

# Expert Forum

## VTE in NZ Hospitals

Making Education Easy

May 2009

This publication is a summary of the recent VTE Experts Forum chaired by Dr Vinod Singh. The forum's objectives included:

- Sharing experiences in managing programmes for the prevention of in-hospital VTE
- Discuss a national policy for effect VTE prophylaxis in NZ hospitals
- Education regarding thrombosis in cancer

The creation of this publication and support for the event has been supplied by sanofi-aventis.

### Contributions from key attendees

**Dr Mary Seddon**, Clinical Director at Quality Improvement Unit/Te Pai Huanga, Counties Manukau DHB, and an attendee at the forum, spoke on the role of her organisation. Following consultation, the organisation has identified areas of patient safety, and currently has a number of projects on the go at different DHBs, including the 'safe major medication management' (focussing on aspects such as e-prescribing and medication reconciliation), and an incident reporting project, in which PE was identified as the cause of death in a number of patients. She also mentioned a MOH perioperative review committee, which will no doubt include aspects relating to VTE in hospitals.

VTE is one of the issues that the organisation has identified as needing attention. Last year, the organisation also attempted to launch a project similar to the 'save 1000 lives' campaign run in Wales and Scotland; this was based on the successful US 'Save 100,000 lives' campaign. However, the project has not gone ahead in NZ due to the change in government, but an attempt to resurrect it is being made this year. The organisation has gained some crucial regional support lately, and it is hoped it will become an umbrella organisation for all these different initiatives. For example, it is envisaged if several hospitals in a region wanted to work on a VTE prophylaxis initiative, access to practical support resources (e.g. data analysis, publishing, etc) would be available. Future projects in planning include a 'safer surgery saves lives' project, involving both private and public hospitals, which has a checklist that includes VTE, and Dr Seddon advised attendees to keep abreast of this project's progress. The checklist has been piloted at Auckland Hospital and is expected to go nationwide soon.

Dr Seddon also pointed out that the organisation faces a number of barriers. One problem she sees is 'pushback' from DHBs, as they have a lot on their plate; however, she maintains that patient safety is their core function, and a lot of time and resources are being spent wastefully within DHBs. Another barrier is communicating medical issues like VTE to politicians and other involved individuals who do not have an extensive medical background.

**Jeff Harrison**, a senior lecturer at the University of Auckland's School of Pharmacy, reported on the findings of a 2006–2007 research project involving all patients with a discharge diagnoses of DVT or PE within the Waitemata DHB. An analysis of the patients' notes revealed that, using ACCP and Australian and NZ guidelines, the findings surrounding the use of VTE prophylaxis were 'quite depressing', but not surprising. He also reported the findings of a survey conducted a couple of years ago to see which DHBs had VTE prophylaxis guidelines and risk assessment tools, and how well the guidelines matched up with international best practice. Although around 20% of DHBs had some guidance in place, rarely did it cover all services. Furthermore, very few DHBs had risk assessment tools, and none were routinely assessing all patients.

## Welcome to this review of the recent NZ venous thromboembolism (VTE) Experts' Forum in Auckland.

One of the main purposes of the forum was to follow-up on the 2008 meeting, in which attendees were encouraged to take steps towards implementing a strategy for VTE prevention at their institutions, and report back on progress at this year's forum. This review is a summary of the background information presented by Dr Singh (chair of the Steering Committee since the 2008 meeting) and the progress that has been made thus far, including summaries of formal presentations and spontaneous reports from attendees on what has been achieved in their regions/institutions. This was followed by a summary of the subsequent workshop session that was scheduled to discuss the implementation of national guidelines.

The forum also heard a presentation on the relationship between thrombosis and cancer, which has been summarised on page 4.

### VTE in hospitals - Presented by Dr Vinod Singh

There is more than enough evidence identifying VTE as a problem in hospitals, with global data from >68,000 patients indicating that around 52% of hospitalised patients are at risk,<sup>1</sup> so the focus now needs to be on implementing strategies to reduce the risk. Guidelines for VTE prophylaxis have been published by the American College of Chest Physicians (ACCP), but they are not extensively used globally, with only 37% and 48% of at-risk medical patients receiving ACCP-recommended prophylaxis in the UK and US, respectively. The extent to which they are used in NZ is unknown, but it is thought to be quite low.

There have been a number of studies providing strong evidence that VTE prophylaxis works that have been accepted by most countries.<sup>2–6</sup> It has also been shown to be safe, with low incidences of clinically important bleeding.<sup>7–8</sup>

### Global Measures

The UK has been the pioneers in VTE prevention, after concerned individuals lobbied the House of Commons Health Committee with data showing that >25,000 people were dying each year from VTE acquired during hospitalisation. They noted that many physicians were unaware there was a problem, as many events occurred following discharge. The House of Commons Health Committee responded with several recommendations, including:

- All patients should be counselled on admission about the risks of VTE, and undergo a risk assessment for prophylaxis
- Increased awareness of postdischarge risk of VTE
- The DH, NICE and Royal Colleges should raise awareness of the extent of VTE and should audit use of the guidelines
- Establish thrombosis committees and teams in hospitals.

The government agreed that more needed to be done and passed legislation, and the CMO wrote to every medical officer informing them of their responsibilities for assessing all hospitalised patients for VTE, and that they would be liable for malpractice if they failed to do so.

In the US, the 'Coalition to Prevent Deep Vein Thrombosis' was formed. It was made up of 50 bodies, including every large organisation from the American College of Haematologists to pharmacists and osteopaths. Similar recommendations were made and the Surgeon General wrote to each physician advising of their responsibility of formally assessing every admitted patient for VTE prevention.

### Specific recommendations for VTE prophylaxis in the UK

- Original doctor to be notified when VTE develops after hospital discharge
- More prominence in undergraduate and postgraduate medical education
- NICE to extend scope to include medical patients and patients undergoing low-risk procedures who are at high risk of VTE
- Currently accepted consensus guidelines to be circulated and implemented
- Procedures for counselling all patients to be supported by hospital specialist thrombosis teams
- All medical and surgical patients admitted to hospital to undergo risk assessment for VTE
- Implementation of systems and structures to improve the NHS's capacity
- A thrombosis committee to be established in each hospital, with a specialist thrombosis team

### Progress by the NZ Steering Committee

While the contribution of sanofi-aventis in supporting the forum was noted with thanks, Dr Singh pointed out that the Ministry of Health (MOH) should be taking a more active role in supporting initiatives aimed at addressing the high rates of in-hospital VTE, including supporting forums such as this one. He commented that due to busy schedules, the committee has not been able to achieve as much as it would have liked. Discussions have been held with the Director General of Health, the Principal Medical Officer of Health and the Health and Disabilities Commissioner, all of whom have expressed their support for the committee's work. The committee has also put together a draft reference document, which was distributed to the forum's attendees. However, an organisation of individuals prepared to go out and ask for help is still needed, and ultimately volunteers are needed to form an MOH-funded group dedicated to ensuring VTE prevention is available in every NZ hospital.

*Dr Vinod Singh, FRACP, is an honorary clinical senior lecturer in medicine, and a consultant physician in internal medicine and stroke with the Waitemata DHB.*

## Expert Forum VTE in NZ Hospitals

### VTE prevention projects in NZ DHBs

The forum included three formal presentations where representatives from DHBs reported back on progress that has been made in their regions towards addressing VTE prevention in hospitals. In addition, Dr Singh asked attendees to report on any other progress that has been made, and also any lack of progress in order to help identify barriers to implementing VTE prevention.

#### Waitemata and Counties/Manukau DHBs Presented by Tracey Woulfe and Elizabeth Brookbanks

The first formal presentation reported on a collaborative team of four (two nurse and two doctors) who conducted a thromboprophylaxis audit within the Waitemata and Counties/Manukau DHBs between October 2006 and April 2007, with financial support from sanofi-aventis; all aspects of the conduct of the audit were hospital based with no industry bias.

##### Audit of medical patients

The eligibility criteria for the audit of medical patients were based on three international studies. Immobility for >3 days was a key criterion to target thromboprophylaxis in the most at-risk patients. Other criteria were age >40 years and acute on chronic CHF, COPD exacerbation or acute respiratory failure, or a standard risk factor along with an acute infective episode, an acute rheumatic disorder or an acute inflammatory condition. The audit involved 263 medical patients, of whom 127 met the eligibility criteria, and 74 (28% of total) had no contraindication for thromboprophylaxis. Of those, 17 (23%) were receiving enoxaparin sodium [Clexane®] and the remainder (77%) were not receiving any VTE preventative measures.

##### Audit of surgical patients

The audit of surgical patients involved 124 general surgical and gynaecological patients, but not orthopaedic patients as there is already a thromboprophylaxis protocol in place at North Shore Hospital for these patients. Risk was defined using ACCP guidelines, type of surgery (major vs. minor), patient age and risk factors. Most (98%) were eligible for thromboprophylaxis, and 96% were receiving some form of thromboprophylaxis. Among patients from the Waitemata DHB (n=60), 20% did not receive any chemoprophylaxis, and nearly 60% were high-risk patients. Although many surgical patients were receiving chemoprophylaxis, around 45% were only receiving enoxaparin sodium at a dose of 20mg when they should have been receiving more based on their bodyweight and renal function.

##### 'Stop the clot'

The audit was followed by implementation of the 'Stop the clot' programme. Prior to implementation, buy-in was obtained from physicians and other key hospital staff, including discussions with registrars about how an assessment tool could be implemented. One week was dedicated to a high visibility, high impact roll-out that included a number of methods including presentations, displays, posters and other promotional materials and events, and teaching sessions for appropriate staff. Assessment tools included: 1) a VTE risk assessment tool (with surgical and medical components) based on criteria used in the audit; 2) a risk assessment card, adapted from one from Tauranga hospital, for quick reference (mainly targeted at junior doctors); and 3) a VTE risk sticker for pharmacists to stick on charts of high-risk patients as a reminder that a thromboprophylaxis assessment should be undertaken. It was felt that pharmacists are key to the implementation of VTE prevention strategies, as they do thorough assessments of the patients.

##### Ongoing impact

Pharmacists have continued to promote VTE prophylaxis on postacute ward rounds, which has been more successful than the stickers or writing on the patients' notes, as their presence seems to have a greater impact and also allows for any issues to be discussed there and then. There has also been an increase in the number of people ringing for prophylaxis advice.

In the medical department, the use of 20mg and 40mg enoxaparin sodium syringes has increased by 90% and 73%, respectively. While the overall use of enoxaparin sodium has not increased much in the surgical wards, there has been a 50% increase in the use of the 40mg syringes.

##### The challenges

One problem that was encountered was the 3-monthly rotation of house officers, necessitating constant re-education, which is an area where a national protocol would be advantageous. Another problem is the issue of having another form to fill out, and feedback has indicated a preference for it to be part of the admission-to-discharge planner. Finally, there were time constraints to reinforce the message in the acute thrombosis service setting.

##### Where to from here?

Plans for the future include: 1) a dedicated VTE prevention nurse; 2) incorporation of the VTE assessment tool into the admission-to-discharge planner; 3) incorporation of VTE management and prevention into the electronic RMO handbook; 4) a VTE section in clinical practice manual on wards and the intranet; and 5) a ward-based resource nurse.

Tracey Woulfe, CNS, is a Thrombosis Nurse Specialist at Waitakere Hospital  
Elizabeth Brookbanks is Team Leader for Medical Pharmacists at North Shore Hospital

#### Bay of Plenty DHB Presented by Dr Neil Graham

Dr Graham presented the second formal presentation with an introduction reiterating the epidemiology of VTE in hospitals and what other countries are doing or attempting to do (including the point that many attempts to get something off the ground in Australia have been unsuccessful). He also quoted data indicating that 40–90% of organisation change initiatives fail, and that overall improvement can be expected to be only 8–10%. Successful strategies need to be active, have a multifaceted approach and include an iterative audit and means of feedback. He also quoted data that in Australia, the cost of VTE has been estimated to be \$1.72 billion (0.15% of GDP), which places it fifth behind CHD, stroke, lung cancer and COPD.<sup>9</sup>

#### VTE prophylaxis at BOP DHB

Advances in VTE prevention within the Bay of Plenty (BOP) DHB were initiated after the CMO (John Kyngdon) received a letter from the Health and Disabilities Commissioner that: 1) outlined a case where a woman who had presented with a leg fracture had been sent home with an undiagnosed DVT despite being symptomatic; and 2) advised the DHB to put together a diagnostic formulation for the management of DVT and PE, introduce a prophylaxis programme with an audit before and after, and provide an education programme for staff and patients.

##### Implementation

The overall strategy was to: 1) develop a risk assessment form; 2) pilot VTE prophylaxis in general medicine, general surgery and orthopaedics (the high-risk areas); 3) develop protocols, guidelines and policies, copies of which were made available in each ward; 4) provide folders with important VTE articles; 5) provide staff education (in wards, departments and groups); 6) develop a patient education pamphlet; 7) provide ongoing motivation, revisiting, updating presentations and modifications; and 8) extension beyond the pilot (which is to include Whakatane).

The risk assessment form was divided into sections for surgical, medical and orthopaedics. However, it was not commonly used during the pilot even though thromboprophylaxis was often prescribed. A small VTE risk assessment card detailing risks, chemoprophylaxis doses, etc, which could be attached to a belt for example, was quite popular with the house officers. There was also evidence of increased patient awareness due to the patient education pamphlets being distributed at admission (where appropriate).

##### Audits

Audits were conducted both prior to and after implementation in 25–26 patients for each department (general medicine, general surgery and orthopaedics). The use of VTE prophylaxis had increased notably in the postimplementation audit (see Figure), and the proportion of patients not considered fell from >60% to 16%.

##### Ongoing issues

Issues that arose or need to be considered include: 1) forms not being completed (it is to be reviewed); 2) limited documentation; 3) therapeutic use modified prophylaxis prescriptions; 4) some prescriptions without risk stated in notes; 5) limited use of stockings in medical patients; 6) timing of enoxaparin sodium administration (8am each day to fit with nurses' rounds); 7) timing of assessments when complete risk data available; 8) ongoing assessments of outcomes, compliance, etc

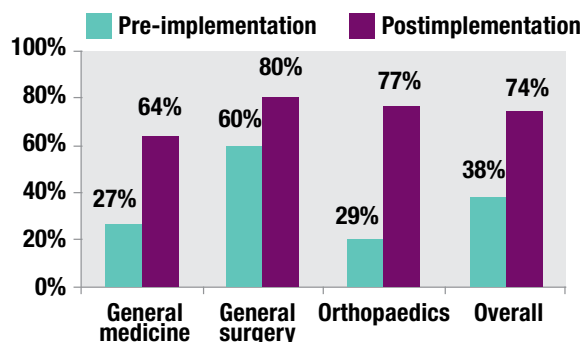


Figure. Proportion of patients receiving VTE prophylaxis at Tauranga Hospital before and after implementation of a pilot VTE prophylaxis strategy

Dr Neil Graham is a physician at Tauranga Hospital

## VTE prevention projects in NZ DHB cont.

### Mid Central Health VTE prophylaxis audit

Presented by **Daryl Pollock**

Daryl Pollock presented findings of a retrospective audit at Mid Central Health designed to ascertain the medical patients who receive adequate VTE prevention in Palmerston North Hospital. To keep it brief they audited every second medical patient over a 2-week period, resulting in the inclusion of 89 patients in whom notes were available. Twelve of the patients were already receiving therapeutic enoxaparin sodium so were not included in the analysis; incidentally, only 6 of those patients had their bodyweight documented. There were three authors who chose the criteria and standards and formulated an audit tool (based on one already in use at Wellington Hospital). Data were collected from Dec 2008 to Jan 2009. Factors taken into account included: 1) individual VTE risk; 2) clinical condition; 3) bleeding risk; and 4) appropriateness of VTE prophylaxis for each patient. Each patient was judged to require VTE prophylaxis if they had one additional risk factor from the study tool (besides being hospitalised).

Among the 77 patients included in the analysis, 6 did not require prophylaxis. Of the remaining 71 patients who should have received some form of VTE prophylaxis, 14 were not suitable for chemoprophylaxis (and did not receive it), and of those 14, mechanical prophylaxis was documented for 4 of them; this also raises the issue of whether the use of mechanical prophylaxis is being documented in all cases. Therefore, there were 57 patients requiring chemoprophylaxis, but only 10 received it. Among the remaining 47 who did not receive prophylaxis, there were 12 patients with questionable suitability.

*Daryl Pollock, CNS, is a haemophilia/thrombosis clinical nurse at Palmerston North Hospital*

### Projects at other hospitals

#### Whangarei Hospital

- Has conducted an audit of 200 general surgical patients.
- Findings were similar to other audits.
- Currently working on guidelines and trying to set up policy.

#### Auckland Hospital

- About to commence data collection in surgical wards.

#### Middlemore Hospital

- Audit completed.
- Findings were similar to other audits.
- Medical and surgical prophylaxis tools have been developed and run as pilots.
- Currently investigating having tools added to the admission-to-discharge planner, and updating anticoagulation policy to make it more accessible/user friendly.
- Next step is to develop a good implementation strategy.

#### Rotorua Hospital

- Audit currently being done, but registrar conducting it is due to leave.

## VTE prevention national guidelines workshop

Dr Singh pointed out that national guidelines can be difficult to develop, and there are medicolegal implications. Ms Wouffe and Dr Graham provided detailed presentations of their respective risk assessment/guideline forms. Both were quite similar, and both have been signed off by their respective DHBs. One attendee also revealed that the Waikato DHB also has endorsed VTE prevention guidelines.

### Problems with the endorsed guidelines

As mentioned in the audits, it was uncommon for the risk assessment/guidelines forms to be filled out. There was much discussion on this. The Waitemata DHB forms were to undergo further development, and a popular solution was to include it in the admission-to-discharge planner. However, there was also a general consensus that they would be far too long to get them accepted. The solution that most attendees seemed happy with was to just have one question on the admission-to-discharge planner asking 'Has the patient's VTE risk been assessed?', and refer to the assessment/guideline forms. Dr Graham also advised not spending too much time worrying about finer points of the assessment/guideline forms that can be dealt with in subsequent audits, as this can result in significant delays getting them out.

With respect to getting the forms filled out, it was suggested that this was not necessarily so important, and the forms could be treated as an educational tool to get clinicians thinking about it, so assessment of VTE prevention is at least being done. However, on the other side of the coin, another attendee noted that as soon as you have a form that is supposed to be filled out and it isn't, then the clinician can be held accountable if things go wrong.

### VTE prophylaxis references

1. Cohen AT et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. *Lancet* 2008; 371(9610):387-94
2. Leclher E et al. The venous thrombotic risk in non-surgical patients: epidemiological data and efficacy/safety profile of a low-molecular-weight heparin (enoxaparin). The Prime Study Group. *Haemostasis* 1996; 26 Suppl 2:49-56
3. Kleber FX et al. Randomized comparison of enoxaparin with unfractionated heparin for the prevention of venous thromboembolism in medical patients with heart failure or severe respiratory disease. *Am Heart J* 2003; 145(4): 614-21
4. Hillbom M et al. Enoxaparin vs heparin for prevention of deep-vein thrombosis in acute ischaemic stroke: a randomized, double-blind study. *Acta Neurol Scand* 2002; 106(2):84-92
5. Sherman DG et al. The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous

## Issues with running VTE prevention projects

- It was pointed out that making VTE prevention part of the culture can facilitate the engagement of SMOs to look for and fill out risk assessment forms. Using checklists, attending their meetings and grand rounds can also help to drive the message home, and it is also important to remember that their behaviour often influences the behaviour of the juniors.
- Orthopaedics may have different ideas (particularly the use of aspirin), so it is important to work with them. One attendee had been told that the orthopaedic association was working on its own VTE prevention guidelines. Dr Singh expressed an interest in working with all other interested groups to develop guidelines.

## Difficulties initiating VTE prevention projects

It was established that there is a general willingness among attendees to get VTE prevention programmes in place; however, the two main barriers that cropped up in the discussions were: 1) lack of know how; and 2) lack of support from seniors.

It was suggested that lack of know how could be addressed by strengthening regional networks, particularly with any organisation that has conducted an audit. Ms Wouffe indicated that attendees were welcome to take copies of the data and forms from their project, and that others would also probably be happy to provide copies of theirs. It was clear that this offer was appreciated by a number of attendees. Another attendee pointed out that sharing resources now should make compiling national guidelines easier (when that happens) as all DHBs should be operating within the same framework.

In response to the lack of support from seniors, Dr Seddon emphasised that the initial audit should provide just enough data to show there is a problem, and Dr Singh reiterated this pointing out that the Waitemata DHBs audit was large, and most hospitals can consider a much smaller audit to confirm they have similar issues. Another concern seniors had raised was industry support of the forum. Ms Wouffe pointed out that the Waitemata DHB's large audit would not have been possible without the support of sanofi-aventis. She commented that it's important that industry sponsors have no input that could compromise the integrity of the findings, and it is equally important to emphasise this fact to seniors.

Dr Singh asked all attendees to write to DHBs, and that this would help improve seniors' participation. However, one attendee felt it would be better to campaign at the level of the MOH and DHBNZ, as they stand a good chance of getting DHB CEO sign-off based on it being a priority for the health of New Zealanders, and once that is obtained, resources usually follow. Dr Seddon also suggested including a patient vignette, with just a brief summary of data and evidence, when presenting to seniors, as this usually gets a better response than a large amount of data. Mr Harrison also pointed out the importance of getting clinicians on board, and suggested a 'veiwpoint' published in the NZ Medical Journal might help achieve this.

## Consensus

Dr Singh felt that in an ideal world there should be one national guideline across DHBs so transient staff have consistency. However, it was acknowledged that this could take a while to achieve, and could be a project for the Steering Committee in collaboration with other specialties/departments, which would help to make it more widely accepted. Most attendees agreed that a national form could take a long time to develop, and under the circumstances, it was concluded that until that happened, there are three guidelines endorsed by DHBs, all of which are freely available, that can be used as is, or tweaked if necessary, to comply with each DHB's requirements.

## The Future

Dr Singh noted that while NZ is miles behind other developed countries with VTE prevention in hospitalised patients, some progress is being made. The next task is to engage the Ministry of Health and DHBs in supporting this venture. It is also hoped to have active participation from Professional Colleges e.g. RACP, RACS, the College of GPs and other Colleges. It is also hoped that there will be at least quarterly meetings of the Steering Committee and an annual meeting of the National Committee.

### Take home messages:

- VTE prevention in NZ hospitals is inadequate
- Effective guidelines are needed
- National guidelines would be preferred, but are likely to take a while to develop
- There are three DHB-endorsed guidelines that other DHBs can adopt or adapt

## Cancer and thrombosis: searching for occult cancer in patients with VTE

Presented by Dr Sharon Jackson

The main purpose of this presentation was to think about which patients presenting with thrombosis should be screened for malignancy. The association between VTE and malignancy has been known about for many years. For patients presenting with a thrombosis, some will also have to deal with a diagnosis of a malignancy soon after, often while still coming to terms with the management of their thrombotic disease. Patients presenting with thrombosis require a bit of thought to determine if further investigations for a malignancy are warranted.

### Incidence of cancer following diagnosis of VTE

Among patients who present with idiopathic VTE, 15–20% will already have been diagnosed with a cancer at presentation. Among those with no known risk factors for VTE, around 2–5% will be diagnosed with cancer around the time of presentation (usually within 1 month). Of the rest with unexplained VTE, 1.5–10% will be diagnosed with cancer during follow-up. Cohort studies have reported incidences of cancer in patients with idiopathic VTE ranging from 2.7 to 25.7%, and in all studies the incidences were greater than the incidences reported for cancer in patients with secondary VTE (0–7.1%).<sup>1–3</sup> One such study showed that the time course of new cancer diagnoses was quite steady, so if patients are to be screened at a set time point, then some patients who will develop a cancer will be missed.<sup>6</sup> The only significant risk factors for cancer identified in a multivariate analysis were unprovoked VTE (hazard ratio 1.86; 95% CI 1.21, 2.87) and advanced age (1.23; 1.05, 1.44; 10-year increments). One population-based study found that 9.3% of patients with VTE or PE (n>26,200) were subsequently diagnosed with cancer, and that many of those cases were diagnosed within the first year following VTE/PE.<sup>7</sup>

An analysis of cancer registry data (n=528,693) found that there were 30% more clots during the year prior to the cancer diagnosis than would be expected.<sup>8</sup> A proportionately large number of these clots occurred within the 2 months prior to the cancer diagnosis. Another important finding was that among patients with unprovoked clots, the incidence of metastatic cancers was relatively high, meaning that there would probably be little impact on prognosis if they had been diagnosed at the time of their thrombosis. A recent meta-analysis revealed that the pooled relative risks for developing occult cancer are 3.2 (95% CI 2.4, 4.5) for patients with any VTE versus no VTE, 2.7 (1.9, 3.9) for patients with idiopathic VTE versus no VTE, and 3.8 (2.6, 5.4) for patients with idiopathic VTE versus secondary VTE.<sup>9</sup> Another recent meta-analysis showed that the baseline likelihoods of a malignancy being diagnosed within 1 month of a clot occurring are 4.1% and 6.1% for any and unprovoked VTE, respectively, and these increased to 6.3% and 10.0% by 12 months.<sup>10</sup>

Data from the RIETE registry indicated that 1.2% of 17,475 consecutive patients with acute VTE were diagnosed with occult cancer within 3 months after VTE presentation, and half of those patients had metastatic cancer.<sup>11</sup> Risk factors identified in this analysis for hidden cancer included older age, anaemia, bilateral DVT and idiopathic VTE.

Cancers that appear to be most likely associated with VTE include ovarian, prostatic, colorectal, gastric, pancreatic, hepatic, haematological, brain, renal and lung malignancies.<sup>8,9,11</sup>

### Natural history of patients with cancer & VTE

Consequences of a cancer diagnosis in patients with VTE include increased incidences of recurrent VTE, major bleeding and mortality.<sup>11</sup> Population-based data from Denmark showed that the 1-year survival rate for patients with cancer at the time of VTE was 12%, compared with 36% for patients with cancer without VTE, and it remained lower thereafter for ≥15 years.<sup>12</sup>

### Risks and benefits of cancer screening

Any screening strategy for cancer in VTE patients would need to be safe, have a high sensitivity and specificity, and improve the outcome for either the malignancy or thrombosis; having effective treatment available is one of the most important criteria for any screening programme. The possible benefits of screening include improved prognosis by reducing morbidity associated with cancer treatment and cancer-related mortality, and reduced costs associated with treatment of the cancer. However, in some cases there may be no benefit, and screening may just advance the date of diagnosis, which could result in an earlier reduction in quality of life for the patient. Other possible drawbacks of screening

include, procedure-related morbidity, psychological burden of having possible cancer and undergoing unnecessary procedures, false security of being classified as cancer free, and the costs associated with the screening procedures, which are not insubstantial.

### Extensive screening vs routine evaluation

One RCT (SOMIT) has compared extensive screening (abdominal and pelvic ultrasound and CT, endoscopy and haemocult, mammography, pelvic exam and cervical smear, sputum cytology and chest x-ray, and tumour markers) with routine evaluation in patients presenting with idiopathic VTE.<sup>13</sup> Extensive screening (n=99) picked up 13 cancers, compared with none in the routine evaluation group (n=102), and cancers were diagnosed during the subsequent 2 years in 1 and 10 of the extensive screening and routine evaluation groups, respectively. Cancer mortality was lower in the extensive screening group (2.0% vs. 3.9%), but the difference was not significant due mainly to the low number of participants. Ten of the cancers were detected by abdominal/pelvic CT, 5 by ultrasound and 1 each by sputum cytology, colonoscopy and mammography. The cancers found by extensive screening were identified an average of 10.6 months earlier than they otherwise would have been identified.

Another study took the approach of investigating possible malignancies in patients presenting with VTE based on a thorough history, physical examination (including pelvic, rectal and breast), and routine laboratory results, followed by targeted investigations based on the results (e.g. colonoscopy if bowel habits had changed) or a limited workup for malignancy (CEA, PSA, CA-125, abdominal/pelvic ultrasound).<sup>14</sup> Occult cancer was suspected in 167 (19%) participants with idiopathic VTE, of whom 34 (3.9%) were diagnosed with cancer. In the participants who underwent the limited workup (i.e. without suspected cancer), 13 were diagnosed with cancer. These data suggest that a fairly routine evaluation will identify around half of the patients with VTE who also have a malignancy. If a limited diagnostic workup with ultrasound and tumour markers is also performed, then half the remaining cases will be identified, and the remainder will become apparent within the following year. The study also showed that the chances of having a cancer in patients aged <70 years with idiopathic VTE was about the same (around 3–3.5%) as they were for patients aged >70 years with secondary VTE, while patients aged >70 years with idiopathic VTE had a 9.3% chance of also having cancer.

### Cost of screening

Costs of the screening methods vary considerably, with CT being more expensive than ultrasound (typical cost \$NZ485 vs. \$160 for pelvis and abdomen), and colonoscopy is the most expensive (\$850–\$1200). In contrast, tumour markers are relatively cheap (\$37 for CEA, CA125 and AFP, and \$13.50 for PSA). There are little data on the cost effectiveness of screening for malignancy in patients with idiopathic VTE, but the various approaches used in the SOMIT study have been analysed.<sup>15</sup> It was determined that around 10 patients need to be screened with CT in order to detect a malignancy, and adding other investigations made little difference. More patients need to be screened with ultrasonography to detect a malignancy. Combining ultrasound with other investigations makes little difference, but does increase the number of patients requiring additional investigations due to the low specificity of the other tests. CT was associated with the lowest cost per diagnosis at €1974, and €1000 per life-year gained. As expected the inclusion of colonoscopy increases the cost per diagnosis and per life-year gained substantially. Despite the low cost of tumour marker investigations and a relatively low cost per diagnosis (€2109), the cost per life-year gained was €2617. Translating to NZ dollars, the cost of CT plus mammography is \$2192 per life-year gained, which may not be much less favourable than screening costs for breast cancer (\$7075) and cardiovascular disease (\$4083) in NZ.

### Take home messages:

- Cancer is relatively common in patients with idiopathic VTE, and a thorough history and physical examination are warranted for all of them.
- Any abnormalities identified should be further investigated.
- Incidence of cancers >3 months after idiopathic DVT is low; routine screening is probably not warranted unless index of suspicion is high.
- CT is probably the most effective modality if screening is warranted.
- Cost effectiveness is not clear.

Dr Sharon Jackson is a haematologist at Middlemore Hospital, Auckland

### Cancer and thrombosis references

1. Aderka D et al. Idiopathic deep vein thrombosis in an apparently healthy patient as a premonitory sign of occult cancer. *Cancer* 1986; 57(9): 1846–9
2. Prandoni P et al. Deep-vein thrombosis and the incidence of subsequent symptomatic cancer. *NEJM* 1992; 327(16): 1128–33
3. Ahmed Z, Mohyuddin Z. Deep vein thrombosis as a predictor of cancer. *Angiology* 1996; 47(3): 261–5
4. Monreal M et al. Occult cancer in patients with venous thromboembolism: which patients, which cancers. *Thromb Haemost* 1997; 78(5): 1316–8
5. Hettiarachchi RJ et al. Undiagnosed malignancy in patients with deep vein thrombosis: incidence, risk indicators, and diagnosis. *Cancer* 1998; 83(1): 180–5
6. Douketis JD et al. The long-term risk of cancer in patients with a first episode of venous thromboembolism. *J Thromb Haemost* 2009; 7(4): 546–51
7. Sorensen HT et al. The risk of a diagnosis of cancer after primary deep venous thrombosis or pulmonary embolism. *NEJM* 1998; 338(17): 1169–73
8. White RH et al. Incidence of venous thromboembolism in the year before the diagnosis of cancer in 528,693 adults. *Arch Intern*

9. Med 2005; 165(15): 1782–7
10. Indice S et al. Venous thromboembolic events and organ-specific occult cancers: a review and meta-analysis. *J Thromb Haemost* 2008; 6(5): 781–8
11. Carrier M et al. Systematic review: the Trousseau syndrome revisited: should we screen extensively for cancer in patients with venous thromboembolism? *Ann Intern Med* 2008; 149(5): 323–33
12. Trujillo-Santos J. Clinical outcome in patients with venous thromboembolism and hidden cancer: findings from the RIETE Registry. *J Thromb Haemost* 2008; 6(2): 251–5
13. Sorensen HT. Prognosis of cancers associated with venous thromboembolism. *NEJM* 2000; 343(25): 1846–50
14. Piccioli et al. Extensive screening for occult malignant disease in idiopathic venous thromboembolism: a prospective randomized clinical trial. *J Thromb Haemost* 2004; 2(6): 884–9
15. Monreal M. Screening for occult cancer in patients with acute deep vein thrombosis or pulmonary embolism. *J Thromb Haemost* 2004; 2(6): 876–81
16. Di Nisio M et al. Decision analysis for cancer screening in idiopathic venous thromboembolism. *J Thromb Haemost* 2005; 3(11): 2391–6