Surgical Treatment of Necrotizing Enterocolitis
Overview

• Necrotizing Enterocolitis

• Indications for operative therapy

• Evidence based review of laparotomy and peritoneal drainage
History

- 1888 Paltauf
  - 5 patients who died of overwhelming peritonitis

- 1953 Schmid and Quaiser
  - Necrotizing Enterocolitis

- 1964 Berdon
  - Case series of 21 patients with NEC

- 1975 Santulli
  - Disease had 3 components
    - Injury to the intestinal mucosa
    - Presence of bacteria
    - Availability of metabolic substrate
Epidemiology

• 1-3 in 1000 live births
• 10-66 in 1000 live births < 1500 g
• Mortality 10-50%
  – Stage 1: 10-30%
  – Stage 2: 8-32%
  – Stage 3: 54-87%
• 90% in premature infants
• 90% babies < 2000 grams
Risk Factors

- Age
- Maturity
- Feedings
- Hyperosmolar formulas and meds
- Medicines
- Cocaine
Age

• Average age of onset 14 days
• Term infants present at earlier age
  – < 7 days of life
  – Increased mortality and complications
• Earlier onset = worse prognosis
Maturity

• Average gestational age 31 weeks
• Younger gestational age and birth weight = worse prognosis
• Preterm GI tract
  – Decreased gastric acid secretion
  – Lower levels of protective mucus
  – Increased mucosal permeability
  – Absence of coordinated peristalsis until 34-35 weeks
Feedings

- 90% occurs after first feeding
- Reduction in incidence when slow feeding protocols instituted
  - < 20 kcal/kg/day
- Randomized controlled trial failed to find a difference in incidence
  - Slow versus fast progression
  - Early versus delayed
  - Continuous versus bolus
Trophic Feeds

- Randomized controlled trial VLBW
- Minimal volume feeding (20 cc/kg/day) x 10 days before advancing to full volume
- OR- Standard advancement
  - 20 cc/kg/day
- Decreased incidence of NEC (1.4 vs 10%)
- May trigger gut maturation

Schanler et al. Pediatrics 1999
Medications

- Theophylline
- Vitamin E
- Indomethacin
  - Retrospective studies which showed increased NEC after indomethacin use for PDA
  - RCTs which showed no difference with low dose indomethacin
Prevention

• Probiotics
• Breast milk
• Slow advancement
• Delayed feeds
Pathology - Macroscopic

- May involve single or multiple segments of bowel
  - Most common in terminal ileum > colon
- Involves both large and small intestine in 44%
- NEC totalis (pan-necrosis) – necrosis of at least 75% of the gut
  - 19% of surgical cases
Pathology - Microscopic

- Coagulation necrosis of superficial mucosa (89%)
- Edema and hemorrhage of submucosa
- Transmural necrosis
- Epithelial regeneration, formation of granulation tissue and early fibrosis
  - Suppurative process
Diagnosis - Clinical

- Physiologic instability
  - Lethargy
  - Temperature Instability
  - Apnea and bradycardia
  - Hypoglycemia
  - Shock

GI symptoms
- Abdominal distension
- Blood per rectum
- Increased gastric residuals
- Emesis
- Diarrhea
Diagnosis - Clinical

• Physical Exam
  – Abdominal distension
  – Abdominal wall erythema
  – “Racing stripes”
  – Tenderness to palpation
Diagnosis - Laboratory

• Thrombocytopenia
• Metabolic acidosis
• C-reactive protein
• Leukopenia
• Positive blood cultures (30%)
• Fungal cultures - negative
Diagnosis - Imaging

• Plain film
  – Pneumatosis – 19-98%
  – Portal venous gas – 10-30%
    • Poor prognosis
    • Present in 61% of NEC totalis
  – Pneumoperitoneum – 12-30%
  – Intraperitoneal Fluid – 11%
  – Persistent dilated loops – 33%
Bell’s Staging

• I – Suspected
  – Any one or more historical factors producing perinatal stress
  – Systemic manifestation
  – Gastrointestinal manifestations

• Ib - above with blood per rectum
Bell’s Staging

• II – Definite
  – Any one or more historical factors
  – Any above signs or symptoms plus persistent occult or gross GI bleeding, marked abdominal distension
  – Radiographic evidence of
    • Intestinal distension with ileus
    • Small bowel separation (edema of bowel wall)
    • Persistent dilated loops of bowel
    • Pneumatosis intestinalis
    • Portal venous gas

• IIa - mildly ill
• IIb – moderately ill
Bell’s Staging

- III – Advanced
  - Any one or more historical factors
  - Above signs and symptoms plus
    - Deterioration of vital signs
    - Evidence of septic shock
    - Marked GI hemorrhage
  - Radiographic evidence of pneumoperitoneum
- IIIa – no perforation
- IIIb - perforation
Isolated Intestinal Perforation

- Pneumoperitoneum with absence of pneumatosis in premature infant
- Sudden onset of illness
- Not associated with metabolic derangements
- At exploration, single perforation in terminal ileum on anti-mesenteric border
- Remainder of bowel is normal
## TABLE 2. Comparison of Characteristics at Enrollment in Infants With Intraoperative Diagnosis of NEC Versus IP

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NEC*</th>
<th>IP*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)</td>
<td>762 (485–997)</td>
<td>735 (555–980)</td>
<td>0.326</td>
</tr>
<tr>
<td>Gestational age (wk)</td>
<td>25.9 (23–31)</td>
<td>25.1 (23–28)</td>
<td>0.067</td>
</tr>
<tr>
<td>Age at operation (days)</td>
<td>27.8 (1–68)</td>
<td>7.4 (2–23)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pneumatosis [n (%)]</td>
<td>34 (57.6)</td>
<td>1 (6.3)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Pneumoperitoneum [n (%)]</td>
<td>27 (45.8)</td>
<td>13 (81.3)</td>
<td>0.022</td>
</tr>
<tr>
<td>Gasless abdomen [n (%)]</td>
<td>2 (3.4)</td>
<td>3 (18.8)</td>
<td>0.0643</td>
</tr>
<tr>
<td>“Blue” abdomen [n (%)]</td>
<td>9 (15.5)</td>
<td>6 (37.5)</td>
<td>0.078</td>
</tr>
<tr>
<td>Portal vein air [n (%)]</td>
<td>14 (24.1)</td>
<td>0</td>
<td>0.031</td>
</tr>
<tr>
<td>Preoperative indomethacin use [n (%)]</td>
<td>37 (63.8)</td>
<td>8 (50.0)</td>
<td>0.390</td>
</tr>
<tr>
<td>Preoperative steroid use [n (%)]</td>
<td>6 (10.0)</td>
<td>3 (18.8)</td>
<td>0.387</td>
</tr>
</tbody>
</table>

*Diagnosis determined intraoperatively by surgeon observation.

†Bluish discoloration on physical examination at enrollment.

Medical Treatment

• Bowel decompression
• Antibiotics
  – Broad spectrum including anaerobic coverage
• Bowel rest
• Fluid resuscitation
• Supportive care
Indication for surgery

• Perforation
  – Pneumoperitoneum on radiograph
  – Aspiration of stool, bile or fluid with a positive gram stain

• Relative indications
  – Portal venous gas
  – Fixed intestinal loop
  – Erythema of the abdominal wall
  – Palpable abdominal mass
ONEIL 1975

- Descriptive study of 52 premature infants with NEC
- 32 treated medically, 20 underwent operation
  - 22/32 (69%) survived with medical management alone
  - 12/20 (60%) survived after surgery

- Indications for surgery
  - Pneumoperitoneum
  - Clinical deterioration
    - Sudden hyponatremia and progressive acidosis
    - Drop in platelets less than 100K
    - Presence of DIC

- Physical findings and Xrays not reliable
- Paracentesis with positive cultures helpful
• Retrospective study of 61 patients with necrotizing enterocolitis
• 10 criteria evaluated
  – Positive findings
    • (1) pneumoperitoneum
    • (2) paracentesis findings positive for gangrenous intestine
    • (3) erythema of the abdominal wall
    • (4) a fixed abdominal mass
    • (5) a persistently dilated loop of intestine on serial abdominal radiographs.
  – Negative findings
    • (1) clinical deterioration
    • (2) persistent abdominal tenderness
    • (3) profuse lower gastrointestinal hemorrhage
    • (4) the roentgenographic finding of gasless abdomen with ascites
    • (5) severe thrombocytopenia.
• Mortality 64% in patients operated on for pneumoperitoneum versus 30% for other findings
Kosloske 1994

- Review of 147 patients with necrotizing enterocolitis (94 gangrene)
- Best indicators (specificity & PPV near 100% & prevalence >10%).
  - pneumoperitoneum
  - positive paracentesis
  - portal venous gas.
- Good indicators (specificity & PPV near 100%, but prevalence <10%).
  - fixed intestinal loop noted on x-ray
  - erythema of the abdominal wall
  - palpable abdominal mass
- Fair indicators (91% specificity, 94% PPV, & prevalence of 20%)
  - "severe" pneumatosis intestinalis-graded by a radiographic system
- Poor indicators (predictive value)
  - clinical deterioration (78%)
  - platelet count below 100,000/mm³ (73%),
  - abdominal tenderness (58%)
  - severe gastrointestinal hemorrhage (50%)
  - gasless abdomen with ascites (0%)
- No test had a high sensitivity for intestinal gangrene.
### Absolute indication for OR - BMJ

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Laparotomy</th>
<th>Drain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure of medical therapy</td>
<td>71%</td>
<td>14%</td>
</tr>
<tr>
<td>Abdominal Mass</td>
<td>36%</td>
<td>1%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Raised inflammatory markers</td>
<td>3%</td>
<td>1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radiologic findings</th>
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<tbody>
<tr>
<td>Pneumoperitoneum</td>
<td>75%</td>
<td>53%</td>
</tr>
<tr>
<td>Fixed intestinal loop</td>
<td>39%</td>
<td>6%</td>
</tr>
<tr>
<td>Portal venous gas</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>Pneumatosis intestinalis</td>
<td>3%</td>
<td>0</td>
</tr>
</tbody>
</table>

Rees et al. Arch Dis Child Fetal Neonatal Ed 2005
Surgical Treatment

• Laparotomy
  – Small bowel resection with enterostomy
  – Resection with primary anastomosis
  – Proximal jejunostomy
  – “Clip and drop”
  – “Patch, drain and wait”

• Intraperitoneal Drain
  – Irrigation
  – May need more than one drain
Meta-analysis

- 5 prospective studies
  - 2 randomized
  - 3 observational
- 523 patients
  - 273 peritoneal drain
  - 250 laparotomy
- Increased mortality of 55% with drain
- PD patients were younger and smaller

NICHD Neonatal Research Network

- Prospective, cohort study of ELBW
- N = 156
  - Laparotomy = 76
  - Peritoneal Drain (PD) = 80
- Enrollment criteria
  - ELBW infants (<1000g)
  - Evidence of NEC or IP requiring surgical intervention
- Overall in-hospital mortality – 49%
- Median time to death – 8.5 days

Indications for Surgery

Surgery

- Pneumoperitoneum
- Clinical deterioration
- Portal venous air
- Infected Ascites
- Abd Wall erythema
- Other
• Death – OR 0.97 (0.43-2.20)
• Death or Neurodevelopmental impairment
  – OR 0.44 (0.16-1.2) favoring laparotomy
• 35% of PD patients survived without laparotomy
• 11% long term parenteral nutrition
• No difference in outcomes in IP patient
NEC Steps

- Prospective, randomized trial VLBW
- N = 117
  - Laparotomy = 62
  - PD = 55
  - closed early due to funding, planned to enroll 130
- Eligibility
  - Pneumoperitoneum
  - Stool, pus or bile aspiration
  - Clinical evidence of perforation
- Laparotomy – necrotic tissue resected with stomas placed proximal to active disease
- Drain – Irrigation until clear, then penrose drain placement
  - Discouraged salvage laparotomy

Moss et al. NEJM. 2006
NEC Steps

• Outcomes
  – Survival at 90 days - 35.5% vs 34.5%, p=0.92
  – TPN dependence – 40% vs 47.2%, p=0.53
  – Hospital LOS – 116 vs 126, p=0.43

• No association with mortality
  – Birth weight
  – Pneumatosis
  – Ventilator status
  – Platelet count
  – Sex
NEC Steps

• No advantage of either treatment in patients
  – With pneumatosis
  – GA < 25 wks
  – pH < 7.30

• 5 (9%) patients in PD underwent laparotomy for clinical deterioration

• 16 (29%) underwent delayed laparotomy for stricture, obstruction or not tolerating feeds
NET trial

- Prospective, randomized trial ELBW
- N = 69
  - Laparotomy = 34
  - Peritoneal Drain = 35
  - Needed 80 patients, closed at 42 months due to low accrual
- Eligibility
  - Pneumoperitoneum
- Exclusion criteria
  - Previous episode of NEC
  - Previous laparotomy or drain
  - Grade IV IVH

NET Protocol

- Laparotomy
  - Surgical procedure not specified by protocol

- Drain
  - Irrigation not recommended
  - Continued deterioration after 12 hours
    - Delayed laparotomy
NET trial

• Outcomes
  – 1 m survival - 76% vs 67%, p=0.4
  – 6 m survival – 64% vs 51%, p=0.3
  – LOS – 85 vs 74 days, p=0.95
  – No difference in respiratory or nutritional outcomes

• 74% PD required subsequent laparotomy
• 11% survived with drain alone
• Salvage laparotomy did not increase survival when compared to primary laparotomy
Salvage Laparotomy after PD

- Retrospective study
- 26 patients
  - 9 laparotomy
  - 17 peritoneal drain
    - Lower birth weight
    - More comorbid conditions
- 56% vs 41%, NS
- 4 patients in PD group underwent salvage laparotomy
  - All died

Conclusions

• The best evidence reveals no difference in mortality with drain versus laparotomy for necrotizing enterocolitis
• Salvage laparotomy may be appropriate after initial drain placement
• Differentiation of NEC from isolated intestinal perforation may affect outcomes