# Manitoba Prostate Cancer SUPPORT GROUP

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**Prostate Oncology Specialists Discuss:** 

#### May 2014

# PERSISTENT DISEASE

Over 50,000 men relapse after surgery or radiation each year. With other types of cancer, colon or lung for example, relapse is detected when a scan shows metastases. Prostate cancer is different. Relapse can be detected by the PSA blood test when the cancer is still microscopic. With prostate cancer, scan-detected metastases may take ten or more years to appear after a PSA relapse occurs. In the context of the broader cancer world, therefore, a "PSA relapse," represents a "twilight

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Thanks!

zone" between two extreme situations— men who are still in remission and men with overt, scandetected metastasis. There are exceptions to the generally reliable rule that PSA is always detectable when cancer is present. These exceptions occur when, 1) There is a positive margin present after surgery and, 2) When there is a positive biopsy after radiation. In the former case, the amount of persistent disease after surgery is too tiny to be detected by PSA. In the latter case, PSA production originating from the residual prostate gland "overshadows" the PSA coming from cancer. Therefore, as a result, without biopsy, detection of relapse after radiation is generally delayed until the PSA rises above the 1 to 2.

#### **Positive Margins**

Newsletter

Positive margins occur after surgery in 10% to 50% of men (the percentage depends on patient variables and surgeon skill). Positive margins are (*Continued on page 2*)

Next Meeting: May 15, 2014 John Dyck, HIFU patient Topic: HIFU treatment: My Story Location: Main Floor Auditorium Seven Oaks General Hospital Leila and McPhillips Time: 7 to 9 p.m





The Manitoba Prostate Cancer Support Group does not recommend treatment modalities, medications, or physicians.

Thought of The Day

I wondered why the baseball kept getting bigger ... and then it hit me.

www.manpros.org

#### (Continued from page 1)

common because the prostate is only a few millimeters from the bladder and rectum. Therefore, even the finest surgeon will leave cancer behind if the cancer invades outside the gland. Cutting out a bigger area around the prostate, i.e. into the bladder or rectum in an attempt to achieve a clear surgical margin, is not an option.

Positive margins are reported a couple days after the operation by a pathologist, a type of doctor who specializes in examining the gland under the microscope. When a positive margin occurs, the risk of future PSA relapse is about 50%.

#### **Minimal Extent**

When surgical margins are positive several studies show that radiation to the prostate fossa, the area of the body where the prostate used to be, lowers PSA relapse rates and may slightly improve the ten-year survival rate. Some experts argue, however, that men with minimal positive margins have a 50% chance of being cured and therefore should only undergo radiation when and if the PSA starts to rise. These doctors recommend monitoring PSA closely, say every 3 months, and starting radiation when the PSA rises up to 0.1 or 0.2. This approach is attractive because we know that half of men with positive margins will never relapse and can be spared the potential side effects from radiation.

#### **Multiple Areas**

Multiple positive margins usually mean the cancer was large, high grade and that surgery was probably illadvised in the first place. In any case, multiple positive margins should be handled like locally advanced disease, i.e. with radiation administered to both the fossa and to the lymph nodes in combination with testosterone inactivating pharmaceuticals and possibly with second generation hormonal agents like Zytiga and Xtandi. A short course of Taxotere might also be considered.

#### Local Relapse

Cancer recurring after surgery, radiation, cryotherapy or HIFU, in the area of the body where the prostate used to be, is termed a local relapse. Local relapses can be detected by a rise in PSA, a nodule felt on digital rectal examination, imaging (ultrasound or MRI) or by a biopsy. In this section about locally relapsed cancer, for the sake of discussion, it is assumed we are talking about isolated local relapse, i.e., that no metastases are detected by bone and body scans. If scans show metastases, systemic therapy is required. When systemic metastases are extensive, local treatment may be superfluous.



#### After Surgery

Radiation is the most common treatment for a local relapse after surgery. While radiation is often effective, the possibility of microscopic metastases outside the prostate fossa needs to be considered since radiation to the fossa alone will fail to be curative if cancer is also present in other parts of the body. The actual presence or absence of microscopic metastasis is never certain since there is no technology capable of detecting them. Microscopic metastases are more likely when the Gleason score is high and when PSA is rising quickly. In these situations, when the likelihood of microscopic metastases is higher, additional radiation to the lymph nodes in combination with testosterone inactivating pharmaceuticals (TIP) should be considered.

#### **After Radiation**

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Biopsy-proven local relapse in the residual prostate after radiation is usually managed with cryotherapy rather than with surgery. Cryotherapy and surgery both potentially cause incontinence. However, the risk of incontinence from cryotherapy is substantially lower than it is with surgery. New experimental approaches are under investigation using genetically altered viruses, laser, and in some cases, a second round of radiation using radioactive seeds.

#### After Cryotherapy

Local relapse after cryotherapy can be treated with an additional attempt at cryotherapy or with radiation.

#### **PSA Relapse**

Even though PSA has been questioned as a tool for screening, it's the Gold Standard for confirming cancer recurrence. However, a PSA rise from a low-grade recurrence that may not require treatment. Determining the difference between a low-grade recurrence and a high-grade recurrence is heavily influenced by the rate of PSA doubling.

For a PSA relapse, treatment usually consists of testosterone inactivating pharmaceuticals (TIP) given intermittently. For example, after TIP is started, PSA usually drops to less than 0.1. Treatment is continued for 6 to 12 months. After TIP is stopped and the effects wear off, testosterone recovers and PSA will begin to rise. A second cycle of TIP is restarted when the PSA reaches a certain threshold (usually between 3 and 6). Immunotherapy administered during the holiday period may slow the rise in PSA and delay the need for restarting TIP.

#### **PSA Doubling Time**

The seriousness of relapsed prostate cancer is determined by the PSA (Continued on page 3)

#### (Continued from page 2)

doubling rate, an indicator of the rate of cancer growth. When PSA doubling requires more than 12-15 months to occur, the disease is low grade and therapy can usually be withheld. PSA doubling that occurs in less than 12 months is usually a sign that treatment will be required. PSA doubling in less than three months signals aggressive disease requiring maximal therapy. Additional factors that are predictive of greater aggressiveness are high Gleason score, a rapid relapse that occurs soon after local therapy and the presence of a high PSA nadir while taking TIP.

#### **PSA Nadir**

The lowest PSA achieved after starting testosterone inactivating pharmaceuticals (TIP) is called the PSA nadir. A favorable drop in PSA (to less than 0.05) after starting TIP predicts survival far better than PSA doubling time or Gleason score. A high PSA nadir in the face of ongoing treatment with TIP is an early indication of castrate resistance. A high PSA nadir strongly indicates the need for additional treatment including radiation, stronger hormone blockade, chemotherapy or immunotherapy.

#### Castrate Resistance (Hormone Refractory)

Hormone refractory is defined as a rising PSA with a low testosterone (academicians prefer calling men with hormone refractory disease castration resistant). The selection of optimal treatment for men with hormone refractory disease depends on balancing two major goals: 1) stabilizing or reversing cancer growth and 2) minimizing side effects to maintain quality of life.

Historically, individual treatments are administered sequentially one by one starting with the mildest treatments and advancing to more powerful agents as dictated by need. However, due to the development of newer drugs with fewer side effects creates the possibility of using them in combination to achieve better results. Medications that are in common use for prostate cancer are Casodex, Nilutamide, ketoconazole, estrogen, Zytiga, Xtandi, Xofigo, Leukine, Cyclophosphamide, Taxotere, Carboplatin, Avastin, Revlimid, Xeloda, Jevtana, Xgeva and Zometa.

Most treatments, when they are effective, will drop or stabilize PSA within 60-90 days after starting therapy (Provenge and Xofigo are exceptions to this rule). So if PSA continues rising or if unacceptable side effects occur, a change in therapy needs to be considered.



#### **Rapid Doubling Time**

Men with hormone refractory disease and a rapidly rising PSA, especially after an antiandrogen like Casodex has been tried, are less likely to respond to secondary hormonal maneuvers such as Nilutamide, ketoconazole and estrogen. However, newer agents such as Zytiga and Xtandi are much more likely to obtain a meaningful remission. Early chemotherapy with Taxotere or Jevtana may also be advisable in cases where the cancer is behaving more aggressively. If a good response is attained and the disease becomes stablized, immune therapy with Provenge can be considered.

#### Local Regional

As discussed in the newly-diagnosed section on early metastasis to pelvic lymph nodes, modern radiation (IMRT) has become much more effective and far less toxic. Men with hormone refractory disease may benefit from radiation to the pelvic lymph nodes if suspic ions are high that disease may be confined to that region of the body.

#### **Bone Metastases**

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Unpublished data released in December 2013 in the Wall St. Journal indicate that early initiation of chemotherapy using Taxotere increases longevity. Additional agents used for men with bone metastasis are Zometa, Xgeva and Xofigo. Beam radiation to a limited number of bone metastases may be beneficial for some men.

#### Pain Management & Radiation

With some exceptions, most bone metastases tend to be painless. Spot radiation controls pain very effectively. However, radiation to bone should be used judiciously because radiation permanently kills bone marrow. Radiation is occasionally recommended to prevent future bone fractures. However, bone fractures from prostate cancer are uncommon. For this reason, undergoing bone radiation simply to prevent a fracture is rarely necessary. Xofigo, an injectable form of radiation, can be effective in reducing pain and seems to have only mild or moderate effects on the marrow.

#### **Bone Scans**

Metastatic disease is monitored with scans. Radioactive technetium bone scans have been the standard bone scanning method for years. More recently, Fluoride PET bone scans have demonstrated better accuracy. MRI is another accurate scanning technique for evaluating bone. Since many prostate cancer metastases occur in the pelvis or spine, MRI of these areas may pick up metastatic disease when all the other methods are read as clear.

Source: Prostate Oncologist Specialists

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# **Early Warning TEST For Recurrent Prostate Cancer.**

Early detection of recurrent prostate cancer has driven a team of Mayo Clinic physicians and researchers to the leading edge of prostate cancer diagnosis and treatment. A recently approved diagnostic test, the C-11 PET scan, allows doctors to detect a recurrence of prostate cancer long before conventional imaging does.

Survivors of prostate cancer often live in fear of their cancer coming back. Physicians and patients alike know that early detection is crucial for beating prostate cancer a second time, so it's even scarier when a doctor says that the cancer is there but that it can't be found.

Oncologists monitor the prostatespecific antigen (PSA) levels of men who have been treated for prostate cancer, and when the PSA goes up, it's a warning sign that the cancer is back. The problem, though, is that the cancer itself sometimes can't be found.

That's because elevated PSA levels can occur long before a lesion can be detected by traditional imaging techniques, such as bone scans, computerized tomography (CT) scans and magnetic resonance imaging (MRI). Even if the scans do detect something, there is no way to tell whether it's active cancer, scar tissue from previous treatments or even cancer at all — the scans only see the anatomical abnormalities and not what is causing it.

However, a Mayo Clinic research team has developed a new imaging method that can often find recurrent prostate cancer months, if not years, earlier than other imaging techniques can.

In September 2012, the Food and Drug Administration (FDA) approved Mayo Clinic's use of choline C-11 positron emission tomography (PET) scans. The choline C-11 PET scan is a diagnostic test used for prostate cancer patients who have undergone previous treatment and then develop rising PSA levels but for whom conventional imaging can't locate a recurrent tumor. The choline C-11 is absorbed by cancer cells and highlights them on the scan.

"For the first time ever, we will have a clear blueprint of where the patient stands, at a far earlier course in treatment failure," says Eugene D. Kwon, M.D., a Mayo Clinic urologist in Rochester, Minn.

For many months, Mayo Clinic was the only health care institution in the country authorized to use the choline C-11 PET scan. But when Mayo Clinic originally filed a new drug application with the FDA for use of the choline C-11 component, Mayo Clinic decided to waive all exclusivity. That's because Mayo Clinic wanted medical providers everywhere to be able to manufacture the drug and have access to the test to better serve their own patients.

## **PET** — The best imaging option

Doctors use a cancer's high rate of

growth as a means of visualizing tumors. Prostate cancer tumors consume choline, a B-complex vitamin, to use as a building block. So when a minute amount of radioactively labeled choline (choline C-11) is inje

(choline C-11) is injected into a patient, it is quickly taken up by the tumor, which then emits radiation.

A PET scanner is able to tell where in the body this radiation is being emitted.

"Then it translates that radiation signal into a computer-digitized picture with a brighter intensity being represented as the site where there is more of this radioisotope localized," Dr. Lowe says. "It's a way of looking at the body three-dimensionally so you can see through the body and around the body."

Dr. Lowe has been interested in positron emission imaging since his early days in college. After medical school, the Canadian-born physician pursued a residency in nuclear medicine and a PET imaging fellowship at Duke University.

Dr. Lowe ran the PET facility at Saint Louis University for five years. During that time in the late 1990s, he says, only about 25 places in the country — all of them academic medical centers — were doing PET scans.

In 1999, Mayo Clinic recruited Dr. Lowe to put together a clinical PET scanning program at its Rochester campus, a program that he says is now one of the two or three busiest practices in the nation, and the fastest

> growing segment of Mayo Clinic's Department of Radiology.

A year later, Dr. Lowe and his colleagues began looking into PET imaging of prostate cancer in animals. The

team compared different radioactive nutrients and found that choline C-11 was the superior imaging agent.

In 2005, the team imaged men with (Continued on page 5)



#### (Continued from page 4)

known prostate cancer, and again choline C-11 emerged as the lead compound. By the latter part of 2007, choline C-11 was being used under a research protocol in a small number of patients at Mayo Clinic, allowing the physicians to gain experience and ultimately integrate the test into clinical practice.

#### Safe and fast

Choline C-11 isn't toxic — it's the same as choline, except that a few of its normal carbon atoms have been replaced by radioactive carbon atoms. The body sees it and treats it the same way as it does regular choline.

"You get it in broccoli and eggs, and in many of the foods you eat," Dr. Lowe notes. "We could give a manythousand-times greater dose of choline than the dose that we would normally inject into somebody for a PET scan, and it still wouldn't approach what the daily recommended vitamin dose is."

PET drugs are different from most other pharmaceuticals. Among other features, for instance, they have a very short shelf life.

The half-life of choline C-11 is only 20 minutes. That means it loses half its radioactivity every 20 minutes; after 40 minutes it's only one-quarter as radioactive and after an hour only oneeighth, with ever-decreasing radioactivity as time ticks on.

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Because the radioactivity is the property that allows the PET scanner to see the cancer, choline C-11 must be used shortly after it's made. It cannot be stored and shipped — it must be manufactured right where it is used.

Mayo Clinic uses a high-energy particle accelerator called a cyclotron to produce C-11, which is then incorporated into choline C-11. Technicians prepare the choline C-11 dose based on the exact time it will be used. A nuclear medicine technologist injects it into a patient waiting on the PET scanner bed.

Because of the demand prompted by patient cases, Mayo Clinic is adding a fourth PET scanning suite and second cyclotron, and it has increased production from twice weekly to twice daily, three times a week.

It takes about 45 minutes to make choline C-11 after the C-11 comes out of the cyclotron. The scan itself takes

only about 20 minutes. The results are analyzed, and a report is typically ready for the doctor half an hour after the scan is completed.

At Mayo Clinic, choline C-11 PET scanning picks up metastatic lesions in about one-third of the men in whom traditional imaging found no lesions. The false-positive rate for the PET scan is low — about 5 percent, Dr. Lowe says. A biopsy is performed on any suspect tissue found by the scan.

For many men with a rising PSA level, it can be difficult to decide whether and when to treat a possible recurrence of prostate cancer. But with the new choline C-11 PET scans, lesions can be seen far earlier and more precisely.

Mayo Clinic researchers are also investigating other imaging agents for prostate cancer, such as choline F-18. It has a half-life of almost two hours. which means that a single production run could be used to scan more men. Researchers are also investigating the use of choline C-11 and choline F-18 for other malignancies.

Source: Mayo Clinic website.

#### \*\*\* program decisions, etc. **Volunteer Opportunity:** · Have a desire to give back and help others Now Recruiting for the who are involved with PCa. Manitoba Prostate Cancer Support Group · We also have other opportunities to volunteer **Board of Directors** for "one time" events such as working at a Does this sound like you? bingo or attending a health fair. · Friendly, enthusiastic, compassionate, There are no requirements – but computer email dependable. skills are helpful. · Able to attend one monthly Board meeting (2<sup>nd</sup> Thurs. of the month at 2 p.m.). Please consider this and call our answering · Would like to join a working committee and machine at 204-989-3433 participate in activities, ☆ become involved in budget, policy and ☆ ☆ \*\*\* www.manpros.org

# Vitamin Supplements - How Best To Use Them

By: Dr. Mike Allan and Dr. James McCormack

According to the Oxford Dictionary. vitamins "are a group of organic compounds essential for normal growth and nutrition and are required in small quantities in the diet because they cannot be synthesized by the body."

As humans, we long for perfect health and longevity. This desire leads us to try an endless variety of interventions to achieve the goal, with varying degrees of success. It may be this yearning for unattainable perfection that leads to decisions which appear logical but, in fact, are not.

The "vitamin logic" states, "if the body needs small amounts of vitamins to function, the body will perform even better if given more." It is important to remember that using the "need a little so take a lot" philosophy has not turned out so well with food, alcohol. medications or vices.

There is the unfortunate reality that multiple large well-designed studies have quite consistently shown no advantage in taking vitamin supplements for relatively healthy people.

To date, well over 100,000 people have been studied over a number of years and the results have confounded vitamin logisticians and sales reps everywhere. Almost without fail, for relatively healthy people without obvious vitamin deficiencies, no change in overall death rate, cancer or cardiovascular disease has been shown. In fact, anti-oxidant vitamins, like Vitamin A, E or beta-carotene, have actually been shown to increase death for approximately one in every 300 who take any of those supplements for roughly three to five years.

B vitamins, believed to potentially reduce cardiovascular disease, have also been shown to have no effect. A very recent review also suggests no overall important clinical benefit from using Vitamin D supplements, except maybe reduced hip fractures, but 300 to 400 people need to take it to benefit one person, so the clinical importance of this is questionable.

"Vitamin logic" is so powerful that many of you may still be reluctant to believe the evidence, so we have devised some fool-proof ways for you to get the maximum benefit from vitamin supplements.

1) After purchasing any vitamin supplements, immediately drive to the house of a friend or family member that is at least five kilometres from your house and ask them

to store these vitamins in a safe place. Every day, when you generally take your vitamin supplement, simply walk to their house, pop that pill, and then immediately walk home. Briskly. The results will astound you.

2) For those of you who swear by higher dose vitamins, choose a home 10 km from your house, run there at a comfortable pace, take two pills, and run home. Note: You can actually just take one and get the same effect, which immediately cuts costs in half. Note 2: You can also take none.

3) If you have no friends or family hopefully not a result of your vitamin "habit" - and are thus forced to keep and take your vitamins at home, there are still ways to maximize their effect. The ultimate technique is to place your favourite vitamins on your dinner plate and surround them with a variety of fresh vegetables, fruit and fish/poultry. Should you at anytime during the meal feel compelled to take one of the vitamins, pick it up, lick it, and then compare it to the taste of any of the food on your plate. If you prefer the taste of the vitamin supplement, go for it.

Delicious Flintstones chewables are, of course, an exception, especially the Dino ones.

4) Fortunately, your body is equipped with a tremendous filtering system known scientifically as "your kidneys." So effective are these organs if you ingest more than the small amount of vitamins required for

health, you pee out the excess. To avoid any possible strain on your kidneys, however, we suggest, before taking your vitamins, place them directly into the toilet and flush. Although this avoids

the "middle man," we'll have to pray it won't harm the fishes.

5) When you purchase vitamins, make sure they come from "natural sources" as it is well known that natural things are completely safe - for example, natural arsenic, natural tornadoes and natural snake venom.

6) Finally, if you can't live without the belief vitamin supplements really do work, then package up the ones you buy and send them to countries where vitamin deficiency is a serious health concern. You will be proven correct, they are vital, and the effect of this generosity may be the only daily supplement you need.

Mike Allan is a family doctor and associate professor and the director of evidence based medicine in the department of family medicine at the University of Alberta. James McCormack is an expert advisor with EvidenceNetwork.ca and professor with the faculty of pharmaceutical sciences at the University of British Columbia in Vancouver.

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# "Free Book"

Beyond Hormone Therapy by Mark A. Moyad, MD, MPH

This book is a unique educational book for individuals dealing with advanced prostate cancer, those with a rising PSA after being on hormone or androgen deprivation therapy. It discusses how the cancer came to be advanced, what factors affect prognosis, and what treatments are available. Many useful tips to lessen or eliminate treatment side effects are included.

I have 10 books to give away – 5 to rural Manitoba and 5 to Winnipeg. I will accept emails dated on, or after, May 15th (Everyone should have received their newsletter copies by this date). The first



May 2014

10 people to send an email to me with your name, address, and telephone number will receive the book. Please put "To the Editor" in the subject line of your email and send it to: manpros@mts.net

This book is courtesy of The Manitoba Prostate Cancer Support Group.

June Sprott - Newsletter Editor

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# New Test Developed To Detect Men At High Risk Of Prostate Cancer Recurrence

Editor's Note: This article was produced by medical express.com prior to the conference that took place in Vienna, Austria on April 5, 2014. This conference is well attended by radiation oncologists from around the world. Note that the research was done in Canada.

A new genetic "signature" to identify prostate cancer patients who are at

high risk of their cancer recurring after surgery or radiotherapy has been developed by researchers in Canada, the 33rd conference of the European Society for Radiotherapy and Oncology in Vienna will hear today (Saturday).

Professor Robert Bristow will tell the conference that although surgery and precision radiotherapy are the mainstays of treatment for cancer that is confined to the prostate, the cancer will return in between 30-50% of patients due to spread of the disease outside the prostate gland that was undetected during the initial treatment. "Men who fail treatment within two years may be at the highest risk of dying from their prostate cancer," he will say. "Existing methods for identifying high risk patients are imperfect, so new tests are required that are better at predicting which patients will have their cancer recur. These men can then be offered additional treatments, such as chemo- and hormone therapy, that will combat the



will combat the prostate cancer throughout their entire body, rather than therapies solely focused on the prostate, in order to improve their chances of survival."

Dr. Bristow, a clinician-scientist at the Princess Margaret Cancer Centre and a Professor at the

University of Toronto, Canada, and Dr. Paul Boutros from the Ontario Institute of Cancer Research, together with their Canadian team, have developed a "signature" based on the DNA of the patient's prostate cancer that can accurately predict treatment failure in patients undergoing radiotherapy or surgery. The tumour's genetic characteristics and its microenvironment were analysed from biopsy tissue taken before the start of treatment.

"This is the first report of a test using this information derived from biopsy samples that can predict with close to 80% accuracy which men are at high or low risk of their prostate cancer recurring," he will say.

The researchers need to validate the test over the next two to three years in different and larger groups of patients to ensure that it will work successfully in hospitals worldwide. "If all goes well, then this will lead to a new test for cancer patients that can be turned around in three days and will tell doctors which patients will do well with local treatment alone – surgery or radiotherapy – and which will need extra treatment," Prof Bristow will say.

Source: medicalxpress.com

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Many Thanks		

Our Prostate Cancer Support Group would like to acknowledge a recent donation from AbbVie Corporation. AbbVie produces Lupron, a drug used for prostate cancer hormone therapy. We are grateful they have chosen to assist us with our work again this year and their kindness is much appreciated. Their involvement helps us to continue our services to the community and we thank them for their generosity.

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## MEETINGS

May 15, 2014 John Dyck HIFU Treatment: My Story

### June 19, 2014

Dr. Ainslie Mihalchuk, Family Physician CMO & Director of Family Medicine, Concordia Hospital *How You Can Help Yourself* 

July, 2014 No Meeting

> All meetings are held at Seven Oaks General Hospital Auditorium 7-9 p.m. Everyone welcome

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