

CLINICAL PROBLEM SET # 14

Patient
Male, 68 years old
Chief Complaint
"My back tooth on the left started bothering me last week, so I have been taking Advil since. But the toothache did not go away, and I see blood when I brush my teeth. Oh, and last night I noticed white stuff in the back of my mouth, but it is not painful."
Background and/or Patient History
Two-vessel coronary artery bypass graft 5 yrs ago Balloon angioplasty 2 yrs ago Idiopathic Hypertension Last visit with dentist was 3 years ago. Medications: Hydrochlorothiazide Ramipril <i>He used to take Warfarin (Coumadin®), but has recently been switched to:</i> Dabigatran (Pradaxa®) Aspirin 81 mg ("baby aspirin")
Current Findings
Extensive endodontic damage of teeth #14 and #15. White lesions in the tonsillar pillar regions on both sides, consistent with the clinical presentation of Candidiasis. Temp: 99.1 F BP: 145/90 mmHg HR: 75 bpm

I. Should the dentist stop any of the prescription medications before dental surgery on this patient? If so, which one(s) and why? If not, what would be the best alternative course of action?

II. If dental extractions needed to be done during this first visit, would the patient-initiated treatment with Ibuprofen (Advil®) have any impact on the treatment plan and the potential outcomes?

III. Now let's assume that the patient is still on Warfarin.

1. What tests and their results would assure an acceptable risk of bleeding in this patient during dental procedures?
2. How would the risk of intraoperative bleeding be affected (increased/decreased) by:
 - A. Fluconazole, an antifungal agent, known to strongly inhibit CYP2C9?;
 - B. a drug that induces CYP2C9?;
 - C. a drug that competes with Warfarin for CYP2C9?
 - D. a drug that is highly bound to plasma proteins?
 - E. Vitamin K-enriched diet (e.g., green leafy vegetables)?

Which of the following describes the mechanism of action of Clopidogrel?

Its active metabolite binds to the platelet glycoprotein (GP) IIb/IIIa receptors	A
Its active metabolite binds to the platelet ADP receptors	B
It irreversibly inhibits Cyclooxygenase	C
It facilitates the action of Antithrombin III	D
It directly binds to Thrombin	E

Answer: B

Clopidogrel is a prodrug

Relative to Enoxaparin, Unfractionated Heparin:

has a longer half-life	A
is monitored by prolongation of aPTT	B
does not cause thrombocytopenia	C
is less likely to be given intravenously	D
is less likely to induce an autoimmune response leading to thrombosis	E

Answer: B

Enoxaparin is low molecular weight heparin.

A: unfractionated has shorter half-life

B: it takes longer for coagulation because this is anti-platelet

C: thrombocytopenia is decreased number of platelets

Which of the following anticoagulants is a direct inhibitor of Thrombin?

Abciximab	A
Dabigatran	B
Rivaroxaban	C
Warfarin	D
Tranexamic Acid	E

Answer: B

A: is not anti-coagulant, is anti-platelet

C: Xa inhibitor

D: vit K reductase inhibitor

E: not anticoagulant, is antifibrinolytic (opposite effect)

Suddenly stopping Apixaban can lead to:

Anaphylaxis	A
Excess bleeding	B
Increase in INR	C
Ischemic Stroke	D
Thrombocytopenia	E

Answer: D

Apixaban is Xa inhibitor, anti-coagulant, so risk of excess bleeding when used chronically.

B: If you suddenly stop it you will not have the risk of excess bleeding is if you overdosed

A: allergic response to drug, not something you get when removing drug

C: INR is not a good way to monitor factor 10, and if anything it would decrease INR

E: this would be from adding the drug, not stopping

The following test would accurately determine the coagulation status of a patient taking Apixaban:

aPTT	A
Factor Xa assay	B
INR	C
PT	D
TT	E

Answer: B

Factor Xa assay uses antibody for it

The other tests are not sensitive for this inhibitor

D: measures fibrinogen and fibrin levels, extrinsic pathway, factor 7, factors dependent on vitK

Allelic variants of CYP2C9 can result in up to 90% reduction in Warfarin clearance because up to 99% of circulating Warfarin is biologically inactive (bound to plasma albumin).

Both the statement and the reason are correct and related.	A
Both the statement and the reason are correct but not related.	B
The statement is correct, but the reason is not.	C
The statement is not correct, but the reason is correct.	D
Neither the statement nor the reason is correct.	E

Answer: B

The first part is about metabolism and the second part about protein binding

The mechanisms of interaction between Warfarin and Antibiotics involve:

increase in gut microflora-derived Vitamin K; CYP2C9 inhibition	A
decrease in gut microflora-derived Vitamin K; CYP2C9 inhibition	B
increase in gut microflora-derived Vitamin K; CYP2C9 induction	C
decrease in gut microflora-derived Vitamin K; CYP2C9 induction	D
None of the above is correct because Warfarin is metabolized only by CYP3A4	E

Answer: B

Antibiotics inhibit CYP2C9, microflora produce vit K

Laboratory analysis shows INR of 7.0 for a patient on Warfarin. The patient should immediately be treated by:

increasing the dose of Warfarin and administration of Vitamin K	A
discontinuing Warfarin and administration of Vitamin K	B
administration of Aminocaproic Acid or Tranexamic Acid	C
administration of Desmopressin	D
administration of Protamine	E

Answer: B

Meaning PT is approx. 7 times longer than it should be so Warfarin would make the situation worse because it would increase the time so administer the substrate for the enzyme that got inhibited by warfarin (vit K)
C: these are anti-fibrinolytic so they improve hemostasis but the key is to **target the mechanism** that caused the problem
E: antidote for heparin

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"...On slide 7 you list some dangerous drug combinations in Dentistry (...)
go over these interactions with some more context
of perhaps how they interact and areas of interaction to watch...."
Kunal Mansukhani

The Most Dangerous Drug Combinations Relevant to Dentistry:

Epinephrine in Local Anesthetics with:

Propranolol (non-selective beta-adrenergic antagonist)

NSAIDs with:

Diuretics and Renin-Angiotensin-Aldosterone System inhibitors (triple therapy)

Lithium (mood stabilizer-Bipolar Disorder)

Warfarin (anticoagulant) with:

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Metronidazole and Fluconazole

Sulfonamides, Macrolide and Quinolone antibiotics

February 26, 2021

Should the dentist stop any of the prescription medications?

YES

A

NO

B

Any of the anticoagulants?
NO

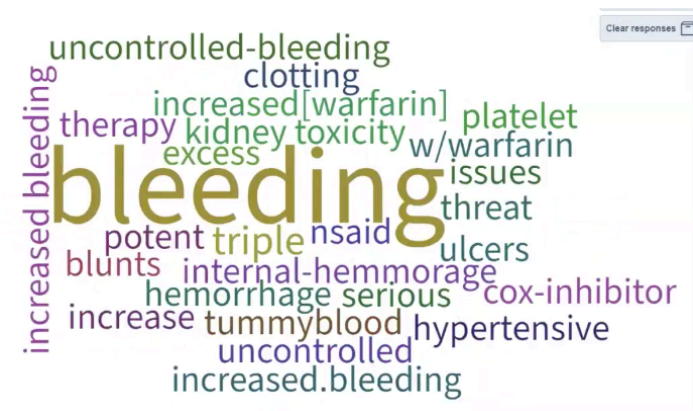
In a SHORT PHRASE, what would be the best first step?

Patient had serious heart surgery so dentist should not make decisions about anti-platelet drugs or other drugs patient is taking



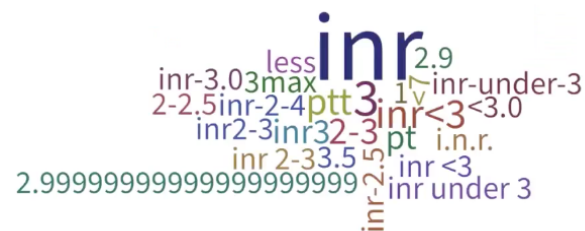
They should consult with the physician. This is very serious. Maybe it is better for the patient to not receive dental treatment.

In ONE WORD or a SHORT PHRASE, what is the additional risk with Ibuprofen (Advil)?



Triple therapy of diuretic and RAA-inhibitor and ibuprofen has risk of bleeding, consider their hemostasis abilities is compromised by the NSAIDs

In ONE WORD and ONE NUMBER: With Warfarin, what test and value would assure an acceptable risk of bleeding?



INR<3 , 2-3

If patient takes warfarin they take it for a reason and if it is below 2, then the anticoagulation is basically not effective, so below 2 the patient is at risk of ischemic stroke

For a patient on Warfarin, adding FLUCONAZOLE, a CYP2C9 inhibitor, would make the risk of bleeding:

Higher	A
Lower	B

Higher because it inhibits the enzyme that degrades warfarin

For a patient on Warfarin, adding a CYP2C9 inducer would make the risk of bleeding:

Higher	A
Lower	B

Lower, but increased risk of blood clotting and issues associated with that

For a patient on Warfarin, adding a drug that competes with Warfarin for CYP2C9 would make the risk of bleeding:

Higher	A
Lower	B

Higher risk of bleeding because less warfarin is metabolized

For a patient on Warfarin, adding a drug that is highly bound to plasma proteins would make the risk of bleeding:

Higher	A
Lower	B

Warfarin cannot bind so more free warfarin so risk of bleeding is higher

For a patient on Warfarin, adding Vitamin K-rich foods to the diet would make the risk of bleeding:

Higher	A
Lower	B

Lower

Those patients are asked to watch their diets and if they add green leafy vegetables they are supposed to increase the warfarin

Relative to Aspirin 81 mg, Aspirin 325 mg stronger inhibits platelet aggregation. Reduce dose of Clopidogrel in liver cirrhosis.

Both statements are true.	A
Both statements are false.	B
The first statement is true, the second is false.	C
The first statement is false, the second is true.	D

Answer: B

For anti platelet effect 81mg is not less effective than 325, you don't need higher dose.
Clopidogrel is prodrug. You don't reduce the dose, you would increase or use a different drug that is not requiring liver to make it effective.

Thrombocytopenia in response to unfractionated Heparin. Which parenteral anticoagulation is a viable alternative?

Abciximab	A
Alteplase	B
Bivalirudin	C
Dalteparin	D
intravenous Vitamin K	E

Answer: C

A: anti-platelet, not anti-coagulant
B: fibrinolytic, we want to prevent coagulation, would be used if you already have MI or stroke
C: direct thrombin inhibitor
D: low molecular weight heparin
E: not anti-coagulant, is pro-coagulant