

# A gut feeling ...

BVN-GBN Autumn meeting 2023

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# Overview

● Case

◆ Differential diagnosis and discussion

★ Take home

# Case V.

Premature born boy (GA 27w4d, BW 1270g=p90)

- Spontaneous uncomplicated pregnancy, normal ultrasounds
- G3P2
  - P1 GA 27w5d: omphalocele, NEC
  - P2 GA 33w6d: no problems
- Emergency cesarean section (uterine dehiscence), no antenatal corticosteroids
- APGAR 7/8/8. Adequate transition. IRDS R/ LISA + NIV.

# Case V. GA 27w4d, BW 1270g

0-48h MEF (MM/PreNAN st 1) + TPN

24-48h First stool (minimal amount)

D2: 4x vomiting/regurgitation (non-billious)

## D6 (28w3d):

- Prolonged MEF → enteral feeding 30ml/kg/d
- Little but no adequate meconial passage
- X-abdomen: no intestinal distension, no signs of obstruction
- 2x glycerin enema → no result
- D7: NAC enema → meconial passage ✓



GA 27w4d  
BW 1270

### Q1 What would you do?

- Imaging studies
- Enema
- Watchful waiting
- Other

# Case V. GA 27w4d, BW 1270g

D8

- Regular meconial passage, gastric intolerance: **8→12 feedings**
- Apnea/bradycardia of premature: caffeine + **doxapram**

**D15 (29w6d)**

- Persisting feeding intolerance (non-billious, non-projectile vomiting, EV 92ml/kg/d)
- Start duodenal (transpyloric), continuous, feeding

D19

- Duodenal feeding well tolerated
- Exclusive enteral feedings, TPN stopped

**Q2: What would you do?**

- Imaging studies
- Duodenal(transpyloric) feeding
- Erythromycin
- Watchful waiting
- Other

GA 27w4d  
BW 1270

**D6**  
Prolonged MEV  
and delayed  
meconial passage

# Case V. GA 27w4d, BW 1270g

D23-D27 trial gastric feeding: no succes **X**

D39(33w1d)-D43 trial gastric feeding + erythromycin: no succes **X**

D49 (34w2d) →

- Start of oral feedings
- Continuous inability to step-up gastric feeding (despite PPI, 2nd trial of erythromycin and change of formula feeding) **X**



# Case V. GA 27w4d, BW 1270g

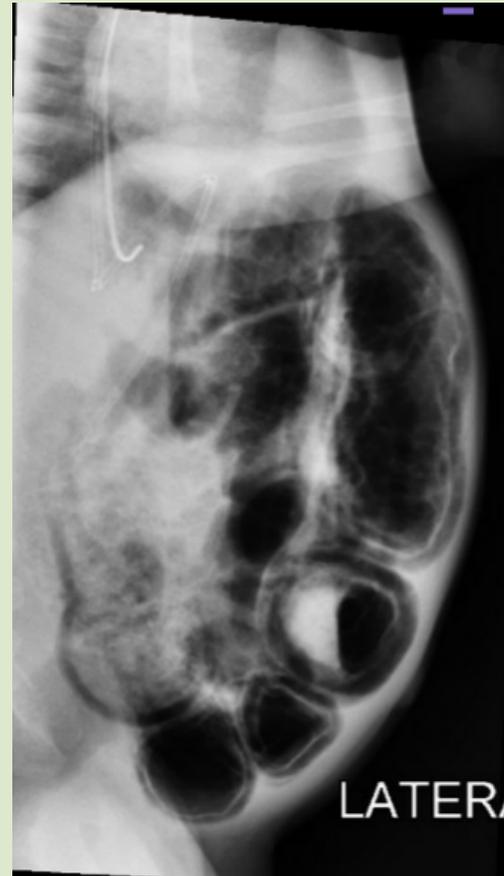
## D63 (36w4d)

- Diaper filled with dark-red bloody stool, 2x in 1h
- Vitals stable, no fever, CR < 2sec, distended abdomen with peristalsis, not shiny, slightly increased resistance on palpation



# Case V. GA 27w4d, BW 1270g

## X-abdomen



## Lab

Hb 10.6g/dL, normal leukocyte and trombocyte count

CRP 1.6mg/L

capBG: pH 7.36, pCO2 43  
Na 130mmol/L  
lactate 2.3mmol/L

GA 27w4d  
BW 1270

**D6**  
Prolonged MEV  
and delayed  
meconial passage

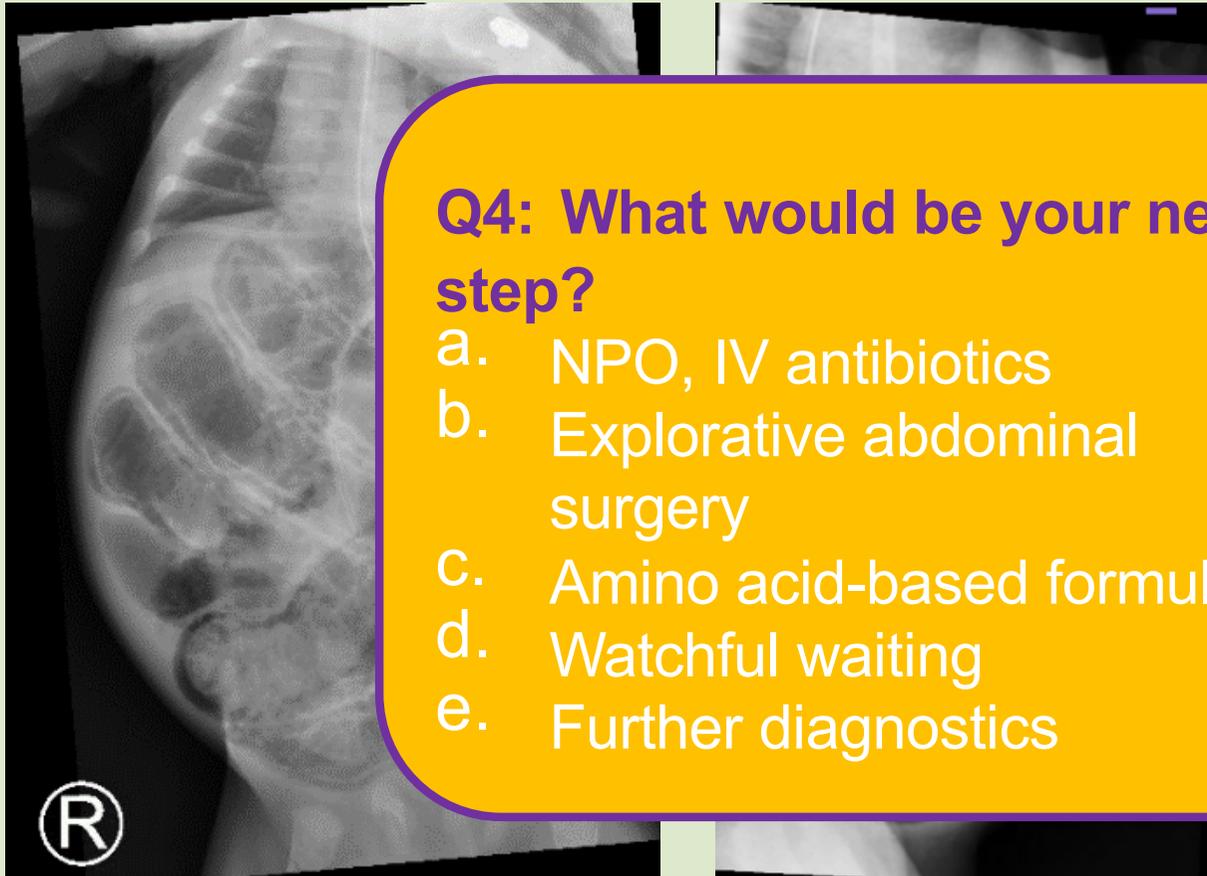
**D15**  
Start duodenal  
feeding  
(continuous)

**D39**  
2nd trial gastric  
feeding +  
erythromycin

**D60**  
Oral + duodenal  
feeding + restart  
erythromycin

# Case V. GA 27w4d, BW 1270g

## X-abdomen



## Lab

Hb 10.6g/dL, normal leukocyte and trombocyte  
6mg/L  
pH 7.36, pCO2 43 mmol/L  
2.3mmol/L

**Q4: What would be your next step?**

- a. NPO, IV antibiotics
- b. Explorative abdominal surgery
- c. Amino acid-based formula
- d. Watchful waiting
- e. Further diagnostics

GA 27w4d  
BW 1270

**D6**  
Prolonged MEV  
and delayed  
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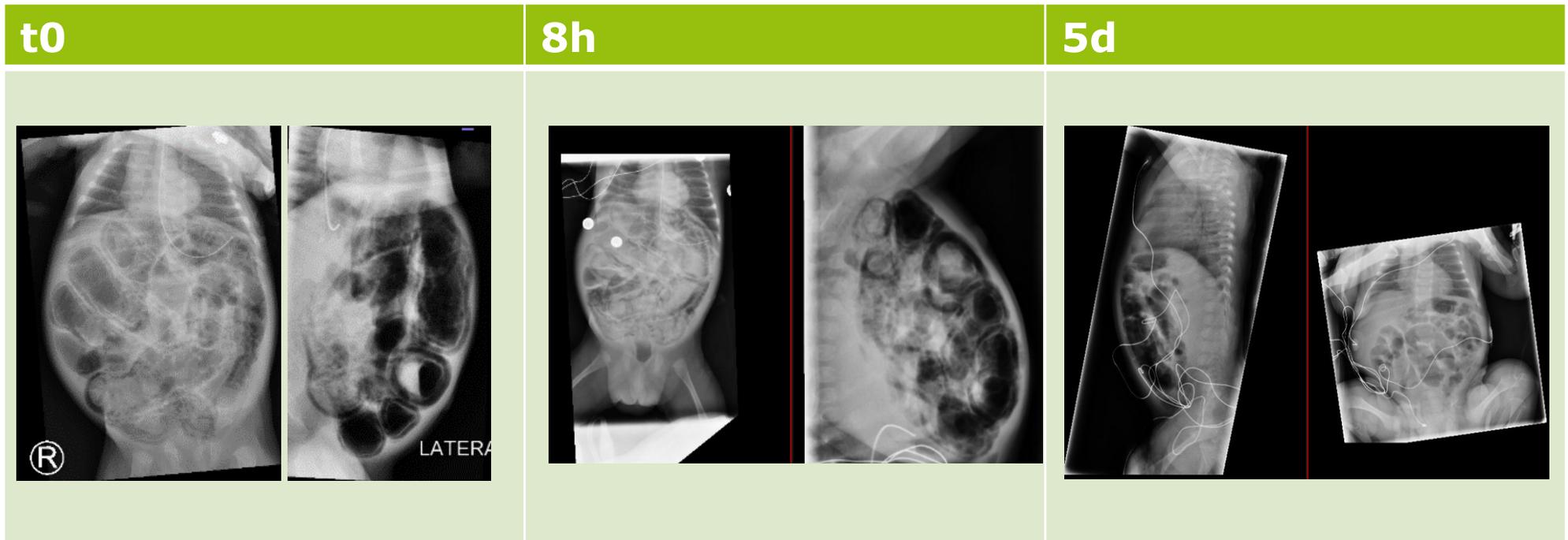
# Case V. GA 27w4d, BW 1270g

## D63 (36w4d)

- WDX Necrotizing enterocolitis
- Treatment
  - NPO, exclusive TPN
  - IV antibiotics (cefotaxim, amikacin, metronidazol)
- Follow-up
  - Vitals stable, no fever, clinically stable
  - CRP max. 5.7mg/L, Hb↓ 8.0g/dL
  - Lactate 2.3-1.7-1.8mmol/L
  - Na 130-139mmol/L, hypokalemia R/ IV KCl
  - Imaging
    - Abdominal US: extended PI of small intestines and colon, normal hepatic findings, no pneumoperitoneum
    - X-abdomen ...



# Case V. GA 27w4d, BW 1270g



# Case V. GA 27w4d, BW 1270g

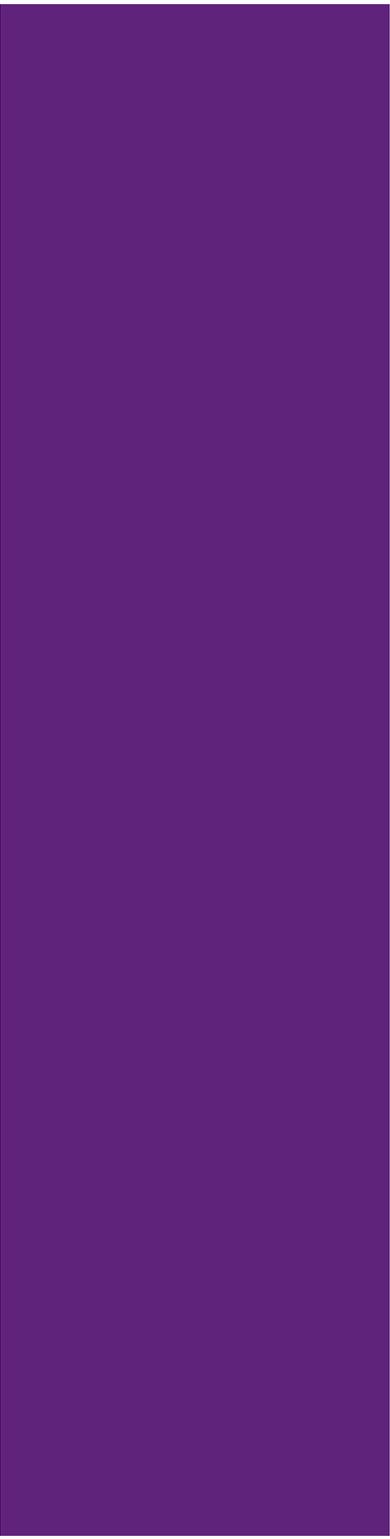
## D63 (36w4d)

- WDX Necrotizing entero-colitis
- Treatment:
  - NPO, exclusive TPN
  - IV antibiotics (cefotaxim, amikacin, metronidazol)

## D67 (37w1d)

- Restart enteral feeding: Puramino®, well tolerated
- D72: fully enteral feeding through NG-tube





# **Differentiation of pathological entities**

# NEC - diagnosis

TABLE 1. NEC Staging System Based upon Historical, Clinical and Radiographic Data

## STAGE I (Suspect)

- a. Any one or more historical factors producing perinatal stress.
- b. Systemic manifestations—temperature instability, lethargy, apnea, bradycardia.
- c. Gastrointestinal manifestations—poor feeding, increasing pre-gavage residuals, emesis (may be bilious or test positive for occult blood) mild abdominal distension, occult blood may be present in stool (no fissure).
- d. Abdominal radiographs show distension with mild ileus.

## STAGE II (Definite)

- a. Any one or more historical factors.
- b. Above signs and symptoms plus persistent occult or gross gastrointestinal bleeding; marked abdominal distension.
- c. Abdominal radiographs show significant intestinal distension with ileus; small bowel separation (edema in bowel wall or peritoneal fluid), unchanging or persistent “rigid” bowel loops, pneumatosis intestinalis, portal vein gas.

## STAGE III (Advanced)

- a. Any one or more historical factors.
- b. Above signs and symptoms plus deterioration of vital signs, evidence of septic shock or marked gastrointestinal hemorrhage.
- c. Abdominal radiographs may show pneumoperitoneum in addition to others listed in II c.

Classification of NEC, Signs & Symptoms of NEC, and NPO/Antibiotic Duration

NEC Category	Bell's Stage	Diagnosis			Management	
		Systemic signs	Abdominal Signs	Radiographic Signs	NPO and antibiotic length	Consults
Suspected	IA	Temperature instability, apnea, bradycardia, lethargy	Gastric retention, abdominal distention, emesis	Normal or mild intestinal dilation, mild ileus	48 hours	Per clinician judgement
	IB	Same as IA	Same as IA, plus grossly bloody stool	Same as IA	48 hours	Surgery
Definite	IIA	Same as IA	Same as IB, plus absent bowel sounds with or without abdominal tenderness	Intestinal dilation, ileus, pneumatosis intestinalis or portal venous gas	7 days	Surgery
	IIB	Same as IA, plus mild metabolic acidosis and thrombocytopenia	Same as IIA, definite tenderness, with or without abdominal cellulitis or right lower quadrant mass	Same as IIA, plus ascites	10 days	Surgery
Advanced	IIIA	Same as IIB, plus hypotension, bradycardia, severe apnea, combined respiratory and metabolic acidosis, DIC, and neutropenia	Same as IIB, plus signs of peritonitis, marked tenderness	Same as IIB	10 days	Surgery
	IIIB	Same as IIIA	Same as IIIA	Same as IIB, plus pneumoperitoneum	14 days	Surgery

# FPIES = food protein-induced enterocolitis syndrome

## Pathophysiology

Non-IgE mediated food allergy

Innate > adaptive immune system

## Clinical presentation

Type	Acute	Chronic
	<ul style="list-style-type: none"> <li>Repetitive, projectile emesis typically &lt; 1 to 4h of trigger food ingestion</li> <li>Diarrhea (bloody) &lt; 6-8h</li> <li>Systemic symptoms: pallor, hypotonia, hypotension, hypothermia</li> <li>Ill-appearing in otherwise appropriate growth and development</li> </ul>	<ul style="list-style-type: none"> <li>Persisting vomiting/diarrhea (bloody)</li> <li>Poor weight gain/FTT</li> </ul>
	Intermittent ingestion	Frequent ingestion
	6m	< 1m

carrot),

# FPIES - diagnosis

**Table 1.** FPIES diagnostic criteria

FPIES diagnostic criteria	Description
<b>Acute FPIES:</b>	Diagnosis requires meeting the <b>major criterion and ≥ 3 minor criteria</b>
Major criterion	Vomiting 1 to 4 hrs after ingestion of suspected food trigger and absence of typical IgE-mediated allergic skin or respiratory symptoms
Minor criteria	<ol style="list-style-type: none"> <li>1. ≥ 2 repetitive episodes of vomiting after ingestion of suspected food trigger</li> <li>2. Repetitive vomiting 1 to 4 hrs after eating a different food</li> <li>3. Extreme lethargy with any suspected reaction</li> <li>4. Need for emergency department with any suspected reaction</li> <li>5. Need for intravenous fluid support with any suspected reaction</li> <li>6. Diarrhea within 24 hrs (typically within 5 to 10 hrs)</li> <li>7. Hypotension</li> <li>8. Hypothermia</li> </ol>
<b>Chronic FPIES</b>	<p>The <b>most important criterion</b> for diagnosis is <b>resolution of symptoms</b> within days of elimination of offending foods and acute recurrence of symptoms when the food is reintroduced with:</p> <ul style="list-style-type: none"> <li>- Vomiting within 1 to 4 hrs</li> <li>- Diarrhea within 24 hrs (typically within 5 to 10 hrs)</li> </ul> <p><b>Milder presentation:</b> lower doses of food trigger result in intermittent vomiting ± diarrhea, as well as poor weight gain/failure to thrive</p> <p><b>Severe presentation:</b> daily ingestion of food trigger result in intermittent but <b>progressive vomiting and diarrhea ± blood ± dehydration ± metabolic acidosis</b></p>
<b>Oral food challenge:</b>	Diagnostic of FPIES (positive) if major criterion and ≥ 2 minor criteria are met
Major criterion	Vomiting 1 to 4 hrs after ingestion of suspected food trigger and absence of typical IgE-mediated allergic skin or respiratory symptoms
Minor criteria	<ol style="list-style-type: none"> <li>1. Lethargy</li> <li>2. Pallor</li> <li>3. Diarrhea within 5 to 10 hrs after suspected food trigger ingestion</li> <li>4. Hypotension</li> <li>5. Hypothermia</li> <li>6. Increased neutrophil count of ≥ 1,500 cells/mL above baseline count</li> </ol>

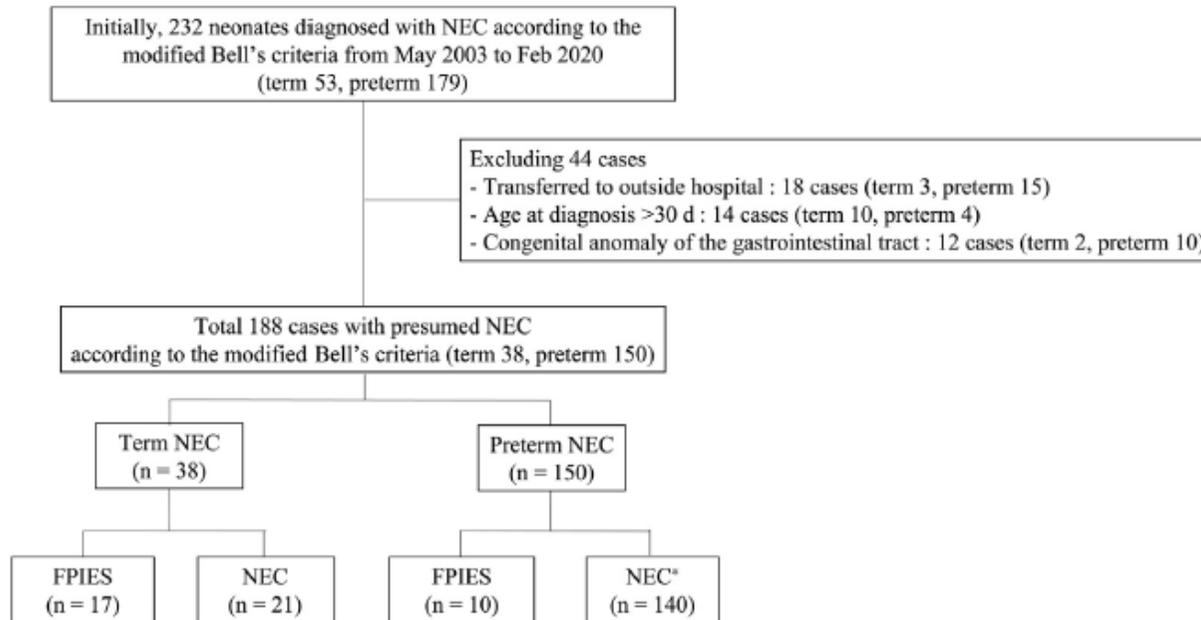
Modified from Nowak-Węgrzyn *et al.*<sup>12</sup>

FPIES, food protein-induced enterocolitis syndrome; IgE, immunoglobulin E.

# FPIES? NEC?

	FPIES	NEC
<b>Clinical</b>	<b>Acute</b> recurrent vomiting/diarrhea ± systemic signs <b>Chronic</b> progressive vomiting and diarrhea ± FTT <b>OFC</b>	Temp instability Apnea/BC↑ Discolorisation abdominal wall
	Distended abdomen, vomiting, bloody stools Systemic: lethargy, hemodynamic instability	
<b>Labographic</b>	Leukocytosis+eosinophilia Thrombocytosis IL27 ?	Thrombocytopenia, DIC, neutropenia
	Metabolic acidosis	
<b>Imaging</b>		Ascites Pneumoperitoneum Portal venous gas
	Intestinal dilatation/ileus Pneumatosis intestinalis (FPIES > NEC?)	

# FPIES? NEC?



**Figure 1.** Process of inclusion and exclusion of cases. The asterisk represents patients who were initially diagnosed with presumed NEC were classified into the FPIES group and the NEC group according to the international guidelines for diagnosing FPIES. FPIES, food protein-induced enterocolitis syndrome; NEC, necrotizing enterocolitis.

# FPIES? NEC?

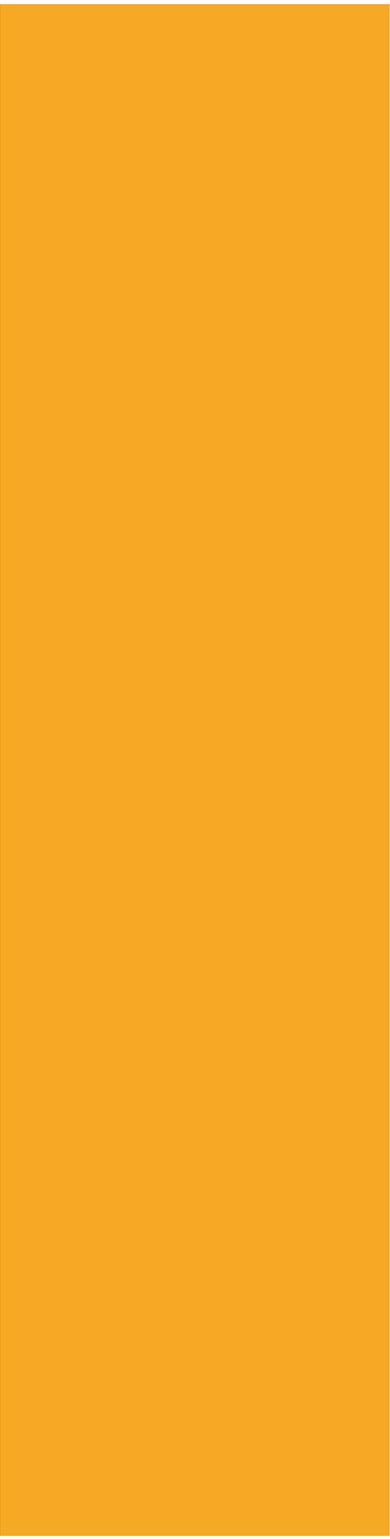
**Table 3**  
Comparison of Clinical Features, Laboratory Findings, Radiologic Findings, and Outcomes Between the Food Protein-Induced Enterocolitis Syndrome Group and the Necrotizing Enterocolitis Group in Term and Preterm Infants With Presumed Necrotizing Enterocolitis

Variable	Term				Preterm				
	Total (n = 38)	FPIES (n = 17)	NEC (n = 21)	P value	Total (n = 150)	FPIES (n = 10)	NEC (n = 140)	P value	
<b>Symptom, n (%)</b>									
Hematochezia	26 (68.4)	16 (94.0)	10 (47.6)	<b>.004</b>	73 (48.7)	8 (80.0)	65 (46.4)	.052	
Vomiting	19 (50.0)	9 (52.9)	10 (47.6)	>.99	45 (30.0)	2 (20.0)	43 (30.7)	.72	
Abdominal distention	13 (34.2)	6 (35.3)	7 (33.3)	>.99	104 (69.3)	4 (40.0)	100 (71.4)	.06	
Shock	10 (26.3)	8 (47.1)	2 (9.5)	<b>.02</b>	56 (37.3)	5 (50.0)	51 (36.4)	.50	
<b>Laboratory finding, median (range)</b>									
Hemoglobin (g/dL)	15.4 (10.7-19.3)	15.4 (10.7-18.6)	15.5 (12.2-19.3)	.05	12.3 (7.4-20.0)	12.4 (9.6-15.5)	12.3 (7.4-20.0)	.14	
WBC (/μL)	11,360 (5600-23,250)	14,770 (9300-22,860)	10,300 (5600-23,250)	<b>.048</b>	9870 (1470-52,850)	10,730 (2760-22,180)	9850 (1470-52,850)	.86	
Platelet (/μL)	314,000 (135 k-384 k)	319,000 (222 k-478 k)	289,000 (135 k-519 k)	.12	257,000 (6 k-770 k)	299,500 (77 k-511 k)	257,000 (6 k-770 k)	.43	
ANC (/μL)	5657.5 (1529-19,065)	6972.0 (2663-13,739)	4426.5 (1529-19,065)	.37	4330.0 (221-34,353)	3839.0 (524-14,861)	4330.0 (221-34,353)	.24	
Eosinophil (%)	3.2 (0-9.2)	4.35 (1.2-8.6)	2 (0-9.2)	<b>.01</b>	2.2 (0-25.1)	2.15 (0-8.0)	2.2 (0-25.1)	.89	
hsCRP (mg/dL)	0.1 (0.01-3.91)	0.1 (0.09-3.91)	0.1 (0.01-0.77)	.35	0.2 (0.01-20.94)	0.1 (0.08-20.94)	0.2 (0.01-15.70)	.47	
<b>Radiologic finding, n (%)</b>									
Normal	8 (21.6)	3 (18.8)	5 (23.8)	.08	.29 36 (24.3)	3 (30.0)	33 (23.7)	.08	
Ileus	21 (56.8)	10 (62.5)	11 (52.4)	>.99	67 (45.3)	2 (20.0)	65 (46.8)	.15	
Pneumatosis intestinalis	7 (18.9)	3 (18.8)	4 (19.0)	.07	34 (23.0)	4 (40.0)	30 (21.6)	.04	
Perforation	1 (2.7)	0 (0.0)	1 (4.8)	<.001	11 (7.4)	0 (0.0)	11 (7.9)	<.001	
<b>NEC grading, n (%)</b>									
1a	16 (42.1)	5 (29.4)	11 (52.4)		.08 50 (33.3)	1 (10.0)	49 (35.0)		
1b	10 (26.3)	5 (29.4)	5 (23.8)		37 (24.7)	3 (30.0)	34 (24.3)		
2a	9 (23.7)	5 (29.4)	4 (19.0)		24 (16.0)	2 (20.0)	22 (15.7)		
2b	2 (5.3)	2 (11.8)	0 (0.0)		14 (9.3)	3 (30.0)	11 (7.9)		
3a	0 (0.0)	0 (0.0)	0 (0.0)		7 (4.7)	1 (10.0)	7 (5.0)		
3b	1 (2.6)	0 (0.0)	1 (4.8)		18 (12.0)	0 (0.0)	17 (12.1)		
<b>Outcome</b>									
NPO duration (d)	3 (0-14)	3 (0-8)	3 (1-14)	.77	5 (0-35)	8 (3-35)	4 (0-21)	.08	
Operation	2 (5.3)	0 (0.0)	2 (9.5)	.49	29 (19.3)	4 (40.0)	25 (17.9)	.10	
Survival	37 (100.0)	17 (100.0)	21 (100.0)	>.99	133 (88.7)	9 (90.0)	124 (88.6)	.89	
Type of feeding at the time of discharge				<.001				<.001	
Cow's milk formula	8 (22.8)	0 (0.0)	8 (42.1)		79 (60.8)	0 (0.0)	79 (64.8)		
Extensively hydrolyzed hypoallergenic formula	9 (25.0)	6 (35.3)	3 (15.8)		7 (5.4)	3 (30.0)	4 (3.3)		
Elemental formula	10 (27.8)	10 (58.8)	0 (0.0)		8 (6.2)	6 (60.0)	2 (1.6)		
Breast milk feeding	7 (19.4)	0 (0.0)	7 (36.8)		33 (25.4)	0 (0.0)	32 (26.2)		
Maternal dietary elimination	2 (5.6)	1 (5.9)	1 (5.3)		3 (2.3)	1 (10.0)	3 (2.5)		

Abbreviations: ANC, absolute neutrophil count; FPIES, food protein-induced enterocolitis syndrome; hsCRP, highly sensitive C-reactive protein; NEC, necrotizing enterocolitis; NPO, nil per os; WBC, white blood cell count.  
NOTE. Data are expressed as number (%) for numeric parameters and median (range) for continuous parameters. Continuous variables were analyzed using the Mann-Whitney test, and categorical variables were analyzed using Fisher's exact test. Statistical significance was set at  $P < .05$ . The bold emphasis is used for statistically significant parameters.

# What I hope you take home

- Pneumatosis intestinalis in a premature  $\neq$  NEC
- Consider FPIES in the differential diagnosis of NEC
- Dare to wait



# **A gut feeling... which isn't as clear as a Bell**

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## **Questions?**

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