

Applying Results of Randomized Trials to a Clinical Practice

Shawn D. St. Peter, M.D.

Director
Center for Prospective
Clinical Trials

Children's Mercy Hospital
Kansas City, MO



VARIATION IN CARE

- ❑ Documented benefits in avoiding wide variation in care
 - ❑ Improved Efficiency
 - ❑ Cost-Effectiveness
 - ❑ Superior Outcomes

Example of Variation - Empyema

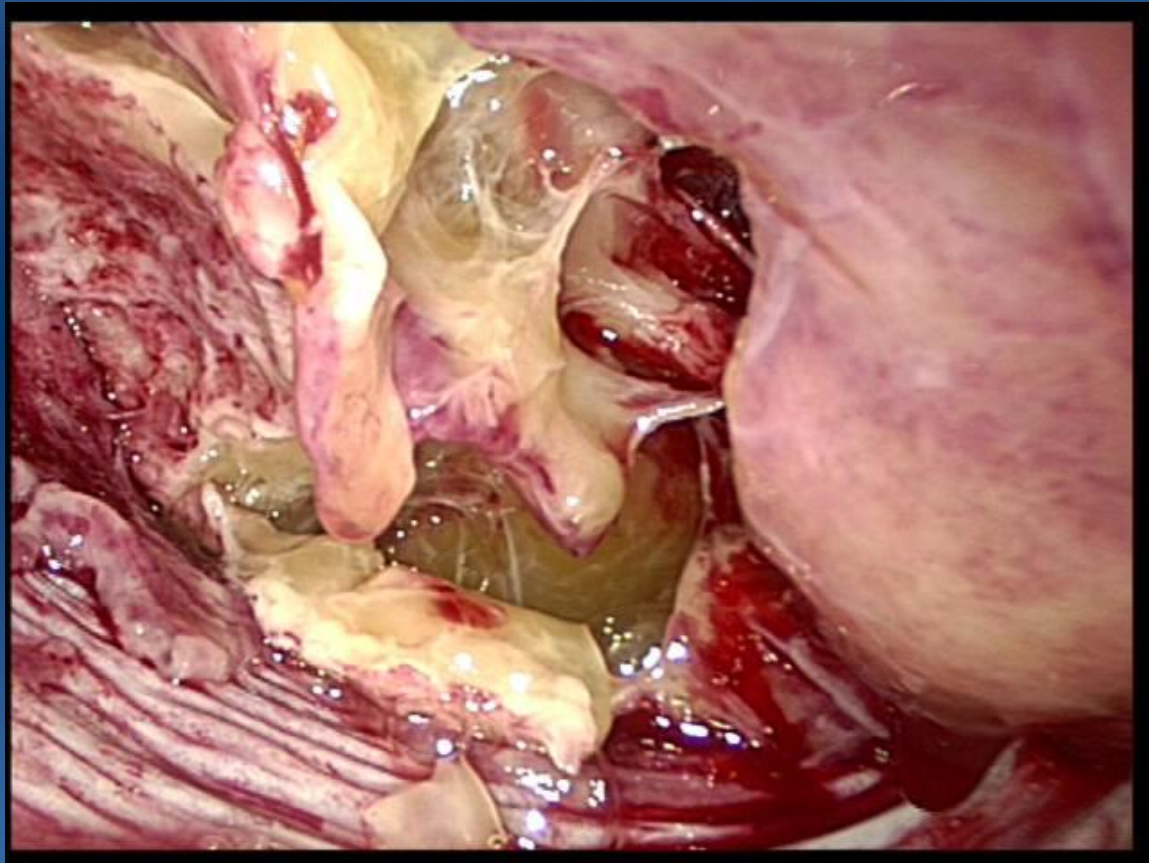
2001-2005

- ❑ Hospitalist A read a journal article that fibrinolysis is superior to chest tube alone
 - ❑ Refer to interventional radiology
- ❑ Hospitalist B read a journal article that primary VATS is superior to chest tube alone
 - ❑ Refer to surgery

CONFLICT WITHIN OUR HOSPITAL

VATS STUDY POPULATION

Inclusion Criteria



VATS STUDY POPULATION

Inclusion Criteria



VATS STUDY PROTOCOL

FIBRINOLYSIS

- ❑ 12 Fr tube placed by IR or surgery in procedure room
- ❑ 4mg tPA in 40ml NS given into tube on insertion and each day for 3 doses

VATS

- ❑ Thoracoscopic debridement with chest tube left behind on – 20 cm H₂O suction

VATS STUDY PROTOCOL

Primary Outcome Measure

Time to discharge after intervention

VATS STUDY RESULTS

Outcomes

	VATS	tPA	P Value
LOS (Days)	6.89	6.83	0.96
O2 tx (Days)	2.25	2.33	0.89
PO Fever (Days)	3.1	3.8	0.46
Analgesic doses	22.3	21.4	0.90
Proc Charges	\$11,660	\$7,575	<u>0.01</u>

16.6% failure rate for fibrinolysis

2007-Present → UNIFORM PROTOCOL

EMPHYEMA

(Loculations or $> 10,000$ WBC/ μ L)



12 Fr chest tube with 3 doses of tPA



Drainage decreased without clinical improvement



Ultrasound or CT



Persistent pleural space disease



No pleural space disease



VATS



Continue Antibiotics

Example of Variation

Perforated Appendicitis

2001 -2004

- ❑ Some surgeons utilized triples
- ❑ Some surgeons utilized rocephin/flagyl
 - ❑ Some surgeons didn't care
- ❑ Variation in definition of perforation, NG tubes, TPN use, discharge criteria, use of home antibiotics, wound management

RETROSPECTIVE REVIEW

Overview

- ❑ Retrospective - 250 patients w/perforated appendicitis
- ❑ Those treated with rocephin/flagyl were compared to those treated with triple antibiotic coverage
- ❑ Parameters included temperature curves for the first 5 post-operative days, abscess rate, length of hospitalization, length of intravenous antibiotic treatment and medication charges

RETROSPECTIVE RESULTS

Outcomes

	RO/FLAG	TRIPLES	P Value
WBC ($\times 10^3$)	9.8 +/- 0.5	11.6 +/- 0.4	0.10
LOS (Days)	6.8 +/- 0.4	7.9 +/- 0.2	<u>0.03</u>
IV Tx (Days)	7.2 +/- 0.5	8.6 +/- 0.4	<u>0.05</u>
Abscess (%)	8.8%	14.2%	0.37

RESULTS

Medication Charges

RO/FLAG

TRIPLES

\$ of Course \$546.01 +/- \$29.34 \$2494.06 +/- \$78.44

P Value < 0.0001

St. Peter et al. **A Simple and More Cost Effective Antibiotic Regimen for Perforated Appendicitis.** *Journal of Pediatric Surgery.* 2006;41(5):1020-4.

NOT SO FAST, MY FRIENDS!!



WHY A TRIAL?

Weaknesses

- ❑ Retrospective
- ❑ Uneven numbers between groups
- ❑ Recent experience vs historical experience creates bias
 - ❑ Far more laparoscopy in recent cohort (Rocephin/Flagyl)
 - ❑ (47% in Ro/Flag group vs 2% in Triples group)
 - ❑ Experience with laparoscopy improved
 - ❑ Pressures to discharge sooner in recent cohort independent of medication regimen

ABX STUDY POPULATION

Inclusion Criteria

- ❑ Under 18 years of age
- ❑ Perforated appendicitis at the time of appendectomy
 - ❑ Stool in the abdomen
 - ❑ Hole in the appendix

Exclusion Criteria

- ❑ Known allergy to one of the medications

MANAGEMENT

- ❑ All patients receive 5 days IV abx
- ❑ Diet begins after flatus
- ❑ WBC drawn on POD 5
- ❑ If elevated, draw again on POD 7, then if elevated, draw on POD 10 and obtain CT
- ❑ N1 WBC count and tolerating PO's w/o fever meets d/c criteria
- ❑ No abx on D/C

RESULTS

Outcomes

	RO/FLAG	TRIPLES	P Value
WBC ($\times 10^3$)	9.4 +/- 3.9	9.9 +/- 4.4	0.56
LOS (Days)	6.27 +/- 2.5	6.20 +/- 3.2	0.85
IV Tx (Days)	6.0 +/- 1.5	6.2 +/- 1.1	0.48
Abscess (%)	20.4%	16.3%	0.79

RESULTS

Medication Charges

	RO/FLAG	TRIPLES	P Value
Total Meds	\$3370	\$3817	0.20
IV Abx	\$1412	\$1940	<u><0.001</u>
% of Med Charges	4.5%	6.1%	<u><0.001</u>

ABX COURSE STUDY

Inclusion Criteria

- ❑ Under 18 years of age
- ❑ Perforated appendicitis at the time of appendectomy
 - ❑ Stool in the abdomen
 - ❑ Hole in the appendix

Exclusion Criteria

- ❑ Severe concomitant process

IV GROUP

- ❑ Receive 5 days IV rocephin/flagyl
- ❑ WBC drawn on POD 5
- ❑ If elevated, draw again on POD 7, then if elevated, draw on POD 10 and obtain CT
- ❑ N1 WBC count and tolerating PO's w/o fever meets d/c criteria
- ❑ No abx on D/C

IV/PO GROUP

- ❑ Receive scheduled IV rocephin/flagyl
- ❑ Diet begins after flatus
- ❑ When tolerating diet, go home to complete 7 day course with oral augmentin

RESULTS

Outcomes

	5 Days IV	IV/PO	P Value
Reg diet (hrs)	68+/-35	61+/-32	0.36
LOS (days)	6.1+/-2.0	4.8 +/- 2.6	0.01
Total visits	3.1+/-1.4	3.1+/-1.2	1.0
Abscess (%)	19%	20%	1.0

58% Stayed 5 Days

Definition of Perforation

PERFORATED

	<u>No Definition</u> (n=131)	<u>Definition</u> (n=161)
Abscess Rate	14.0%	18%
LOS (days)	9.4 +/- 4.2	7.4 +/- 8.8

NON-PERFORATED

	<u>No Definition</u> (n=292)	<u>Definition</u> (n=388)
Abscess Rate	1.7%	0.8%
LOS (days)	1.9 +/- 1.3	1.5 +/- 1.5

IRRIGATION FOR PERFORATION (N=220)

Irrigation Group

- ❑ Irrigate with NS from suction/irrigator
- ❑ Must irrigate with at least 500 ml

No Irrigation Group

- ❑ No bag on the suction/irrigator
- ❑ Suction only

All patients managed with the IV/PO antibiotic course

Perforated Appendicitis

2011- Where are we after 3 Trials?

Patient Benefits

- ❑ No NG tubes
- ❑ No TPN ---No early PICC lines
- ❑ Opportunity for early d/c
- ❑ No diphenhydramine or ranitidine
- ❑ No uncertainty about plan
- ❑ Know exact risk of adverse events

Perforated Appendicitis

2011- Where are we after 3 Trials?

Caregiver Benefits

- ❑ Know the exact course
- ❑ Can answer family/nurse questions with certainty
- ❑ No need to run down each individual staff for daily management

Perforated Appendicitis

2011- Where are we after 3 Trials?

Scientific Benefits

- ❑ Can use a defined population for a variety of investigations
- ❑ Currently have 270 patients enrolled in the past 2 trials with the same IV/PO abx protocol and no difference in abscess rate among the variables studied over those cases

OBSERVATION STUDY

Prior Cohort

- 270 patients with IV/PO antibiotic course

Experimental Group

- If ready to go home early, check a WBC if elevated they go on oral abx, if normal go home with no abx

NON-RANDOMIZED STUDIES

- Attenuated protocol for spleen/liver injury
- Management and outcomes for blunt renal injury

SPLEEN/LIVER PROTOCOL

- Grade 1-2
 - 1 night bedrest
- Grade 3-5
 - 2 night bedrest
- *Night is defined as patient in the bed on AM rounds*

SPLEEN/LIVER PROTOCOL

- ❑ 131 patients
- ❑ Mean age 10
- ❑ Spleen 55%, Liver 42%, Both 2%
- ❑ Bedrest applied to 110 pts (84%)
 - ❑ Mean grade 2.6, mean rest 1.6, LOS 2.2 days
- ❑ Bedrest limited stay in to 86 pts (66%)
 - ❑ Mean grade 2.6, mean rest 1.6, LOS 1.8 day

All management heterogeneity is removed

BLUNT RENAL TRAUMA

Management

- ❑ ALL Grades
 - ❑ May ambulate in AM
 - ❑ Hematuria has no influence on clinical decision making
 - ❑ Home when eating and pain controlled

BLUNT RENAL TRAUMA

Outcomes Measures

- ❑ Daily UA while in hospital until clear
- ❑ F/U at 2 weeks for BP & UA
 - ❑ UA every 2 weeks until clear
 - ❑ US in 4-6 wks for urinary extravasation on initial CT
- ❑ BP every 6 months to 3 years

INSTITUTIONAL BENEFITS OF IMPLEMENTING RCT's

- ❑ Protocols for common conditions homogenize care
 - ❑ Consistent care plans for fellows/residents/NP's
 - ❑ Improves communication and expectations with patients, floor nurses, clinic personnel
 - ❑ Decrease/eliminate intradepartmental disagreements about practice habits
- ❑ Multi-departmental studies
 - ❑ Improves working relationship
 - ❑ Fosters more collaboration

VARIATION IN CARE NOW REMOVED

Appendicitis

Pyloric Stenosis

Blunt Spleen/Liver Trauma

Blunt Renal Trauma

Fundoplication

Burns

HOW DO WE IMPLEMENT PROTOCOLS?

Try

- Agree to disagree
 - Recognize practice can be more evidence based and less art
 - Abandon ego that personal preference is only safe form of care
 - You have the power to monitor the effect
 - Simple protocols are more likely to produce consistent compliance
 - Ask very little of the staff surgeon