

The Winston Churchill Memorial Trust of Australia

Report by Jill Margo AM

2011 Churchill Fellow

“Putting Humpty Dumpty together again”

The Bob and June Prickett Churchill Fellowship to study penile rehabilitation following surgery for prostate cancer

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Dated 09/07/2013.

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Introduction

Once men are over the shock of the diagnosis of prostate cancer and recover from their radical surgery, there is often another shock in store for them. Their cancer may be gone but they are stripped of functions they took for granted. Even if they had superior nerve-sparing surgery, their sex lives are altered forever. Their sensations are different, they have lost length, a number have urinary worries and almost all have some issues with potency. For many, the consequences of surgery are shattering.

This report focuses on only one of their numerous concerns. It concentrates on the rehabilitation of potency following surgery and explores what forms of penile rehabilitation are being offered in major centres of excellence around the world.

The field is relatively new and while there is debate about the value of penile rehabilitation, there is evidence that some things can help. Studies have been published on individual components of the rehabilitative process but these 'dots' have not yet been joined into one definitive strategy and there is presently no consensus on how the process should proceed.

Some centres say there is enough evidence to offer comprehensive recovery plans which involve intensive initial therapy with years of maintenance. Other centres offer little as they wait for a higher level of evidence to prove the strategies really work before they recommend men put time and money into them.

Penile rehabilitation is best understood using the concept of an injury in an otherwise healthy man. When another part of his body is injured, such as the knee, there are protocols to promote its recovery. During radical prostate surgery the erectile nerves are injured and take time to recover. Rehabilitative protocols are focused on keeping the rest of the penile machinery in working order while this wiring slowly repairs itself, sometimes over two or more years.

While there are no established ways of protecting the nerves before surgery or accelerating their recovery afterwards, there are established ways of preventing the machinery from falling into disuse. The highest aim of penile rehabilitation after prostate cancer surgery is to keep the engine running while the wiring is repaired, in the hope that it will eventually run on its own or with a little help. If this fails there are other ways of keeping a man sufficiently functional to have intercourse.

After decades of shattering despair, it seems "all the king's horses and all the king's men" now have some improved prospects of putting Humpty together again.

Acknowledgements

Without Bob Prickett's generosity, this report would not have been possible. He and his late wife, June, have sponsored many Churchill fellows over the years and I am grateful for not only the assistance but for the warmth, interest and kindness with which their sponsorship was delivered.

To the administrators of the Churchill Trust, thank you for your exemplary management, your unfailing decency, efficiency and your responsiveness on any issue at any time.

To members of the Churchill Trust committees who conduct the interviews and select fellows, the time and effort that you selflessly give to the process is remarkable. During the interviews I was conscious that you have busy lives and were giving up your weekends. Your contribution is the foundation upon which any contribution by fellows is made.

Thank you for selecting me and I hope this report eventually leads to some material improvement in the lives of men recovering from prostate cancer surgery.

This manuscript was run under the well trained eye of Bernie O'Shea, a fine sub-editor, who picked out its errors and smoothed it. Of course, my referees played a crucial role and I would like to thank Chris Short, who is now Editor of the Weekend AFR, and Emeritus Professor Tom Reeve AC, the *éminence grise* of cancer medicine in Australia who has been a mentor to so many, including myself.

Executive Summary

Penile Rehabilitation Following Surgery for Prostate Cancer

By Jill Margo AM, Health Editor, *The Australian Financial Review*, 1 Darling Island Road, Pyrmont, Sydney, NSW, 2009. T 02 93717916, M 0412054605

The fellowship took me to several centres of excellence in the management of prostate cancer and rehabilitation. Highlights included:

- Memorial Sloan Kettering Cancer Centre, in New York, where Professor John Mulhall is the acknowledged champion of rehabilitation.
- Johns Hopkins University School of Medicine in Baltimore, where Professor Arthur Burnett, a world authority, has a sobering perspective on the limitations of rehabilitation.
- UCSF, where renowned Professor Tom Lue believes rehabilitation definitely has value.
- RAMBAM Health Care Campus, in Haifa, Israel, where Professor Yoram Vardi is a respected innovator in the field, and the Sackler Faculty of Medicine, Tel-Aviv University, where Professor Juza Chen is currently Director at the Sexual Dysfunction Clinic of the Sourasky Medical Centre.

There is disagreement about the value of penile rehabilitation following surgery for prostate cancer. While good evidence supports individual components of the rehabilitation process, there is no consensus on the optimum way to run a program. There is, however, agreement that expectations are being raised too high by the prospect of rehabilitation and that a more realistic approach should be taken.

On balance, the view is that there is something to be gained through rehabilitation, although it takes considerable commitment, expense and not all benefit. Advocates say that, at the very least, men should have the option of making the effort.

In Australia, rehabilitation is conducted on an *ad hoc* basis. Most men are not fully informed about it and do not have the choice of deciding if it is worthwhile. Their prospects would improve if information was readily available about the potential benefits and the limitations. For this to occur, existing evidence needs to be evaluated and simple consumer guidelines drawn up.

The Prostate Cancer Foundation of Australia, PCFA, has now undertaken to hold a workshop with stakeholders on this issue. In collaboration with Cancer Council Australia, the PCFA now has responsibility for updating existing guidelines on prostate cancer and where necessary drawing up new guidelines.

Should rehabilitation be recommended, questions of public education and implications for the health insurance industry would need to be addressed. In the meantime I intend to continue the conversation in the pages of the *AFR*.

Program

April 2013

Israel: 2 – 6 April

- Souransky Medical Centre, Tel Aviv. Professor Juza Chen.
- Rambam Health Care Campus, Haifa. Professor Yoram Vardi.

Germany: 11 – 16 April

- Urologische Klinik, Prostatakrebszentrum
Charité Universitätsmedizin, Berlin
Dr. Christian Klopff.
Dr. Ahmed Magheli.

United Kingdom: 16 – 21 April

- King's College London Urology Centre, London Bridge, and Guy's Hospital. Dr Paul Hegarty.
- The Prostate Centre, Wimpole Street, London. Professor Roger Kirby and Professor Michael Kirby.
- St Peter's Andrology Clinic based at The London Clinic, Harley Street, London. Dr David Ralph.

United States: 22 April – 2 May

- **New York** – Memorial Sloane Kettering Cancer Centre
Dr Joseph Narus
Professor John Mulhall
Megan Newcomer
Dr Christian Nelson
- **Baltimore** – Brady Urological Institute, Johns Hopkins Medical Institution
Professor Arthur Bennet
Associate Professor Trinity Bivalacqua
- **San Francisco** – University California San Francisco/Veterans Affairs Hospital.
Professor Tom Lue
Professor Maurice Garcia

Main Text

There are many facets to the way men sexually adapt following a radical prostatectomy. Apart from dealing with the mechanical breakdowns and changes in sensations, most have to deal with complex psychosexual issues such as libido, intimacy and meaning-making in their relationships. All these issues need to be considered in the rehabilitation process to help them live as best as they can with what has been lost. This report, however, focuses only on one aspect of sexual rehabilitation. It looks at penile rehabilitation and at what is being offered around the world to try to help men regain some erectile capacity. It is not a scientific report but an observational one from an informed perspective.

How things used to be

In the past, men were grateful to have their prostate cancer treated and accepted that once it was surgically removed they had no option but to live with the consequences. Apart from the social and psychological impact, which cannot be underestimated, every man was left impotent and about 25 per cent had severe problems with urinary control.

The sole aim of surgery was to remove the cancer and because there was so much blood in the operating field, critical structures around the prostate could not be seen clearly. When methods were found to control bleeding, surgery became more precise and the rates of urinary incontinence dropped dramatically.

But as the orthodoxy held that the nerves that govern erectile function ran through the prostate and would inevitably be lost when the prostate was removed, no attempts were made to preserve potency. Then in 1977, a leading urologist from Baltimore encountered the unexpected. Three months after his operation, a patient reported he was potent. This meant the nerves had not been removed with the prostate. So where were they?

Four years later they were located outside the capsule of the prostate. They were in a bundle of arteries and veins that run along the edge of the gland. Although too fine to be seen during surgery, if the bundle could be preserved without compromising the curative intention of the operation, then the nerves could be saved, if not completely then at least partially.

In 1982 the first deliberate nerve-sparing radical prostatectomy was successfully performed. The method has since been through many revisions and improvements.

How things changed

Nerve-sparing surgery is the only way of preserving the potential for natural potency and although it can be achieved with a scalpel, a laparoscope or a robot, it is not routinely offered. It takes skill and extra time and not all men ask for it.

If a man is not fully potent before his cancer surgery, should the surgeon make the extra effort to preserve his nerves? Or, if a man clearly states he wants his cancer out and has no interest in sex, should the surgeon make the effort anyway?

Yes, says Professor Arthur L. Burnett, II, a neuro-urologist and world-authority in the science and medicine of male erectile dysfunction from Johns Hopkins University School of Medicine in Baltimore. He says some surgeons today are too ready to dismiss a man who is somewhat dysfunctional and do not do their best to preserve the modest level of function that he may have. "I believe that we need to preserve nerve function under all circumstances as long as it does not compromise disease control and as long as the necessary steps are taken to ensure the cancer is addressed. Irrespective of his initial presentation, the man's potential quality of life should be maximised." He says some patients don't want to do anything at the time of the operation but come back six months later when their continence is good and their health is back and ask 'where are my erections, doctor?'

So the tables have turned. Until 30 years ago, regardless of what men wanted or hoped for when they went into their operation, their nerves were removed. Today, the view of the world's leading experts is that the nerves should be preserved regardless of what men want going into the operation but providing this does not reduce their chance of a cure.

For many men, however, nerve sparing is not enough. Even if the surgeon believes they are fully preserved - and it is difficult to know - the nerves can take two years to recover and some even longer. In this period the erectile machinery can fall into disuse. With less blood flow it does not get the nutrients it needs and scar tissue develops. The penis becomes fibrotic, with connective tissue (collagen) replacing penile tissue. It is important that while men wait for their nerves to recover, they keep their erectile tissues in good condition and the machinery in working order. This is the essence of penile rehabilitation.

When they go in for surgery, men hope to win the 'trifecta'. They want to emerge cancer free, with their continence intact and with the capacity to regain their potency. But even if they are diligent and comply with the entire penile rehabilitation program, potency does not always return. Younger men with good pre-existing potency have the best chance of a strong recovery.

How things are now

"Shattering" is a word still commonly used by men to describe their experience with prostate cancer. At the time of diagnosis their focus is on getting rid of the cancer but once the surgery is over and they begin to feel better, many find themselves facing a long future with erectile dysfunction.

While grateful for the high survival rate, the emasculating effect of the surgery leaves many in pieces. There is nowhere to turn and for many more, there is nowhere they want to turn except to the wall. The possibility of a natural sex life has gone and their world has irrevocably changed. The effects of this inevitably reverberate through their relationships and their families.

About 20,000 men are diagnosed with prostate cancer in Australia every year and more than 90 per cent are still alive five years later. The great majority of these men live way beyond this and often do so without natural potency. In addition, some have to cope with the ongoing stress of imperfect continence.

Restoring urinary continence is usually their first priority. While methods for achieving this are not within the remit of this report, potency and continence are closely linked. Incontinence is not only a significant burden itself but it can sabotage potency in a man who otherwise has good erectile function. The prospect of uncontrolled leakage in an intimate situation is embarrassing.

Over the past decade new expertise has emerged aimed at helping men regain some of the potency they have lost through their cancer surgery. While there is no promise of a return to full pre-operative function, in many cases some function can be retrieved. The amount depends on several factors, the main ones being:

- His age
- His pre-existing potency
- His general health
- Him having had nerve-sparing surgery

Depending on who is discussing it, penile rehabilitation takes many forms. It is best understood on a spectrum. At the highest end, the aim is to help a man regain his capacity for natural and spontaneous intercourse. Initially, he may need drugs or devices but the hope is that he can eventually function unassisted. At the lowest end, the aim is to fit a man with a prosthesis that enables him manually to create an erection whenever he wants one. Such implants have been available for many years and are a last resort. They work, the reported level of satisfaction is high but they are mechanical and once a man has had an implant, there is no going back. He has no other options for restoring potency.

For the purposes of this report, rehabilitation focuses on what can be done with drugs and devices in the period following surgery to restore some natural function, before the man either gives up on penetrative sex or resorts to an implant.

In the past 20 years, the public profile of prostate cancer has risen considerably and the disease is now a major concern for men. Controversies about testing, about the interpretation of results and about treatment of this cancer generate anxiety in the community. Although national and international research into prostate cancer is now at its height, our understanding and management of this cancer is at least a decade behind breast cancer.

The table below demonstrates how prominent prostate cancer is in the lives in of Australian men.

Snapshot of Prostate Cancer in Australia

- Prostate cancer is the most common cancer in Australian men (excluding non-melanoma skin cancer).
- In 2009, there were 19,438 new cases of prostate cancer in Australia.
- This accounted for 30.2 per cent of all new cancers in men that year.
- The risk increases with age.
- In 2009, the average age at diagnosis was 67.4 years
- In 2010, there were 3,235 deaths from prostate cancer
- This accounted for 13.3 per cent of all cancer deaths in men in Australia.
- Relative survival rates for this cancer have increased in recent years.
- Between 1982-1987 and 2006-2010, the five-year relative survival increased from 58.2 per cent to 92.0 per cent.
- By the end of 2007, there were an estimated 129,978 men in Australia who had been diagnosed with prostate cancer in the previous 26 years.
- Of this number, 72,582 had been diagnosed in the previous 5 years.
- In 2012, prostate cancer was estimated to account for 15 per cent of the total burden of cancer in men in Australia, second only to lung cancer.

- Source: Australian Government/ Cancer Australia
Updated May 2013

The need for evidence

“Common sense often turns into scientific evidence at some stage; you just have to wait for it. That’s the question. Do you wait?”

While studies have provided evidence for parts of the penile rehabilitation process, these individual pieces of evidence have not been joined into one definitive strategy. Although there is considerable overlap in practice around the world, each centre of excellence offers its own version of rehabilitation.

Some offer rigorous programs that taper off over years. Others offer minimal intervention because there is no Level 1 evidence to support them offering more. Until this highest level is achieved, they fear it may be a waste of time and resources and they don't want to inflate men's expectations.

Evidence-based medicine, EBM, is a relatively recent phenomenon and in its classic form, it is considered to provide the most reliable evidence on the effects of health interventions. It is essentially a mathematical exercise which involves estimating the potential harms and benefits of interventions. These estimates are derived from high-quality research on population samples and predict whether a particular treatment will do more good than harm. There are different classifications of evidence but broadly, there are three levels:

- Level I is derived from randomised controlled studies.
- Level II is derived from other types of studies or series that are less rigorous.
- Level III is comprised of the opinions of respected authorities, reports from expert committees or descriptive studies.

Not everyone, however, believes the highest level of evidence must be reached before an intervention can be offered. There is also debate about the limitations of EBM and the notion that it can be applied in all areas of medicine. In the last few years, the credibility of individual trials and systematic reviews has been undermined by reporting biases in the published medical literature.

With sexual rehabilitation, there is a philosophical difference between those who set great store on EBM and those who do not. Experts who are waiting for Level 1 say they need the scientific solidity it offers before they can be confident enough to offer rehabilitation to their patients – which, in places like the United States, can cost \$600 a month.

At a major urology clinic in Berlin, for example, rehabilitation is not routinely offered because of lack of evidence. "We don't recommend it but we do say there is some data that has shown there might be a positive effect on penile rehabilitation for long-term erectile function," says Dr Ahmed Magheli, Director of the Urologische Klinik, Prostatakrebszentrum, Charité Universitätsmedizin in Berlin. Although the data was initially very promising in both animals and humans, he says it is now not clear that rehabilitation has an effect. But equally, he says there is no data to say it does not have an effect.

In Germany there is a clear demarcation between what is offered in the public and private sectors. Public hospitals used to offer the 'Kiel Protocol' of rehabilitation but through lack of evidence and cost it fell away. Now public hospitals do limited rehabilitation which is not tailored to individual men.

Sceptical, is how Professor Yoram Vardi, a neuro-urologist from Israel, describes his position on penile rehabilitation. Based at the Rambam Health Care Campus in Haifa, with an excellent reputation for research into erectile dysfunction, he thinks the available data is not convincing and that there is a tension between this and the strong psychological need to be seen to be doing something about the situation.

"Men want something to be done but it is expensive, it takes many months without results and I am not sure we are really doing something real. I tell men they can have it if they wish but I don't push it. My feeling is that the majority who have rehabilitation don't remain compliant for long and stop treatment after a month or two because they can't see the result immediately."

On the other hand, those who offer comprehensive rehabilitation programs say there is enough evidence to proceed and it is up to the patients, not the doctors, to decide if they want to put in the effort. Some also say that Level 1 has limited application in this situation.

While it is very important in evaluating the risks of bringing new drugs to market, as a paradigm it is not easily imposed on the complex process of rehabilitation. It is generally difficult to apply to surgery, too, and it has been noted there was never any Level I evidence for the DaVinci Robot, which was enthusiastically adopted and is now widely used in surgery for prostate cancer.

There is no more passionate an advocate for penile rehabilitation than Professor John Mulhall, Director of the Male Sexual and Reproductive Medicine Program of Memorial Sloan-Kettering Cancer Centre, in New York. He says as the rehabilitation process offers potential benefit and causes no harm other than cost, "why wouldn't men try it!"

Professor Mulhall's rehabilitation program, the best known in the world, is part of MSKCC's Survivorship Initiative. It aims is to permit men and couples to resume

satisfactory sexual relations (or preserve their fertility potential) irrespective of their diagnosis or the kinds of treatment they have received for their cancer.

"The definitive study to demonstrate whether rehabilitation works and in which fashion it works - which drug works, when to start it, how much to give and for how long - has not yet been done," he says. "But we do have circumstantial evidence from different areas, from studies in humans and studies in animals, and all the signals are that there is benefit. The magnitude of that benefit can only be defined with a large, randomised, controlled trial that is under way at MSKCC at the moment."

"When a patient declares his sexual function is incredibly important and asks what he can do to maximise his recovery, I tell him we do not have all the data for rehabilitation. But I also tell him there is probably some significant upside and no downside except money."

"Rather than making the decisions for patients, I believe we should give them information, in as comprehensive a way as they can manage. Then let them decide whether they want to go ahead and do rehabilitation."

This sentiment was repeated by Dr Paul Hegarty, a consultant urological surgeon who specialises in sexual rehabilitation post-prostatectomy at the Urology Clinic of Guy's and London Bridge Hospital, London. "Does it have to be evidence based in classical form? The feedback we have from our patients is very positive and they vote with their feet." In addition to rehabilitation, his clinic offers pre-habilitation, to get men into an optimum state before they have their surgery.

Professor Tom Lue, an eminent figure in penile rehabilitation from the University of California San Francisco, says the absence of Level 1 and even Level 2 evidence does not render a treatment valueless. "Clinicians have to use their common sense. We don't have Level 1 for most of the surgery we do but we do operations every day. How can you do a heart operation within a double blinded placebo controlled study?" He believes Level 1 is a construct, a purpose-driven statistical exercise with the designer's bias inherent in the methodology.

Some centres take a middle course. While they acknowledge the evidence is not solid, they say it is probably worth engaging in some rehabilitative activities because they may provide some benefit. Doctors at these centres are extremely careful to moderate men's expectations.

Associate professor of urology and oncology, Trinity Bivalacqua of the Brady Urological Institute at Johns Hopkins in Baltimore, guards against exaggerating the benefits of rehabilitation. "I am very realistic with patients in helping them understand what their recovery is really about." He says the problem with the medical literature is that there are no standardised definitions, and assessments are

often subjective and not verified. What one person regards as reasonable erectile function, another might regard as poor.

While an analysis of the published evidence for rehabilitation is beyond the scope of this report, reviews have been conducted by others. In a recent article in the *Journal of Sexual Medicine*, Eric Chung from Australia and Gerald Brock from Canada describe the various types of sexual dysfunction identified among prostate cancer survivors and review the management strategies currently available for sexual rehabilitation after treatment.

They conclude that several preventive and treatment strategies for the preservation and recovery of sexual function are available but no consensus guidelines exist regarding the optimal rehabilitation protocol. "While medical and surgical therapies are effective in erectile function recovery and/or preservation, psychological and sexual counselling are equally important in sexual rehabilitation."

So what do patients think about the need for Level 1 evidence? Dr Christian Nelson, a clinical psychologist on the MSKCC's rehabilitation program, says it is not issue for them. From all those who have consulted him over the years, only one has ever asked for some literature and inquired whether there was a randomised controlled trial for the intervention.

While acknowledging the evidence is not strong, he tells men there is some data and that those who use injections (a major component of MSKCC's rehabilitation program) are more likely to recover their erectile function than those who don't. This, he says, is generally enough because the level of evidence is not the psychological barrier for them.

It agreed that young, potent men have the best prospects of recovering good potency, but of the 32 men who are diagnosed with prostate cancer in Australia every day, the great majority are in older age brackets, as can be seen from this table:

An Australian man's chance of being diagnosed with prostate cancer today:

- For a man in his 40s - 1 in 1000
- For a man in his 50s - 12 in 1000
- For a man in his 60s - 45 in 1000
- For a man in his 70s - 80 in 1000
- One in 9 men will develop prostate cancer in their lifetime.

- Source: The Prostate Cancer Foundation of Australia

Men seeking information

It is not easy for Australian men to collect reliable information to make up their own minds. There is no clarity and only bits and pieces are available. On the Internet, depending how they search, they will find a mixed offering of worthy sites interspersed with sites that are commercially driven and others that promote counterfeit and potentially dangerous drugs. The amount of information online can be overwhelming. A Google search using the phrase *sexual rehabilitation after prostate cancer* yielded more than seven million listings in late June 2013.

It takes much understanding to navigate the world of sexual or penile rehabilitation, and consulting the family doctor is not always a help. Last year a survey of 136 general practitioners across the country showed 80 per cent acknowledged they lacked confidence when it came to managing continence or erectile dysfunction in men who had received treatment for prostate cancer. The survey was conducted by the Australian Prostate Cancer Research Centre, Epworth, Melbourne.

Another issue for men is that rehabilitation works best if it is commenced almost immediately after surgery. This means they do not have the luxury of slowly recovering from surgery and then exploring the issues of rehabilitation at their leisure. Proponents of the process say the need for early intervention cannot be overemphasised because of the risk of disuse syndrome. If men “don’t use it, they lose it!” This does not mean they have to engage in actual intercourse sex after surgery. It just means they have to keep exercising their organ to prevent the tissue from deteriorating. But unlike a calf muscle that wastes through disuse and can then be rebuilt, once penile tissue is ‘wasted’, it can’t repair in the same way. The damage is likely to be irreversible.

Exercise of the organ is not always visible. While injections and devices can bring on erections, some drugs can help individual cells stay healthy and increase the likelihood of nocturnal erections returning. But men need information on more than just erectile function. They also need to know about:

- Penile curvature (Peyronies)
- Penile shortening
- Loss of ejaculation
- Changed sensation of orgasm
- Reduction in sexual desire
- Altered dynamics with their partner
- Mood and mental health issues

Most don't understand the impact of the treatment they are about to have, according to Dr Christian Nelson. He helps men and their partners optimise intimacy before, during, and after treatment for prostate cancer and says in the beginning they not only lack information but are overoptimistic about the outcome of treatment. They listen selectively and think they'll be fine in a few months.

Compound bad news is difficult to absorb. When several pieces of bad news are delivered at once, people naturally prioritise and try and deal with one issue at a time, in order of perceived importance. So it is with prostate cancer. He says when men hear they have cancer and there are consequences of treatment, they focus on the word cancer. The rest can wait. First and foremost they want the cancer out. Then they will deal with the consequences of treatment.

Even if they were told in detail about the consequences of treatment, after surgery men routinely ask "why didn't anyone tell me what was in store?" They are angry, frustrated and disappointed and don't recall being told the details. Some were never told in a meaningful way, some never heard what was said or read what they were given and some just couldn't confront it because the cancer used all their oxygen and they had nothing left.

Dr Nelson says the message about the after effects needs to be given repetitively but, like the proverbial horse taken to the water, these men can be given the information but can't be made to confront and understand what it means for them. The after effects exist on the other side of the mountain and, for the moment, all they can see are the hazardous rock faces and steep peaks ahead.

There are, however, some men who are not so sure they want treatment because of the sexual implications. It's a decision point but most go ahead because of pressure from their partner and family.

When men emerge from surgery and things are not working, they try to figure out what is happening. If they have incontinence and are leaking and dripping, many don't even think about sex. When this is under control and when they have their energy back they start to think about it. Some just hope it will get better naturally. Some privately try Viagra and when it doesn't work, they become scared and, in desperation, think they are done. At this point, a host of men slip away.

When Dr Nelson he sees desperate men and informs them of the available rehabilitation strategies, there is some relief but also frustration that they have wasted time and should have started sooner. The strongest theme is 'why didn't my surgeon tell me about it before surgery?'

Nerve injury

One way to cut through the noise surrounding sexual rehabilitation after prostate cancer is to draw on the fundamental principle of rehabilitation in general and see it as a way of assisting recovery from an injury.

In this case, the primary injury is to the erectile nerves, says assistant adjunct professor Maurice Garcia, urologist at the UCSF School of Medicine. This injury results in a change of blood flow and injury to the tissue responsiveness of the penis.

Just as there are protocols to rehabilitate muscle injuries, so there are protocols for erectile nerve injuries. Damaged nerves cannot send effective signals to the base of the penis to increase blood flow and initiate the changes necessary for an erection to occur. They can't do this in response to sexual stimuli and they can't produce normal episodes of nocturnal tumescence when the man is asleep.

Without this regular exercise, the penis falls into disuse. But unlike a voluntary calf muscle that can be rebuilt with physiotherapy, with disuse the penis can deteriorate to a point beyond which its responsiveness cannot be restored. It contains smooth muscle which is autonomically driven and cannot be voluntarily exercised. It also contains tissues which may become fibrosed and scarred. After nerve injury, the penis may seem shorter and may also develop a curve.

While other aspects of sexual function are affected by surgery, such as the loss of normal fertility, the loss of ejaculation and a change in the sensation of orgasm, the main injury to the erectile machinery is to the nerves.

Nerve preservation during surgery is essential if the man is to have any hope of recovering spontaneous potency. Because this requires so much skill, some say the procedure should be described as neurosurgery rather than prostate surgery. They say removing the prostate is not the challenge, unless it is high grade and bulky. The challenge is sparing the nerves and this takes far longer than the standard 90 minutes. It can take 2.5 to 3 hours with no pulling or stretching of the nerves and no cautery to get the best results.

If the nerves are removed, the man has no chance of spontaneous potency although later he may be able to use injections, devices or implants to achieve assisted potency. The reasons a surgeon may remove these nerves include: the cancer has invaded them; bad scarring makes it difficult to separate them; a man says potency is not important to him; the surgeon decides potency is not important or the surgeon does not want to make the extra effort unless specifically asked.

But saving the nerves of a potent man does not guarantee his potency will be restored. Like almost every other aspect of prostate cancer treatment, nerve sparing is contentious. It certainly was a major breakthrough but what concerns experts is

that so many nerve-sparing procedures are performed but only few patients do regain good potency. Some are not expected to regain it because of age or diseases, but even the proportion which is otherwise expected to recover is small.

One explanation is that the damaged nerves take too long to recover and by the time they do, the rest of the machinery has fallen into disuse and can't respond. Another could be that what looks like full nerve sparing was, in reality, only partial. Another is that the cancer's location may mean that only nerves on one side of the prostate are saved. If all are saved, the man is told he has had successful bilateral nerve-sparing surgery.

Professor Juza Chen, of the Tel-Aviv Sourasky Medical Center, is not certain that 100 per cent nerve-sparing surgery is possible. "Although I do bilateral nerve sparing, I am not sure this is really complete nerve sparing because the micro-nerves close to the operating field are probably damaged in the process."

There is a subjective element to nerve sparing, according to Professor Yoram Vardi. He says there is little objective data to confirm what has been saved because when the prostate is on the laboratory bench, there is no histological evidence to prove nerve sparing has been successfully achieved. Further, the fact that there are several techniques means there is no gold standard for nerve sparing.

He says the problem is visibility. "You don't see the nerve but because you are close to the prostate you know it should be there. You see a bundle, it is very diverse in different patients and it is not a defined anatomical structure that you can be sure about. With complete nerve sparing men should be potent a month later but we know 90 per cent are not even able to have an erection after surgery."

This means there has been some nerve damage. If the nerves are spared they should have a capacity to repair but after a year, 40 per cent of men still have no erection. Professor Vardi suggests that perhaps something is wrong with the definition of nerve sparing and that, in many cases, it is only partial.

Exquisitely sensitive, the nerves are easily bruised and injured. They can be injured by being touched, stretched or by energy in the operating field, such as heat from diathermy. Some surgeons no longer use diathermy for this reason.

Professor Vardi says much work has been done trying to develop nerve protectants but there are no results yet. There was an attempt to identify the nerve during surgery by stimulating it with a needle, but this was not effective.

Researchers are planning to injecting stem cells pre-operatively to see if they help preserve the neurovascular bundles. Another study, further down the line might try and place stem cells or a pharmacologic agent directly onto the bundles to protect them. A growth factor called GGF2, glial growth factor 2, has shown benefits in

animals and is currently being evaluated being evaluated. The fact that these nerve injuries occur at a predictable time, during scheduled surgery, offers a unique opportunity to limit the damage at an early time point. It is different to treating an unexpected injury hours after the fact.

Surgeons have various ways of describing these nerves. One says they form a sort of hairnet over part of the gland. Another says they can be found in a veil over a section of the prostate but warn that when it is peeled back in order to remove the prostate, the nerves sustain traction and percussion injuries.

The analogy of a hardboiled egg has been used by Dr. Christian Klopff, from the Urology Clinic at the Prostatakrebszentrum Charité Universitätsmedizin Berlin. Just as the egg has a thin membrane covering it, so the prostate has a thin mesh membrane containing some 50 parasympathetic nerves over part of it. Keeping it intact as the prostate is extremely delicate work and some damage is inevitable.

Professor Arthur Burnett describes the nerves as “a diffuse network of very fine fibrous webbing, almost like spider webbing, encased in a fascia and mixed with blood vessels. They are very delicate and as they are not easily identified visually, we use surgical landmarks to guide us. There is nothing simple about their preservation and it does require a high level of technical skill.”

“These nerves encase the prostate but also lie over the side wall of the rectum. We still don’t understand exactly how they are traumatised even with the most delicate operation. We don’t understand the science behind why they seem dormant and why it takes a year or more even with the best operations to regain neural transmission. We understand the macroscopic concepts not the minutia.”

Dr Paul Hegarty says just as blood vessels can be stained preoperatively, so a stain is needed for nerves so they can be seen. He finds it useful to use the analogy of a tent and says the nerves exist in a kind of veil between the two layers of the tent, in the space between them. “As long as you preserve both layers of the tent tissue you are probably preserving the nerves to the penis. Even though you may not cut them, you may bruise or injure them with too much energy – too much heat or too much cold. Bruising causes neuropraxia. The sheath remains intact but the nerve crenates, it atrophies back.” It grows back very slowly, can take 18 months and can still improve up to two years.

Professor Tom Lue has spent many years researching these nerves. In animals they are visible, particularly in the rat, which has one nerve which is easily seen. They are more difficult to see in the monkey, where there is a praxis (web) and electro-stimulation is needed to find the right one. An erection “pacemaker” was tried in animals to stimulate tumescence but when tried in humans, it failed.

While there is a long way to go in understanding what happens to erectile nerves after surgery and how they recover, Professor Lue recently had two insights: one in saving nerves and the other in how they grow.

Nerve cells have projections that bring information to them and then take it away. If these projections are injured, the nerve cell body dies. He says there is a way to save the cell body from dying. Secondly, he says Schwann cells, which support and feed nerve cells, also direct their growth in this case. They provide the tracks upon which the erectile nerves can travel towards their target. How to make Schwann cells grow is a target of research.

Tissue damage and shrinkage

Professor John Mulhall tells men after their surgery the most important thing is to get an erection anyway they can. "We get three at least every night of our lives (nocturnal erections) and the goal here is to replicate that while we are waiting for the nerves to recover from the trauma of surgery over a 12 – 24 month timeframe. Whether the erection is nocturnal, sexual or masturbatory it doesn't matter, it's about oxygen, blood flow and stretch of erection tissue."

He explains what happens to a muscle in a plaster case: it shrinks. "Well, that is what happens to your penis if you are not getting erections and it is permanent because it is not atrophy as in those muscles, it is scarring, collagen deposition. With nerve injury and chronic absence of erections – it turns to collagen and is no longer pliable and stretchy. That is true in humans. There is evidence to show as early as two months after surgery there is a significant increase in collagen deposition."

The penis shrinks for two reasons. First, he says in the early stages it becomes hyper-contractile because of what is called "competitive sprouting" or sympathetic hyperinnervation. When the nerves are injured, the sympathetic contraction nerves are in the ascendancy and the muscle gets contracted. When men ask: "What happened to my penis doctor? It is being sucked back into my body!" he tells them this nerve contractility is not permanent. The second reason is cellular changes. Smooth muscle fibrosis with scarring and collagen as well as structural changes in the tunica of the penis are permanent.

When researchers at MSKCC measured penile length two months, six months and then two years after surgery, Professor Mulhall says they found the only men who did not have measurable loss were those using regular oral medication, Viagra, Levitra or Cialis. These drugs boost the thin layer of cells that line the interior surface of blood vessels and lymphatic vessels. This layer is called the endothelium and the drugs are known to be endothelial protectants. They are potential anti-fibrotic agents and may also have a mild impact on neural regeneration. Most men lose about 1cm.

Circulatory damage

Damage to the blood vessels and blood supply involved in erectile function is not much discussed after surgery. The accessory pudendal arteries run in periprostatic region and are at risk of injury during a radical prostatectomy. Professor Chen says there are studies showing the preservation of blood supply is beneficial for the later recovery of erectile function. One study showed the effect of artery preservation doubled the likelihood of erectile function recovery and shortened the time to recovery. These results have not been confirmed. Another study showed no effect.

When the prostate is being dissected out of the body, even in highly skilled hands, some of the very fine blood vessels that supply the tiny nerves can be disrupted or damaged.

Vascular damage can also cause difficulties. Professor Yoram Vardi says it is extremely difficult after surgery to say if the problem results from nerve damage alone or whether there is vascular damage or both. A trick he uses is to test men with injections. Those with pure nerve damage respond well. Men who can't hold their erections because blood leaks away probably have vascular issues.

He has developed a novel form of therapy that changes the haemodynamics of the penis. Called shock wave therapy, it increases blood flow, probably by encouraging the growth of tiny blood vessels or regenerating the epithelium to increase its function. Although 100 or shock wave therapy machines are now in use around the world, this form of penile remicrovascularisation is still regarded as experimental, particularly post prostatectomy. It is just beginning to be used to promote potency in men with other disorder such as cardiovascular disease or diabetes.

Nocturnal Erections

Healthy men get between three and six erections every night while they are asleep. These are a good way to assess their erectile capacity because during sleep there is no adrenaline to compromise them. As there is no anxiety or stress, they just take their course.

When the erectile nerves are removed, men no longer get nocturnal erections. If they do have them after surgery, it is a sign the nerves are functioning. Nocturnal erections still occur when men age, but are milder, less rigid and less prolonged. Dr Paul Hegarty says between the ages of 60 and 70 men would have three or four a night which would be 70 per cent firm. They won't wake because they occur at the deepest part of sleep when the body is actually paralysed. If men wake suddenly and need to go to the toilet, they think their full bladder is giving them their erection, but it is not so, it is coincidental.

His clinic conducts nocturnal tumescent studies to delineate which men have functional erectile problems from those who have psychological dysfunction. Cardiovascular disease, diabetes and other neurological issues can stop nocturnal erections. So can aging. After a nerve injury from surgery, men notice shrinkage partly because they are not getting night stretching anymore. This leads to fibrosis and an increase incidence of Peyronie's.

Peyronie's Disease

Peyronie's is a bend in the penis which many find distressing, depressing, disfiguring and difficult to talk about. Sometimes it reverses spontaneously. It happens because a plaque forms and on erection, the penis is made to bend around it. While only 50 per cent of men have a penis that is straight as an arrow, a gentle bowing of up to 20 degrees, in any direction, is very common. Peyronie's is an angulation and frequently occurs after a radical prostatectomy.

Mr David Ralph, a London uro-andrologist, says if the penile tissue is not regularly stretched after surgery, cell death occurs and there is a sevenfold to tenfold instance of Peyronie's. "If a man is referred to me with erectile dysfunction after a radical prostatectomy, I examine him thinking I am going to feel Peyronie's. The thickening or lumps can be felt in the flaccid state. Men sometimes think they have a tumour but they are two a penny because of the fibrosis and scar tissue that shrinks the penis down. I am particularly interested if I am going to put in an implant because I want to know how difficult it is going to be. Peyronie's does not need to be removed before because the implant overrides it."

Ejaculation and Orgasm

After surgery, all men lose the capacity for ejaculation. The prostate which supplies much of the volume of ejaculate is gone and the change in plumbing means, once they have recovered, their experience of climax is dry. Men cope differently with this but it is known to be a major issue for gay and bisexual men for whom semen exchange is an important part of sex play and an important manifestation of sexual satisfaction.

While it is not possible to restore ejaculation, Dr Paul Hegarty has found a way of helping some men minimise the loss. He gives them a jelly they can squeeze into the urethra before sex begins and which is pushed out at the time they would normally ejaculate. He found it by chance though a patient who was having pain and needed an anaesthetic jelly. He has a jelly, not licenced for this use but nevertheless

appreciated. Through a little nozzle, men squirt in 2ml to 3ml of the jelly. He says some men who had painful ejaculation before surgery have less pain afterwards.

Orgasm is a mental event and while the sensation remains after surgery, it can be altered by it. Some men describe it as being more internal than it previously was. Some say it is more difficult to control, they can't prolong it and the sensation is shorter. Some say the reverse!

Incontinence

This is a broad and deep area of concern for men after surgery but is only covered in this report in relation to potency. Professor John Mulhall says even if men are grossly wet when they consult him, he still wants them to have erections. "Men who are wet generally delay presentation because they have no interest in sex and they think rehabilitation is about having sex. It is not it is about having erections."

There are two forms of sexual incontinence. The first is climacturia when men pass urine at the point of orgasm. He says this occurs in 90 per cent of men at least once after their surgery. Some 20 per cent of men will leak consistently at orgasm in the first year. It will be uncommon in the second year and rare in the third. It is an aesthetic problem and not all men dislike it.

The second type is arousal incontinence which causes men to drip during foreplay, is unpredictable and causes distress.

Dr Paul Hegarty, who has a special interest in treating men with both incontinence and erectile dysfunction, says incontinence is difficult to define because it is so subjective. Men don't cope well with it and many change their daily activities to accommodate it and stay dry by staying at home. If they go for a walk or a pint of beer, they become wet.

In the demographic that attends his clinic, many become inactive. In the worst cases, when they can't afford pads, they sit at home on the couch, dripping onto a towel. "We get them dry with whatever we can and they become more active and their lives open up. But then they end up becoming wet because they are doing so much more."

In the same operation he sometimes puts in a sling for incontinence and a penile implant for potency. The sling works almost immediately and can be life changing. The prosthesis takes longer. The man has to wait four to six weeks for his wounds to heal before he starts putting pressure on the area. Thereafter he can use the prosthesis.

Some men say for a period after surgery, they can't read their body's own impulses. The signals are scrambled. They'll feel like they have just wet themselves and rush to the bathroom to find they are dry. When the reverse happens it is embarrassing.

The toolbox

Numerous medical tools are used in penile rehabilitation. There is no standardisation in their use and while some centres use one or two, others use many. This report does not cover the use of alternative and complementary therapies such as acupuncture and herbal remedies. It also does not cover sexual nutraceuticals or dietary supplements that make claims about boosting potency

1. Oral medications

Viagra, Levitra and Cialis are known as PDE5 inhibitors (phosphodiesterase type 5 inhibitors) and are a first line of treatment in rehabilitation. A trial of Viagra showed significant improvement in erectile capacity when compared to placebo or no rehabilitation.

It is largely agreed these drugs should be instituted early after surgery to help lessen damage to the architecture of the penis by preventing corporal endothelial and smooth muscle damage. The time, the frequency, the dose and the duration of treatment are not agreed. Some centres have patients on daily low doses so they have a consistent level of PDE5 inhibitor in their blood. Against this background, they have men challenge themselves with a full dose, from time to time. Other centres recommend men take a full dose three times week, while others suggest men just use a full dose on demand.

There are some centres that use these drugs as part of a 'pre-habilitation' process, to condition and boost the endothelial lining of blood vessels before surgery.

There is also no agreement of the use of PDE5 in men who have not had nerve-sparing surgery.

2. Injections

Injections were the first tools used in penile rehabilitation and still play a very important role in oxygenating and stretching the penis which helps to protect its tissue structure. Men are taught to self-inject and told to expect a high success rate. They work in some 70 per cent of cases and can be formulated to suit individual needs. When they fail, it usually means damaged veins allow the blood to flow out.

The drug mix in the injection is not strong enough to counter this. There is a high dropout rate as many men find self-injection uncomfortable, unattractive and unromantic. In unskilled hands, it can cause scarring.

Despite their widespread use, in terms of evidence injections do not yet have definitive support in their role in rehabilitation.

3. Muse

This therapy is no longer available in Australia but is used overseas. It stands for Medical Urethral System for Erections and involves plunging a rice-sized pellet into the penis. The pellet contains a drug called alprostadil and dissolves, triggering an erection. Some men complain of burning and say the resulting erection is not very hard.

4. Vacuum Devices

These electrical or manual pumps can induce an erection through producing negative air pressure in a cylinder. The vessels in the penis fill with blood which is then kept there by a tension ring placed at the base of the penis. The erection may last 30 minutes and while it stretches the penis and helps to prevent contraction, it is said not to oxygenate the tissues because blood is venous rather than arterial. Some note the penis is cold and semi-rigid. There is no evidence vacuums work as a monotherapy in rehabilitation.

5. New Drugs

The drug pentoxifylline (Trental) promotes micro-vascular blood flow to ischaemic tissue. An old, safe drug, it has been in use since the seventies primarily for neuropathies, mostly peripheral neuropathy in people with diabetes. It improves flow to tissues at the extremities that are starved of blood.

While its mechanism is not fully understood, Professor Tom Lue thought it might be useful to treat Peyronie's and conducted some basic experiments. He found it reduced scarring, reduced inflammation and, in animals, assisted nerve growth.

Professor Maurice Garcia, who works with Professor Lue, says they began using the drug in rehabilitation almost two years ago. It helps to stop Peyronie's scarring. In rare cases it can reverse some of its effects and enable a mild curve to straighten out. It appears to have the potential to improve the quality of erections too and probably

takes at least three months to start having an effect. The tissue changes can be detected on ultrasound.

Professor Lue says the drug also has a slight Viagra-like effect. "We damaged the erectile nerve in rats, gave them the medication and after a certain time they had better erections," he says. The drug is now given to all men who come with erectile dysfunction and who can tolerate it. It must be taken with a meal or it causes stomach upsets. About 90 per cent can tolerate it.

6. Shock Therapy

Shockwave therapy, which uses energy produced by sound, has been used in medicine for many years. Lithotripsy uses sound energy to shatter kidney stones, and in varying intensities is also used in orthopaedics where it has an anti-inflammatory effect on joints and tendons.

Professor Yoram Vardi was the first to use it for erectile dysfunction (see above). The idea came from its use in cardiac medicine. In people who are not fit enough to have bypass surgery, shockwave therapy is sometimes used on their myocardium to increase blood flow. Professor Vardi thought perhaps it could work on the penis too, because it is a vascular organ and is easier to access than the heart. About four years ago, he conducted a pilot study on men with vascular problems such as heart disease, diabetes and hypercholesterolemia. After six or seven weeks, their erectile response was impressive. Today 500 men have been through trials.

Professor Vardi says because of their nerve damage and their vascular issues, this therapy does not have the same level of success in men post-radical prostatectomy patients. But in those for whom oral medication had not helped, after a year of this therapy, some 40 per cent of men were able to penetrate. The therapy is already in clinical use for erectile dysfunction and has almost no side effects. "We now have around 2.5 years of follow-up and the 65 per cent of responders say the effects last at least two years."

"We think it probably encourages the growth in new vessels, but we are not entirely sure. But we do know the haemodynamics of the penis changes after treatment in responders." He believes it is too early to use as part of a rehabilitation program. Professor Chan who did some of the early work with shock therapy is now working on new methods of delivering it.

Professor Tom Lue has conducted some basic science experiments to see how it works. Based on laboratory work and animal models, he believes it can be helpful in men for rehabilitation after treatment for prostate cancer. Professor Maurice Garcia is

taking this further. He says it is not witchcraft. The strong clinical results show it can be effective and the solid animal data explain the rationale for it.

Professor Lue has shown low-intensity shockwave therapy improves the recruitment of the body's own stem cells to damaged tissue. This recruitment is part of the natural rehabilitative process. When you injure a tissue, adult stem cells migrate towards it and help to restore its health. Some differentiate into the tissues that were harmed and died. Others differentiate to make co-enzymes and growth factors that help drive rehabilitation and the normal function of those tissues. And other stem cells dedicate themselves to producing new blood vessels.

In an experiment with rats, Professor Lue injured the erectile nerve and then gave one group shockwave therapy. Those that received the therapy had better erectile function than the others and also, tests showed they had more endothelial cells and more of other cells types that are part of the healing process.

7. Testosterone

As testosterone is known to feed prostate cancer, can it be given once the prostate has been removed? There much debate about this. What if some cancer remained behind? As part of the rehabilitation process, some centres do give testosterone to selective patients when their levels are low, their mood is down and they feel lethargic. It is given not to preserve erectile function but rather to boost their energy and their libido, and must be carefully monitored to minimise the risks associated with prostate cancer recurrence.

Pre-habilitation

Most centres prepare men for their prostate surgery. They offer information about what is ahead and provide counselling for the man and his partner. This may be on an individual basis or in groups. It is not unusual for men's potency to be assessed pre-operatively too. Most do this is with a questionnaire, followed by a chat to verify it. A few clinics strive for a more objective appraisal. After the questionnaire they physically test men's erectile capacity to produce a set of data that can be used for comparison post-operatively. They do sensory neurologic, vascular and hormonal tests. In addition, they monitor the response to oral PDE5 inhibitors and penile injections to document pre-operative function. These measures are useful because they benchmark performance before the operation and counter a tendency to exaggerate how much was lost afterwards.

Some clinics, however, go further. They try to get men into an optimum state before their surgery. They not only want them fit for surgery in the usual way, but they want their potency to be as good as possible as well. They recommend men take oral medication for some time before surgery. This is controversial.

Professor Juza Chen, who has no doubt rehabilitation works, has his doubts about pre-habilitation. "There is no objective evaluation for pre-habilitation and it may just be wishful thinking. I have seen men who have had wonderful preparation pre-surgery and had brilliant nerve sparing surgery and they still have a problem when they get here."

At Professor John Mulhall's clinic, men are recommended to take a PDE5 inhibitor, such as Viagra, for a few weeks before surgery. He makes a passionate case:

"No one really knows how important this is or how long before surgery the drugs should be taken but there is data to support men taking it. Animal models show if Viagra is given to animals three days before nerve-sparing surgery, they do better than if they receive the Viagra on the day of surgery.

"The drugs are taken for 'endothelial pre-conditioning', to bolster these cells ahead of the nerve injury which will in turn cause them damage. As this does not interfere with the operation or with bleeding, there is no reason not to do it, apart from expense.

"Although all the animal data is positive, in the absence of a high level of evidence for pre-habilitation, it is matter of looking critically at the available data and making a best judgement assessment. Viagra, Levitra and Cialis are potent endothelial protectors. It is irrefutable that in humans they protect endothelium. We know the endothelium is damaged with nerve injury. So why wouldn't you put somebody on these drugs purely an endothelial protectant?

"Personally, I have taken Viagra for six years. So potent is the endothelial effect that most sexual medicine practitioners are on PDE5 inhibitors. I take a quarter pill, 25mg, which gives me at least 24 hours of endothelial protection."

At the Prostate Centre in London, all men are assessed pre-operatively and if they have suboptimal erectile function they are put on daily mini doses of Cialis. Professor Michael Kirby says men are kept on these pills for as long as possible, depending on when they first present and when the operation is necessary. "Ideally, we want to treat them for three months to get erectile capacity as good as possible. "

Rehabilitation

In broad terms, Professor Arthur Burnett describes rehabilitation perfectly when he says it is somewhere between hypothesis and proof. "Here we are in the middle, trying to put forward various concepts and people are in earnest, but we still have a way to go. I don't think we have come close enough to having good answers. We have put together all these ideas and strategies, all are purposeful and probably make some sense, probably offer some help, but there is still no great proof of definitive success."

Personally, he takes a realistic approach because he has seen how extremely disappointed men are when, despite all their efforts, rehabilitation does not work for them. The clinicians are to blame and need to speak in frank terms. "Most important, in my mind, is to stop kidding patients and ourselves otherwise we will make no real scientific progress."

"Institutions are climbing over each other with promises of what they can deliver. Advertisements are everywhere. As a result we are creating false expectations and we are guilty in society and in the medical field about what we promise to deliver. I think that is a shameful thing."

He says this is about people trying to get market share and showing they are best. "If I make a discovery in my research laboratory and we think it is a great advance, I know it is going to be 10 to 15 years before it comes to the bedside. But I get the media asking if I can promise it in the next three months."

Against this background, he still believes rehabilitation is important.

Of all the descriptions of penile rehabilitation, the most original is from Professor John Mulhall, who says it is like "babysitting the erectile tissue while waiting for the nerves to recover".

Despite the debate, there are some points of consensus about 'babysitting'. It's agreed the nerve injury eventually produces profound changes in the architecture of the penis which influences its ability to respond to an inflow of blood and leads to end organ failure.

It's agreed the early use of PDE5 inhibitors are a first line of treatment for men who have had nerve-sparing surgery. These drugs help to prevent corporal endothelial and smooth muscle damage. There is no agreement on exactly when they should be started, how much should be taken, at what intervals and for how long. There is a signal that the daily use of Viagra increases a man's chance of regaining his pre-operative function.

Injection therapy is widely used to oxygenate and stretch the penis. This is believed to help protect its structure and function but no definitive study has proved its benefit. There is also nothing to support vacuum devices as a stand-alone therapy although they are used to support other therapies and provide stretch.

The principal arguments against penile rehabilitation are that it raises unrealistic expectation, there is no high level evidence to support it and that it is expensive and time consuming. The arguments for it are that after their surgery, men live on for decades and without reasonable erectile function their quality of life can be severely reduced. It is agreed erectile tissue damage is time dependent and there are serious risks to waiting for a spontaneous recovery which could take two years or may never occur.

If sexual intercourse is important to a man, then he should be in penile rehabilitation after prostate cancer surgery, says Professor John Mulhall. There is no definitive data but there is a signal from evidence in animals and humans that erectile function is better with rehabilitation.

There is much overlap of the interventions used in various rehabilitation strategies around the world. Some places suggest men just use oral medication on demand, when they want to try to have intercourse, and offer men little else. Some have complex programs. Below are examples of the protocols used in different centres.

1. Preserving the architecture of erectile tissue: Professor John Mulhall, MSKCC

If men consult him before their surgery, they are put on oral medication. If they consult him afterwards, they begin their oral medication when their catheter is removed after the operation.

Once it is removed, all men take mini doses of oral medication every night after surgery. At two or three weeks, if they want to try intercourse they have full dose once a week for the occasion.

At six weeks they see Professor Mulhall. By then, about 15 per cent of men will be responding to the oral medication. They will be given a new pill regime to follow. The intervention lasts about a year and then they are watched to see what happens with their natural erections. Some need encouragement to keep their belief strong because most of the recovery is in the second year. There are men who improve beyond that but that could partly be confidence rather than biology.

The 85 per cent who are not responders remain on oral medication and move onto injection therapy too, for a period. Most men respond to injections within six months

of the operation. The aim is to get them off the injections eventually and back onto an oral medication regime once they become good responders.

"If men come in for surgery under the age of 60 with excellent erections and have good nerve-sparing surgery and do rehabilitation, the MSKCC data shows they have an 80 per cent chance of responding to pills two years later."

But there is a high dropout rate partly because it takes so long to produce results and there is no certainty the results will be satisfactory. The pills are expensive, the injections are offputting and men are generally not good at compliance, says Professor Mulhall. In addition, they get anxious about their performance in a sexual situation and if they do have success, it may compare poorly to how it used to be. Those who are successful at rehabilitation, particularly with injections, focus on the long-term gain.

The dropout rate is particularly high between six and nine months, which is when hopelessness usually sets in. This is the time men need real encouragement.

2. Two points of difference: Professors Tom Lue and Maurice Garcia, UCSF

They believe rehabilitation makes good sense for men who have reasonable to good erectile function before surgery but that it has less to offer those with poor function.

Unlike other centres, they time their medication differently. After surgery, they recommend men take their PDE5 inhibitors at night just before sleep, on an empty stomach. As the men are not using the pills for sex, Professor Garcia says they may as well take them in a way that maximises their rehabilitative benefit. "Our rationale is that by taking the drugs in homeostatic state during sleep, there is no sympathetic outflow from the brain working to overcome erections. If the goal is to take a pill to bring a rush of blood to your penis then it is best not to interrupt the benefit. If being awake, anxious, active and making dinner interferes with this, it makes no sense to take the drugs while you are awake."

The drugs stimulate the return of blood flow, which brings important co-factors and nutrients and should also help with nocturnal erections. They recommend PDE5 inhibitors at least three times a week. The dose depends on which drugs the men use and what they can afford. If only half doses are affordable, this still confers benefits.

Their second point of difference is their use of the old drug pentoxifylline (Trental) which promotes micro-vascular blood flow and wound healing. It improves flow to tissues in the extremities and, in men with erectile dysfunction, appears to improve

the quality of their erections. It helps with rehabilitation from Peyronie's and must be taken for three months before it starts to have an effect.

As a second line of therapy, they use injections therapy and also offer vacuum devices for stretching.

Conditioning expectations is crucial and they always discuss the importance of pre-existing potency and explain that compliance with the rehabilitation program provides the best chance of recovery.

3. A realistic approach: Professor Arthur Burnett, Johns Hopkins

If a man expects Professor Burnett to deliver an excellent nerve-sparing operation, followed by excellent erection restoration, but he is going to MacDonald's every day, is smoking and is in bad shape, he is clearly told to take some ownership of his recovery. "I am very frank. It is an absolute priority that they take responsibility for better fitness," he says.

He believes rehabilitation is very important but men need to know where they stand with their own health conditions. If they present with cardiovascular disease, diabetes or hypertension, they have a number of strokes against them with regard to the likelihood of recovery. "On completion of standardised questionnaires, if a man believes his function is so-so, I can't promise him the world afterwards. He may get to be functional but it may be somewhat worse."

Professor Burnett suggests oral medication be used in some form but it is not known which form is the best. He questions extrapolations from animal work and does not believe the role of these medications in rehabilitation, taken daily like a vitamin, is established as effective. Their benefits are most established when taken on demand for sexual activity.

While there may be a benefit in preserving some vascular function, whether that could have a dramatic effect in recovering function faster or better is still unknown. If his patients want to explore these medications, he consents and also tries to get them attuned to other options to stay sexually intimate, such as vacuum devices and injections. But, he says, the psychological impact is important and no matter what the treatment, there is always a mind-body dimension which can be a challenge.

His team at Johns Hopkins is working on novel ideas for rehabilitation such as the use of Erythropoietin. Patients have slowly been enrolled over the past few years in a randomised controlled trial to see if this drug, given perioperatively, can help to jump start the nerves. He says it has a good scientific basis to be vascular and neural protective.

4. *We don't give up: Professor Michael Kirby, The Prostate Centre, London*

Following a radical prostatectomy, Professor Kirby says, the nerves sulk for about 18 months. Some take as much as four years to get over the trauma and his clinic never gives up. It won't consider an implant until the four-year mark.

As soon as men are ready, after the operation, they are offered oral medication. From week 4 to 6, they are recommended to use vacuum devices, to draw blood into penis and let it drain out for four to five minutes. They don't use the ring because the point is not to have intercourse but to induce stretch and hopefully restore length and keep the structure of the penis healthy. At three months they start injections.

Professor Kirby says it is a struggle and only 5 to 10 per cent of men get good erections quite quickly. These are usually younger men. Overall, about 60 per cent of men can be helped in some way.

Spiritually, it is a big investment for men. They put much hope into the process and they need support in several areas, not just in the mechanics of erectile function. He tries to see the man and his partner and explain the importance of stimulation, physically, emotionally and mentally. Professor Kirby believes this may assist nerve recovery.

A partner touching a man in an intimate way will send a message to his brain. If he has also been watching blue movies or reading sexy magazines, his brain will be sending messages down his body. This traffic encourages the nerves. Although it is never going to be the same again, you have to keep encouraging them and supporting them.

The Prostate Centre has a holistic approach and takes the opportunity to try to get men back in good shape in general.

5. *How I understand the biology: Professor Trinity Bivalacqua, John Hopkins*

Before their operation, he carefully assesses men and conditions their expectations. He is wary of creating false hope. "I help them understand what their recovery is really about. They are all going to emerge with sexual dysfunction. The nature of orgasm changes, rigidity is nowhere near the same and there will be no ejaculate." He is also frank with older men who have erectile dysfunction or are at risk of it.

When the catheter comes out ten days after the operation, his patients move into an intense pelvic floor exercise program. They do *kegels* and other exercises. For the first six to eight weeks, the focus is on the return of continence. At the same time he

presents them with data about the use of erectile aids in their recovery. "I say we know that PDE5 inhibitors are no better on demand than every day and that vacuum devices only preserve length and do not help erectile function."

If they want to use pills he encourages them to do so three times a week. This does not provide erections but helps with blood flow and potentially helps to preserve the erectile tissue for when the nerves start to fire. He generally recommends Viagra and prescribes 100mg which the men cut in half and take on Monday, Wednesday and Friday. Should they want to have sex one night, they take a full pill on demand. It doesn't matter that they might have taken a half in the morning.

He sees the patients again 8 weeks after the catheter is removed, by which time most are dry. If they are, he inquires about their erections. Most don't have any. If they want to have intercourse, he recommends they move to injection therapy.

If they are continent and functional on injections and having intercourse, they should still be on their Viagra three times a week. He has them challenge themselves at intervals by using a full Viagra rather than an injection. By 12 to 18 months, the hope is that younger men who were potent before their nerve-sparing surgery will be able continent and don't like injections, an implant is suggested. to do away with the injections. If not, they go back to injections.

"This is not evidence based, it is just me putting together what I understand about the biology and clinical sides." He waits 18 to 24 months before thinking about an implant. Men whose nerves were removed go straight to injections. If they are

6. When it is time to consider an implant: Mr David Ralph, The London Clinic

Mr Ralph is said to be the biggest implanter of penile prostheses in the UK. He believes 100 per cent of erectile nerves are never spared because if they were, men would not be left with erectile dysfunction. Despite patchy evidence, he says most British men are offered some form of rehabilitation.

Once the catheter is removed after surgery, he uses 5mg of Cialis daily and says there should be no intercourse for the first couple of months while men are still experiencing a little urinary leakage and are recovering from surgery. They remain on the Cialis for three months and use a vacuum device intermittently to stretch out the penis to try to prevent excessive shortening.

At eight weeks but more usually at 12 weeks, if they feel like having sex and their erections are not good enough, Mr Ralph starts active treatment with a maximum

dose of 20mg Cialis on demand. This is given against a background of 5mg daily of Cialis. Sometimes he prescribes Viagra.

If this is not enough, the men go onto Caverject injections, not for rehabilitation but for the occasions they want to have sex. If their results are poor a year later, he says they are candidates for an implant. By now, some 18 months have probably passed and many are ready to consider an implant.

Mr Ralph implants about 200 penile prostheses a year, mostly in men who have diabetes or blood pressure issues. About 40 are in men who have had their prostate removed for cancer. There are two basic types of implants. The malleable rods that can be bent up or down leave the man with a permanent semi-erection and are used less often because of concealment issues. The popular type is the three-part inflatable device.

Conclusion

Even in the hands of the most experienced surgeon, erectile nerves always sustain some injury during a radical prostatectomy. The aim of penile rehabilitation is to “babysit” the erectile tissue until these nerves recover. The goal is to keep the tissues well exercised and healthy so they can respond spontaneously when the nerves again start sending signals. If these tissues are not well maintained they fall into disuse and lose their ability to respond. This eventually results in organ failure.

The evidence for penile rehabilitation is patchy and there is no agreement on the way it should be delivered. It takes a lot of time, commitment and energy and does not always work. In addition, it is expensive.

But, it does no physical harm and offers potential benefits. It is very important because it is the only thing available to try to help men regain partial or full erectile function after surgery and, as such, it should be accessible should they want it.

There is no suggestion it should be mandatory. Rather, it should be available without hyperbole to those men who want to give it their best shot, to those men who might otherwise be facing decades unable to have intercourse unless they have an implant.

Recommendation

That a working party be convened on the issue of penile rehabilitation. It should address the following four questions:

- What forms of penile rehabilitation are offered in Australia, who has access and who funds it?
- What is the state of evidence in the world literature?
- Could we do better in Australia?
- Should we have recommendations or at least rudimentary guidelines for men and their clinicians?

APPENDIX

Drawn from discussions at the Male Sexual and Reproductive Medicine Program,
Memorial Sloan-Kettering Cancer Centre, New York

- Q&A
- Challenges of injection therapy
- What the partners say

Q&A

With Professor John Mulhall

What would you recommend to men about to have surgery?

"Enter your surgery with your eyes wide open. Communicate the importance of potency to your surgeon. Emphasise the need for the surgeon to do the best job possible. At MSKCC, which is a paragon of good prostate surgery, if you have baseline erectile dysfunction, you are five times less likely to get a nerve-sparing procedure. Nerve sparing can be complicated, it adds time and the surgeon thinks 'oh well, he's got ED anyway so he doesn't need those nerves. Why take the time and effort? I say of course you need those nerves.

"The other problem is that after being diagnosed with prostate cancer, a man talks to people and goes to see a big-name surgeon. Two weeks prior to surgery his erectile function is not as good as it was six months before because he is stressed and anxious. The surgeon says 'ah, his erections are not good' and he doesn't get nerve sparing although, in fact, his machinery was perfect.

"That is human nature, so my message is to empower you so you communicate that this is very important, that the surgeon does the best nerve-sparing procedure possible."

What is the best outcome you've seen?

"On rare occasions I have seen men get back to where they were before surgery. These men are usually under 45, have done rehabilitation for up to 24 months and had excellent nerve-sparing surgery. Whether this would have been achieved without rehabilitation, I cannot say.

"The function of rehabilitation is to try to get a man back to where he was before surgery. It is called 'back to baseline' and at MSKCC only 6 per cent of men over the age of 60 get there. In younger men it is around 20 per cent."

Challenges of injection therapy

With Dr Joseph Narus, director of penile injection therapy

Depending on their response to oral medication, most men go through the injection phase which involves self-injecting with a three-part mix titrated to their personal needs.

To help men overcome their anxiety about putting a needle into their penis, they are introduced to the process over two visits. On the first, they don't have to worry about filling the syringe or doing the injecting because it is done for them. They relax and see how they respond. The first dose is usually low.

They stay for half an hour and all usually respond. On a scale of 0-10, with a low dose men will score at least to 2-4. A few have a prolonged result which is reversed before they leave. "After all the trauma and anxiety they have been through, when they see the result they have a smile on their faces and their fear goes out of the window," says Dr Narus.

On the second visit the dose is adjusted and they are taught to self-inject using a small diabetic needle. Thereafter, every time they inject at home, they call in to report the results. Careful records are kept and over time the dose is titrated exactly for them. This management process runs for 24 months.

If their nerves were removed and they have poor circulation, are diabetic or have cardiovascular diseases, Dr Narus says they still respond as long as their penile tissue is healthy. If a man is two years post-radical prostatectomy and has done nothing in the interim, his tissues may be fibrotic. With an injection he may get partial erection.

The clinic uses its own three-drug formulation of alprostadil, phentolamine and papaverine and asks men to inject three times a week at home, expecting they will inject twice. The point is to get oxygenated blood into penis, not to have intercourse, which they can have, if they are sufficiently rigid. Some men who eventually respond to pills alone decide to continue with injections because the results are predictable.

Men are shown how to integrate injections into the sexual experience. One way is to fill a syringe, leave it at bedside and after some foreplay, roll over and take ten seconds to inject. They then exert a little pressure with an alcohol pad to minimise bleeding or bruising and if the partner is involved, this eventually becomes natural.

There is a concern about scarring. "Some men come in for their first injection two to six months after surgery and have never had a curvature. I inject them for first time and they have a significant curve on erection. I can't say it is because of the injection." Some men get fibrosis because of lack of use.

In the eight years he has been on the program, the numbers using injections and the knowledge base has grown considerably. From a single sheet to educate patients, there is now a book that has been revised three times. And there are take home instructions which include how to deal with a prolonged erection.

Some men are reluctant to leave the program. Even though they are stable users after five years, they still want the security of supervision. Dr Narus says they need to be discharged to make room for new patients.

"The oldest man I have ever trained was 96. He walked in, was healthy and able to inject himself. His wife was in her 70s."

For men who do not respond to injections, the next option is an implant.

What partners say

with Dr Christian Nelson, psychologist

With gay couples, the partner usually has a good understanding of the complexities of the loss that results from prostate cancer surgery. By dint of their gender, female partners don't have the same appreciation.

When a heterosexual couple consults Dr Christian Nelson for the first time, he can almost predict the scenario. The man will express how upset he is about his lack of erections and the woman will say it is no big deal. The man will say 'what do you mean?' and get angry. The wife will then get upset because her husband is mad at her for something she doesn't think is so important.

The wife is thinking the first priority is for him to be alive and she's relieved he doesn't have cancer anymore. Often, she couldn't care less about whether they have penetrative sex. If they want to be intimate there are other things they can do. The trade-off for her is inconsequential.

For the man it is entirely different. Penetration is a core male issue and even oral sex is only enjoyable with an erection. Many won't cuddle, kiss or hug because they fear it will initiate a sexual encounter they can't complete. They avoid treatment because it is so emotionally charged. In the past everything just worked and they never thought about it. Now, not only is it stressful, but the stress undermines their capacity to perform. The whole exercise becomes self-sabotaging so they avoid it. They shut down their libido.

Dr Nelson says the focus of counselling for many couples is not the sexual piece, but the non-sexual piece – the absence of hugs, snuggling, warmth, attention and closeness. Injection therapy can bridge this gap. Although it works very quickly, the emotional bridging takes time because of the psychological baggage. Generally partners are supportive and by working as a team, the couple is more successful.

Men who usually go for an implant have tried all treatments and are motivated enough to go to the next step. They are sexually active and the implant opens the world of sexuality again to them. It's a life saver.