藥訊

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手術前後該如何服用抗血栓藥品？

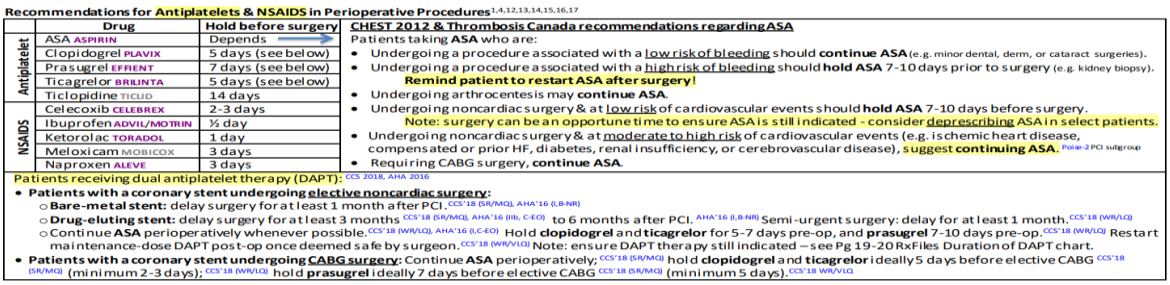
曾煌証藥師

某日民眾致電藥局，詢問明天或下週要拔牙，有吃抗血栓藥物，請問藥師要怎麼辦呢?這是門診藥師常會接到的諮詢電話，過去會依病人服用的抗血栓藥物特性提供停藥的天數，而參考美國及歐洲建議準則：「牙科執行拔除一至三顆牙齒、牙周手術與植牙等術式，並不需要停止新型抗凝血劑或改變原本用藥處方」。因此，對於低出血風險的拔牙手術，一般而言是不需要停藥的。不過牙醫師是主要負責手術者，出血風險及處置還是交由牙醫師評估。因此建議民眾，要詢問牙醫師的意見才能確保整個手術過程中的安全。

醫師會根據手術出血風險及病人發生栓塞可能評估手術前後該如何服用抗血栓藥品。一般來說簡單的門診小手術屬於極低/低出血風險，例如白內障手術、洗牙、拔牙、表淺皮膚手術或是不切除息肉的胃鏡等，不需停用抗血栓藥品；而中度或高度出血風險的手術，例如：心臟手術(CABG 或瓣膜置換)、胃造口術、內視鏡止血等，則需根據抗血栓藥品的種類、病人發生栓塞的可能性及病人的

檢驗數值（如腎功能或凝血功能），由醫師來決定需要如何停用抗

血栓藥品(可見下表)。



Recommendations for Antiplatelets & NSAIDS in Perioperative Procedures[1,4,12,13,14,15,16,17]

	Drug	Hold before surgery
Antiplatelet	ASA ASPIRIN	Depends
	Clopidogrel PLAVIX	5 days (see below)
	Prasugrel EFFIENT	7 days (see below)
	Ticagrelor BRILINTA	5 days (see below)
	Ticlopidine TICLID	14 days
NSAIDS	Celecoxib CELEBREX	2-3 days
	Ibuprofen ADVIL/MOTRIN	½ day
	Ketorolac TORADOL	1 day
	Meloxicam MOBICOX	3 days
	Naproxen ALEVE	3 days

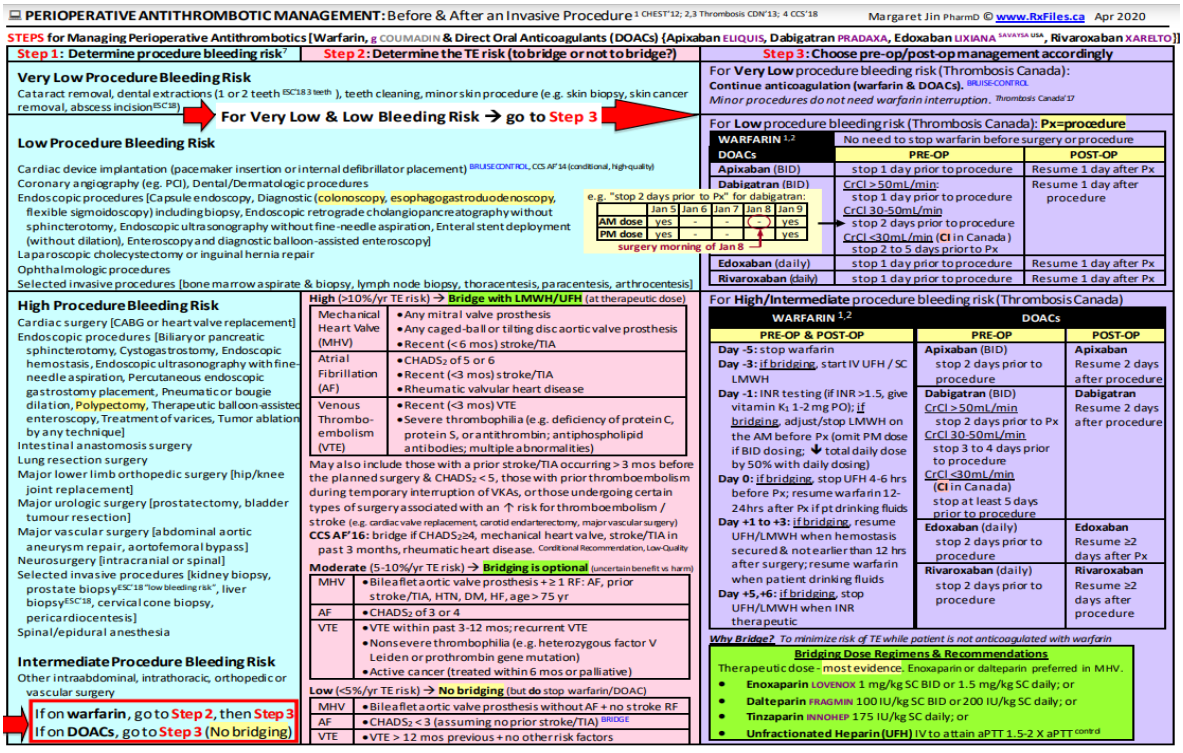
CHEST 2012 & Thrombosis Canada recommendations regarding ASA

Patients taking **ASA** who are:

- Undergoing a procedure associated with a low risk of bleeding should **continue ASA** (e.g. minor dental, derm, or cataract surgeries).
- Undergoing a procedure associated with a high risk of bleeding should **hold ASA** 7-10 days prior to surgery (e.g. kidney biopsy).
  Remind patient to restart ASA after surgery!
- Undergoing arthrocentesis may **continue ASA**.
- Undergoing noncardiac surgery & at low risk of cardiovascular events should **hold ASA** 7-10 days before surgery.
  Note: surgery can be an opportune time to ensure ASA is still indicated - consider deprescribing ASA in select patients.
- Undergoing noncardiac surgery & at moderate to high risk of cardiovascular events (e.g. ischemic heart disease, compensated or prior HF, diabetes, renal insufficiency, or cerebrovascular disease), suggest **continuing ASA**. Poise-2 PCI subgroup
- Requiring CABG surgery, **continue ASA**.

Patients receiving dual antiplatelet therapy (DAPT): CCS 2018, AHA 2016

- **Patients with a coronary stent undergoing elective noncardiac surgery:**
  - **Bare-metal stent:** delay surgery for at least 1 month after PCI. CCS'18 (SA/MQ), AHA'16 (I,B-NR)
  - **Drug-eluting stent:** delay surgery for at least 3 months CCS'18 (SA/MQ), AHA'16 (IIb, C-EO) to 6 months after PCI. AHA'16 (I,B-NR) Semi-urgent surgery: delay for at least 1 month. CCS'18 (WR/LQ)
  - Continue **ASA** perioperatively whenever possible. CCS'18 (WR/LQ), AHA'16 (I,C-EO) Hold **clopidogrel** and **ticagrelor** for 5-7 days pre-op, and **prasugrel** 7-10 days pre-op. CCS'18 (WR/LQ) Restart maintenance-dose DAPT post-op once deemed safe by surgeon. CCS'18 (WR/V/LQ) Note: ensure DAPT therapy still indicated – see Pg 19-20 RxFiles Duration of DAPT chart.
- **Patients with a coronary stent undergoing CABG surgery:** Continue **ASA** perioperatively; CCS'18 (SA/MQ) hold **clopidogrel** and **ticagrelor** ideally 5 days before elective CABG CCS'18 (SA/MQ) (minimum 2-3 days); CCS'18 (WR/LQ) hold **prasugrel** ideally 7 days before elective CABG CCS'18 (SA/MQ) (minimum 5 days). CCS'18 WR/V/LQ



PERIOPERATIVE ANTITHROMBOTIC MANAGEMENT: Before & After an Invasive Procedure [1 CHEST'12; 2,3 Thrombosis CDN'13; 4 CCS'18] Margaret Jin PharmD © www.RxFiles.ca Apr 2020

STEPS for Managing Perioperative Antithrombotics [Warfarin, g COUMADIN & Direct Oral Anticoagulants (DOACs) {Apixaban ELIQUIS, Dabigatran PRADAXA, Edoxaban LIXIANA SAVAYSA USA, Rivaroxaban XARELTO}]

Step 1: Determine procedure bleeding risk[7] | **Step 2: Determine the TE risk (to bridge or not to bridge?)** | **Step 3: Choose pre-op/post-op management accordingly**

Very Low Procedure Bleeding Risk

Cataract removal, dental extractions (1 or 2 teeth ESC'18 3 teeth), teeth cleaning, minor skin procedure (e.g. skin biopsy, skin cancer removal, abscess incision ESC'18)

For Very Low & Low Bleeding Risk → go to Step 3

Low Procedure Bleeding Risk

Cardiac device implantation (pacemaker insertion or internal defibrillator placement) BRUISECONTROL, CCS AF'14 (conditional, high-quality)
Coronary angiography (eg. PCI), Dental/Dermatologic procedures
Endoscopic procedures [Capsule endoscopy, Diagnostic (colonoscopy, esophagogastroduodenoscopy, flexible sigmoidoscopy) including biopsy, Endoscopic retrograde cholangiopancreatography without sphincterotomy, Endoscopic ultrasonography without fine-needle aspiration, Enteral stent deployment (without dilation), Enteroscopy and diagnostic balloon-assisted enteroscopy]
Laparoscopic cholecystectomy or inguinal hernia repair
Ophthalmologic procedures
Selected invasive procedures [bone marrow aspirate & biopsy, lymph node biopsy, thoracentesis, paracentesis, arthrocentesis]

High Procedure Bleeding Risk

Cardiac surgery [CABG or heart valve replacement]
Endoscopic procedures [Biliary or pancreatic sphincterotomy, Cystogastrostomy, Endoscopic hemostasis, Endoscopic ultrasonography with fine-needle aspiration, Percutaneous endoscopic gastrostomy placement, Pneumatic or bougie dilation, Polypectomy, Therapeutic balloon-assisted enteroscopy, Treatment of varices, Tumor ablation by any technique]
Intestinal anastomosis surgery
Lung resection surgery
Major lower limb orthopedic surgery [hip/knee joint replacement]
Major urologic surgery [prostatectomy, bladder tumour resection]
Major vascular surgery [abdominal aortic aneurysm repair, aortofemoral bypass]
Neurosurgery [intracranial or spinal]
Selected invasive procedures [kidney biopsy, prostate biopsy ESC'18 "low bleeding risk", liver biopsy ESC'18, cervical cone biopsy, pericardiocentesis]
Spinal/epidural anesthesia

Intermediate Procedure Bleeding Risk

Other intraabdominal, intrathoracic, orthopedic or vascular surgery

If on **warfarin**, go to **Step 2**, then **Step 3**
If on **DOACs**, go to **Step 3** (No bridging)

High (>10%/yr TE risk) → **Bridge with LMWH/UFH** (at therapeutic dose)

Mechanical Heart Valve (MHV)	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (< 6 mos) stroke/TIA
Atrial Fibrillation (AF)	• $CHADS_2$ of 5 or 6 • Recent (<3 mos) stroke/TIA • Rheumatic valvular heart disease
Venous Thrombo-embolism (VTE)	• Recent (<3 mos) VTE • Severe thrombophilia (e.g. deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)

May also include those with a prior stroke/TIA occurring > 3 mos before the planned surgery & $CHADS_2$ < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an ↑ risk for thromboembolism / stroke (e.g. cardiac valve replacement, carotid endarterectomy, major vascular surgery)
CCS AF'16: bridge if $CHADS_2$≥4, mechanical heart valve, stroke/TIA in past 3 months, rheumatic heart disease. Conditional Recommendation, Low-Quality

Moderate (5-10%/yr TE risk) → **Bridging is optional** (uncertain benefit vs. harm)

MHV	• Bileaflet aortic valve prosthesis + ≥ 1 RF: AF, prior stroke/TIA, HTN, DM, HF, age > 75 yr
AF	• $CHADS_2$ of 3 or 4
VTE	• VTE within past 3-12 mos; recurrent VTE • Nonsevere thrombophilia (e.g. heterozygous factor V Leiden or prothrombin gene mutation) • Active cancer (treated within 6 mos or palliative)

Low (<5%/yr TE risk) → **No bridging** (but do stop warfarin/DOAC)

MHV	• Bileaflet aortic valve prosthesis without AF + no stroke RF
AF	• $CHADS_2$ < 3 (assuming no prior stroke/TIA) BRIDGE
VTE	• VTE > 12 mos previous + no other risk factors

For **Very Low** procedure bleeding risk (Thrombosis Canada):
Continue anticoagulation (warfarin & DOACs). BRUISE-CONTROL
Minor procedures do not need warfarin interruption. Thrombosis Canada'17

For **Low** procedure bleeding risk (Thrombosis Canada): **Px=procedure**

WARFARIN [1,2]	No need to stop warfarin before surgery or procedure	
DOACs	**PRE-OP**	**POST-OP**
Apixaban (BID)	stop 1 day prior to procedure	Resume 1 day after Px
Dabigatran (BID)	CrCl > 50mL/min: stop 1 day prior to procedure CrCl 30-50mL/min stop 2 days prior to procedure CrCl <30mL/min (**CI** in Canada) stop 2 to 5 days prior to Px	Resume 1 day after procedure
Edoxaban (daily)	stop 1 day prior to procedure	Resume 1 day after Px
Rivaroxaban (daily)	stop 1 day prior to procedure	Resume 1 day after Px

e.g. "stop 2 days prior to Px" for dabigatran:

	Jan 5	Jan 6	Jan 7	Jan 8	Jan 9
AM dose	yes	-	-	-	yes
PM dose	yes	-	-		yes

surgery morning of Jan 8

For **High/Intermediate** procedure bleeding risk (Thrombosis Canada)

WARFARIN [1,2]		DOACs	
PRE-OP & POST-OP		**PRE-OP**	**POST-OP**
Day -5: stop warfarin **Day -3:** if bridging, start IV UFH / SC LMWH **Day -1:** INR testing (if INR >1.5, give vitamin K_1 1-2 mg PO); if bridging, adjust/stop LMWH on the AM before Px (omit PM dose if BID dosing; ↓ total daily dose by 50% with daily dosing) **Day 0:** if bridging, stop UFH 4-6 hrs before Px; resume warfarin 12-24hrs after Px if pt drinking fluids **Day +1 to +3:** if bridging, resume UFH/LMWH when hemostasis secured & not earlier than 12 hrs after surgery; resume warfarin when patient drinking fluids **Day +5, +6:** if bridging, stop UFH/LMWH when INR therapeutic		**Apixaban** (BID) stop 2 days prior to procedure	**Apixaban** Resume 2 days after procedure
		Dabigatran (BID) CrCl > 50mL/min stop 2 days prior to Px CrCl 30-50mL/min stop 3 to 4 days prior to procedure CrCl <30mL/min (**CI** in Canada) stop at least 5 days prior to procedure	**Dabigatran** Resume 2 days after procedure
		Edoxaban (daily) stop 2 days prior to procedure	**Edoxaban** Resume ≥2 days after Px
		Rivaroxaban (daily) stop 2 days prior to procedure	**Rivaroxaban** Resume ≥2 days after procedure

Why Bridge? *To minimize risk of TE while patient is not anticoagulated with warfarin*

Bridging Dose Regimens & Recommendations

Therapeutic dose - most evidence. Enoxaparin or dalteparin preferred in MHV.

- **Enoxaparin** LOVENOX 1 mg/kg SC BID or 1.5 mg/kg SC daily; or
- **Dalteparin** FRAGMIN 100 IU/kg SC BID or 200 IU/kg SC daily; or
- **Tinzaparin** INNOHEP 175 IU/kg SC daily; or
- **Unfractionated Heparin (UFH)** IV to attain aPTT 1.5-2 X aPTT control

資料來源：

References- Perioperative Management – Before & After an Invasive Procedure