PSA North of England

Prostate Matters

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Prostate Matters Issue 2

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SURVIVING PROSTATE CANCER - A CAUSE FOR CELEBRATION

Stepping Hill's urology department recently reached a milestone having successfully carried out 300 radical prostatectomies at Stepping Hill and the Alexandra Hospitals. They chose to celebrate by inviting all their patients who had undergone prostate surgery and who continue to enjoy good health to an event at the Old Trafford Football Club.

The event, which was being held in association with Astra Zeneca, was opened and compered by Stuart Hall who kept the audience entertained and the speakers on their toes with his own brand of wit. Even prostate cancer can be amusing, especially when patients tell their stories, and Denis Law, who was the guest of honour, and Martin Ferguson both created much amusement in the way that they talked of their own recent experiences - both had been operated on by Paddy O'Reilly, Consultant Urological Surgeon Stockport NHS Foundation Trust.

There were also a number of presentations from the medical professionals at Stepping Hill.

Mr O'Reilly, Head of the Urology Department, who, it was announced, had recently been appointed President of BAUS (British Association of Urological Surgeons), talked of the history of the Radical Prostatectomy in this country and in particular in the North West of England; how he and a small number of other surgeons had travelled to the USA to learn the technique. He took the opportunity to name and thank many people who had a part in establishing the high level of service both at Stepping Hill and at the Alexandra. He said that by publicising this event he hoped it would help to en-

A cause for celebration - Denis Law takes part in the celebration

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Chairman's Comment

In this, the second of our general newsletters, we devote more space than is usual to medical features. This is largely because of the negative publicity, appearing in the popular press, concerning PSA testing. We hope that the supplement included (pages 5-8) will introduce some balance into the PSA debate.

This year has seen some developments in the activities of our charity and these will be reviewed in the forthcoming chairman's report. To make further progress, in 2005, we need your help and I would like to ask all of you to consider ways in which you might like to become involved.

More seasonably, as the year comes to an end, it is a great pleasure, on behalf of all the committee members, to wish you all a very happy time over the festive season, and a good and healthy new year.

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Over 20,000 men are diagnosed with prostate cancer every year in the UK

It affects men from all walks of life and often goes unnoticed in the early stages.

Symptoms to look out for:

Frequent need to pass urine

Delay or hesitancy before urinating

Pain in passing urine

Dribbling

Blood in urine

Inability to get or maintain erection

Back pain

RAYS OF HOPE—The Christie talk by Dr John Logue

In September Dr John Logue addressed an audience at the Christie meeting. Dr Logue has an ability to introduce the subject at a level that is well received by newcomers as well as being able to hold the interest of those in the audience who have a more advanced level of knowledge. As on previous occasions Dr Logue's presentation was well received and appreciated by the audience.

This article is based on notes taken at that meeting.

The purpose of the talk was specifically to make known the various ways of treating Prostate Cancer through radiation and to point out where they come into play. Also, where the future lies in the treatment of Prostate Cancer, and in particular the significant improvements to both the procedures and reduction in side effects of the treatments.

P.C. is a disease which is becoming increasingly common as years go on. It is more common in the African/Asian people. Data available suggests that the percentage of men with Prostate Cancer increase with each age group and in the 80+ group it is around 50%. In the U.S.A. the percentage that die of P.C. is reducing considerably, believed to be mainly due to earlier detection and the screening of all males over the age of 50, rather than the fact that their treatments are more effective than in the U.K.

In the UK the number of men diagnosed with P.C. is more than 20,000 p.a. Five years from now if the increase in ad hoc PSA testing continues, this will increase to 70,000+. If a formal early screening system could be established in the U.K. as in the U.S.A. then approximately 97% of those diagnosed would still be alive five years later. If regular screening could be developed, then it would be diagnosed at an early age and treated; men would respond well especially in the early years.

What causes us to see a Prostate Cancer patient?

The majority of men present today show no symptoms. Men come along with a raised PSA from a routine blood test, or rectal examination.

In others symptoms develop if the Prostate becomes enlarged, putting pressure on the bladder, causing urinary problems, or impotence. Pressure on the kidneys can cause kidney failure. In advanced cases there is pain, which usually means that the cancer has spread into the bones.

If diagnosed with P.C. what do we need to know about the disease?

We need to know what stage it is at. Whether it is contained within the prostate or whether it has spread beyond. A bone scan will determine if there is any spread. Also how aggressive is the P.C? Biopsy results and the PSA test will guide on this.

T1 is where men have positive biopsy results, but the prostate feels normal and looks normal on a scan.

T2 is where there is a lump within the prostate.

T3 is where the cancer has spread out of the gland.

T4 is where the cancer is invading the bladder or rectum.

The Gleason score tells how the cancer is behaving and how aggressive it may be.

The majority of scores are between 6 and 7 which are O.K. 9 to 10 means it is more aggressive.

In some cases various types of scans are carried out which give a lot more information about the cancer.

The procedure which follows is:-

Diagnosis - Staging - Multi Disciplinary Team planning - Treatment - Follow-up - Long term survival.

Treatment for early P.C. include:-

Do nothing except "watch and wait" (actively monitor).

Remove the prostate - a radical prostatectomy.

Radical external beam radiotherapy.

Brachytherapy.

Cryotherapy is where the prostate is frozen.

HIFU - High intensity focused ultrasound. This effectively cooks the cancer and kills it.

Hormone Therapy - a treatment suitable for most cancers, which can keep it under control, often for many years, but will not be a cure.

40% of men have prostate cancer, but die of other causes. Treatment may not be necessary.

The benefits versus the toxicity of treatment needs to be weighed up - hence the "watch and wait"

By careful monitoring it may be possible to see which cancers are the "pussycats" and which are "tigers"

<u>Surgery versus "watch and wait."</u>
Radical prostatectomy involves the removal of the prostate, which is a good treatment for early cancer in the situation where the PSA is below, say, 20 and the cancer is contained within the prostate It has potential side effects; it is a relatively major operation and may not be something which older men can withstand, therefore usually confined to men under the age of 75.

A trial has been carried out on Surgery v. Observation, but there is no evidence to suggest that men who have surgery necessarily live longer than those who just have an eye kept on them, but it does suggest that as time goes on those who have surgery may benefit, as more men under observation develop secondaries.

<u>Cryotherapy</u> is another option, which is not normally freely available, but this is now being looked at more closely.

<u>IMRT</u> - Intensity Modulated Radiotherapy.

Treatment by radiotherapy has increased quite dramatically. At The Christie 100 cases were treated in 1991, but 525 cases in 2003 going up to 600+ this year.
There has been a significant improvement in the way the treatment is delivered, especially where accuracy is concerned.
It is now possible to shape the radiotherapy to the shape of the cancer, thus reducing the side effects considerably. Also Hormone treatments can be used try to improve the chances of cure. It is possible with the use of scanners to plan Image Guided radiotherapy sometimes by implanting markers which are visible on X-

Continued page 3, col. 1

Nutrition and Prostate Cancer

In our first edition of *Prostate* Matters we included an article on Nutrition based upon information produced by the Prostate Cancer Foundation. In future editions we shall take one or more of the headings in turn and provide more detail:

Reduce or eliminate consumption of red meat.

• Minced turkey: Can be used in place of anything calling for minced beef
• Sliced roasted turkey breast: For sandwiches, wraps, salads
• Skinless chicken breast: Roasted, grilled, skewered, baked, stir-fried
• Almost anything coming from the sea: Grilled, baked, steamed, poached, even barbecued if in foil.
• Soya burgers: There are many brands to choose from. Try several to find your favourite. (try mushroom burgers)
• Vegetarian sausages: Grill them for the best taste
• Soya mince (e.g. Realeat brand Vege Mince from good supermarkets): Can be used in place of anything calling for minced beef (makes delicious Chilli and Bolognese).

Reduce or eliminate high fat, farm-raised fish

Salmon, trout, mackerel and sardines are fatty fish. The type of fat in these fish is the healthy omega-3 type, so it's okay to eat this fish if it is fresh and wild. Unfortunately, the majority of salmon available in markets and restaurants is farm-raised. We would not recommend this due to the use of chemicals, growth promoters and anti-biotics used in intensive fish farming. We would prefer to see the use of wild salmon or organically farmed salmon, where such methods of production are not allowed. When you go to the fishmonger , you need to ask whether they have any wild salmon, trout, etc. Be sure to specify that you don't want farm-raised fish.

There are many other delicious fish and seafood you can eat. Try these:

- Tuna
- Halibut
- Snapper
- Cod
- Haddock
- Hake
- Monkfish
- Red mullet
- Plaice
- Sea-Bass (but beware much of this is now farmed, despite the name)
- Sole
- Squid
- Whiting
- Swordfish
- Skate
- Crab
- Prawns
- Lobster
- Clams
- Mussels

Nutrition Goals

- Decrease percentage of dietary fat to 15 to 20% of total energy intake
- Increase vegetable servings to 3 to 5 per day
- Increase fruit servings to 2 to 4 per day
- Increase dietary fibre intake to 25 to 35 grams per day
- Substitute soy protein for some animal protein so that you are getting 25 to 40 grams of soy protein per day

RAYS OF HOPE

continued from page2.

rays on the machine. In addition a new machine at the Christie can create a CT scan at the same time as the treatment is being delivered. This machine at is one of only three in the world. In the last 10 years the necessity for bowel operations following the use of radiotherapy has been negligible, due to the improved techniques in administering radiotherapy.

Brachytherapy - Treatment of P.C. by the implanting of radioactive seeds.

Those at T1 and T2 stages with no prior TURP are eligible for this treatment . Average time of treatment - 2 days.

Conclusions:

- There is increasing diagnosis of EARLY prostate cancer. (Ed comment: through increased awareness)

- Evidence that early treatment is curative.

- Advances in treatment (IMRT, Brachytherapy).

- Research to outline behaviour of cancer.

- Advances in management of advanced cancer.

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A short Question and Answer session followed.

Q: Is it possible to have a second course of radiotherapy if other forms of follow up treatment cease to be effective.

A: No, because if the dose of radiotherapy is too high, it may cause damage to the rectum. This is why only one course of radiotherapy is given.

Q: The longer hormone treatment continues the more side effects it produces. How about HRT holiday once the PSA count becomes very low?

A: It is possible to use hormone treatment in an intermittent way with pulses of treatment over 6 – 9 months given as necessary.

Q Is it possible to treat cancer if it returns in the prostate following radiotherapy?

A: If the cancer returns to the prostate following the treatment with radiotherapy then Cryotherapy. Or HIFU may be useful treatment.

Christie Talk Summaries

In the past many members have asked if we could provide a summary of the Christie presentations.

We have often attempted to do this with a speakers approval, but unless there is a transcript, which is rare, it has proved extremely difficult. This is particularly so when a speaker has no notes.

Eva Lomas, one of our members from the Bolton Group, has offered to take notes and to make them available to us for checking and collation into a summary. This is an onerous task and we are very grateful to Eva for making this offer.

Dr John Logue's talk has been put together from Eva's notes and we hope that we can bring you a summary of the most recent talk in each of our *Prostate Matters.*

Personality - Ron Turner

Ron, born in Manchester on Jan 2nd 1920, was raised and educated in the city. His childhood and youth, during the 1920's and 30's saw the period of the depression and the build up to war. In his first job, in the textile industry (aged 17); he was the youngest member of the Royal Exchange, which now houses the theatre. In Ron's time people met there to discuss business, and it was the largest floor in Europe available for this purpose.

Ron joined the Royal Airforce on Monday June the 17th 1940. It was the day France "fell" (Ron accepts no blame for this) and he was discharged, by coincidence on Monday June 17th 1946. During this period Ron saw service in India, both in hill stations in the Simla hills, and at an air base in Bengal which was used to bomb Japanese submarine bases. Later he was moved to Penang, and he still remembers with great pleasure, the white bread and 'best' butter (which he hadn't tasted for 3½ years) supplied by the Royal Navy. Well the Navy is the senior service!

Following the atom bombing of Japan, he returned to the UK and resumed employment with his old firm (F. R. Sewell) where he was subsequently appointed to the board of directors. In 1946 he married Betty his wife of nearly 60 years and, later, they had two children, both boys. As the Textile industry changed with the larger companies taking increased share of the market, Ron moved to Courtaulds where he became a Marketing Executive, "dealing with customers of yarn and fibre clients "down the line" to many of our major retailers and mail order catalogue companies; educating them about our forthcoming advertising campaigns for new products as and when we launched them". This was a time of rapid change in textile technology, and much of Ron's time was spent in the education of retailers about the new materials and new methods of dyeing and finishing. When Ron retired, Courtaulds was the largest company

in textiles. Considering the position now, and taking into account the fall of France, it does seem that Ron's comings and goings can be very significant, which takes us to prostate support.

Ron was diagnosed (aged 69) in 1989 and, within three months, he was given a TURPS followed by radiation therapy at Christies. His consultant at Christies (Dr. Read, who preceded Dr. Logue) thought that all might be clear, but his urologist P. J. O'Reilly at Stepping Hill decided to monitor him and has continued to do so for more than 15 years. During this period Ron has been fortunate, in that he has experienced no pain, although he has had to cope with the problems associated with zoladex and, latterly, with oestrogen. He is possibly the longest survivor in our group.

Ron first became aware of prostate support, like so many men, when his wife drew his attention to a message in a local paper by two men who were meeting in the 'Church Inn' inviting other patients to meet with them to provide mutual support. These men were, of course, Roy Nixon and Ray Dalton. Ron joined them and the group built up to numbers where there became a need for formality, and Ron, who was then secretary of the Pownall PROBEX club, arranged with the manager of the Hesketh Tavern that a room be made available for meetings. These meetings still take place (at 1.00pm on the second Monday of each month).

Ron is very grateful to the initiators of the support group, and is particularly grateful for the tremendous efforts made by Roy Nixon, in the development of our support group, and also to Stepping Hill NHS Hospital, especially to Paddy O'Reilly.

Ron, who is clearly a very courageous man, had two hip replacements 13 years ago and two cataracts removed within the last two months, for which he is also very grateful to the NHS. In fact he can now read without glasses for the first time in 40 years.

Support groups

In the last *Prostate Matters* we talked of Local Support Groups—mentioning the existing ones at Bolton, Cheadle, Crewe and Trafford and new areas on which we are focussing. We are pleased to say that progress is being made in all of the new areas mentioned and we are confident that in the New Year we shall achieve our first meetings in Oldham and the Wirral. Chester is also progressing and there are promising signs for Stoke-on-Trent. If any members would like to assist in the creation of a new group, or feel that an area is lacking a group, please contact Mike Lockett through the office. If you don't already attend a group, but would like to, or have someone else in mind who might benefit, please contact the office to determine the specific location and meeting times of your nearest one.

The Prostate Cancer Support e-group

This is another way to keep in touch with other survivors of prostate cancer, their partners, carers, friends and others who are interested in the subject. What happens is if you, as a member, send an e-mail it pops up in the inbox of everyone who is a member of the group, and you get the messages other members send. The etiquette is that the e-mails are titled to cover the subject of the text. This then gives the option to delete the ones that you have no interest in.

There are two rules – 1) No spam and 2) Be kind to others on the group.

This allows a wide range of discussion and support but in a kindly manner and also allows for members to point people to the place where the best information is available for them. We advertise group meetings and other events and recent research too.

To join the group you can request an invitation from the group owner, Bryan Metcalf at bryan.metcalf@virgin.net. Who, when he can, escapes the jungles of Yorkshire to come to the Manchester meetings.

Bryan Metcalf - 01757 228394

SPECIAL SUPPLEMENT

Testing for Prostate Cancer using the PSA test!

Following considerable recent press (mainly negative) about the PSA test there have been many concerns expressed by members and other callers to both our helpline and to the committee about the tests effectiveness, reliability and relevance to patients. As a result we have printed, in the next four pages, responses from medical professionals and also a paper produced by our Chairman, John Dwyer.

Experts: PSA Test Still Valuable for Prostate Cancer Screening

By E.J. Mundell, *HealthDay Reporter*

SATURDAY, Nov. 13 (HealthDayNews) -- Earlier this autumn, the researcher who first identified the prostate-specific antigen (PSA) blood test -- used for nearly two decades to screen men for prostate cancer -- announced the test had become "all but useless."

Writing in the October issue of the *Journal of Urology*, Stanford University's Dr. Thomas Stamey said the test is now more likely to spot benign prostate enlargement or very slow-moving malignancies than "significant," aggressive cancers, raising risks for misdiagnosis and unnecessary surgeries.

The news left millions of older American men confused about whether their annual PSA test was worth it, and whether its results could be trusted.

But according to experts representing two leading medical groups, rumours of the demise of the PSA test may be premature.

Dr. Durado Brooks, director of prostate and colorectal cancer at the American Cancer Society, noted that "Dr. Stamey's article is countered by a wealth of other literature, so there's a lot of dispute right now among experts as to the level of value PSA testing offers."

He believes PSA screening remains "a useful test, in terms of detecting prostate cancer in its early stage."

The PSA test -- which measures blood levels of a compound secreted at higher levels as prostates enlarge -- may well be a victim of its own success. Experts generally agree that when the test was first put into widespread use in the 1990s, it picked up a lot of advanced cancers that had previously been missed.

But as annual screenings have become more commonplace, PSA screening is now detecting much smaller cancers -- many of them slow-growing and worthy of "watchful waiting" rather than more radical prostate-removing surgery.

What's needed, according to Brooks, are improvements to the existing PSA test "so that we can differentiate those 'bad actors' -- prostate cancers that are more likely to be aggressive and to cause problems -- from the indolent [slow-growing] tumours that are often found."

Dr. J. Brantley Thrasher is chairman of urology at the University of Kansas Medical Centre and a spokesman for the American Urological Association. He agreed with Brooks that the PSA test needs to be refined, not discarded.

"The fact of the matter is that death rates from prostate cancer have dropped precipitously from the 1990s," he said, although there's no clear evidence that decline is due to PSA-linked early detection.

"What we're trying to do now is find better markers, tweaking PSA to make it better," he said.

"What bothers me a little bit, especially in the lay press, is that when we start to see a little controversy around something like PSA screening, people out there will say 'Well, there's no use for PSA, don't even get one,'" he said.

"Then I worry that we'll go back to the situation we had 10 or 15 years ago, where we are seeing a lot of advanced-cancer patients walking through the door, crippled with bony metastases because they're not finding it till it's very late, and we don't have anything to offer them."

Thrasher pointed out that, despite better early detection, prostate cancer is still the second leading cause of cancer death in men, killing more than 30,000 American males each year.

According to both Thrasher and Brooks, Stamey's dismissal of the PSA test came as no real surprise, since debate has simmered among urologists and cancer specialists for years as to the exam's continued efficacy in spotting cancers worthy of aggressive treatment.

"It's always been a controversial issue," Thrasher said, "because PSA can be elevated for a number of reasons besides cancer," including the benign prostate enlargement that occurs naturally as men age.

The challenge for researchers is to find better blood markers, to make the test more specific, Thrasher said. "Almost every quarter I'm seeing literature coming out with new molecular markers," he said. "I'm truly convinced that we're going to come up with something that -- either combined with PSA, a PSA [variant], or by itself -- will be better."

In the meantime, the American Cancer Society continues to recommend that doctors offer annual PSA screening, plus a digital rectal exam, to all normal-risk male patients over 50 years of age.

According to Brooks, the challenge for patients is to "understand the benefits and the limitations of the PSA test and decide for themselves, in consultation with their physicians, exactly what they want to do, and whether they want to be tested or not."

SOURCES: Durado Brooks, M.D., M.P.H., director, prostate and colorectal cancer, American Cancer Society; J. Brantley Thrasher, M.D., chairman, department of urology, University of Kansas Medical Center, Kansas City; October 2004 *Journal of Urology*

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PSA TESTING AND SCREENING
- A PATIENT'S VIEW (J. Dwyer Nov.2004)

A recent paper by Thomas Stamey (NEJM 2004) led to much discussion, especially in the popular press, about the validity of the PSA test in the diagnosis of prostate cancer (PCa), and provided much ammunition for those against screening. The comment that "The PSA era in the US is over- -" is not the last word on this topic. We include a surgeon's response in this letter. A good review by A. M. Murphy et al. (J. Urol.2004) compares the cost and reliability of screening for PCa & Breast Cancer. Here is a patient's response.

PSA in Diagnosis

It is clear that the PSA test is not specific for PCa. In general PSA serum levels of healthy men change with age. The data reported by (J.E.Oesterling 1993) are usually quoted (see table 1)

Additionally, serum PSA levels can vary in an individual due to: prostatitis, recent ejaculation, prostate massage (e.g. riding a bicycle) etc. The benign growth of the prostate (BPH) can also result in an increased expression of PSA. In BPH the PSA level is reported to increase (linearly) with increase in prostate volume.

These features make it difficult to select a PSA level for use as a 'cut off' for selecting patients for biopsy. Consequently, the benefits of a screening programme are considered by many to be outweighed by problems associated with: unnecessary referral for biopsy, anxiety associated with testing men for cancer, unnecessary treatment of indolent cancers and (of course) resource.

The choice of a 'cut – off' PSA level is compounded by the observation (I.M. Thompson et. al 2004) that PCa can be present at very low levels of serum PSA. From a very large fully randomised trial, involving 18 882 men aged between 62 and 91 years, 2950 cases were randomly selected from the placebo (no treatment arm) and their PSA levels were followed over 7 years. In all of these cases PSA never exceeded 4.0, and none showed any irregularity in DRE. Biopsies at the end of the trial showed that 449 of the 2950 cases had prostate cancer, and 67 of these had a Gleason score ≥ 7 (suggesting aggressive cancer). The results are summarised below in table 2.

Clearly a 'cut off' at PSA = 4 will miss some aggressive cancers, but lowering the threshold could lead to many men being offered, or asking for, treatment which might be unnecessary, costly and result in a reduced quality of life.

Eventually there will be other markers for PCa and several, showing promise, are currently under investigation. In the meantime we have the PSA level and DRE as the starting point for initial diagnoses. From the patient's point of view we would like to see these used most effectively.

Table 1. PSA Level and Age (Oesterling 1993)

Age/Years	40 - 49	50 - 59	60 - 69	70 - 79
PSA level/ µg/L	0 – 2.5	0 – 3.5	0 – 4.5	0 – 6.5

Table 2. Prostate Cancer and low PSA Level (Thompson 2004)

PSA	0 – 0.5	0.6 – 1.0	1.1 – 2.0	2.1 – 3.0	3.1 – 4.0
% with PCa	6.6	10.1	17	23.9	26.9

For reasons of error a single PSA test is not a basis for referral for biopsy and I imagine it is rarely used as such (feedback from our members might be interesting).

However, the pattern of dependence of PSA level, on time, is more relevant. In this context there is now more emphasis on evaluating the PSA velocity and the doubling time for patients. These parameters require the use of several measurements over a period of time and we should encourage consultants to provide these parameters along with confidence intervals (error bars). Sometimes PSA velocity is calculated from the slope of a line based on two points which is statistically meaningless.

In short, whereas the PSA level is not readily related to the extent or grade of PCa, its dependence on time is more relevant. A pattern where PSA level, although it may be elevated, which presents, on average, a flat profile (which may show significant oscillations) is not so indicative of problems as a pattern which shows a steady increase of PSA level with time. For example A.V.D'Amico et al. (2004), suggested that, before diagnosis, men with an annual PSA velocity of more than 2 µg/L were significantly more likely to have metastasis than men with annual PSA velocity < 2µg/L. More elaborate models for PSA dependence on time, which attempt to factor in a contribution to PSA level from both age and the presence of BPH have recently been proposed (L. Klotz 2004) but their predictive properties, for diagnosis, have yet to be established. G. J. Kelloff et al. (2004) provide an interesting qualitative assessment of PSA in relation to *before* and *after* treatment (Table 3, page 6). This table gives the relative magnitude of the effect of each condition on the indicated measure (PSA or PSA doubling time (PSADT)). The blank '-' indicates no change. The degree of change is indicated by the number of + signs.

The table indicates the importance of using doubling times in diagnosis and their increasing significance during treatment (+ indications relate only to metastatic PCa). In addition, these authors list a series of recommendations for the use of PSA doubling time in the evaluation of oncological drugs for prostate cancer.

Other features associated with PSA levels are also reported to assist in diagnosis. The total PSA in serum includes 'free'

PSA and PSA complexed to a_1 - ACT and to macroglobulin. The use of both ‘free’ and ‘complexed or ‘bound’ PSA are well described in the book by S. Strumm. Several reports suggest that the use of the ratio of free (or complexed PSA) to total PSA, can enhance the utility of PSA in differentiating BPH and PCa [e.g. W.J. Catalonia (1995, 1997, and 1998); F. Martinez (1997, 2000, and 2002]. The papers by Martinez distinguish between the two forms of complexed PSA, and suggest that PSA complexed to a_1 ACT gives the better discrimination. P. J. O’Reilly et al. (1999), consider results over time and suggest that a progressive increase in total PSA (positive velocity) combined with a decrease in ‘free/total’ PSA (negative velocity) provides an indicator for re-biopsy. Recent reports (S.Sozen et al. (in press) 2005) suggest that complexed PSA alone might be a better initial test for PCa and Xavier Filella et al. (2004) report advantages in using the ratio (free PSA/total PSA). Other reports suggest that, for African-Americans the use of these measures results in only a modest improvement (B. Martin 2003).

PSA Screening. Summary

As a screening tool PSA level presents some problems, which must (of course) be taken into account. Nevertheless, the view expressed at the recent meeting of BPG/BAUS (Nov.2004) was that PSA testing would continue to increase because men were asking for it. This is clear evidence that there is growing awareness in the general public. As patients we are concerned that PSA test results are used optimally and we should encourage appropriate bodies to resource this and also release funding to: - (1) clarify the role of PSA derivatives and precursors and (2) evaluate the merits of new techniques and markers in the diagnosis of PCa. Some very interesting progress is being made in this field. The development of effective programs of “Active Surveillance”, already in use at some centres in the UK should clarify criteria for both diagnosis and treatment selection. The present report considers recent studies concerned with increasing the effectiveness of diagnosis in relation to screening. It must also be said that many authors focus on the (high) probability that older men will develop PCa but are unlikely to die of it. They conclude that there is no overall benefit from screening. However, in reporting on a recent randomised screening study having a 15 year follow up (G. Sandblom 2004), the authors, whilst accepting there was insufficient power to provide definitive evidence for improved mortality, nevertheless concluded that “screening in general practice is an effective way to detect PCa whilst it is still localised”. I will comment on this at a later date.

PSA as a tool to follow progression of PCa

The situation is very different for men (now patients) who have been diagnosed and have had their cancer graded and staged. In good circumstances they are invited to become involved in decisions about the most appropriate treatment for their condition. Prior to this discussion, regarding treatment, there is usually sufficient data to establish a baseline level for PSA, and PSA is then monitored over time. Measured PSA levels become most important, when a treatment procedure has been implemented, and this is recognised in the paper by Stamey. Additionally, in all of the applications for funding of clinical trials that I have been invited to see, PSA levels are used as an indicator of ‘biological failure’ in trial treatments: usually as PSA velocity or PSA doubling time. Table 3 emphasises the importance of PSA testing, particularly the use of doubling times, when following the progression of PCa.

PSA Progression. Summary

PSA testing is still of considerable importance to men already diagnosed with PCa. Dynamic criteria: PSA velocity and PSA doubling times etc., along with appropriate errors should be established. Kelloff et al. (2004) refer to a significant relationship between PSA doubling time and prostate specific mortality, after treatment, and recognise this as a “clinically meaningful benefit to the patient”. When treatment options are discussed consideration should be given to the use other forms of PSA and to the value of available nomograms/ algorithms as predictors. Data feedback from “Active Surveillance” programmes could be useful in the clarifying the role of existing (and new) markers for recognition of cancer type.

Future

There is a need for (1) optimal use of PSA levels and derivatives with more sophisticated data manipulation (e.g. artificial neural networks (B. Djavan 2002)) and (2) more specific tests for PCa, which differentiate between indolent and aggressive cancers. Newer molecular markers and newer procedures including spectroscopic; spectrometric; and imaging techniques, along with the identification of relevant gene patterns are currently being developed. These will be discussed in another letter.

Table 3 Relative Effectiveness of PSA Measures (Kelloff 2004)

	Before local Treatment		**After local Treatment**	
	Total PSA	PSA-DT	Total PSA	PSA-DT
BPH	+ + +	++	-	-
Prostatitis	+ +	-	-	-
Trauma	++	-	-	-
Organ Confined PCa	+++	+++	-	-
Micrometastases	-	+++	+	+++
Distant Metastases	+++	+++	++++	++++

Further Comment on PSA test

Further comment was provided by a response to Dr Stamey's paper by Dr William J Catalona who is a Urologist and Surgeon.

He believes that a direct association has been demonstrated between the serum PSA level and the likelihood of prostate cancer, even at low PSA levels. He states that PSA screening advances the date of diagnosis by 5 to13 years and in the USA prostate cancer-specific mortality rates have decreased by more than 20% since 1995 in the PSA screening era.

Dr Catalona's recommendation for prostate cancer screening is: annual PSA and digital rectal examination beginning at age 40, or earlier in men with a family history of early age-at-onset prostate cancer (PSA levels should be 0.6 to 0.7 ng/ml in men in their 40s and 50s without prostate disease); prospectively monitoring PSA velocity; biopsies for men with a suspicious digital rectal examination, PSA higher than 2.5 ng/ml, or a PSA velocity higher than 0.75 ng/ml per year; considering measuring androgen levels in interpreting PSA results; and using percent free PSA, percent complexed PSA, PSA density, and PSA velocity measurements to determine the need for repeat biopsies. The most effective and acceptable treatments eradicate the tumour at a very early stage before it has a chance to spread.

Every man hopes to be cured with primary treatment without additional therapy. No one wants to hear about long-term hormonal therapy, chemotherapy, or harsh experimental treatments. The risk of unnecessary treatment is low when good clinical judgment is exercised.

This article is an extract based on a paper produced by William J. Catalona, M.D. Professor of Urology, Director, Clinical Prostate Cancer Program, USA and Robert H. Lurie Comprehensive Cancer Center, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA. If you would like a copy of the full paper, please contact the PSA NoE office.

The Prostate Cancer Diet

You will see many articles on Diet and Nutrition in *Prostate Matters*, as the editorial team are passionate believers in the importance of this to patients. Few patients are initially aware of diet as a contributor to the development of prostate cancer. And yet, when only a smattering of awareness occurs, it becomes a subject of great interest.

A common complaint expressed by patients is that they have been given no information by their medical advisers, which of course causes some people to question its significance.

Partly for this reason we are delighted to see that Stepping Hill Hospital are now displaying on the Urology Department Notice Board a document entitled "The Prostate Cancer Diet".

With their permission we have reproduced this document below.

<u>The Prostate Cancer Diet</u>

Background

Fat intake is associated with prostate cancer. Animal fat and alpha-linoleic acid from vegetable sources may be the most important components, but the mechanisms involved are unclear. Fatty meat such as beef and lamb should be limited.

Beta-carotene is protective, as in other epithelial cancers.

The high soya intake in Japan and China may also be protective, prostate cancer is very rare in these countries.

Soya beans are a dietary source of isoflavine genistein, which is a specific inhibitor of protein tyrosine kinases, and inhibits DNA topo-isomerases as well as other enzymes involved in signal transduction. Genistein has been shown to suppress proliferation of prostate cancer cells in laboratory experiments.

Lycopene reduces the risk of prostate cancer by 2 or 3 fold. Remember Lycopene is only released when raw tomatoes are treated or cooked - thus grilled tomatoes, tomato ketchup, tomato juice and pizzas are all beneficial (*Ed. Comment choose pizzas without cheese)*.

In addition the above, multivitamin and antioxidant supplements should be taken daily- "Centrum", available at most pharmacies, is the one I recommend.

There is anecdotal evidence that green lipped mussel extract, available from herbal outlets, is also of considerable value. It is an old Maori recipe for arthritis, but is said to have some effects on the prostate.

<u>Recommendations</u>

ANTIOXIDANTS - Centrum Multivitamins, these also contain immune system enhancers (eg. Vit E) and trace elements

LYCOPENE - Found in grilled and treated tomatoes, or in tablet form from health food shops

SOYA MILK/BEANS - To supply isoflavines genistein

SELENIUM - As pills from health food shops

ALLIUM/ALLIN - Found in garlic, onions, shallots and chives

VEGETABLES - Especially broccoli, sprouts, cabbage, kale, cauliflower

SPICES - Chilli, turmeric, cumin

GREEN LIPPED MUSSEL EXTRACT.

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<u>Editorial Comment</u>

Generally multivitamins are a comprehensive formula of vitamins and minerals, specifically designed to maintain your complete well-being and to supplement your daily diet.

If you choose to take a multivitimin, we would suggest that you check the level of certain ingredients. The following figures are recommended levels of supplements which may help to fight prostate cancer and can be obtained individually

- 200 mcg of selenium a day.
- 200 IU of Vitamin E a day.
- 30 mg of lycopene a day (this is better taken as 10mg three times.

The benefits of Red Wine

Moderate wine consumption has multiple health benefits. It probably plays a major role in the health-promoting properties of the Mediterranean diet, which have been widely promoted .

Furthermore, according to a recent publication from the Fred Hutchinson Cancer Centre in Seattle, Washington (one of the leading cancer epidemiology groups) red wine consumption probably has a dramatic impact on the risk of prostate cancer. The publication showed that men who consumed four or more ounces of red wine four or more times a week had a 50% reduction in prostate cancer risk. And the greatest impact was on the risk of *aggressive, life-threatening forms* of prostate cancer.

For men with low-grade prostate cancer who are on a "watchful waiting" programme, their major risk is that their cancer might suddenly become more aggressive and spread before it can be effectively treated. Perhaps **moderate** red wine consumption, if coupled with other agents that foster cancer dormancy, can reduce that risk and make an active monitoring approach more effective!

Donations

A way of helping ourselves to maintain and improve upon what we do, is to encourage donations from various sources. Some of the recent ones, for which we are very grateful, are:

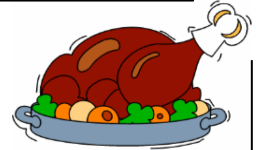
- ASTLEY ROTARY - £400
- The PROVINCIAL GRAND LODGE OF CHESHIRE FREEMASONS - £1000
- The MAYOR OF RAWTENSTALL'S CHARITY - £100

One of our members has raised over £300 by just asking that on his birthday (instead of another tie from his favourite Aunty, etc) a donation be sent to the PSA North of England. The administrators in our office collated the donations, acknowledged receipt and advised him of the value. Should anyone wish to do the same using a memorable event of their own, we would be delighted to help in a similar fashion.

The PSA North of England charges an annual membership fee of £12 - less than the cost of the material and information that is communicated to members on an ongoing basis. This fee is set at a modest level so as not to present a barrier for any person who would benefit from becoming a member. As a result we are dependant on external funding and very grateful to all who give donations.

Any member who would like to help in raising funds should contact our office, as there are many fund raising events available.

Enjoy your Christmas lunch!



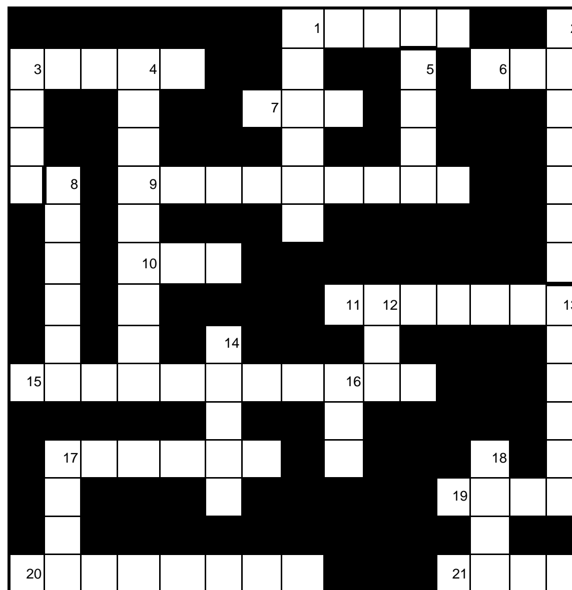
One of the great attributes of the Xmas lunch is that it is so appropriate for the Prostate Cancer Diet. The main meat is turkey and plenty of vegetables. Low fat/vegetarian Christmas pudding can be chosen. Sauces such as onion and rum can be made very well with Soya Milk. Those additional sauces—especially cranberry— are also good. Always remember that wherever possible, organic is best. So Eat well and healthily and Enjoy your Christmas lunch!

Prostate Matters Crossword

In this issue we have provided a seasonal teaser for you. The theme to the crossword is DRINKS. So to encourage you to complete the crossword, all correct entries will be placed in a bag and one will be picked out (blindly). That person will receive one bottle of organic red wine as a prize (see page ? of *Prostate Matters* for article on red wine). Closing date for the competition is 21st January 2005, to be sent to the PSA North of England office and addressed CROSSWORD.

ACROSS

1. Robust
3. Old periodical
6. Comes before you by the sound of it
7. Queer
9. Bovine tremble produces it
10. To be unwell
11. Pancakes
15. Type of monk
17. A colour
19. A body carriage
20. Bird's end
21. Unspoilt



DOWN

1. To flatten
2. Island cake
3. Anywhere in a storm
4. To malinger
5. Part of a horse
8. Has been
12. Type of trap
13. Was employee of the Iron road
14. Found in decide right
16. 12 down isn't cool without it!
17. Character from the Mikado
18. To moan

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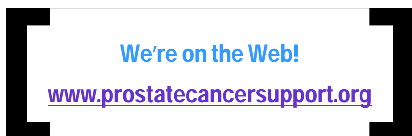

● Prostate Cancer - Information and Support

helpline 0845 456 0678

Aims of PSA North of England

To provide help, support and information to men who have Prostate Cancer, and to their families and carers.

To give a voice to all those affected by Prostate Cancer by raising awareness and by making representation to appropriate bodies -The public, Health professionals and Government.

Next Regional Meeting at Christie Hospital
19th February 2005.
Chris Parker from the Royal Marsden will be talking on:
Active surveillance of early prostate cancer and Advances in the Management of Hormone Refractory Disease.
Tea and coffee at 1pm.

Surviving prostate cancer - a cause for celebration :

continued from page 1

courage more men to take the appropriate steps to get early diagnosis and treatment for this, the most common cancer in men over 50 and the most common cause of cancer death in men, with over 21,000 new cases being diagnosed each year. Awareness of the disease is crucial in encouraging more men to take appropriate steps to get early diagnosis and treatment for prostate cancer.

In talking of the team's aspirations for the future he handed over to Stephen Brown, Clinical director of the Urology Department, who talked about HIFU, an exciting new technique in the treatment for prostate cancer, which is being piloted at Stepping Hill, and which was covered in some detail in our previous edition of *Prostate Matters*.

Mr Brown also announced the establishment of a new charity - The Stockport Prostate Cancer Fund - which was officially launched during this event. It is hoped that £25,000 will be raised in the first year of this new charity, which has been set up to help fund further developments in prostate cancer diagnosis and care.

As an attendee, who had also undergone surgery by Paddy, I was very pleased to see so many healthy looking men and their partners, a number of whom were PSA North of England members.

Listening intently to Denis Law talking were Martin Buggy, Astra Zenica, Stephen Brown, Paddy O'Reilly and Stuart Hall

Article by Mike Lockett