



OBJECTIVE:

To provide information on the use of acetylsalicylic acid in the prevention of vascular thromboembolic events.

BACKGROUND:

Acetylsalicylic acid (ASA) is well-established in the management of acute myocardial infarction and in the secondary prevention of cardiovascular disease among both men and women, based on large randomized trials. ASA may also be considered in selected patients for prevention of recurrent venous thromboembolism and for prophylaxis following joint arthroplasty. The net benefit of ASA use depends on weighing the anticipated reduction in cardiovascular events against the increased risk of gastrointestinal bleeding.

MECHANISM OF ACTION OF ASA:

ASA irreversibly inhibits platelet aggregation by inhibiting thromboxane A₂ (TxA₂) synthesis.

INDICATIONS FOR ASA:

Antiplatelet therapy is recommended for all patients with the following, unless contraindicated:

- 1) Cardiac:** For all patients with symptomatic coronary artery disease (CAD), including:
 - i. Acute coronary syndrome (ACS) patients with and without ST segment elevation
 - ii. Chronic stable angina
 - iii. Following percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG)
 - iv. Prosthetic heart valves:
 - i. ASA 81 mg daily is recommended in addition to VKA in selected high-risk patients with a mechanical valve prosthesis [see Clinical Guide: Mechanical and Bioprosthetic Heart Valves: Anticoagulant Therapy]
 - ii. ASA 81 mg daily is reasonable in all patients with a bioprosthetic aortic or mitral valve who are not taking an oral anticoagulant [see Clinical Guide: Mechanical and Bioprosthetic Heart Valves: Anticoagulant Therapy]
- 2) Cerebrovascular:**
 - i. For patients with non-cardioembolic ischemic stroke or transient ischemic attack (TIA) [see Clinical Guide: Stroke: Secondary Prevention]
 - ii. Following carotid endarterectomy
- 3) Peripheral arterial disease (PAD):**
 - i. Symptomatic patients [see Clinical Guide: Peripheral Arterial Disease]

4) Primary prevention of cardiovascular morbidity and mortality:

- i. Only in special circumstances in patients without manifest vascular disease in whom vascular risk is considered high and bleeding risk is considered low. Examples include: asymptomatic carotid or coronary atherosclerosis demonstrated on vascular imaging studies and patients at very high risk of vascular events due to multiple cardiovascular risk factors.

5) Secondary prevention of recurrent VTE:

- i. In patients at high risk of VTE recurrence following completion of initial anticoagulant therapy for a minimum of 3-6 months, ASA may be considered as an option to decrease recurrent VTE only if extended anticoagulant therapy is not acceptable to the patient. [see Clinical Guide: Venous Thromboembolism: Duration of Treatment]

6) Thromboprophylaxis following joint arthroplasty:

- i. For patients not at high risk of VTE, consideration can be given to rivaroxaban 10 mg orally per day until post-operative day 5, followed by ASA 81 mg daily for an additional 9 days following total knee arthroplasty or for 30 days after total hip arthroplasty. [see Clinical Guide: Thromboprophylaxis: Orthopedic Surgery]

DOSING OF ASA:

- The usual antiplatelet dose of ASA is 81 mg daily. Higher doses increase the risk of adverse events with no evidence of increased efficacy.
- A single initial dose of 162 mg chewed or crushed is recommended in patients suffering an ACS event, and then indefinite therapy with 81 mg daily.
- An initial dose of 81 mg once daily should be utilized in patients suffering a TIA or ischemic stroke of noncardiac origin.

Note: For patients with a history of, or at risk of, gastrointestinal bleeding, co-administration of a gastroprotective agent should be considered (i.e. proton pump inhibitor (PPI), H₂ antagonist) or consideration given to an alternate antiplatelet agent such as clopidogrel.

ADVERSE EFFECTS OF ASA:

- Bruising and other minor bleeding is very common with use of ASA
- Dyspepsia
- The most common serious adverse effect of ASA is bleeding into the gastrointestinal tract (which is dose-related)
- Allergic reactions, asthma (may be severe)

PERI-PROCEDURAL MANAGEMENT FOR PATIENTS TAKING ASA:

Patients receiving ASA and:

- a) undergoing an invasive diagnostic test,

- i. associated with a low risk of bleeding, should continue ASA without interruption.
 - ii. associated with a high risk of bleeding, should discontinue ASA 7 to 10 days prior to the procedure.
 - iii. Patients with coronary stents deserve special consideration, and consultation with a specialist is advised.
- b) undergoing arthrocentesis, continue ASA through the time of the procedure.
 - c) undergoing a minor surgery, dental, eye, or skin procedure, generally continue ASA around the time of the procedure.
 - d) undergoing elective major non-cardiac surgery, should discontinue ASA 7 to 10 days prior to the procedure except in those undergoing carotid endarterectomy, or with recent coronary artery stenting. When ASA is interrupted, it should be resumed when the risk of bleeding related to surgery has passed, between 8 to 10 days after major noncardiac surgery (See Clinical Guide: Perioperative Management of Antiplatelet Therapy).
 - e) undergoing coronary artery bypass grafting (CABG), should continue ASA (See Clinical Guide: Perioperative Management of Antiplatelet Therapy).

SPECIAL CONSIDERATIONS:

- 1) **Concomitant use of therapeutic doses of anticoagulants and ASA** is discouraged and should only be considered in patients with an indication for anticoagulation who are at relatively low bleeding risk AND have one of the following indications:
 - i. Recent ACS
 - ii. Recent PCI +/- coronary artery stent
 - iii. High risk prosthetic heart valve (e.g. older generation valve or mitral valve replacement with atrial fibrillation, LV dysfunction or previous systemic embolus on therapeutic anticoagulation)
 - iv. Proven TIA/ischemic stroke while on therapeutic doses of anticoagulation alone

In **most** other patients taking ASA, if anticoagulation is started, the ASA should be stopped.
- 2) Patients taking ASA for vascular protection should avoid the concomitant use of **NSAIDs**. If a patient taking low-dose ASA for vascular protection requires an anti-inflammatory agent, specific cyclooxygenase-2 inhibitors should be chosen over traditional NSAIDs.
- 3) ASA should be avoided or used with caution in patients with **asthma or nasal polyps**, in those at **high risk of bleeding** or with recent major bleeding, and in patients with **severe thrombocytopenia** or with familial or **acquired bleeding disorders**.

PEDIATRICS:

When possible, pediatricians with expertise in thromboembolism should be involved when ASA is being considered for antiplatelet therapy. When this is not possible, a combination of a neonatologist/pediatrician and an adult hematologist, supported by consultation with an experienced pediatric hematologist, is recommended.

OTHER RELEVANT THROMBOSIS CANADA CLINICAL GUIDES:

- Mechanical and Bioprosthetic Heart Valves: Anticoagulant Therapy
- Perioperative Management of Antiplatelet Therapy
- Peripheral Arterial Disease
- Stroke: Secondary Prevention
- Thromboprophylaxis: Orthopedic Surgery
- Venous Thromboembolism: Duration of Treatment

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Date of Version: 2018July 24

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