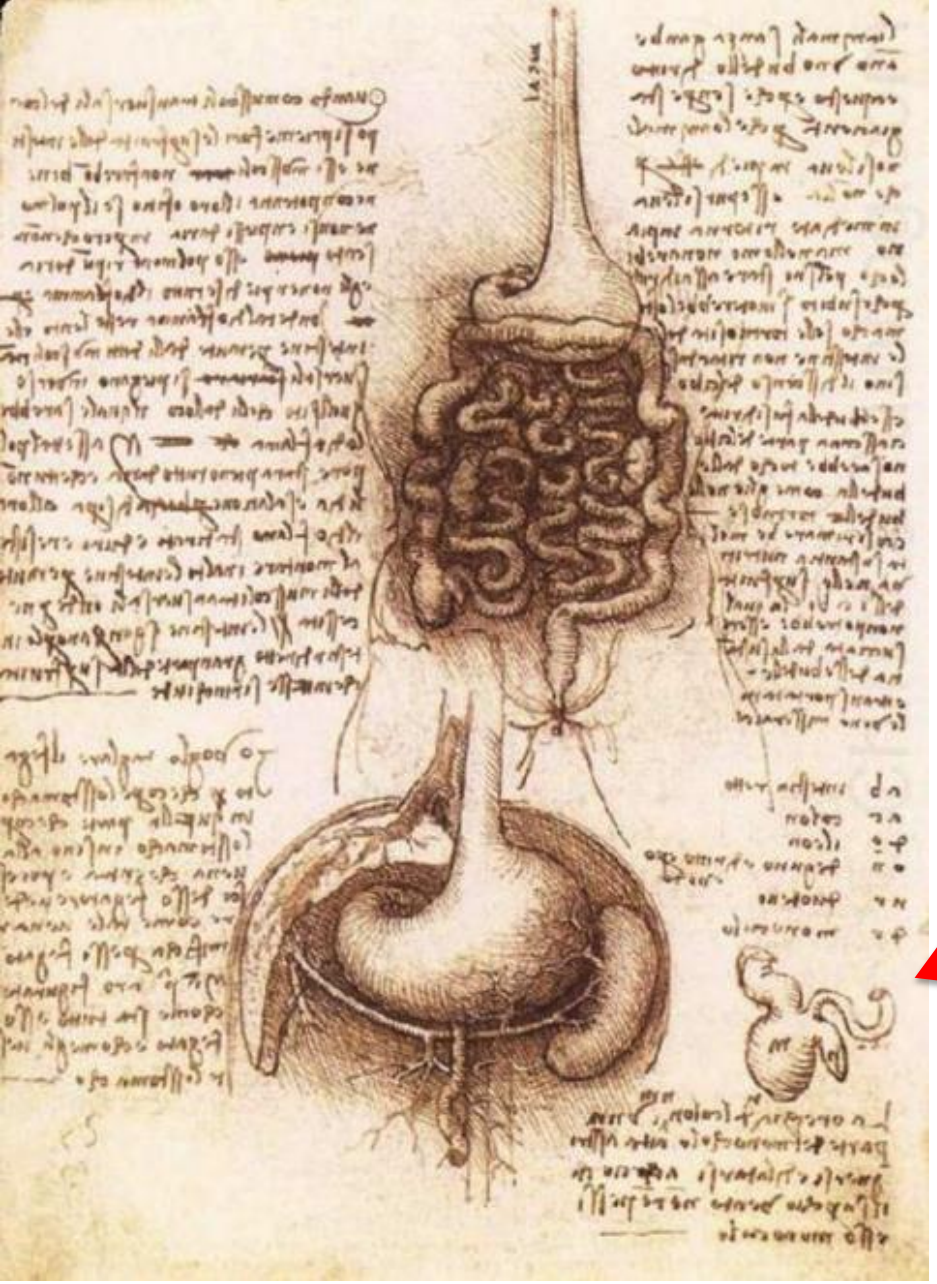
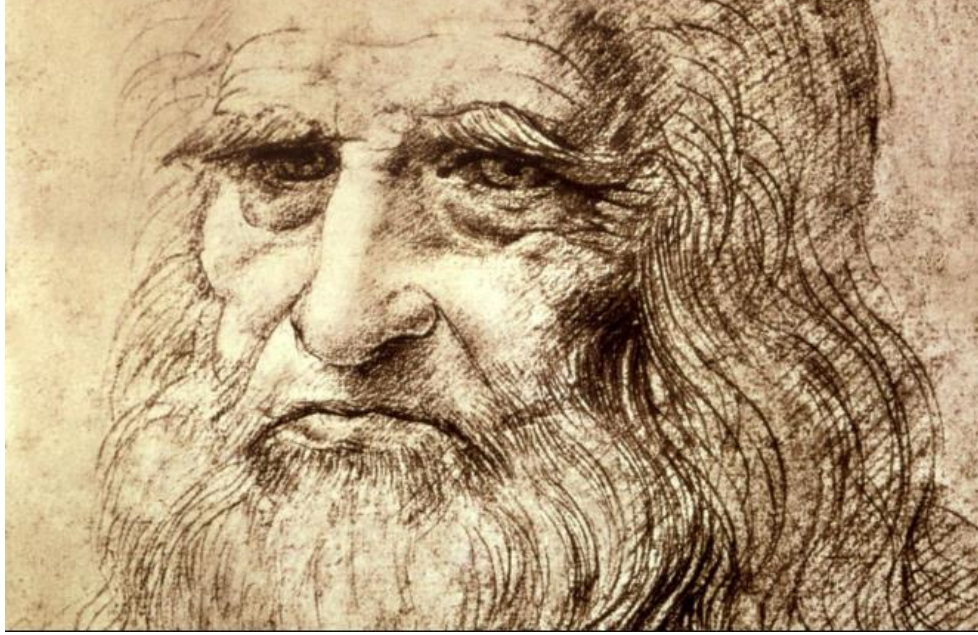
APPENDIX

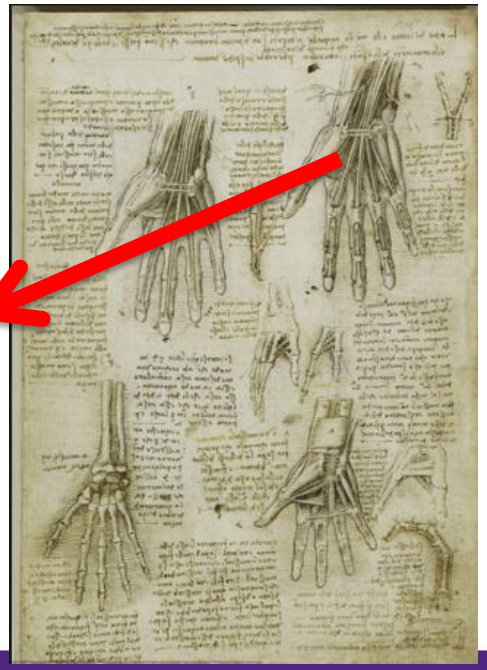
Sanjay VB Patel

February 17, 2016

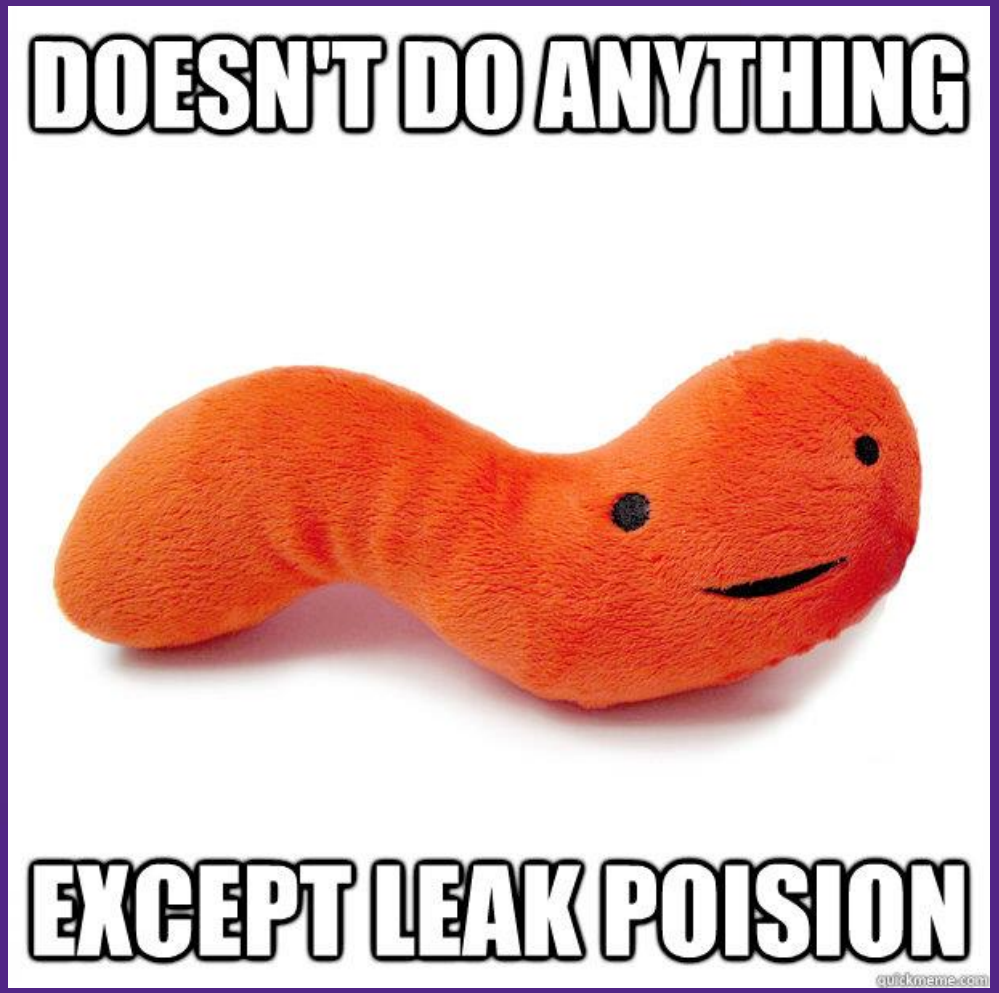
Dr. M. Brackstone

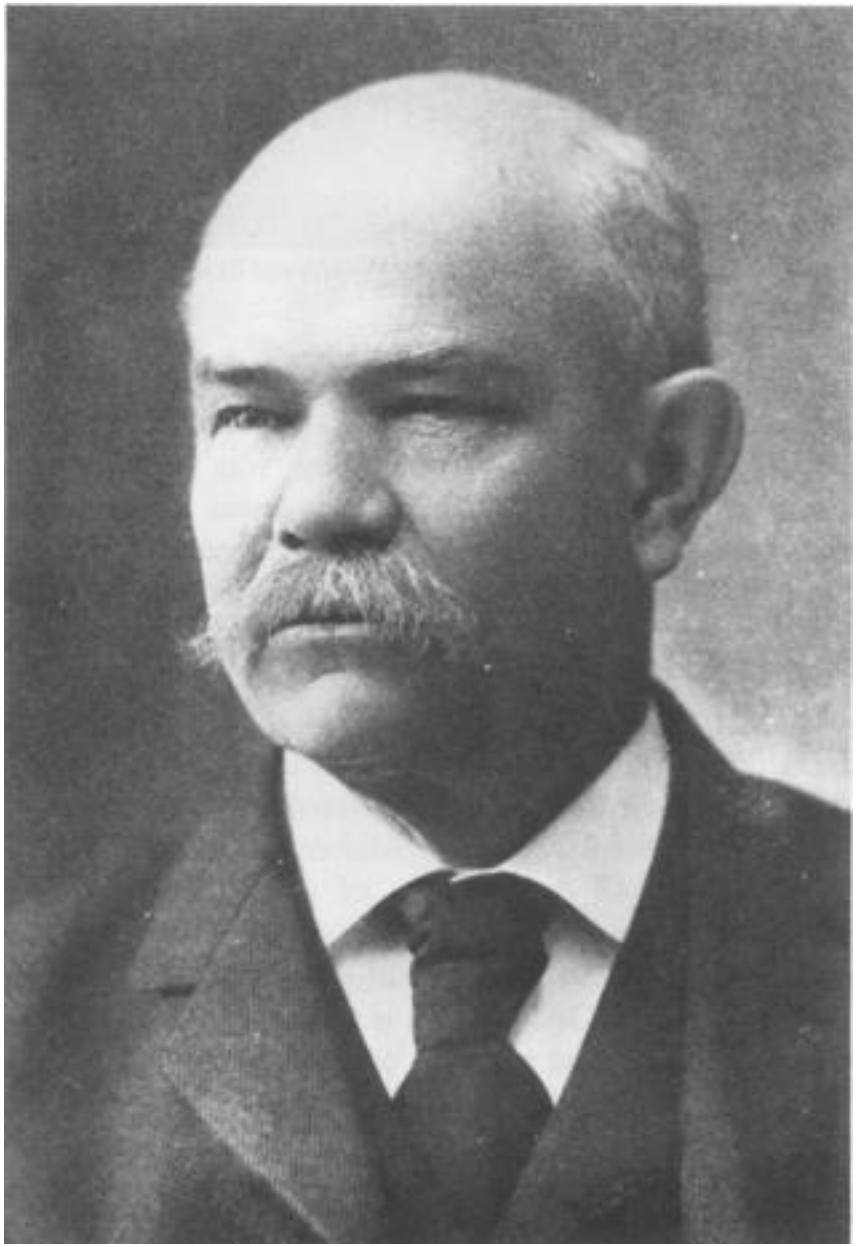






BENIGN APPENDIX





Reginald Herbert Fitz

Shattuck Professor of Pathological Anatomy Harvard
American
(1843 – 1913)

First to describe appendicitis
(The American Journal of the Medical Sciences 1885)

"Perforating Inflammation of the Vermiform Appendix; With Special Reference to Its Early Diagnosis and Treatment"

Clinical Presentation of Acute Appendicitis
Epidemiology

- Most common cause of emergency surgery worldwide
- Most commonly occurs in 10-30 years of age.
- More common in men (1.4 : 1)
- Life time incidence 6.7 – 8.6 %

Clinical Presentation of Acute Appendicitis
History and Physical Examination

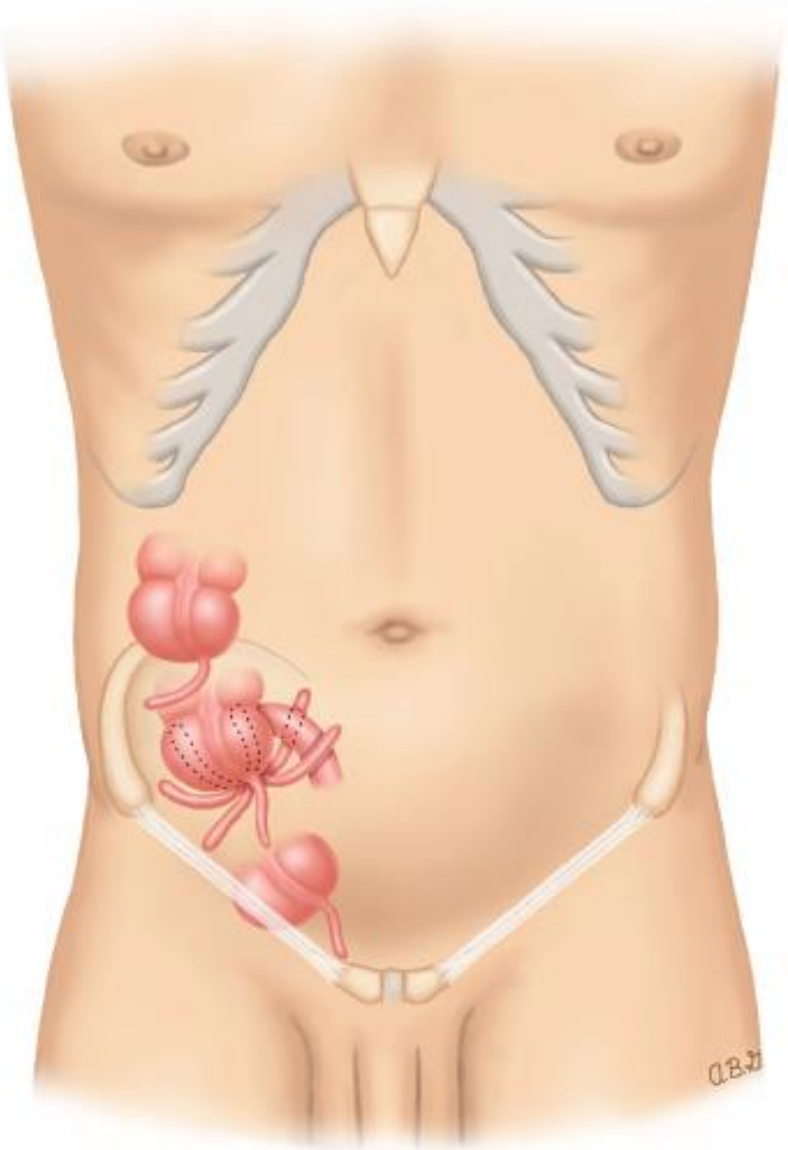
Classic constellation of symptoms

- **Abdominal pain, anorexia, nausea and vomiting**

Non-specific symptoms

- **Indigestion, malaise, tenesmus, diarrhea, dysuria, and atypical pain**

Migratory abdominal pain – occurs in 50-60% of patients



Behind the caecum (ascending retrocaecal): 65%

Inferior to the caecum (subcaecal): 31%

Behind the caecum (transverse retrocaecal): 2%

Anterior to the ileum (ascending paracaecal preileal): 1%

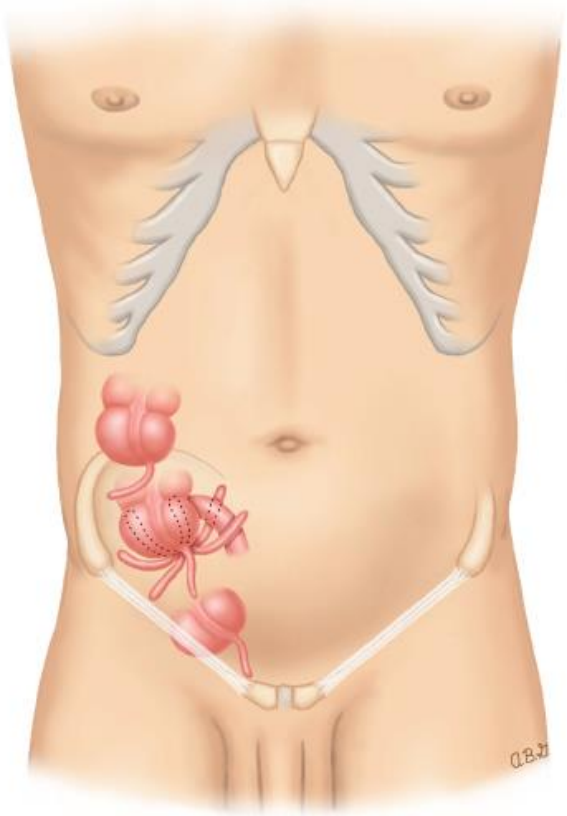
Posterior to the ileum (ascending paracaecal retroileal): 0.5%

Clinical Presentation of Acute Appendicitis
History and Physical Examination

Tachycardia
Fever

Abdominal pain RLQ
Focal Peritonitis
Rebound tenderness
RLQ mass

Pelvic examination
Rectal examination



Charles McBurney

American
(1845 – 1913)

McBurney's Point
(Ann Surg 1894)

Uptodate:
Maximal tenderness typically 1.5 - 2 inches from the anterior superior iliac spine, on a straight line drawn from the ASIS to the umbilicus.

"The incision in the skin is an oblique one about four inches long. It crosses a line drawn from the anterior iliac spine to the umbilicus nearly at right angles about one inch from the iliac spine, and is so situated that its upper third lies above that line" - McBurney

Niels Thorkild Rosving

Danish
(1862 – 1927)

Rosving's Sign
(Zentralblatt für Chirurgie1907)

Uptodate:
Pain in the right lower quadrant when palpated in the left lower quadrant.

"Smerter i højre nedre kvadrant med palpering af den venstre nederste kvadrant" - Rosving

Sir Vincent Zachary Cope

English
(1881 – 1974)

Cope's Psoas Sign
Cope's Obturator Sign

(Cope's Early Diagnosis of the Acute Abdomen, 1921)

1

Psoas Sign - Right lower quadrant pain with passive right hip extension

Obturator Sign - Right lower quadrant pain with passive flexion of the right hip and knee followed by internal rotation of the hip

Clinical Presentation of Acute Appendicitis
History and Physical Examination

Sign	Specificity	Sensitivity	Utility
McBurney's Point Tenderness	50 – 94%	75 – 86%	✔✔✔
Rosving's sign	22 – 68%	58 – 96%	✔✔
Cope's Psoas Sign	13 – 48%	79 – 97%	✔
Cope's Obturator Sign	8%	94%	✗

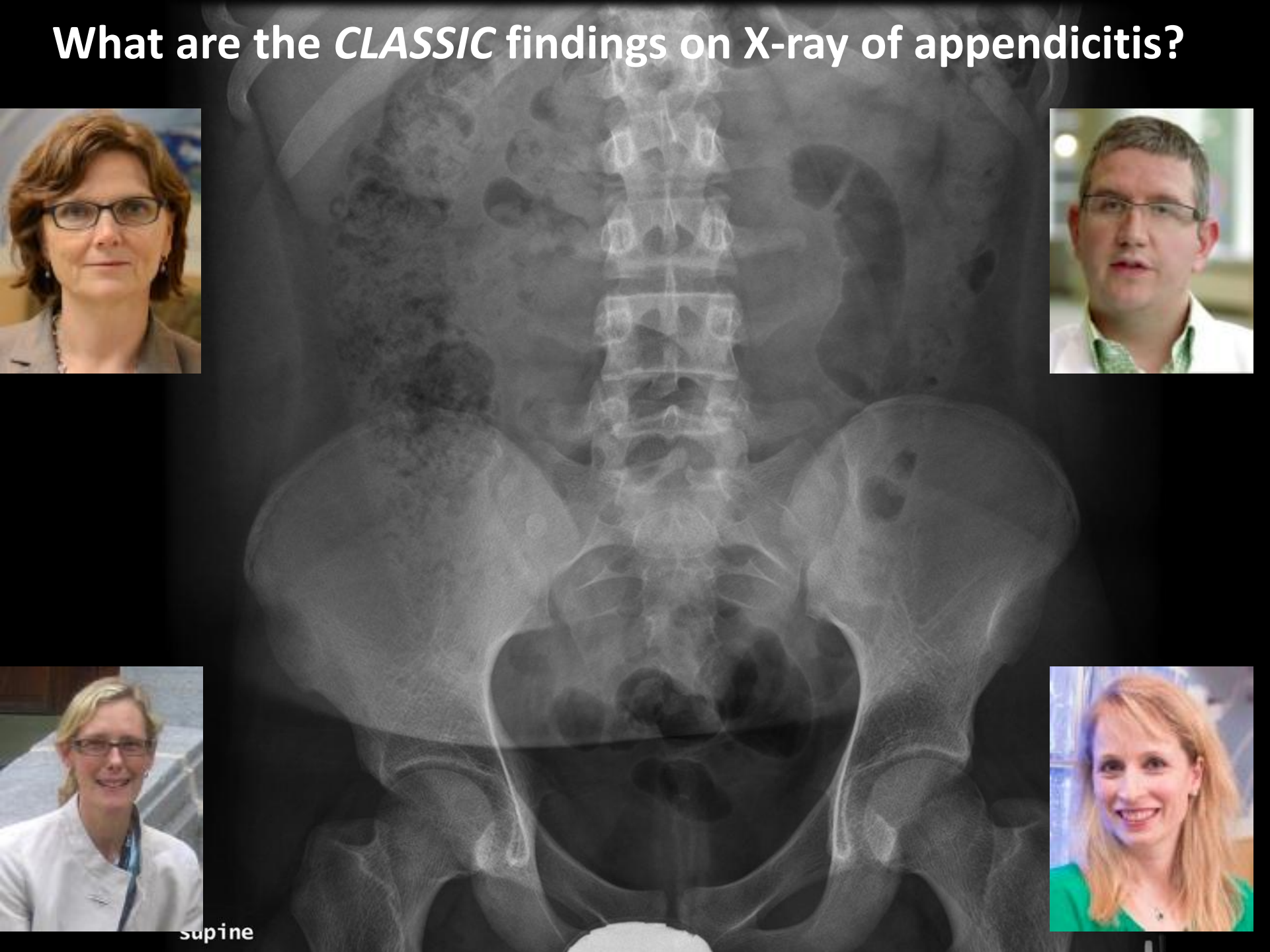
Clinical Presentation of Acute Appendicitis
Investigations

- CBC, electrolytes, CRE, bHCG
- Urine dip/culture

- WBC > 10,000 (sens 80%, spec 55%)
- Total Bilirubin >10 (sens 70%, spec 86%)

- Abdominal X-ray
- CT
- Ultrasound

What are the *CLASSIC* findings on X-ray of appendicitis?



Imaging in Acute Appendicitis
Investigations – X ray

1. Fecalith
2. Dilated loops of bowel with air fluid levels
3. Scoliosis of the spine
4. Obliteration of the right lower psoas shadow
5. Obliteration of the preperitoneal fat line
6. Paucity of gas in the RLQ
7. Small bowel obstruction
8. Air bubbles in the RLQ
9. Free air

Imaging in Acute Appendicitis
Investigations - Ultrasound

- Dilated appendix (>6 mm outer diameter)
- Non-compressible
- Appendicolith/Fecalith/Poopalith
- Prominent echogenic pericaecal fat
- Periappendiceal fluid collection
- Target appearance (axial section)

Imaging in Acute Appendicitis
Investigations – CT Scan

- Dilated appendix with distended lumen (>6 mm diameter)
- Thickened and enhancing wall
- Thickening of the cecal apex (up to 80%):
  - Cecal bar sign, arrowhead sign
- Periappendiceal inflammation
- Extraluminal fluid
- Inflammatory phlegmon
- Abscess formation
- Appendicolith

Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

ORIGINAL RESEARCH CONTRIBUTION

Performance of Ultrasound in the Diagnosis of Appendicitis in Children in a Multicenter Cohort

Manoj K. Mittal, MD, Peter S. Dayan, MD, MSc, Charles G. Macias, MD, MPH, Richard G. Bachur, MD, Jonathan Bennett, MD, Nanette C. Dudley, MD, Lalit Bajaj, MD, MPH, Kelly Sinclair, MD, Michelle D. Stevenson, MD, MS, Anupam B. Kharbanda, MD, MSc, for the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics*

Impression	Sensitivity	Specificity
Diagnostic of appendicitis	72.5%	97.0%
Appendicitis cannot be out ruled	79.9%	84.0%

THE AMERICAN SURGEON January 2013 Vol. 79

Accuracies of Diagnostic Methods for Acute Appendicitis

JONG SEOB PARK, M.D.,* JIN HO JEONG, M.D.,* JONG IN LEE, M.D.,† JONG HOON LEE, M.D.,*
JEA KUN PARK, M.D.,* HYOUN JONG MOON, M.D.*

*From the *Department of Surgery, Myongji Hospital, Kwandong University, Goyang, Korea; and the †Department of Surgery, Ajou University School of Medicine, Suwon, Korea*

Modality	N	Diagnostic	Sensitivity	Specificity	Negative Appendectomy
Ultrasound	1777	1101	99.1	91.7	5.2
CT	965	473	96.4	95.4	4.3
Physical Exam	303	218	99.0	76.1	12.2

Comparison of Imaging Strategies with Conditional Contrast-enhanced CT and Unenhanced MR Imaging in Patients Suspected of Having Appendicitis: A Multicenter Diagnostic Performance Study[1]

All patients had MRI
Ultrasound first

If US equivocal then CT was performed

N=230

Modality	Sensitivity	Specificity
Ultrasound only	77%	94%
CT	97%	91%
MRI	97%	83%

A Practical Score for the Early Diagnosis of Acute Appendicitis

We conducted a retrospective study of 305 patients hospitalized with abdominal pain suggestive of acute appendicitis. Signs, symptoms, and laboratory findings were analyzed for specificity, sensitivity, predictive value, and joint probability. The total joint probability, the sum of a true-positive and a true-negative result, was chosen as a diagnostic weight indicative of the accuracy of the test. Eight predictive factors were found to be useful in making the diagnosis of acute appendicitis. Their importance, according to their diagnostic weight, was determined as follows: localized tenderness in the right lower quadrant, leukocytosis, migration of pain, shift to the left, temperature elevation, nausea-vomiting, anorexia-acetone, and direct rebound pain. Based on this weight, we devised a practical diagnostic score that may help in interpreting the confusing picture of acute appendicitis. [Alvarado A: A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med May 1986;15:557-564.]

Alfredo Alvarado, MD
Plantation, Florida

From the Department of Surgery, Plantation General Hospital and Humana Hospital Bennett, Plantation, Florida.

Received for publication April 5, 1985. Revision received September 11, 1985. Accepted for publication November 11, 1985.

Address for reprints: Alfredo Alvarado, MD, 4101 NW 4th Street, Suite 407, Plantation, Florida 33317.

Clinical Scoring Systems - Alvarado

Criteria	Score
Migratory Abdominal Pain	2
Anorexia	1
Nausea AND Vomiting	1
Tenderness RLQ	1
Rebound tenderness	1
Elevated temp (>37.5)	1
Leukocytosis (>10,000)	2
Shift (Left shift/bands)	1

MANTRELS

Highly Suspicious (7-10)
-Operate
-*Surgical consultation
-Sensitivity 58-88%

Intermediate (5-6)
-Imaging with US or CT
-*4-6 obtain CT

Low (1-4)
-Discharge from ER
-* <3 No imaging indicated
- Sensitivity 98% for non-acute appendicitis

*McKay, R. Ann Emerg Med 2007

Ohle *et al. BMC Medicine* 2011, **9**:139
http://www.biomedcentral.com/1741-7015/9/139

BMC Medicine

RESEARCH ARTICLE Open Access

The Alvarado score for predicting acute appendicitis: a systematic review

Robert Ohle[†], Fran O'Reilly[†], Kirsty K O'Brien, Tom Fahey and Borislav D Dimitrov[*]

- A cut point of 5 performs well as a rule out CPR in all patient groups with suspected appendicitis
- This CPR calibrates well in men, over-predicts in women and is inconclusive in children.
- The Alvarado scoring system compares similarly to other CPR currently in use (Ottawa ankle)
- **Sensitivity (non-appendicitis) at a score of 5: 94-99%**

- There is not enough evidence to support a decision to go to surgery at a cut-point of 7.
- **Sensitivity 88%, Specificity 81%, negative appendectomy rate 13.3-16.7%**

Management of Acute Appendicitis

The goal of management is early diagnosis and prompt surgical intervention

- ***Resuscitate the patient – IV access, fluid administration, urinary catheter, correction of electrolytes and antibiotics.***
- ***Antibiotics:***
  - ***Within 60 minute window of cutting skin***
  - ***Non-complicated:***
    - ***Cefazolin (1-2 gm IV) + metronidazole (500mg IV)***

  - ***Complicated (perforated):***
  - ***Piperacillin-Tazobactam or Ceftriaxone + metronidazole***
- ***Within 24 – 72 hours of symptom onset***
- ***Operation Open or Laparoscopic***

Open Appendectomy

Claudius Amyand

French/British
(1680-1740)

First appendectomy
(Phil. Trans 1735)
-11yo boy with incarcerated hernia
-"Poppin" caused appendiceal perforation.

Amyand's Hernia
-Inguinal hernia with the appendix within the sac.

"This operation proved the most complicated and perplexing I ever met; with many unsuspected oddities and events concurring to make it as intricate as it proved laborious… 'Tis easy to conceive that this operation was a painful to the patient as laborious to me - it lasted nearly half an hour."

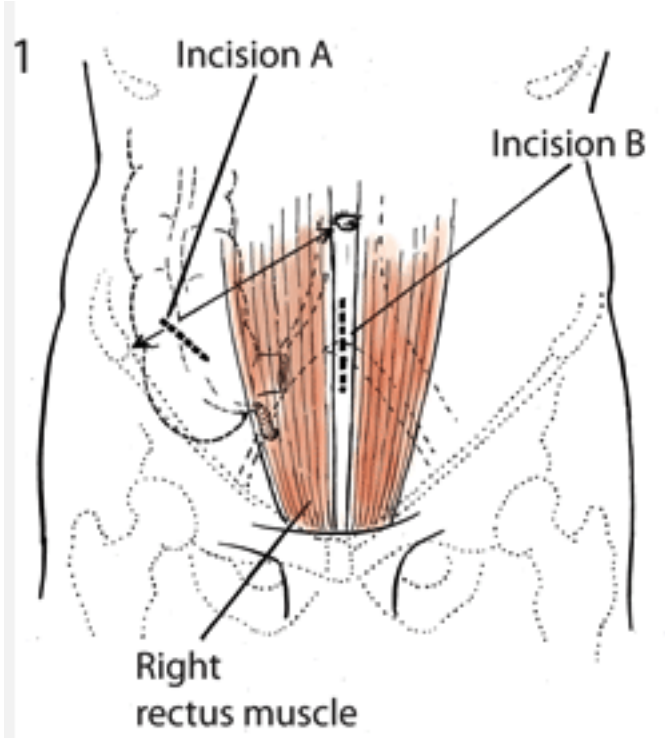
Ann Surg. 1894 Jul; 20(1): 38–43.

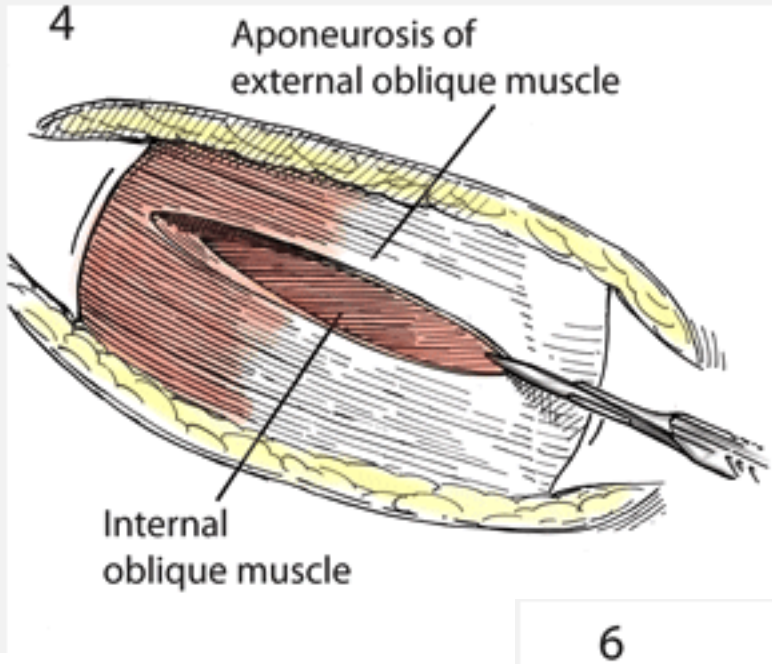
THE INCISION MADE IN THE ABDOMINAL WALL IN CASES OF APPENDICITIS, WITH A DESCRIPTION OF A NEW METHOD OF OPERATING.

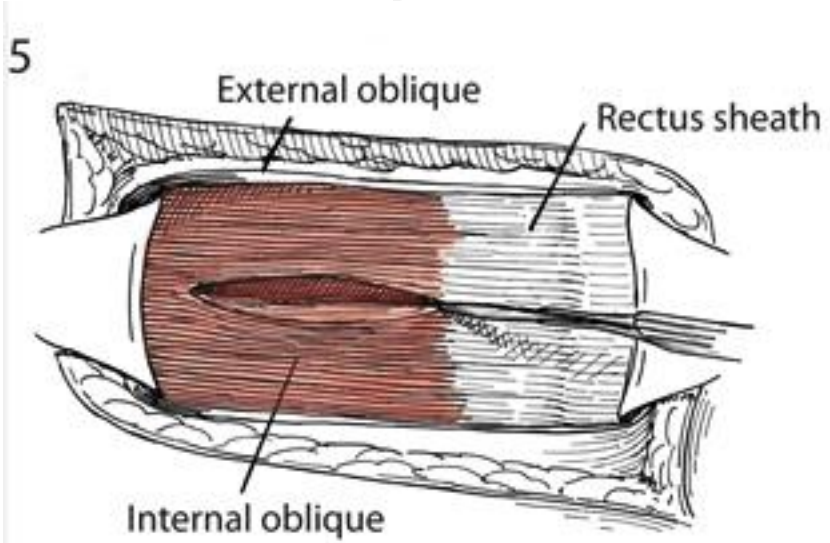
By CHARLES McBURNEY, M.D.,

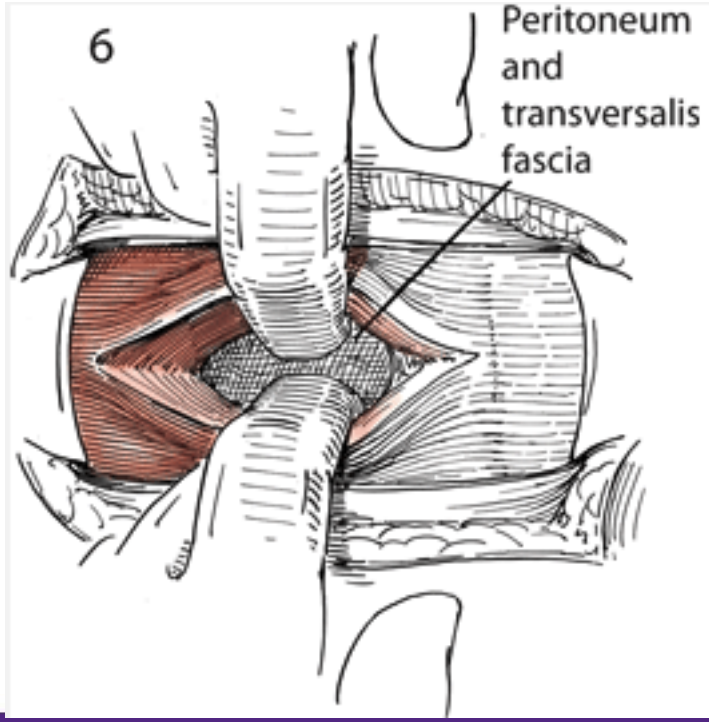
OF NEW YORK,

SURGEON TO THE ROOSEVELT HOSPITAL.

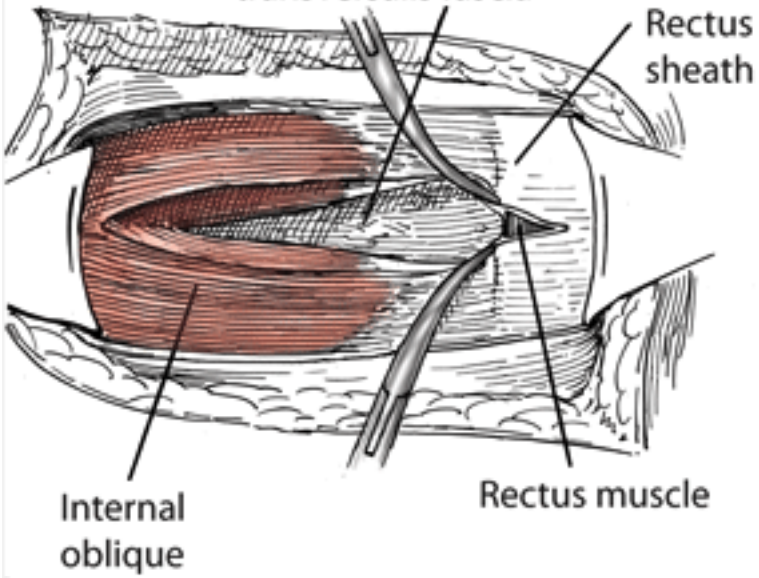

1
Incision A
Incision B
Right
rectus muscle


4
Aponeurosis of
external oblique muscle
Internal
oblique muscle

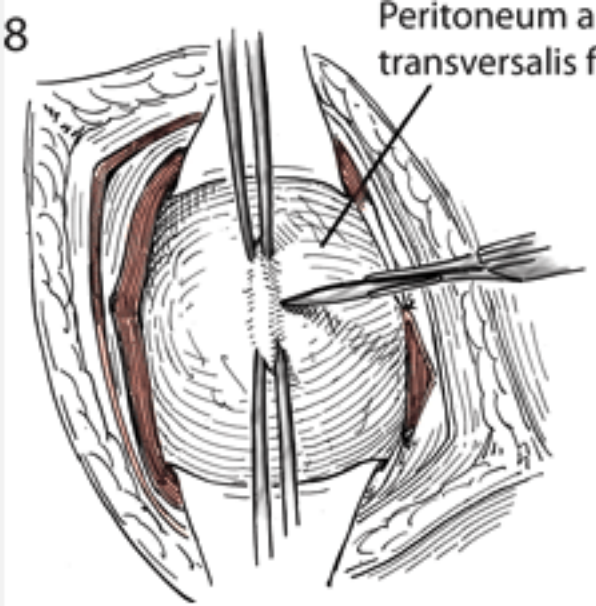

5
External oblique
Rectus sheath
Internal oblique


6
Peritoneum
and
transversalis
fascia

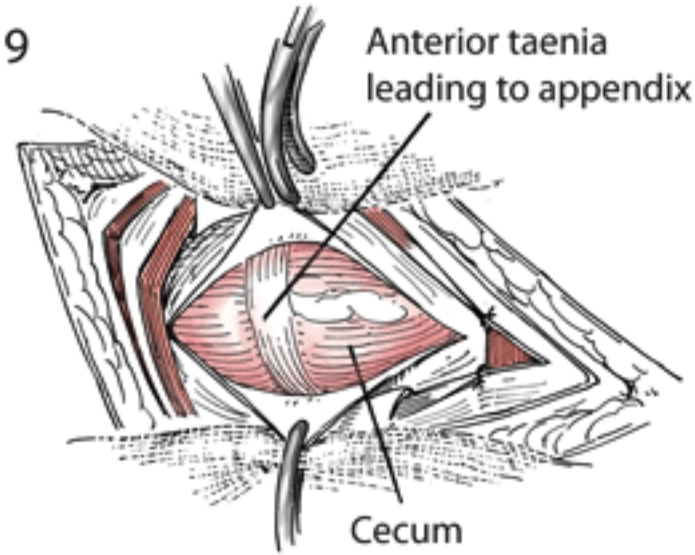
7


Peritoneum and transversalis fascia
Rectus sheath
Internal oblique
Rectus muscle

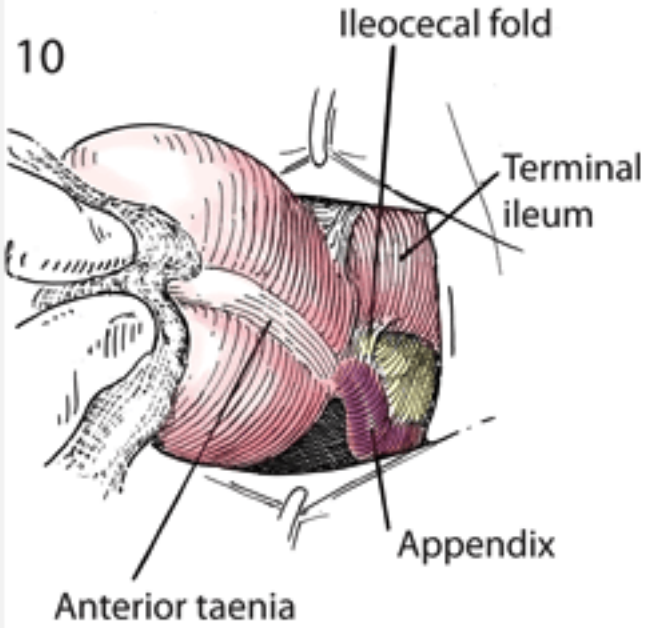
8

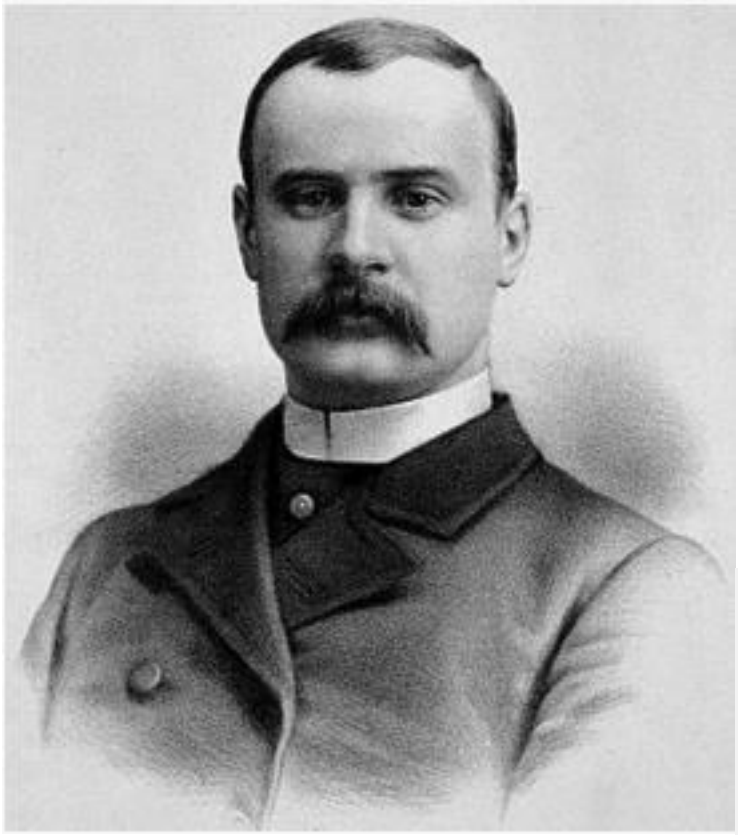

Peritoneum and transversalis fascia

9


Anterior taenia leading to appendix
Cecum

10


Ileocecal fold
Terminal ileum
Appendix
Anterior taenia



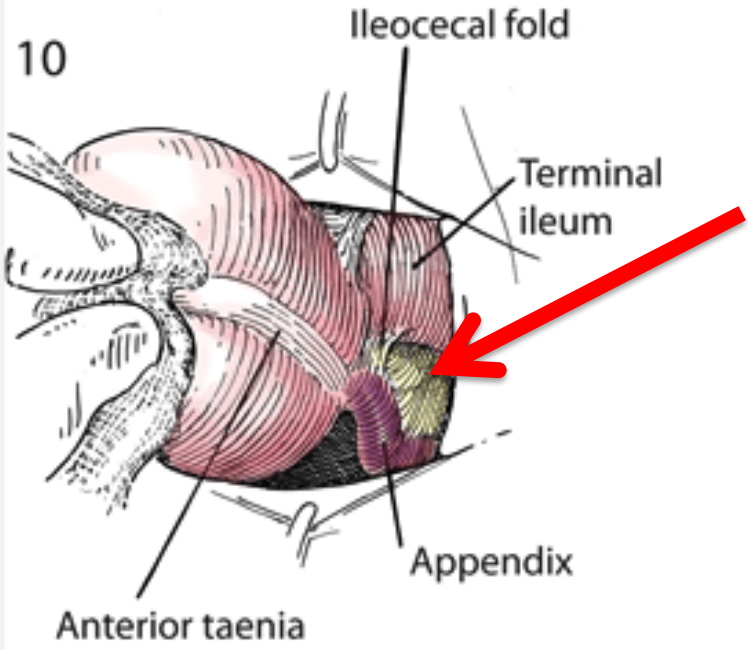
Sir Fredrick Treves

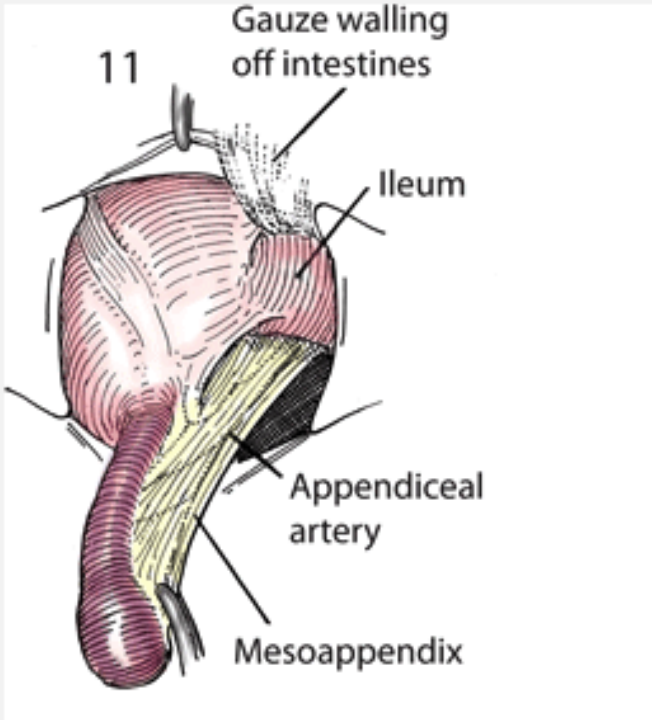
British

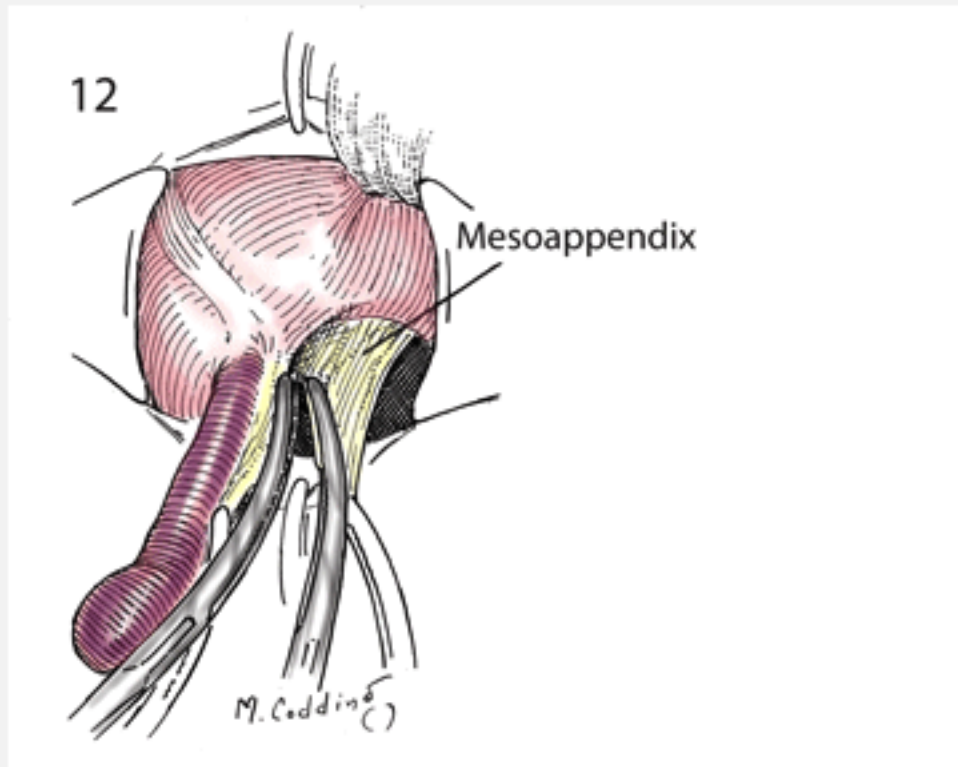
(1853-1923)

Bloodless Fold of Treves

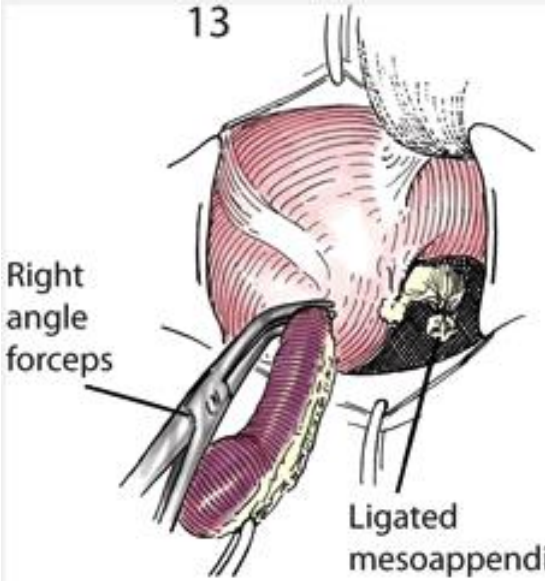
Friends with John Merrick
AKA Elephant man



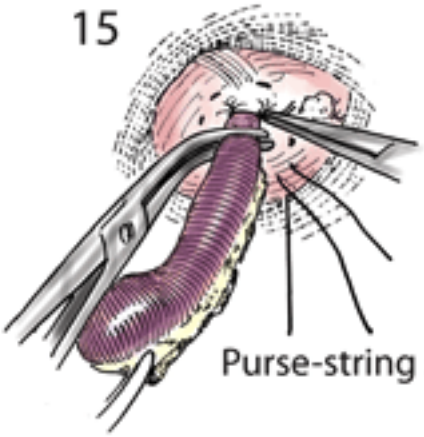

11
Gauze walling off intestines
Ileum
Appendiceal artery
Mesoappendix


12
Mesoappendix
M. Cadding ( )

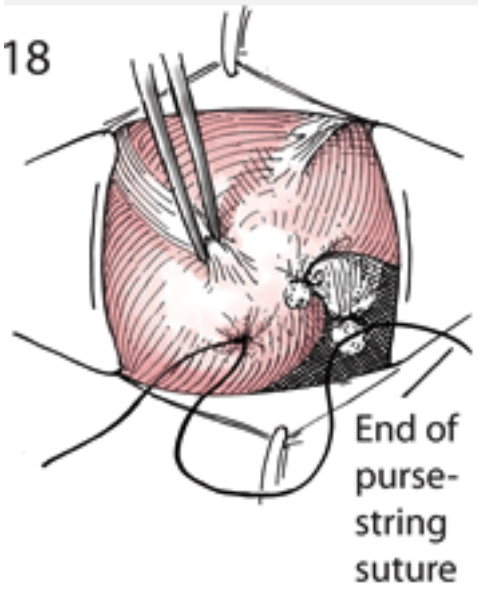
13


Right angle forceps
Ligated mesoappendix

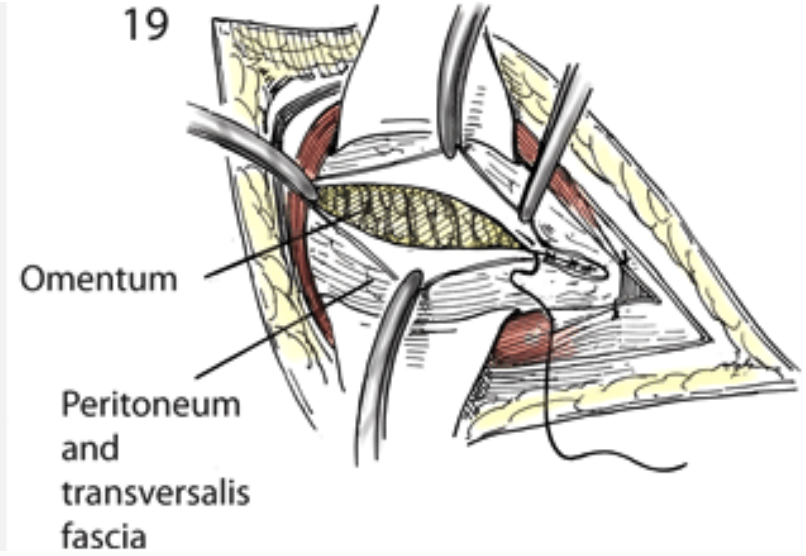
15


Purse-string suture

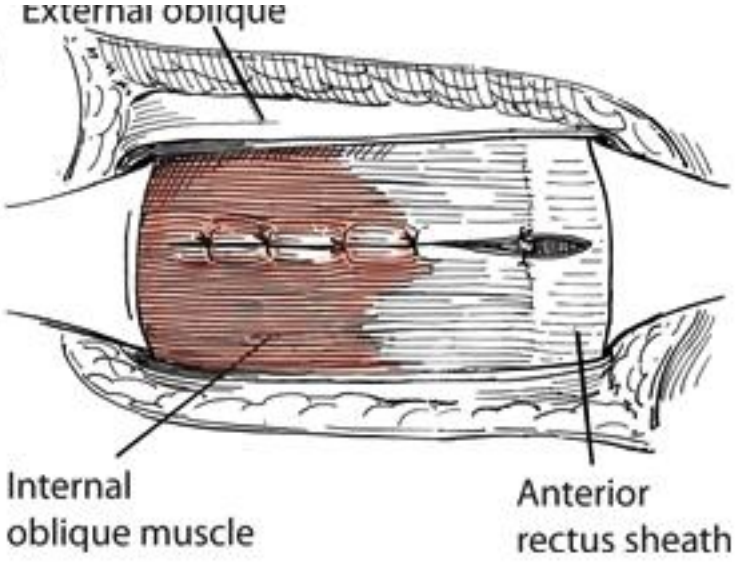
18

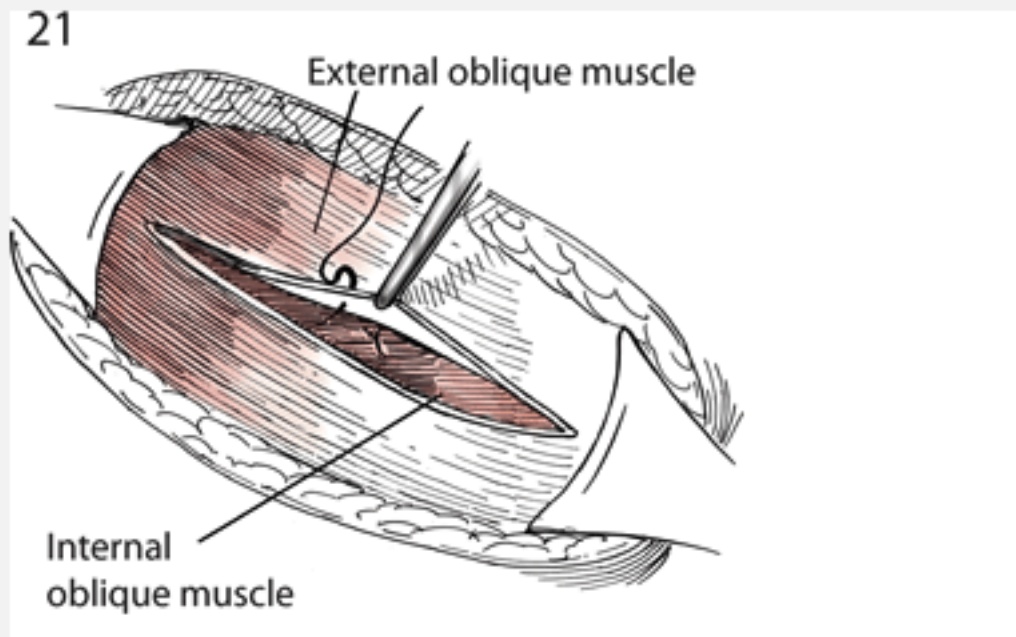

End of purse-string suture

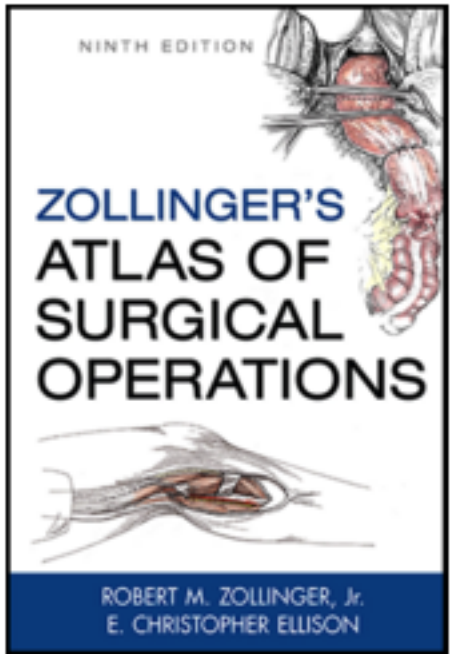
19


Omentum
Peritoneum and transversalis fascia

20


External oblique
Internal oblique muscle
Anterior rectus sheath


21
External oblique muscle
Internal
oblique muscle



Zollinger's Atlas of Surgical Operations, 9e

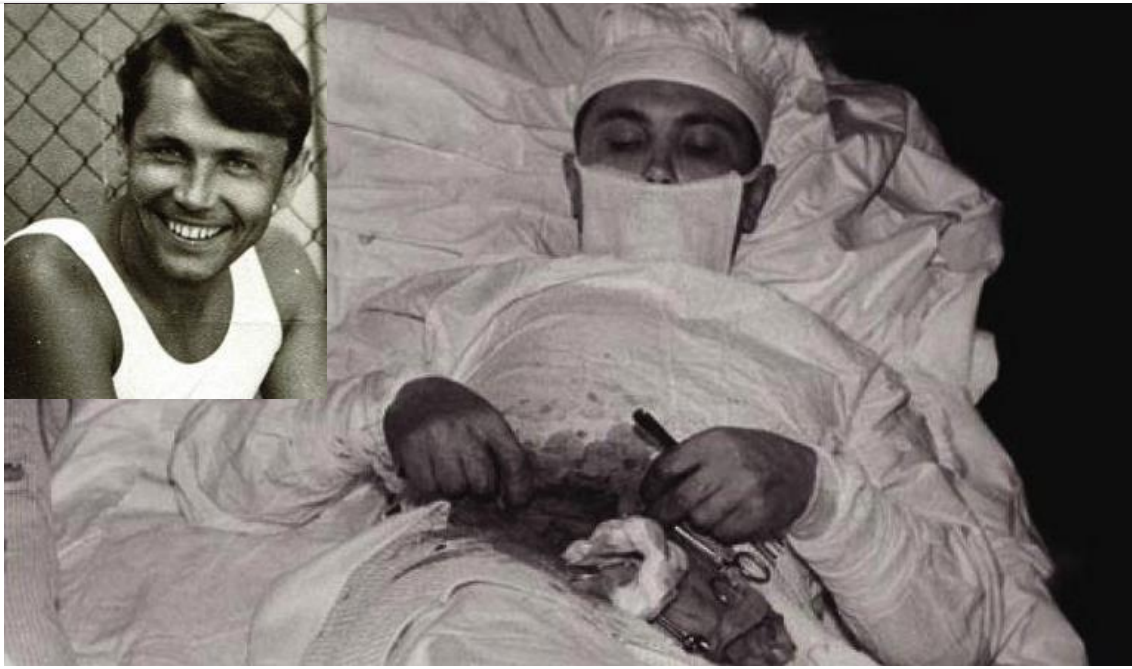
Robert M. Zollinger Jr, *Author*, E. Christopher Ellison, *Author*, Marita Bitans, *Illustrator*, Jennifer Smith, *Illustrator*

Auto-appendectomy in the Antarctic: case report

BMJ 2009 ; 339 doi: http://dx.doi.org/10.1136/bmj.b4965 (Published 15 December 2009)
Cite this as: *BMJ* 2009;339:b4965

Leonid Ivanovich Rogozov
Russian
(1934 - 2000)

First auto-appendectomy
(BMJ 2009)
-1960-61 Antarctic Expedition
-May 1961 2am
-27 year old first medical post



- OR time 1:45min

Laparoscopic Appendectomy

Kurt Semm

German
Obstetric and Gynecology
(1927 - 2003)

First laparoscopic appendectomy (1980)
-Attempts to publish were rejected for 5 years – "unethical"
-German Surgical Society tried to suspend his license.
-Muhe used Semm's instruments to perform first lap chole

"Both surgeons and gynecologists were angry with me, they were throwing stones at me. All my initial attempts to publish on laparoscopic appendectomy were refused, with the comment that such nonsense does not and will never belong to general surgery,"

SAGES - Appendectomy

Laparoscopic versus open surgery for suspected appendicitis

Stefan Sauerland[1], Thomas Jaschinski[2], Edmund AM Neugebauer[3]

[1]Department of Non-Drug Interventions, Institute for Quality and Efficiency in Health Care, Cologne, Germany. [2]Institute for Research in Operative Medicine, University of Witten/Herdecke, Cologne, Germany. [3]Institute for Research in Operative Medicine, Medical Faculty, University of Witten/Herdecke, Cologne-Merheim, Germany

Laparoscopic Versus Open:

Wound infections (OR 0.43, 0.34 – 0.54)
Less pain (p<0.05)
Return to normal activity 5 days (4 – 7days)
Intraabdominal infections (OR 1.77, 1.14 – 2.76)
Operative time 10 minutes longer
Return to work 2 (-2 to 4 days)
Actual cost ???

THE COCHRANE COLLABORATION®

Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial

Corinne Vons, Caroline Barry, Sophie Maitre*, Karine Pautrat, Mahaut Leconte, Bruno Costaglioli, Mehdi Karoui, Arnaud Alves, Bertrand Dousset, Patrice Valleur, Bruno Falissard, Dominique Franco*

Lancet 2011; 377: 1573–79

N= 239 (randomized)
119 in Appendicectomy group
120 in Antibiotic group

Primary endpoint: 30 – day abdominal peritonitis rate

- Antibiotic: Dx at appendicectomy or on CT-scan
- Appendicectomy: Persistent fevers, elevated wbc, elevated CRP, CT-scan
- Non-inferior 2% versus 9%

*18-34% recurrent appendicitis within 1-year in antibiotic group

thebmj

CCBYNC Open access
Research

Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials

BMJ 2012; 344 doi: http://dx.doi.org.proxy1.lib.uwo.ca/10.1136/bmj.e2156 (Published 05 April 2012) Cite this as: BMJ 2012;344:e2156

Krishna K Varadhan, research fellow[1], Keith R Neal, professor[12], Dileep N Lobo, professor[1]

[1] *Division of Gastrointestinal Surgery, Nottingham Digestive Diseases Centre NIHR Biomedical Research Unit, Nottingham University Hospitals, Queen's Medical Centre, Nottingham NG7 2UH, UK*
[2] *Department of Epidemiology and Public Health, Nottingham University Hospitals*

Included 4 RCT

Results:

- Peri-operative complications – RR 0.69 (RR 0.61) favoring antibiotic group
- Length of stay – no difference
- Treatment efficacy – Heterogenous
  - Successful treatment 44 - 85% in the antibiotic group

Conclusions:

- Antibiotics can be used safely (no increased complications).
- Perhaps acute uncomplicated appendicitis could be treated like uncomplicated diverticulitis with an early trial of antibiotic therapy

Annals of Surgery • Volume 253, Number 2, February 2011 www.annalsofsurgery.com | 309

ORIGINAL STUDY

Improving Outcomes After Laparoscopic Appendectomy

A Population-Based, 12-year Trend Analysis of 7446 Patients

Lukas Brügger, MD, Laura Rosella, PhD†, Daniel Candinas, MD*, and Ulrich Güller, MD, MHS**

Surgical outcomes are improving…

- Conversion from laparoscopic to open 1.2% (2.2%)
- Intraoperative complications 0.7 % (3.1%)
- Post op complications 1.9 % (6.1%)

Management of Acute Appendicitis

Conclusion:

- *Open and Laparoscopic approaches are equivocal, however certain populations may benefit from a laparoscopic approach.*

- **Diagnostic uncertainty – allows for assessment of other Intraabdominal viscera if appendicitis is not the true diagnosis**
- **Female patients – Shown to have higher negative appendectomy rates compared to men (~20%).**
- **Elderly patients – Shown to have lower morbidity in some studies**
- **Obese patients – Exposure can be difficult in the open approach**

Clinical Presentation of Acute Appendicitis

Management of Acute Appendicitis

- **The goal of management is early diagnosis and prompt surgical intervention.**
- ***But….***
- ***Patients presenting with >5 days of symptoms***

Or

- ***Mass in the RLQ with localizing pain***
  ie. walled off abscess

Clinical Presentation of Acute Appendicitis

Management of Missed Appendicitis

Operating on missed appendicitis

- ***Risk of bowel and enterocutaneous fistula***
- ***Right hemicolectomy or cecostomy***

Non-operative management:

- ***NPO***
- ***Antibiotics***
- ***Observation***
- ***Interventional radiology – drains***

- ***If patient does not respond then operative intervention is indicated. Patient should be aware of the risk of bowel resection.***

Clinical Presentation of Acute Appendicitis
Management of Missed Appendicitis

Interval Appendectomy

- ***Appendectomy performed electively 6-8 weeks after recovery.***
- ***Colonoscopy should be performed in patients >50 before surgery.***

- ***Equipoise concerning the evidence to support elective appendectomy versus watchful waiting.***

POSTER SESSION

Routine Interval Appendectomy Is Not Justified After Initial Nonoperative Treatment of Acute Appendicitis

Anna Kaminski, MD; In-Lu Amy Liu, MS; Harry Applebaum, MD; Steven L. Lee, MD; Philip I. Haigh, MD, MSc, FRCSC

Arch Surg. 2005;140:897-901

32398 patient were diagnosed at 12 medical centers
1012 were treated non-operatively
- 148 were not treated with interval appendectomy
- 864 were treated with interval appendectomy

Recurrence rates were 5% over a 4 year follow-up
Length of hospital stay was 6 days for interval appendectomy
Length of hospital stay was 4 days for recurrent appendicitis (P=0.006)

Nonsurgical Treatment of Appendiceal Abscess or Phlegmon

A Systematic Review and Meta-analysis

Roland E. Andersson, PhD, MD,† and Max G. Petzold, PhD‡*

Annals of Surgery • Volume 246, Number 5, November 2007

Results:

- Risk of "enclosed inflammation" ie missed appendicitis was 3.8% (n= 59,448)
- Failure rate of non-operative management 7.8%
- Risk of recurrent appendicitis in non-operative groups 7.2%
- Rate of malignant disease on follow-up 1.2% (n= 2775)
- Rate of significant non-malignant disease at follow-up 0.7% (i.e crohn's)

- *Morbidity was compared, showed a significantly greater morbidity with surgical invention compared to non-operative management with out interval appendectomy.*
  - *Significant heterogeneity in these outcomes*

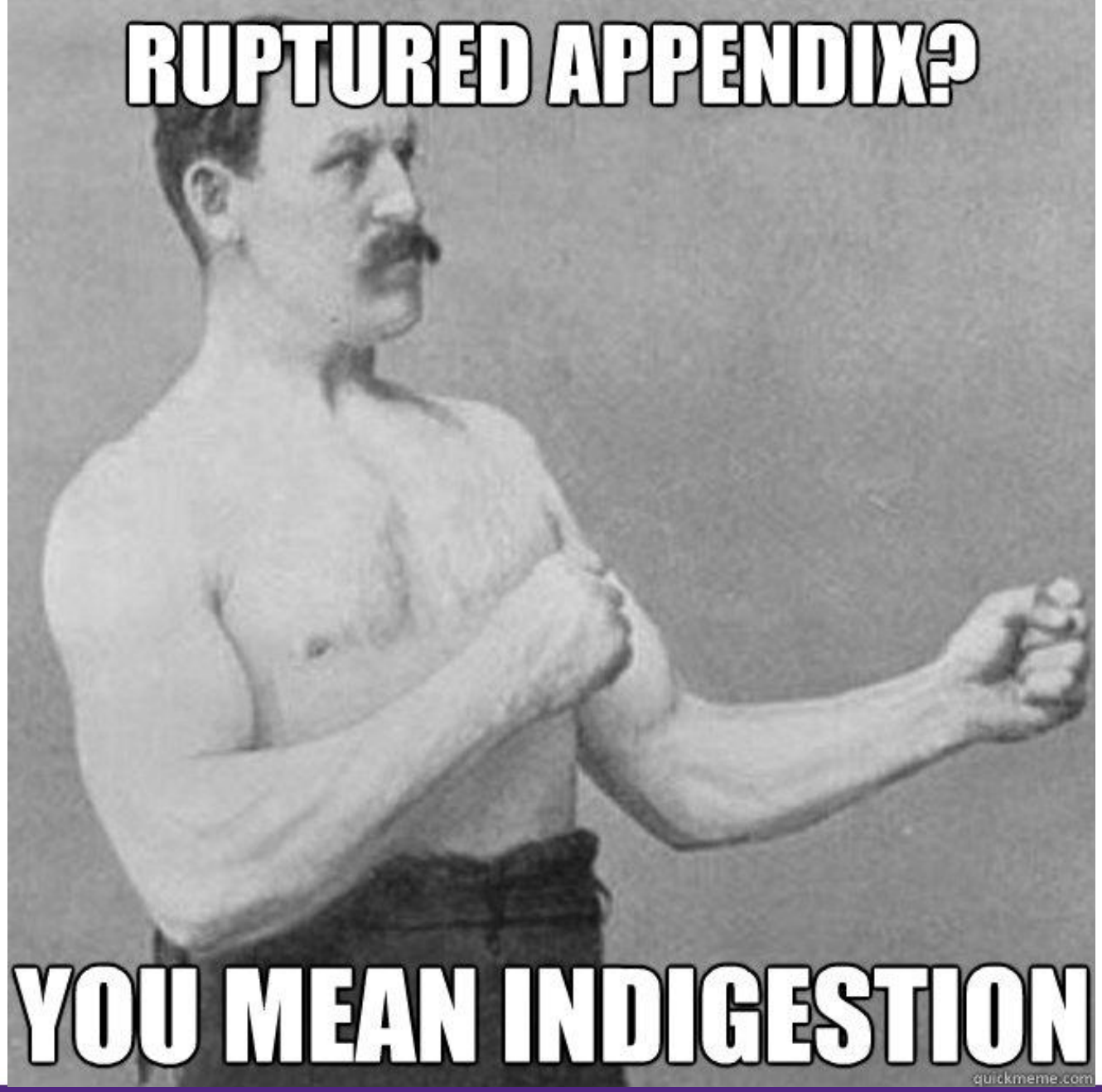
Harry Houdini (1874 – 1926)

Joselyn Gordon Whitehead - McGill

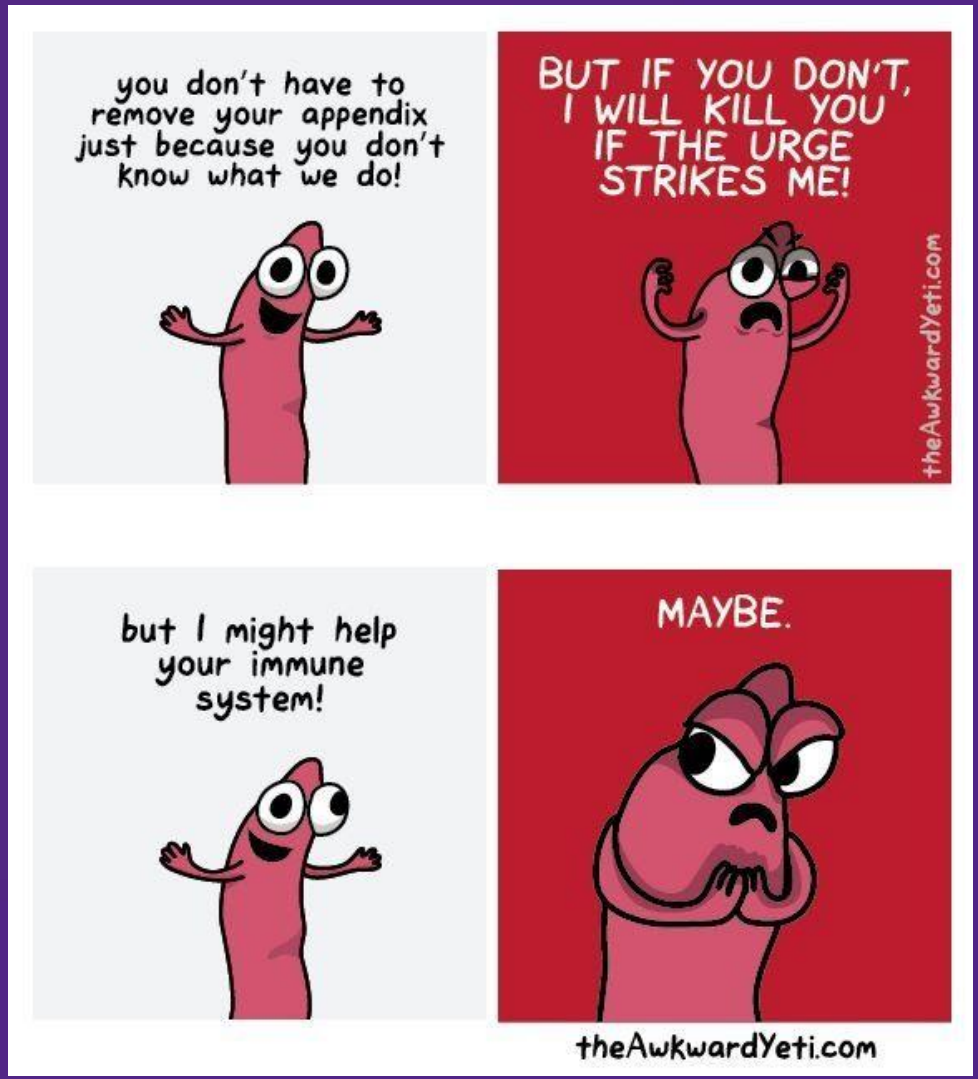
Jack Price's description

Author - Sir Arthur Conan Doyle

The first-year McGill student asked Houdini whether it was true that punches in the stomach did not hurt him. Houdini remarked rather unenthusiastically that his stomach could resist much, though he did not speak of it in superlative terms. Thereupon he gave Houdini some very hammer-like blows below the belt, first Securing Houdini's permission to strike him. Houdini was reclining at the time with his right side nearest Whitehead, and the said student was more or less bending over him. These blows fell on that part of the stomach to the right of the navel, and were struck on the side nearest to us, which was in fact Houdini's right side; I do not remember exactly how many blows were struck. I am certain, however, of at least four very hard and severe body blows, because at the end of the second or third blow I verbally protested against this Sudden onslaught on the part of this first-year student, using the words, "Hey there. You must be crazy, what are you doing?"


RUPTURED APPENDIX?
YOU MEAN INDIGESTION
quickmeme.com

NEOPLASTIC APPENDIX

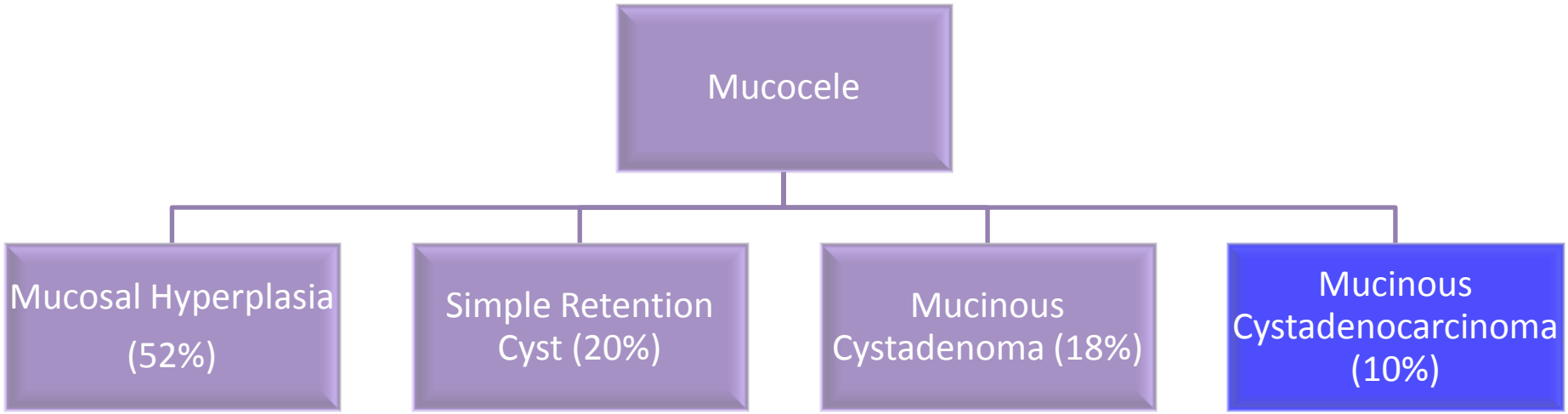


Classification of Appendiceal Neoplasms

- Appendiceal malignancy is rare
  ~1% of appendectomy specimens
- Mucocele (Benign)
- Adenocarcinomas
- Carcinoid Tumors

Appendiceal Neoplasms: Mucoceles

- Appendiceal mucocele is a lesion characterized by a distended mucus-filled appendix
- Rare – 0.3% of appendix specimens

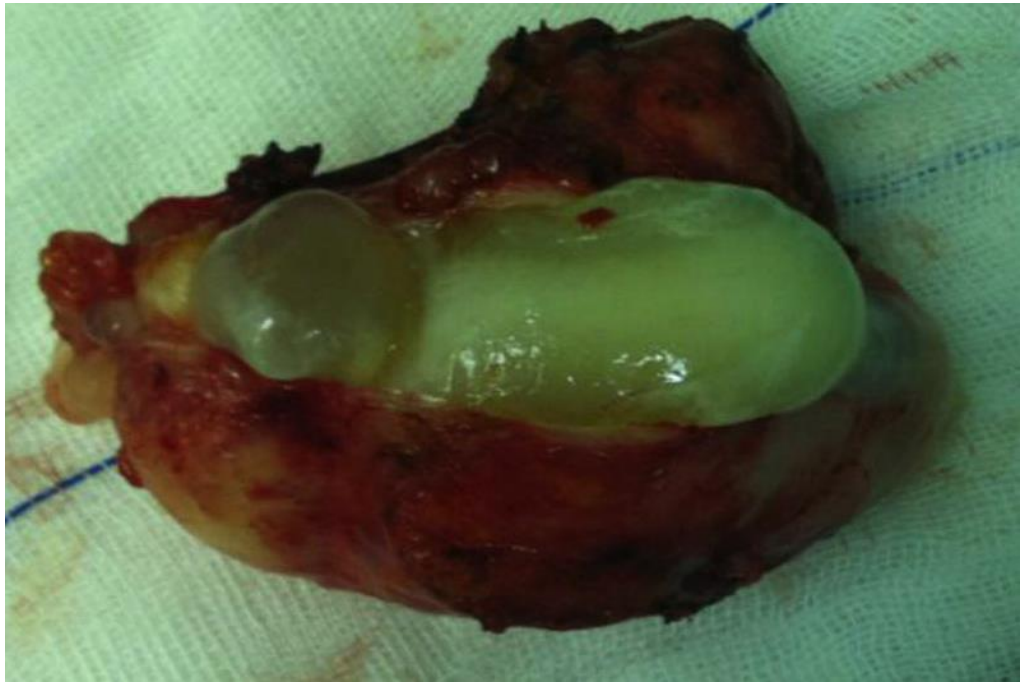


* Relative frequency

Appendiceal Neoplasms: Mucocele

Clinical Presentation:

- Asymptomatic (Most common)
- RLQ abdominal pain
- Colicky abdominal pain
- GI bleeding – intussusception
- Bowel obstruction
- Hydroureter
- Acute abdomen if ruptures



Laboratory Findings:

- CA 19-9
- CEA
- ESR

*Evidence is not great to support these for diagnostic purposes

Appendiceal Neoplasms: Mucocele

Imaging:
- Ultrasound
- CT

Findings to suggest mucocele:
- Calcification in the appendiceal wall
- Cystic lesion
- Irregular wall, but normal wall thickness
- Hypodense spots in the peritoneum

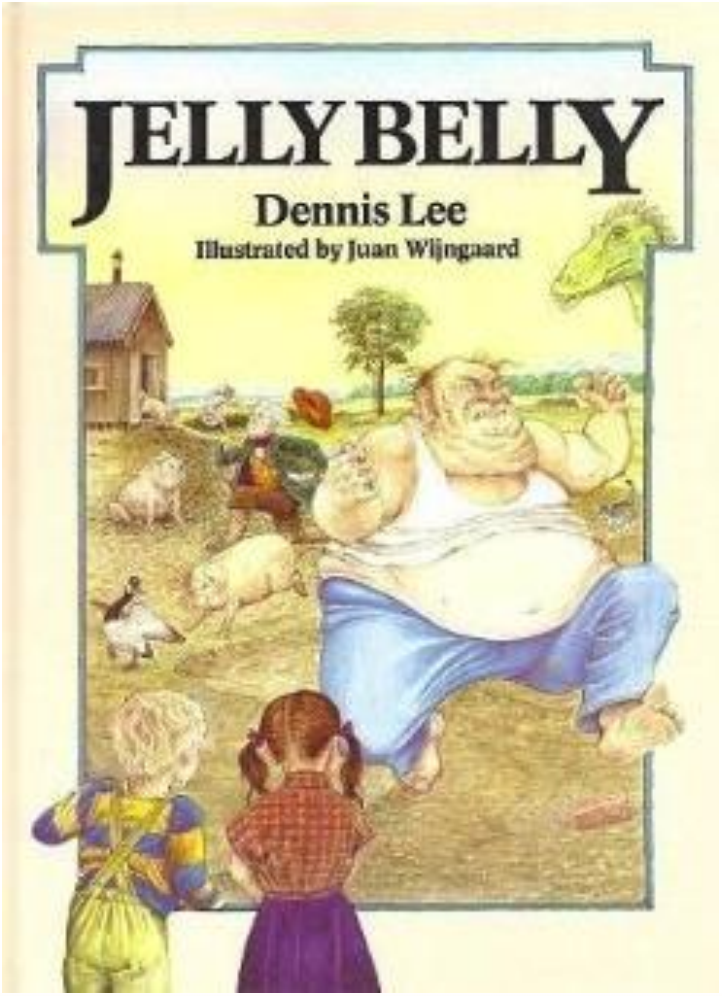
Endoscopy

Appendiceal Neoplasms: Mucocele

Management:

- **Early diagnosis and surgical resection**
- **Appendectomy – staple across the base of the cecum**
- **Right hemicolectomy – if malignant features (cystadenocarcinoma), or obvious invasion into the terminal ileum, cecum or adjacent mesentery at the time of operation.**
- **Rule out synchronous cancer – 20%**
  - **Check colon, ovaries, endometrium, breast and kidney**

Pseudomyxoma Peritonei



"Jelly Belly bit with a big fat bite…" – Denis Lee

Pseudomyxoma Peritonei

Originally used to describe Intraabdominal spread of a cystadenoma of the appendix.

Cystadenoma of the appendix ruptures, spreading mucous producing cells throughout the peritoneum.

Mucous accumulates in the abdomen (Jelly Belly) until it causes obstruction, which has no curative surgical treatment.

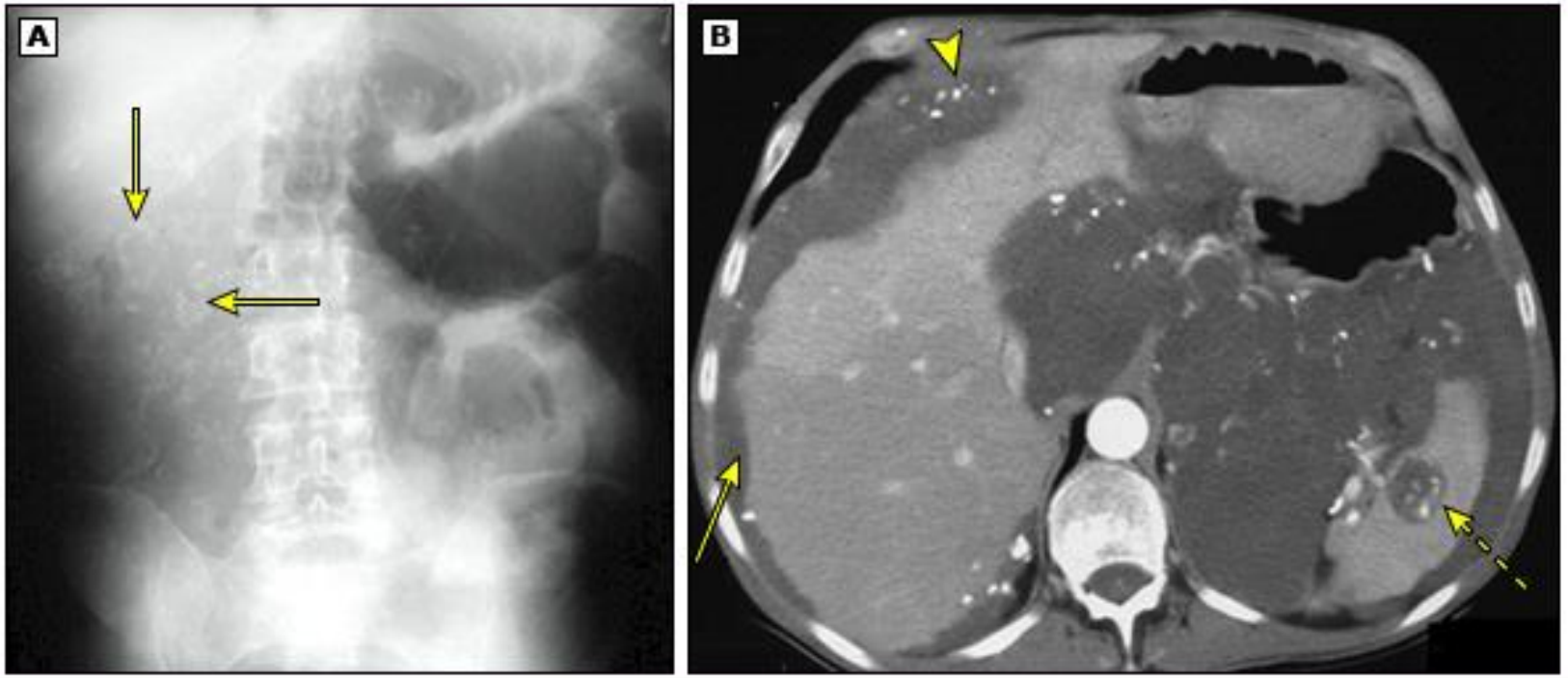
Some also include peritoneal carcinomatosis from malignant mucous producing tumors of the appendix, small and large bowel, lung, pancreas, stomach, breast and ovaries in the definition

Prognosis is very different for indolent cystadenoma type versus all others.

Clinical Presentation of Pseudomyxoma Peritonei
Presenting Symptoms

Non-specific Symptoms

- *Increasing abdominal girth*
- *Inguinal hernia in men*
- *Ovarian mass on pelvic examination*



Typical CT findings:

Mucin same density as water

Calcifications are common

Scalloping of the liver, spleen and peritoneum

Spares the central portion of the abdomen (redistribution phenomenon)

Pseudomyxoma Peritonei: HIPEC and CRS

Hyperthermic Intraperitoneal Chemotherapy and Cytoreductive Surgery

Theory behind the treatment:

- *Intraabdominal administration increases the effective concentration 7-fold (mitomycin or 5-FU)*
- *Limits systemic effects*
- *Heating increases the depth of penetration*

Patient Selection (Surgarbaker, PH)

1. *Histopathological assessment*
    - *Non-invasive neoplasms (better)*
2. *Radiological assessment*
    - *No liver, lung mets or lymphadenopathy*
    - *Segmental obstruction of small bowel (worse)*
    - *Tumor deposit >5cm (worse)*
3. *Peritoneal Cancer index*
4. *Complete Cytoreduction*

Pseudomyxoma Peritonei: HIPEC and CRS

MANAGEMENT OF
PERITONEAL SURFACE MALIGNANCY
USING
INTRAPERITONEAL CHEMOTHERAPY
AND
CYTOREDUCTIVE SURGERY

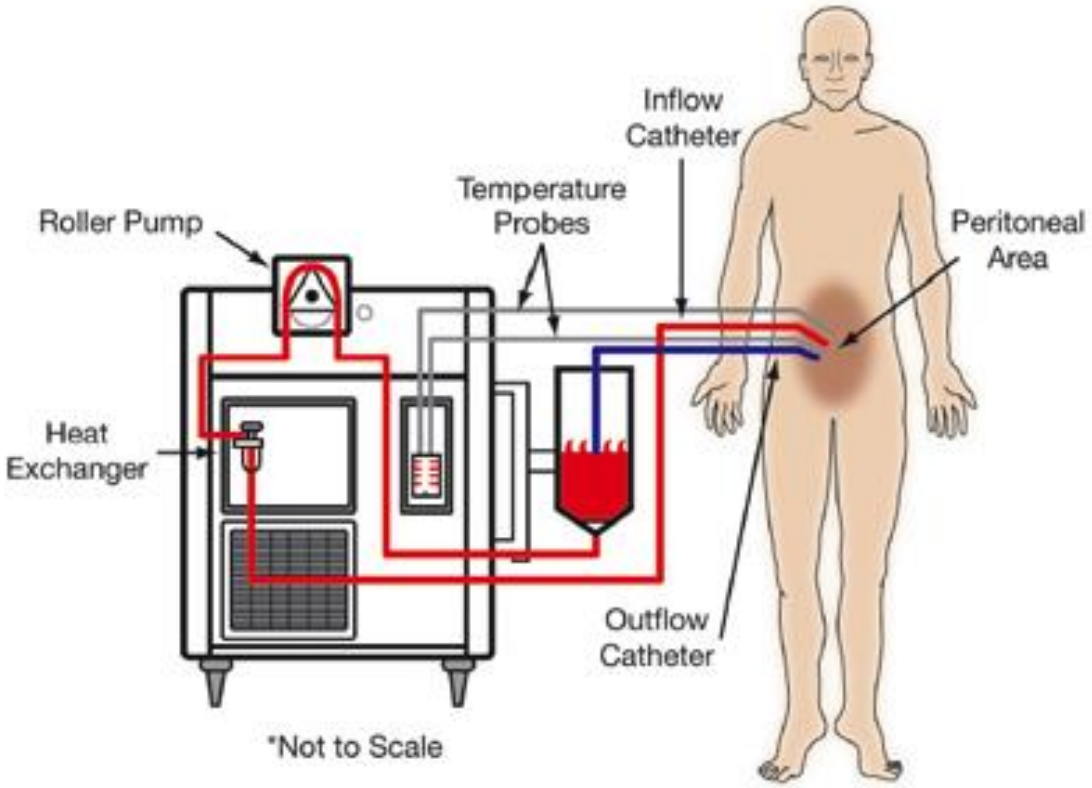
A Manual for Physicians and Nurses

Paul H. Sugarbaker, M.D., F.A.C.S.

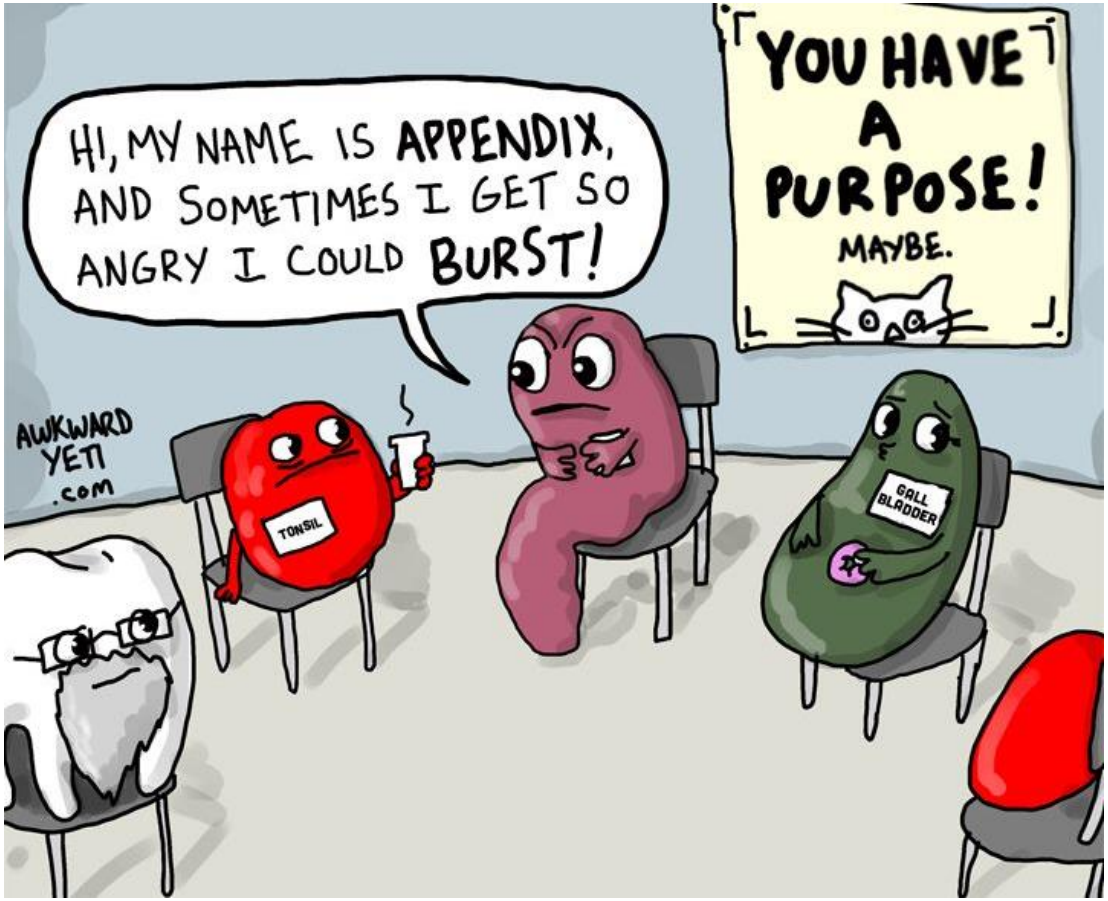
Washington Cancer Institute

110 Irving Street NW Washington, DC 20010

http://www.surgicaloncology.com/gpmtitle.htm



Appendiceal Neoplasms: Adenocarcinoma



Appendiceal Neoplasms: Adenocarcinoma

Histologic Subtypes

- Mucinous cystadenocarcinoma (Most Common)
- Intestinal type adenocarcinoma
- Signet ring cell adenocarcinoma

Histology	Frequency	5 year Disease Specific Survival
Mucinous cystadenocarcinoma	37%	58%
Intestinal type adenocarcinoma	27%	55%
Signet Ring adenocarcinoma	6%	27%
Carcinoid Tumors	11%	93%

AJCC, 10th Edition, 2010

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria*
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through muscularis propria into subserosa or into mesoappendix
T4	Tumor penetrates visceral peritoneum, including mucinous peritoneal tumor within the right lower quadrant and/or directly invades other organs or structures¶Δ
T4a	Tumor penetrates visceral peritoneum, including mucinous peritoneal tumor within the right lower quadrant
T4b	Tumor directly invades other organs or structures

Regional lymph nodes (N)◇	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 3 regional lymph nodes
N2	Metastasis in four or more regional lymph nodes

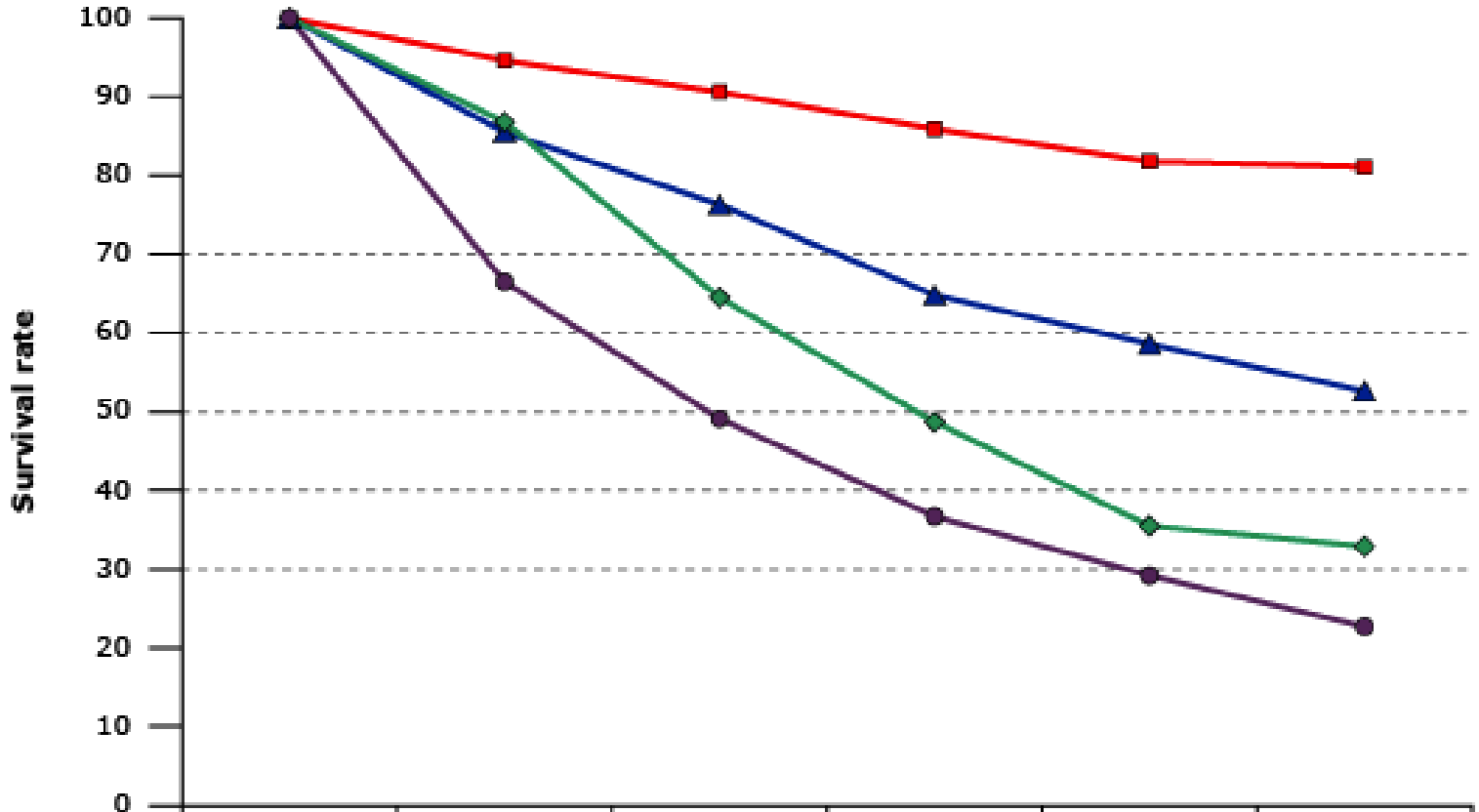
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
M1a	Intraperitoneal metastases beyond the right lower quadrant, including pseudomyxoma peritonei
M1b	Nonperitoneal metastases

pTNM pathologic classification. The pT, pN, and pM categories correspond to the T, N, and M categories.

pN0. Histological examination of a regional lymphadenectomy specimen will ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Histologic grade (G)§		
GX	Grade cannot be assessed	
G1	Well differentiated	Mucinous low grade
G2	Moderately differentiated	Mucinous high grade
G3	Poorly differentiated	Mucinous high grade
G4	Undifferentiated	

Anatomic stage/prognostic groups				
Stage 0	Tis	N0	M0	
Stage I	T1	N0	M0	
	T2	N0	M0	
Stage IIA	T3	N0	M0	
Stage IIB	T4a	N0	M0	
Stage IIC	T4b	N0	M0	
Stage IIIA	T1	N1	M0	
	T2	N1	M0	
Stage IIIB	T3	N1	M0	
	T4	N1	M0	
Stage IIIC	Any T	N2	M0	
Stage IVA	Any T	N0	M1a	G1
Stage IVB	Any T	N0	M1a	G2, 3
	Any T	N1	M1a	Any G
	Any T	N2	M1a	Any G
Stage IVC	Any T	Any N	M1b	Any G



	0	1	2	3	4	5
I	100.0	94.6	90.6	85.9	81.8	81.1
II	100.0	85.5	76.3	64.8	58.6	52.6
III	100.0	86.8	64.5	48.7	35.5	32.9
IV	100.0	66.5	49.1	36.7	29.2	22.7

Years from diagnosis

Appendiceal Neoplasms: Adenocarcinoma

Management

- Diagnosis made pre-op
  - Right hemicolectomy
  - However, some evidence to suggest survival is no different for early lesions with simple appendectomy

- Found post-appendectomy
  - Right hemi-colectomy
  - No further operation if:
    - Adenocarcinoma confined to the mucosa
    - Well differentiated lesions no deeper then submucosa

Appendiceal Neoplasms: Adenocarcinoma

Adjuvant Therapy

- No randomized evidence exists due to the rare nature of these types of malignancy

- Chemotherapy ???
  - Retrospective evidence to suggest some patients with advanced disease may benefit from treatment.
- Radiation ???

Appendiceal Neoplasms: Peritoneal Mucinous Carcinomatosis

Adenocarcinoma

Role of HIPEC and CRS

J Clin Oncol. 2003 Oct 15;21(20):3737-43.

Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer.

Verwaal VJ[1], van Ruth S, de Bree E, van Sloothen GW, van Tinteren H, Boot H, Zoetmulder FA.

Only RCT looking at HIPEC and cytoreductive surgery

105 Patient with peritoneal carcinomatosis

- 87 with colon cancer
- 18 with appendiceal cancer

Control – Standard therapy

- 5-FU and leucovorin chemotherapy
- Palliative surgery if required

Experimental – HIPEC and debulking surgery

- Debulking to <2.5mm lesions
- HIPEC – 90 minutes of isotonic dialysis fluid with mitomycin at 41 degrees.
- 5-FU and leucovorin started 6 weeks post

Median Survival: 22.4 months versus 12.6 months

Original article

Right hemicolectomy does not confer a survival advantage in patients with mucinous carcinoma of the appendix and peritoneal seeding

S. González-Moreno and P. H. Sugarbaker

Program in Peritoneal Surface Malignancy, The Washington Cancer Institute, Washington, DC, USA
Correspondence to: Dr P. H. Sugarbaker, Department of Surgical Oncology, Washington Cancer Institute, 110 Irving Street NW, Suite CG-185, Washington, DC 20010, USA (e-mail: Paul.Sugarbaker@medstar.net)

British Journal of Surgery 2004; **91**: 304–311

Cohort of 501 patients with mucinous adenocarcinoma of the appendix

- 17-year experience
- Compared appendectomy versus right hemi-colectomy
- All patients were treated with HIPEC and CRS

Overall results:

- 5 year survival 74% (SEER stage IV 22%)
- 10 year survival 52%

Ann Surg Oncol. 2012 May ; 19(5): 1386–1393. doi:10.1245/s10434-012-2241-6.

Aggressive Management of Peritoneal Carcinomatosis from Mucinous Appendiceal Neoplasms

Frances Austin, MD[1], Arun Mavanur, MD[1], Magesh Sathaiah[1], Jennifer Steel, PhD[2], Diana Lenzner, MS[3], Lekshmi Ramalingam, MD[1], Matthew Holtzman, MD[1], Steven Ahrendt, MD[1], James Pingpank, MD[1], Herbert J. Zeh, MD[1], David L. Bartlett, MD[1,4], and Haroon A. Choudry, MD[1,4]

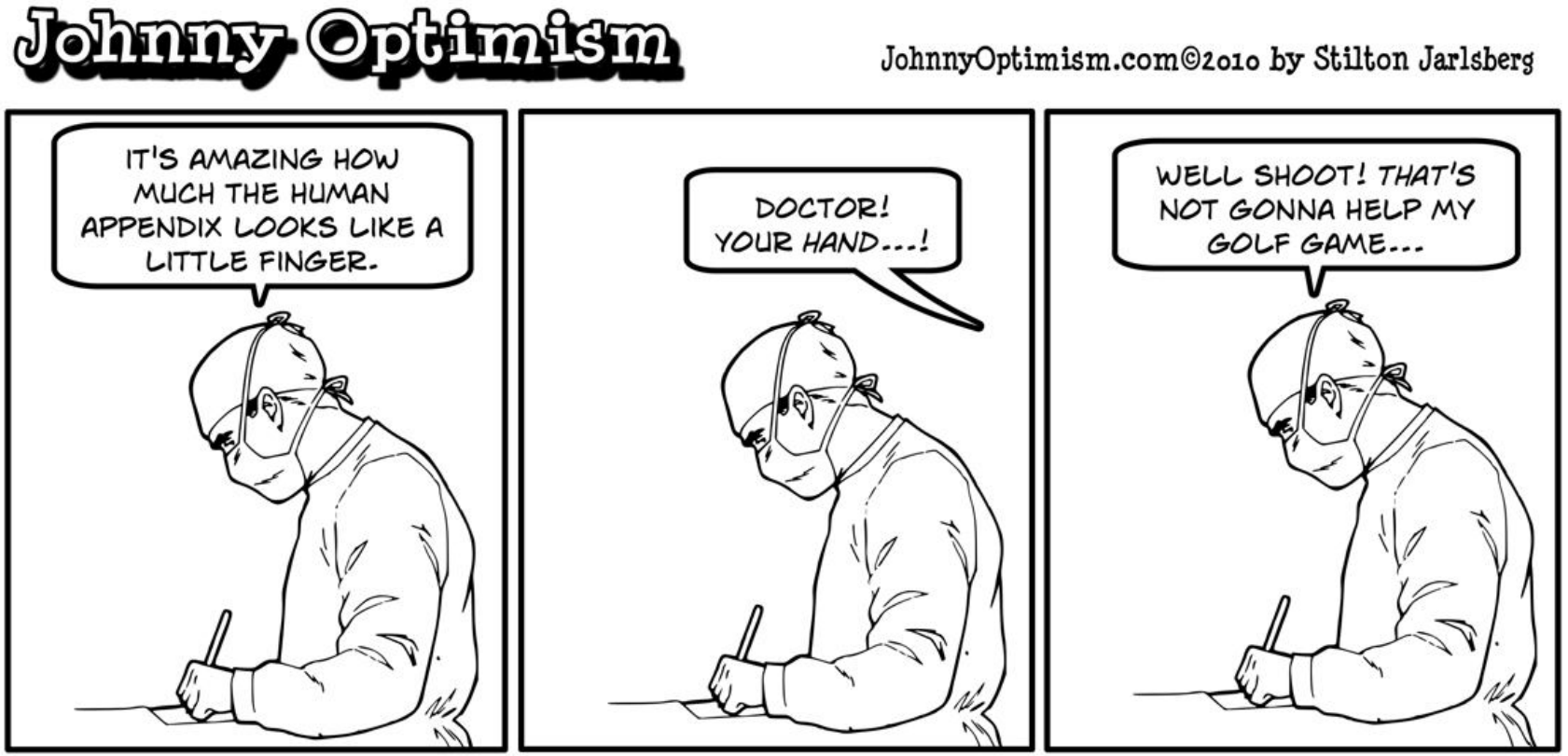
282 patients with peritoneal carcinomatosis undergoing HIPEC and CRS

Simplified peritoneal cancer index (SPCI) – pre-operative tumor load
Complete cytoreduction score (CC-score) – visible disease remaining

Lower SPCI showed better survival
Lower CC-score showed better survival

Survival 3 year – 67%
Survival 5 year – 52%

Appendiceal Neoplasms: Carcinoid Tumors



Appendiceal Neoplasm: Carcinoid Tumors

- *Approximately 11% of appendiceal malignancies*
- *Age 40 – 50 years*
- *More common in women*
- *Occur most often in the distal third of the appendix*
- *Large tumors cause obstruction*

Carcinoid Syndrome: Metastatic Disease

- *Episodic Flushing (EtOH, emotional stress, eating, liver palpation and anesthesia)*
- *Venous telangiectasia*
- *Bronchospasm*
- *Diarrhea*

Carcinoid Crisis:

- *Significant hemodynamic instability*
- *Octreotide Prophylaxis (300-500mcg IV), repeat PRN*

Appendiceal Neoplasm: Carcinoid Tumors
Clinical Presentation

- *Most patients are symptomatic at time of diagnosis*
- *Appendicitis (10% reside at base of appendix)*
- *Bowel obstruction*
- *Carcinoid Syndrome*
- *Incidental finding*

Work-Up of Carcinoid Tumors

- *CT abdomen*
- *CT chest*
- *Octreotide scan*
- *24-Hour 5-HIAA (5-hydroxindolacetic acid)*
- *Chromogranin A*

Endoscopic image of an appendiceal carcinoid

TNM staging of appendiceal carcinoid

AJCC 7th edition, 2010

Primary tumor (T)*	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 2 cm or less in greatest dimension
T1a	Tumor 1 cm or less in greatest dimension
T1b	Tumor more than 1 cm but not more than 2 cm
T2	Tumor more than 2 cm but not more than 4 cm or with extension to the cecum
T3	Tumor more than 4 cm or with extension to the ileum
T4	Tumor directly invades other adjacent organs or structures, eg, abdominal wall and skeletal muscle¶
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

pN0. Histological examination of a regional lymphadenectomy sp
include 12 or more lymph nodes. If the lymph nodes are negative
ordinarily examined is not met, classify as pN0.

Anatomic stage/prognostic groups			
Stage I	T1	N0	M0
Stage II	T2, T3	N0	M0
Stage III	T4	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

Appendiceal Neoplasm: Carcinoid Tumors
WHO Grade

TABLE 4. Grading Systems for Neuroendocrine Tumors of the Midgut

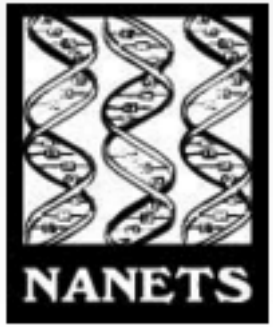
Grade	Criteria
Low grade (G1)	<2 Mitoses/10 high-power fields, and <3% Ki-67 index
Intermediate grade (G2)	2–20 Mitoses/10 high-power fields, or 3%–20% Ki-67 index
High grade (G3)	>20 Mitoses/10 high-power fields or >20% Ki-67 index

Appendiceal Neoplasm: Carcinoid Tumors Management:

NANETS

- *<1cm tumors with no evidence of lymphovascular invasion or invasion into the mesoappendix are considered a cure.*

- *Right Hemicolectomy*
  - *>1cm at the base of the appendix*
  - *>2cm or size cannot be evaluated*
  - *Grade 2 and 3 tumors*
  - *Lymphovascular invasion*
  - *Invasion of mesoappendix*
  - *Positive margins*



Appendiceal Neoplasm: Carcinoid Tumors Management:

ENETS

- *<2cm tumors with no evidence of lymphovascular invasion or invasion into the mesoappendix are considered a cure.*

- *Right Hemicolectomy (within 3 moths):*
  - *>2cm or size cannot be evaluated*
  - *Invasion of mesoappendix*
  - *Positive margins*

European ENETS Neuroendocrine Tumor Society

Appendiceal Neoplasm: Carcinoid Tumors Follow-Up:

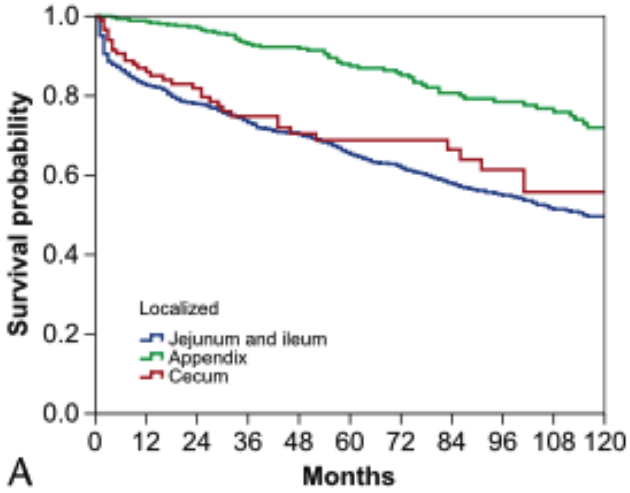
ENETS

- *Curative Tumors – Chromogranin A at 6-12 months*
- *All others – CT, Octreotide scan, Chromogranin A q6-12 months indefinitely*

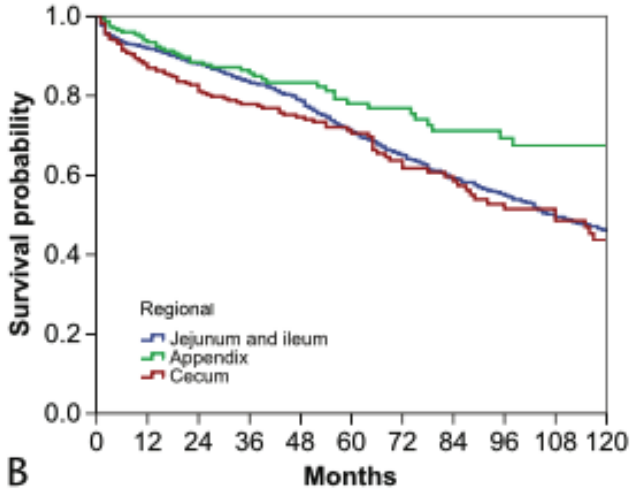
NANETS

- *Curative Tumors – (G1, <1cm) no follow up*
- *All others – Restage at 3 – 6 months*
  - *HIAA, Chromogranin A, CT/MRI and Octreotide scan q6-12 months for 7 years.*

- Appendix



A



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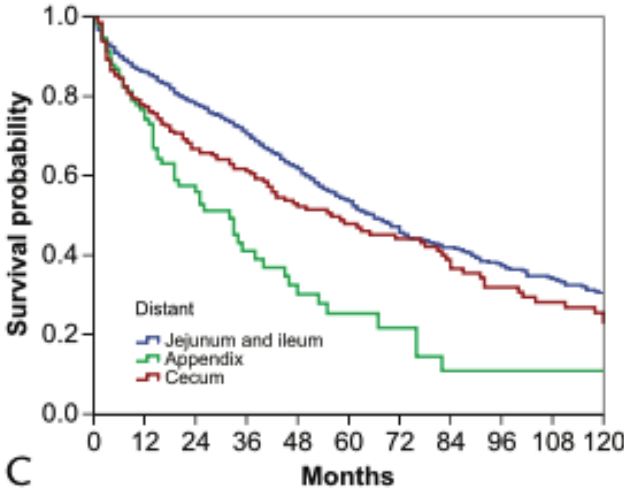


C

D

Primary Tumor Site	Localized				Regional				Distant			
	Median Survival Duration, months	3-Year Survival Rate	5-Year Survival Rate	10-Year Survival Rate	Median Survival Duration, months	3-Year Survival Rate	5-Year Survival Rate	10-Year Survival Rate	Median Survival Duration, months	3-Year Survival Rate	5-Year Survival Rate	10-Year Survival Rate
Appendix	NR	93%	88%	72%	NR	86%	78%	67%	31	42%	25%	11%
Jejunum/ileum	115	73%	65%	49%	107	83%	71%	46%	65	70%	54%	30%
Cecum	135	74%	68%	55%	107	78%	71%	44%	55	61%	48%	23%

FIGURE 2. Overall survival among patients with midgut NETs. Survival by stage and primary site in patients with G1/G2 NETs diagnosed from 1988 to 2004. Cases were selected from SEER database (1973–2004) using International Classification of Diseases for Oncology third edition histology codes 8150–8157, 8240–8246, and 8249. Localized disease (A), regional disease (B), distant disease (C), survival by disease stage and primary tumor site (D).

Appendiceal Neoplasm: Carcinoid Tumors
Advanced Disease:

Systemic Therapy
- *Octreotide alone*
  - *Improved time to progression*
  - *Survival advantage suspected*
- *Octreotide + INF alpha*
- *Cytotoxic Chemo (5FU – based)*
- *Everolimus/Sirolimus (mTOR)*
- *Bevacizumab (anti-VEGF)*

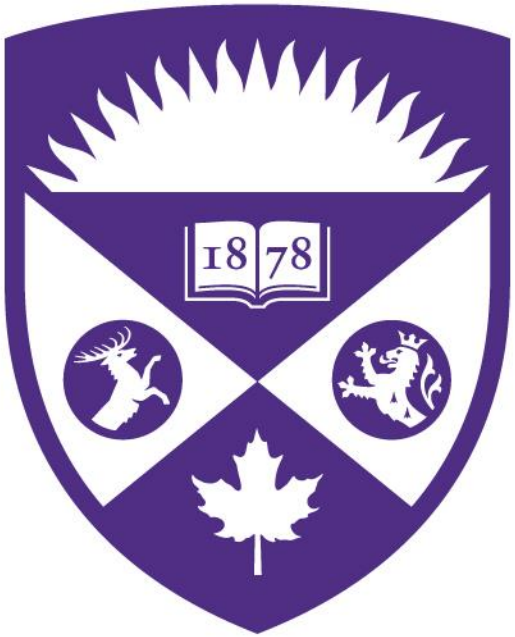
Cytoreductive Surgery
- *Hepatic Resection*
- *Liver directed therapy*
  - *Cryo, radio or microwave ablation*
  - *Embolization (Bland, chemo or radioactive)*
  - *Peptide receptor radiotherapy*

“Idleness is the appendix to nobility…” - Robert Burton

Dr. Elizabeth Pomfret, MD, PhD, FACS

Chair, Dept. of Transplantation and Hepatobiliary Diseases,
Lahey Medical Center, Burlington, Massachusetts
Professor of Surgery, Tufts University School of Medicine

Wednesday, February 17, 2016
5:00-6:00pm, Auditorium B, UH



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