




OMED COLORECTAL CANCER SCREENING COMMITTEE MEETING
Saturday, May 1, DDW New Orleans, 2010
Presenter: James E. Allison

*The human mind is like a parachute.
It doesn't work unless it is open.*

**Most Colonic Polyps are Sheep
Dressed in Wolves' Clothing**



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Lecture Outline

- Colon polyps/adenomas - definitions
- The Wolves and the Sheep
- The Hype - The influence of investigators, specialty societies, media, and guidelines
- The Consequences
- The Facts
- Conclusions and Recommendations

Polyp - Definition

- Polyp – any mucosal protrusion into the lumen of the colon
- Adenoma – a polyp that has been examined histologically and found to be composed of benign gland like structures

Koretz RL. Annals of Int Med 1993 ;118:63-68

Polyp - Definition

- Adenoma – A benign **precancerous** growth which may develop into colon cancer in the future if not removed. Removal prevents that polyp from becoming cancerous but you are still at risk to develop new polyps in your colon. Close follow up is recommended

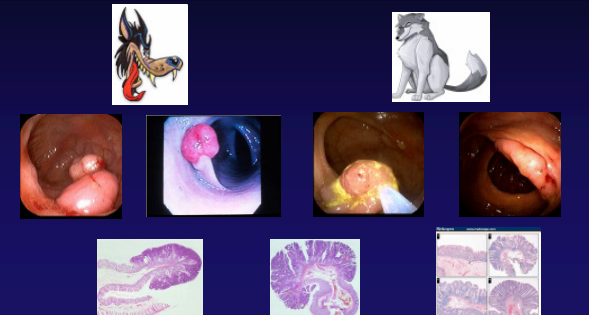
*2010 ASGE Colon Cancer Awareness Month Resources
Polyp Information Sheets for Patients and Referring Physicians
Sponsored by partial funding from the ASGE Foundation Fujinon Fund
through a charitable gift from Fujinon, Inc.*

Advanced Adenoma - Definition

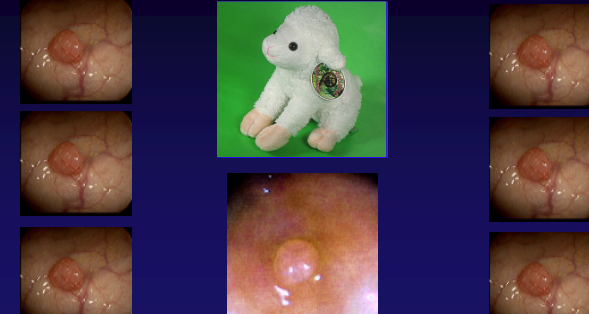
Adenomatous polyps > 1cm or with >20% villous component or any high-grade dysplasia

Rozen P, Comaneshter D, Levi Z et al Cancer 2010


**The Wolves;
Large TA, TVA, VA, Atypia,
Serrated Adenoma**



**The Sheep:
Small Tubular Adenomas**



**Most Colonic Polyps
Sheep in Wolves' Clothing**



Koretz RL Annals of Int Med 1993 ;118:63-68

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Screening Colonoscopy Studies
The Findings

Screening Program	Sensitivity for Advanced Neoplasia (%)
FOBT alone	24
Sigmoidoscopy alone	70
FOBT + Sigmoidoscopy	76

Lieberman DA, Weiss DG VA Cooperative Study Group NEJM 2001, 345:555-560

Screening Colonoscopy Studies
The Message

We found that one-time screening of asymptomatic subjects with FOBT plus sigmoidoscopy fails to identify about one quarter of subjects with advanced neoplasia and one half of subjects with advanced proximal neoplasia.

Lieberman DA, Weiss DG VA Cooperative Study Group NEJM, 345:555-560

The Danger Lurking in the Small Adenoma

Subject characteristics	With high grade dysplasia	Without high grade dysplasia	Total	P
Largest Polyp Size Category				
1-5mm	6 (3%)	215 (97%)	221	<.001
5-9mm	19 (16%)	100 (84%)	119	
> 10mm	227 (51%)	217 (49%)	444	

Bretagne JF, Manfredi F, Piette C et al Dis Colon Rectum 2010; 53:339-345

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Small Adenoma Studies The Message

- CTC surveillance of small polyps will lead to missed high grade dysplasia
- Optical colonoscopy and removal of all polyps is the preferred approach

The Opinion Leaders Speak - 2000

"There is suspicion among physicians that in recommending flexible sigmoidoscopy to screen persons for colorectal cancer, we are promoting a suboptimal approach. Relying on flexible sigmoidoscopy is as clinically logical as performing mammography of one breast to screen women for breast cancer.

The failure of insurance companies to cover the costs of colonoscopic screening is no longer tenable."

Podolsky DK Editorial NEJM 2000;343:207-208

The Opinion Leaders Speak - 2009

"It is impractical for a PCP to discuss 6 different options for CRC screening with each patient. Recommending one preferred strategy simplifies the discussion. Colonoscopy is the preferred strategy because it is the best test."

*Rex D, Johnson DA, Anderson JC et al Am J Gastroenterol. 2009;104:739-750
Rex D Medscape Medical News March 10,2009*

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The Media Speaks

“The results of the Lieberman study may put doctors in a ethical --- and possibly legal --- bind. How can I in good conscience still advise patients to use sigmoidoscopy given we have evidence it will miss a significant number of early polyps.”

*Dr. Timothy Johnson
ABC News Medical Editor*

The Media Speaks

The Katie Couric Effect



It's considered the most effective test for detecting colon cancer, and as Katie Couric says in her special report, "It really didn't hurt." Katie's first colonoscopy

Cram P, Fendrick MA, Inadomi J, et al. Arch Intern Med 2003;1601-1605

***ACS/USMSTF and ACR Guidelines
Precautions Re Menu of Options***

- *If fecal tests are used the “opportunity for prevention is both limited and incidental and not the primary goal of CRC screening with these tests.”*
- *“It is the strong opinion of this expert panel that colon cancer prevention should be the primary goal of CRC screening and that providers and patients should understand that noninvasive tests are less likely to prevent cancer compared with the invasive tests.”*

The Result – Polyp/CA Phobia



***The Consequences
An Elephant Emerges in the Screening Room***



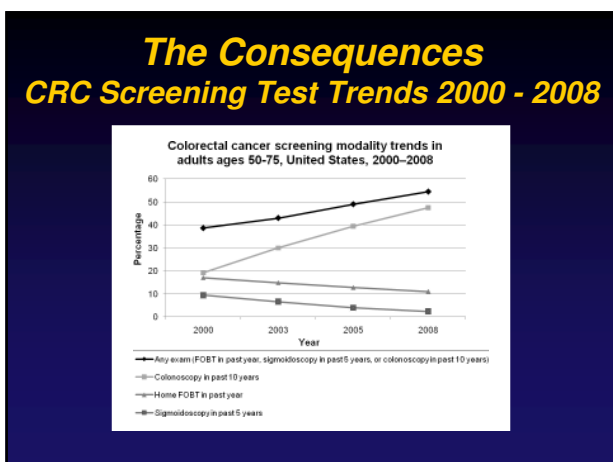
Optical Colonoscopy

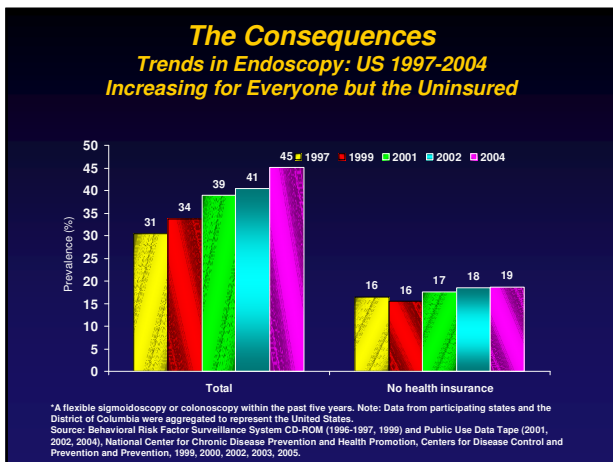
***The Consequences - Cecal Stampede
The Headlong Rush for Screening Colonoscopy***



Lawson MJ, Tobi M Dig Dis Sci. 2008 Apr;53(4):871-4

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The Facts – Large Adenomas

- Large polyps (>1cm) become colorectal cancers at a rate of roughly 1% per year
- A large polyp, left in situ, has a cumulative risk of malignancy at 20 years of only 24%

Ransohoff DF Editorial. *The Lancet* 2002; 359:1266-7.
Stryker S, Wolff B, Culp C, et al. *Gastroenterology* 1987; 93:1009-13.
Eide T. *Int J Cancer* 1986; 38:173-6.

The Facts – Small Adenomas

- Only about 2.5/1000 polyps per year progress to cancer
- The development of invasive cancer from a small (<10mm) adenoma is extremely unlikely in less than five years

*Ransohoff DF Editorial. The Lancet 2002; 359:1266-7.
Stryker S, Wolff B, Culp C, et al. Gastroenterology 1987; 93:1009-13.
Eide T. Int J Cancer 1986; 38:173-6.*

The Facts: Advanced Adenomas

- Most polyps, even the “advanced” ones, do not directly lead to death from colon cancer
- Advanced neoplasia may be considered a convenient proxy for colorectal cancer but its use as an outcome measure may be misleading in screening studies because the natural history of this lesion is unknown

Imperiale TF et al NEJM. 2002 346:1781-1785

Dysplasia in Small Adenomas The Facts

- The prevalence of high grade dysplasia in subjects found with small adenomas was only 1% in a large U.S. colonoscopy study
- Longitudinal studies assessing follow-up of unresected small colorectal adenomas harboring high grade dysplasia is lacking
- We have no idea how many will progress to fatal cancer or over what period of time

Lieberman D, Holub J, Eisen G et al. Gastro 2008;135:1100-05.

The Importance of Small Polyps

“The exaggerated hypothesis that every polyp regardless of how benign appearing, must be treated as a cancer waiting to happen demonstrates reasoning as flawed as managing every pigmented skin nevus as though it were a melanoma.”

*David Morowitz, MD Clinical Professor of Medicine Georgetown University
School of Medicine Gastroenterology & Endoscopy News September, 2006*

Overdiagnosis - Definition

Overdiagnosis - labeling innocuous tumors cancer and treating them as though they could be lethal when in fact they are not dangerous.

“Overdiagnosis is pure, unadulterated harm,”

*Barnett Kramer MD, Associate Director for disease prevention NIH
The NY Times October 21, 2009*

Summary

- The term “advanced adenoma” is misleading because the natural history of this lesion is unknown
- The definition of an advanced neoplasm as used in the gastroenterology literature is very different from that found in a standard pathology textbook
- Most advanced neoplasms are polyps and only a small percentage of them present a risk of progression from benign to malignant status

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Summary

- At present, our ability to identify those that will is limited and based on phenotype
- Adenomas as they are portrayed by the U.S. media and some specialty societies could qualify as good examples of “overdiagnosis”

Conclusions/Recommendations

- Hopefully, new biological tests (stool or serum markers) will be developed that are superior indicators of risk than polyp phenotype
- Until we have such tools we must be mindful of our budget deficits and limited medical resources.
- We must educate the public and legislators that the real risk of any polyp progressing to fatal cancer is small.
- Education will give patients the proper perspective about the real importance of finding or missing a polyp at screening and may both decrease fear and curb the enthusiasm for population screening with expensive and possibly harmful tests



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Flexible Sigmoidoscopy

• There has been the overused analogy of FS as being similar to screening for breast cancer with mammography of a single breast. The "1 breast" argument, while a catchy sound bite, is grossly misleading. If performing mammography on 1 breast detected 67% to 80% of breast cancers and adding an examination of the other breast required sedation, another specialist, a more difficult preparation, a driver, additional time lost from work, a longer wait for scheduling, and carried 15 times the risk of serious complications, cost 3 to 4 times more, and had substantially less supporting outcomes data, we might be performing (or in the United States, at least discussing) single-breast mammography.

Fisher DA 2007 Gastrointestinal Endoscopy 65:646-7

A New Industry Emerges



The Polyp Finding Industry

- Narrow-band imaging (NBI)
- High definition colonoscopy
- Chromocolonoscopy
- Third Eye Retroscope
