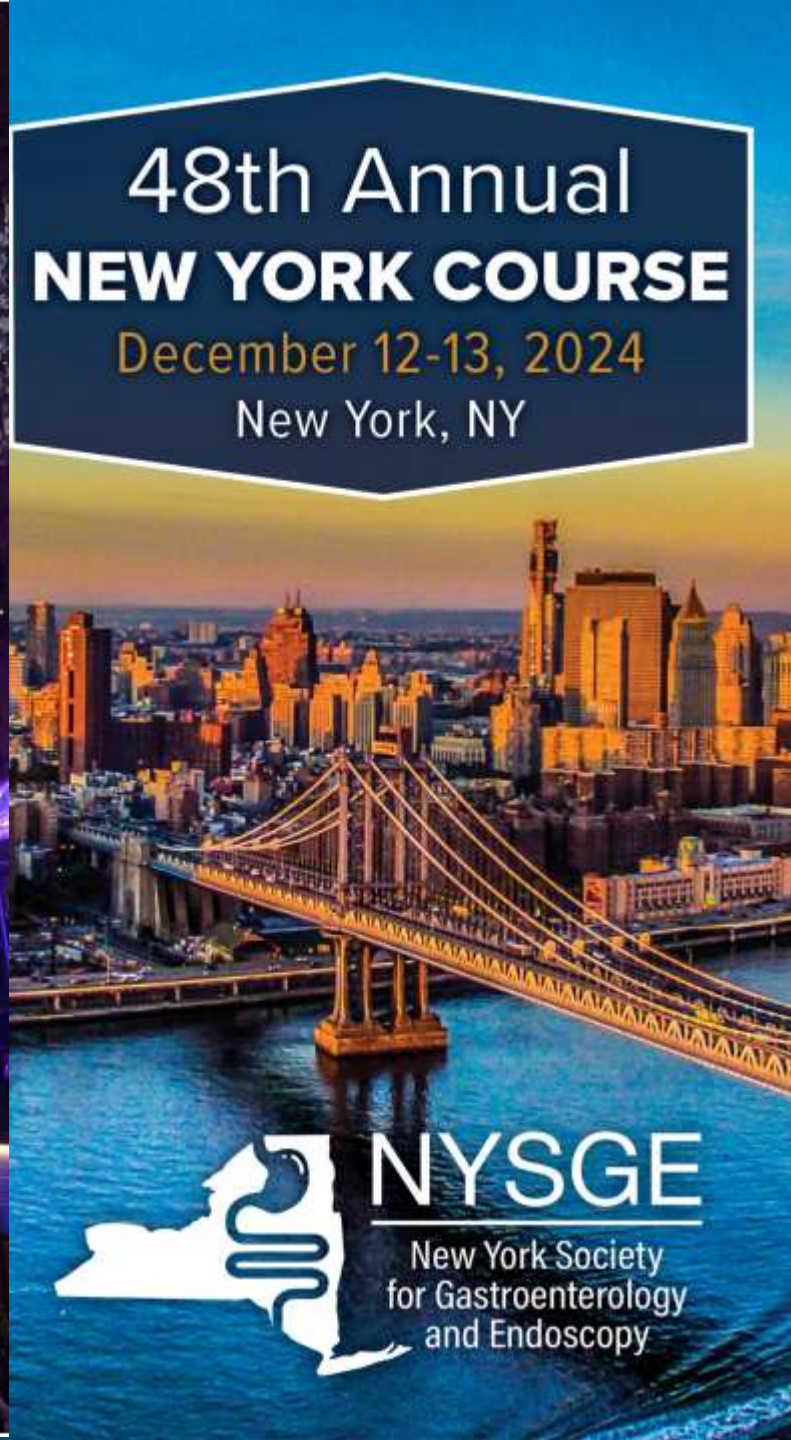
Thank you!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