

- > New Oral Anticoagulants  
by Dr Peter Davidson
- > FISHing for Melanomas  
by Dr Inara Strungs
- > 2013 Influenza (Flu) Vaccine  
by Dr Shalinie Perera



## New Oral Anticoagulants (NOACs)

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Anticoagulation is a cornerstone of management of thrombotic conditions including PE, DVT, AF and the post surgery patient. The haemostatic cascade provides several points for therapeutic intervention in delivering some form of anticoagulation/antithrombotic (see Diagram 1 overleaf). Traditionally, Warfarin has been the principal choice in short-term and long-term anticoagulation. However, its use for this purpose resulted in significant burden on physician, patient and pathology providers due to its need to be closely monitored.

The advent of the New Oral Anticoagulants (NOACs) promises to provide equivalent benefit with less or no need for repeated haematologic monitoring. In this article we hope to provide an overview of these new medications, their uses and their pitfalls.

There are two main classes of these new drugs:

1. **Direct Thrombin Inhibitors** - these often have 'agatran' ending to their drug name
2. **Direct Xa Inhibitors** - these often have 'xaban' ending to their drug name.

Presently there are 3 new drugs on the Australian market: Rivaroxaban (Xarelto® Bayer), Dabigatran (Pradaxa® Boehringer Ingelheim), and Apixaban (Eliquis® Pfizer).

In future, more choice is likely to become available. TGA and PBS listings for the current drugs is not uniform and may be a potential cause for confusion (See Table 1 overleaf). There is a fourth drug, Edoxaban (Lixiana), which has not yet to made it onto the Australian market.

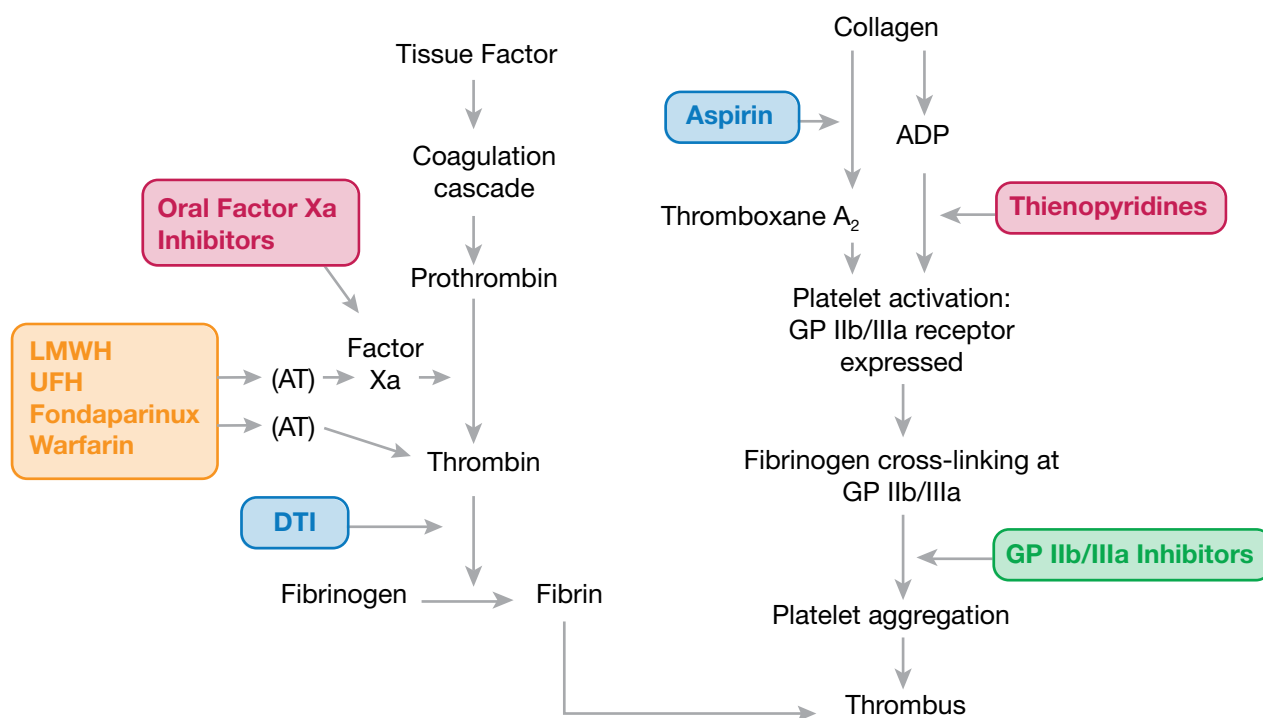


DIAGRAM 1: COAGULATION CASCADE AND SITES OF ACTION

## Efficacy of NOACs compared to Warfarin

In view of recent approvals by international agencies such as the US FDA, it is likely all three drugs will have TGA approval for the treatment of AF. The results of the trials of these drugs in the setting of non-valvular AF are summarised in Table 2.

Warfarin itself (at an INR target range of 2 - 3) provides roughly a 60 - 70% reduction in risk of thromboembolic events compared with no treatment in the setting of AF.

The risk of major bleeding with Warfarin is around 3% per annum in contrast to a background untreated population risk of 0.1 - 0.5% per annum.

Interestingly with Warfarin the major bleeding tended to be intracranial whereas the NOACs were associated with less intracranial bleeding. However, GI bleeding was more often a feature of major bleeding with the NOACs.

## NOAC pharmacology

The pharmacology of the drugs is summarised in Table 3.

Of clinical relevance it is important to note the degree to which the drugs are dependent on renal excretion, as renal impairment can lead to toxic accumulation and overdosage.

Depending on the choice of NOAC, accurate estimation of renal function is important in regard to safe dosing of the patient. The eGFR should not be relied upon in these circumstances and creatinine clearance should be measured with a 24 hr urine test or calculated using the Cockcroft-Gault formula. Many of the electronic medical record programs such as Medical Director have an in-built formula calculator.

Drug	INDICATION		
	Non Valvular AF	Post op Prophylaxis THR/TKR	DVT/PE Treatment
Warfarin	TGA Approved PBS Listed	TGA Approved PBS Listed	TGA Approved PBS Listed
Dabigatran	TGA Approved Non PBS	TGA Approved PBS Listed	Not Approved Presently
Apixaban	TGA Pending	TGA Approved PBS Listed	Not Approved Presently
Rivaroxaban	TGA Approved Non PBS	TGA Approved PBS Listed	TGA Approved PBS Listed*

TABLE 1: TGA APPROVED INDICATIONS AND PBS LISTING

Drug	TRIAL		
	RE-LY	ARISTOTLE	ROCKET-AF
Stroke/ thromboembolism	34% reduction	20% reduction	Non-inferior to Warfarin
Haemorrhagic stroke	74% reduction	50% reduction	40% reduction
Major bleeding	Similar	30% reduction	Similar

TABLE 2: MAJOR RESULTS OF PHASE 3 TRIALS OF NEW ANTICOAGULANTS VS WARFARIN IN AF

Those drugs that have less than 65% renal excretion are dependent on hepatic elimination, and caution must be used when treating patients with liver failure. Use is not recommended in those with severe impairment (Child-Pugh Class C).

DRUG	DABIGATRAN	APIXABAN	RIVAROXABAN
Target	Thrombin	FXa	FXa
Half-life (h)	12 - 17	9 - 14	9 - 13
Dosing	110 - 150 mg BD	2.5 - 5 mg BD	10 - 30 mg OD
Peak plasma conc.	2 - 3 h	1 - 3 h	2 - 4 h
Plasma protein binding	34 - 35%	87%	92 - 95%
Renal elimination	80%	25%	66%
Metabolism	Potent P-gp inducers / inhibitors	CYP3A4 P-gp inducers / inhibitors	CYP3A4 P-gp inducers / inhibitors
Coagulation monitoring	Not required	Not required	Not required

TABLE 3: NOAC PHARMACOLOGY

## RIVAROXABAN

Rivaroxaban (Xarelto® Bayer) is a factor Xa inhibitor and is the only agent PBS listed for the Treatment and Prevention of VTE. Its pharmacology is summarised in Table 3. Its dosing guide is provided below in Table 4.

	INDICATION		
Creatinine Clearance (CrCl)	VTE Prevention (total hip & knee replacement)	Stroke prevention in atrial fibrillation	DVT treatment & prevention
Normal >80 mL/min	10 mg once daily	20 mg once daily	15 mg twice daily for 3 wks, then 20 mg once daily
Mild 50 - 80 mL/min			
Moderate 30 - 49 mL/min	10 mg once daily	15 mg once daily	15 mg twice daily for 3 wks, then 20 mg once daily
Severe 15 - 29 mL/min	10 mg once daily (Use with caution)	Xarelto® is contraindicated	
Severe <15 mL/min	Xarelto® is contraindicated		

TABLE 4: RIVAROXABAN DOSAGE AND ADMINISTRATION ADVICE FOR PATIENTS WITH REDUCED RENAL FUNCTION OVER 65 YEARS

Note: PBS reimbursement is not available for all indications. A quick reference for streamlined authority is provided at the end.

Trial studies in AF (Rocket Study) and VTE (Einstein Study) have shown Rivaroxaban to be as effective as the present standard of care (Warfarin), with a risk event rate on worse than the present standard of care.

Contraindications to the use of Rivaroxaban include: Hypersensitivity, active bleeding, lesions at high risk of spontaneous bleeding, severe hepatic disease (with coagulopathy), severe renal disease (CrCl <30 mL/min), pregnancy, lactation, and concomitant treatment with strong inhibitors of both CYP3A4 and P-glycoprotein (Ketoconazole, Clarithromycin, Ritonavir).

Precautions for the use of Rivaroxaban include a general increased bleeding risk, bronchiectasis or a history of pulmonary bleeding, renal impairment, hepatic impairment, surgery and interventions, spinal/epidural anaesthesia or puncture. There is also no clinical data in patients with prosthetic heart valves or lactose intolerance.

Care should be taken if there is concomitant administration of medication which may affect coagulation such as NSAIDs, platelet aggregation inhibitors or other anticoagulants.

Common (>2%) adverse reactions reported during the trials were bleeding (post procedural, gingival, rectal, haematuria, menorrhagia, epistaxis, haematoma, ecchymoses, contusion), biochemical (increased liver transaminases), GI (constipation, diarrhoea, nausea), and general (pyrexia, peripheral oedema, pain in extremity, headache, dizziness, fatigue).

## APIXABAN

Apixaban (Eliquis® Pfizer) is also an orally active Factor Xa inhibitor; it has been PBS listed for the prevention of VTE in patients undergoing hip or knee replacements and authority is required. Its pharmacology is summarised in Table 3. Its dosing guide is provided below in Table 5.

	INDICATION		
Creatinine Clearance (CrCl)	VTE Prevention (total hip & knee replacement)	Stroke prevention in atrial fibrillation	DVT treatment & prevention
Normal >80 mL/min	2.5 mg BD	5 mg BD or 2.5 mg BD if > 75 yrs age	Not TGA approved
Mild 50 - 80 mL/min			
Moderate 30 - 49 mL/min		2.5 mg BD	
Severe 15 - 29 mL/min	Cautious use	Cautious use	
Severe <15 mL/min	Contraindicated	Contraindicated	
Note: TGA Approval for use in AF is still pending			

Note: TGA Approval for use in AF is still pending

TABLE 5: APIXABAN DOSAGE AND ADMINISTRATION ADVICE

Contraindications to the use of Apixaban include clinically significant active bleeding (including GI), lesions or conditions at increased risk of bleeding (recent CVA, active PUD, and those with pre-existing impairment of haemostasis), severe hepatic disease with associated coagulopathy, concomitant treatment with strong inhibitors of both CYP3A4 and P-glycoprotein (azoles, HIV PIs), concomitant therapy with any other anticoagulant.

Precautions for the use of Apixaban include situations at high risk of bleeding and the use of medications that might affect haemostasis (NSAIDs etc.). The use of thrombolytics for a CVA or AMI, while on Apixaban, should be avoided if possible. Inducers of CYP3A4 and P-gp (e.g., rifampin, phenytoin, carbamazepine, St John's Wort) reduce apixaban exposure but paradoxically have been shown to increase bleeding risk. Apixaban should be used with caution in those with mild to moderate hepatic impairment.

The most common adverse reaction recorded during large clinical trials was bleeding. Other adverse reactions reported at >1% of participants included nausea, anaemia, hepatic enzyme derangement; however the reported rate in the comparator drug arm was similar. Rectal bleeding, gingival bleeding and haematuria were only increased when compared to ASA.

## DABIGATRAN

Dabigatran (Pradaxa® Boehringer Ingelheim) is an orally active direct thrombin inhibitor that has been PBS listed for the postoperative prevention of VTE in patients undergoing hip or knee replacement and authority is required. Its pharmacology is summarised in Table 3. Its dosing guide is provided overleaf in Table 6.



Care must be taken in the elderly to accurately assess their renal function prior to consideration of Pradaxa.

	INDICATION		
Creatinine Clearance (CrCl)	VTE Prevention (total hip & knee replacement)	Stroke prevention in atrial fibrillation	DVT treatment & prevention
Normal >80 mL/min	220 mg daily (2 x 110 mg caps)	300 mg daily or 220 mg daily if >75 yrs age	Not TGA approved
Mild 50 - 80 mL/min			
Moderate 30 - 49 mL/min	150 mg daily	220 mg daily	
Severe 15 - 29 mL/min	Contraindicated	Contraindicated	
Severe <15 mL/min			
Note: PBS reimbursement for use in AF is still pending.			

TABLE 6: DABIGATRAN DOSAGE AND ADMINISTRATION ADVICE

The contraindication most significant with Dabigatran is that it must not be used in those with renal impairment (CrCl<30 mL/min) and care must be taken in the elderly to accurately assess their renal function prior to consideration of Pradaxa. Other contraindications include the usual high bleeding risk situations (current or recent significant bleeding, especially GI or intracerebral, bleeding diatheses, planned surgical procedures) as well as hepatic impairment and concurrent treatment with Ketoconazole or Verapamil.

Drug interactions found to be significant in trials included Proton Pump Inhibitors (PPIs) which were found to reduce the absorption, SSRIs were found to be associated with increased bleeding risk, and NSAIDs should be used only for very short periods if at all. Strong inducers of P-glycoprotein (Rifampicin, St John's Wort, Carbamazepin) are expected to reduce Pradaxa concentrations. P-glycoprotein inhibitors (Amiodarone, Clarithromycin, Ritonavir, Verapamil) should be used with caution and patients kept under close clinical surveillance due to their potential to increase Dabigatran levels and potentiate its anticoagulant effect.

Risk and benefits

Precautions that must always be taken into account when commencing a patient on anticoagulant therapy such as the assessment for situations and conditions that will place a person at increased risk of bleeding while anticoagulated and the education of the patient and their family must be observed. The renal function of those over 75 years of age should be carefully monitored while they are being treated with the new agents, particularly Pradaxa and Rivaroxaban.

Concomitant use of antiplatelet agents

Studies with Dabigatran, Rivaroxaban and Apixaban in patients with acute coronary syndromes, receiving combined antiplatelet therapy with Aspirin and Clopidogrel, have generally shown a dose-dependent increase in the risk of major bleeding and any bleeding. Nevertheless, there is a possibility for a net clinical benefit of concomitant therapy as recently shown for Rivaroxaban.

Need for monitoring

Although designed to not require any therapeutic monitoring, certain situations may demand and assessment of coagulation or drug level.

- Patients with low body weight or obese patients
- Pediatric patients
- Renal or hepatic impairment
- Accidental or deliberate overdose
- To measure adherence
- To evaluate patients with haemorrhagic or thrombotic complications
- To assess levels prior to surgery

To monitor these drugs new coagulation assays are required.

Some of the standard assays of a coagulation profile which are frequently used to monitor heparin and Warfarin are unsuitable for the NOACs because the assay is insensitive or too sensitive to these newer agents. Furthermore, the assay sensitivity may also depend on the reagents used for that assay as different manufacturers provide slightly differing reagents.



	Direct Thrombin Inhibitors	Direct FXa Inhibitors	Indirect FXa Inhibitors
PT in sec and INR	↑	↑	No
aPTT	↑	↑	No
Thrombin time	↑↑	No	No
Fibrinogen (Clauss)	No/↑	No	No
Derived fibrinogen	No/↓	No/↓	No
D-dimers	No	No	No

**TABLE 8: INFLUENCE OF ANTICOAGULANTS ON STANDARD COAGULATION ASSAYS**

Both a prolonged APTT and TCT suggest clinically important levels of Dabigatran are present. An APTT trough level > 80 sec is associated with increased bleeding risk.

Whereas with Rivaroxaban, TCT will be unaffected, and a prolonged PT (INR > 1.2) and to a lesser extent APTT, will suggest clinically important levels of Rivaroxaban are present.

Usefulness of lab tests	Dabigatran	Rivaroxaban	Apixaban
	ECT	Chromogenic anti-Xa	Chromogenic anti-Xa
	TT	aPTT, PT	
	aPTT		
	PT / INR		

**TABLE 9: LABORATORY TESTING NEW ORAL AGENTS**

Assays with the strongest linear correlation with the drug dose/concentration are preferred for monitoring the individual drugs.

QML Pathology offers a Chromogenic Anti Xa assay for Rivaroxaban. Presently no formal reference ranges have been ratified. Moreover, analysis is dependent on the timing of the last dose and to some extent the strength of the tablets.

As these drugs become more widely used in the management of venous thromboembolic disorders one also needs to be aware of potential interference of these drugs in some of the common thrombophilia assays (see Table 10).

Depending on the assay the lab uses, there may be no impairment to the measurement, or a falsely higher estimate of the level. This usually makes it all the more important to get screening bloods done before the first dose.

**Note:** It will not affect molecular tests such as a PCR for Factor V Leiden and Prothrombin 20210 mutations.

		Direct Thrombin Inhibitors	Direct FXa Inhibitors	Indirect FXa Inhibitors
Antithrombin	FIIa-based assay	↑	No	No
	FXa-based assay	No	↑	No
Protein C	Coagulometric	↑	↑	No
	Chromogenic	No	No	No
Protein S activity	Coagulometric	↑	↑	No
DVRRT assay (lupus anticoag diagnostics), LA screen & confirm	Clotting Times	↑	↑	No
ProC Global, APCR	Clotting Times	↑	↑	No
FXIII	Chromogenic determination, FXIII activation via thrombin	↓	No	No

**TABLE 10: INFLUENCE OF ANTICOAGULATIONS TO COMMON THROMBOPHILIA ASSAYS**

## Managing side-effects

- Bleeding may occur due to a number of factors, such as:
  - Toxic levels due to overdosage or deterioration in renal flow/output (or liver dysfunction in those drugs dependent on hepatic metabolism)
  - Drug interaction though altering metabolism
  - Other anticoagulant effects, e.g., anti-platelet agents, NSAIDs or Vitamin K deficiency
  - Focal pathology, e.g., infection (UTI), ulceration or polyps.
- Treatment will depend on the severity of the bleeding
- Always consider the anatomical site of the bleeding. Do not immediately assume the anticoagulant is responsible– although it could be!
- Order an urgent coag profile, FBC, E/LFT, blood group and screen

### MILD BLEEDING

- Withhold next dose of NOAC or discontinue treatment as appropriate
- Apply local measures and treat any aggravating factors

### MODERATE BLEEDING

As above, plus:

- Administer fluid replacement to maintain good urine output to improve renal excretion
- Consider platelets if levels less than 70 - 80 x 10<sup>9</sup>/L or patient on anti-platelet agent
- Consider tranexamic acid
- Consider Vitamin K – if risk of deficiency or recent Warfarin use
- Administer oral charcoal if ingested in last 2 hours.

### ADDITIONAL INTERVENTIONS – SEVERE ONGOING BLEEDING

As above, plus consider the following therapeutic options:

- Rivaroxaban:** Prothrombinex, Novo7
- Dabigatran:** Dialysis, Prothrombinex, Novo 7

Non-bleeding side effects may occur such as GI upset or rash, or perhaps there is renal deterioration over time, which may require the patient to be switched to Warfarin.

## Changing from NOACs to Warfarin

Complicated high risk patients may require a 3 way switch with cessation of the NOAC, and commencement of a Heparin, then commencement of warfarin, and ceasing the heparin when the INR is therapeutic. Uncomplicated cases can be managed with a simple switch. Warfarin is started up to 3 or 4 days before the planned cessation of the NOAC. Warfarin should be commenced at the estimated maintenance dose (EMD) rounded up to the nearest mg, and the first INR done on Day 0 (See Table 11 below).

$$EMD = \sqrt{\frac{WT \times (100 - Age)}{100}}$$

DRUG	START DAY WITH WARFARIN		
Calculated creatinine clearance, mL/min	> 50	31 - 50	15 - 30
Dabigatran*	Day -3	Day -2	Day -1
Rivaroxaban*	Day -4	Day -3	Day -2
* Dabigatran/Rivaroxaban is stopped on Day 0. The longer overlap with Rivaroxaban is justified by its half-life being shorter than that of Dabigatran and by the concern about thromboembolic events shortly after transitioning from Rivaroxaban to Warfarin.			

TABLE 11: TRANSITIONING FROM NOAC TO WARFARIN

## Changing from Warfarin to NOACs

The reverse situation may apply and patients who become difficult to management on Warfarin may be more suitably managed on a NOAC. As general rule, avoid switching from Warfarin if the patient is well controlled on Warfarin and there are no good reasons to switch. If there are good reasons, always assess the patient for contraindications to a NOAC before switching (See Table 12 below).

Day -1	Take Warfarin for last time
Day 0	No Warfarin
Day +1	Check INR if < 2.5* commence NOAC^ if INR > 2.5 delay NOAC and repeat INR day +2
Day +2	If INR < 2.5 commence NOAC if INR > 2.5 delay NOAC and repeat INR next day
* INR <2.5 or INR <2.0 in case of Pradaxa	
^ Commence NOAC at a dose appropriate to age and renal function	

TABLE 12: TRANSITIONING FROM WARFARIN TO NOAC

## Conclusion

With the advent of newer anticoagulants the management of patients can become simpler yet more complex

Presently, Warfarin will continue to remain the first option for many AF patients as PBS listing of the NOAC for this condition is non-existent, and likely to be on authority only when granted.

Initial treatment of confirmed acute symptomatic deep vein thrombosis (DVT) without symptomatic pulmonary embolism (PE)			
Form & strength	Max qty	Repeats	Streamlined authority code
Tablet 15 mg	42	0	4098
Continuing treatment of confirmed acute symptomatic DVT w/out PE			
Form & strength	Max qty	Repeats	Streamlined authority code
Tablet 20 mg	28	5	4099
Continuing treatment for prevention of recurrent VTE			
Form & strength	Max qty	Repeats	Streamlined authority code
Tablet 20 mg	28	5	4132
Note: Authority is required for prescribing Xarelto for VTE prophylaxis following orthopaedic surgery.			

TABLE 13: QUICK GUIDE TO PBS AUTHORITY FOR STARTING XARELTO IN VTE

### References

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## Pathologist Profile

**Dr Peter Davidson MBBS FRCPA**  
PATHOLOGIST IN CHARGE - HAEMATOLOGY

A graduate of the University of Queensland (1985), Dr Davidson practiced as a GP in Beenleigh and Chermide from 1989-1990, before returning to the hospital system to complete his pathology training. He trained in haematology at the Royal Brisbane Hospital, Greenslopes Repatriation Hospital, and the Australian Red Cross Blood Transfusion Service, before obtaining his fellowship.

Based at the central laboratory in Brisbane, Dr Davidson has been a haematologist with QML Pathology since 1996, as well as acting as Visiting Consultant Haematologist to the ARCBS (1996-1997) and the Mater Hospital (1996-present).

Dr Davidson is currently Head of the Haematology Department.

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## FISHing for Melanomas

Dr Inara Strungs MBBS FRCPA BA

*Diagnosis of melanocytic lesions is one of the most difficult areas of histopathology.*

*While most lesions can be designated as benign or malignant, similar features can be found in both groups, and there is a subset of tumours which cannot be definitively classified even by experts. They are referred to as tumours of 'uncertain malignant potential', or 'borderline', 'ambiguous' or 'controversial' tumours.*

*Histology remains the gold standard for diagnosis of melanomas and a second, expert opinion is often obtained for difficult tumours.*

*Recently molecular testing has been introduced as an adjunct to histology.*

### Molecular testing

- Benign naevi are driven by point mutations in selected oncogenes without chromosomal abnormalities. In contrast, melanomas show chromosomal instability with gains, amplifications and losses of chromosomal material which can be detected by genetic techniques (CGH and FISH).
- **Comparative genomic hybridisation (CGH)** – hybridises and compares the entire genome of a tumour to reference DNA. It can be performed on paraffin-embedded tissue but requires a significant amount of tissue, special equipment and expertise and is time consuming since microdissection is needed. It is only performed in specialist centres overseas and costs over \$1000.
- **Fluorescence in situ hybridisation (FISH)** – hybridises short DNA fragments (probes) to paraffin-embedded sections of tumour. At present only four targets can be evaluated on a single FISH test. The FISH test which has been found to have the highest diagnostic discrimination, and is available from Abbott Molecular, targets chromosome 6p25, 6 centromere, 6q23 and 11q13. FISH is simple, rapid and cheaper than CGH but requires highly trained technical staff.
- Discrepancies between CGH and FISH are expected if both are used (because FISH can pick up abnormalities in only a few cells, whereas CGH needs a high percentage of cells to be affected).

## Sensitivity/Specificity and uses of FISH for melanocytic tumours

- Several studies of histologically unequivocal melanomas and naevi have shown a **specificity** of 82-94% and a **sensitivity** of 90-98% (Fang). Other studies (Gaiser; Leboit - unpublished data quoted in McCalmont, 2011) report lower results, but this may be due to differences in methodology and case selection.
- **False positive** FISH results for unequivocally benign naevi may occur because of tetraploidy (four copies per nucleus of a chromosome) which needs to be corrected for, and because some benign lesions have chromosomal aberrations.
- **False negatives** may occur since some melanomas have chromosomal changes other than those targeted by the assay, i.e., a negative FISH result does not exclude the diagnosis of melanoma.
- The only current justification for use of the FISH test is in histologically ambiguous lesions since it is not needed in unequivocal cases. But there is a problem in assessing the effectiveness of the FISH test in these cases. Sensitivity and specificity is unable to be established since there are no objective validation data to serve as a reference as in unequivocal naevi and melanomas. Even follow up data are not always useful since not all melanomas are lethal.
- FISH is useful in small lesions with scanty tissue, and in distinguishing conjunctival naevi, intranodal naevi, mitotically-active naevi and cellular blue naevi from melanoma.

## Limitations of FISH for melanocytic lesions

- As noted before, a negative FISH does not exclude melanoma.
- The sensitivity of FISH for evaluation of spitzoid lesions is suboptimal (unless extra probes are added which at present make the cost prohibitive).
- Most experts are of the opinion that FISH should only be used as an adjunct and not an alternative to careful microscopy and expert consultation. Many remain sceptical about its use and think that more follow up is needed.

## Availability of FISH for melanocytic lesions at QML Pathology

- FISH has recently become available at QML Pathology and is performed at Royal Prince Alfred Hospital in Sydney at a cost of \$950 (non-rebatable). Because of the aforementioned problems with sensitivity and specificity, cases submitted for this test need to be reviewed by QML pathologists in conjunction with pathologists at the Sydney Melanoma Unit.

## Summary

The four probe FISH test should only be used for assessment of ambiguous melanocytic lesions and only as an adjunct to careful histologic assessment and expert opinion. A positive FISH is supportive of melanoma, but a negative result does not exclude it. The jury is still out on the exact usefulness of the test, but it may become more useful in the future when more probes can be added.

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## Pathologist Profile



### Dr Inara Strungs MBBS FRCPA BA CONSULTANT HISTOPATHOLOGIST

Dr Strungs graduated from the University of Queensland in 1981 and worked at Royal Brisbane Hospital and Royal North Shore Hospital in Sydney. She trained in histopathology at the Queen Elizabeth Hospital in Adelaide and obtained her fellowship in 1990.

Dr Strungs has worked as Staff Pathologist at Toowoomba Base Hospital and Gramp Skin Pathology in Adelaide, and VMO at Princess Alexandra and Nambour Hospitals. She joined QML Pathology in November 2001.

Dr Strungs is a member of the International Academy of Pathology, the Australian Medical Association and Australasian Dermatopathology Society.

Dr Strungs has a special interest in dermatopathology.

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# 2013 Influenza (Flu) Vaccine

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## Overview

Every year, the flu is responsible for the deaths of approximately 2800 Australians (either directly, or through complications caused by the virus). Adults older than 65 years, pregnant women, very young children, Aboriginal and Torres Strait Islanders older than 15, and those with chronic medical conditions are at high risk of serious complications.

## This Year's Flu Season

This year the flu season started earlier in the countries of the northern hemisphere and influenza activity has been continuing to increase. Indicators of severity in USA and Canada have been high compared to last year, with the number of hospitalisations and deaths due to pneumonia and influenza beginning to exceed the national threshold. The age group most affected is adults more than 65 years, followed by children 0-4 years. 37 deaths have been reported in the paediatric age group already in the USA up to the week ending 19/01/13.

Australia is expected to experience a similar situation, therefore, it is important to be prepared in advance. Flu vaccination is the most effective action in helping fight the spread of flu in the community. Vaccination is recommended in autumn to allow time for immunity to develop before the flu season starts.

## Vaccination

Each year, flu vaccines are tailored to match the expected strains that circulate around the world. The flu vaccine is constantly changing, and the immunity following vaccination wanes after one year. Therefore, it is necessary for vaccination to be performed every year for the vaccine to remain effective.

The flu vaccine for 2013 contains the following strains:

- A (H1N1): an A/California/7/2009 (H1N1) - like strain
- A (H3N2): an A/Victoria/361/2011 (H3N2) - like strain
- B: a B/Wisconsin/1/2010 - like strain.

Note: The H1N1 is the same as the H1N1 virus that was included in the 2012 vaccine, but the influenza H3N2 and influenza B vaccine viruses are different for 2013.

Early estimates have shown that the majority of the subset of strains characterised by the CDC so far are antigenically similar to the strains in the vaccine.

The 2013 influenza vaccine is available for purchase from QML Pathology (please see below). To order, please contact our Vaccines Department on (07) 3121 4523.

## References

1. Australian Government Department of Health and Ageing (2012) *Seasonal Influenza Vaccination Program* [Brochure]. Retrieved from: [www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/ITO150-cnt](http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/ITO150-cnt).
2. World Health Organization (2013) *Global Health Observatory (GHO): Global influenza virological surveillance*. Retrieved from: [www.who.int/gho/epidemic\\_diseases/influenza/virological\\_surveillance/en/index.html](http://www.who.int/gho/epidemic_diseases/influenza/virological_surveillance/en/index.html).



## Flu Vaccine Now Available

*The 2013 Flu Vaccine is now available to buy in boxes of 10 and in single doses. As stock is in high demand, it is recommended that you place your order early.*

**For orders and enquiries, please contact the QML Pathology Vaccines Department on (07) 3121 4523 or email [VaccCustServ@qml.com.au](mailto:VaccCustServ@qml.com.au).**



## Warfarin Care Clinic Easter Hours

QML Pathology wishes to advise that over the upcoming Easter period, the Warfarin Care Clinic will not be accepting any NEW REGISTRATIONS from Wednesday, 20 March 2013. This service will re-open from Tuesday, 2 April 2013.

Patients who are currently monitored by QML Pathology and are being discharged from hospital will still be accepted during this time.

## Cytopathology Staff Achievements

QML Pathology Cytopathology department is proud of the high quality Scientists involved in screening cervical smears and non-gynaecological samples. All staff undergo extensive training and after two years are eligible to sit for the CT (ASC) exam set by the Australian Society of Cytology (ASC).

**Congratulations to Sasha Milenkoff, Phuong Do and Sara Hall (pictured right) for passing the difficult ASC exam.**



## Anti-MuSK Antibody Tests

Anti-MuSK antibody tests received by QML Pathology are sent to NSW Health Pathology Concord Hospital. Until now, this test has been performed by NSW Health Pathology as a bulk billed item. Recently we have been advised that this is no longer feasible and NSW Health Pathology is now charging for this test in order to cover costs incurred. Patients will now be required to pay \$100.00.

# Collection Centres

## NEW COLLECTION CENTRES

### BALLINA WEST ..... 02 6686 6424

Ballina West Medical Centre  
Shop 12-13, Ballina West Shopping Centre  
Pacific Terrace  
Opening Hours:  
Mon - Fri: 8.00am – 12.00pm

### BLI BLI..... 07 5448 4577

Shop 15, River Markets Shopping Centre  
314 – 328 David Low Way  
Opening Hours:  
Mon - Fri: 7.00am – 12.00pm  
12.30pm – 3.00pm

### FOREST LAKE ..... 07 3279 9241

The Tower Medical Ctr, 241 Forest Lake Blvd  
Opening Hours:  
Mon - Fri: 8.00am – 12.00pm  
1.00pm – 4.30pm  
Sat: 8.30am – 12.30pm

### KINGSCLIFF..... 02 6674 4501

40 Marine Pde  
Opening Hours:  
Mon - Fri: 9.00am – 12.00pm

### LISMORE ..... 02 6622 4421

22 Keen St  
Opening Hours:  
Mon - Fri: 8.00am – 1.00pm  
1.30pm – 4.00pm

### MARYBOROUGH ..... 07 4123 6765

Good Price Pharmacy, 168b Bazaar St  
Opening Hours:  
Mon - Fri: 7.30am – 12.00pm  
12.30pm – 2.30pm

### MARYBOROUGH ..... 07 4121 6856

Luxton's Pharmacy, 264 Bazaar St  
Opening Hours:  
Mon - Fri: 9.00am – 1.00pm

### MITCHELTON ..... 07 3121 4444

24 Blackwood St  
Opening Hours:  
Mon - Fri: 8.00am – 12.00pm

# Doctor's Noticeboard

**AMA QUEENSLAND** will be hosting their Workplace Relations Training in various locations throughout Queensland. With topics focusing on eHealth, Telehealth and Personally Controlled Electronic Health Record: your medico-legal obligations. General practitioners, Practice managers and support staff are encouraged to attend. For more information or to register, please call (07) 3872 2216.

## CONSULTATION ROOM FOR PSYCHIATRIST OR PSYCHOLOGIST – GOLD COAST

Do you want to join an adult psychiatrist and a child psychiatrist on the Gold Coast? A professional consulting room is available at the Mermaid Waters Therapy Clinic.

This is a modern, purpose-built psychiatric clinic in the central Gold Coast, close to transport, local general practitioners, a major shopping centre and the beach. There is dedicated off street car parking, a large waiting room, children's room and secretarial support is included in the lease. Sessional or full-time rental available.

For further information, please email [mermaidwaterstherapyclinic@gmail.com](mailto:mermaidwaterstherapyclinic@gmail.com) or call Carole or Jonathan on phone (07) 5578 5022 or 0400 819 316.



### DR JAN LAWRENCE

MBBS., RANZCP, Cert. POA

Dr Lawrence is most interested in working with older persons with depression, anxiety and

cognitive impairment, and those adjusting to serious medical illness, pain, or the end of life.

She consults from her private practice on Level 7 at St Vincent's for those referred from the community, and to in patients of St Vincent's Brisbane, and the residents of Marycrest and Lilian Cooper Nursing Homes. Dr Lawrence has also established a multi-disciplinary Memory Clinic at St Vincent's, with two geriatrician colleagues, a psychologist and allied health. The clinic offers assessment and management of cognitive impairment and associated conditions. Capacity assessment available.

The Link Consulting Rooms, St Vincent's 411 Main St, Kangaroo Point QLD 4169

Phone: 07 3240 1387

Fax: 07 3240 1287



### DR JOHN PISKO,

Melbourne University.

FRACS – General Surgery and Urology

*Over 20 years of providing Urology services to the Gold Coast, public and private.*

#### Clinical interests:

- General urology
- Erectile dysfunction
- Urological cancer
- Urological stone management
- Surgery for prostate obstruction inc. greenlight PUP laser Prostatectomy.

Suite 2, Level 5, 123 Nerang Street Southport QLD 4215

Email: [johnpisko@gmail.com](mailto:johnpisko@gmail.com)

Enquiries to Emily on (07) 5532 7655.

**DR JOSEPHINE CHEUNG**, Obstetrician & Gynaecologist, has relocated her northside practice to North West Private Hospital, 137 Flockton St, Ramsey Place, Suite H, Everton Park. She is still practising at her main surgery at the Mater Private Clinic, 550 Stanley St, Level 3 Suite 8 and 9, South Brisbane.



### DR PHILIP HALL,

Gynaecologist, Fertility Specialist, City Fertility Ctr

MBBS MRMed FRANZCOG FRCOG FACRRM

Dr Philip Hall has recently joined City Fertility Centre Brisbane. He is highly experienced and qualified in fertility management and ART with over 30 years experience. He has a Masters of Reproductive Medicine from UNSW.

In addition to his interest in reproductive medicine, Dr Hall treats polycystic ovaries, endometriosis and premature menopause. He is a skilled laparoscopic and hysteroscopic surgeon and highly supportive of complementary medicine in the holistic management of fertility problems. His other major interest is pelvic floor reconstruction and incontinence.

S 6.1, St Andrew's Hospital, Wickham Tce, Spring Hill / 31 Markwell St, Kingaroy QLD

Phone: (07) 3831 6202

[www.cityfertility.com.au](http://www.cityfertility.com.au)

**DR SUSAN ROBERTS**, Perinatal Psychiatrist, has moved to:

The Wellness Medical Precinct  
21 Carrara Street  
Benowa QLD 4207

Phone: (07) 5539 2362

Fax: (07) 5597 7195

## GP POSITION AVAILABLE AT GREENSLOPES MEDICAL CLINIC AND SKIN CANCER CLINIC

Opportunity for F/T or P/T GP to join our modern medical practice. The practice is fully equipped, computerised, very visible and offers mixed billings.

Family friendly working hours and excellent working conditions.

Please contact director on 0404 884 914.

## GP's VR FT/PT REQUIRED

- Join our team of 5 doctors
- Long established practice, located on busy road near shopping and close to the beach
- Large modern premises, fully equipped treatment room
- Accredited and fully computerised
- Full time nursing and reception support.
- Good working hours 8.00am to 5.00pm Monday to Friday
- Saturday mornings only on rotation
- No after hours
- We are a mixed billing practice with QML Pathology, chemist and allied health on site.

Phone: (07) 5491 9044

Email: [currimundi@cmcnet.com.au](mailto:currimundi@cmcnet.com.au)

*The Doctor's Noticeboard is a free service for practitioners to advise changes to their practice.*

*If you would like to place a notice, please email details to [info@qml.com.au](mailto:info@qml.com.au).*

# Infectious Diseases Report

GEOGRAPHIC DISTRIBUTION - DECEMBER 2012

ORGANISM	Regions (as per key below)															TOTAL			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	DEC	NOV	OCT	SEP
Adenovirus (not typed)		6	3	1			4		6		8	4	3	3		38	69	78	104
Adenovirus (typing pending)	1	4	1							2		3		1		12	20	15	23
Barmah Forest virus		1					4		1	1		3	2	5	3	20	35	13	17
Bordetella pertussis	3	27	16	5	1		17		27	6	52	18	14	25	5	216	261	221	236
Brucella species	1		1	1						2		1		1		7	7	9	10
Campylobacter jejuni																0	1	3	1
Chlamydia pneumoniae																0	0	0	0
Chlamydia trachomatis, not typed	59	87	37	28	2		74		36	28	134	36	10	42	15	588	773	731	754
Coxiella burnetii	1	1	2						1				1			6	4	4	6
Cryptococcus species												1				1	2	1	3
Cytomegalovirus (CMV)	1	8	6	2			4		4	1	8	4		3		41	73	65	82
Entamoeba histolytica		1														1	0	0	1
Enterovirus - not typed																0	1	0	1
Epstein-Barr virus (EBV)	5	21	16	3			22		11	2	32	18	9	9	11	159	156	108	137
Flavivirus unspecified	3	1					1		1	1	3	2		2	1	15	13	12	14
Hepatitis A virus	1			1							1					3	4	1	6
Hepatitis B virus	4	7	5				14	1	4		45		1	2		83	96	81	100
Hepatitis C virus	12	38	21	4			30		27	8	39	20	10	7	10	226	323	309	288
Hepatitis D virus																0	0	1	0
Hepatitis E virus																0	0	0	0
Herpes simplex Type 1	14	51	13	9	3		40		31	3	78	23	8	10	9	292	364	292	354
Herpes simplex Type 2	6	26	10	4			20		17	3	32	14	6	8	3	149	172	159	183
Herpes simplex virus - not typed																0	0	0	0
HIV-1		3	2				3		1		5					14	9	3	13
HTLV-1																0	1	0	0
Human Metapneumovirus		13	7	1		1	8		14	3	10	6	3	8	1	75	111	154	185
Influenza A virus	1	1	1					2	2	2	6	5	3			23	73	360	2219
Influenza B virus	1		2			1	1		1		1	2				9	94	438	685
Legionella pneumophila (all serogroups)																0	0	0	1
Legionella species		1														1	5	3	3
Leptospira species		1		1												2	0	3	4
Measles virus																0	0	1	0
Mumps virus							1								1	2	0	0	1
Mycoplasma pneumoniae	27	73	35	14	3		70		52	18	139	56	31	11	12	541	743	961	1337
Neisseria gonorrhoeae	7	7	3				14		1	1	11	4	1	4		53	53	35	38
Parainfluenza virus	4	6	9				8		12	4	18	10	9	9	2	91	129	105	100
Parvovirus		4	2				7		3	2	12	7	2			39	87	32	25
Pneumocystis carinii		1														1	1	1	0
Respiratory Syncytial virus	1	11	6	1		1	2		3	1	9	2		3		40	74	126	190
Rhinovirus (all types)	1	20	7	2		2	23		12	8	41	11	6	9		142	233	171	270
Rickettsia - Spotted Fever Group	1		1										1		1	4	4	4	3
Ross River virus	1	2	1	1			2		2	4	4	3	2	2	1	25	43	32	20
Rubella virus		1							1							2	0	0	1
Salmonella paratyphi A																0	0	0	
Salmonella paratyphi B																0	0	0	
Salmonella typhi																0	0	0	
Streptococcus Group A	3	4	5		1		7		5	6	17	6	4	3	1	62	98	84	90
Toxoplasma gondii																0	4	0	1
Treponema pallidum	13	8	9		3		35	1	3	2	37	6	11	13	2	143	159	143	164
Trichomonas vaginalis	12	1			2		1							2		18	21	35	28
Varicella Zoster virus	5	30	14	4	1		37		23	4	55	21	4	5	2	205	235	218	235
<b>TOTAL</b>	<b>188</b>	<b>466</b>	<b>235</b>	<b>82</b>	<b>16</b>	<b>5</b>	<b>449</b>	<b>4</b>	<b>301</b>	<b>112</b>	<b>797</b>	<b>286</b>	<b>141</b>	<b>187</b>	<b>80</b>	<b>3349</b>	<b>4551</b>	<b>4919</b>	<b>7933</b>

## REGIONS:

1 Cairns

2 Gold Coast/Northern Rivers

3 Ipswich

4 Mackay

5 Mount Isa

6 New England

7 North Brisbane Suburbs

8 Northern Territory

9 Redcliffe

10 Rockhampton

11 South Brisbane Suburbs

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](mailto:INFO@QML.COM.AU).

