**Feedback to MCQs – HCP Content**

**1. The use of anticoagulants for stroke prevention**

a) Atrial fibrillation increases the risk of stroke five-fold

**True** / False

b) CHADS2 is the preferred tool to assess an individual’s risk of stroke

True / **False**

c) Warfarin and aspirin are equally effective in preventing stroke in those with atrial fibrillation

True **/ False**

**Adjusted-dose vitamin K anticoagulants (including warfarin) reduce stroke, disabling stroke, and other major vascular events for those with nonvalvular atrial fibrillation by about one third when compared with antiplatelet therapy. Applied to all-comers with atrial fibrillation, aspirin reduces stroke by 20 percent, whereas warfarin reduces it by 65 percent. (Hart RG, Halperin JL, Pearce LA, et al. Lessons from the Stroke Prevention in Atrial Fibrillation trials. *Ann Intern Med*. 2003;138(10):831–838.)**

d) Warfarin and the NOACs are equally effective in preventing stroke in those with atrial fibrillation

**True**  / False

**The NOACs have similar stroke prevention efficacy to warfarin. However, the evidence base and their use in clinical practice is relatively limited.**

**2. Indications for oral anticoagulation**

a) The most common site of origin of a deep vein thrombosis is the deep vein is of the calf (distal DVT)

**True** / False

b) Which of the following are signs or symptoms of a DVT (select all that apply

i) **Hot, painful leg**

**ii) Leg oedema**

**iii) Skin discolouration**

iv) Numbness

c) When treating a DVT, heparin can be stopped once the INR in in therapeutic range

True / **False**

**Heparin should be continued for at least two days after the INR is therapeutic. In rare instances, warfarin initiation can paradoxically cause clot extension through rapid depletion of the anticoagulant factors Protein C and Protein S. Overlapping heparin treatment prevents this from happening.**

**d) All those who have a DVT should have a thrombophilia screen**

True / **False**

**Thrombophilia screening is expensive and time-consuming and should not be used indiscriminately. Positive results often cause unjustified concern to the individual, and a negative result may provide false reassurance. Also, there should be a plan of how the results will affect management.**

**Its main indications are:**

* **VTE at age < 40 yrs**
* **Recurrent VTE**
* **VTE in an unusual anatomical site**
* **Positive family history of VTE**
* **Recurrent miscarriage**
* **Skin necrosis**

**e) Which of the following are signs or symptoms of a PE (select all that apply**

i) **Shortness of breath**

ii) Rash

iii) **Tachycardia**

**iv) Apprehension**

**f) Antiphospholipid syndrome (Hughes Syndrome) is an inherited thrombophilia**

True / **False**

**g) All patients with bioprosthetic heart valve replacements require lifelong anticoagulation**

True / **False**

**h) There is a higher risk of systemic embolisation with a valve in the mitral position compared with an aortic valve replacement**

**True** / False

**3. The effect of anticoagulants on blood clotting**

1. Blood is made up of red cells, white cells, platelets and plasma **T**/F
2. The function of red blood cells are: the carrying of oxygen and carbon dioxide together with phagocytosis of foreign cells and viruses T/**F**

**Red cells carry oxygen throughout the body and transport carbon dioxide from the capillaries back to the lungs to be excreted when exhaled. However, they they are not responsible for the phagocytosis of foreign cells and viruses. This is the role of white blood cells.**

1. At the point of blood vessel or tissue damage, or exposure of blood to air, platelets circulating in the blood, become sticky and adhere together **T**/F
2. Loose platelet aggregation is characterised by cross linking of fibrin through active GIIb/IIIa receptors with fibrinogen bridges T/**F**

**Platelet aggregation is the first stage of clot formation. This describes the final stage of clot formation. Soluble fibrinogen is converted into insoluble fibrin, which emeshes the fibrin plug to create a stable clot.**

1. The clotting cascade consists of two separate systems. The intrinsic pathway which has all its components within the blood and the extrinsic pathway which is activated by extravascular tissue damage. **T**/F
2. Following the conversion of prothrombin to thrombin (factor II), thrombin is involved in converting insoluble fibrin fibres to soluble fibrinogen T/**F**

**Thrombin converts soluble fibrinogen into insoluble fibrin.**3 factors (known as Virchow’s triad) are involved in the formation of a clot:

* Local trauma to a vessel wall
* Hypercoagulability
* Blood stasis **T**/F

8. Tissue factor released when blood clots are formed is also known as Factor III **T**/F

1. Venous clots consist of red and white blood cells with a small amount of platelets within a fibrin mesh. **T**/F

10. Clots naturally break down because of the body’s natural production of fibrinogen T/**F**

**Plasmin is the enzyme that naturally breaks down blood clots**

11. Antiplatelet agents are useful for preventing venous thromboembolism

True / **False**

**Antiplatelet agents are useful in preventing arterial thrombosis**

12. Arterial thrombi are mainly composed of platelets

**True** / False

13. Aspirin exerts its antithrombotic effect by inhibiting cyclo-oxygenase (COX), preventing the synthesis of prostacyclin in the vascular walls

True / **False**

**This is paradoxical effect of aspirin. Prostacyclin is a vasodilator which has anti-aggregating properties and is thus potentially anti-thrombotic. By inhibiting COX, aspirin prevents its synthesis which is, in effect, a pro-coagulant effects. However, COX inhibition also prevents the synthesis of the thromboxane A2, a vasoconstrictor that causes platelet aggregation, and is thus potentially thrombotic.**

14. Large doses of aspirin will have an immediate antithrombotic effect

**True**  / False

15. Warfarin blocks production of the following clotting factors (please select one response):

**i) Factor II (prothrombin), VII, IX and X**.

ii) Factor II (prothrombin), VII, IX and XI.

iii) Factor VII, IX, X and XI

iv) Factor II (prothrombin), IX, X and XII

16. The time for warfarin to achieve an antithrombotic effect depends on the clearance of Factor VII, the clotting factor with the longest half-life

True / **False**

**The antithrombotic effect of warfarin depends on the clearance of functional factor II (prothrombin.**

17. Warfarin can have a paradoxical pro-coagulant effect through inhibition of Protein C and Protein S

**True**  / False

18. Low molecular weight heparins inhibit antithrombin III and directly inhibit thrombin

True / **False**

**Low molecular weight heparins act by activating** [**antithrombin**](http://en.wikipedia.org/wiki/Antithrombin) **III (ATIII), which then inactivates** [**thrombin**](http://en.wikipedia.org/wiki/Thrombin) **and** [**factor Xa**](http://en.wikipedia.org/wiki/Factor_Xa) **.**

19. Low molecular weight heparins have a longer half-life than unfractionated heparin

**True** / False

**4. How the effect of vitamin K antagonists is monitored**

a) The INR measures how thin the blood is

True / **False**

**Although people often refer to the INR as a measure of how thin the blood is, this is not strictly true. It is a measure of how long it takes the blood to clot (clotting time).**

b) The INR is a reflection of the prothrombin time (PT)

**True**  / False

c) The higher the value of the thromboplastin ISI, the more reliable the INR result is likely to be.

True / **False**

**As the value of the ISI increases above a value of 1.0, the INR result will become less reliable.**

d) The INR value for some who has had a PE is expressed either as a target INR 2.5 or as a range 2.0 - 2.5

**Tru**e / False

e) A patient who has had a recurrent DVT whilst on oral anticoagulation should have an INR target of 3.0

True / **False**

**The INR target for this indication is 3.5**

f) Prior to cardioversion, a target INR of 3.0 can be aimed for.

**True**  / False

g) Which of the following will determine the INR target in someone with a mechanical heart valve (select all that apply)

1. **The position of the valve**
2. **The type of valve**
3. **If the person has atrial fibrillation**
4. The age of the person

**5. Pharmacokinetics and pharmacogenomics of warfarin**

a) The relationship between plasma concentration of warfarin and its effect on blood coagulation, as measured by the INR, is linear

True / **False**

**As warfarin’s effect on vitamin K clotting factors is a function of both their synthesis rate and degradation rates, there is no simple correlation between plasma concentration and therapeutic effect.**

b) The mean-plasma half-life of warfarin is approximately 40 hours. On initiating a fixed dose of warfarin, it would take 200 hours or 8 days to reach constant plasma concentration (or steady state)

**True** / False

c) As warfarin is 99% bound to albumin, hypoalbuminaemia caused by renal impairment can cause a reduction in anticoagulation response by reducing plasma protein binding.

True / **False**

**Clinical conditions that reduce the levels of albumin may increase the toxicity of warfarin, as the reduced plasma protein binding results in more free (unbound) warfarin circulating.**

d) Liver impairment can result in an increased anticoagulant effect by impairing the metabolism of warfarin

**True** / False

f) Because of warfarin’s long half-life of 40 hours, it takes at least 2 days to see the effect of a dose adjustment on the INR

**True**  / False

g) Which of the following factors may influence an individual’s response to warfarin? (select all that apply)

1. **Ethnicity**
2. **Variability in clotting factor turnover**
3. Eye colour
4. **Age**

**6. Factors affecting the INR**

a) Which of the factors listed below are likely to alter the effect of warfarin? (please select any that apply)

1. **Other medication**
2. **Alcohol**
3. Taking warfarin on a full stomach
4. **Changes in diet**
5. **Getting a dose of ‘flu**
6. Taking warfarin with a glass of milk

**The main factors that alter the effect of warfarin, increasing or decreasing the INR, are other medication, changes in dietary vitamin K and alcohol intake and acute health changes.**

**b)** The most common way that drugs affect the action of warfarin is by reducing its excretion by the kidneys.

True **/ False**

**The most common way that other drugs interact with warfarin is by reducing or increasing its metabolism by cytochrome P-450 in the liver.**

c)On introducing a drug that inhibits the cytochrome P450 system to a patient taking warfarin, the following takes place:

* 1. **INR increases, necessitating a warfarin dose reduction**
  2. INR increases, necessitating a warfarin dose increase
  3. INR drops, necessitating a warfarin dose reduction
  4. INR drops, necessitating a warfarin dose increase

d) Rifampicin is an enzyme inducer. When taken with warfarin, this means that warfarin is:

* 1. **metabolised more rapidly, resulting in a lower INR**
  2. metabolised more rapidly, resulting in a higher INR
  3. metabolised more slowly, resulting in a lower INR
  4. metabolised more slowly, resulting in a higher INR

e). On the introduction of an interacting drug to be taken for 1 week or more, it is important to check the INR on a weekly basis

**True** / False

f). It is reasonable to halve the dose of warfarin if a broad-spectrum antibiotic like co-amoxiclav is introduced.

True **/ False**

**If you know someone is starting a broad-spectrum antibiotic for a week or more, it may be prudent to decrease the dose of warfarin to minimise the predicted INR rise. However, only a slight decrease in warfarin dose (e.g. 0.5 mg / 1mg) is advised**

g). The use of alternative medicines such as glucosamine and cod-liver oil, together with warfarin is safe

True / **False**

**Alternative medicines may interact with warfarin and should be treated with caution. Glucosamine enhances the effect of warfarin and should be avoided. Cod-liver oil may increase the risk of bleeding.**

h) Those taking warfarin should be advised to avoid food containing vitamin K

True / **False**

**Vitamin K-containing foods form part of a healthy diet, and patients should not be advised to omit these completely. Instead, patients should be counseled to keep the amount of vitamin K-containing foods in their diet consistent, and to inform their anticoagulant practitioner if they have changed their diet since the last INR test.**

i) Binge drinking reduces the INR

True / **False**

**Binge drinking increases the INR**

**7. The adverse effects of warfarin**

a) Which of the following are adverse affects associated with warfarin? (Select all that apply)

1. **Nose bleed**
2. **Skin rash**
3. **Skin necrosis**
4. Dry eye
5. Actinic keratosis
6. **Alopecia**

b) Which of the following can be evidence of bleeding? (Select all that apply)

1. **Black, tarry stools**
2. **Severe headache**
3. **Pink or brown urine**
4. **Severe bruising**

**All of these could be evidence of severe bleeding. Black, tarry stools can be a sign of passing blood in the stools (malaena). A severe headache may be a sign of a intracranial bleed. Pink or brown urine may indicate that there is blood in the urine (haematuria). Severe bruising, especially that which appears without an apparent reason, may also indicate a severe bleed.**

c) You should advise patients that if they notice a little bit of blood whilst brushing your teeth they should go straight to their nearest Emergency Department

True / **False**

**Bleeding gums can occur whilst taking warfarin. Unless this bleeding is severe, there is no need to go the Emergency Department. Instead, reassure the patient.**

d) What should an anticoagulated patient do if they have had a severe headache over a few days? (Please select the response that best answers this question)

1. They do not need to do anything
2. They should take a pain killing medicine (e.g. paracetamol tablets)
3. They should discuss it with their anticoagulant practitioner at their next clinic appointment
4. **They should go straight to their nearest Emergency Department**

**A severe headache may be an intracranial bleed and needs to be urgently investigated.**

e) What should an anticoagulated patient do if they notice that they have black, tarry stools? (Please select the response that best answers this question)

1. They do not need to do anything
2. They should take a laxative (e.g. senna tablets)
3. They should discuss it with their anticoagulant practitioner at their next clinic appointment
4. **They should go straight to their nearest Emergency Department**

**Black, tarry stools can be a sign of passing blood in the stools (malaena) and needs to be urgently investigated.**

f) If a woman takes warfarin in early pregnancy, it can damage the unborn child

**True** / False

**Warfarin can affect the development of a baby in early pregnancy, causing birth defects.**

g) A woman who takes warfarin should not breast-feed her infant

True / **False**

**As warfarin does not pass into breast milk, it is safe to breast feed while taking warfarin.**

h) Patients should stop warfarin 48hours before a dental extraction

True / **False**

**If the INR is less than 4.0, warfarin does not need to be stopped or reduced before a dental extraction. The INR should be checked no more than 72hours before the planned dental procedure (ideally 24hours before).**

i) Renal impairment is a contraindication to warfarin

True / **False**

**Although patients with renal impairment may require lower doses of warfarin and closer management, this is not considered to be a contraindication to warfarin. Current indications are as follows (MHRA, 2009):**

* **Known hypersensitivity to warfarin or to any of the excipients**
* **Haemorrhagic stroke**
* **Clinically significant bleeding**
* **Within 72 hours of major surgery with risk of severe bleeding**
* **Within 48 hours postpartum**
* **Pregnancy**
* **Concomitant use of fibrinolytic drugs**

**8. Practical management of warfarin therapy**

1. Loading doses of warfarin are required on initiation of warfarin because of the long half-life of warfarin **T**/F
2. Centres typically use loading doses of warfarin 10mg for 3 days when initiating warfarin in newly diagnosed VTE patients T/**F**

**High loading doses of warfarin may increase the patient's risk of bleeding complications early in therapy and cause a paradoxical hypercoagulable state. Due to these risks high loading doses are generally not recommended. Consequently, many centres now use lower doses of 5mg, 5mg, 5mg, or 8mg, 8mg, 8mg on the first three days of warfarin treatment.**

1. In patients with newly diagnosed VTE, it is appropriate that the patient receives additional heparin as cover whilst the warfarin loading doses are given **T**/F

**If the event being treated is new – for instance an acute proximal DVT - or new-onset atrial fibrillation - warfarin loading doses should be given together with heparin.**

1. When initiating anticoagulation, heparin can be stopped once a therapeutic INR has been reached T/**F**

**Heparin should not be discontinued until the INR is within therapeutic range for at least 2 consecutive days. . In rare instances, warfarin initiation can paradoxically cause clot extension through rapid depletion of the anticoagulant factors Protein C and Protein S. Overlapping heparin treatment prevents this from happening.**

1. There is an increased risk of warfarin-induced skin necrosis on initiation of warfarin in those with Protein C or S deficiency. **T**/F
2. When considering initiation of warfarin, the following factors need to be taken into account: patients age, liver function, concomitant disease states such as heart dysfunction and other medications **T**/F

**When considering initiation of warfarin, the following factors need to be taken into account:**

* **Patient’s age**
* **Liver function**
* **Renal function**
* **Interacting drugs**
* **Concomitant disease states (e.g. heart dysfunction)**

1. Initiation of warfarin is a relatively safe time for warfarin management and you can take a relaxed approach to this whole phase T/**F**
2. There is little point in determining what is the cause of an abnormal INR in someone who is being monitored long term – the changed dose would be the same whatever the cause T/**F**
3. Fluctuations in INR in an otherwise well patient, may be addressed by looking at temporary causes such as lifestyle changes including alcohol and diet **T**/F

**Unexpected fluctuations of the INR in an otherwise stable patient should always be investigated. Subsequent management will depend on the cause. Causes include:**

**• Non-compliance - including missed doses or deviations from the instructed regimen**

**• Initiation of an interacting drug**

**• Change in diet or alcohol intake**

**• Acute worsening in health**

**• Increased emotional stress (e.g. moving house, bereavement, family troubles)**

1. An adjustment of 50% of the maintenance dose is the maximum adjustment in a patient, whose INR is consistently out-of-range T/**F**

**As a general rule, dose increments are of the order of 5 – 10%. Very occasionally a dose adjustment of up to 20% may be needed.**

1. In stable patients with atrial fibrillation, the maximum interval between appointments is 16 weeks. T/**F**

**For those with a stable INR, the maximum testing interval is 12 weeks.**

1. There is good evidence to demonstrate that time spent in the therapeutic INR range (TTR) results in less emboli and strokes **T**/F
2. The interval before the next INR test should always be 4 weeks. T/**F**

**The frequency of monitoring depends on the stability of INR control. On average, patients are monitored every four to six weeks, but this can vary from every week (or twice a week if very unstable) to a maximum of 12 weeks.**

1. The interval before the next INR test is determined mainly by the change

in INR level in the current test and the preceding one **T**/F

1. Patients with AF who have an INR >5 who are not bleeding should have 1 to 2 doses of warfarin withheld **T**/F
2. The follow up interval should always remain the same in someone taking low dose warfarin whatever the INR result T/**F**

17. A follow up interval of more than 4 months is safe and cost effective T/**F**

**For those with a stable INR, the maximum testing interval is 12 weeks.**

18. An advisory system using a built in algorithm is much better than a clinician at getting the next dose correct and you should always accept the dose recommendation given Y/**N**

20. Computerised decision support systems (CDSS) should always supply patient specific advice. **True** / False

21. There is no evidence that electronic maintenance dosing algorithms result in better control of the INRs and better outcomes for the patient. True / **False**