

WARFARIN & ITS EFFECTS - by Pauline Goodwin RGN, FPSPract

In Ancient times people recognised the healing power and properties of indigenous plants. This knowledge accumulated over many generations, often kept alive by chant, story-telling and human experience. Today, the understanding and use of plants has evolved significantly beyond the use of herbs, to medicines that can be synthesised and reliably predicted to save lives. Warfarin is among these medicines. For thousands of people who suffer life threatening illnesses or blood clots, Warfarin is a life-line.

DISCOVERY

In the 1920s in Wisconsin, America, cattle were dying. The food (roughage) that the cows ate often scratched their throats and digestive system. Normally, these minor wounds healed - but no longer - the wounds continued to bleed, so the cows slowly bled to death. The farmers and local vet were baffled, so they asked a researcher, Karl Paul Link who worked for the Wisconsin Alumni Research Fund to help. He analysed everything in the cows' environment: the water they drank and the feed they ate, eventually discovering that the substance causing the cows to die was their winter feed (sweet clover hay) which had been spoiled by unusually wet weather conditions. The substance was called Coumarin. Coumarin is the substance that gives new mown hay its characteristic smell. Link decided to call the substance WARFARIN derived from Wisconsin Alumni Research Foundation = WARF = CoumARIN = ARIN = Warfarin.

In the 1940s, this discovery eventually led to the commercialisation of Warfarin under the name Dicoumarol. This product had many impurities but they were not considered to be a problem because Dicoumarol was only used to kill rats and mice. Then, in the 1950s, Link, working with another scientist, Harold Campbell, performed further research on the substance which led to the synthesis and approval of Warfarin to be used for human consumption, although it was not used until Dr Armand Quick and his colleagues developed *Prothrombin time*, PT. This is a blood test that measures the time it takes for the liquid portion of the blood (plasma) to clot. Prothrombin is a plasma protein that is the precursor to thrombin. A normal prothrombin time is measured in seconds: 11 to 13.5 is considered normal. This was how patients' blood was checked whilst taking Warfarin until the 1980s, when Tom Kirkwood from the UK devised a new measure, the *International Normalised Ratio*, now most commonly known as the INR. This provided a more consistent way of expressing prothrombin ratio, which was quickly accepted world-wide after being endorsed by the World Health Organisation, and has been used subsequently as a measure of activity for Warfarin when used therapeutically.

INR ranges can vary from person to person when on Warfarin therapy - an average range would be between 2 and 3. When the INR result is too low, blood will clot. If too high, blood will not clot. The INR reference range is different for healthy people compared to those undergoing anticoagulant therapy using Warfarin. Patients taking Warfarin need to have a blood test regularly to monitor their INR. The result determines how much Warfarin will be prescribed, and when the next test will be arranged. All patients on Warfarin are given a small yellow booklet where all their INR results are noted, and a small card. These should be kept with the patient at all times to warn medical staff of current dosage. In the case of a sudden emergency such as an accident or sudden illness, this information could be invaluable.

HOW DOES WARFARIN WORK?

Warfarin works by extending the time it takes for blood to clot by slowing down the production of Vitamin K in the liver.

VITAMIN K

K vitamins are a group of fat soluble vitamins known as Quinones that are essential for the synthesis of prothrombin in the liver, and of several related proteins involved in the clotting of blood and electron transport. The vitamin is widely found in foods, especially green vegetables, pork, liver, yogurt, egg yolk, kelp, and fish liver oils, (to name but a few), and is synthesised by the bacterial flora of the gastrointestinal tract.

Vitamin K deficiency is very rare – it can occur when the body cannot absorb the vitamin from the gastrointestinal tract, or after a long-term course of antibiotics. People with this deficiency will have bruising or bleeding because without vitamin K the blood will not clot.

DIET

When taking Warfarin, patients may need to limit their intake of Vitamin K. They are given a list of foods to limit in their diet (but not avoid). A balanced diet must be maintained. This delicate balance can be difficult to maintain because INR results can change due to alterations in the diet: for example, too many green vegetables at one meal can upset the delicate balance. When the Warfarin dose is too low, and the INR is below the reference range, blood is apt to clot within blood vessels. This can lead to vital organs such as the heart, lungs, or brain losing their blood supply. However when the dose is too high and the INR is above the reference range, this will reduce clotting and may result in bruising, or dangerous bleeding into the gastrointestinal tract, urine, and even the brain. This can be fatal.

NB.... Vitamin K and the mineral Potassium often are confused due to the chemical symbol of Potassium being 'K' Vitamin K and Potassium have very different functions in the body.

WHY USE WARFARIN?

For thousands of people who suffer life-threatening illnesses, Warfarin is a life-line. It is often used to prevent recurrent events, or conditions such as Deep Vein Thrombosis (DVT). Every year, 60,000 people in Britain develop a DVT. The most common cause is simply being immobile for long periods of time: for example, if legs are immobile for more than 90 minutes the blood flow in the vessels can drop by 50% making a clot more likely to occur. People most at risk are bed bound patients, in hospital after an operation, or those sitting still for long periods on an aeroplane.

Ischaemic strokes are known as Cerebral Vascular Accidents (CVAs). They are caused by the blockage of an artery within the brain. The affected area is starved of oxygen. Brain cells cease to function, and movement, vision and speech are lost. Bleeding within the brain, 'Haemorrhage' is another form of stroke. Strokes are the third most common cause of death in the UK, and the single largest cause of disability in the UK. Heart conditions such as Atrial Fibrillation (fast irregular heartbeat) can be caused by thickening of the arteries. Atherosclerosis which restricts blood flow may cause clots to form, which in turn can cause a heart attack (Myocardial Infarction), or death. Valve disorders (stenoses) occur when a valve outlet is too narrow, or when valves cannot close properly due to disease. This causes the heart to work harder and affects the bloodflow which can lead to clot formation. Some people who have valve replacements may take Warfarin depending on the type of valve used. All of these states may necessitate Warfarin therapy to maintain blood flow, and life.

PROBLEMS ASSOCIATED WITH WARFARIN THERAPY

The numerous interaction pathways and variability in patient responses makes a clinical consequence of alterations in metabolism difficult to predict, especially in the elderly population. Unfortunately, there are at least 60 different drugs that may increase or decrease the effects of Warfarin. Polypharmacy is on the rise, and many over 60s are prescribed twice as many medications as they were just 10 years ago. *Prescriptions dispensed in the community, 1997 to 2007* reveals 'Older people receive more prescriptions per head than any other group'. Instructions can be misread, or misunderstood. This can lead to an incorrect dose being taken, causing adverse effects which can lead to hospital admission. This is serious enough, but when taking Warfarin, the effects are life-threatening.

CODE OF PRACTICE

The Association of the British Pharmaceutical Industry, ABPI, is the trade association that represents manufacturers of all prescribed medicines. Formed in the 1930s, it now represents 80 companies which supply 80% of the medicines used by the National Health Service. Members must abide by their code of practice in the spirit, and to the letter. The association monitors medicines and ensures they are administered in an ethical, and professional manner.

The professional standards for hospitals and pharmacies are patient centred. Their aim is to optimise patient outcomes from medicines, and ensure we are given information and support:

- 1 Systems are in place to identify patients who may need support.
- 2 Allow patients to request support.
- 3 Ensure regular supply of medicines.
- 4 Monitor all side effects.
- 5 Optimise outcomes from medicines.

6 All patients are given written information about their medicines, and have their expressed needs for information met.

All patients must be given evidence-based estimates of the benefits and risks of treatment - then they can make personal choices about their treatment. As an example, and related to the above: patients may be told that Warfarin gives around a 60% relative reduction, but seven out of one hundred people will still have a stroke even though they take Warfarin.

POINTS TO NOTE

1 How long people remain on Warfarin varies, six to twelve weeks for DVTs, three to six months for pulmonary embolisms. However many people remain on Warfarin for life.

2 In an emergency patients can be given Vitamin K to reverse the action of Warfarin.

3 Before an operation Warfarin is usually stopped at least five days prior.

4 Warfarin is rarely used during pregnancy.

5 If patients are not taking Warfarin, a normal INR is 0.8 to 1.1.

6 An adult daily recommended dose of Vitamin K is 90 mcg/daily.

7 Warfarin is also called a Vitamin K antagonist.

8 The most serious side effect when taking Warfarin is bleeding.

9 When on Warfarin for life patients need to be weighed regularly - fluctuations in weight can affect the INR result.

10 Grapefruit juice and cranberry juice are to be drunk in moderation only. They alter the effects of Warfarin.

11 Alcohol is permitted, but only two units per day: for example, one pint of beer or two small glasses of spirits.

12 Many dietary supplements contain Vitamin K, so seek a doctors' advice before taking - they may reduce the effect of Warfarin.

13 Warfarin comes in different strengths indicated by a tablet colour code in the UK:

0.5mg white tablet	1mg brown tablet
3mg blue tablet	5mg pink tablet.

14 Warfarin is taken once daily, usually in the evening. It is important it is taken at the same time each day, with or without food.

GOOD PRACTICE

All foot workers must ensure they take a full history from their clients. This must include a full medical history to include all medications being taken. When doing this, ask the client why they take each medication. This allows a clear summary of past and present medical history and allows the client time to add new information which is often forgotten. This helps the practitioner maintain good records, whilst maintaining client health and safety. Remind your client to check with their GP or Pharmacist when purchasing over the counter medicines - some of these interact with Warfarin. Aspirin and Ibuprofen, for example, increase risk of bleeding.

Podiatrists and Foot Health Practitioners take pride in their profession and always aim to provide best practice. Any abnormality in the clotting time of the blood can affect treatment, and clients' health and safety. If on Warfarin, ask when was their last INR test? This will assure the practitioner that the client is on the correct dosage. You can ask to see their yellow INR book, and note the dosage, although this changes often. Good scalpel technique is necessary at all times, fragility of blood vessels should be managed carefully.

THICKENED CALLOUS may need to be pared over several visits to avoid bleeding. The area can be padded (off-loaded) between visits. Remember, bleeding also increases the risk of infection.

VASCULAR CORNS. If a corn has grown quite large and capillary blood vessels are visibly bleeding into the corn itself, the result can be layers of skin and dried blood in a 'laminated', layered sandwich. Small blood vessels in close proximity to the nucleus can bleed during and after treatment. Deep and direct pressure may be needed using gauze, and wearing gloves. Chemical agents may be used to control bleeding: Ferric chloride 15% soln., Hydrogen peroxide 10%, or Kaltostat (Calcium alginate). Once bleeding ceases, a dressing of choice can be applied.

WARFARIN INDUCED SKIN NECROSIS

This is rare, but well-recognised. This is a skin and soft tissue complication of anticoagulants. The site is initially painful, oedematous, red in colour. The symptoms often appear between the third and tenth day after commencing Warfarin therapy. Often patients believe they have bumped against something causing a bruise. The condition is more common in women than men, main areas affected are areas with a high fat content (areas where the blood vessels are compromised – buttocks, breasts, thighs, and abdomen), but can appear on extremities: fingers, toes, etc. If necrosis, purpura, or bruising is visible refer your client immediately to their GP or hospital.

Treatment: Warfarin is stopped. Heparin may be used instead. Vitamin K can be administered to reverse effects. Small areas are left to heal, whilst larger areas may need surgery, or skin grafts.

FUNGAL NAILS

Fungal nails often need reduction using a bur - care needs to be taken not to catch the surrounding tissue as a bleed may ensue. Fluconazole increases Warfarin concentration, and increases risks of bleeding.

SIDE EFFECTS

If your client suffers any side effects, notify their GP or Pharmacist. Side effects can be reported by yourself or your client on the *MHRA yellow card scheme*, and this is used to make Doctors, Nurses, and Pharmacies aware of any new side effects. This can be done online at the following web address:

<https://yellowcard.mhra.gov.uk/the-yellow-card-scheme/>

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Answers should be submitted on A4 paper and should be of sufficient length to demonstrate full understanding of the topic. Single word answers are not permissible. Try to answer in one or two short paragraphs, not more than 1/3rd page per answer.

- 1 What is PT? Describe its function.
- 2 How does Warfarin work?
- 3 Why do we need Vitamin K and what function does it perform.
- 4 What are the symptoms of Vitamin K Deficiency?
- 5 Why do some people need to take Warfarin? Name and explain three conditions.
- 6 What problems, as well as bleeding, do we need to be careful about?
- 7 Explain the aims of the Association of British Pharmaceutical Industry ABPI and the professional standards for hospitals, and pharmacies.
- 8 Which age group typically receives the most prescribed drugs? Explain the problems this can cause, and how they can be avoided.
- 9 Why, as practitioners, do we need to know if our clients are on Warfarin therapy?
- 10 Describe the problems we may encounter as practitioners, and how best to manage them safely.

*Return this page with the administration fee (see website CPD Download page) and your answers to:
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