PHC721 - CLINICAL PROBLEM SET # 10

Patient
Male, 62 years old
Chief Complaint
"Last week, I lost a filling in my lower tooth on the right side."
Background and/or Patient History
Atherosclerosis; Diabetes, Type 2, poorly controlled; Diabetic neuropathy; Myocardial Infarction (6 years ago); Obesity; Peptic Ulcer Disease; Alcohol abuse (> 10 years); Smokes tobacco, 40-pack-years Medications: Cimetidine (Tagamet®), H2 receptor antagonist Clopidogrel Digoxin Metformin, anti-diabetic, 500 mg twice daily Propranolol
Current Findings
Acetone smell in patient's breath. A missing filling in #30 – restorable. Temp: 98.8 F BP: 120/75 mmHg HR: 64 bpm 240 lb; BMI: 35

1. How would the patient's systemic health condition affect the local anesthesia administered for the tooth restoration procedure?

A. Upon contact with the extracellular fluid, is the ionized fraction of the local anesthetic expected to be larger or smaller?

B. Is the onset of the anesthesia expected to be normal, faster or slower?

2. Propranolol is a weak base, highly bound to plasma proteins (primarily alpha-1-acid glycoprotein), non-selective competitive antagonist of beta-adrenergic receptors. It is known to reduce hepatic blood flow.
If a poorly-trained dentist decided to use Lidocaine with Epinephrine for local anesthesia in this patient:

A. How would the efficacy, potency, Emax, and EC50 of Epinephrine acting through beta-adrenergic receptors be affected by Propranolol?

B. How would the risk of Lidocaine systemic toxicity be affected by Propranolol? Please explain the underlying mechanisms.

3. What are other patient-related factors or medications that would be likely to affect the severity of a potential systemic toxicity of Lidocaine?

4. What are other potential drug interactions in this patient?

5. Metformin (CL 500 mL/min, Oral Bioavailability (F) 50%), is excreted unchanged by the kidney.

A. Assuming the patient takes Metformin as prescribed (no skipped doses or increased intervals between doses) and there are no patient- or drug-related modifiers, what is the expected plasma concentration of Metformin?

B. How would the plasma concentration of Metformin be affected by other conditions or medications of this patient?

6. PHARMACODYNAMICS BONUS:
Imagine you have a full arsenal of agonists and antagonists (competitive and non-competitive) for: **1)** the receptor mediating desired (therapeutic) actions of a drug, and **2)** the receptor responsible for the drug's toxic effects. Which of the pharmacological tools would you use to **increase the Therapeutic Index** of that drug?