

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: John Baillie, MB ChB, FRCP

Chromoendoscopy

Firas H. Al-Kawas, MD
Chief of Endoscopy
Georgetown University Hospital
Professor of Medicine
Georgetown University School of Medicine

G&H What is chromoendoscopy?

FA Chromoendoscopy is a diagnostic technique that combines staining and endoscopy. Different areas visible through the endoscope are highlighted with one of a variety of available stains. Magnifying endoscopy further enhances this technique

G&H In what specific settings is chromoendoscopy typically used?

FA Chromoendoscopy is used in many different settings, but the most common and important use is in the diagnosis of precancerous lesions or early cancer. This technique helps identify areas that can be targeted for biopsy or treatment. Different stains highlight areas of cellular change that can then be targeted for biopsy.

G&H When was chromoendoscopy first developed?

FA Investigators in Japan were the first to use staining in combination with endoscopy; these researchers used chromoendoscopy to highlight the surface of polyps and to screen areas of the stomach for early gastric cancer. This method was used for many years in Japan before its introduction in the United States.

G&H Could you describe your study of chromoendoscopy in the evaluation of colonic polyps?

FA The main purpose of this study was to see if chromoendoscopy using indigo carmine staining could enable endoscopists to differentiate between precancer-

ous polyps, such as adenomas, and hyperplastic polyps that do not progress to cancer. Generally, it is difficult to determine whether a polyp, which can be quite small, is precancerous without a biopsy. Staining polyps with indigo carmine enabled endoscopists to correctly predict for the majority of polyps whether or not they were precancerous. The accuracy was not 100%, but this study and others have shown that chromoendoscopy is a very effective way to distinguish between adenomatous and nonadenomatous polyps.

G&H Is chromoendoscopy being used to detect precancerous conditions in patients with Barrett's esophagus?

FA Yes, this area is currently being explored. There are some studies in this setting suggesting that methylene blue highlights potentially precancerous areas. The endoscopist would then biopsy this specific area in order to determine whether the cells are indeed precancerous, that is, exhibiting high dysplasia. The data in this setting are still preliminary and there is some debate about whether the findings have been successfully duplicated in other studies. However, this approach appears promising so far.

As mentioned above, the same approach is being evaluated for diagnosing precancerous conditions in the stomach. A stain is sprayed, followed by an endoscopy with magnification. Investigators are currently evaluating whether this technique can distinguish between normal and abnormal areas. Biopsies can then be targeted to the potentially abnormal areas, rather than being done in a blind or random fashion.

G&H Could you describe how this technique works?

FA The technique of chromoendoscopy is very simple, varying slightly according to the specific dye that is used. In general, the area to be stained is washed using a catheter passed through the working channel of the endoscope, and then the dye is applied.

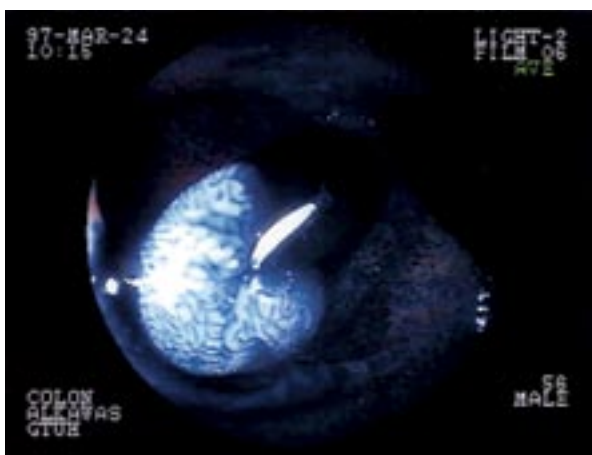


Figure 1. Colon adenoma: typical appearance with indigo carmine staining.



Figure 2. Early esophageal cancer. (A) Before Lugol staining. (B) After Lugol staining.

G&H Does this approach add time or expense to the normal endoscopy procedure?

FA Adding staining to the endoscopy procedure does not add a significant expense. Many endoscopists are concerned about the additional time required, and therefore in busy endoscopy units staining tends not to be used. However, emerging data from studies in the United States, Europe, and Japan show that staining adds only a few minutes to the standard endoscopy procedure and in certain situations, such as examining polyps or Barrett's esophagus, may be highly beneficial.

G&H Is chromoendoscopy being underutilized?

FA Yes, although in the United States endoscopists are becoming more aware of the value of chromoendoscopy, particularly in targeting biopsies in Barrett's esophagus and precancerous lesions, and in further identifying lesions prior to mucosectomy. At the present time, however, the technique is still underutilized.

G&H What are the different dyes that are used, and what are their specific purposes?

FA The dyes that are most commonly used are those that enhance the appearance of the surface (ie, contrast dyes), thus better revealing the details of the mucosa, particularly when using a magnifying endoscope. The two dyes in this category are methylene blue and indigo carmine (Figure 1).

Other dyes are called absorptive dyes and they help to identify the type of cell that is present in the esophagus or stomach. For example, Lugol's solution would be the dye of choice when searching for squamous mucosa in the esophagus (Figure 2). Here, the areas that do not absorb Lugol's solution would be suspected for cancer, because cancerous cells do not contain glycogen and therefore do not absorb this dye.

Methylene blue is another example. Intestinal metaplasia cells will absorb methylene blue, which is why this dye is used in evaluating patients with Barrett's esophagus. Additionally crystal violet and toluidine blue are absorbed by malignant cells and can help identify early cancer.

G&H In what other settings is chromoendoscopy being used?

FA This technique is also being used in evaluating patients with ulcerative colitis undergoing screening for dysplasia or small areas of cancer. In this setting, methylene blue can be sprayed during colonoscopy to help highlight suspicious areas. Alternatively, the dye may be taken orally the day before a colonoscopy. When the colonoscopy is performed, the colon is already stained. There are some early data, mainly from Japan, showing the potential benefit of this approach. Data also suggest that magnification endoscopy may be needed in this setting.

Another application of contrast dyes is to highlight hard-to-see flat lesions and residual tissue after polypectomy and mucosectomy, thereby allowing more precise management.

In the research setting, indigo carmine has been used to identify aberrant crypt foci in the rectum. Methylene blue has been used during endoscopic retrograde cholangiopancreatography to help identify the pancreas opening in the minor ampulla or after biliary sphincterotomy of the major ampulla (Figure 3).

G&H How does tattooing work?

FA One of the major problems with endoscopy occurs when a polyp is removed and is found to be cancerous. If the patient subsequently undergoes surgery, the surgeon needs to know exactly where the malignant polyp or cancer was in order to remove that specific portion of

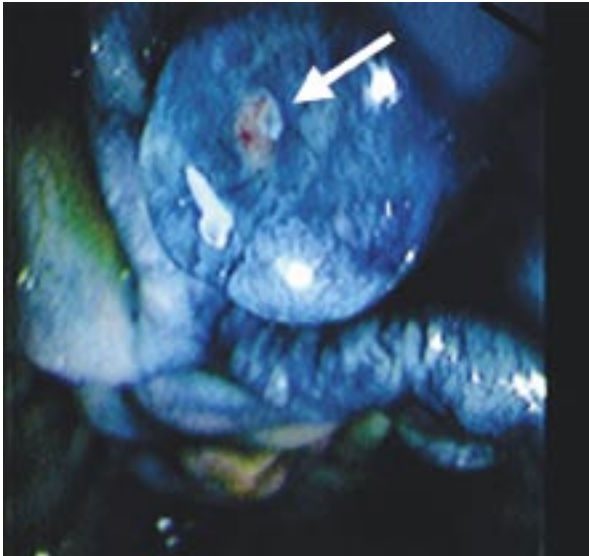


Figure 3. Minor papilla after application of methylene blue. Arrow points to pancreatic duct opening.

the bowel. Because of the looping in the bowel, it can be difficult to distinguish between different areas or provide reliable distance.

Permanent tattooing was initially done with India ink, but this dye was found to be associated with severe local reactions when injected into the bowel wall. A purified form of India ink and a suspended sterile carbon preparation (SPOT, GI Supply) were subsequently developed. The ink is injected in the vicinity of the lesion so that the surgeon will be able to see it, or so the endoscopist will know exactly where the polyp was for further therapy or follow up.

There is also nonpermanent tattooing with methylene blue. This dye is mixed with saline and injected submucosally to raise polyps. This technique allows for safer polypectomy and helps the pathologist identify the cut surface of a sessile polyp in case of advanced pathology. Nonpermanent tattooing is also useful when performing a mucosectomy or removing flat polyps because it provides a simple way to identify the boundaries of the area that has been removed.

G&H What side effects have been associated with chromoendoscopy?

FA Rarely, patients experience nausea, abdominal pain, or heartburn. Very rarely, patients can have an allergic reaction to the dye used. Methylene blue is absorbed and patients may be concerned about blue urine, and should be made aware of this in advance.

If tattooing is performed properly, there are no significant risks. Cases have been reported in which the fluid has been injected outside the bowel. As mentioned above, if the older preparations of India ink are used, patients may experience severe local tissue reaction.

Suggested Reading

- Hurlstone DP, Fujii T. Practical uses of chromoendoscopy and magnification at colonoscopy. *Gastrointest Endosc Clin N Am.* 2005;15:687-702.
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- Canto M. Chromoendoscopy and magnifying endoscopy for Barrett's esophagus. *Clin Gastroenterol Hepatol.* 2005;3(7 suppl 1):S12-S15.
- Eisen GM, Kim CY, Fleischer DE, et al. High-resolution chromoendoscopy for classifying colonic polyps: a multicenter study. *Gastrointest Endosc.* 2002;55:687-694.