MULTIPLE CHOICE QUESTIONS

1. Platelet dense granules contain high concentrations of:

A. Thromboxane A$_2$
B. Adenosine diphosphate
C. Cyclo-oxygenase 1
D. P-selectin
E. P2Y$_{12}$ receptors

Correct answer: B. Adenosine diphosphate (ADP). Platelet dense granules containing ADP are released upon platelet activation. ADP acts on the platelet P2Y$_1$ and P2Y$_{12}$ receptors, the latter having a central role in the amplification of platelet activation. Platelet alpha granules contain pro-inflammatory and pro-coagulant factors, including P-selectin.

2. Aspirin exerts its antiplatelet effect via inhibition of:

A. P2Y$_{12}$ receptor stimulation
B. Thromboxane A$_2$ generation
C. Glycoprotein IIb/IIIa binding
D. Prostacyclin release
E. Factor X activation

Correct answer: B - Thromboxane A$_2$ generation. Aspirin (acetylsalicylic acid) is an irreversible inhibitor of cyclo-oxygenase (COX1) enzymes. Platelet COX1 is responsible for converting
arachidonic acid to prostaglandin H$_2$, which is then converted to thromboxane A$_2$ by thromboxane A synthase. Thromboxane A$_2$ is a potent pro-aggregatory and vasoconstrictive substance. Inhibition of platelet COX1 by aspirin therefore reduces thromboxane A$_2$ generation. Less preferentially and more at higher doses, aspirin may reduce prostacyclin release from the endothelium. Prostacyclin inhibits platelet aggregation and leads to vasorelaxation, therefore inhibition of its release is counterproductive. However, aspirin’s overall effect of greater inhibition of thromboxane generation than prostacyclin release results in its net antiplatelet action.

3. You are asked for advice on the optimal antithrombotic strategy going forward for a 67-year old female with a history of non-ST elevation myocardial infarction (MI) one year ago. Angiography was performed at that time and showed diffuse multivessel coronary artery disease. Her MI was conservatively managed i.e. she did not undergo revascularisation. She has been receiving dual antiplatelet therapy since her MI and has tolerated this well. Her resting ECG shows sinus rhythm with left bundle branch block. She has normal renal function.

Which one of the following additional risk factors would confer high ischaemic risk as defined in the ESC 2019 CCS guidelines?

A. Hypertension
B. Frailty
C. Peripheral artery disease
D. Liver failure
E. Diet-controlled type 2 diabetes mellitus
Correct answer: C – Peripheral artery disease. The ESC 2019 CCS guidelines identify those at high ischaemic risk as those with multivessel coronary artery disease plus one of peripheral artery disease, drug-treated diabetes mellitus, recurrent myocardial infarction or eGFR 15-59 ml/min/1.73m\(^2\). Frailty and liver failure are examples of factors for high bleeding risk.

4. You assess that she is at high ischaemic risk, but not high bleeding risk.

Of the following regimens of dual antiplatelet therapy (DAPT), which would be a recommended option to consider in this patient’s case?

A. Aspirin 75-100 mg once-daily plus prasugrel 5 mg once-daily
B. Aspirin 75-100 mg once-daily plus prasugrel 10 mg once-daily
C. Aspirin 75-100 mg once-daily plus ticagrelor 60 mg twice-daily
D. Aspirin 75-100 mg once-daily plus ticagrelor 90 mg twice-daily
E. Aspirin 75-100 mg once-daily plus clopidogrel 300 mg once-daily

Correct answer: C - Aspirin 75-100 mg once-daily plus ticagrelor 60 mg twice-daily. This lady is one year after an MI and has tolerated DAPT for this duration. Given she is at high ischaemic risk but not high risk for bleeding, long-term DAPT should be considered. Whilst the licensed dosing regimen in the first year after an acute coronary syndrome event is 90 mg twice-daily, it is 60 mg twice-daily that is recommended for long-term treatment after this time. Prasugrel is not recommended in this case because the patient’s MI was not treated by percutaneous coronary intervention. Clopidogrel would be a recommended option, but the maintenance dose is 75 mg.
once-daily, not 300 mg once-daily as stated in option E. Low-dose dual antithrombotic therapy with aspirin 75-100 mg once-daily and rivaroxaban 2.5 mg twice-daily would also be a recommended regimen to consider in this case.

5. The patient’s General Practitioner writes to you around a year later to say this lady has now been diagnosed with atrial fibrillation. They ask for your advice as to what antithrombotic therapy would now be best in this case.

Which one of the following is most appropriate to advise?

A. Where possible, warfarin should be preferred over a non-vitamin-K-antagonist oral anticoagulant (NOAC) when combining antiplatelet and anticoagulant therapy.

B. It is reasonable to remain on antiplatelet therapy alone in this case.

C. The long-term combination of an oral anticoagulant and single antiplatelet therapy should not be considered.

D. The long-term combination of an oral anticoagulant and dual antiplatelet therapy should not be recommended.

E. Long-term treatment with apixaban plus ticagrelor is a recommended option in this case.

Correct answer: D - The long-term combination of an oral anticoagulant (OAC) and dual antiplatelet therapy should not be recommended. This patient, who is female, aged over 65 and with a previous history of myocardial infarction, will have a CHA2DS2-VASC score of at least 4,
therefore oral anticoagulation is strongly recommended. In patients with high ischaemic risk but not high bleeding risk, combination of an OAC with single antiplatelet therapy can be considered. Where possible, a non-vitamin-K-antagonist oral anticoagulant (NOAC) should be preferred to a vitamin K antagonist, including in patients requiring concurrent anticoagulant and antiplatelet therapy. Combining a NOAC and a potent P2Y₁₂ inhibitor (ticagrelor or prasugrel) can be considered as an alternative to triple therapy with aspirin, clopidogrel and an OAC in the immediate post-PCI period, but is not recommended for routine long-term use. In this case, if a P2Y₁₂ inhibitor was continued, clopidogrel would be the recommended agent.

6. You see the same patient two years later in your clinic as she has developed symptoms of stable angina that have not been improved by medical therapy. Her resting ECG continues to show atrial fibrillation (AF). You arrange elective coronary angiography, which shows a focal severe stenosis in the mid left anterior descending artery not present on the previous angiogram. You decide to proceed with percutaneous coronary intervention (PCI), implanting one drug-eluting stent. The procedure is successful and uneventful.

Which one of the following statements is correct regarding the management of antithrombotic therapy in this patient’s case concerning the time around PCI?

A. If warfarin is prescribed, the target international normalised ratio (INR) should be 2.0 to 2.5.

B. Patients on full-dose oral anticoagulation undergoing PCI do not require additional antiplatelet therapy.

C. It is recommended to routinely continue triple therapy with aspirin, clopidogrel and an oral anticoagulant for 12 months after PCI in patients with AF.
D. If prescribed triple therapy with aspirin, clopidogrel and an oral anticoagulant after PCI, it is recommended to stop clopidogrel after one week and continue aspirin for 6 months.

E. Aspirin 75 mg once-daily plus clopidogrel 75 mg once-daily plus rivaroxaban 2.5 mg twice-daily is a recommended combination after PCI in patients with AF requiring oral anticoagulation.

Correct answer: A - If warfarin is prescribed, the target international normalised ratio (INR) should be 2.0 to 2.5. This patient with AF, requiring oral anticoagulation, has undergone PCI. In this scenario, it is recommended to prescribe a period of triple therapy with aspirin, a P2Y₁₂ inhibitor and an oral anticoagulant, then stop aspirin after around a week if low risk for stent thrombosis or up to six months if high risk. Where possible, a NOAC should be preferred to a VKA. However, in the case of the latter, the target INR should be 2.0-2.5, aiming for >70% of time in the therapeutic range. Very low-dose rivaroxaban (2.5 mg twice-daily) is neither licensed nor recommended in patients with atrial fibrillation, and is unlikely to provide adequate stroke prevention in this setting.