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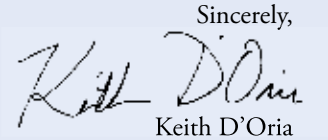
# Table of Contents



# A Message From the Editor

We at Physician's Weekly are excited to present you with an eBook dedicated to feature stories we've covered that are pertinent to oncology physicians. In recent months, our publication has published a variety of news items in this field, focusing on clinical and evidence-based research. The content in these articles relies on the expertise of our contributing physician authors. We anticipate that Physician's Weekly will continue to feature news in primary care in the coming months. We hope that you find this information useful in your practice. Please let us know your thoughts by contacting us at keithd@physweekly.com.

Sincerely,



Keith D'Oria
Managing Editor, *Physician's Weekly*

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# Preve
# to Impr

# nting Delayed CINV rove Patient Outcomes

*CINV, particularly delayed-onset CINV, is a significant adverse effect of chemotherapy, but prophylactic medications are available to effectively prevent the problem in many patients receiving treatment for their cancer.*

**John W. Mucenski, PharTmD**
Director of Pharmacy Operations
University of Pittsburgh Medical Center
Cancer Centers

Chemotherapy-induced nausea and vomiting (CINV) remains a major adverse effect of cancer chemotherapy, despite the availability of several antiemetic drug classes. Although not life-threatening, CINV has a major impact on a patient's quality of life (QOL) and ranks high on the list of factors most feared by patients receiving chemotherapy. Additionally, symptoms from CINV can be severely debilitating and often result in patients refusing further courses of chemotherapy, which can minimize the likelihood of achieving optimal outcomes. "Failure to control acute nausea and vomiting on the first day of chemotherapy will increase the risk of nausea and vomiting on subsequent days and in subsequent cycles of chemotherapy," says John W. Mucenski, PharmD. "The downstream economic effects of not adequately controlling CINV with the first course of chemotherapy cannot be underestimated. These include calls to the office, additional visits for intravenous (IV) hydration and antiemetics, and the potential for hospitalization."

CINV is not always confined to the acute period. "Most patients at risk for CINV will be treated with IV antiemetics therapy initially, but will be discharged with oral medications, which are not always as effective as IV agents," explains Dr. Mucenski. "In many cases, patients will develop delayed-onset CINV, in which nausea and vomiting occur more than 24 hours after

> *It's imperative to control delayed-onset CINV before it starts and utilize therapies that will most effectively address this issue.*
>
> — John W. Mucenski, PharmD

**Table 1 Characterizing Delayed-Onset CINV**

- Nausea and vomiting occur more than 24 hours after chemotherapy.
- Nausea and vomiting may continue for up to 7 days.
- Stomach upset is usually most severe 48 to 72 hours after treatment.
- Causes are not well understood.
- Common in patients who are not treated correctly for acute CINV.
- Occurs more commonly in women and in people treated with high doses of chemotherapy.
- Often difficult to control.

**Source:** Adapted from: CancerNausea.com. Available at: www.cancernausea.com/treatment_options/delayed_onset_nv.asp.

chemotherapy administration and last for 5 to 7 days or even longer [Table 1]."

Providers tend to underestimate the number of patients who suffer from delayed-onset CINV, which evidence suggests affects as many as 50% to 70% of patients and occurs more often than acute-onset CINV. This may occur in part since patients often do not report side effects they experience at home following chemotherapy treatments. This type of CINV can significantly reduce QOL, increase treatment costs, and greatly impair a patient's ability to provide care to themselves or others once they have been discharged. "It's imperative to control delayed-onset CINV before it starts and utilize therapies that will most effectively address this issue," Dr. Mucenski says. "Physicians need to make efforts to become informed on proper prophylaxis against delayed-onset CINV and better protect their patients after they leave outpatient or inpatient settings."

## Analyzing Treatment Options

Current guidelines call for use of a 5-hydroxytryptamine (serotonin) type 3 ($5\text{-HT}_3$) receptor antagonist in patients receiving moderately and highly emetogenic chemotherapy. The $5\text{-HT}_3$ receptor antagonists are now included in most regimens for antiemetic control, but there are pros and cons to consider when using different agents. All approved $5\text{-HT}_3$ receptor antagonists are approved to prevent acute CINV, but palonosetron has a distinct advantage over the other agents in this class because it has been approved by the FDA for the prevention of delayed CINV in addition to acute CINV. Palonosetron has been shown to provide significantly higher complete response rates when compared with ondansetron in both acute and delayed phases of CINV in moderately emetogenic chemotherapy recipients. The agent binds differently to $5\text{-HT}_3$ receptors and has a 40-hour half life.

In other studies, significantly more patients who received palonosetron were nausea-free on Days 3-5 following moderately emetogenic chemotherapy when compared with those who received ondansetron. In addition, palonosetron has been demonstrated to be noninferior to ondansetron in the acute phase of CINV for patients receiving highly emetogenic chemotherapy (Table 2). Studies have also shown that palonosetron yields significantly higher rates of complete response in delayed-onset CINV when compared with dolasetron.

## Combination Therapy Yields Greater Benefits

Substance P, which is mediated through the neurokinin-1 ($NK_1$) receptor, is another recently identified neurotransmitter with activity in CINV. Substance P is one of a group of peptides located throughout the central nervous system and found in the gastrointestinal tract along with $5\text{-HT}_3$ receptors. "Aprepitant is a substance $P/NK_1$ receptor antagonist approved by the FDA for the prevention of acute and delayed CINV when used with a $5\text{-HT}_3$ antagonist and dexamethasone,"

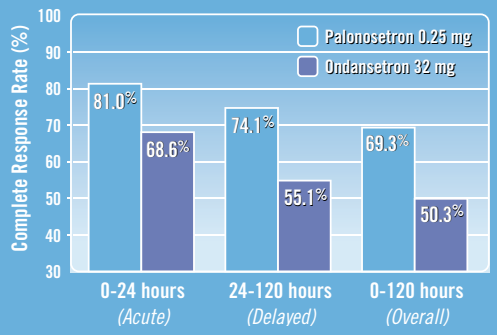
says Dr. Mucenski. "The development of novel agents has given patients more options for management and improved control of CINV." Recent data indicate that the combination of palonosetron plus aprepitant and dexamethasone is highly effective in the prevention of both acute and delayed-onset CINV following a variety of moderately to highly emetogenic chemotherapy regimens. Complete responses—no emesis and no additional medication for nausea and vomiting—have been achieved in the vast majority of patients during both acute and delayed phases of CINV.

The prevention of CINV allows for significantly greater QOL for patients during and following treatment, and can help patients achieve a higher compliance rate with subsequent treatments for their cancer. This can optimize their chances to improve long-term outcomes. "When patients are undergoing chemotherapy associated with moderate-to-severe nausea and vomiting, clinicians should consider combining palonosetron with aprepitant plus dexamethasone to improve outcomes," Dr. Mucenski says. "Furthermore, guidelines from the American Society of Clinical Oncology are expected soon. These will provide clinicians with evidence-based recommendations to further improve CINV prophylaxis."

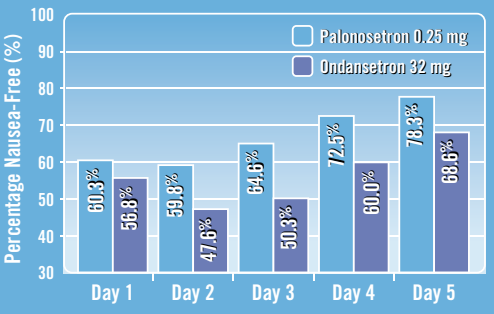
*John W. Mucenski, PharmD, has indicated to* Physician's Weekly *that he has worked as a paid speaker for Amgen, Eisai, and Merck. For more information on this article, including references, visit: www.physiciansweekly.com.*

## Table 2 Comparing Efficacy

In a clinical trial, palonosetron provided significantly higher complete response* rates when compared with ondansetron in both acute and delayed phases of CINV in moderately emetogenic chemotherapy recipients:




Data also demonstrate that significantly more patients who receive palonosetron were nausea-free on Days 3-5 following moderately emetogenic chemotherapy than those receiving ondansetron:




*Complete response: defined as no emetic episode and no use of rescue medication was required.

**Source:** Gralla RJ, et al. *Ann Oncol.* 2003;14:1570-1577.

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# Overcoming Oncology Workforce Shortages

**Dean F. Bajorin, MD, FACP**
Professor of Medicine
Memorial Sloan-Kettering Cancer Center
Weill Medical College of Cornell University
Co-Chair, Workforce Advisory Group
American Society of Clinical Oncology

In March 2007, results of a study commissioned by the American Society of Clinical Oncology (ASCO) Board of Directors on supply and demand for oncology services through 2020 were released. The study indicated that that the United States is likely to face a nearly 50% increase in demand for oncology services by 2020, largely because of the expected increases in both cancer survivorship and cancer incidence caused by the aging population. The anticipated increase in the supply of oncologists during that timeframe will not meet the growing demand.

Results from the 2007 ASCO study were likely conservative with regard to predictions. As the general population gets older, it's likely to seek more healthcare services than those who are currently 65 or older. Furthermore, improvements in cancer treatments are enabling patients to live longer. In turn, these individuals may eventually be faced with other cancer diagnoses and/or chronic illnesses later in life. Oncology workforce shortages can affect the entire medical community. Unless actions are taken, it's likely that we'll face a crisis in our ability to provide quality cancer care for patients.

## New Initiatives

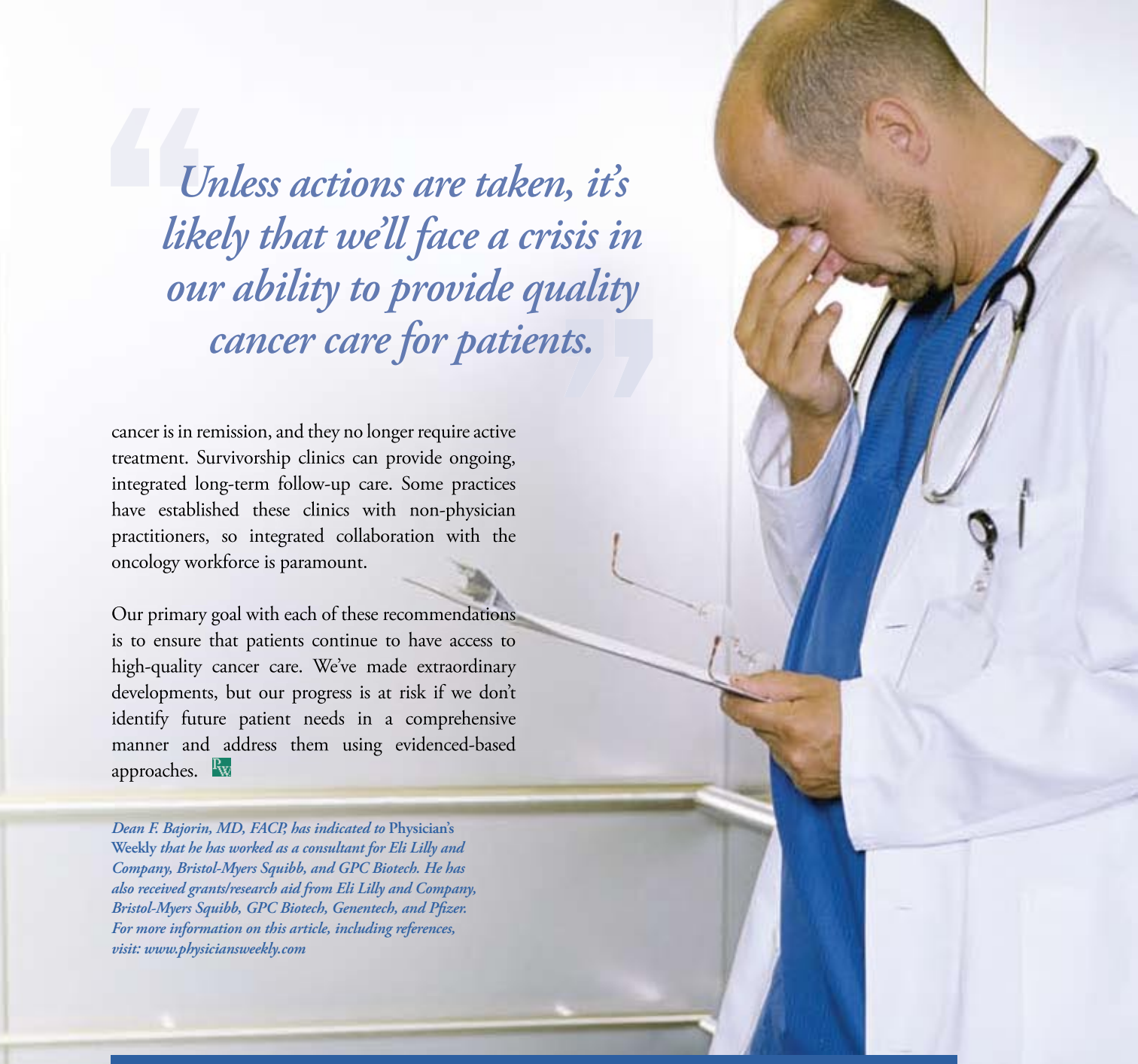
In the November 2008 *Journal of Oncology Practice*, ASCO's Workforce Advisory Group issued a strategic plan to address projections indicating that demand for oncology services will surpass the supply of practicing oncologists in the years to come. While no single action will fulfill the supply and demand gap completely, efforts are being made to develop multifaceted approaches that address oncology workforce shortages so that future demands can be met.

One of the major actions that ASCO and other associations are currently undertaking is to develop an information database that tracks real-time trends in the oncology workforce. The goal of this database is to monitor the oncology workforce supply. It will gather actual figures on the number of practicing oncologists in the U.S. and compare these data to benchmarks established in 2007.

## Important Recommendations

ASCO also recommends evaluating in greater detail the delivery of oncology care by collaborating with other physicians and non-physicians. Most oncologists already work with non-physician practitioners (eg, nurse practitioners and physician assistants), but only about half of these providers perform advanced activities like helping with new patient consults or ordering routine chemotherapy. Identifying the most productive elements of innovative practice models is necessary to improve delivery of care.

Another area where improvements can be made to increase the oncology workforce supply is to expand the number of oncology training slots in residency and fellowship programs. Currently, the number of these positions in oncology is limited. Efforts are also needed to increase medical student and resident exposure to oncology. In addition, ASCO is examining the use of "survivorship clinics." These clinics have developed paradigms to optimally manage patients once their



*Unless actions are taken, it's likely that we'll face a crisis in our ability to provide quality cancer care for patients.*

cancer is in remission, and they no longer require active treatment. Survivorship clinics can provide ongoing, integrated long-term follow-up care. Some practices have established these clinics with non-physician practitioners, so integrated collaboration with the oncology workforce is paramount.

Our primary goal with each of these recommendations is to ensure that patients continue to have access to high-quality cancer care. We've made extraordinary developments, but our progress is at risk if we don't identify future patient needs in a comprehensive manner and address them using evidenced-based approaches.

*Dean F. Bajorin, MD, FACP, has indicated to* Physician's Weekly *that he has worked as a consultant for Eli Lilly and Company, Bristol-Myers Squibb, and GPC Biotech. He has also received grants/research aid from Eli Lilly and Company, Bristol-Myers Squibb, GPC Biotech, Genentech, and Pfizer. For more information on this article, including references, visit: www.physiciansweekly.com*

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# CRC Surveillance in Patients With IBD

**Francis A. Farraye, MD, MSc**
Clinical Director, Section of Gastroenterology
Boston Medical Center
Professor of Medicine
Boston University School of Medicine

Certain patients with inflammatory bowel diseases (IBD), including ulcerative colitis and Crohn's disease of the colon, have an increased risk of developing colorectal cancer (CRC) when compared with patients without IBD. While IBD is relatively rare in the general population, it remains one of the important high-risk conditions predisposing patients to CRC. The majority of patients with IBD will not develop CRC, but two factors that increase CRC risk have been identified: 1) CRC risk increases after 8 to 10 years of having ulcerative colitis, and 2) the more extensive the colonic involvement, the higher the CRC risk. Patients with disease limited to the rectum do not have an increased risk of CRC, while patients with ulcerative proctosigmoiditis or left sided colitis have an intermediate risk. The greatest risk is for those whose entire colon is diseased. The risks are similar for those with extensive Crohn's colitis.

In the February 2010 issue of *Gastroenterology*, the American Gastroenterological Association (AGA) released a medical position statement and technical review on the diagnosis and management of colorectal neoplasia in IBD. The recommendations were designed to help identify high-risk individuals and develop individualized surveillance plans based on each patient's unique situation.

## Assessing Risks

The AGA position statement provides important information on assessing CRC risk in IBD patients.

*An individualized and sensible approach to CRC surveillance in patients with IBD is essential.*

Disease duration, more extensive disease, severity of inflammation, primary sclerosing cholangitis, and a family history of sporadic CRC have all been associated with an increased risk of developing CRC in patients with IBD. Colonic strictures in patients with ulcerative colitis and/or a shortened colon, and/or multiple post-inflammatory pseudopolyps are also associated with an increased risk of CRC. Furthermore, increasing degrees of histologic inflammation has been identified as a risk factor for progression to colorectal neoplasia.

The literature indicates that dysplasia detected on biopsy is currently the best marker for CRC risk in IBD. Use of chromoendoscopy in high-risk patients appears to be a viable strategy to identify dysplasia and cancer. More research is needed to identify genetic, molecular, or biochemical markers that can be measured in tissue, blood, or stool and are associated with an increased risk of colorectal neoplasia.

## Treatment Recommendations

Current data indicate that patients with IBD and a non-adenoma-like dysplasia-associated lesion or mass that doesn't lend itself to being completely removed by colonoscopy should be treated with colectomy. Conversely, patients with an adenoma-like dysplasia-associated lesion or mass removed endoscopically and without evidence of flat dysplasia elsewhere in the colon can be managed safely by polypectomy and continued surveillance. Flat high-grade dysplasia found on random biopsies and confirmed by a pathologist with expertise in IBD is associated with undiagnosed synchronous cancer (present in 42% to 67% of cases) and therefore should be treated with colectomy. However, the current evidence is insufficient on the benefits and harms of colectomy for flat low-grade dysplasia found on random biopsies.

In general, surveillance colonoscopy appears to result in at least a moderate reduction of CRC risk in patients with IBD, and those with extensive ulcerative colitis or Crohn's disease of the colon are the most likely to benefit. With more research, there is hope that we'll determine more conclusively if certain medications used to treat IBD might also help to prevent colorectal neoplasia. PW

*Francis A. Farraye, MD, MSc, has indicated to* Physician's Weekly *that in 2010 he received research support from Prometheus Laboratories, has been a consultant and a member of the speaker's bureau for Abbott, Centocor and Shire, and has been a consultant for UCB. For more information on this article, including references, please visit: www.physiciansweekly.com*

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# Redefining Screening Guidelines for Certain Cancers

*The University of Texas MD Anderson Cancer Center has released comprehensive, risk-based screening guidelines for breast, cervical, and colorectal cancer, highlighting important new evidence to guide practices.*

**Therese B. Bevers, MD, FAAFP**

Professor of Clinical Cancer Prevention
Medical Director, Cancer Prevention Center and Prevention Outreach Program
University of Texas MD Anderson Cancer Center

According to the American Cancer Society, more than 40% of Americans will develop cancer at some point in their lifetime. It is also estimated that cancers that can be prevented or detected earlier by screening account for at least half of all new cancer cases. Estimates from 2009 indicate that about 192,370 women will be newly diagnosed with breast cancer, and another 40,170 will die from it. About 11,270 new cases of cervical cancer will be diagnosed in women, and 4,070 women will die from it. New cases of colorectal cancer will be diagnosed in 106,100 men and women and 49,920 of these people are estimated to die from the disease.

## Building on Previous Recommendations

Considering the magnitude of these cancers, researchers at the University of Texas MD Anderson Cancer Center released comprehensive, risk-based screening guidelines for breast, cervical and colorectal cancers. Available at www.mdanderson.org, the recommendations translate best practices in cancer prevention employed at the university into accessible guidelines for the public to follow. It identifies risk categories and provides information about when to begin and discontinue screening exams. "The guidelines reconstruct and expand upon previously published guidelines for screening," says Therese B.

### Table 1 Breast Cancer Screening Recommendations

- Starting at age 20, encourage women at all risk levels to become familiar with how their breasts look and feel, and to immediately report any changes to their provider.
- Encourage women aged 40 and older at average risk to get annual mammograms and breast exams.
- For women at increased risk, the type and frequency of exams (eg, clinical breast exams, mammograms, and breast MRI) should depend on risk factors such as:
  - History of radiation treatment to the chest.
  - Genetic predisposition.
  - Diagnosis of lobular carcinoma *in situ*.
  - Gail Model score of 1.7% or greater in women 35 years or older.
  - Lifetime risk of 20% or greater based on family history.

**Source:** Adapted from: University of Texas MD Anderson Cancer Center.

> *Cancer screening is not a one-size-fits-all strategy.*
>
> —Therese B. Bevers, MD, FAAFP

Bevers, MD, FAAFP. "The guidelines were developed by multidisciplinary panels of MD Anderson disease site experts across several areas." Those areas include medical oncology, surgical oncology, cancer prevention, and imaging as well as others.

## Adjusting for Individual Risk

"Cancer screening is not a one-size-fits-all strategy," says Dr. Bevers. "The new risk-based recommendations from the University of Texas MD Anderson Cancer Center are more personalized, precise, and detailed than what has previously been released by other cancer organizations. The new guidelines build on established cancer screening practices and offer more specific recommendations for individuals at increased risk for these three cancers [Tables 1, 2, and 3]."

Cancer screening recommendations have historically been targeted largely to patients at average risk for developing cancer based on characteristics such as age, family history, or genetic predisposition. However, average risk has not been previously defined, and recommendations for individuals at increased or high risk have not been outlined. Dr. Bevers says, "Providing physicians and patients with more knowledge about how decisions are made about risk levels and screening tests may provide a deeper understanding of disease processes and enable them to put cancer risk into perspective."

The new screening guidelines define risk categories and offer recommendations for those at increased and high risk of developing cancer. "For example," says Dr. Bevers, "there are now five different sets of screening recommendations for those at increased risk for breast cancer. There are also four categories of age-based risk recommendations for cervical cancer. For colorectal cancer, patients need to be proactive about obtaining results from their screening tests. For example, if a colonoscopy reveals polyps, it's critical to know the type of polyps, how many were found, and the size of the polyps. This information factors heavily into what colorectal cancer risk category patients should fall under and the intervals at which screenings are needed."

Dr. Bevers also notes that the guidelines state that it is critical for women who do not require annual cancer screenings to continue with annual appointments to obtain other appropriate healthcare. "Clinicians need to stop linking specific visits for preventive care with one activity. We must remember to continue treating the whole patient and take every opportunity to provide preventive measures to ensure the well-being of each individual."

### Table 2 Cervical Cancer Screening Recommendations

- For women at average risk, women younger than 21 are recommended to get a liquid-based Pap test within 3 years of initiating vaginal intercourse.
- Encourage continued Pap tests annually until women have had 3 consecutive negative test results.
- After 3 consecutive negative test results, a liquid-based Pap test is recommended every 2 years unless women are at increased risk of cervical cancer based on the following risk factors:
  - History of cervical cancer or severe cervical dysplasia.
  - Persistently testing positive for human papillomavirus (HPV).
  - Exposure to diethylstilbestrol before birth.
  - HIV infection.
  - A compromised immune system.
- Beginning at age 30, adding HPV testing to the liquid-based Pap test is the preferred screening option.
  - If both HPV and Pap testing are negative, women should be screened every 3 years unless they are at increased risk based on the risk factors cited above or unless the optional HPV test was not done.

**Source:** Adapted from: University of Texas MD Anderson Cancer Center.

## More to Come

The new recommendations represent the first wave of an effort by MD Anderson to improve the effectiveness of cancer prevention and detection efforts at their earliest, most treatable stages. Risk-based screening guidelines for prostate, liver, skin, endometrial, and ovarian cancers are currently in development. Furthermore, an online risk assessment tool integrating the new screening guidelines is expected to be launched on the MD Anderson website in 2010. "Our guidelines are designed for patients who are at increased risk for cancer," says Dr. Bevers. "The hope is that providing more tools to clinicians and their patients will help us catch cancers at their earliest stages, ultimately improving our chances of treating the disease effectively and reducing the enormous burden of cancer."

*Therese B. Bevers, MD, FAAFP, has indicated to* Physician's Weekly *that she currently has no financial interests to report. In the past, she has received grant support, been part of a speaker's bureau, and been a consultant for Eli Lilly, and she has been on an advisory board for Merck. However, none of these companies are current financial interests. For more information on this article, including references, please visit: www.physiciansweekly.com*

### Table 3 Colorectal Cancer Screening Recommendations

- For men and women aged 50 and older who are at average risk, they should do one of the following:
  - A colonoscopy every 10 years.
  - A virtual colonoscopy every 5 years.
  - A fecal occult blood test every year.
- For men and women at increased or high risk, the type and frequency of exams (eg, colonoscopy and flexible sigmoidoscopy) depend on the following factors:
  - Personal history of adenomatous polyps.
  - Personal history of colorectal cancer.
  - Family history of colorectal cancer or adenomatous polyps.
  - Genetic diagnosis of familial adenomatous polyposis.
  - Genetic history of hereditary nonpolyposis colorectal cancer, or a clinical history suggesting such.
  - Inflammatory bowel disease (eg, ulcerative colitis or Crohn's disease).

**Source:** Adapted from: University of Texas MD Anderson Cancer Center.

## References


To access cancer screening guidelines from the University of Texas MD Anderson Cancer Center, go to http://www.mdanderson.org

For resources for clinicians from the University of Texas MD Anderson Cancer Center's website, go to http://www.mdanderson.org/education-and-research/resources-for-professionals/index.html

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# Cryosurgery for Localized Prostate

**Richard J. Babaian, MD**
Senior Medical Director and Professor
MD Anderson Physician's Network

*An American Urological Association best practices statement provides evidence supporting the use of cryosurgery for the treatment of localized prostate cancer.*

Most men currently diagnosed with localized prostate cancer are likely to have the disease eradicated by one of the available treatment modalities, but the focus on health-related quality of life associated with treatment has intensified. In 2007, the American Urological Association (AUA) released guidelines for the management of clinically localized prostate cancer. This guideline, however, did not address the role of cryosurgery for treatment of the disease because of insufficient long-term efficacy data on metastasis-free, prostate-cancer specific, or overall survival. In the November 2008 *Journal of Urology,* the AUA released a new best practice statement on cryosurgery for the treatment

# Cancer

of localized prostate cancer. "This is the first time the AUA has released official guidance on this treatment modality," says Richard J. Babaian, MD, who chaired the panel that published the statement.

According to the AUA guidelines, several investigations have reported the efficacy and morbidity of cryosurgery for the disease. "Prostate cryosurgery has been found to result in acceptable outcomes with regard to health-related quality of life," says Dr. Babaian. "It has been associated with reduced costs when compared with other local therapeutic options." Studies have also shown that short-term PSA relapse-free survival outcomes following cryoablation of the entire prostate are comparable to that of radiation therapy in men with intermediate- and high-risk disease.

## Cryosurgery Options

According to the AUA best practice statement, cryosurgery can be used as primary therapy or salvage therapy (Table 1). The minimally invasive treatment involves freezing cancerous tissue. As a result of this process, tumors are destroyed. Thermal probes

## Table 1 Assessing the Options

**Primary Cryosurgery:**

Primary cryosurgery is an option for men who have clinically organ-confined disease of any grade with a negative metastatic evaluation.

- High-risk patients may require multimodal therapy.
- There are limited data regarding the outcomes for clinical T3 disease; the role of cryosurgery in this setting is currently undetermined.

**Salvage Cryosurgery:**

Salvage cryosurgery can be considered as a treatment option for curative intent in men who have failed radiation therapy.

- The most appropriate candidates have:
  - Biopsy-proven, persistent organ-confined prostate cancer.
  - A PSA <10 ng/mL.
  - A negative metastatic evaluation as determined by standard assessment (eg, imaging modalities).

**Source:** Adapted from: Babaian RJ, et al. *J Urol.* 2008;180:1993-2004.

are placed into the prostate, where a controlled freezing-thawing process ensues. Clinicians must monitor patients closely and pay special attention to temperature, freeze cycles, and thaw rates. Although cryosurgery is often performed in outpatient settings, research has indicated that some patients may require an overnight hospital stay. The average operative time associated with the procedure is about 2 hours.

Cryosurgery, according to the AUA panel, is an option when appropriate patients do not want or are not good candidates for radical prostatectomy because of certain comorbidities. Dr. Babaian says that cryotherapy as a first treatment may be a viable option for men with clinically localized prostate cancer of any grade with no metastasis. "High-risk patients may require multimodal therapy," he adds. "In some larger glands, neoadjuvant cytoreduction can be considered to overcome technical limitations in treatment. It should be noted, however, that neoadjuvant or concomitant hormonal therapy has not been shown to positively impact subsequent cryosurgery outcomes."

Radiation patients with biochemical recurrence and a PSA of less than 10 ng/mL could be considered candidates for salvage cryotherapy. It is a secondary treatment for patients without evidence of metastasis and whose local recurrence is detected early. Several major variables, especially PSA doubling time, must be considered prior to using cryotherapy as a salvage therapy. "Salvage cryotherapy should only be used in patients with a positive prostate biopsy," says Dr. Babaian. "Radiation therapy reduces the size of the prostate, so gland volume is not as much a limiting factor as it is when cryotherapy is used as a primary treatment."

## Optimizing Results

There are several complications of cryosurgery that should be considered when making decisions about utilizing the procedure. In addition to incontinence and erectile dysfunction, complications include urinary retention, swelling, and fistula formation. Although a concern, the rates of these complications have been less than 10% in current investigations. "To optimize results, it's important that clinicians have a keen ability and awareness of how to appropriately use ultrasound," Dr. Babaian says. "Success of the procedure depends on it. It's also paramount to closely monitor tissue freeze rates, temperatures, thaw rates, and freeze cycles [Table 2]. The good news is the mortality rate associated with cryosurgery for localized prostate cancer is very low."

The AUA best practice statement on cryosurgery provides clinicians with a current understanding of the principles and strategies for performing cryosurgery in localized prostate cancer. It is based on reviews of medical literature, clinical experience, and expert opinion. "Unlike a clinical guideline," Dr. Babaian explains, "best practice statements do not use formal meta-analyses of the literature. However, the hope is the document will provide more helpful information on this emerging prostate cancer treatment option. Decisions to use one treatment over others should be made by physicians and patients collaboratively after all other available options and potential complications are exhaustively reviewed. Cryosurgery will continue to be explored, and there is further evidence that more minimally invasive options will continue to be developed in the coming years."

## Table 2 Maximizing the Effect

To both maximize the destructive effects of cryosurgery and to permit comparisons of outcomes among treatment centers, specific procedural requisites should be followed.

**Tissue freeze rate:**

- Rapid freezing is recognized as being more destructive than slow freezing.
- Cancer cells have the opportunity to "adapt" under conditions of slow freezing by losing water to the extracellular milieux, thereby reducing the probability of intracellular ice formation.

**Temperature monitoring:**

- Use of thermocouples is strongly advised when performing cryosurgery.
- Real-time measurements of tissue temperature at critical locations within and proximal to the prostate provide urologists with an important indication of the status of the freezing process; it also protects key vital structures.
- Temperature monitoring is also facilitated by ultrasound images.

**Nadir temperature:**

- –40°C has been used as the end-temperature goal historically.
- Prostate cancer is comparatively temperature labile with a lower lethal temperature near –20°C.

**Thaw rate:**

- Prostate cancer ablation is improved with slow thawing.
- Activation of the heating mode in the cryoneedle/cryo-probe placement (CN/P) does not affect the thaw rate of the distal edges of the gland.
- Probe heating affects only the frozen tissue mass juxtaposed to the CN/P and not the distally frozen tissue.

**Freeze cycles:**

- Use of a double freeze-thaw cycle is recommended.
- Data demonstrate that a clear benefit accrues with the use of a dual cycle.
- Those cancer cells not killed by the first freezing are sufficiently stressed so that a second cycle is lethal.
- Damage to tumor vascularity permits the second freeze to occur more rapidly and extends the –40°C isotherm further from the CN/P.

**Source:** Adapted from: Babaian RJ, et al. *J Urol.* 2008;180:1993-2004.

*Richard J. Babaian, MD, has indicated to* Physician's Weekly *that he has worked as a consultant for Endocare and Gen-Probe, and has received grants/research aid from Gen-Probe. For more information on this article, including references, please visit: www.physiciansweekly.com*

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