



Systematic Review of the Medication List: A Resource for Risk Assessment and Dental Management

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ABSTRACT Polypharmacy, besides representing a risk in and of itself, points to the potential risk the underlying diseases that necessitated the drugs can present in the dental office. These diseases and medications can also present a risk to oral health. A sequence for categorizing drugs in a medication list is presented here to aid in the identification of potential risks in the dental treatment and management of patients with complex medical histories and drug regimens.

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As our population ages and people live longer, with more chronic diseases and longer medication lists, identifying potential risks for the dental patient becomes more difficult. By the year 2030, the number of Californians aged 65 and older will have increased by 130 percent from the year 2000.¹ Approximately 20 percent of people over age 65 take at least five medications, not including over-the-counter products.² In California, 45 percent of adults have one or more chronic conditions including diabetes, asthma, hypertension, and heart disease or rate their health as fair or poor.³ A systematic method for breaking down a lengthy drug list that will not only help highlight medication

issues, but also emphasize important considerations in caring for a medically complex population, is presented here.

Prior to administering a drug or writing a prescription, three questions should always be asked:

- Is this person allergic to this drug?
- Have they experienced an adverse drug reaction while taking it?
- Could the drug I plan to prescribe interact with any of the patient's current drug regimen?

These are basic requirements for keeping patients safe as dentists administer and prescribe drugs to them, whether they are taking many prescription drugs or none. Any patient can have an adverse drug reaction to single or multiple drugs as an expected or unexpected side effect.⁴

However, familiarity with drugs commonly used by patients with increasingly complex medical problems will help us identify potentials for problems in the dental management of these patients. These problems may arise from the use of the drug alone or by virtue of the fact they have a disease that requires management with a particular drug.

The fact that the patient is on medication suggests they have underlying disease with which dental professionals should be concerned. Some medications are prescribed in the event of an emergency. Some of the conditions for which the medications are prescribed will require laboratory evaluation to determine the risk of an adverse outcome. Some will require consultation with the patient's physician regarding alteration of their drug regimen or use in concert with other medication.

Some drugs may alter what a dentist chooses to prescribe. Some will require alteration of a dental treatment plan, treatment regimen, or plan for maintenance. In all cases, it is important to identify these potential risks when first evaluating the patient or upon review of any new diagnoses and medications with which a patient may present at any given appointment.

See **TABLE 1** for drugs that should draw the practitioner's attention.

Drugs Needed in the Event of Emergency

Any patient could have a medical emergency in the office at any time, even before they are called from the waiting room. The first drugs to look for on a medication list are those that may be necessary in an emergency, such as nitroglycerin used for angina or bronchodilators inhaled during acute exacerbation of chronic obstructive pulmonary

TABLE 1

Four Categories and Examples of Drugs That Should Draw Attention in a Medication List

DRUGS NEEDED IN THE EVENT OF EMERGENCY

- nitroglycerin
- short-acting bronchodilators — inhalers (albuterol, pirbuterol)

DRUGS THAT HAVE THE POTENTIAL TO RESULT IN AN ADVERSE EVENT OR TELL US THE PATIENT IS AT HIGHER RISK FOR AN ADVERSE EVENT

- insulin
- anti-coagulants (warfarin [Coumadin], clopidogrel [Plavix], aspirin, NSAIDS)
- bisphosphonates (alendronate [Fosamax], ibandronate [Boniva], zoledronic acid [Zometa], clodronate [Bonefos])
- chemotherapeutics (vincristine, 5-fluorouracil, methotrexate, doxorubicin)
- immunosuppressants (prednisone, cyclosporin)
- MAO inhibitors (isocarboxazid [Marplan], phenelzine [Nardil], and tranylcypromine [Parnate])
- opioids (methadone, Fentanyl, Pentazocine)
- recreational drug use
- sedative hypnotics (diazepam [Valium], alprazolam [Xanax], alcohol)

DRUGS THAT HAVE A SPECIFIC AND POTENTIALLY SIGNIFICANT ADVERSE INTRAORAL SIDE EFFECT

- ACE inhibitors (captopril [Capoten], enalapril [Vasotec], lisinopril [Zestril])
- calcium channel blockers (amlodipine [Norvasc], felodipine [Plendil], nifedipine [Procardia, Adalat])
- cyclosporin (Sandimmune)
- phenytoin (Dilantin)
- xerostomic medications (e.g., anti-hypertensives, diuretics, antidepressants, antihistamines)
- chemotherapeutics (vincristine, 5-fluorouracil, methotrexate, doxorubicin)

OVER-THE-COUNTER AND NATURAL DRUGS THAT MAY CONTRIBUTE TO AN ADVERSE TREATMENT OUTCOME

- | | |
|-----------------|--|
| ■ Aspirin | ■ St. John's wort |
| ■ Ibuprofen | ■ Echinacea |
| ■ Feverfew | ■ Ephedra (ma-huang) |
| ■ Garlic | ■ Bitter orange |
| ■ Ginger | ■ Valerian |
| ■ Ginkgo biloba | ■ Kava kava |
| ■ Gilberry | ■ Dong quai ^{5,7,8,11,12,15,16} |

disease.^{5,6} While it is important to stress to patients they need to bring these medications with them to each appointment, it is also necessary to keep these medications in an emergency

kit. If the patient brings them to each appointment, they should place them out at each visit so time is not wasted looking through their belongings for the medication during an emergency.

TABLE 2

Drugs That Have a Potential to Result in an Adverse Effect or Indicate That the Patient Is at High Risk for an Adverse Event^{4,6,15,17}

Drug Groups	Example Drugs	Potential Management Problems
Anti-coagulants	Aspirin, warfarin* (Coumadin)	Excessive bleeding
Immunosuppressants	Corticosteroids* Azathioprine (Imuran)	Increase risk of bacterial and fungal infection, poor stress response
Chemotherapeutic agents	Vincristine (Oncovin) Methotrexate (Rheumatrex)	Delayed healing, mucositis, fungal infections
Sedative hypnotics*, narcotics, barbiturates	Tylenol #3, diazepam (Valium), meperidine (Demerol)	Fall risk, respiratory suppression
Hypoglycemics	Insulin*, sulfonylureas	Hypoglycemia
Bisphosphonate bone stabilizers (esp. IV bisphosphonates)	Pamidronate (Aredia) Zoledronic acid (Zometa) Alendronate (Fosamax)	Delayed bone healing, Bone necrosis
Recreational drugs	Alcohol, cocaine, heroine	Drug interactions Respiratory suppression Liver function Pain control
Opioid analgesics, anti-addictive	Methadone (Amidone)	Pain control Liver function Respiratory suppression

* Denotes drugs that are highly titrated with a narrow margin of safety¹⁵

Drugs That have the Potential to Result in an Adverse Event or Indicate the Patient Is at Higher Risk for an Adverse Event

The second group of drugs to identify is those that may contribute to an adverse treatment outcome or adverse event in the office. Many of these drugs have a narrow margin of safety and are highly titrated (TABLE 2). One of the most recognizable in this group is insulin. Insulin itself is not generally a problem in the provision of care, but it does give some information about the patient. The first is that they are risk of developing hyper- or hypoglycemia in the office. Instructions must be clear to the patient that they follow their usual medication and diet regimen prior to treatments. An in-office finger stick blood sugar test can be useful to assess patient status prior to treatment. If they are not able to eat for some time after treatment, for instance, following multiple extractions or extensive periodontal surgery, a physician

consultation should be completed to determine if this regimen should be altered on the side of mild hyperglycemia for a short period to ensure they do not become hypoglycemic during the postoperative period.

The use of insulin by a patient with type 1 or type 2 diabetes should also signal this patient may be at risk of delayed healing or even infection following treatment. As opposed to a finger stick blood test that indicates only about that patient at the date and time given, a glycosylated hemoglobin test or HbA_{1c} is the test used to determine long-term control for the patient with diabetes. The target is generally 7 percent or less; however, this number may be altered by other conditions in older adults.⁵⁷ A physician consultation should be requested in order to determine their long-term control and whether or not this patient would benefit from a perioperative course of antibiotics. For patients who do not have well-controlled diabetes it is also important to inquire whether or not their kidney func-

tion may be impaired as a result of their disease, especially if they have been diagnosed with diabetes for many years. In these cases it is important to consider whether prescription dosages need to be changed as a result of impaired renal function (TABLE 3).

Anti-coagulants are drugs commonly used in the prevention of cardiac and cerebrovascular events such as myocardial infarction, atrial fibrillation, and stroke. Drugs such as aspirin, Plavix, and Coumadin are among the most commonly seen. While it is usually not necessary to alter these regimens, and, in fact, may present more of a risk than treating the patient on the drug, it is prudent to get the appropriate lab work to minimize the chance of excessive bleeding during or following a procedure.

While there are no recommended treatment modifications for patients taking clopidogrel (Plavix), there is still the potential for complications that arise as a result of anti-coagulant therapy, for

TABLE 3

Guidelines for Prescribing Commonly Used Drugs in Dentistry That Are Metabolized by the Kidney (Amoxicillin, Cephalosporin, Penicillin, Tetracycline) to Patients With Impaired Renal Function^{5,7,18}

Renal Function Test	Laboratory Value	Guideline for Dental Prescribing
Glomerular filtration rate (GFR)	<10 ml/min 10-50 ml/min >50 ml/min	One dose q 24 hrs One dose q 8-12 hours One dose q 8 hours

TABLE 4

Lab Values of Concern for Patients Receiving Chemotherapeutics, Immunosuppressants or Anti-coagulants That Could Result in Impaired Healing, Risk of Infection or Excessive Bleeding Following Dental Treatment^{5,7}

Test	Value of Concern	Consideration
Absolute neutrophil count (neutropenia)	Less than 500/mm ³	Antibiotic prophylaxis, consult MD if concurrent with chemotherapy prior to treatment
Lymphocyte count (lymphopenia)	Less than 1,500/mm ³	Patient is predisposed to fungal and viral infections
Granulocyte	Less than 2,000/mm ³	Consider antibiotic prophylaxis or delay tx
Platelet count (thrombocytopenia)	Less than 50,000/mm ³ Less than 10,000/mm ³	Consider platelet replacement or delay until count increases Risk of life threatening spontaneous bleeding
PFA-100	Greater than 175 seconds	Consider stopping aspirin for 3 days, with MD permission
INR	Greater than 3.0	Consider consultation with MD to decrease Coumadin dosage to reach desired INR

example excessive bleeding following procedures – although rare, neutropenia, thrombocytopenia and eccymoses. A PFA-100, platelet function analyzer 100, can be requested for the patients on aspirin. A PT and INR should be requested within 48 hours prior to surgery for those patients taking Coumadin.

As a general guideline, it is safe to treat a patient with an INR of 3.5 or less if only one or two teeth are to be removed. However, the general health condition of the patient should be taken into consideration. If the patient is having extensive oral surgery, has multiple medical conditions, has other conditions which may impair coagulation, is taking other drugs that may impair coagulation, or is of an advanced age, it may be best to work at an INR of 3.0 or less, or refer the patient to an oral surgeon, and/or complete the

treatment in a hospital setting in the event there is an adverse event during or following treatment.^{5,7} Practitioners should use their judgment in these cases based upon their knowledge of the patient as well as knowledge about their own skills.

When a patient is on anti-coagulants, attention should be paid to surgical technique to minimize trauma and tearing of adjacent tissues. Provide sutures or primary closure where possible. The use of topical hemostatic agents such as gel foam, Surgicel or Thrombostat should also be considered.⁵ Carefully review post-operative instructions with the patient or their caregiver to be sure they do not disrupt the clotting process after they have left the office. If the planned surgery is extensive and/or the patient is at risk for heavy or excessive bleeding, refer to a specialist for evaluation and treatment.

The use of oral bisphosphonates to manage patients with osteoporosis is becoming increasingly common. Many patients with breast cancer, multiple myeloma, prostate, renal, lymphatic, lung cancers, and many other cancers are receiving treatment with IV bisphosphonates. While these drugs are invaluable with regard to the management of these diseases, it has become evident that the use of these medications creates a risk of osteonecrosis following bony oral surgical procedures and sometimes from recurrent trauma such as from an ill-fitting prosthesis or even spontaneously secondary to untreated dental disease. Most practitioners will more commonly see patients taking oral bisphosphonates in their practices, which carries a much lower risk than the IV form. However, patients must be made aware of this risk prior to

TABLE 5

Guidelines for Prescribing Commonly Used Drugs in Dentistry That Are Metabolized by the Liver (Acetaminophen, Codeine, Diazepam, Erythromycin, Ibuprofen, Ketoconazole, Lidocaine, Lorazepam, Prednisone) to Patients With Impaired Hepatic Function^{5-7,18}

Liver Function Test	Normal Value	Guideline for Dental Prescribing
AST, ALT, liver transaminases	30-40 u/l	If greater than 4 times normal, do not use drugs that are toxic to or metabolized by the liver

consenting to or refusing procedures that place them at risk of osteonecrosis.^{8,9}

Patients taking the IV form of the medication to treat cancer should also be carefully evaluated prior to proceeding with dental treatment since they may also be taking immunosuppressants, placing them at risk for other adverse outcomes in the dental office.⁵ A physician consultation and thorough review of relevant laboratory values should be completed prior to treating patients taking immunosuppressants as they are at risk for poor healing and possibly excessive bleeding following treatment (TABLE 4). They may be suffering other adverse side effects of their treatment such as nausea, mucositis, or fatigue and may not be motivated to pursue or be able to tolerate general dental treatment at this time.^{5,7}

Dental practitioners can aid these patients by helping them create an individualized oral hygiene/prevention regimen and careful treatment planning during this time to minimize the adverse effects of their cancer treatment on their oral health. This will not only help maintain their oral health during this time, but it can maximize their potential to complete their cancer treatment by maintaining oral comfort and nutritional intake.⁵

Some of the more commonly prescribed immunosuppressants: glucocorticoids, cyclosporine, azathioprine (Imuran), methotrexate (Rheumatrex), and chemotherapeutics such as vincristine (Oncovin) may be readily recognizable to some practitioners.⁶ However, because there are so many drugs available and new drugs are constantly coming into use, it may be more efficient to review the medical history for conditions or diseases that may warrant their use, such

as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, organ transplant, or cancer and then carefully review the patient's medication list for the drugs used to manage these diseases.

As the name suggests, these drugs impair the immune system making the patient susceptible to delayed healing or infection following a procedure or refractory conditions such as periodontal disease, fungal infections, or other opportunistic infections. This may result in a need to aggressively treat recurrent or opportunistic infections and/or provide only palliative treatment until the cancer therapy is complete, assessing and reassessing laboratory values related to immune function and treating as appropriate.^{5,7}

Recreational drug use can also place a patient at risk for an adverse event in the dental office. It is important to ask patients about recreational drug use during review of the medical history and medication list. The information may need to be taken into consideration as determinations are made about the use of anesthetic with vasoconstrictors or pain medication that may be prescribed.⁵ Some patients may report they are on methadone to manage their drug addiction.⁶ In these cases it is appropriate to consult with the patient's physician and/or pharmacist with regard to the use of pain medications. Methadone also interacts with a number of drugs that might be prescribed in dentistry, such as anti-bacterial and anti-fungal drugs.⁶

Some patients may have impaired liver function, for example those who have abused alcohol or those who have hepatitis B or C secondary to IV drug use⁵ (TABLE 5). Working in conjunction with the patient's

physician and/or pharmacist is important in making sure their pain is adequately addressed while also reducing the chances for an adverse outcome as a result of medication choice or dosages prescribed. Patients who are on methadone or other opioids for chronic pain conditions also will benefit from coordinated care between the dentist, physician, and pharmacist to appropriately manage oral/dental pain. The use of opioids, sedative hypnotics, narcotics and barbiturates, by prescription or otherwise, alerts the practitioner that the patient is at risk for respiratory depression and possibly falls; and this should be taken into consideration if medication for pain or sedation is to be prescribed.^{5,6,15}

Antidepressants are another group of commonly prescribed medications. Most do not present a direct impact on the provision of oral health care, however the class of drugs known as MAO inhibitors can enhance the effect of vasoconstrictors such as epinephrine and levonordefrin and should be avoided.^{5,6} A careful cross-check for drug interactions should be completed prior to prescribing because these drugs also have a high potential for adverse drug interactions.⁶

Drugs That Have a Specific and Potentially Significant Adverse Intraoral Side Effect

The next group of drugs to consider is those that have specific intraoral side effects, such as gingival enlargement secondary to poor oral hygiene and use of calcium channel blockers used to treat hypertension, cyclosporine used to manage autoimmune disorders, and Dilantin used to manage seizure disorders.^{6,10,11} ACE inhibitors can cause lichenoid or ery-

TABLE 6

Strategies and Considerations for Managing Patients Taking Medications That Have Intraoral Side Effects^{5,7,10,11,15}

Side Effect	Drug Class	Example (Generic)	May Be Used to Treat	Strategies and Considerations
Xerostomia	Antihistamine	Claritin (loratadine)	Hay fever	Consider consultation with MD to inquire about a permanent or temporary change in medication to see if it resolves. If this is not possible, or if the patient is taking numerous drugs that impair salivary flow, provide palliative care and counsel patients about caries prevention.
	Antidepressant	Zoloft (sertraline)	Obsessive compulsive disorder	
	Calcium channel blocker	Norvasc (amlodipine)	High blood pressure	
	Diuretics	Lasix (furosemide)	High blood pressure	
Fungal infection	Antibiotics	Tetracap (tetracycline)	Periodontal disease	Emphasize good oral hygiene. Prescribe anti-fungals. Monitor for resolution and recurrence.
	Immunosuppressant	Cortan (prednisone)	Rheumatoid arthritis COPD	
Mucositis	Anti-neoplastic	Adrucil (5-fluorouracil)	Chemotherapeutic for breast cancer	Provide palliative care if not already done by oncologist. Develop individualized oral hygiene routine with the patient.
Gingival hyperplasia	Anti-convulsant	Dilantin (phenytoin)	Epilepsy	In all cases, advise patients that poor oral hygiene will contribute to the problem, create an individualized oral hygiene plan.
	Calcium channel blocker	Procardia (nifedipine)	High blood pressure	
	Immunosuppressant	Sandimmune (cyclosporin)	Prevent organ transplant rejection	
Stomatitis lichenoid reactions	ACE inhibitor	Capoten (captopril)	High blood pressure	To confirm diagnosis, consult with MD to inquire about a temporary change in medication to see if it resolves. If this is not an option, consider biopsy and/or careful history of and monitoring of the lesion.
	Diuretics	Thiazide (HCTZ)	High blood pressure	
Mucosal burns	Anti-inflammatory	Ecotrin (aspirin)	Osteoarthritis	Instruct patients to swallow, not dissolve, the aspirin.

thema multiforme reactions.^{6,7} And, there are a whole host of other medications that count xerostomia and diminished salivary flow as an oral side effect (TABLE 6).

Physician consultation may be required to inform the physician of the adverse effect and to inquire whether or not there is an alternative drug choice. It is important to provide the patient with strategies for minimizing or coping with these side effects, especially if there is not an alternative treatment for them. Subjects with significantly reduced salivary flow should be counseled with regard to caries prevention to limit the potentially disastrous effects of impaired salivary flow on the dentition.

Salivary substitutes and stimulants may be useful for these patients, especially those with prostheses who may be experiencing discomfort or difficulty wearing them due to their impaired salivary flow.

Patients who have salivary impairment as a result of head and neck radiation or Sjögren's disease may be prescribed pilocarpine or cevimeline to stimulate salivary flow, however these drugs should be used cautiously, particularly in patients of an advanced age and/or those who are medically compromised.^{5,7} They should not be used in patients with uncontrolled asthma, narrow angle glaucoma or severe hepatic impairment.⁶

Over-the-counter and Natural Drugs That may Contribute to an Adverse Treatment Outcome

There are several natural and over-the-counter medications that can play a role in adverse treatment outcomes. Valerian used for its sedative effects, often in the treatment of insomnia, can potentiate the adverse effects of sedative hypnotic or anti-anxiety medications that may be prescribed. Several other natural drugs can increase bleeding, such as St John's wort, Dong quai, Gingko biloba, garlic and ginger. Ephedra combined with anxiety and/or a vasoconstrictor can increase blood pressure and heart rate. Patients who take high

doses of aspirin or NSAIDs over-the-counter are also at risk in increased bleeding.¹²⁻¹⁴

Conclusion

Once a drug list is reduced to manageable segments and the potential risks identified, we can return to our original questions as we begin our treatment in the office or dismiss the patient with a prescription:

- Is the patient allergic to this drug?
- Have they had an adverse reaction to it?
- Could the drug I plan to prescribe interact with any of the drugs in the patient's current regimen?

This list of drugs and conditions that should draw the practitioner's attention is dynamic. Specific patient populations, such as pediatric, may have specific drugs or additional criteria that need to be considered.

As new drugs and treatments are developed and new side effects become evident, it will be necessary to review and add or delete items from this list as indicated by the most current information. Practitioners must use the health history and the medication list in concert, using one to make sense of the other and utilizing all the information available from reviewing each one carefully in order to manage their increasingly complex patients safely and effectively. ■■■■

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