

OMED COLORECTAL CANCER SCREENING COMMITTEE MEETING

Saturday, May 1, DDW New Orleans, 2010

Presenter: Paul Rozen

What is the Perfect Fecal Test in 2010? An Overview

Paul Rozen

Prof. (Emeritus) Tel Aviv University;
Director, Sestopali Fund for Gastrointestinal
Cancer Prevention;
Dept. of Gastroenterology,
Tel Aviv Medical Center, Israel



World Organisation of Digestive Endoscopy

Colorectal Screening Committee

What is the Perfect Fecal Test in 2010?

An Overview

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Fecal test for colorectal (CR) neoplasms
detect **occult blood** (FOBT) or **other** tumor products

Test **characteristics** needed include:

- Ease of Preparation & Transport
- Stability & Standardized Processing
- Highly Sensitive for CRC, or CRC + AAP
- Highly Specific: minimizing **unnecessary** colonoscopies
- Program Sensitivity & Specificity:
- Costs:
- Non-FOBTs:
- Test Comparison with Recognized Methodologies:

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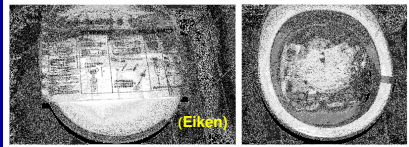
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Fecal occult blood tests (FOBT) & Others	
Office Processed <i>Guaiaac</i> Not Human Hb Specific <ul style="list-style-type: none">▪ Hemoccult 11▪ Hemoccult SENSa	Laboratory Processed <i>Immunochemical</i> Fixed Sensitivity for Hb <ul style="list-style-type: none">▪ MagStream HemSp▪ InSure
<i>Immunochemical</i> Human Hb Specific Fixed Sensitivity for Hb <ul style="list-style-type: none">▪ Hemoccult ICT (FlexSURE)▪ InSure▪ OC-Hemodia	Hb Quantified <ul style="list-style-type: none">▪ OC-Sensor /MICRO Other Fecal Constituents <ul style="list-style-type: none">▪ Genetic products▪ Cellular products▪ Cytology

Easy Preparation & Stool Sampling

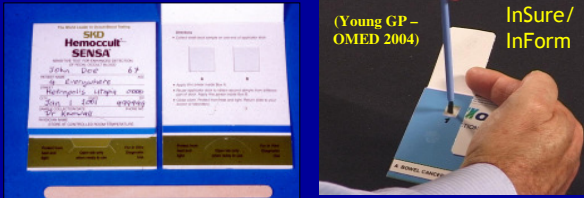
Need to provide toilet-**disposable** stool **collection paper**

- This “floats” in the toilet bowl & flushed after stool sampling.
- Feces collected using sampling stick.



Most test-kits provide sampling stick or probe or brush that should be **convenient to use**.

G-FOBT	InSure I-FOBT
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- Uses **stick** for fecal sampling
- **6** samples during **3d**

- (Young GP – OMED 2004)
- Uses **brush** to sample toilet water adjacent to feces
- **2** samples during **2d**

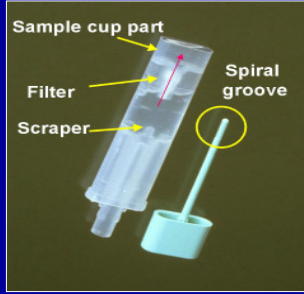
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OC-MICRO: Stool sampling

- After fecal sampling, stick reinserted into tube, pushed thru a scraper & membrane
- ~10 mg of feces remain attached to grooves on tip (depending on fecal consistency)
- Feces then dissolved in 2 mL buffer & stable ~21 days at 4°C



Courtesy of ALFA WASSERMANN, Milan, Italy

Characteristics Needed: Transportation

- Most **dry** & **some fluid** FOBTs can be sent by **mail**.
- Multiple **fluid** samples, in a hot climate, are best **refrigerated** & **hand-returned**, ± cold-pack, to refrigerated collecting points.

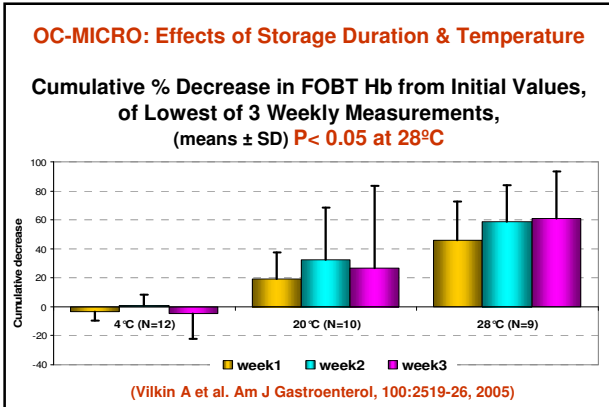
Characteristics Needed: Sample Stability

- There is rapid **degradation** of fecal Hb in non-frozen **whole stool** collections.
- **Dry** FOBTs are stable at room temperature for ~2 wks.
- Fecal Hb stability in **fluid** FOBTs depends on **buffer** used & **ambient temperature** which effects **rate** & **degree** of Hb degradation.

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Characteristics Needed: Standardized Processing Office FOBTs (G-FOBT)

Test processing & interpretation by **trained** personnel

Hemocult 11 vs. Hemocult SENS^a

(more sensitive)
(Beckman Coulter)

Hemocult[®] and Hemocult[®] SENS^a
COMPARISON OF OCCULT BLOOD TEST RESULTS

Processing Office- I-FOBTs:

Hemocult ICT (FlexSURE) (Beckman Coulter),
& InSure (Enterix)

More complex test processing & interpretation by **trained** personnel

1. Sample window
Collection card front

2. Collection card back

3. Sample tab
Test card

4. Test card complete
Test card positive reading

Control
Kontrolle
Contrôle
Controllo

Test

Pos

Neg

Invalid

Ungültig / Non valide
No válido / Non valido

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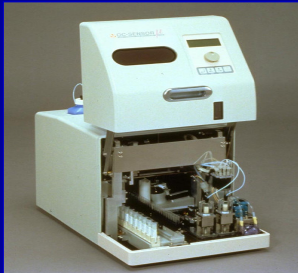
InSure Automated Laboratory Processing

(Young GP OMED 2004)

- Fully automated:
- Barcode identification
- Reagent added
- Wait five minutes
- Capture image
- Read result

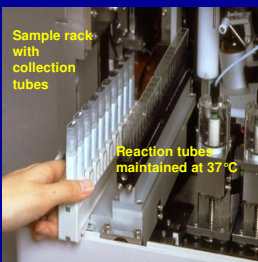


Processing I-FOBTs (OC-MICRO - Eiken) Automated processing & Hb quantified



- Bar code labels on collection tubes.
- Tubes loaded in rack

Automated processing & Hb quantified



Courtesy of ALFA WASSERMANN, Milan, Italy

- Hb-antibody flocculation measured by LED
- Hb concentration calculated. Range 50-2,000ngHb/mL buffer = 10- 400µg Hb/g feces.
- Print-out:
 - Hb measurements,
 - ID numbers,
 - error messages.

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Characteristics Needed: Sensitivity Should be Maximal for CRC

- A **number** of samples are needed to **compensate** for:
 - **intermittent** bleeding, **non-representative** or non-standardized sampling.
 - **effects** of ambient temperature, transport & duration before processing.
- Depending on **No. of samples & Hb threshold** used, **quantified** I-FOBT allows determining sensitivity for **CRC**, or **CRC & AAP**, or **CRC & AAP & non-AAP**.

Characteristics Needed: Specificity

Determines the **need for colonoscopy** follow-up:

- Should **maximize** the diagnosis of CRC & AAPs for polypectomy.
- **Least** number of colonoscopies for positive FOBTs to identify a CRC &/or AAP.

Fecal Hb giving **maximum sensitivity** for CRC, or CRC or AAP
& **No. colonoscopies** for positive I-FOBTs

From **ROC** results in **1,682 colonoscopy** patients with **3 I-FOBTs** analyzed by OC-MICRO

P Rozen, et al. Cumulative evaluation of a quantitative immunochemical fecal occult blood test to determine its optimal clinical use. *Cancer* 2010;116:2115-25.

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Fecal Hb giving maximum sensitivity & associated specificity (%) for CRC (20), CRC or AAP (149)

Fecal Hb ng/mL buffer	1st I-FOBT		Higher of 2 I-FOBTs		Highest of 3 I-FOBTs	
	Sens.	Spec.	Sens.	Spec.	Sens.	Spec.
CRC						
64.5	75	92.3				
56			95	88.4		
56.5					100	85.7
CRC or AAP						
60	41.6	94.1				
51.5			55	90.5		
54.5					61.6	88.7

No. colonoscopies needed for positive I-FOBTs for each CRC ± AAP detected

No. colonoscopies depends on:

- fecal Hb **threshold** chosen to determine a positive test
- **No.** fecal samples examined

No. colonoscopies needed for positive I-FOBTs for each CRC ± AAP detected

At **50ng threshold**, for CRC or AAP, examining:

- **1st** test required colonoscopy on **2.7** persons
- Higher of **2** tests required colonoscopy on **2.8** persons, detecting **32.3% more** neoplasms ($P < 0.001$)
- Highest of **3** tests required colonoscopy on **3.1** persons, detecting **11% more** neoplasms ($P = 0.004$)

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Program Sensitivity & Specificity

Screening tests are **repeated** during “dwelling time” period that disease **remains curable**.

➤ **Initial** screening should identify **almost all asymptomatic CRC ± some AAP**, & their endoscopic removal prevents CRC

▪ With **minimal** unrewarding **colonoscopies** for positive tests.

➤ **Cumulative** screening should reduce CRC **mortality** by identifying **AAPs**, & their endoscopic removal prevents CRC

FOBT Costs

Vary from:

▪ <\$10 for the **guaiac** FOBT

▪ to >\$20-30 for **I-FOBT**

▪ to >\$100 for fecal **DNA** tests.

❖ The **acceptable cost & neoplasia yield** depend on the screening **policy**.

Non-FOBTs

Include fecal :

▪ **DNA**

▪ **cellular products**

▪ **cytology**.

They have **not** been shown to be **cheaper** or more **sensitive or specific** than the **quantified I-FOBT**

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Test Comparison with Recognized Methodologies

New tests need to be compared with proven screening tests such as:

- Colonoscopy
- Guaiac FOBT

P Rozen et al. Quantitative colonoscopic evaluation of relative efficiencies of an immunochemical fecal occult blood test and a sensitive guaiac test for detecting significant colorectal neoplasms. *Aliment Pharmacol Ther.*29:450-457, 2009

Comparative Sensitivities & No. colonoscopies for positive FOBTs for each neoplasm (CRC or AAP) detected

- 3 x 2 HOS had 53.1% sensitivity & required 8.1 colonoscopies.
- 1st I-FOBT at 50ngHb/mL buffer had 53.1% sensitivity & required 2.1 colonoscopies.
- Higher of 2 I-FOBTs at 50ng had 68.8% sensitivity (29.5% more) & required 2.1 colonoscopies.
- Highest of 3 I-FOBTs at 50ng had 75.0% sensitivity (9.1% more) & required 2.6 colonoscopies.

Conclusions

The quantified immunochemical human-Hb-specific FOBT is probably the most efficient screening test available, reducing the No. of unneeded colonoscopies.

- eliminates diet restrictions
- provides quality-control of development
- allows selection of a Hb level for colonoscopy

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**Acknowledgments &
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