

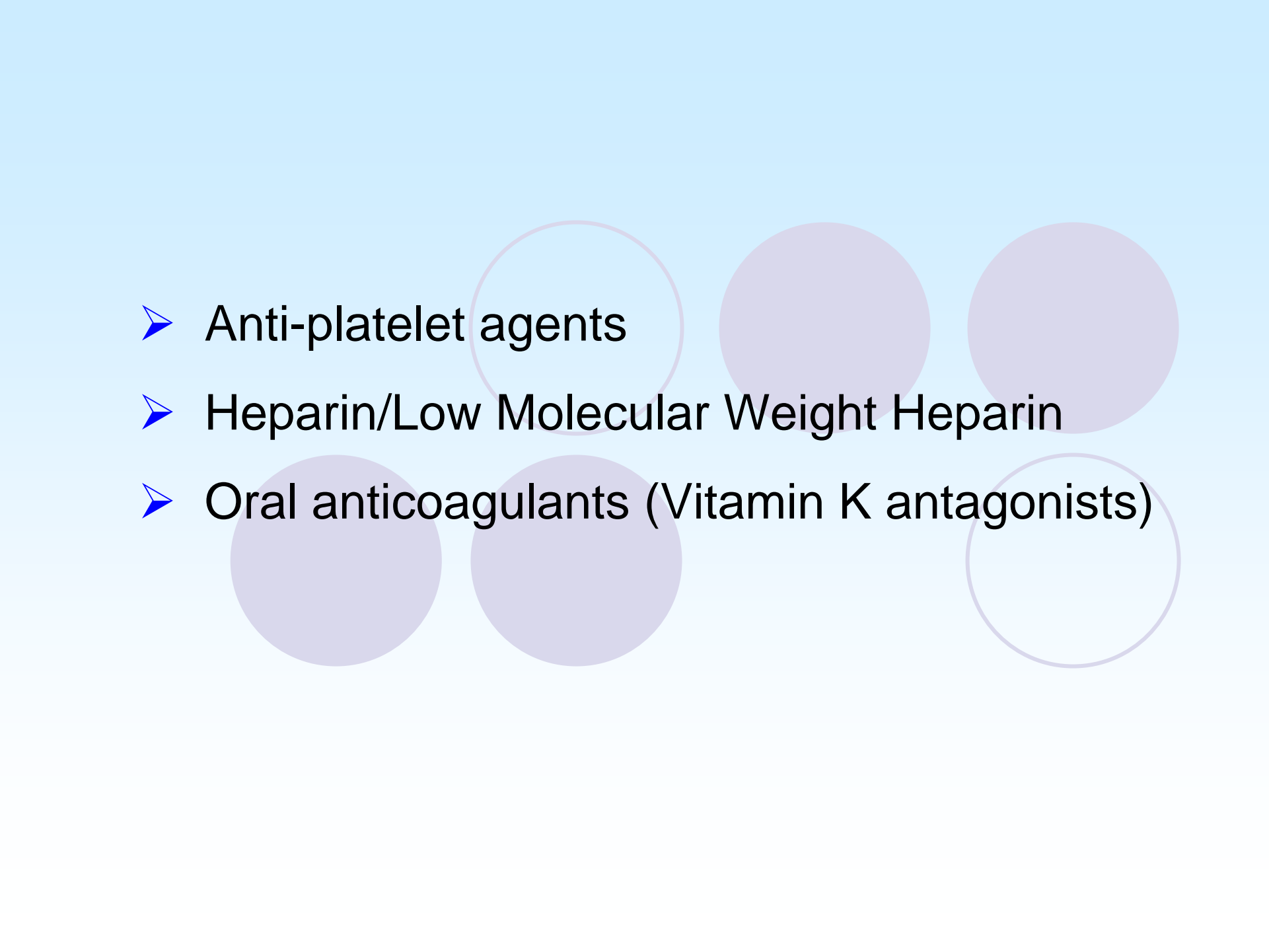


# **Managing Critical Bleeding in Patients on Routine Antithrombotics**

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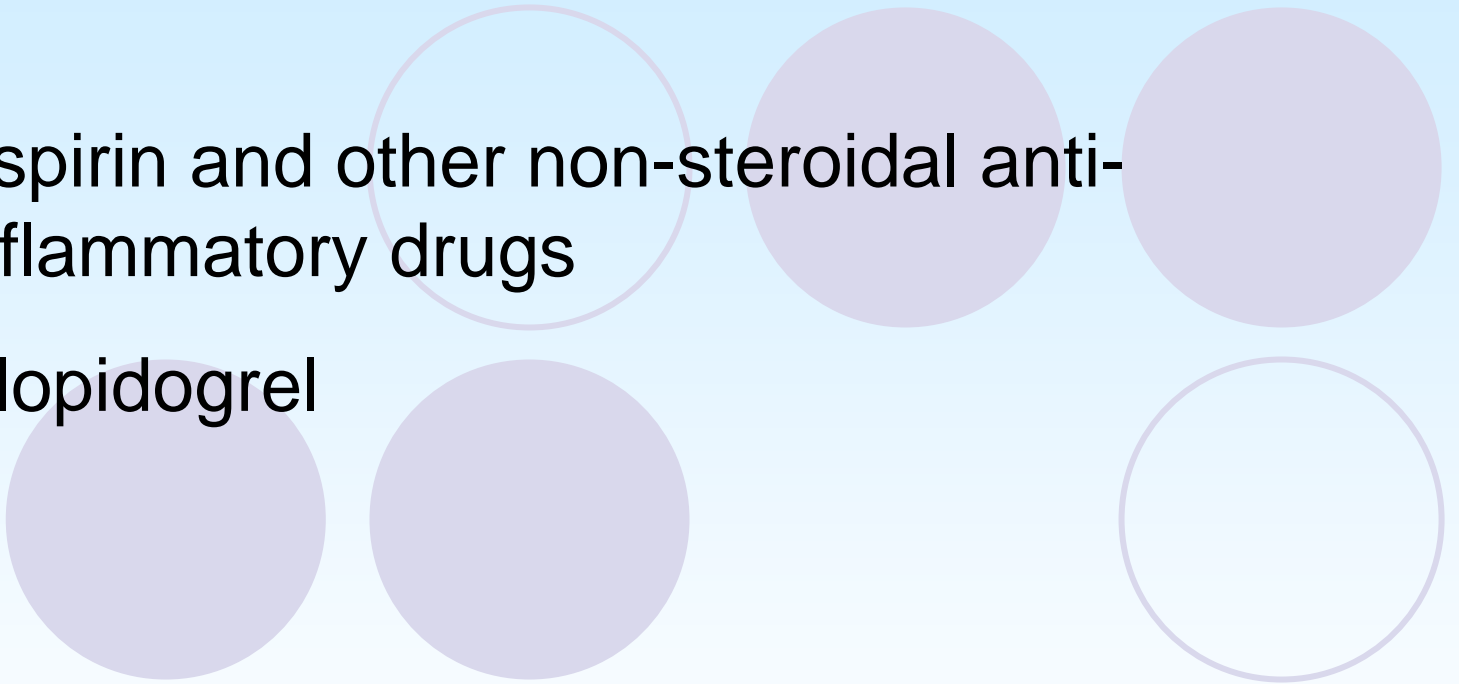
## The consequence of :

- a rising incidence of thrombotic disorders
- an aging population
- the most likely to require surgery and blood
- large numbers of people presenting for procedures/surgery on anti-thrombotics at risk of bleeding

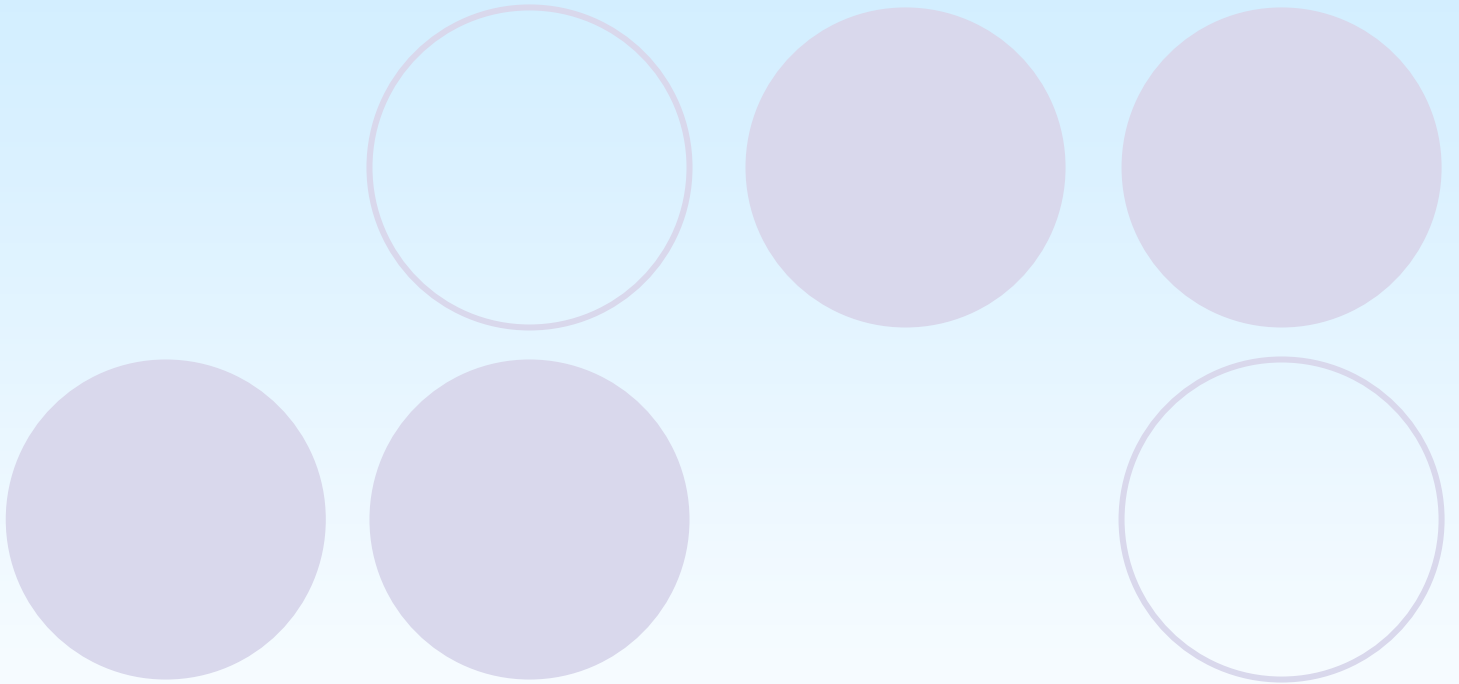
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- Anti-platelet agents
  - Heparin/Low Molecular Weight Heparin
  - Oral anticoagulants (Vitamin K antagonists)

# Anti-platelet Agents

- Aspirin and other non-steroidal anti-inflammatory drugs
- Clopidogrel



# Aspirin



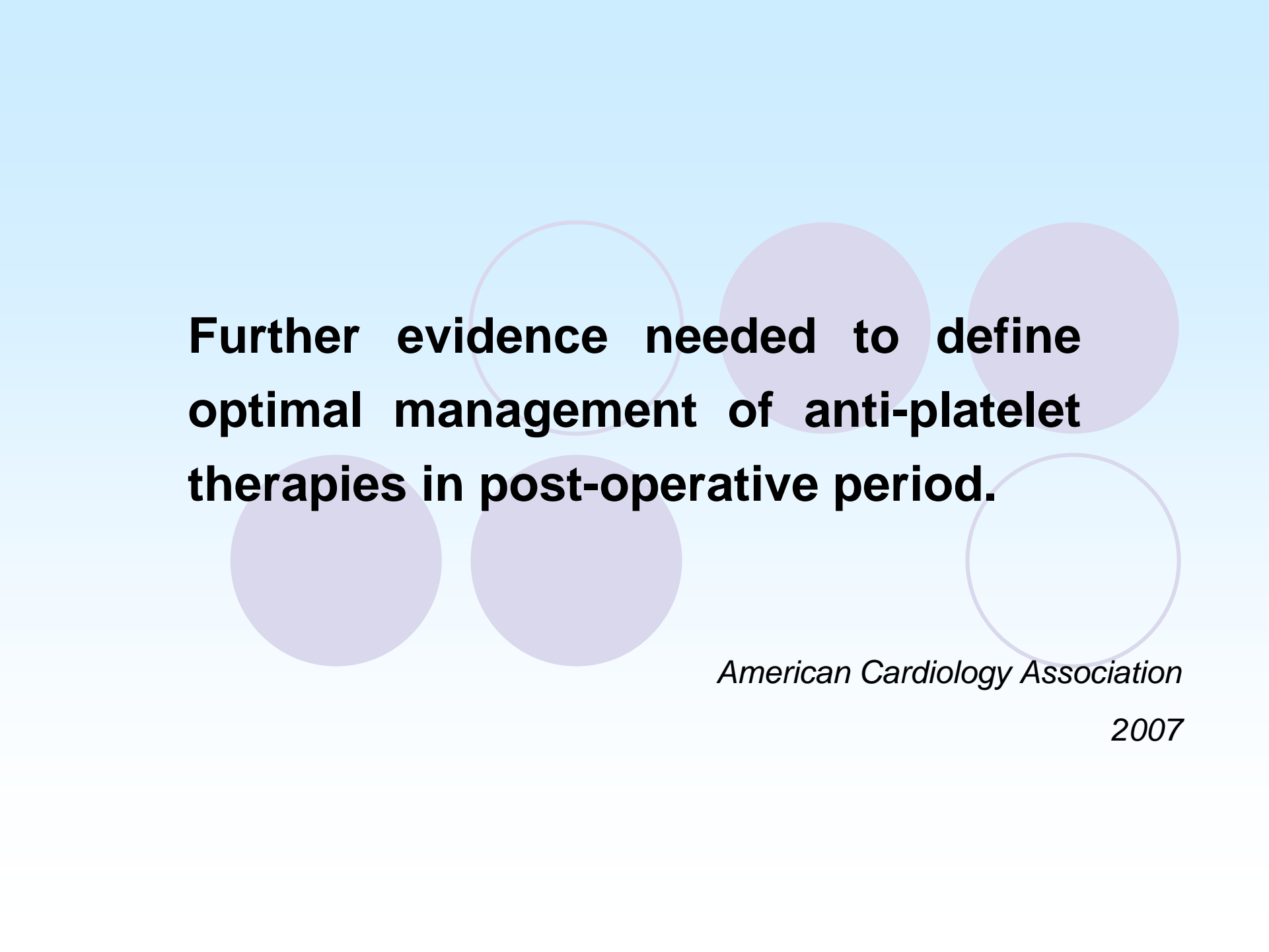
## Aspirin and NSAIDs

- May be used without prescription
- Ingestion may not be disclosed to family or clinicians
- Despite data to suggest increased post-operative bleeding rates/volumes particularly in cardio-thoracic surgery, the current practice is to encourage continuation of ASA unless the bleeding risk is considered unacceptably high, e.g. neurosurgery, ophthalmic surgery, prostate surgery?

- The risk of peri-operative cardiac ischaemic events is 2%-5% in patients over 40.
- Associated mortality of myocardial infarction is 25%.
- Associated mortality of cardiac arrest is 65%.

# Can we stop aspirin to reduce bleeding risk?

- PEP study (orthopaedic prophylaxis) with aspirin increased ischaemic events!
- ASA as 2° prophylaxis for symptomatic atherosclerosis reduces risk of stroke and myocardial infarction by 30% and risk of cardiovascular death by 15%.
- ASA withdrawal increases risk of acute coronary syndrome ~8 days later and is responsible for ~10% of cases.



**Further evidence needed to define optimal management of anti-platelet therapies in post-operative period.**

*American Cardiology Association*

*2007*

# Appropriate Use of Platelets

*“Platelet function disorders:*

*May be appropriate in inherited or acquired disorders, depending on clinical features and setting. In this situation, platelet count is not a reliable indicator.”*

## **Potential impact on ARCBS:**

- Increased usage of Red Cell concentrates.
- Increased usage of platelet concentrates.

No data on how frequently platelets are given for drug-induced functional defects.

# Indications:

*Prevention of recurrence of ischaemic stroke or transient cerebral ischaemic events in patients:*

- (1) With a history of symptomatic cerebrovascular ischaemic episodes while on therapy with low-dose aspirin; or*
- (2) Where low-dose aspirin poses an unacceptable risk of gastrointestinal bleedings; or*
- (3) Where there is a history of anaphylaxis, urticaria or asthma within 4 hours of ingestion of aspirin, other salicylates, or NSAIDs;*

*Prevention of recurrence of myocardial infarction or unstable angina in patients:*

- (1) With a history of symptomatic cardiac ischaemic events while on therapy with low-dose aspirin; or*
- (2) Where low-dose aspirin poses an unacceptable risk of gastrointestinal bleeding; or*
- (3) Where there is a history of anaphylaxis, urticaria or asthma within 4 hours of ingestion of aspirin, other salicylates, or NSAIDs.*

**Off-label use common**



# Cardiac Stents

- A well-established alternative to coronary artery bypass grafting.
- Bare metal stents – require at least four weeks treatment with dual anti-platelet therapy to prevent thrombosis/stent closure and allow ‘endothelialisation’.
- Drug eluting stents – delay endothelialisation but requires long-term (?more than twelve months) treatment.

# Implications

- Because surgery can be complicated by excessive bleeding
- AND
- Because cessation of Clopidogrel acutely in patients with stents can cause occlusion and fatal myocardial infarction
- ARCBS TMS and Operations Units will be involved!

**“The pre- or intra- operative transfusion of 10-15 (single) units of platelets may adequately reverse Clopidogrel induced platelet disaggregation to facilitate post-operative haemostasis.”**

## Heparin/low molecular weight heparin:

➤ Used in :

- Intravascular procedures
- Cardiopulmonary bypass
- Acute thrombotic disorders

As the action is not reversed by blood products, bleeding, as the main risk, will be managed by red cell transfusions.

## Anti-thrombin concentrates:

- Used in patients with deficiency:
  - Hereditary
  - Acquired (e.g. DIC)

# Oral Anticoagulant Indications

- 1° and 2° prophylaxis against stroke in atrial fibrillation.
- 2° prophylaxis against venous thromboembolism.
- Very little use in 1° thromboprophylaxis in Australia.

# Reversal of Warfarin

There are choices of :

- 'Time' ±bridging anticoagulation
- Vitamin K
- Replacement products

According to clinical circumstances.

# Clinical indications for use of FFP from NHMRC/ANZSBT guidelines:

- Single factor deficiencies where a specific or combined factor concentrate is not available.
- Warfarin effect in presence of life threatening bleeding in addition to Vitamin K-dependent concentrates.
- Acute disseminated Intravascular Coagulation with bleeding and prolonged coagulation. Not indicated for Chronic Disseminated Intravascular Coagulation.
- Thrombotic thrombocytopenic Purpura.
- Coagulation inhibitor deficiencies in patients undergoing high risk procedures or with spontaneous thrombosis requiring heparin therapy and when specific factors are not available.
- Following massive transfusion or cardiac bypass in presence of bleeding and prolonged coagulation.
- Liver Disease in presence of bleeding and prolonged coagulation.

Warfarin reversal is emerging as the major indication for FFP use at a tertiary hospital.

*“Careful monitoring of warfarin therapy, stringent implementation of warfarin reversal guidelines and introduction of newer products for warfarin reversal would help reduce the consumption of FFP.”*

In studies in which Prothrombin Complex Concentrates (PCC) have been compared with Fresh Frozen Plasma (FFP), PCCs are associated with a shorter time to INR correction with a low risk of thrombotic events.

Evidence based treatment guidelines are needed to optimise the use of PCCs for Warfarin reversal.

# Current recommendations for the use of PCCs for Warfarin Reversal

US 7 <sup>th</sup> ACCP Consensus Conference on Antithrombotic Therapy	PCCs or rFVIIa for serious or life-threatening bleeding at any INR elevation
UK Guidelines on Oral Anticoagulation	PCCs (50 IU/kg) for major bleeding
Australian Consensus Guidelines on Warfarin Reversal	PCCs for clinically significant bleeding; or PCCs for INR >9 without bleeding
Italian Federation of Anticoagulation Clinics	PCCs for serious bleeding (e.g. CNS, gastrointestinal)

## Implications for ARCBS

Continuing plasma supply for PCC production.

Education about use of PCC and FFP.

# References:

## Clopidogrel

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## Oral Anticoagulants

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