BACKGROUND

Adenomatous polyps are the most common neoplasm found in people who are screened or who have a diagnostic work-up (1–4). Removal of these adenomas reduce the risk for future colorectal cancer and advanced adenomas (5,6). Patients with adenomas usually are placed into a surveillance program of periodic colonoscopy to remove missed synchronous and new metachronous adenomas and cancers (7–9). The dramatic increase in screening colonoscopy places a huge burden on medical resources applied to surveillance (10–12).

The US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society (USMSTF/ACS) issued updated guidelines on post-polypectomy surveillance (7) (Table 1, 2). These guidelines differ from the earlier guidelines in several ways (7–9): it offered a consensus statement that strengthens the guidelines; it specifically examined predictors of advanced adenomas and incorporated them into the guidelines; and we emphasized the quality of baseline colonoscopy and its impact on detection of post-polypectomy colorectal cancer (5,13). Risk stratification could reduce markedly the intensity of follow-up evaluation in a substantial proportion of patients, so that colonoscopy resources could be shifted from surveillance to screening and diagnosis (14,15). The USMSTF/ACS performed a Medline search of the postpolypectomy literature under the subject headings “colonoscopy” and “adenoma,” “polypectomy surveillance,” and “adenoma surveillance,” limited to English language articles from 1990 to 2005. The final review was based on 15 studies (5,13,21,16–18,19–26).

RATIONALE FOR THE NEW GUIDELINES

Some characteristics of colorectal adenomas at baseline colonoscopy are associated with subsequent adenoma detection and the histologic severity of subsequent adenomas. These data can be used as the
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Table 1
Surveillance Recommendations

1 Patients with small rectal hyperplastic polyps should be considered to have normal colonoscopies, and therefore the interval before the subsequent colonoscopy should be 10 years; an exception is patients with a hyperplastic polyposis syndrome; they are at increased risk for adenomas and colorectal cancer and need to be identified for more intensive follow-up evaluation.

2 Patients with only one or two small (<1 cm) tubular adenomas with only low-grade dysplasia should have their next follow-up colonoscopy in five-to-ten years; the precise timing within this interval should be based on other clinical factors (such as prior colonoscopy findings, family history, and the preferences of the patient and judgment of the physician).

3 Patients with three to ten adenomas, or any adenoma 1 cm, or any adenoma with villous features, or high-grade dysplasia should have their next follow-up colonoscopy in three years providing that piecemeal removal has not been performed and the adenoma(s) are removed completely; if the follow-up colonoscopy is normal or shows only one or two small tubular adenomas with low-grade dysplasia, then the interval for the subsequent examination should be five years.

4 Patients who have more than 10 adenomas at one examination should be examined at a shorter (<3 years) interval, established by clinical judgment, and the clinician should consider the possibility of an underlying familial syndrome.

5 Patients with sessile adenomas that are removed piecemeal should be considered for follow-up evaluation at short intervals (two-to-six months) to verify complete removal; once complete removal has been established, subsequent surveillance needs to be individualized based on the endoscopists judgment; completeness of removal should be based on both endoscopic and pathologic assessments.

6 More intensive surveillance is indicated when the family history may indicate HNPCC.

Table 2
Additional Surveillance Considerations

1 The present recommendations assume that colonoscopy is complete to the cecum and that bowel preparation is adequate; a repeat examination should be performed if the bowel preparation is not adequate before planning a long-term surveillance program.

2 There is clear evidence that the quality of examinations is highly variable; continuous quality improvement process is critical to the effective application of colonoscopy in colorectal cancer prevention.

3 A repeat examination is warranted if there is a concern that the polyp was removed incompletely, particularly if it shows high-grade dysplasia.

4 Endoscopists should make clear recommendations to primary care physicians about when the next colonoscopy is indicated.

5 Given the evolving nature of guidelines, it is important that physicians and patients should remain in contact so that surveillance recommendations reflect changes in guidelines.

6 Pending further investigation, performance of FOBT is discouraged in patients undergoing colonoscopic surveillance.

7 Discontinuation of surveillance colonoscopy should be considered in patients with serious comorbidities with less than 10 years of life expectancy, according to the clinician’s judgment.

8 Surveillance guidelines are intended for asymptomatic people; new symptoms may need diagnostic work-up.

9 The application of evolving technologies such as chro-mendoscopy, magnification endoscopy, narrow band imaging, and computed tomography colonography are not established for postpolypectomy surveillance at this time.
basis for decisions about safe and effective post-polypectomy surveillance intervals by stratifying patients into lower-risk and higher-risk groups for future advanced adenomas (27). The available body of evidence is the basis for these recommendations. Advanced Adenomas are defined as \( \geq 1 \) cm, or with villous features, or with high-grade dysplasia (HGD).

**QUALITY OF INITIAL COLONOSCOPY**

The baseline colonoscopy needs to be of high quality for the baseline adenoma characteristics to be used for planning surveillance intervals. As defined by the USMSTF, a high-quality colonoscopy reaches the cecum, has little fecal residue, and has a minimum time of withdrawal from the cecum of six-to-ten minutes (28). Baseline colonoscopy without a good clearing of the colon places the patient at increased risk for subsequent neoplastic findings (29). Adenomas, advanced adenomas, and cancers are missed by colonoscopy (30–32) (Tables 3, 4). Sensitivity could be increased by continuing quality improvement programs for the performance of colonoscopy (28). A trial designed specifically to evaluate surveillance, in which colonoscopy is performed by experienced endoscopists, have shown that a low incidence of cancer can be achieved in postpolypectomy patients (5,17).

**CHARACTERISTICS OF REMOVED ADENOMAS AS PREDICTORS OF ADVANCED ADENOMAS AT FOLLOW-UP (TABLE 5).**

**Multiplicity**

Multiplicity at \( \geq 3 \) adenomas baseline has been shown to predict subsequent detection of advanced adenomas. Of the RCT’s, the National Polyp Study (17), the European fiber and calcium study (20), and the pooled analysis of chemoprevention studies (13) showed that multiplicity conferred an increased risk for advanced neoplasia at surveillance. The pooled analysis did not report OR’s but did report a significant difference in mean number of prior lifetime adenomas at baseline in those with and without advanced neoplasia at surveillance. The observational cohort studies also showed that multiplicity was a risk factor for subsequent advanced adenomas and cancer.

**Size**

Adenoma size larger than 1 cm also was shown to predict metachronous advanced adenomas in the wheat bran study (19). Adenoma size was important in seven of eight of the observational cohort studies assessing advanced neoplasia.

**Pathology**

Histologic type of adenoma at baseline was not a significant predictor of advanced neoplasia in the ran-
domized trials but was for several of the observational cohorts. Histology is a particularly difficult predictor to evaluate because of the somewhat subjective nature of classifying tubular, tubulovillous, and villous adenomas (34). High-grade dysplasia is related to larger adenoma size and villous component at baseline and is an important predictor for subsequent advanced neoplasm in the observational cohort studies (16,21). By definition all adenomas have some level of dysplasia. In the past, dysplasia has been classified as mild, moderate, severe, or carcinoma in situ. Currently, severe dysplasia or carcinoma in situ are considered the equivalent of high-grade dysplasia and mild or moderate dysplasia are considered the equivalent of low-grade dysplasia.

Proximal Location
In two studies, a proximal adenoma at baseline was associated with an increased risk for subsequent advanced adenomas (19,20).

Other Risk Factors
Family history of colorectal cancer and adenomas at a young age (35) is an established risk factor for the development of colorectal cancer (36,37). However, few studies have addressed specifically the relationship between family history and metachronous advanced adenomas in postpolypectomy patients. The National Polyp Study showed that a family history of colorectal cancer in patients age 60 or older predicted a 4.8-fold increased risk for advanced adenomas at follow-up evaluation (18).

COMMENTARY
From the 1970s to the 1990s, annual follow-up colonoscopy was common practice after polypectomy and there were no guidelines available that addressed how clinicians should best follow-up these patients. In 1993, a report from the National Polyp Study showed that it was safe to defer the first follow-up examination for three years (17). This evidence, along with the knowledge of the long natural history of the adenoma-carcinoma progression, led to guidelines in 1997 that recommended a three-year interval for the first follow-up examination after removal of adenomas (9). Practice began to evolve along the lines of this evidence. Guidelines have been used in the courts of law as indicating the standard of practice (41).

Recent guidelines have introduced the concept of risk stratification of patients at the time of polypectomy into those more likely or less likely to develop subsequent serious neoplasia (7). The most consistent evidence for predicting subsequent advanced adenomas indicates that multiplicity, size, villous histology, and high-grade dysplasia are the important factors at baseline (Table 5). Based on these factors, patients can be stratified at the time of colonoscopy into lower or higher risk for subsequent advanced adenomas (Table 6). The most consistent evidence for predicting subsequent advanced adenomas indicates that multiplicity,
size, villous histology, and high-grade dysplasia are the important factors at baseline. Based on these factors, patients can be stratified at the time of colonoscopy into lower or higher risk for subsequent advanced adenomas.

Patients who have had a polypectomy and long-term surveillance have been shown to have a reduced incidence of colorectal cancer (5,6). When one separates out the effect of initial polypectomy from the subsequent surveillance, modeling has shown that more than 90% of the reduced incidence over the first five-to-six years is the result of the initial polypectomy. However, there is a subgroup that can be identified as having a higher risk for subsequent cancer by using the advanced adenoma as a surrogate marker (44). These observations support the concept of stratifying patients by baseline factors so that the group at increased risk can be identified for more intensive surveillance and the group at lower risk can be identified for less intensive surveillance. Reduction in the intensity of surveillance could free up endoscopic resources that could be shifted to screening and diagnosis, thereby increasing the benefit and reducing the procedural risk.

The use of fecal occult blood testing (FOBT) after colonoscopy in postpolypectomy patients has been reported to be a widespread practice (38% of patients had FOBT after adenoma removal at colonoscopy) (45). The National Polyp Study has shown that the use of FOBT after colonoscopy results in a substantial number of unnecessary colonoscopies; 77% of colonoscopies performed to evaluate positive surveillance FOBT results detected no advanced adenomas or cancer (i.e., the positive predictive value was 23%) (46). In a recent report by Bampton, et al (59) of 785 patients who had a recent surveillance colonoscopy, the positive predictive value for an immunochemical FOBT was 27%. This was in a high-risk cohort composed of patients with a history of colonic neoplasia or with a strong family history. A lower positive predictive value would be expected in a lower-risk population. The possible benefit of FOBT in patients having surveillance colonoscopies needs further study, but with the present available evidence this should be discouraged.

In the present guidelines, recommendations for the lower-risk group are intentionally flexible because follow-up colonoscopy studies are limited to five-to-six years (16,17). Some physicians and patients may elect to have a follow-up colonoscopy at five years because they wish to be assured that future risk has been reduced to less than that of the average-risk population. Others may feel confident that this risk already has been reduced to less than that of the general population by adequate clearing of the colon and would be satisfied with either a 10-year follow-up colonoscopy or choosing other screening options currently recommended for individuals at average risk (7,8).

Risk stratification and recommended follow-up intervals are based on the presumption that a high-quality colonoscopy was performed at baseline. However, variable colonoscopic miss rates for adenomas and cancer have been shown (5,13,30–32,48–50). This variability in colonoscopic baseline quality could translate into either a lower rate of subsequent cancers detected during surveillance or a higher rate as seen by Robertson, et al (13) and others (30–49). For example, in the National Polyp Study, if the baseline colonoscopy did not clear the colon with high confidence (excellent preparation, complete polypectomy), the examination was repeated before entering the patient into the surveillance program. Repeat examinations were required in 13% of the patients (17). Such rigor contributed to a marked reduction in colorectal cancer incidence in the National Polyp Study that was not observed in other studies (13,49). In Australian and Japanese studies (48–50) low miss rates were seen in patients in whom the cecum was intubated.

The quality of the baseline examination can be evaluated to some extent by the number of cancers detected earlier versus later in a surveillance program. Thus, the major benefit of the baseline colonoscopic polypectomy rests on the quality of that examination (28,29). The concern by clinicians of missed adenomas and cancers can be assuaged by high-quality baseline performance of colonoscopy. Protection can never be 100%, but it is excellent (5,28,51).

There was insufficient evidence to include family history in the guidelines as a predictor of metachronous advanced adenomas. Clearly, however, family history of colorectal cancer in a close relative does increase the risk for colorectal cancer in other relatives and needs further study in the postpolypectomy setting.

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Table 7
Conclusions about Guidelines

- Based on totality of evidence currently available
- Updated with new data
- Meant to help the clinician & patient decisions
- Clinicians and patients should act with a comfort zone of evidence, experience and personal philosophy of medical practice
- Clinicians are ultimately responsible for patient care and decisions

Table 8
Reasons for Interval Neoplasia

- Technological Limitations
- Technique
  - Incomplete Colonoscopy
  - Inadequate Bowel Prep
  - Fast Withdrawal Time
  - Piecemeal Removal of Large Sessile Polyps
- Biology
  - Fast Track Cancers—MMR Pathway (15%–20%) (documented in HNPCC)
  - Flat Adenomas

(36,37). Issues such as this must be considered on an individual basis when clinicians are determining appropriate follow-up evaluation. Patients with a family history indicating HNPCC require special screening and surveillance (7,9,37,52).

Other issues evolving in the literature that require further study and may affect future guidelines include different recommendations for men and for women by age (53). Given the evolving nature of guidelines, it is important that physicians and patients remain in contact so that surveillance practices will reflect changes in guidelines.

There is no evidence that patients with small distally located hyperplastic polyps have an increased risk for colorectal cancer and therefore they should be pre-screened as appropriate for average-risk patients (54). The present guidelines state this explicitly. It has been shown recently, however, that hyperplastic polyps are not a homogenous histologic category and there is accumulating evidence from molecular genetic studies that some histologic variants of hyperplastic polyps may evolve into a unique type of adenoma that resembles a hyperplastic polyp with dysplasia, called a serrated adenoma (55). This form of adenoma in turn has been linked to the ultimate development of sporadic microsatellite instability adenocarcinoma. This form of colonic adenocarcinoma shares with HNPCC the genetic attribute (in this case, acquired) of microsatellite instability (sporadic microsatellite instability cancers) because of mismatch repair deficiency. Hyperplastic polyps at risk for such a progression show atypical architectural and cytologic features, often are large, sessile, and usually are located proximally. Other terms for these hyperplastic polyp variants are sessile serrated adenoma or serrated polyp with abnormal proliferation. Some investigators have suggested that complete removal and surveillance, as for typical adenomas, may be warranted in these cases (56).

All endoscopists must remain alert to the syndrome of hyperplastic polyposis. Hyperplastic polyposis was defined by Burt and Jass (57) for the World Health Organization International Classification of Tumors as:

1. at least 5 histologically diagnosed hyperplastic polyps proximal to the sigmoid colon, of which 2 are greater than 1 cm in diameter
2. any number of hyperplastic polyps occurring proximal to the sigmoid colon in an individual who has a first-degree relative with hyperplastic polyposis
3. more than 30 hyperplastic polyps of any size distributed throughout the colon.

Studies have found an increased risk for colorectal cancer in these patients (58,59). The pathway may be through the serrated adenoma (56,60). The magnitude of the increased risk has not been determined. A recent case series of 15 patients found no cancer developed within three years of follow-up evaluation (61). The optimal management of hyperplastic polyposis has not yet been defined and requires further study.

Technologic advances such as computed tomography colonography, chromoendoscopy, narrow band imaging, and magnification endoscopy may one day be shown to be important in postpolypectomy surveil-
lance (66–65). Some of these techniques may have a special role in detecting flat adenomas (66). However, at this time, there is insufficient evidence that any of these techniques should be part of routine post-polypectomy surveillance.

In conclusion, it must be emphasized that for surveillance to be effective certain criteria need to be met (Table 2); and it should be noted that guidelines are dynamic and change with new evidence. The ultimate responsibility lies in the hands of the clinicians’ judgment (Table 7). Finally, we need to recognize that colonoscopy is not a perfect tool. There are technological and biological (67) reasons for interval neoplasia, but high quality technique can bring this examination to its highest potential (Table 8).

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