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Vulva Squamous Cell Cancer and its precursors – An update

Dr Jason Stone, Pathologist in Charge: Cytopathology, QML Pathology

Vulva cancer is rare and affects approximately 280 Australian women annually. Squamous cell carcinoma (SCC) accounts for 90% of vulval malignancies. The remainder are made up by melanoma (4%), metastatic tumour (5%) and other rare tumours (e.g. cutaneous adnexal tumours, sarcomas and lymphoma).

The putative precursor for vulva squamous cancer is vulvar intraepithelial neoplasia (VIN). The incidence of VIN has greatly increased over the last three decades, although the rates of invasive tumour are relatively constant.

Histologically, two distinct forms of VIN are observed:

1. VIN of usual type (uVIN) and
2. VIN of differentiated type (dVIN)

Both forms of VIN have different aetiology, morphology and risk of progression to invasive squamous cell carcinoma.

uVIN is driven by human papilloma virus (HPV) infection. Many of the high-risk HPV types (especially types 16, 33 and 18) that cause cervical intraepithelial neoplasia (CIN) and cervical squamous carcinoma are also responsible for causing uVIN. The risk factors for uVIN and CIN are similar (number of sexual partners, smoking and immunosuppression).

uVIN tends to occur in younger women (aged 30-50), whereas dVIN is typically seen in post menopausal women. The most common presentation of uVIN is pruritis or dysuria, although a quarter of patients will be asymptomatic.

Clinically, uVIN presents as white or erythematous macules which may evolve into verrucous plaques. More than half of cases are multifocal on the vulva and 18-52% of patients have similar lesions at other sites (e.g. cervix or anus). It will be interesting to observe the impact of the HPV vaccine on VIN rates in the future.

dVIN is usually seen in the sixth to eighth decade and is not related to HPV infection. dVIN is often associated with lichen sclerosus (LS) or other chronic inflammatory dermatoses. It is much less common than uVIN (10-15% of cases of VIN) but has much higher risk of progression to invasive carcinoma than uVIN (32% vs 5%) and progression to invasion is much quicker (22 months vs 41 months). dVIN is more likely to be unicentric than uVIN. Clinically dVIN will present as a thickening or white plaque, particularly on the background of LS. The risk of LS progressing to invasive SCC is reported to be up to 6%.



Clinical appearance of HSIL (uVIN3) Clinical appearance of dVIN

On a molecular level, the **pathogenesis** also differs.

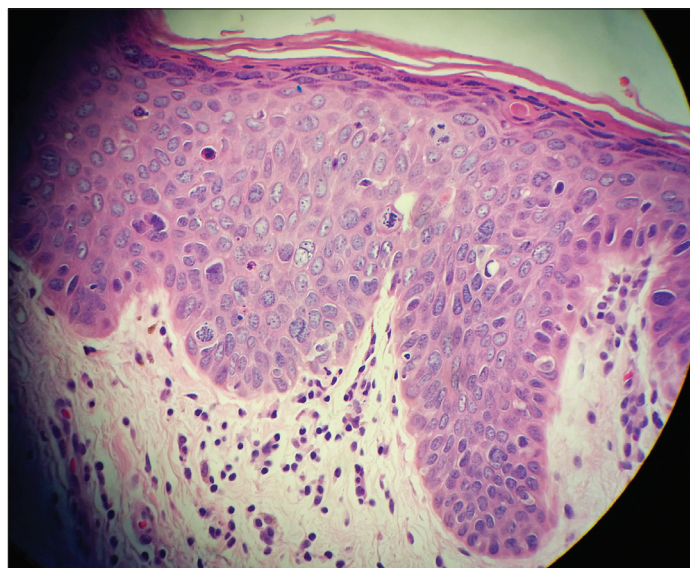
uVIN requires integration of the HPV E6 and E7 genes. The oncogenic protein products of these two genes adversely affect the host cells' tumour suppression capabilities by disrupting the retinoblastoma (pRB) tumour suppressor, p53 protein and the human telomerase (hTERT). In addition, the host cell growth regulating factors cyclin A/E and p21 are disrupted leading to increased cellular proliferation.

The molecular pathogenesis of dVIN is less well understood. Emerging studies implicate several mutations in the TP53 gene (which is an important human tumour suppressor gene). These TP53 mutations are believed to be induced by the ischaemic stress and oxidative stress associated with chronic inflammatory disorders e.g. LS. Other genetic mutations involving CDKN2A, HRAS and PIK3CA have also been described.

The **diagnosis** of VIN is made by a generously sized punch biopsy or excision biopsy for histological assessment. Vulva smears for cytology are not recommended as the sensitivity and specificity of this investigation is very poor and not comparable to cervical smear cytology. With all vulva biopsies it is important to include a detailed clinical history and description. Many vulva biopsies will show co-incidental minor inflammatory or pigmentary changes which may mislead the pathologist if the clinical findings are not provided. High risk HPV testing is only clinically validated on cervical cytology and plays no role in the investigation of vulval lesions.

For completeness, brief mention will be made of a distinct entity called bowenoid papulosis. This is a condition, typically affecting pregnant women, with multiple small vulval papules which are histologically identical to uVIN but show spontaneous regression clinically. This again illustrates the value of the clinical history in interpreting the histology.

Histologically, uVIN is a relatively straightforward diagnosis to make. The combination of cytological and architectural features of malignant epithelium without evidence of dermal invasion are well recognised by most anatomical pathologists. Conversely, dVIN is an exceptionally difficult histological diagnosis, even for expert gynaecological pathologists. The microscopic features are subtle and overlap with those seen in many benign conditions. The presence of background LS, especially the hyperplastic variant of LS, makes histological assessment for an invasive component difficult.



Histology of vulval HSIL (uVIN3)

From a clinical perspective, the **management** of invasive SCC of the vulva is very different to that of other cutaneous sites. SCC of the skin will only metastasize in rare circumstances, and those are usually cases of a large, deep and poorly differentiated tumour. Conversely, vulval SCC with a depth of

invasion just over 1mm has up to 20% chance of regional nodal metastases. Therefore these cases require specialist referral.

The rare variant of SCC known as verrucous carcinoma has a much better prognosis with lower propensity for metastases.

The **terminology** of VIN has been previously complicated by various classification systems existing concurrently. Fortunately, recent years have seen a convergence of nomenclature. The current WHO classification (2014) and the International Society for the Study of Vulvovaginal Disease (2015) have both adopted the recommendations of the 2012 LAST group (Lower Anogenital Squamous Terminology) and use a two-tiered system for uVIN:

- Low-grade squamous intraepithelial lesion (LSIL) and
- High-grade squamous intraepithelial lesion (HSIL).

This two-tiered system is now used in all anogenital sites, and replaces the historical three-tiered (CIN1/2/3, VIN 1/2/3, AIN 1/2/3 etc).

As dVIN is not HPV related it still retains its own diagnostic category, separate from LSIL and HSIL.

In conclusion, the precursor lesions to vulval SCC comprise two clinically and histologically different lesions, each with their own distinct molecular pathway to oncogenesis.

TAKE HOME MESSAGES

- There are two distinct precursors to vulval SCC.
- The most common is an HPV related pathway called LSIL (uVIN1) or HSIL (uVIN2/3).
- The second (Differentiated VIN, dVIN) occurs in older patients, has increased progression to SCC and is often associated with chronic lichen sclerosis.
- Thickened plaques/nodules in long standing lichen sclerosis require biopsy.

- Histological examination is the examination of choice.
- Vulval smears and/or HPV testing are not recommended.
- A diagnosis of SCC or a precursor should initiate specialist referral.

REFERENCES

1. WHO Classification of Tumours of Female Reproductive Organs. 2014.
2. Pathology. April 2013. 45(3), p214-228
3. Pathology. June 2016. 48(4), p291-302
4. Journal Virology 2004 Nov;78(21): 11451-11460

PATHOLOGIST PROFILE

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Dr Stone joined QML Pathology in 2010.

In 2012 Dr Stone was appointed as Head of Cytopathology. In addition to his work at the Brisbane Laboratory, Dr Stone also oversees histology and cytology for the Mackay region. His special interests encompass cytopathology; breast, gynaecological and GP skin histopathology.

Dr Stone's professional memberships and associations include the International Academy of Cytology, Australian & New Zealand Vulvovaginal Society, United States and Canadian Academy of Pathology and Australian Society of Cytology (former Queensland State Councillor).

Changes to Cervical Screening due in 2017 – An update*

Dr J Stone

As you are aware, cervical screening in Australia will change from May 2017 ("The Renewal").

Instead of microscopically screening a two yearly cervical smear, there will be five yearly testing for high-risk HPV on a cervical liquid based sample starting at age 25. The option of a "supervised" self-collection will also be available.

The programme will be identical for both vaccinated and unvaccinated women. Depending on the result of the high-risk HPV test, patients will be stratified into low risk (negative result), high risk (positive for HPV16 or 18) or intermediate

risk (positive for non-HPV16/18 subtype). A microscopic slide will only be assessed on those with a positive high-risk HPV result.

Women in the high-risk category will be referred for colposcopy. Women in the intermediate risk category will either undergo repeat testing in a year or will be referred for colposcopy. This decision will be based on the cytological findings on the microscopic slide that will be made after the positive result.

>>> CONTINUED OVERLEAF

The exact details of the new programme are still being finalised at a national level.

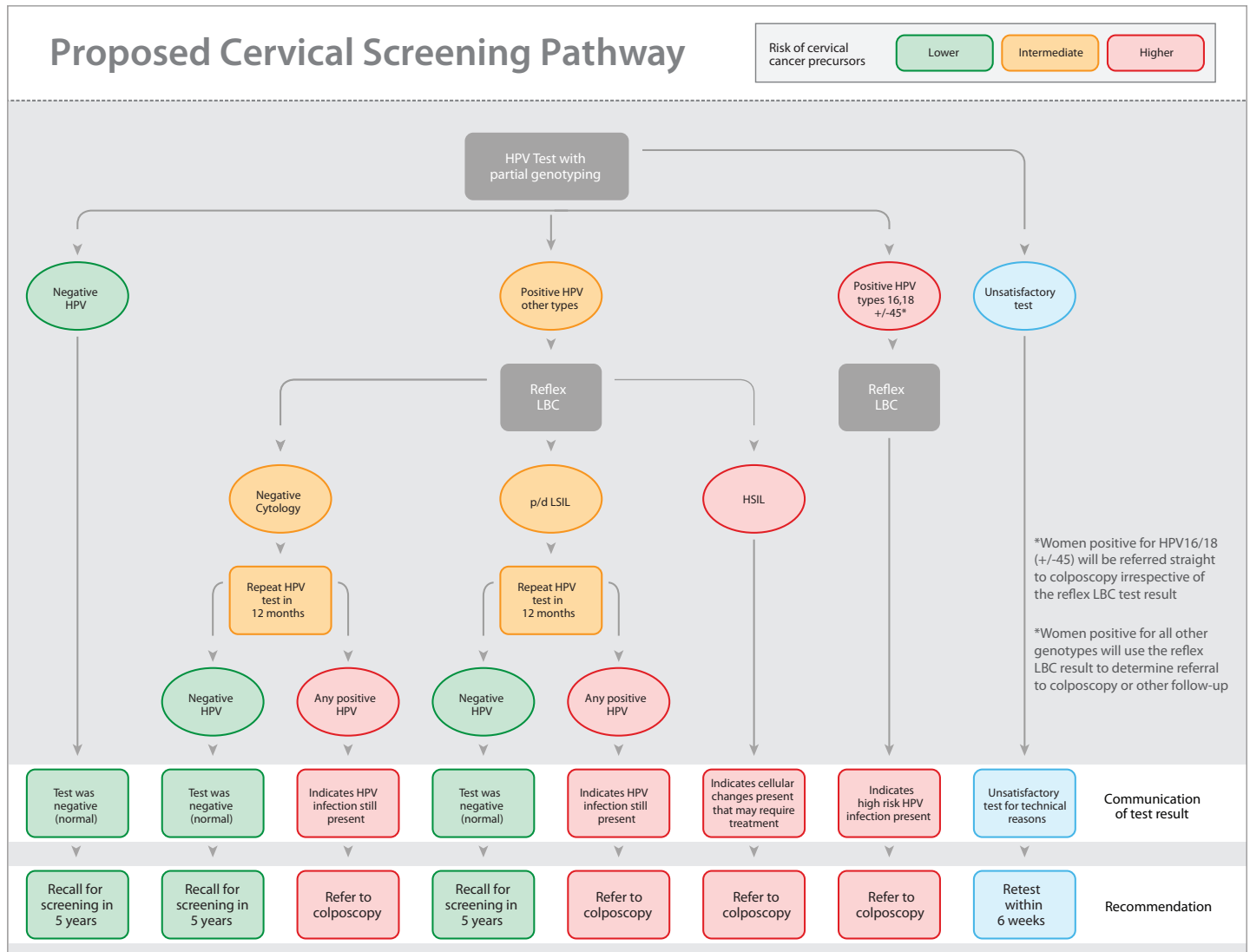
QML Pathology will keep you informed of developments as soon as they are finalised and national guidelines are published. QML Pathology will be distributing detailed information sheets and running educational sessions in the lead up to the new program commencing in May 2017.

In the interim, more detailed information can be obtained from the Australian Government website at:

www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/overview-of-the-renewal.

TAKE HOME MESSAGES

- 1 May 2017 will be the date of change. Contrary to initial expectations, **there will not be a transition period.**
- Women will still need a cervical sample for the high-risk HPV test.
- High-risk HPV testing is still just a screening test. There is a small but definite proportion of women who will develop high grade cervical squamous intraepithelial lesions (HSIL) or cervical carcinoma, despite a negative high-risk HPV result.



MSAC Recommendations for the New Cervical Screening Pathway. (MSAC Outcomes, Application number 1276. Accessible from www.msac.gov.au)

♦For further information please reference the full article 'Changes to the National Screening Program' by Dr Michelle Alizart, which featured in Issue 1, 2015, of the QML Pathology Doctor Newsletter.

Paternity and Relationship Testing

Genomic Diagnostics offers the highest standard of quality in relationship testing

INTRODUCTION

Genomic Diagnostics is the nationally co-ordinated genetic testing service for QML Pathology. Performing paternity and relationship testing in its purpose built Australian laboratory since 1998, Genomic Diagnostics has been responsible for testing more people every year than any other testing facility in the country.

Our team of highly qualified scientists offer a comprehensive DNA testing service, and our facilities are accredited to international standard ISO 17025 by NATA.

Privacy and autonomy is important to us. Genomic Diagnostics does not outsource testing, and is the only DNA organisation in Australia to offer results by encrypted email as well as post.

RELATIONSHIP TESTING

Relationship testing may be useful in a variety of situations, and is available to any required legal standard:

- Paternity testing for legal or peace of mind purposes, including during pregnancy
- Confirming other relationships such as mother, brothers/sisters, uncles/aunts, grandparents, and identical or fraternal twins
- Family relationships for immigration matters
- Adoption and surrogacy testing cases
- Individual profiling for deceased estates, or to establish relationships with recently deceased relatives.

HOW THE TEST WORKS

DNA testing is currently the most advanced and accurate technology to determine parentage.

Using a panel of proven STR (Short Tandem Repeat) profiling techniques, similar to those used in DNA forensic analyses, DNA profiling compares DNA patterns from the parties concerned to determine biological relatedness.

SPECIMEN REQUIREMENTS

EDTA blood or dry swab - Swabs are provided as part of the collection kit that is sent out to the chosen collection centre.

HOW TO ORDER

An application must be completed by the patient, and can be downloaded from the Genomic Diagnostics website. Alternatively, to request forms to be sent via email or post, please email info@genomicdiagnostics.com.au or call 1800 822 999. Once the completed forms are received by Genomic Diagnostics, a case is created, payment taken, and a collection kit is either sent out to the client (for non-legal 'peace of mind' tests), or to the QML Pathology collection centre where the collection has been booked.

TURNAROUND TIME

Standard testing is 10 working days. However, if there is specific requirement for an urgent result (e.g. international surrogacy cases), a faster TAT of 4-5 working days may be possible in consultation with the laboratory.

PRICING STATEMENT

The cost of a non-legal 'peace of mind' test is from \$390*, with legal testing from \$690* (determination of parentage of one child).

Immigration cases are quoted based on the individual family scenario (i.e. number of persons being considered for immigration and number of persons required to be tested to establish relatedness).

An immigration case quote also includes transportation and the cost of contacting embassies in other countries, etc.*

No Medicare rebate is available for this testing.

TERMS AND CONDITIONS

Testing must be paid for in advance. If a case is cancelled once it has been set up and samples collected, only a 50% refund will apply.

FURTHER INFORMATION

Talk to our friendly customer care team today, call **1800 822 999** between 9:00am and 5:00pm (EST) or email info@genomicdiagnostics.com.au

*Prices are correct at time of printing and are subject to change without notice.

•For a full list of inclusions, please contact Genomic Diagnostics.

General Recommendations for Antenatal Screening

Dr Charles Appleton, Dr Kerry DeVoss, Dr Julia Chang, Dr Peter Davidson,
Dr Rebecca Adams, Dr Renu Vohra, Dr Sally Appleton

The following investigations are recommendations only and provide a guideline to antenatal screening.

TO CONFIRM PREGNANCY

HCG

- Please note LMP on request form
- Test is usually positive 10 – 14 days post conception

FOLLOWING POSITIVE CONFIRMATION OF PREGNANCY, THE FOLLOWING INVESTIGATIONS ARE RECOMMENDED AT THE FIRST ANTENATAL VISIT:

Full blood count	Review haematological findings
Blood group and antibody screen	The antibody screen should be repeated at the beginning of each pregnancy
Rubella IgG antibody status	Rubella antibody titre should be measured for each pregnancy
Syphilis serology	Assess status
Midstream urine	Biochemical analysis and culture
HIV serology	Counselling should be provided prior to requesting the test
Hepatitis B sAg serology	To determine if Hep B carrier
Iron studies	Consider iron study if multiparous, last pregnancy was less than 18 months ago, or patient has a history of menorrhagia or iron deficiency
Oral glucose tolerance test (OGTT)	Women with risk factors for hyperglycaemia in pregnancy should have a pregnancy OGTT to screen for gestational diabetes at the first antenatal visit. Women without risk factors for hyperglycaemia in pregnancy should undergo a 75g OGTT at 24 – 28 weeks gestation

OTHER TESTS THAT MAY BE CONSIDERED IN EARLY STAGES OF PREGNANCY

Screening for haemoglobinopathies as per local protocol.

As a minimum, all women should be screened using mean cell volume (MCV) and mean cell haemoglobin concentration (MCHC) as indicators of the need for further investigation (e.g. iron studies, haemoglobin studies). Consideration should be given to haemoglobinopathy testing in women from high risk groups for haemoglobinopathies, particularly those associated with normal MCV (e.g. sickle cell anaemia).

Hepatitis C serology	Assess status
CMV serology	Assess status if potential for exposure
Toxoplasmosis serology	Assess status if potential for exposure
Varicella serology	Testing for varicella antibodies should be considered if there is no history or uncertain history of previous illness
Vitamin D	High-risk populations should be tested in early pregnancy
TSH	Targeted screening for at risk groups is recommended

INVESTIGATIONS RECOMMENDED DURING SUBSEQUENT ANTENATAL VISITS

Prenatal tests for chromosome abnormalities (counselling and testing discussed as appropriate)

Prenatal screening tests available in first trimester	<ul style="list-style-type: none"> First Trimester Screening (between 8-13 weeks gestation) is the combination of free bHCG and PAPP-A results, together with Nuchal Translucency measurement by Ultrasound in the 11-13 week window or Non-invasive Prenatal Testing (NIPT) Generation™ - from 10 weeks gestation
Prenatal screening tests available in second trimester	<ul style="list-style-type: none"> Second trimester Down Syndrome and Spina Bifida screening (between 15-18 weeks gestation) The test assays for bHCG, AFP and free Oestriol or Non-invasive Prenatal Testing (NIPT) Generation™ - from 10 weeks gestation
Prenatal diagnostic tests on fetal cells obtained from amniocentesis and chorionic villus sampling	<ul style="list-style-type: none"> Conventional Karyotyping Rapid aneuploidy tests e.g. FISH or Chromosomal microarray analysis
Obstetric ultrasound scan (usually at 18-20 weeks gestation)	Ultrasound for fetal morphology and placental localization
Gestational diabetes (24-28 weeks gestation)	High risk women with an early normal OGTT should have a repeat 2 hour 75g OGTT at 24-28 weeks gestational age. If GTT is positive then Gestational Diabetes is diagnosed. Retest 3 months post-partum
Blood group antibody testing (28 weeks gestation)	Further screening is recommended for Rh negative women at approximately 28 weeks gestation (prior to 28 week anti-D injection)
FBC and iron studies (28 weeks gestation)	The haemoglobin level and platelet count should be repeated at 28 weeks gestation
Syphilis, Hepatitis B, Hepatitis C, HIV (28 weeks gestation)	Consider repeat screening at 28 weeks in high-risk populations
Group B Streptococcal Disease (35-37 weeks gestation)	GBS carriage is best predicted by prenatal screening at 35-37 weeks gestation

INVESTIGATIONS POST DELIVERY

Paediatric collection	Phenylketonuria-Heel prick test post delivery
TSH	7-30 days post-partum (If Thyroiditis was present earlier in the pregnancy)
Iron Studies	Follow up if iron levels are low during pregnancy
FBC	Consider for history of excessive tiredness
Cytology	Pap smear 6-8 weeks post-partum if patient has not had a smear in previous 2 years

REFERENCES

- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). Routine antenatal assessment in the absence of pregnancy complications: College statement. 2015.
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- RANZCOG. Maternal Group B Streptococcus in pregnancy: screening and management: College Statement. 2012.
- GDM reference group Queensland Clinical Guideline. Recommendations for the diagnosis of gestational diabetes mellitus. 2015.

Thyroid Function Testing

Thyroid Stimulating Hormone (TSH) and Thyroid Function Test (TFT)

THYROID STIMULATING HORMONE (TSH)

TSH is a glycoprotein which is synthesised and secreted by the thyrotrope cells in the anterior pituitary gland. It is the first-line test for the diagnosis of thyroid disease in high-risk individuals and it is the only test funded by Medicare to screen for thyroid disease when there is no history of thyroid problems. TSH can also be used to monitor patients who are receiving treatment for thyroid disease and differentiated thyroid cancer.

THYROID HORMONES

TSH stimulates the thyroid gland to secrete the hormone thyroxine (T4) which is then converted to triiodothyronine (T3). T3 is the active hormone that stimulates and regulates (most) metabolism in the body. This conversion of T4 to T3 mostly takes place in end organ tissues and some in the thyroid itself.

Medicare will rebate for FT4/FT3 testing only if the clinical criteria listed in Table 1 are satisfied.

Table 1: Medicare Clinical Criteria

Medicare rules provide that a Medicare eligible request for "TFT" (TSH + FT3/FT4) testing MUST have a complying clinical indicator written on the pathology request slip by the requesting doctor. Those complying TFT eligible clinical indicators (one of which must be indicated on the request slip) are:

A	the patient has an abnormal level of TSH;
B	for the purpose of monitoring thyroid disease in the patient; or
C	to investigate the sick euthyroid syndrome if the patient is an admitted patient; or
D	to investigate dementia or psychiatric illness of the patient; or
E	to investigate amenorrhoea or infertility of the patient;
F	the medical practitioner who requested the tests suspects the patient has a pituitary dysfunction;
G	the patient is on drugs that interfere with thyroid hormone metabolism or function.

COMMON RESULT PATTERNS OF TFTs

Low TSH with elevated FT4

Common: Graves' disease, toxic multinodular goitre, toxic adenoma.

Less Common: Early stages of Hashimoto's thyroiditis, subacute granulomatous thyroiditis, postpartum and painless forms of subacute lymphocytic thyroiditis.

Rare: Thyroxine ingestion (intentional), drug-induced e.g. iodine, amiodarone; with confirmed pregnancy e.g. hyperemesis gravidarum, hydatidiform mole.

Low TSH with normal FT4 and FT3

Common: Subclinical hyperthyroidism common in elderly patients with toxic multinodular goitre, toxic adenoma, thyroxine ingestion.

High TSH with low FT4

Common: Hashimoto's thyroiditis, hypothyroid phases of postpartum and painless forms of subacute lymphocytic thyroiditis, after ablative (radio-iodine, subtotal thyroidectomy) therapy.

Rare: Post head and neck irradiation, drug-induced (lithium, anti-thyroid therapy, amiodarone, interferon therapy, steroid therapy, dopamine and dobutamine infusion), non-thyroidal illness.

High TSH with normal FT4 and FT3

Common: Subclinical hypothyroidism with autoimmune thyroid disease (early Hashimoto's thyroiditis).

Rare: Late phase subacute granulomatous thyroiditis, drug-induced (amiodarone, sertraline, cholestyramine), congenital TSH receptor defects.

Normal or high TSH with high FT4 and FT3

Common: This pattern may be seen in non-compliant patients with pretest medicating.

Rare: This is an unusual pattern that may alert and require further evaluation to exclude rarely diagnosed disorders such as thyroid hormone resistance and TSH secreting pituitary tumours.

Important: Presence of interfering antibodies may also be a cause e.g. Human Anti Mouse Antibodies (HAMA).

Normal or low TSH with low FT4 and FT3

This is a typical pattern seen in unwell patients with nonthyroidal illness. In otherwise healthy individuals, possible pituitary disease with secondary hypothyroidism should be considered.

FOR DIAGNOSIS

(**Note:** In all cases inclusion of a clinical note will allow the laboratory to perform and bill Medicare for the FT4 and FT3.)

Goitre

TSH+/- (FT3, FT4), urine iodine (note marked day to day variations), anti-thyroid peroxidase antibodies (anti-TPO Abs), anti-thyroglobulin antibodies (anti-Tg Abs), if hyperthyroid anti-TSH receptor antibodies (TRAb).

Graves' disease

TSH +/- (FT3, FT4), anti-TSH receptor antibodies

Hypothyroidism

TSH +/- (FT4), anti-TPO Abs

Thyroiditis

(Hashimoto's): TSH +/- (FT3, FT4), anti-TPO Abs, anti-Tg Abs (less useful)

Monitoring Levothyroxine Therapy

Levothyroxine replacement therapy in hypothyroid patients should be adjusted to maintain a normal TSH. In patients with persistent symptoms of hypothyroidism, aiming for a TSH level in the lower reference range is reasonable.

The therapeutic TSH targets in patients with differentiated thyroid cancer taking suppressive doses of thyroxine should be individualised according to the postablation risk stratification. Guidelines suggest that patients who present with a high risk of disease but are clinically free of disease, are advised to maintain a TSH between 0.1 and 0.5 mU/L. For patients with persistent disease, the TSH should be kept below 0.1 mU/L.

Thyroid function tests in pregnancy

Thyroid dysfunction affects 2-3% of pregnant women and overt maternal hypothyroidism is associated with adverse

pregnancy outcomes. Due to changes to thyroid physiology in pregnancy, pregnancy specific reference intervals are required to define thyroid conditions in pregnancy.

It has been recommended that specialists should be involved in the management of raised TSH levels with four weekly thyroid function monitoring to 20 weeks gestation and the frequency of monitoring can decrease thereafter.

Table 2: Pregnancy specific reference intervals

	TSH (mU/L)	FT4 (pmol/L)
First Trimester	0.2-2.8	10-21
Second Trimester	0.2-3.6	11-18
Third Trimester	0.2-3.6	9-17

HOW TO ORDER TSH

Requests for TSH **should include clinical indicators on the request form**. Please note if you only request a TSH, you will only receive a TSH result issued and no "default" TFT testing will be automatically reported for patients with an abnormal TSH. If relevant, please note all Thyroid medication.

TURNAROUND TIME

Tests are performed daily with results available the next working day.

THYROID FUNCTION TEST (TFT)

A TFT is a TSH + one, or more, of the following:

- FreeT4
- FreeT3

A TFT is recommended if the clinical conditions listed in Table 1 are suspected.

HOW TO ORDER TFT

To obtain TFT testing on the patient, the requesting doctor must submit a request that specifies "TFT" testing. If you require a TFT (TSH+T4) please specify TFT on the request form AND write one of the clinical indicators listed in Table 1 on the request form.

If you require a TSH, T4 and T3, please specify TFT+T3 on the request form AND write one of the clinical indicators listed in Table 1 on the request form.

TURNAROUND TIME

Tests are performed daily with results available the next working day.

FURTHER INFORMATION

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Pathologist in Charge - Endocrinology

T: 61 7 3121 4412

Dr Julia Chang MBBS (Hons), BSc (MED), (Hons) FRCPA



a new *era* in
prenatal testing



Generation® Non-Invasive Prenatal Testing (NIPT) represents a major advance in screening and risk assessment for chromosomal abnormalities.

Generation® is a highly efficient, accurate, non-invasive prenatal screening test, based on Whole Genome Sequencing ("WGS") with proprietary algorithms, that analyses circulating cell-free fetal DNA from a maternal blood sample from as early as 10 weeks gestation.

The clinical utility and benefit of the **Generation®** test has been demonstrated in all pregnant women - regardless of age or risk category - in numerous publications, including studies in the New England Journal of Medicine, as well as reports with cohorts of over 34,000 patients^{1, 2, 3, 4}.

What does the **Generation®** NIPT test for?

Generation® NIPT screens for the most commonly seen and tested chromosomal anomalies, including

- ✓ Trisomy 21 (Down syndrome)
- ✓ Trisomy 18 (Edwards syndrome)
- ✓ Trisomy 13 (Patau syndrome)
- ✓ Sex chromosome abnormalities

The following more rarely occurring genetic abnormalities can also be tested for by requesting **Generation® Plus**:

- ✓ Trisomy 9*
- ✓ Trisomy 16*
- ✓ Common microdeletions*
 - DiGeorge syndrome (22q11.2 deletion syndrome)
 - Angelman syndrome
 - Prader-Willi syndrome
 - Wolf-Hirschhorn syndrome
 - Cri-du-chat syndrome

References

1. Bhatt S, Parsa S, Snyder H, et al. Clinical Laboratory Experience with Noninvasive Prenatal Testing: Update on Clinically Relevant Metrics. ISPD 2014 poster.
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Why use **Generation®** NIPT?

Generation® uses whole genome / genome-wide sequencing which investigates more abnormalities, requires less fetal DNA, and has a lower failure and re-collection rates, compared to other methods^{5, 6, 7, 8}.

Who should be offered the **Generation®** NIPT test?

Numerous studies have conclusively demonstrated the benefits for NIPT in women with a high risk pregnancy, including:

- ✓ Women aged over 35
- ✓ Women with abnormal first trimester combined biochemical and ultrasound findings
- ✓ Women with a family history of chromosomal abnormalities
- ✓ Women with a high risk for invasive testing (e.g. IVF)

In addition, there is significant evidence to suggest that women in a normal risk population could also benefit from NIPT, particularly for peace of mind.

How much does **Generation®** NIPT cost?

The cost of this test is \$395* (or \$450* if requesting **Generation® Plus**) and is NOT Medicare rebatable.

*Prices are correct at time of printing and are subject to change without notice. This testing will incur additional costs. It is highly recommended that testing for microdeletion syndromes be accompanied by specialised genetic counselling.

For more information on **Generation®** NIPT

Please visit genomicdiagnostics.com.au
or call us on **1800 822 999**



Genomic Diagnostics

From the Education Desk of QML Pathology

Cat 1 Quality Improvement - Important information for all Doctors

- There will be no new registrations for the QML Pathology Surgical Skin Audit and Cytology Pap Smear Audit after the 31st August 2016.
- Completion of both audits and final upload of points will be 30th November 2016.

Both QML Pathology audits are RACGP QI approved. As we are rapidly approaching the end of the triennium both Tina and I are working very hard to ensure completion of all your QI requirements, if you have any queries please contact your local QML Pathology Medical Liaison Officer, or contact either Tina or I at education@qml.com.au.

IMPORTANT INFORMATION FOR AUDITS

- If you have not been receiving your monthly reports for either audit please contact the QML Pathology Education department, as we may need to check your registration particulars.
- Both Surgical Skin and Cytology Pap audits have specialised request forms, please ensure these requests are utilised for specimen inclusion. To order, please use your stores request forms.
- For the Surgical Skin Audit please complete the reverse of the request form.
- For the Cytology Pap Smear Audit, please ensure you tick all relevant clinical boxes applicable.
- Please note- with the 2017 changes to cytology screening rapidly approaching, the QML Pathology Cytology Pap smear audit was designed from the outset

to report your patients +HPV, Chlamydia, Gonorrhoea and Trichomonas, so please include all relevant clinical pathology and include in the clinical tick box area.

- Please make sure we have your RACGP & ACRRM numbers and email address available to us at registration, as having your numbers at registration will guarantee a smooth transition for processing your achievements.

Jo Wilson-Farr

Manager - Dr Education and Private Practice Development

Education department contact details:

Phone: **07 3121 4453** or **07 3121 4565**

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Email: education@qml.com.au

DOCTORS NOTICEBOARD

Dr James Leonard McKeon

MBBS (QLD), FRACP

Dr James McKeon is an established thoracic and sleep physician operating from Holy Spirit Northside Private Hospital (HSNPH) in Chermside. Experienced in fibre-optic bronchoscopy, endobronchial ultrasound, pleural aspiration and intercostal catheter placement, he manages the Respiratory Function Testing service at HSNPH, including an additional lung function laboratory at the North West Medical Centre.

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Cairns Haematology & Oncology Clinic

Cairns Haematology & Oncology Clinic (CHOC) provides advice, support and treatment for all types of blood and malignant disease. Offering a full range of services, including medical oncology, radiation oncology and haematology, and having close links to other services across the district, CHOC is able to ensure access to the most appropriate treatment and support for all patients.

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Fertility Solutions

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Fertility Solutions is a local and respected clinic, assisting individuals and couples with all matters relating to fertility. With clinics at the Sunshine Coast and Bundaberg, Fertility Solutions offer patients the choice of 7 Fertility Specialists.

P: 1300 FERTILITY / W: fssc.com.au

Infectious Diseases Report

GEOGRAPHIC DISTRIBUTION - AUG 2016

ORGANISM	Regions (as per key below)															TOTAL			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	JUL	JUN	MAY	APR
Adenovirus (not typed)	3	16	11	1			21		12	5	30	10	7	2	1	119	102	87	74
Adenovirus (typing pending)	1		2	2			2	3	1	2	1	4				18	14	14	10
Barmah Forest virus																0	5	9	8
Bordetella pertussis	2	52	20	4			27		34	12	43	46	8	8	5	261	313	337	294
Brucella species														1		1	4	3	12
Campylobacter jejuni												2				2			
Chlamydia pneumoniae																	1	1	
Chlamydia trachomatis, not typed	68	142	60	20	2		112	2	84	38	219	69	18	42	38	914	942	985	952
Coxiella burnetii	1	1	3	3						2	2	1	1		1	15	15	9	20
Cryptococcus species	1		1												1	3	2		4
Cytomegalovirus (CMV)	2	6	4	2			2		6		10	4	1	1	1	39	32	64	45
Entamoeba histolytica																			
Enterovirus - not typed																	1	1	
Epstein-Barr virus (EBV)	5	21	5	2			16		12	2	35	15	6	6	11	136	138	157	137
Flavivirus unspecified		1					4				2	2	1			10	14	21	25
Hepatitis A virus		1									3		1			5	1	2	8
Hepatitis B virus	7	11	3				17		10	4	77	1		1	1	132	142	155	141
Hepatitis C virus	20	63	23	5	1		51		32	10	101	29	17	13	24	389	402	448	469
Hepatitis D virus																	1		
Hepatitis E virus							1									1	2		1
Herpes simplex Type 1	14	60	32	8	2		59		39	21	115	39	19	13	22	443	442	389	415
Herpes simplex Type 2	13	40	8	8	1		23		13	5	51	27	5	5	5	204	223	248	208
Herpes simplex virus - not typed																			
HIV-1	1	1					6		2							10	19	21	13
HTLV-1																			
Human Metapneumovirus		12	10	1			11		21	1	29	10	2	11	1	109	57	49	99
Influenza A virus	16	122	37	7	3	1	96	3	70	15	168	117	25	21	29	730	179	143	189
Influenza B virus	7	12	1				6	1	2		11	5	1	2		48	34	33	46
Legionella pneumophila (all serogroups)																	3		2
Legionella species											1					1	1		
Leptospira species	2	2											1	1	1	7	8	9	4
Measles virus																	2	1	
Mumps virus		2					1		1		1	2				7	4	2	2
Mycoplasma pneumoniae	5	27	10	5			9		13	8	25	13		1	3	119	134	130	204
Neisseria gonorrhoeae	5	18	3	1	1		20	2	5		28	2	2	5	3	95	77	71	79
Parainfluenza virus	4	7	10	2			18		12	2	25	6	2	7	3	98	121	150	200
Parvovirus									1			1			1	3	5	5	8
Pneumocystis carinii											1	3				4	1		1
Respiratory Syncytial virus	1	63	32	3		1	42		39	17	101	20	31	2	8	360	399	473	460
Rhinovirus (all types)	7	54	22	8	2		45	1	62	21	107	45	13	25	10	422	503	490	354
Rickettsia - Spotted Fever Group		2													1	3	2	3	1
Ross River virus	3	1	3						2	1	1	5		3	4	23	41	201	331
Rubella virus		1							1		1					3	1	2	
Salmonella paratyphi A																			
Salmonella paratyphi B																			
Salmonella typhi		1														1	1	1	1
Streptococcus Group A	10	13	5	1			8	55	7	6	9	8	2	3	2	129	153	154	154
Toxoplasma gondii		2	1	1			1				3	1			1	10	5	7	10
Treponema pallidum	33	17	4	2	14		50	1	19	10	40	8	3	34	2	237	237	266	248
Trichomonas vaginalis	5				2		1		2	3	5		2	6		26	37	29	37
Varicella Zoster virus	7	72	20	3			42		41	5	75	54	6	15	9	349	338	326	325
Yersinia enterocolitica																			
TOTAL	243	843	330	89	28	2	691	68	543	190	1320	549	174	228	188	5486	5158	5496	5591

REGIONS:

1 Cairns

2 Gold Coast/Tweed

3 Ipswich

4 Mackay

5 Mount Isa

6 New England

7 North Brisbane

8 Northern Territory

9 Redcliffe

10 Rockhampton

11 South Brisbane

12 Sunshine Coast

13 Toowoomba

14 Townsville

15 Wide Bay/Burnett

FURTHER HISTORICAL CLINICAL DATA CAN BE OBTAINED BY CONTACTING MARKETING ON INFO@QML.COM.AU.