



Lahey Hospital
& Medical Center

Colorectal Cancer Screening Using Automated Immunochemical FOBT

Gyorgy Abel, MD, PhD

Medical Director, Clinical Chemistry

Immunology / Molecular Diagnostics / POCT

Department of Laboratory Medicine

Lahey Hospital & Medical Center

gyorgy.abel@lahey.org

Medical Grand Rounds, May 4, 2016

Beverly Hospital, MA

OBJECTIVES:

After completing this activity the attendees will be able to:

- Describe the clinical utility and performance of various CRC screening methods
- Contrast immunological and guaiac based fecal occult blood testing
- Formulate a plan using iFOBT in clinical practice based on evidence and guidelines

CONFLICT OF INTEREST: None.

CDC Report

An estimated 50% to 60% of colorectal cancer deaths could be prevented if all persons aged 50 years or more were screened routinely.

Nearly 140,000 new cases of colorectal cancer are diagnosed annually, and the disease claims more than 56,000 lives, making it the second leading cause of U.S. cancer-related death after lung cancer.

CDC Report

The proportion of Americans 50 or older who had a colonoscopy or sigmoidoscopy within the past 10 years rose to 50.6% in from 45.2%

57.3% of adults aged ≥ 50 years reported having had an FOBT within 1 year preceding the survey and/or a lower endoscopy within 10 years, compared with 54.4 %.

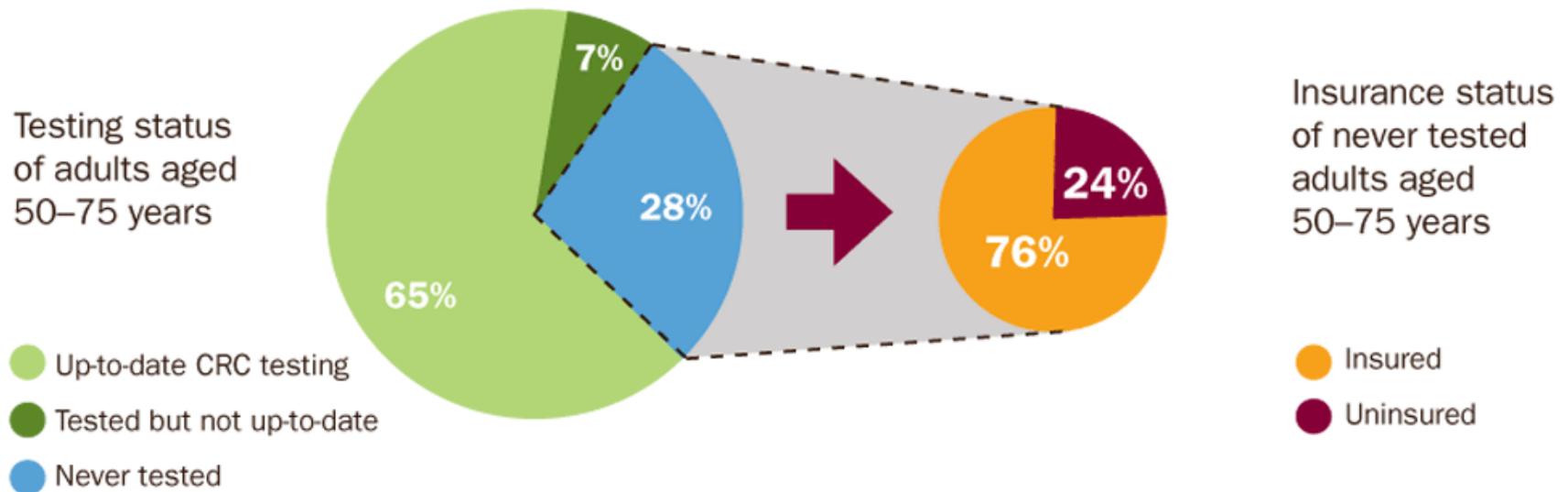
At the same time, the proportion of Americans who had a fecal occult blood test (FOBT) within the past year declined from nearly 22% in to about 19%.

The state with the highest overall screening rate was Minnesota (68%), and the state with the lowest rate was Mississippi (nearly 48%).

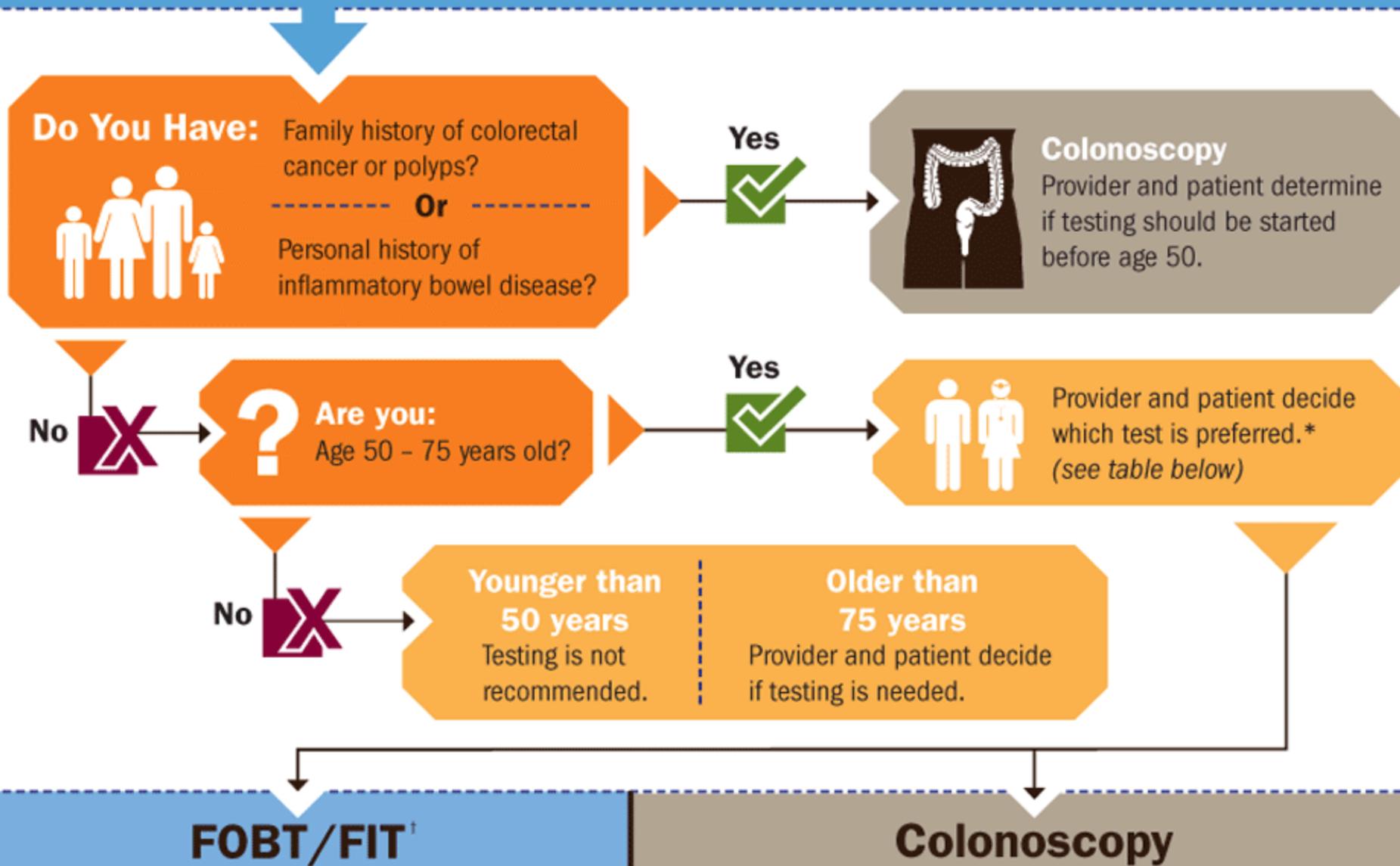
For colonoscopy or sigmoidoscopy in the past 10 years, Minnesota had the highest rate (63.7%) and Mississippi the lowest (41.8%).

(Massachusetts: 66.2%. ACS goal: >80% by 2018.)

Many adults are not being tested



Choosing the right test



FOBT/FIT

Key facts

- Reduces death from colorectal cancer
- Safe, available, and easy to complete
- Done on your own at home
- Finds cancer early by finding blood in the stool
- Finds most cancers early when done every year

Things to consider

- May produce positive test results, even when no polyps or cancer are in the colon
- When the test is positive colonoscopy is required
- Person testing themselves comes into brief close contact with stool samples on a test kit and must mail it or take it to a doctor's office or lab

† *Guaiac Fecal Occult Blood Test (FOBT) or Fecal Immunochemical Test (FIT)*

Colonoscopy

Key facts

- Reduces death from colorectal cancer
- Can prevent cancer by removing polyps (or abnormal growths in the colon) during test
- Examines entire colon
- Finds most cancers or polyps that are present at the time of the test
- Done every 10 years if no polyps are found

Things to consider

- Stomach pain, gas or bloating is possible before, during or after test
- Must be performed at a hospital or clinic, usually with sedation or anesthesia, and someone must go with the person to take him or her home after the test
- A clear liquid diet is required before test
- Must take medication that will cause loose bowel movements to clean out the colon prior to test
- Likely needs to take a day off work/activities
- Small risk of serious complications (for example, bleeding or perforated colon)

**Flexible sigmoidoscopy may not be readily available and has largely been replaced by colonoscopy in the US.*

| FOBT/FIT | Colonoscopy |
|--|---|
| <p>Key facts</p> <ul style="list-style-type: none"> • Reduces death from colorectal cancer • Safe, available, and easy to complete • Done on your own at home • Finds cancer early by finding blood in the stool • Finds most cancers early when done every year <p>Things to consider</p> <ul style="list-style-type: none"> • May produce positive test results, even when no polyps or cancer are in the colon • When the test is positive colonoscopy is required • Person testing themselves comes into brief close contact with stool samples on a test kit and must mail it or take it to a doctor's office or lab <p>†Guaiac Fecal Occult Blood Test (FOBT) or Fecal Immunochemical Test (FIT)</p> | <p>Key facts</p> <ul style="list-style-type: none"> • Reduces death from colorectal cancer • Can prevent cancer by removing polyps (or abnormal growths in the colon) during test • Examines entire colon • Finds most cancers or polyps that are present at the time of the test • Done every 10 years if no polyps are found <p>Things to consider</p> <ul style="list-style-type: none"> • Stomach pain, gas or bloating is possible before, during or after test • Must be performed at a hospital or clinic, usually with sedation or anesthesia, and someone must go with the person to take him or her home after the test • A clear liquid diet is required before test • Must take medication that will cause loose bowel movements to clean out the colon prior to test • Likely needs to take a day off work/activities • Small risk of serious complications (for example, bleeding or perforated colon) |
| <p>*Flexible sigmoidoscopy may not be readily available and has largely been replaced by colonoscopy in the US.</p> | |
| <p>SOURCE: Vital Signs 2013 and USPSTE </p> | |

Colorectal Cancer Screening: Multiple Option Approach* for Average-Risk Persons†

Options

- Annual fecal occult blood testing
- Flexible sigmoidoscopy every 5 years
- Annual fecal occult blood testing plus flexible sigmoidoscopy every 5 years
- Double-contrast barium enema every 5 years
- Colonoscopy every 10 years

*This approach was originally proposed by a multidisciplinary consortium often referred to as the American Gastroenterological Association consortium and subsequently followed by the American Cancer Society.

†Average-risk persons are age 50 or older without other risk factors for colorectal cancer.

Evidence Based Medicine

“The recommendation that all women and all men aged 50 years or older undergo screening for colorectal cancer is supported by a large body of direct and indirect evidence. At present, the available evidence does not currently support choosing one test over the other.”

“If either the FOBT or the sigmoidoscopy has an abnormal result, then complete colonoscopy is indicated.”

Sensitivity, specificity, positive and negative likelihood ratios of immunochemical FOBT for cancer alone and cancer and high-risk adenomatous polyps

| | Sensitivity, % (95% CI) | Specificity, % (95% CI) | Positive likelihood ratio (95% CI) | Negative likelihood ratio (95% CI) |
|---|----------------------------|----------------------------|---------------------------------------|---------------------------------------|
| Cancer | 95.0 (81.8–99.1) | 39.5 (36.0–43.1) | 1.57 (1.43–1.72) | 0.13 (0.03–0.49) |
| Cancer and high-risk adenomatous polyps* | 90.1 (84.4–94.0) | 47.8 (43.9–51.8) | 1.73 (1.58–1.89) | 0.21 (0.13–0.33) |

Negative=N/N and N/P. Positive=P/P. *polyps > 10 mm diameter or >3 adenomatous polyps.

Table 4: Sensitivity, specificity, positive and negative likelihood ratios of immunochemical FOBT for cancer alone and cancer and high-risk adenomatous polyps

Lancet Oncology, February 2006; 7:127

Colonoscopy Is the Preferred Approach to Average-Risk Screening:

Proposed by the American College of Gastroenterology

Preferred Strategy:

Colonoscopy every 10 years

Alternate Strategy:

Annual fecal occult blood testing plus flexible sigmoidoscopy every 5 years

“Serial guaiac-based FOBT is simple, inexpensive, and proven effective at reducing mortality from CRC.

Immunochemical FOBTs facilitate compliance and offer improved specificity.”

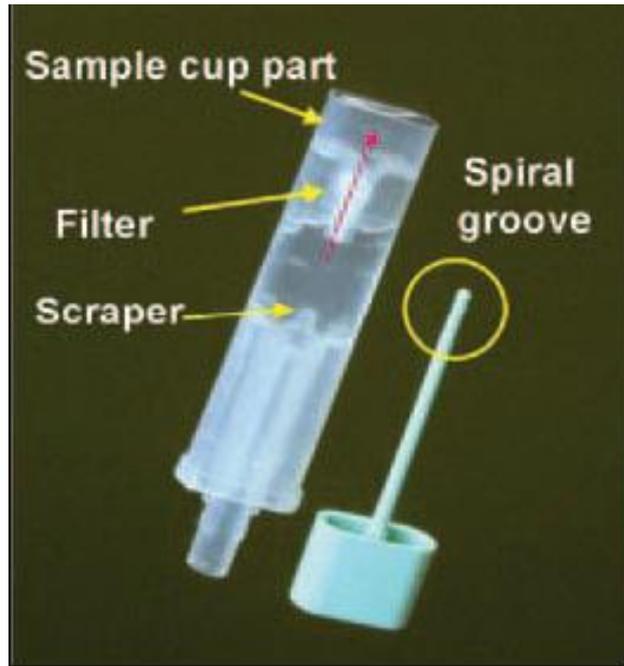
Performance Characteristics and Evaluation of an Automated- Developed and Quantitative, Immunochemical, Fecal Occult Blood Screening Test.

Am J Gastroenterol 2005; 100:2519

OBJECTIVES:

Guaiac fecal occult blood colorectal cancer (CRC) screening tests (FOBT) are faulted for low sensitivity and nonspecificity for human hemoglobin (Hb). Automated-developed, immunochemical, human Hb FOBT (I-FOBT) is specific, eliminates diet restrictions, and Hb quantification allows selection of a threshold for colonoscopy.

Aims were to determine 1) test reproducibility; 2) test stability; 3) intrapatient daily i-FOBT variation; 4) test sensitivity and specificity for neoplasia in 500 symptomatic/high-risk patients undergoing colonoscopy; and 5) to correlate fecal Hb measurements with findings.



Left: Stool probe and fecal sample storage tube. The closed tube is 8 cm long, 2 cm wide. On each tube there is a unique bar code and space to write name and date.

Right: Desktop instrument and accessories. The instrument is 32 cm wide, 53 cm deep, and 42 cm high.

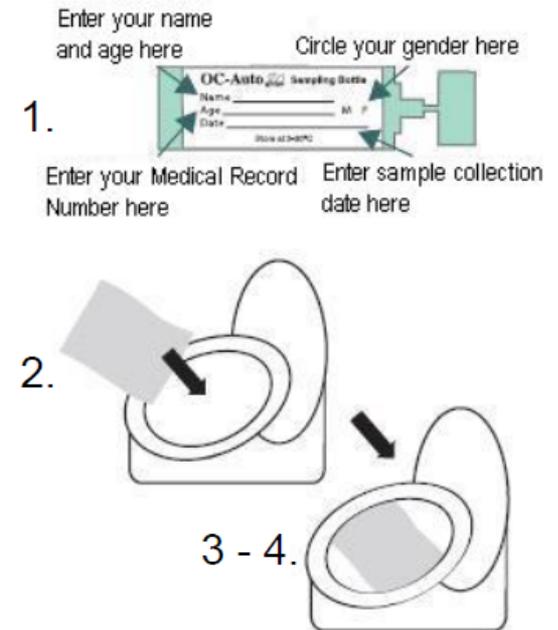
Polymedco Fecal Occult Blood Collection Kit

Read these instructions carefully before taking the stool (fecal) sample.

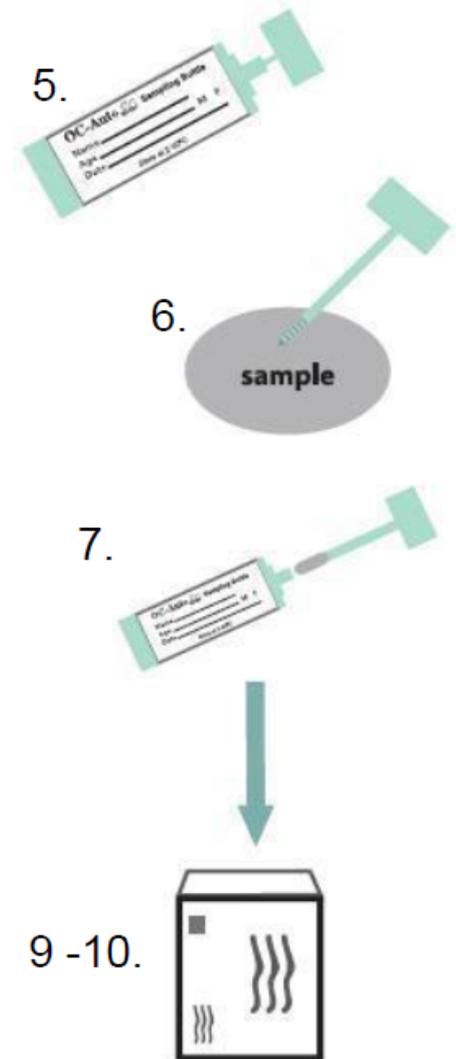
It is important to follow all of the steps: If you do not collect the sample as described below, your test result may be affected. If you have blood in your stool (rectal bleeding) right now, please wait until after the bleeding has stopped to collect your sample.

You do not need to change your diet or medications to collect this sample.

1. If the collection bottle is not already pre-labeled with a bar code, please write your **Name**, **Medical Record Number**, and **Collection Date** on the sample bottle. **Please print clearly.**
2. When you are ready to collect the sample, unfold the large collection tissue paper. (At this point, do **not** use the small absorption pad included in the return envelope. This is used for mailing your sample.)
3. Place the collection tissue paper inside the toilet bowl on top of the water.
4. Produce a stool sample so that it falls on top of the tissue paper.



5. Open the sample bottle by gently twisting and lifting the green cap straight out. The sample probe with a grooved tip is attached to the green cap. The sample bottle contains a liquid preservative that is needed to process your sample. **Do not throw away this liquid.**
6. Scrape the surface of the stool with the grooved tip of the sample probe. Cover the grooved tip completely with stool.
7. Gently insert the sample probe, with the stool on it, directly into the sample bottle. Push in the green cap until you hear it click into place. **Do not reopen.** If some stool sample is on the outside of the bottle, please wipe it off before mailing the bottle.
8. Flush the toilet. (Collection tissue paper will not harm septic systems.)
9. Place your sample bottle and the small absorption pad inside the plastic bio-hazard bag. Securely zip the plastic bag. Insert the plastic bag inside the return envelope. Place the lab order form in the same envelope and seal.
10. Mail the envelope within 3 days of your sample collection. No postage is required.



*If you have any questions or need help using this test kit,
please call your doctor's office directly.*

Thank you for helping us keep you healthy!

**Sensitivity and Specificity for Significant Colorectal Neoplasia,
(N = 34)* at Differing Fecal Hb Levels (N = 500)†**

| Fecal Hb (ng/mL) | Sensitivity (%) | Specificity (%) |
|---------------------|--------------------|--------------------|
| 50 | 79.4 | 89.7 |
| 75 | 76.5 | 93.3 |
| 100 | 76.5 | 95.3 |
| 125 | 70.6 | 95.7 |
| 150 | 70.6 | 95.9 |
| 200 | 64.7 | 96.3 |

* Six colorectal cancers and 28 advanced adenomatous polyps.

†Utilizing the highest of the three I-FOBT measurement in each patient.

Colon Cancer Screening Guidelines 2005: The Fecal Occult Blood Test Option Has Become a Better FIT

- The overall positivity rate in the automated FIT was **5.6%**.
- The sensitivity of the FIT for colon cancer was 66% and 20% for polyps > 1 cm.
- A 66% sensitivity for cancer is a marked improvement over the colonoscopy confirmed 13%–39% sensitivity reported for the most commonly used guaiac tests (GT).

Gastroenterology 2005; 129:745. Editorial

The Guaiac Test:

Heme either as intact hemoglobin or free heme has peroxidase-like activity therefore, in the presence of heme and a developer (hydrogen peroxide), guaiac acid is oxidized producing a blue color.

Heme is present in red meat, and peroxidase activity is present in fresh fruits and vegetables such as radishes, turnips, and broccoli. These foods, therefore, have the potential to produce false-positive results.

Results are affected by vitamin C, which inhibits the guaiac reaction.”

*“The fecal immunochemical tests (FIT) address many of the weaknesses of the GT. They have superior sensitivity and specificity. **The application sensitivities for cancer are good (66%–82%)** but for polyps > 1 cm they are more modest; however, the use of a program of fecal occult blood test (FOBT) screening (in which screening is performed yearly or every other year) may result in a **cumulative sensitivity** of the program that is competitive with a program of a more sensitive test performed less frequently. A combined program of FOBT plus sigmoidoscopy may be as effective as or more effective than a program of colonoscopy screening every 10 years because improved FOBT tests such as FIT are more sensitive than the widely used Hemoccult II.”*

Gastroenterology 2005; 129:745. Editorial

Eiken OC automated FOBT – FDA approved

Cost per test: \$8-10

Immunoassay FOBT Testing coverage:

CPT Code-82274 (*Blood occult by fecal hemoglobin determination by immunoassay qualitative feces 1-3 simultaneous determinations*)

HCPS Code-G0328 (*Fecal blood screening immunoassay*)

\$21.67 Medicare National Average

\$20.19 Massachusetts Medicare

\$14.65 Massachusetts Medicaid

... at Lahey Hospital & Medical Center and Lahey Health

About 14,000 colonoscopies performed annually.

5,340 automated iFOBT tests performed annually
279 positives (positive rate = 5.2%)

We are currently reviewing the follow-up and outcomes from the testing (clinical performance and follow-up of the positives).

New test codes in Epic:

“**LAB4369** Occ Bld, Fecal Immunochemical, Cancr Scr”

“**LAB 4368** Occult Blood, Guaiac, Non Cancer Screen”

Lahey Health-wide expansion of automated iFOBT CRC screen is underway.

About the Cologuard Fecal DNA Test (Exact Sciences)

- Heavily marketed in full page ads in the Boston Globe and NYTimes
- Test performed at the Cologuard laboratory in Wisconsin, patients send the specimen directly to them.
- They directly bill the insurer, and balance bill the patient for any additional charges. The patient agrees to this on the requisition.
- The 'maximum out of pocket charge' is \$649, but it is not clear how this works with Medicare (seems to depend on the plan).
- The Cologuard test needs a physician's order.
- While the Cologuard test is FDA cleared, it is NOT recommended by the USPSTF for colorectal cancer screening
- The Cologuard costs \$599.
- Specimen collection is more involved (300 g specimen required, need packaging of full bowel movement) with the Cologuard test.

About the Cologuard Fecal DNA Test (Exact Sciences)

- A recent comparison study published in JAMA demonstrated slightly *higher sensitivity* but *somewhat lower specificity* of the DNA test than the automated FIT-CHECK.
- Cologuard performs better than FIT in the detection of *serrated polyps*.
- May be O.K. in rare cases if self-pay or if insurance payment is secured, or in certain executive health programs.
- I do not recommend it as a routine alternative or replacement of our current automated FIT CRC screening assay. The costs of the DNA test would be prohibitive and the benefits have not been clearly established.

DNA Blood Test for CRC Screening – *Epi proColon*

- Manufactured by Epigenomics.
- The first molecular DNA blood test FDA approved for patients who have refused colonoscopy and/or a FIT test.
- Sensitivity of 71%, and specificity of 82% for CRC.
- Overall patient compliance of 99%.
- More information is needed before larger scale introduction.

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