DOUGLASS HANLY MOIR PATHOLOGY

Quality is in our DNA

Doctors' Newsletter

ISSUE 2 | 2018

Focus on men's health

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As we leave behind the winter solstice for 2018, it's my pleasure to introduce this issue of the DHM Doctors' Newsletter.

While it's always cheering to move past the shortest day and longest night of the year, the harsh reality is that the coldest and windiest weeks of winter are yet to be endured and, with them, the flu season. Increased vaccine uptake this year will, hopefully, be reflected in reduced morbidity and mortality compared with 2017. However, as always, while we may have passed halfway, it's too soon to relax.

In this Newsletter, Adjunct Clinical Professor Warick Delprado has contributed an article on prostate cancer and Dr Fiona Maclean writes on testicular cancer. Despite the significance of such diseases in men and the fact that early diagnosis and intervention are both possible, engaging men in health programs and services which focus on such gender-specific conditions remains a challenge.

I hope you find the DHM Doctors' Newsletter Issue 2, 2018 both interesting and informative.

Dr Colin Goldschmidt
MBBCh, FRCPA, FAICD
CEO, Douglass Hanly Moir Pathology

Focus on men's health

Two opposing caricatures exist of men as far as their attitudes to health and responses to illness are concerned. The fretting hypochondriac, with pain threshold set to zero, contrasts with the long-suffering stoic, in permanent symptom-denial, to whom a visit to the doctor is an admission of defeat.

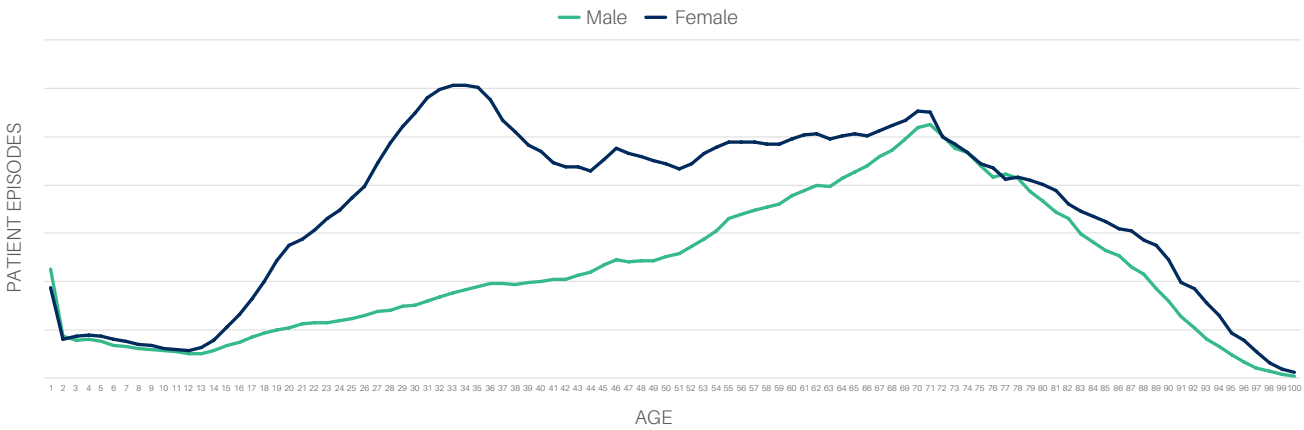
Men are, in fact, less likely than their wives or girlfriends to see a doctor, especially in their younger years, and when they are sick, most will defer seeking medical advice for as long as possible.[1] Of the leading causes of death in Australia, overall, men lead women in most of them and also have a lifespan which is six years shorter than women.[1]

The accompanying graph shows the annual number of pathology testing episodes by gender, which is directly related to the number of individual visits to a medical practitioner.[2]

The almost lifelong gender-difference which it illustrates is easily explained by participation in screening programs for cervical cancer, prenatal care, etc. However, the difference which it represents in the experience which each gender has of the healthcare system, and exposure to concepts of disease prevention and health promotion, may itself be significant. Activities which become normalised for women after decades of experience, but which remain unfamiliar to most men, may have something to do with gender-based differences in attitudes towards healthy lifestyle choices, preventative measures and early detection of disease.

While this Newsletter is narrowly focused on prostate and testicular cancer, in future issues we plan to broaden that focus to include other important aspects of men's health.

DHM Patient Episodes by Gender & Age | May 2017–April 2018



Reference

1. Woods, M. (2014) *Practitioners' Guide to Accessible Health Care for Men,* Men's Health Resource Kit 1, Penrith, MHIRC, Western Sydney University
2. DHM data: Patient episodes by gender and age, 2018

Tumours of the prostate

Prostate carcinoma is the most commonly diagnosed cancer in men in Australia, with 17,729 men expected to be diagnosed in 2018. Yet there is still potential confusion about treatment and prognosis, so understanding the pathology of the disease is critical for informed decision-making for any patient. In this article we focus on the histopathology report as it relates to the diagnosis of prostate cancer and therefore its role in that clinical decision-making process and understanding prognosis.

Adj. Clin. Prof. Warick Delprado
MBBS, FRCPA, FIAC
Director, Sonic Uro Dx

The Gleason grading system has been the mainstay of histopathologic grading of prostate adenocarcinoma since the 1960s. Inherent in this system, however, are certain features which limit its clinical correlation and which can misrepresent the aggressiveness of a given tumour to a patient. The introduction of the Grade Group system (reported in addition to the Gleason Score, and not replacing it) provides a truer depiction of the range from low-grade to high-grade carcinoma and simplifies the prognostic steps.

How the Grade Groups are applied

The Grade Group is a recently adopted categorisation derived from the ISUP Modified Gleason Score. It allocates the patient into one of five prognostic categories or groups, with the lowest number indicating a very good prognostic tumour, and higher numbers indicating a poorer prognosis.

The application of Grade Groups varies according to the specimen type.

Needle biopsy specimens – the Grade Group is derived from the score of the core biopsy/location with the highest ISUP Modified Gleason Score, NOT the composite score.

Radical prostatectomy specimens – the Grade Group is derived from the index carcinoma within the prostate, NOT the composite carcinoma score. The index area of carcinoma ('index carcinoma') is defined for this purpose as the area of carcinoma in the prostate that has the highest clinical significance based upon grade, volume or stage, or any combination of the three.

The five Grade Groups and their corresponding ISUP Modified Gleason Scores are:

Prostate Prognostic Grade Groups	
Grade 1	Gleason Score ≤6
Grade 2	Gleason Score 3+4=7
Grade 3	Gleason Score 4+3=7
Grade 4	Gleason Score =8
Grade 5	Gleason Score ≥9

Changes to staging

Some pathologists previously subcategorised pT2 tumours depending on laterality of disease. This is now formally discouraged. Clinical staging still contains this information.

A picture paints a thousand words

Patients are now brought into discussions concerning their disease and its management to an extent far greater than ever before. In order to achieve this clinicians, need to be able to convey complex medical findings and explain jargon-replete written reports simply, accurately and memorably. To assist in this we have developed a range of contemporary reports which allow clinicians to provide clearer answers to difficult questions.

Where is my cancer? How extensive is my cancer?

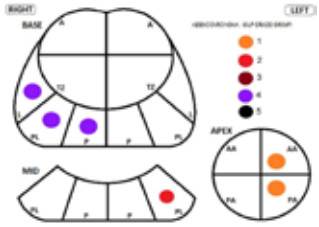
The answers to these common questions can be illustrated using graphical mapping of prostate needle biopsy results, showing the location of cancer and the Grade Groups. This can lead to different treatment options when high-grade carcinoma is localised to a part of the prostate.

Graphical maps can be included in all biopsy reports when biopsies are performed and labelled using standard templates.

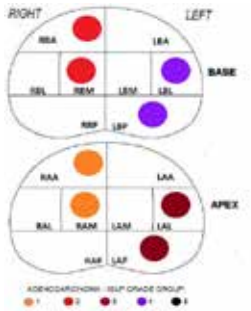
For example:

Transperineal biopsies

1) Grade Group 4 carcinoma is present in the right posterior quadrant in the bladder base region with only lower-grade carcinoma (Grade Groups 1 and 2) on the left near the apex.

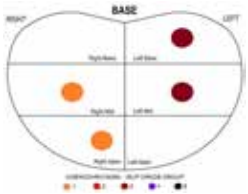


2) Higher-grade carcinoma (Grade Groups 3 and 4) is present along the whole of the left side of the prostate posterolaterally, with lower-grade carcinoma (Grade Groups 1 and 2) on the inner/medial aspect of the right lobe.



Transrectal biopsies

3) Higher-grade carcinoma (Grade Group 4) in the bladder base region on the left, with focal Grade Group 1 on the right.



How bad is my cancer?

The Grade Group (and the inherent Gleason Score) illustrate how far the carcinoma has deviated from the original tissue architecture. Lower Grade Groups indicate a small deviation, resulting in well-formed glands with a small impact on the patient. Intermediate Grade Groups show increasing deviation, with abnormal glands or loss of glandular architecture. Higher Grade Groups have loss of glandular architecture, resulting in a greater impact or poorer prognosis.

Glandular architecture goes from donuts, to squashed donuts, to Swiss cheese, to solid masses.

Illustrations in reports can convey this clearly to patients.

Prostate specific antigen (PSA)

The publication, in 2016, of clinical practice guidelines[1] for PSA testing provides clinicians with evidence-based recommendations necessary to maximise the potential benefits of testing, while minimising the potential harms. The importance of being well-informed when deciding whether to be tested or not is discussed, as well as specific risk-based recommendations for screening and the decision-making and actions to be taken following a positive result. The following is a summary of the key elements and recommendations made in these guidelines.

Key facts

- Prostate cancer is the second most commonly diagnosed cancer and second most common cause of death from cancer in Australian men
- The risk of being diagnosed with prostate cancer increases with age
- High five-year survival rate (95%)
- PSA testing carries potential benefits and potential harms
- PSA is not specific to prostate cancer and is not recommended for use in a population-based screening program, BUT:
- Rates of testing suggest that it is being used as such

Key recommendations

- Age-based screening of all men is not recommended
- Awareness of benefits and harms must precede decision to test
- Average risk of prostate cancer: PSA every two years from age 50 to 69
  - Investigate if > 3.0 ng/mL
- Family history of prostate cancer: PSA every two years from age 40/45 to 69
- Testing of men ≥ 70 years: harms of screening may outweigh benefits
- If PSA ≥3.0 ng/mL
  - Biopsy, MRI, active surveillance, watchful waiting

Potential harm of PSA screening

- Over-diagnosis: cancers detected by PSA screening which would be clinically inconsequential if undiagnosed (20-40%)
- Consequences of unnecessary treatment: incontinence, erectile dysfunction

Ref: 1. PSA Testing and Early Management of Test-Detected Prostate Cancer. Prostate Cancer Foundation of Australia and Cancer Council Australia, Sydney (2016). http://www.prostate.org.au/publications/clinical-practice-guidelines-on-psa-testing (Accessed May 2018)

Tumours of the testis

Testicular germ cell tumour (GCT) is the most common malignancy amongst men in the 20-50 year age bracket. Seminoma is the most common type of testicular cancer but several types of non-seminomatous tumour (e.g. embryonal carcinoma, teratoma) also occur in younger men, particularly in their 20s.

Dr Fiona Maclean
MBBS (Hons), BAppSc, FRCPA, GAICD
Deputy Director, Sonic Uro Dx

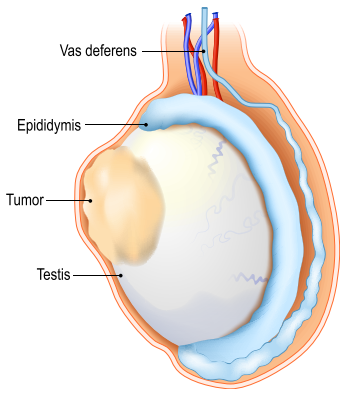
In 2014, 852 new cases of testicular cancer were diagnosed in Australia; for reasons which are unknown, the incidence of testicular cancer has risen by more than 50% over the last 30 years.

The emerging understanding of molecular pathways of histogenesis and their integration with traditional histopathologic morphological assessment has improved classification and thus allowed for optimisation of therapy.

At a glance

- New classifications allow for optimisation of therapy
- The term germ cell neoplasia-*in-situ* (GCNIS) has replaced intratubular germ cell neoplasia (ITGCN) for the initial precursor lesion of germ cell neoplasia of the testis
- The WHO classification of germ cell tumours divides tumours depending on their association with 12p amplification

Testicular cancer



What comes first?

Precursor lesions

Germ cell neoplasia-*in-situ* (GCNIS) is the initial precursor lesion for germ cell neoplasia in the testis, and was formerly known as intratubular germ cell neoplasia (ITGCN). Intermediate precursor lesions are intratubular seminoma and intratubular embryonal carcinoma, and the late precursor lesion is micro-invasive testicular germ cell tumour.

12p, or not 12p, that is the question

The importance of 12p amplification in classification of testicular germ cell tumours

Amplification of chromosome 12p (either as the presence of isochromosome 12p or as 12p over-representation) is the genetic hallmark of malignant GCT and is the key to understanding the current tumour classification.

Tumours associated with 12p over-expression are termed 'post-pubertal tumours' and include seminoma, embryonal carcinoma, yolk sac tumour, choriocarcinoma and post-pubertal teratoma. All have malignant potential and arise from a malignant germ cell, often through GCNIS. In contrast, prepubertal yolk sac tumour, prepubertal teratoma (including dermoid cyst) and spermatocytic tumour arise through other mechanisms, where GCNIS is not involved. This reinforces the concept that spermatocytic tumour (previously known as spermatocytic seminoma) has no relationship to seminoma. Additionally, as prepubertal teratoma arises through a non-transformed germ cell, it does not have metastatic potential. As long as there is no association with GCNIS and thus 12p amplification, the term 'prepubertal teratoma' is applied, regardless of the patient's age or pubertal status.

Tumour type	Amplification of 12p	Association with GCNIS
Seminoma, embryonal carcinoma, yolk sac tumour, choriocarcinoma and post-pubertal teratoma	Present	Usually present
Prepubertal yolk sac tumour, prepubertal teratoma (including dermoid cyst) and spermatocytic tumour	Not present	Not present

Other tumour types

Sex cord stromal tumours are the second most common testicular neoplasm, representing up to 5% of tumours.

Other less common tumour types that arise in the testis and paratesticular tissues include haematolymphoid tumours, mesenchymal tumours and metastatic tumours.

Changes to staging

When it comes to staging, testis wins the prize as the genitourinary system organ that has been subjected to the most updates in the 8th edition of the AJCC. The most important change is in pT categorisation, with the tumour type taken into consideration when assigning T stage.

Staging for pure seminoma relies upon the size of the tumour within the pT1 category. It is substaged as pT1a if the tumour measures <3 cm and pT1b if it measures ≥3 cm. In all tumour types, epididymal infiltration and hilar soft tissue infiltration are categorised as pT2.

Centralised reporting or review of testicular tumours has been shown to lead to better categorisation and staging, with much of the difficulty centred around the presence of lymphovascular invasion in seminoma. Due to the friable nature of the tumour, in units where these tumours are not commonly reported, the presence of artifactually displaced tumour cells within lymphovascular spaces can be mistaken for true lymphovascular invasion, which would incorrectly result in a designation of pT2.

CASE REPORT: REASSURANCE FROM THE PATHOLOGY REPORT

Max was just completing his Commerce degree and looking forward to his post-university life, when he noticed a lump in his right testicle. After a few weeks missing sleep while he was investigated and surgery was planned, he underwent an orchidectomy. He was relieved when the tumour was removed.

Depending on the diagnosis and the stage of the tumour, the next steps could have involved chemotherapy, radiotherapy or a further surgery in the form of a lymph node dissection. Max was steeling himself to find out which of those options lay ahead for him. He had also been told that there would be many years of follow-up ahead with blood tests and scans required – news that was hard to hear at a young age.

Fortunately, Max was diagnosed with prepubertal teratoma, an unexpected result that meant that the tumour had no malignant potential. Max can now move ahead with his life, with no need for further treatment or follow-up.

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Our Doctors' Newsletters contain articles written by our pathologists which focus on current issues and recent developments in pathology. Suggestions from you, which we invite wholeheartedly, are the best guarantee that our Doctors' Newsletter becomes a resource of maximum possible interest, information and relevance. If you have any topics you would like to suggest please feel free to contact Dr Ian Chambers (Medical Editor, DHM Publications) at med.ed@dhm.com.au.

Please note, this Newsletter can also be viewed on our website via the Clinician Publications link.

We look forward to hearing about your topics of interest and encourage your participation.

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Medical Editor

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