

INDIGO: The Fourth Shade

MARK SCHOLZ, M.D.

Men in this category have recurrent or persistent disease after previous local therapy, as defined by a persistent or rising PSA, a positive biopsy after surgery or radiation, a nodule felt on digital rectal examination or documented spread to pelvic lymph nodes.

Cancer recurrence after initial surgery or radiation can be a discouraging development.

With most other cancer types, recurrence means the cancer is incurable, and likely to be fatal. The good news is that prostate cancer is not like other cancers.

Many types of prostate cancer relapses can still be cured – and even those that can't are still treatable, so that a normal life expectancy is usually maintained. Some relapses are so slow growing, that the best approach is simply to watch and wait before taking further action.

Several factors need to be considered before a PSA rise can be attributed to cancer. Sometimes small amounts of PSA are detectable after surgery because the surgeon may have failed to remove the whole prostate gland. This possibility can be evaluated with color Doppler ultrasound and endorectal MRI.

A PSA rise after radiation (also known as a PSA “bump”) may also be due to a noncancerous cause.

This phenomenon is more common after seed implants, but can also occur after undergoing intensity-modulated radiation therapy (IMRT).



Mark Scholz, MD
Prostate Oncology Specialists

In this case, the rise in PSA is a sign of inflammation in the prostate, not cancer recurrence.

Deciphering PSA levels after radiation can also be challenging because a “normal” PSA is higher in men with large prostate glands.

The prostate gland is not eradicated by radiation.

Just as a woman's breast is not eradicated when radiation is used to treat breast cancer, the prostate gland also persists after radiation. Therefore, even when the cancer is cured, the residual prostate gland still emits PSA. Long experience with the thousands of men who have undergone radiation has taught us that the PSA level will usually drop to under 1.0 ng/ml in men who are cured.

Recurrence after surgery is a different situation. Since the whole prostate has been removed, even tiny elevations in PSA usually signal a cancer relapse (unless the surgeon left some prostate behind, as noted above). The next step is to decide whether or not to aggressively pursue radiation.

When PSA levels are low, body and bone scans are almost always clear. Radiation directed at the previous site of the surgically removed prostate (called the *fossa*) is the most common type of treatment administered. Radiation is relatively easy to administer, and is often quite effective. Potential side effects of fossa radiation include the worsening of incontinence or impotence.

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A challenging dilemma is deciding whether or not to extend the radiation field to cover the pelvic lymph nodes, which is where the cancer frequently spreads.

Pelvic node radiation has experienced a renaissance, because IMRT is far less toxic than older radiation technologies. As a result, IMRT dramatically reduces the risk of damage to the intestines, compared to older conformal techniques.

Men embarking on fossa radiation should, at the very least, ensure their radiation therapist designs his radiation fields in a way that makes future node radiation feasible. That way, if fossa radiation fails to control

the relapse (i.e., the PSA keeps rising), the option to administer further radiation to the nodes is still kept open.

If a biopsy confirms an isolated relapse in the prostate after radiation, a second attempt to control the cancer with cryotherapy or seed implants can be considered, as long as body and bone scans are clear. (Please refer to the August 2011 issue of *Insights* for more detailed articles reviewing cryotherapy and seed implants.) The most common side effects from these treatments are impotence and incontinence. Success rates can vary, depending on the patient's original "shade," the Gleason score of the recurrent cancer, the extent of disease, PSA levels and PSA doubling time.

Testosterone Inactivating Pharmaceuticals (TIP)

While many doctors favor further local therapy with radiation or cryotherapy, local therapy invariably is associated with the risk of incontinence or impotence. Also, the odds for success vary. As a result, some patients prefer to stall with testosterone inactivating pharmaceuticals (TIP).

But before we discuss TIP as a standalone treatment for relapse, it should be recognized that TIP is often administered in conjunction with radiation, seed implants or cryotherapy to improve cure rates. In this scenario, the duration of TIP varies from six to 24 months, depending on the perceived seriousness of the relapse.

Relatively few studies have proven that adding TIP to local therapy will enhance cure rates in men with relapsed disease. The policy of adding TIP to local therapy is mostly based on extrapolating from extensive studies showing a benefit in men with newly diagnosed disease.

TIP as a sole therapy is frequently substituted entirely for radiation, cryotherapy or seed implants in men who feel these treatments are either too toxic or unlikely to be successful. TIP is also the ultimate fallback plan that will be used when the PSA continues to rise despite having tried these various local treatments.

Cures with TIP alone are very rare, but the duration of PSA control can be phenomenal. In fact, studies have shown that TIP will keep the PSA in check for an average of about 11 years! (continued on page 6)

TIP can be used either continuously or intermittently. The latter approach is usually more popular, because there are fewer side effects, and studies have demonstrated that the cancer control rates are equivalent to staying on TIP continuously.

TIP can consist of Lupron, Casodex or a combination of the two. When given intermittently, treatment is administered for six to 12 months, assuming the PSA drops to below 0.1, as is almost always the case (a PSA that fails to drop below 0.1 is termed a “high PSA nadir.” High PSA nadir indicates androgen independent prostate cancer, which is in the fifth “shade” of blue — Royal).

After TIP is stopped, men are monitored every three months for testosterone recovery and PSA levels. Testosterone usually recovers after 3-6 months. In a minority of men over 70, when testosterone fails to recover, testosterone replacement with Androgel® or Testopel® can be considered. The rate of PSA rise can be substantially slowed by taking Avodart® or Proscar®, leading to breaks, or “holiday periods” off TIP that are about twice as long. Treatment with a second cycle of TIP is usually initiated when the PSA levels rise up into the 3 to 6 range.

Preliminary studies indicate that further slowing down of the rate of PSA rise, leading to longer holiday periods, can also be accomplished with a combination of medications to stimulate the immune system. Three medicines in particular — Leukine (500 mg by injection three times a week), Cytosan (200 mg by infusion twice a month) and Revlimid (5 mg daily every other week) — appear to be effective, resulting in much longer holiday periods. Side effects are rare, consisting of occasional rashes and heartburn (from Leukine) and occasional low platelet counts (from Revlimid).

TIP also has notable side effects, including loss of libido, weight gain, muscle weakness and hot flashes. Side effects such as osteoporosis and breast enlargement are preventable with medications such as Boniva, Actonel, Prolia, Zometa and Femara. (Please see the November 2010 issue of *Insights* for an in-depth article on TIP. For a detailed review of the side effects of TIP, visit <http://prostate-cancer.org/pcricms/node/16> and scroll down to “Systemic Therapies.”

Summary

Ultimately, management of cancer for men in the Indigo shade varies, depending on a variety of factors related to the cancer — the original shade at diagnosis, PSA doubling time and body scan results all play a role.

Additional factors related to the patient’s age and sexual functionality are also important to consider. Treatment deliberations are being increasingly influenced by the expectation of further new discoveries.

All these factors influence the deliberation process about how aggressively the recurrence should be treated. Some men may choose to delay aggressive treatment and local therapies such as radiation, cryotherapy and seed implant by using intermittent TIP, with the hope that better options will be discovered in the future. ♦

What’s Your SHADE?



Join the Prostate Cancer
Blue Community

CALL FOR SUBMISSIONS

IF YOU HAVE A STORY TO TELL, WE WANT TO HEAR FROM YOU!

PCRI is looking for human interest stories for our weekly e-newsletter.

In December 2011, PCRI launched a brand-new publication, *PCRI Weekly*, to provide our readers with more frequent updates on prostate cancer news and research. A majority of PCRI articles are written by physicians and healthcare professionals, who provide valuable knowledge about the science and mechanics behind prostate cancer and various treatment options.

This is your opportunity to give readers a different perspective. PCRI will consider articles from any of the following:

- Prostate cancer patients and survivors
- Family members and advocates (wife/partner, children, parents, friends, etc.)
- Support group leaders
- Awareness event organizers

Guidelines:

- **Articles should be roughly 300-800 words.** Unlike *Insights*, *PCRI Weekly* aims to publish brief, concise articles. Please also submit a photo or image for your story. If you strongly believe you will require additional space, let us know and we will place it under consideration for a future issue of *Insights*.
- **Use simple language.** This is not a call for medical articles! We care more about your experience. Assume your reader knows little to nothing about prostate cancer.
- **Don't be shy.** Along with a prostate cancer diagnosis comes sensitive issues which can be difficult to talk about. Stay within your own comfort zone, but don't be afraid to write about the personal and the uncomfortable. On the flip side, if you have something more lighthearted or humorous to share, feel free to do so!
- **Have fun!** This is your chance to educate and empower others from an everyday person's perspective — be creative and thoughtful! What do you wish you had known earlier? What advice do you have for others who may be having a similar experience?

How to submit: Please direct all questions and article submissions (with contact information) to the editor at madhu@pcri.org, or mail your article to 5777 W. Century Blvd. Los Angeles, CA 90045.

PCRI will notify applicants if their story has been approved for publication. We look forward to hearing from you!