

CANCER OF THE APPENDIX

Rare, neoplastic lesions found in 0.5% of appendices

- Primary malignant tumors in 1.4% of appendices
- Benign tumors in 4.6% of appendices

Most common is carcinoid (90% of primary appendiceal tumors)

Clinical presentation is often similar to acute appendicitis

Diagnosed usually at time of appendectomy or on pathologic examination of specimen

Can sometimes be perforated and lead to localized abscess

Histologic Types:

- Carcinoid
- Mucocele (Cystic Neoplasms)
- Primary Adenocarcinoma
 - Signet Ring
 - Metastases
 - Stromal tumors (leiomyoma, leiomyosarcoma, lipoma)
 - Lymphoma (in AIDS)

Carcinoid:

- Most common appendiceal tumor
- 45% of carcinoids in GI tract are in appendix
- arise from argentaffin cells lining the crypts; small, firm, circumscribed, yellow-brown
- 50% of the time they are found incidentally at surgery
- 50% of the time they present like acute appendicitis
- Most (75%) found at tip or distal 1/3 of appendix; <10% are at base
- Carcinoid syndrome accompanying appendiceal carcinoids - "rare"
- Generally benign and metastases in 3% of carcinoids less than 2cm
- BUT metastases more common when greater than 2cm, hence.....
- Management according to SIZE:
 - Less than 2cm -> Appendectomy
 - More than 2cm -> Right hemicolectomy
- If not recognized until pathology and greater than 2cm and/or close to base, re-explore and do Right hemicolectomy
- Distal metastases (grow slowly): use chemotherapy protocols for carcinoids: 5 year survival greater than 50%

Adenocarcinoma: 41 cases in a series of 5000 appendectomies

- Can histologically be mucinous or colonic
- *Colonic Subtype* - arises from glandular epithelium of mucosa; resembles colon cancer microscopically, grossly, and biologically
- *Mucinous Subtype* - more favorable than colonic type even when staging differences taken into account
- Presents as acute appendicitis (in 50% of cases) or as right colon carcinoma
- Lymph node involvement or metastases in 50% of cases
- 15-30% can also have another primary CA such as colon or ovary
- Right hemicolectomy produced higher survival rate vs. appendectomy alone (68% vs. 20%): these results are from patients with distant metastases at time of diagnosis:
(Nitecki, SS, Wolf, BG, Schlinkert, R, Sarr, MG: The natural history of surgically treated primary adenocarcinoma of the appendix, Ann. Surg., 219:51, 1994.)
- If diagnosed by pathology after simple appendectomy, re-exploration is recommended
- 5 year survival rates for adenocarcinoma at Mayo Clinic:
Dukes A - 100%, Dukes B - 67%, Dukes C - 50% Dukes D - 6%

Mucocele:

- Definition - a cystic dilation of the appendix containing mucoid material
- Pathophysiology - secretion of mucus by hyperplastic or neoplastic tissues obstructs lumen proximally
- Simple Mucocele (chronic occlusion by mucous), treat by appendectomy
- 75-85% of Mucoceles are caused by Cystic Neoplasms:
- cystadenomas ("grade 1 adenocarcinoma")
- cystadenocarcinomas
- Most of these cystic neoplasms are benign cystadenomas
- Presentation: incidental findings on CT, painless mass, acute appendicitis
- if benign & mucocele is unruptured/ruptured, Appendectomy is curative
- if malignant & mucocele is unruptured → Appendectomy
- if malignant & mucocele ruptures.....Pseudomyxoma Peritonei
 - spillage of malignant mucin secreting cells into peritoneum, leads to recurrent inflammation, adhesions, obstruction, fistulas
 - Wide resection if possible; 5 year survival rates above 50% for ruptured malignant mucoceles

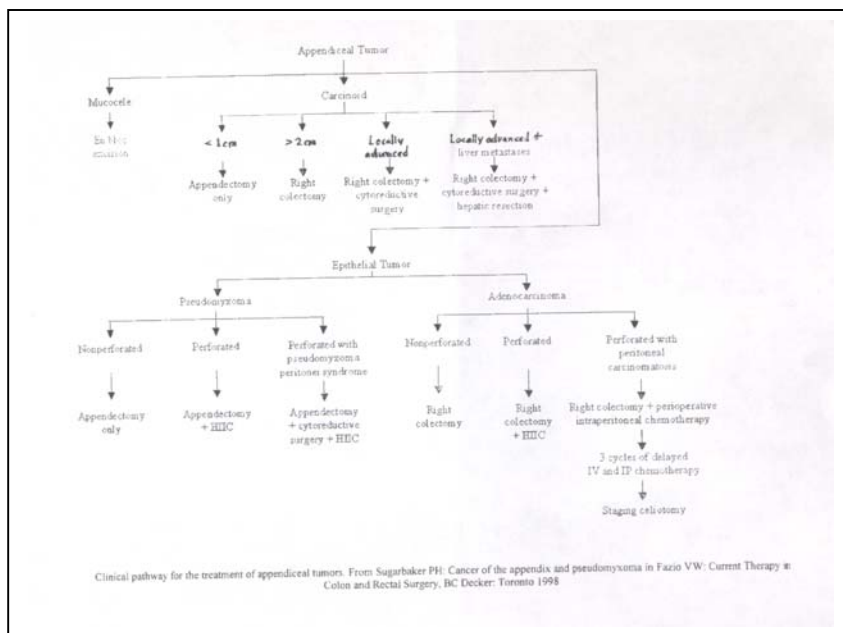
Comparison of Colorectal and Appendiceal Malignant Tumors:

	<u>Colon</u>	<u>Appendix</u>
Adenocarcinoma incidence	85%	10%
Carcinoid incidence	< 1%	70%
Mucinous adenocarcinoma	10-15%	20%
Signet-ring adenocarcinoma	1/1,000	1/10
Mucinous adenocarcinoid	Not reported	Rare
Differentiation carcinoma	20% Well 60% Moderate 20% Poor	60% Well 20% Moderate 20% Poor
Associated malignancy	Unusual	Common

Survey of appendiceal tumors. From Sugarbaker PH: Cancer of the appendix and pseudomyxoma (in) Fazio VW: Current Therapy in Colon and Rectal Surgery. BC Decker: Toronto 1998.

	Carcinoid	Cyst-adenocarcinoma	Adenocarcinoma	Adenocarcinoid	Linitis Plastica* (Signet Ring)
Incidence	66%	20%	10%	Rare	Rare
Location	Tip of appendix	Variable	Base of appendix	Diffuse along appendix wall	Diffuse
Major symptom	Incidental finding	Appendicitis, mucinous ascites	Appendicitis	Appendicitis or right lower quadrant mass	Appendicitis
Prognosis	< 1 cm 100% cure > 2 cm 50% cure	Localized 90% cure Peritoneal seeding-poor prognosis	Follows Duke's stages A - 80% cure B - 50% cure C - 20% cure	84% cure at 5 years	Poor
Clinical syndromes	Carcinoid	Pseudomyxoma peritonei	Peritoneal carcinomatosis		
Treatment	< 1 cm appendectomy only > 2 cm right colectomy + cytoreductive surgery	Appendectomy + intraperitoneal chemotherapy + cytoreductive surgery	Right colectomy + intraperitoneal chemotherapy	Appendectomy only unless advanced	Radical surgery + intraperitoneal chemotherapy +

- In separating cystadenocarcinoma, adenocarcinoma, and signet-ring cancer, it must be remembered that these represent a spectrum of these and are not distinct clinical entities. Benign mucocele is not included as an appendiceal tumor but is rather a cystic process.



Intraperitoneal Chemotherapy (HIIC - Heated Intraoperative Intraperitoneal Chemotherapy)

- For cancers that have lead to implants on peritoneal surfaces
- Eliminating peritoneal spread may prevent carcinomatosis, which leads to intestinal obstruction
- Current indications for HIIC along with cytoreductive surgery:
 1. Large volume of noninvasive peritoneal carcinomatosis or sarcomatosis.
 2. Peritoneal mesothelioma
 3. Low volume peritoneal seeding from invasive cancer.
 4. Perforated gastrointestinal cancers.
 5. Cancer adherent to adjacent organs or structures.
 6. Gastrointestinal cancer with positive peritoneal cytology.
 7. Gastrointestinal cancer with ovarian involvement.
 8. Tumor spill intraoperatively.
 9. Systemic chemotherapy for recurrent ovarian cancer after a long disease-free interval
 10. Palliation of patients with malignant ascites.

This approach requires changing the ROUTE and TIMING of chemotherapy administration
INTRAPERITONEAL ROUTE:

- Surgeon manually manipulates surfaces to uniformly distribute heat and drug
- This assures high concentration of anticancer therapy at the peritoneal surfaces

PERIOPERATIVE TIMING:

- Can begin in the OR and continue for first five postoperative days
- Early postoperative HIIC- before adhesions develop and irrigates away old blood or fibrinous debris
- More effective after surgical debulking so that chemo will contact only microscopic residual disease
- Done prior to creation of any anastomoses, which may help eliminate recurrence at suture lines
- Patients selected by a PCI- Peritoneal Cancer Index (combines a distribution assessment and size of lesions)

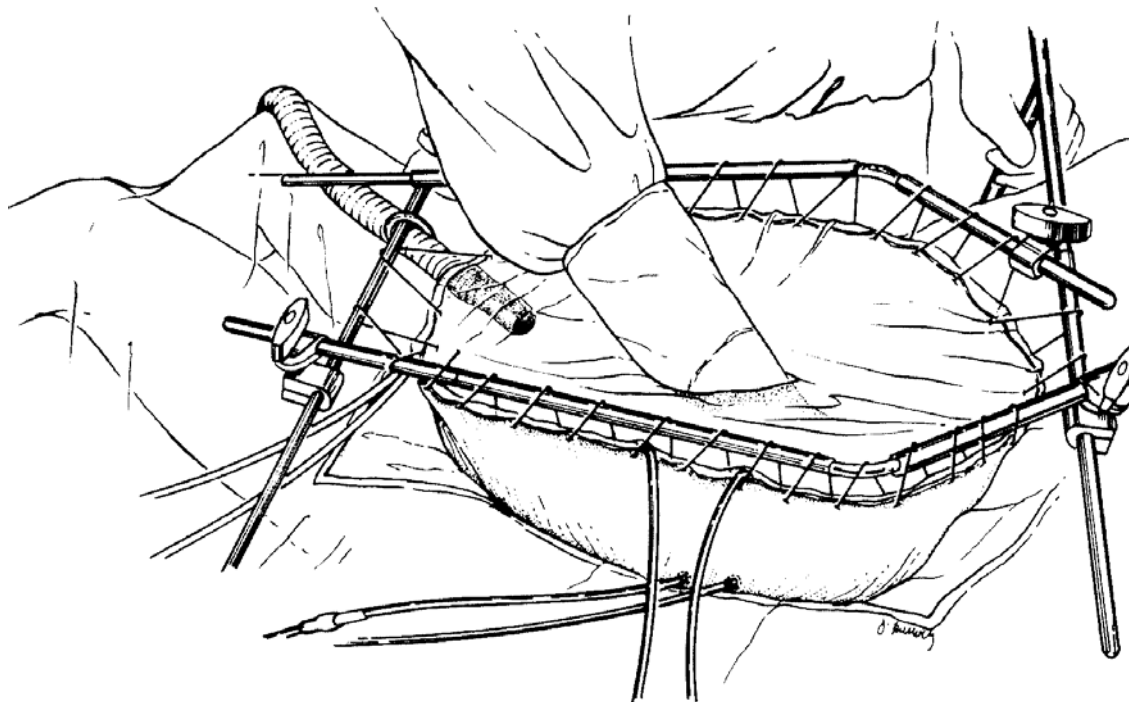
QUESTION: Patient s/p appendectomy with pathologic findings of mucinous adenocarcinoma with uncertain malignant potential by immunohistochemical investigation. The computerized tomography scan, colonoscopy, and liver function tests are normal. Right hemicolectomy is planned. What is your opinion about intraperitoneal chemotherapy in this case?

RESPONSE: Mucinous tumors of uncertain malignant potential are associated with a good prognosis as long as the tumor is completely removed (usually with right hemicolectomy), there are no lymph node or distant metastases (in which case the uncertainty of malignant potential would be eliminated), and there are no signs of extension of the tumor outside the appendix. Carr reported that these tumors behave as benign tumors with prognosis determined by mucin found

outside of the appendix and extra-appendiceal epithelial cells.[1] Sugarbaker and Jablonski reported a large experience with early postoperative intraperitoneal chemotherapy done for patients with peritoneal carcinomatosis.[2] They observed generally good results, especially in patients with tumors arising from the appendix. However, they emphasized the significant morbidity and mortality that accompanies this approach. Their results would strongly suggest that there is no role for intraperitoneal chemotherapy unless peritoneal carcinoma implants are documented. Even if peritoneal carcinomatosis is documented, chemotherapy should probably be done as part of an investigational effort.

Grant Disick, M.D.

Perioperative Intraperitoneal Chemotherapy



Coliseum technique for HICC: A running suture on the self-retaining retractor suspends the skin of the abdominal wall. A sheet of plastic is incorporated into the running suture, so that the abdomen is covered. This helps to hold the heat in the abdomen and prevents splashing as the viscera are vigorously manipulated. Temperature probes are placed at the inflow site for the heated chemotherapy and at a distant site within the abdomen or pelvis. Three or four closed suction drains are placed through the abdominal wall and positioned beneath the hemidiaphragms and within the pelvis. These drains return chemotherapy solution to the reservoir. A smoke evacuator is placed beneath the plastic sheet so that airflow is always from the operating theater, into the abdomen, and then out into a charcoal filter. The surgeon's double-gloved hand is placed through a cut in the plastic sheet. Vigorous scrubbing of all surfaces is a crucial part of the dislodgment of fibrin and entrapped tumor cells.

