Hot Topics: Latest Issues Affecting Pharmacotherapy in Dentistry, Including Issues on Mitigating the Prescribing of Opioids

Presenter: Richard L. Wynn, Professor of Pharmacology

University of Maryland Dental School

Topics

1. The national PDMP concept update and scheduled drug prescribing
2. Mitigation of opioid availability and the increase in heroin markets
3. Analgesics – non-narcotic pain relievers to reduce opioid prescribing
4. Drug interactions involving NSAIDs and opioids with other drugs and supplements
5. Antibiotics: current issues on bacterial resistance
6. Antibiotic Stewardship, Odontogenic Infections
7. Antibiotics as Premedications – more recs by Orthopedic Association
8. More drugs associated with osteonecrosis of the jaw (ONJ)
9. Updating medical marijuana
10. Updating "non-permit level" minimal sedation guidelines from ADA-previously known as "anxiolysis"
11. New blood thinners and emerging guidelines for patient management
12. Nitrous oxide

Course Benefits

The attendee will be able to:

1. List situations where opioid prescribing is a necessary part of therapeutics
2. Describe CDC's concern about bacterial resistance to antibiotics and the stewardship concept
3. Describe the "appropriate use concept" from Orthopedic Surgeons on premedicating the joint prosthetic patient undergoing dental surgery
4. List strategies using non-narcotic pain relievers to reduce opioid use
5. List the NIH purported medical benefits and adverse reactions of medical marijuana;
6. List the most recent findings on cardioprotective aspirin and the management of patients on Pradaxa, Eliquis and other new blood thinners;
7. Summarize ADA "minimal sedation guidelines"

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The opioid crisis will become even more deadly

HEALTH
LENNY
BERNSTEIN

As bad as it is, the U.S. drug crisis is almost certain to get worse before it gets better.

This year ended with a grim announcement from the Centers for Disease Control and Prevention: Drug overdose deaths had soared 21 percent, to 63,632, in 2016 (official statistics lag by a year). That's about equal to the population of Portland, Maine.

Opioids killed more than 42,000 people, a 28 percent increase from 2015.

The drug death toll is so high that it is now primarily responsible for the second straight year of decline in overall U.S. life expectancy — a trend basically unheard of in the developed world.

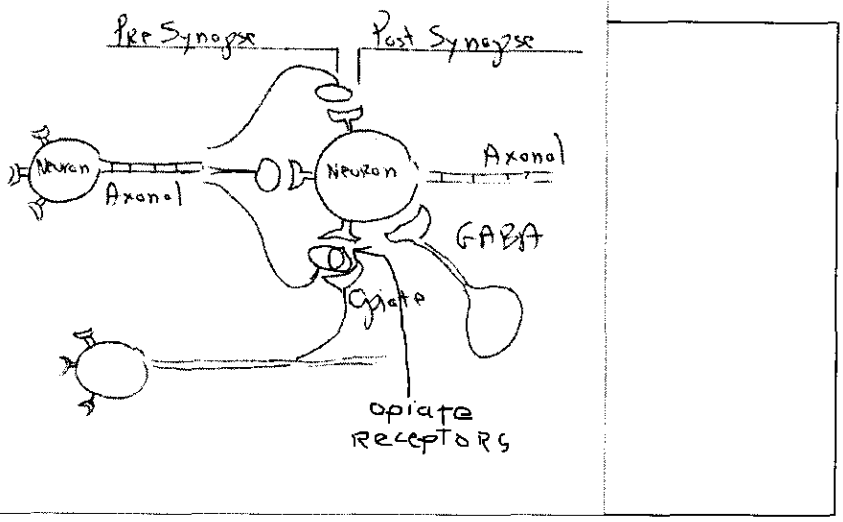
Brace for worse news in 2018. Bob Anderson, who studies mortality statistics for the CDC, said the data through May 2017 is "at least as bad" as the 2016 numbers. People are still being killed by overdoses of pills and heroin, and in increasing numbers. But the problem now is clearly fentanyl, an illegal synthetic opioid that is smuggled from China and mixed with heroin — creating a stronger high and a greater likelihood of death. Fentanyl and similar synthetic opioids killed 19,413 people in 2016, more than double the number in the previous year. That's an incredible leap in just 12 months. (Because many users die with more than one drug in their bodies, a single death can be attributed to two or more drugs.)

So what are we doing about this? Not enough, according to most authorities. The number of prescriptions for opioids is down a bit in recent years, and some doctors are trying to give each patient fewer pills. That might help patients avoid dependence and keep unused extras off the street. Meanwhile, stopping fentanyl and heroin from entering the country has proved difficult. And although President Trump has declared the drug crisis a national emergency, the government has devoted little money to making treatment more available.

Twitter: @LennyMBernstein

Lenny Bernstein is a health and medicine reporter.

New York Times Jan 10, 2018


Pre Synapse
Post Synapse
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GABA
Opiate
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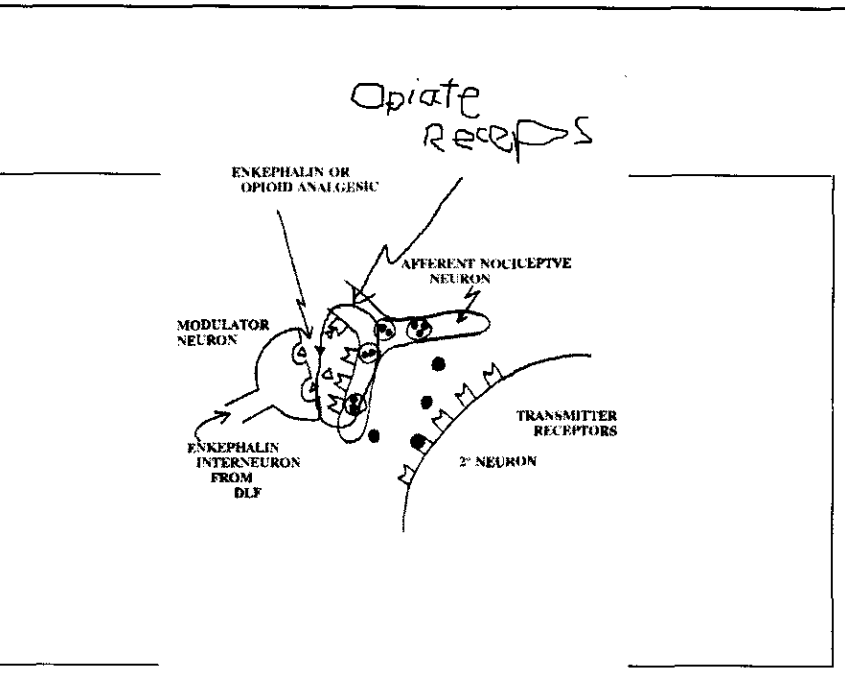
Receptors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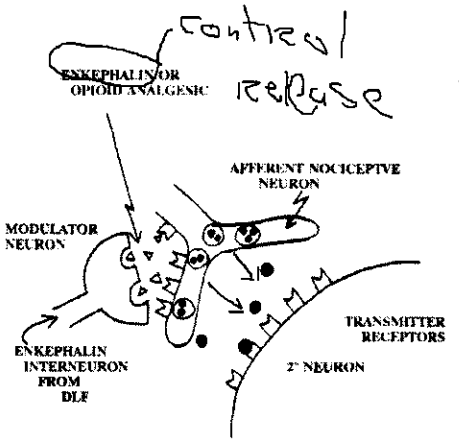
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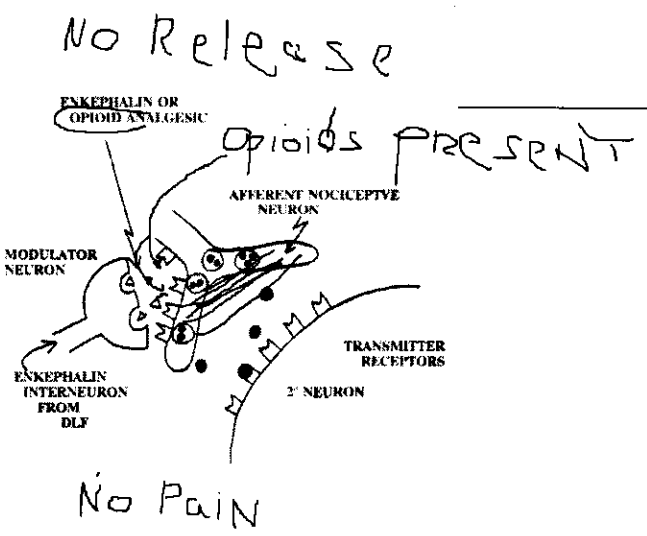
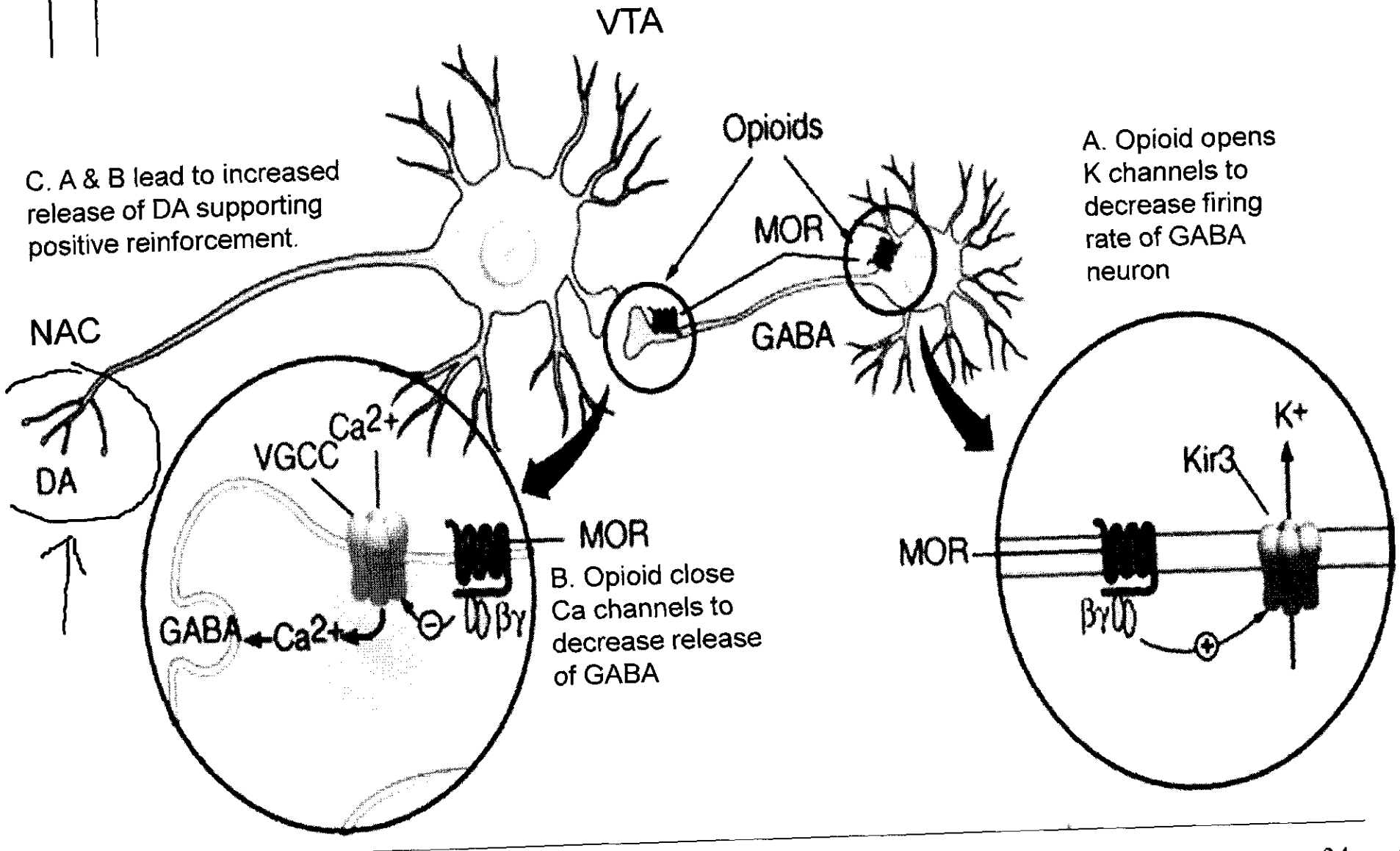
ENKEPHALIN OR OPIOID ANALGESIC
AFFERENT NOCICEPTIVE NEURON
MODULATOR NEURON
TRANSMITTER RECEPTORS
2° NEURON
ENKEPHALIN INTERNEURON FROM DLF

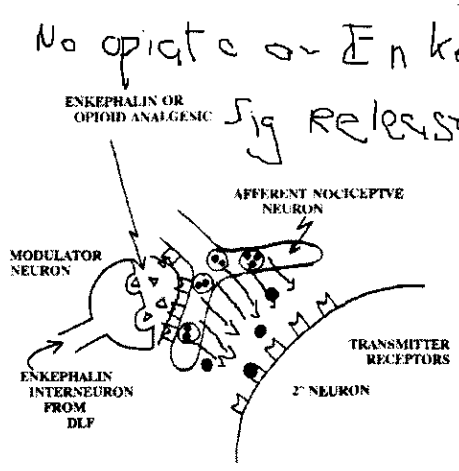
29


No Release
ENKEPHALIN OR OPIOID ANALGESIC
Opioids present
AFFERENT NOCICEPTIVE NEURON
MODULATOR NEURON
TRANSMITTER RECEPTORS
2° NEURON
ENKEPHALIN INTERNEURON FROM DLF
No Pain

30

Purported Mechanisms of Opioid Reinforcement Mediated Via Dopaminergic Enhancement





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Major pathways in full mode - Symptoms

- Pain, sickness
- Flu-like feeling
- Insomnia
- Stomach cramps, nausea
- Sweating
- Psychological disturbances, etc
- Unbearable need for next fix

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INTERNAL OPIATES SITES OF ACTION

DIFFERENT BINDING SITES TERMS

- MU
- DELTA
- KAPPA
- EPSILON
- SIGMA

MAY BE SEPARATE & DISTINCT OR PHYSICALLY LINKED

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RECEPTOR FUNCTION

Mu

- SUPRASPINAL ANALGESIA
- RESPIRATORY DEPRESSION
- EUPHORIA
- PHYSICAL DEPENDENCE

Kappa

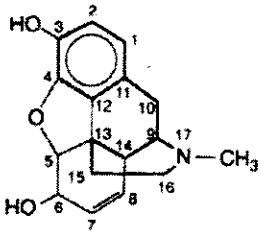
- SPINAL ANALGESIA
- MIOSIS
- SEDATION

Sigma

- DYSPHORIA
- HALLUCINATIONS
- RESPIRATORY STIMULATION
- VASOMOTOR STIMULATION

52

Table 21–5
Structures of Opioids and Opioid Antagonists Chemically Related to Morphine



MORPHINE

Morphine	—OH	—OH	—CH_3	—
Heroin	—$OCOCH_3$	—$OCOCH_3$	—CH_3	—
Hydromorphone	—OH	=O	—CH_3	(1)
Oxymorphone	—OH	=O	—CH_3	(1), (2)
Levorphanol	—OH	—H	—CH_3	(1), (3)
Levallorphan	—OH	—H	—$CH_2CH{=}CH_2$	(1), (3)
Codeine	—OCH_3	—OH	—CH_3	—
Hydrocodone	—OCH_3	=O	—CH_3	(1)
Oxycodone	—OCH_3	=O	—CH_3	(1), (2)
Nalmefene	—OH	$=CH_2$	—CH_2— 	(1), (2)
Nalorphine	—OH	—OH	—$CH_2CH{=}CH_2$	—
Naloxone	—OH	=O	—$CH_2CH{=}CH_2$	(1), (2)
Naltrexone	—OH	=O	—CH_2— 	(1), (2)
Buprenorphine	—OH	—OCH_3	—CH_2— 	(1), (4)
Butorphanol	—OH	—H	—CH_2— 	(1), (2), (3)
Nalbuphine	—OH	—OH	—CH_2— 	(1), (2)

*The numbers 3, 6, and 17 refer to positions in the morphine molecule, as shown above. †Other changes in the morphine molecule are: (1) Single instead of double bond between C7 and C8; (2) OH added to C14; (3) No oxygen between C4 and C5; (4) *Endo*etheno bridge between C6 and C14; 1-hydroxy-1,2,2-trimethylpropyl substitution on C7.

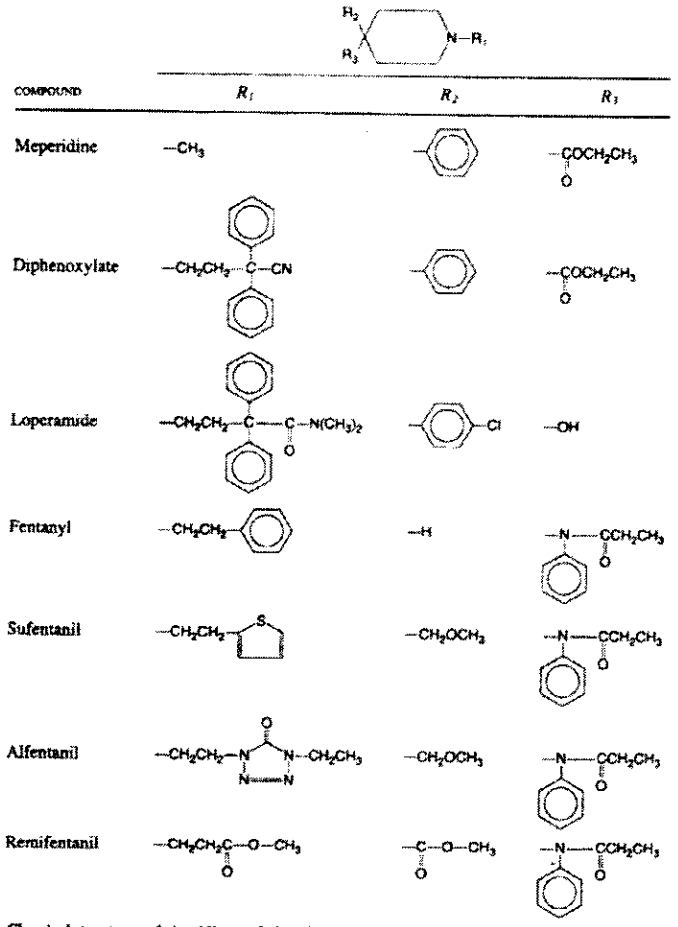
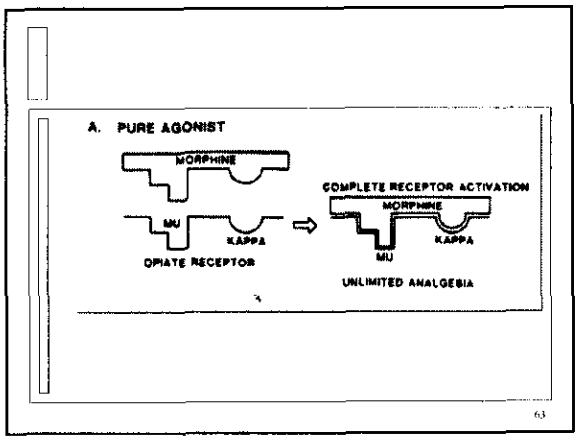
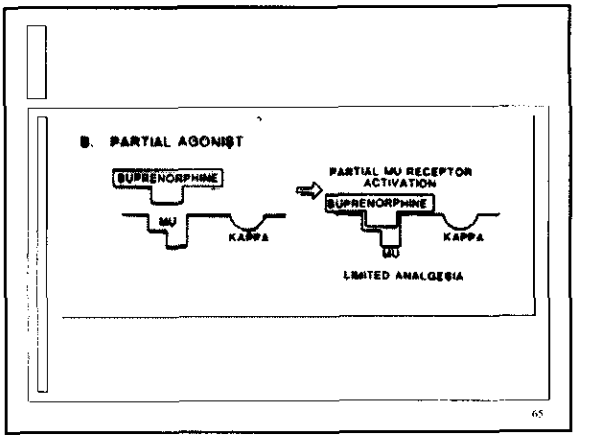


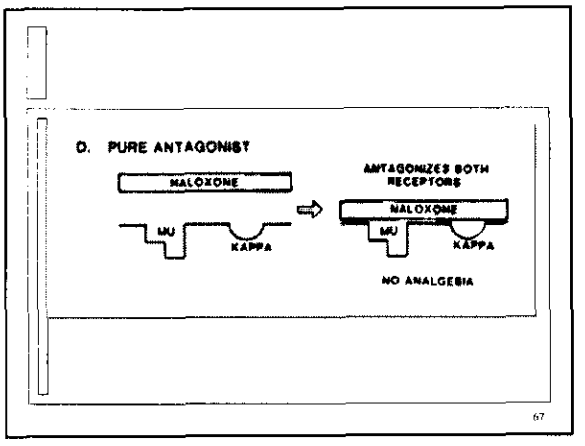
Figure 21–4. *Chemical structures of piperidine and phenylpiperidine analgesics.*

Absorption, Fate, and Excretion. Meperidine is absorbed by all routes of administration, but the rate of absorption may be erratic after intramuscular injection. The peak plasma concentration usually occurs at about 45 minutes, but the range is wide. After oral administration, only about 50% of the drug escapes first-pass metabolism to enter the circulation, and peak concentrations in plasma usually are observed in 1 to 2 hours.

In humans, meperidine is hydrolyzed to meperidinic acid, which, in turn, is partially conjugated. Meperidine also is *N*-demethylated to normeperidine, which then may be hydrolyzed to normeperidinic acid and subsequently







Pure agonists

- Most potent
  - Fentanyl – 100 times more potent than morphine

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What is Carfentanil?

- 100 times more potent than fentanyl
- 10,000 times more potent than morphine

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Pure agonists

- Next most potent
  - Morphine
  - Heroin
  - Hydromorphone (Dilaudid)
  - Hydrocodone (in Vicodin, Lorcet)
  - Oxymorphone (Numorphan)
  - Methadone (Dolophine)
  - Oxycodone (in Percodan, Tylox)

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Pure agonists

- Less potent
  - Codeine
  - Dihydrocodeine (in Synalgos DC)
  - Meperidine (Demerol)

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Pure antagonists

- Naloxone (Narcan)
- Nalmefene (Revex)
- Naltrexone (ReVia)

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Morphine

- Mechanism
  - Same as internal enkephalins, G-protein mediated receptor function
- 1. Analgesia – agst severe pain
- 2. sedation
  - sedation potentiates analgesia
- 3. Respiratory depression
  - Reduced respiratory rate; reduced tidal volume

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Morphine

- 4. Nausea and emesis
  - Stim chemoreceptor trigger zone (CTZ)
- 5. Cough suppression
  - Depress cough center in medulla
- 6. Gastrointestinal effects
  - Decr motility, dec propulsive contractions, constipation
- 7. Renal actions – stim ADH to cause urinary retention

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Morphine

- 8. Miosis
  - Pupillary constriction, atropine counteracts
- 9. Bronchiolar constriction – aggravates asthma
- 10. Biliary colic- constricts biliary duct

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The opioid tolerance effect and death by overdose

- To maintain pain relief, and/or euphoria, person becomes dependent on the need for more and more and higher opioid doses.
- Unfortunately, tolerance to resp dep by opioid is of much less magnitude. Resp remains more dose sensitive than euphoria
- Overdosing to achieve a high inadvertently shuts down respiration (death by overdose).

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Suboxone

- Buprenorphine and naloxone combined in same tablet
- Used for maintenance treatment of opioid dependence
- C=III
- Buprenorphine component provides maintenance narcotic effect through partial agonistic effect at mu receptors

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Suboxone

- Buprenorphine and naloxone combined in same tablet
- Used for maintenance treatment of opioid dependence
- C=III
- If addict shoots IV, naloxone gets in CNS to block effects of IV buprenorphine

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DEA Drug Schedules

https://www.dea.gov/druginfo/ds.shtml

Accessed Aug 27, 2016

Drug Schedules

Drugs, substances, and certain chemicals used to make drugs are classified into five (5) distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential. The abuse rate is a determinate factor in the scheduling of the drug; for example, Schedule I drugs have a high potential for abuse and the potential to create severe psychological and/or physical dependence. As the drug schedule changes-- Schedule II, Schedule III, etc., so does the abuse potential-- Schedule V drugs represents the least potential for abuse. A Listing of drugs and their schedule are located at Controlled Substance Act (CSA) Scheduling or CSA Scheduling by Alphabetical Order. These lists describes the basic or parent chemical and do not necessarily describe the salts, isomers and salts of isomers, esters, ethers and derivatives which may also be classified as controlled substances. These lists are intended as general references and are not comprehensive listings of all controlled substances.

Please note that a substance need not be listed as a controlled substance to be treated as a Schedule I substance for criminal prosecution. A controlled substance analogue is a substance which is intended for human consumption and is structurally or pharmacologically substantially similar to or is represented as being similar to a Schedule I or Schedule II substance and is not an approved medication in the United States. (See 21 U.S.C. §802(32)(A) for the definition of a controlled substance analogue and 21 U.S.C. §813 for the schedule.)

Schedule I

Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Some examples of Schedule I drugs are:

heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote

Schedule II

Schedule II drugs, substances, or chemicals are defined as drugs with a high potential for abuse, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous. Some examples of Schedule II drugs are:

Combination products with less than 15 milligrams of hydrocodone per dosage unit (Vicodin), cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyl, Dexedrine, Adderall, and Ritalin

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Schedule III

Schedule III drugs, substances, or chemicals are defined as drugs with a moderate to low potential for physical and psychological dependence. Schedule III drugs abuse potential is less than Schedule I and Schedule II drugs but more than Schedule IV. Some examples of Schedule III drugs are:

Products containing less than 90 milligrams of codeine per dosage unit (Tylenol with codeine), ketamine, anabolic steroids, testosterone

Schedule IV

Schedule IV drugs, substances, or chemicals are defined as drugs with a low potential for abuse and low risk of dependence. Some examples of Schedule IV drugs are:

Xanax, Soma, Valium, Ativan, Talwin, Ambien, Tramadol

Schedule V

Schedule V drugs, substances, or chemicals are defined as drugs with lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes. Some examples of Schedule V drugs are:

cough preparations with less than 200 milligrams of codeine or per 100 milliliters (Robitussin AC), Lomotil, Motofen, Lyrica,

The FDA will no longer allow opioid-containing cough and cold medicines to be prescribed for children younger than 18 years.

The agency is ordering the safety labeling changes in cough and cold medicines containing codeine or hydrocodone "because the serious risks of these medicines outweigh their potential benefits in this population," the agency said in a statement.

After safety labeling changes are made, the products will no longer be indicated for use to treat cough in any pediatric population, and will be labeled for use only in adults aged 18 years and older.

"Given the epidemic of opioid addiction, we're concerned about unnecessary exposure to opioids, especially in young children. We know that any exposure to opioid drugs can lead to future addiction. It's become clear that the use of prescription, opioid-containing medicines to treat cough and cold in children comes with serious risks that don't justify their use in this vulnerable population," said FDA Commissioner Scott Gottlieb, MD.

At the same time, the FDA is taking steps to help reassure parents that treating the common cough and cold is possible without using opioid-containing products, Gottlieb added.

Related article: 3 New Initiatives Target Opioid Crisis

Labeling for the medications is also being updated with additional safety information for adult use. The cough and cold drugs will now include an expanded Boxed Warning — the FDA's most prominent warning — notifying about the risks of misuse, abuse, addiction, overdose, death, and slowed or difficult breathing that can result from exposure to codeine or hydrocodone.

"The new labeling will provide safety warnings on these products that are consistent with the labeling of other opioid-containing drug products, including immediate-release opioid analgesics and extended-release and long-acting opioid analgesics," FDA said.

Last year, the FDA required the addition of a contraindication to the labeling of prescription codeine products alerting that codeine should not be used to treat pain or cough in children younger than 12 years, due to a specific risk of ultra-rapid metabolism in certain patients.

The FDA also held an expert roundtable and convened a meeting of its Pediatric Advisory Committee to look at all the risks associated with the use of codeine- or hydrocodone-containing cough and cold products in children and adolescents younger than 18 years old.

"Experts indicated that although some pediatric cough symptoms do require treatment, cough due to a cold or upper respiratory infection typically does not require treatment. Moreover, the [redacted] of using prescription opioid cough products in children of all ages generally outweigh the [redacted]fits," FDA said.

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STATE OF MARYLAND
DHMH Maryland State Board of Dental Examiners
Maryland Department of Health and Mental Hygiene
Spring Grove Hospital Center • Benjamin Rush Building
55 Wade Avenue/Tulip Drive • Catonsville, Maryland 21228
Martin O'Malley, Governor – Anthony G. Brown, Lt. Governor – Joshua M. Sharfstein, M.D., Secretary

July 25, 2014

IMPORTANT NOTIFICATION REGARDING TRAMADOL

Effective August 18, 2014, Tramadol will be classified as a Schedule IV controlled dangerous substance (CDS) under federal regulation. If you dispense Tramadol to your patients, you are required to report this to the Prescription Drug Monitoring Program (PDMP). If you write a prescription for Tramadol, but do NOT dispense this medication, you are not required to report to the PDMP.

The Division of Drug Control (DDC) has posted the following information on its web site: USDOJ/DEA, 21 CFR (Federal Register) Part 1308: Schedules of Controlled Dangerous Substances: Placement of Tramadol into Schedule IV (Final Rule).

The link is:

DEA (CFR Final Rule) Tramadol Schedule IV Placement (Effective: 8/18/14)
http://dhmh.maryland.gov/laboratories/drugcont/docs/DEA%20%28CFR%20Final%20Rule%29%20Tramadol%20Schedule%20IV%20Placement%20%28Eff.8-18-2014%29.pdf.

The Maryland State Board of Dental Examiners is pleased to provide Maryland dentists with this notification regarding the upcoming Schedule IV placement of Tramadol. Please adjust your practice accordingly.

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News & Events
FDA NEWS RELEASE

For Immediate Release: January 13, 2011
Media Inquiries: Shelly Burgess, 301-796-4651; shelly.burgess@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA limits acetaminophen in prescription combination products; requires liver toxicity warnings

Agency strategy caps maximum at 325 milligrams to reduce risk of liver toxicity

The U.S. Food and Drug Administration is asking manufacturers of prescription combination products that contain acetaminophen to limit the amount of acetaminophen to no more than 325 milligrams (mg) in each tablet or capsule.

The FDA also is requiring manufacturers to update labels of all prescription combination acetaminophen products to warn of the potential risk for severe liver injury.

Acetaminophen, also called APAP, is a drug that relieves pain and fever and can be found in both prescription and over-the-counter (OTC) products. It is combined in many prescription products with other ingredients, usually opioids such as codeine (Tylenol with Codeine), oxycodone (Percocet), and hydrocodone (Vicodin). OTC acetaminophen products are not affected by today's action.

"FDA is taking this action to make prescription combination pain medications containing acetaminophen safer for patients to use," said Sandra Kweder, M.D., deputy director of the Office of New Drugs in FDA's Center for Drug Evaluation and Research (CDER). "Overdose from prescription combination products containing acetaminophen account for nearly half of all cases of acetaminophen-related liver failure in the United States; many of which result in liver transplant or death."

The elimination of higher-dose prescription combination acetaminophen products will be phased in over three years and should not create a shortage of pain medication. Patients and health care professionals are being notified of the new limitation on acetaminophen content, and of the labeling change, in a drug safety communication issued by CDER. The FDA believes that prescription combination products containing no more than 325 mg of acetaminophen per tablet are effective for treating pain.

"There is no immediate danger to patients who take these combination pain medications and they should continue to take them as directed by their health care provider," said Kweder. "The risk of liver injury primarily occurs when patients take multiple products containing acetaminophen at one time and exceed the current maximum dose of 4,000 milligrams within a 24-hour period."

Acetaminophen is also widely used as an over-the-counter pain and fever medication, and is combined with other OTC ingredients, such as cough and cold ingredients. The actions FDA is taking for prescription acetaminophen products do not affect OTC acetaminophen products.

Because of continued reports of liver injury, FDA proposes that boxed warnings, the agency's strongest warning for prescription drugs, be added to all acetaminophen prescription products. Most of the cases of severe liver injury occurred in patients who took more than the prescribed dose of an acetaminophen-containing product in a 24-hour period, took more than one acetaminophen-containing product at the same time, or drank alcohol while taking acetaminophen products.

An FDA advisory committee discussed the issue at a meeting in June, 2009, and recommended strengthening the warning about severe liver injury on the drug labels of prescription products containing acetaminophen.

For more information and a list of affected products, please visit: www.fda.gov/acetaminophen[1]

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Hydrocodone combinations presently available with the lower amount of acetaminophen

C-II

Tablet, oral:

Hydrocodone bitartrate 5 mg and acetaminophen 300 mg

Hydrocodone bitartrate 5 mg and acetaminophen 325 mg

Hydrocodone bitartrate 7.5 mg and acetaminophen 300 mg

Hydrocodone bitartrate 7.5 mg and acetaminophen 325 mg

Hydrocodone bitartrate 10 mg and acetaminophen 300 mg

Hydrocodone bitartrate 10 mg and acetaminophen 325 mg

Norco®:

Hydrocodone bitartrate 5 mg and acetaminophen 325 mg

Hydrocodone bitartrate 7.5 mg and acetaminophen 325 mg

Hydrocodone bitartrate 10 mg and acetaminophen 325 mg

Vicodin®: Hydrocodone bitartrate 5 mg and acetaminophen 300 mg

Vicodin ES®: Hydrocodone bitartrate 7.5 mg and acetaminophen 300 mg

Vicodin HP®: Hydrocodone bitartrate 10 mg and acetaminophen 300 mg

Codeine combinations presently available with the lower amount of acetaminophen

C-III

Tablet, oral

Acetaminophen 300 mg and codeine phosphate 15 mg

Acetaminophen 300 mg and codeine phosphate 30 mg

Acetaminophen 300 mg and codeine phosphate 60 mg

Tylenol with Codeine No. 3 acetaminophen 300 mg and codeine phosphate 30 mg

Tylenol with Codeine No. 4 acetaminophen 300 mg and codeine phosphate 60 mg

Oxycodone combinations presently available with the lower amount of acetaminophen

C-II

Table, oral

2.5/325; oxycodone hydrochloride 2.5 mg and acetaminophen 325 mg

5/325; oxycodone hydrochloride 5 mg and acetaminophen 325 mg

7.5/325; oxycodone hydrochloride 7.5 mg and acetaminophen 325 mg

10/325; oxycodone hydrochloride 10 mg and acetaminophen 325 mg

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Prescription Writing

Whether a prescription is electronic, typed, printed-out, or hand written, the information below is to be included on any prescription order to the pharmacy.

Prescriber's Name

Address

Phone Number

Patient's Name Date

Patient's Address Age

Rx

Drug Name Dose form, Strength

Disp: Directions to the pharmacist. For example, number of tablets, capsules, or ounces to be dispensed including the number written out (i.e. Dispense Twelve (12) tablets)

Sig: Directions to the patient, i.e. direction on how drug is to be taken. Should be written out with no abbreviations. This is the information that the pharmacist will place on the dispensed medication.

Refills indicated if prescriber desires.

Prescriber's signature

State license number

DEA number (if prescribed drug is a controlled substance, this number is required)

Preventing Prescribing Errors (Edited from LexiDental Drugs)

Prescribing errors account for the majority of reported medication errors and have prompted health care professionals to focus on the development of steps to make the prescribing process safer. Prescription legibility has been attributed to a portion of these errors and legislation has been enacted in several states to address prescription legibility. Eliminating handwritten prescriptions and ordering medications through computerized prescriber order entry (CPOE)] has been the primary recommendation. Whether a prescription is electronic, typed, or hand-printed, additional safe practices should be considered for implementation to maximize the safety of the prescribing process. Listed below are suggestions for safer prescribing:

1. Ensure correct patient by using at least 2 patient identifiers on the prescription (eg, full name, birth date, or address). Review prescription with the patient or patient's caregiver.

2. If pediatric patient, document patient's birth date or age and most recent weight. If geriatric patient, document patient's birth date or age.

3. Use care when prescribing drugs that look or sound similar (eg, look- alike, sound-alike drugs). Common examples include: HydroCODONE vs oxyCODONE, CeleBREX vs CeleXA, diAZEPAM vs triAZOLAM, lorAZEPAM vs alprAZOLAM.

4. Try to avoid using abbreviations. For example write twice daily rather than using B.I.D. Avoid dangerous, error-prone abbreviations (eg, regardless of letter-case: QD, QOD Additionally, text messaging abbreviations (eg, "2Day") should never be used.

   For more information, see http://www.ismp.org/tools/errorproneabbreviations.pdf.

5. Always use a leading zero for numbers <1 (0.5 mg is correct and .5 mg is **incorrect**) and never use a trailing zero for whole numbers (2 mg is correct and 2.0 mg is **incorrect**).

6. Do not write vague or ambiguous orders which have the potential for misinterpretation by other health care providers. Examples of vague orders to avoid: "Resume pre-op medications," "give drug per protocol," or "continue home medications."

7. Review each prescription with patient (or patient's caregiver) including the medication name, indication, and directions for use.

8. Take extra precautions when prescribing *high alert drugs* (drugs that can cause significant patient harm when prescribed in error). Common examples of these drugs include: opioids, and sedatives.

   For more information, see http://www.ismp.org/tools/institutionalhighalert.asp or http://www.ismp.org/communityRx/tools/ambulatoryhighalert.asp.

~~2-fe~~

9/14/2016

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Name_____ Age____

Address_____ Date____

Rx

Hydrocodone 5mg/acetaminophen 300 mg

Disp: Twelve (12) tablets

Sig: Take one tablet as needed for pain.

Refills 0 Signature

DEA No. 613349072

1. This prescription is for the hydrocodone formulation now available with the amount of acetaminophen.
2. The amount to be dispensed is both written and numerically indicated [i.e Twelve (12)].
3. With this specific drug, a 5 mg strength has been indicated. In order to avoid a possible tampering to 7.5 mg, especially if written in handwriting, the prescriber may want to also write out "five mg only".
4. This is a controlled DEA schedule II drug and the DEA number is required on the prescription.
5. This prescription cannot be called in to the pharmacy over the telephone. The prescription has to be taken to the pharmacy or submitted electronically by an appropriate "electronic prescribing of controlled substances" application. Also, no refills are allowed on the original prescription.
6. In this example, the prescription was written for 12 tablets. In case the prescriber feels it necessary to provide additional tablets as a result of patient complaint of continuing postoperative pain, pain in which in the prescriber's judgement cannot be alleviated with a non-opioid pain reliever, a new prescription would have to be submitted.
7. If possible, the clinician should re-examine and evaluate the patient to ensure such a need for a new schedule II prescription is warranted.

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Name_____ Age____

Address_____ Date____

Rx

Ibuprofen tablets 600 mg

Disp: Twenty (20) tablets

Sig: Take one tablet by mouth every six hours for pain and swelling as needed

Refills X 1 Signature

DEA No.

1. This prescription example is for a non-opioid pain reliever ibuprofen.
2. Although ibuprofen is available over-the-counter, the above example is for *a "prescription strength" ibuprofen. One brand name for prescription* ibuprofen is Motrin. However, if the prescriber wrote for Motrin, the pharmacy would dispense the generic ibuprofen.
3. The amount to be dispensed is both written and numerically indicated. It is good prescription writing practice to include the amount both in writing and numerically.
4. This is not a controlled (scheduled) drug and a DEA number is not required.
5. Refills – In this example the prescriber indicated one refill can be given, in case the patient may need more after completing the initial dose regimen.

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Narcotics Get a Name Change

Opioid is Preferred Term in Medical Circles

This report is from Harvard Health Letter November 2010

"Any drug, natural or synthetic, with morphine-like properties is called an opioid (pronounced OH-pee-oid). The terms narcotic and opioid are often used interchangeably, but narcotics has a legal and regulatory pedigree that opioid doesn't, so opioid has become the preferred term in medical circles."

"The prototypical opioids are morphine and codeine (which is milder than morphine). Fentanyl (Duragesic), hydromorphone (Dilaudid) and meperidine (Demerol) have been available for years. Methadone, which is better known as a treatment for heroin addiction, is also prescribed for pain. The opioid drugs are also combined with other drugs into a single pill. Vicodin is the brand name for a combination of the opioid hydrocodone and acetaminophen. Percocet is oxycodone with acetaminophen, and Percodan is oxycodone with aspirin. "

"As opioids became more acceptable, drug makers reformulated some of them so they stay active longer. OxyContin, a sustained-release form of oxycodone, is the prime example. "

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EPIDEMIC: RESPONDING TO AMERICA'S PRESCRIPTION DRUG ABUSE CRISIS

The White House Executive Report can be found at:

http://www.whitehouse.gov/sites/default/files/ondcp/policy-and-research/rx_abuse_plan.pdf

Accessed June 16, 2013

2011

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EPIDEMIC: RESPONDING TO AMERICA'S PRESCRIPTION DRUG ABUSE CRISIS

Contents

https://www.whitehouse.gov/sites/default/files/ondcp/policy-and-research/rx_abuse_plan.pdf

Accessed October 8, 2016

The following summarizes some key points in the White House report

This Report provides data describing the extent to which the prescription drug abuse problem in America has grown over the last decade, and should serve to highlight the critical role parents, patients, healthcare providers, and manufacturers play in preventing prescription drug abuse.

1. Nearly one-third of people aged 12 and over who used drugs for the first time in 2009 began by using a prescription drug non-medically.
2. Over 70% of people who abused prescription pain relievers got them from friends or relatives.
3. Only 5%of people who abused prescription pain relievers got them from a drug dealer or from the Internet.
4. In U.S. military, illicit drug use increased from 5 % to 12 % among active duty service members over a three-year period from 2005 to 2008, primarily attributed to drug abuse.
5. From 1997 to 2007, the milligram per person use of prescription opioids in the U.S. increased from 74 milligrams to 369 milligrams, an increase of 402 percent.
6. In 2000, retail pharmacies dispensed 174 million prescriptions for opioids; by 2009, 257 million prescriptions were dispensed, an increase of 48%.
7. Opiate overdoses, once almost always due to heroin use, are now increasingly due to abuse of prescription pain relievers.

A report published in the Journal of the American Medical Association (JAMA Feb 20 2013; 309) presented more data.

That report said that from 1999 to 2010 the number of people in the United State dying annually from prescription opioid related overdoses quadrupled, from 4030 to 16,651.

The number of reported drug overdose deaths in the United States in 2010 was 22,134. The top three classes of prescribed drugs involved in those overdose deaths were opioids (16,651 deaths), benzodiazepines (6,497 deaths) and antidepressants (3,889 deaths).

More data for a New England Journal of Medicine report of 2010: Okie, S. A flood of opioids, a rising tide of deaths. Vol 363(21):1981-1985.

1. Deaths from unintentional drug overdose in the United States are the second leading cause of accidental death, with 27,658 deaths recorded in 2007.
2. According to the CDC, the magnitude of increase was propelled by a rising number of overdoses of prescription opioids, which caused 11,499 of those deaths in 2007. This number of opioid-associated deaths was more than heroin and cocaine combined in 2007.
3. Visits to emergency rooms for opioid abuse more than doubled between 2004 and 2008, and admissions to substance-abuse treatment programs increased by 400% between 1998 and 2008, with prescription pain killers being the second most prevalent type of abused drug after marijuana.
4. In addition, there was a dramatic shift in the prevalence of fatal drug overdoses from urban to rural communities. According to this 2010 report, up to that time, the highest rates of fatal drug overdoses occurred in West Virginia, New Mexico, Utah, Louisiana, Oklahoma, Nevada, Kentucky and Tennessee. The theory was that increases in opioid prescribing and sales during the 1990s brought abusable drugs into rural areas where no efficient distribution network had existed for illicit drugs such as heroin or cocaine.

Numbers of prescriptions for specific opioids.

According to a published survey by SDI Vector One: National (Drug Topics June 2011 Issue) the total prescriptions were written for the following opioids.

Hydrocodone with acetaminophen - 122,806,850 prescriptions were written in the U.S. in 2010. This was an increase of 2.1% from the previous year. This drug was the number one on the list of top 200 drugs by total prescriptions. .

Oxycodone with acetaminophen - 28,705,243 prescriptions were written in the U.S. in 2010. This was an increase of 6.8% from the previous year. This drug was number 18 on the list of top 200 drugs by total prescriptions.

Codeine with acetaminophen was not within the top 200 drugs by prescriptions in 2010 so there was no information on how many prescriptions were written for this opioid.

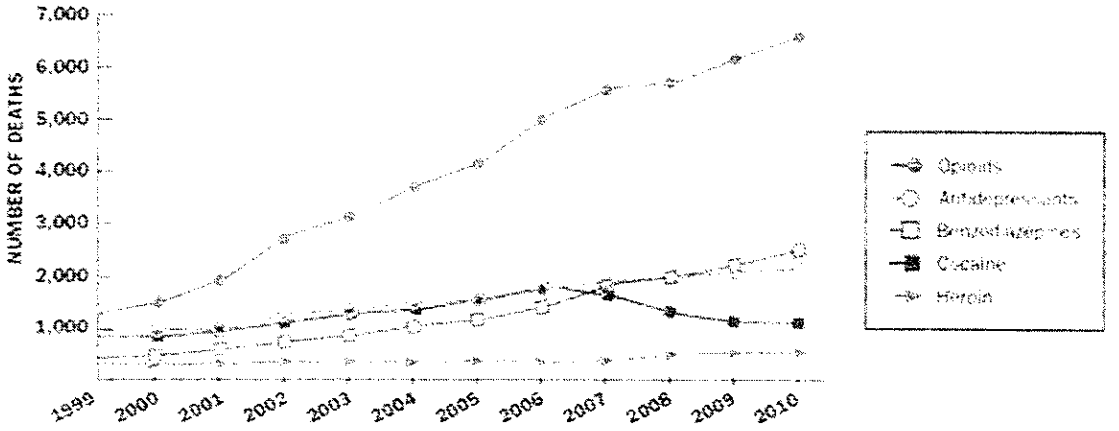
Drug overdose deaths in the United States hit record numbers in 2014

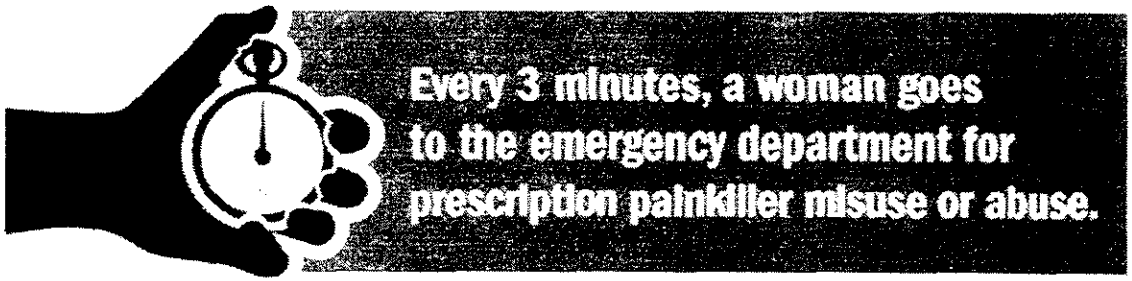
More people died from drug overdoses in 2014 than in any year on record. The majority of drug overdose deaths (more than six out of ten) involve an opioid.[1] And since 1999, the number of overdose deaths involving opioids (including prescription opioid pain relievers and heroin) nearly quadrupled.[2] From 2000 to 2014 nearly half a million people died from drug overdoses. 78 Americans die every day from an opioid overdose.

We now know that overdoses from prescription opioid pain relievers are a driving factor in the 15-year increase in opioid overdose deaths. Since 1999, the amount of prescription opioids sold in the U.S. nearly quadrupled,[2] yet there has not been an overall change in the amount of pain that Americans report.[3,4] Deaths from prescription opioids—drugs like oxycodone, hydrocodone, and methadone—have also quadrupled since 1999.[5]

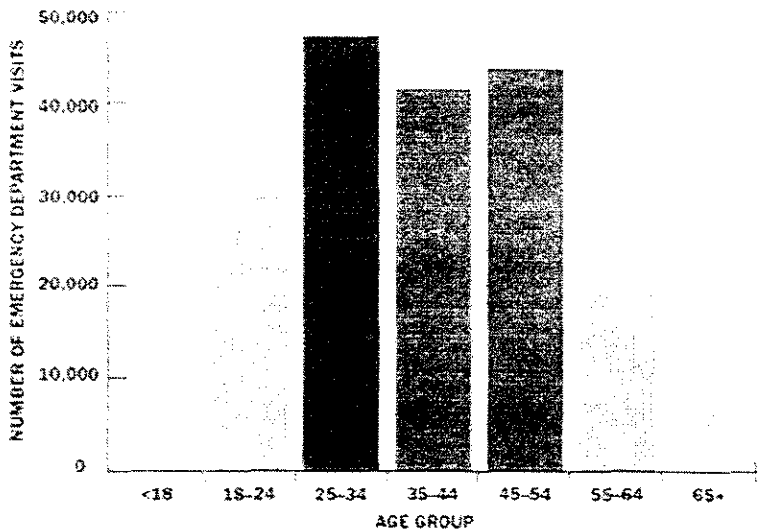
Learn more about prescription opioids

Prescription painkiller overdose deaths are a growing problem among women.





Women between the ages of 25 and 54 are most likely to go to the emergency department because of prescription painkiller misuse or abuse.



SOURCE: Drug Abuse Warning Network, 2010. (Suicide attempts are included for the cases (.03% of total) where opioids were combined with illicit drugs in the attempt.)

Read text version

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http://bha.dhmh.maryland.gov/OVERDOSE_PREVENTION/Documents/2007-2012%20intox%20report_final.pdf

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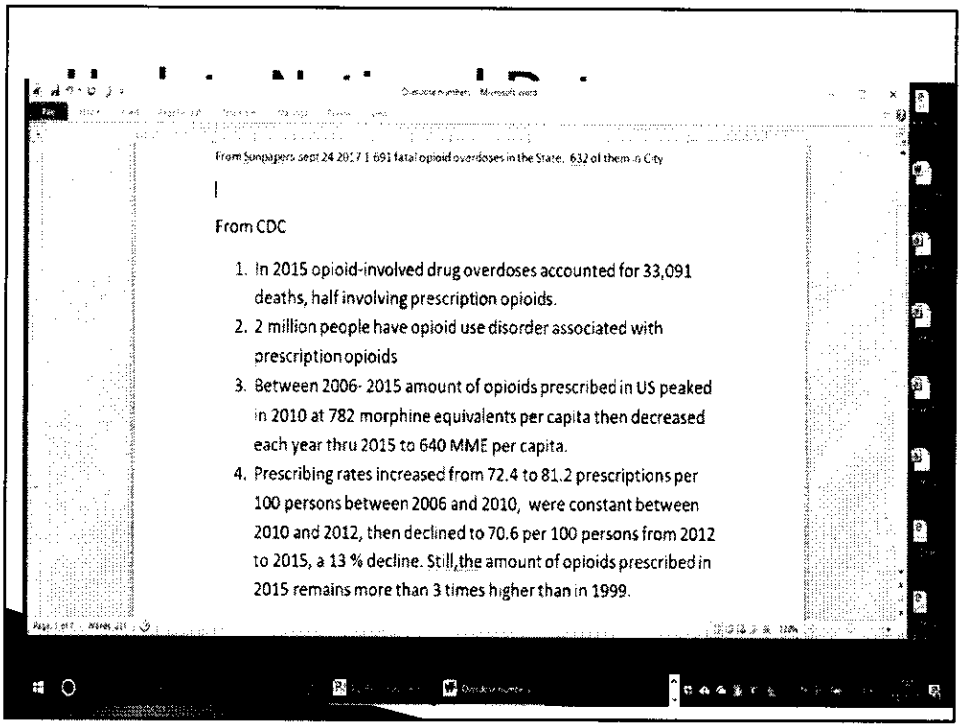
Update National Data

- CDC – 2017
- 64,000 overdose deaths last year nationwide
- 22% jump over previous year
- Leading cause of death in Americans under 50 yrs



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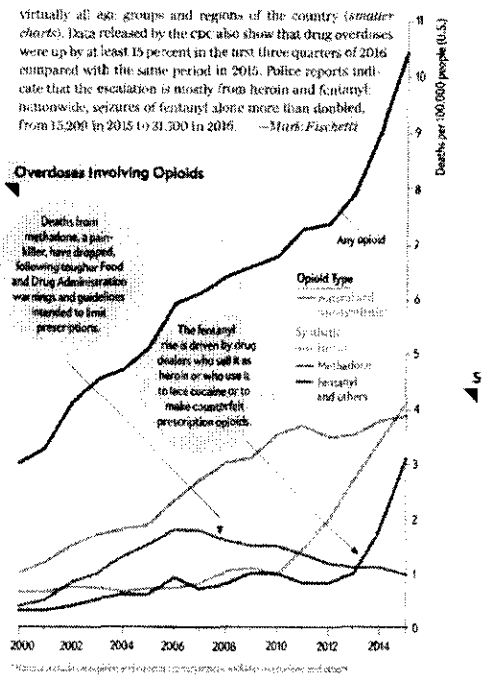
From JAMA viewpoint Aug 1, 2017 318 p 425

Use of PDMP data

Ohio and Kentucky in 2012 implemented pain clinic regulations and began requiring clinicians to review PDMP data. From 2010 to 2015 per capita opioid prescribing decreased in 85% Ohio counties and 62% Ky counties. In Fl, from 2010 to 2015 per capita opioid prescribing decreased in 80% of counties.

Nationally, despite reduction in opioid prescribing, opioid-involved overdose death rates continue to increase, driven largely by heroin and fentanyl.

virtually all age groups and regions of the country (*smaller charts*). Data released by the CDC also show that drug overdoses were up by at least 15 percent in the first three quarters of 2016 compared with the same period in 2015. Police reports indicate that the escalation is mostly from heroin and fentanyl: nationwide, seizures of fentanyl alone more than doubled, from 15,200 in 2015 to 31,300 in 2016. —*Mark Fischetti*



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Denisco RC et al. Prevention of prescription opioid abuse; the role of the dentist. JADA 2011; 142(7):800-809

Background Information from Denisco et al

1. There has been an increase in recent years in prescribing opioids, particularly to manage chronic non-cancer pain.
2. Parallel to that is the growing trend of nonmedical use, and nonfatal and fatal overdoses with opioids.
3. It is estimated that 5 to 23 % of all prescription opioid doses dispensed are used nonmedically.
4. The most frequently abused opioids are immediate-release (IR) opioids, particularly hydrocodone and oxycodone.
5. Family physicians prescribe 15% of the IR opioids in the United States while dentists prescribe 12% of IR opioids.
6. Prescribers of opioids have a responsibility to minimize the potential for drug misuse and diversion while maintaining legitimate access to opioids for patients in need of such pain relievers.

Definitions

1. **Misuse**: use of a medication (prescribed for a medical purpose) other than as directed or as indicated, whether willfully or unintentionally and whether or not harm results.
2. **Abuse**: any use of an illegal drug or the intentional self-administration of a medication for a nonmedical purpose such as altering one's state of consciousness (for example, "getting high").

Sources of misused prescription opioids

1. Having them prescribed for therapeutic use
2. Given by a friend or relative
3. Bought from a friend or family member
4. Left over from their own prescription provided for a legitimate medical problem.

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Denisco RC et al. Prevention of prescription opioid abuse; the role of the dentist. JADA 2011; 142(7):800-809

Practice patterns for managing acute dental -related pain.

Oral and Maxillofacial surgeons prescribing practices after third-molar extractions.

1. A survey was taken of 563 surgeons from a sample from the American Dental Association Survey Center
2. 74% of surgeons said that the most preferable post operative pain reliever was ibuprofen.
3. 85% of surgeons said they almost always prescribed an opioid.
4. 64% of surgeons said that the opioid of choice was hydrocodone with acetaminophen.
5. The average number of prescribed tablets for hydrocodone with acetaminophen was 20 tablets.
6. The instructions for taking hydrocodone with acetaminophen in 96% of the cases was "as needed for pain".

General dentists prescribing patterns

1. A survey was taken of West Virginia dentists' analgesic prescribing patterns. Fifty two percent of all dentists in West Virginia responded to the survey and 79 % were general dentists.
2. Among dentists who did not prescribe opioids, the most frequently prescribed analgesics were non-steroidal anti-inflammatory drugs (64%), followed by acetaminophen (28%).
3. Among dentists who prescribed opioids, the most frequently prescribed opioid was hydrocodone with acetaminophen (73%).
4. The amount of opioids prescribed after third molar extraction varied between 10 and 20 doses (66%)
5. The amount of opioids prescribed after third molar extraction were enough to provide two to five days of treatment (86%).

6. When asked about doses of IR opioids that dentists suspect patients have left after third molar extractions, 41% of dentists expected patients to have leftover drugs.

Denisco RC et al. Prevention of prescription opioid abuse; the role of the dentist. JADA 2011; 142(7):800-809

Use of opioids for the treatment of dental pain

Summary of statements by the American Dental Association on the use of opioids in the treatment of dental pain.

1. Dentists who prescribe opioids for the treatment of dental pain are encouraged to be mindful of the inherent abuse potential of opioids.
2. Dentists are encouraged to recognize their responsibilities for ensuring that prescription pain medications are available to the patients who need them, for preventing these drugs from becoming a source of harm or abuse and for understanding the special issues in pain management for patients already opiate dependent.
3. Dentists who are practicing in good faith and who use professional judgment regarding the prescription of opioids for the treatment of pain should not be held responsible for the willful and deceptive behavior of patients who successfully obtain opioids for non-dental purposes.

Information reported on numbers of doses of opioids for dental pain

1. Available data suggest that clinicians prescribe no more than the number of doses needed based on the usual duration of acute pain severe enough to require opioids for that condition. It is the clinician's judgment as to the expected duration of the acute pain and how many doses of the opioid that may be needed.
2. The Denisco et al paper cites three examples of numbers of opioid doses that are usually prescribed

a. After dental surgery, the typical dosing period for hydrocodone with acetaminophen was between two and three days, although there was some flexibility in the number of days, as some patients legitimately will need analgesics for seven days or more.
b. Results of another study showed that 24 % of patients reported that they still were taking analgesics 10 days after the removal of four third molars. It was not reported as to whether the analgesics were opioids.
c. Oral and maxillofacial surgeons in the United States reported that they prescribe hydrocodone with acetaminophen in quantities of up to 10 to 20 doses after third-molar extractions.

Opioid Medications Drug Safety: Attention Prescribers – FDA seeks you help in curtailing the U.S. opioid epidemic

http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm

Accessed October 8, 2016

Prescription opioids are powerful pain-reducing medications that include prescription oxycodone, hydrocodone and morphine, among others, and have both benefits as well as potentially serious risks. These medications can help manage pain when prescribed for the right condition and when used properly. But when misused or abused, they can cause serious harm, including addiction, overdose and death.

Recently, too many citizens have been impacted by the serious harms associated with these medications. In response to the current opioid crisis facing our country, FDA has developed a comprehensive action plan to take concrete steps toward reducing the impact of opioid misuse and abuse. Part of the action plan is in maintaining a thorough knowledge of the drug labels to help prescribers inform their decision making to ensur e safe, appropriate, and effective use.

The drug label, or package insert, that accompanies all FDA-approved medications is he most complete source of information on the drug. Drug labels provide important safety and efficacy information and clinical data to prescribers on the benefits, risks and appropriate use for all FDA-approved drugs. The FDA-approved drug label is one of the most useful tools prescribers have for providing safe and effective opioid therapy to their patients.

An example of drug labeling is on the following pages describing hydrocodone and acetaminophen taken from LexiComp Online Drug Information for Dentistry, October, 2016.

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Hydrocodone and Acetaminophen (Dental Lexi-Drugs)

Pronunciation

(hye droe KOE done & a seet a MIN oh fen)

ALERT: U.S. Boxed Warning

The FDA-approved labeling includes a boxed warning. See Warnings/Precautions section for a concise summary of this information. For verbatim wording of the boxed warning, consult the product labeling or www.fda.gov.

Brand Names: U.S.

hycet®; Lorcet® 10/650; Lorcet® Plus; Lortab®; Margesic® H; Maxidone®; Norco®; Stagesic™; Vicodin ES®; Vicodin HP®; Vicodin®; Xodol® 10/300; Xodol® 5/300; Xodol® 7.5/300; Zamicet™; Zolvit®; Zydone®

Generic Availability (U.S.)

Yes: Oral solution, tablet

Use

Relief of moderate-to-severe pain

Effects on Dental Treatment

Key adverse event(s) related to dental treatment: Xerostomia (normal salivary flow resumes upon discontinuation). See Dental Health Professional Considerations.

Adverse Effects

Frequency not defined.

Cardiovascular: Bradycardia, cardiac arrest, circulatory collapse, coma, hypotension

Central nervous system: Anxiety, dizziness, drowsiness, dysphoria, euphoria, fear, lethargy, lightheadedness, malaise, mental clouding, mental impairment, mood changes, physiological dependence, sedation, somnolence, stupor

Dermatologic: Pruritus, rash

Endocrine & metabolic: Hypoglycemic coma

Gastrointestinal: Abdominal pain, constipation, gastric distress, heartburn, nausea, peptic ulcer, vomiting, xerostomia

Genitourinary: Ureteral spasm, urinary retention, vesical sphincter spasm

Hematologic: Agranulocytosis, bleeding time prolonged, hemolytic anemia, iron deficiency anemia, occult blood loss, thrombocytopenia

Hepatic: Hepatic necrosis, hepatitis

Neuromuscular & skeletal: Skeletal muscle rigidity

Otic: Hearing impairment or loss (chronic overdose)

Renal: Renal toxicity, renal tubular necrosis

Respiratory: Acute airway obstruction, apnea, dyspnea, respiratory depression (dose related)

Miscellaneous: Allergic reactions, clamminess, diaphoresis

Controlled Substance C-II

Dental Usual Dosage Postoperative pain: Oral:

Children and Adults ≥50 kg: Average starting dose in opioid naive patients: Hydrocodone 5-10 mg 4 tim acetaminophen should be limited to ≤4 g/day (and possibly less in patients with hepatic impairment or ethanc

Dosage ranges (based on specific product labeling): Hydrocodone 2.5-10 mg every 4-6 hours; maximum: 6 (maximum dose of hydrocodone may be limited by the acetaminophen content of specific product)

Elderly: Doses should be titrated to appropriate analgesic effect; 2.5-5 mg of the hydrocodone component e exceed 4 g/day of acetaminophen.

Dosing: Adult **Pain management (analgesic):** Oral (doses should be titrated to appropriate analgesic eff dose in opioid naive patients: Hydrocodone 5-10 mg 4 times/day; the dosage of acetaminophen should be limited possibly less in patients with hepatic impairment or ethanol use).

Dosage ranges (based on specific product labeling): Hydrocodone 2.5-10 mg every 4-6 hours (maximum dose limited by the acetaminophen content of specific product)

Dosing: Geriatric Doses should be titrated to appropriate analgesic effect; 2.5-5 mg of the hydrocodone hours. Do not exceed 4 g/day of acetaminophen.

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Dosing: Pediatric **Pain management (analgesic):** Oral (doses should be titrated to appropriate analges

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Children 2-13 years or <50 kg: Hydrocodone 0.1-0.2 mg/kg/dose every 4-6 hours; do not exceed 6 dose recommended dose of acetaminophen

Children ≥50 kg: Refer to adult dosing.

Dosing: Renal Impairment No dosage adjustment provided in manufacturer's labeling; use with cau

Dosing: Hepatic Impairment Use with caution. Limited, low-dose therapy usually well tolerated in h disease/cirrhosis; however, cases of hepatotoxicity at daily acetaminophen dosages <4 g/day have been reported hepatic impairment.

Mechanism of Action Hydrocodone, as with other opioid analgesics, blocks pain perception in the cer to specific receptor molecules (opiate receptors) within the neuronal membranes of synapses. This binding result synaptic chemical transmission throughout the CNS thus inhibiting the flow of pain sensations into the higher cent the two subtypes of the opiate receptor which hydrocodone binds to cause analgesia.

Acetaminophen inhibits the synthesis of prostaglandins in the CNS and peripherally blocks pain impulse antipyresis from inhibition of hypothalamic heat-regulating center.

Contraindications Hypersensitivity to hydrocodone, acetaminophen, or any component of the formulatic severe respiratory depression

Warnings/Precautions

Concerns related to adverse effects:

- CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients m performing tasks which require mental alertness (eg, operating machinery or driving).
- Constipation: Hydrocodone may cause constipation which may be problematic in patients with unstat post-myocardial infarction. Consider preventive measures (eg, stool softener, increased fiber) to r constipation.
- Hepatotoxicity: **[US Boxed Warning]: Acetaminophen may cause severe hepatotoxicity, pote transplant or resulting in death; hepatotoxicity is usually associated with excessive acetamino in adults).** Risk is increased with alcohol use, preexisting liver disease, and intake of mor acetaminophen-containing medications. Chronic daily dosing in adults has also resulted in liver damag
- Hypersensitivity/anaphylactic reactions: Hypersensitivity and anaphylactic reactions have been report use; discontinue immediately if symptoms of allergic or hypersensitivity reactions occur. Use with hypersensitivity reactions to other phenanthrene derivative opioid agonists (codeine, hydrom oxycodone, oxymorphone).
- Hypotension: May cause hypotension; use with caution in patients with hypovolemia, cardiovascular d MI), or drugs which may exaggerate hypotensive effects (including phenothiazines or general anesthe
- Skin reactions: Rarely, acetaminophen may cause serious and potentially fatal skin reactions such exanthematous pustulosis, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). severe skin reactions develop.

Disease-related concerns:

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- Abdominal conditions: Hydrocodone may obscure diagnosis or clinical course of patients with acute abdo
- Adrenocortical insufficiency: Use with caution in patients with adrenocortical insufficiency, including Addi opioid use may cause secondary hypogonadism, which may lead to sexual dysfunction, infertility osteoporosis (Brennan, 2013).
- Biliary tract impairment: Use hydrocodone with caution in patients with biliary tract dysfunction, including cause constriction of sphincter of Oddi.
- Drug abuse: Use opioids for chronic pain with caution in patients at increased risk for misuse; factors as risk include previous substance use disorder, younger age, concomitant depression (major), and p use. Consider offering naloxone prescriptions in patients with factors associated with an increased ris history of overdose or substance use disorder, higher opioid dosages (≥50 morphine milligram equi concomitant benzodiazepine use (Dowell [CDC 2016]).
- Ethanol use: Use with caution in patients with alcoholic liver disease; consuming ≥3 alcoholic drinks/day i liver damage. Have patients avoid ethanol or limit to <3 drinks/day.
- G6PD deficiency: Use with caution in patients with known G6PD deficiency.
- Head trauma: Use with extreme caution in patients with head injury, intracranial lesions, or elevate exaggerated elevation of ICP may occur.
- Hepatic impairment: Use with caution in patients with hepatic impairment.
- Mental health conditions: Use opioids with caution for chronic pain in patients with mental health con anxiety disorders, post-traumatic stress disorder) due to increased risk for opioid use disorder and o monitoring is recommended (Dowell [CDC 2016]).
- Obesity: Use with caution in patients who are morbidly obese.
- Prostatic hyperplasia/urinary stricture: Use hydrocodone with caution in patients with prostatic hyp stricture.
- Psychosis: Use with caution in patients with toxic psychosis.
- Renal impairment: Use with caution in patients with renal impairment.
- Respiratory disease: Use hydrocodone with caution in patients with pre-existing respiratory compr hypercapnia), COPD or other obstructive pulmonary disease, and kyphoscoliosis or other skeletal di respiratory function; critical respiratory depression may occur, even at therapeutic dosages. May sup with caution postoperatively and in patients with pulmonary disease.
- Sleep-disordered breathing: Use opioids with caution for chronic pain and titrate dosage cautiously in p for sleep-disordered breathing, including HF and obesity. Avoid opioids in patients with moderate to s breathing (Dowell [CDC 2016]).
- Seizures: Use with caution in patients with a history of seizure disorders.
- Thyroid dysfunction: Use with caution in patients with thyroid dysfunction.

Concurrent drug therapy issues:

- Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detaile

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- Sedatives: Effects may be potentiated when used with other sedative drugs or ethanol. In the setting prescribing opioids and benzodiazepines concurrently whenever possible; epidemiologic studies increased risk for potentially fatal overdose with concurrent use (Dowell [CDC 2016]).

Special populations:

- CYP2D6 "poor metabolizers": Due to the role of CYP2D6 in the metabolism of hydrocodone to hyd metabolite with higher binding affinity to mu-opioid receptors compared to hydrocodone), patients w CYP2D6, including "poor metabolizers" or "extensive metabolizers," may have decreased or inc formation, respectively. Variable effects in positive and negative opioid effects have been reported in t limited data exists to determine if clinically significant differences of analgesia and toxicity can CYP2D6 phenotype (Hutchinson, 2004; Otton, 1993; Zhou, 2009).
- Debilitated patients: Use with caution in debilitated patients; there is a greater potential for critical respirat therapeutic dosages.
- Elderly: Use with caution in the elderly; may be more sensitive to adverse effects. Use opioids for chro this age group; monitor closely due to an increased potential for risks, including certain risks such as impairment, and constipation. Clearance may also be reduced in older adults (with or without renal im narrow therapeutic window and increasing the risk for respiratory depression or overdose (Dowell [CD
- Pediatric: Respiratory depression may occur even at therapeutic dosages; use with extreme caution in ch

Dosage form specific issues:

- Propylene glycol: Some dosage forms may contain propylene glycol; large amounts are potentially toxic a associated hyperosmolality, lactic acidosis, seizures and respiratory depression; use caution (AAP, 19

Other warnings/precautions:

- Appropriate use: Chronic pain (outside of end-of-life or palliative care, active cancer treatment, medication-assisted treatment for opioid use disorder) in outpatient setting in adults: Opioids should therapy for chronic pain management (pain >3-month duration or beyond time of normal tissue short-term benefits, undetermined long-term benefits, and association with serious risks (eg, overdo risk of developing opioid use disorder). Preferred management includes nonpharmacologic therapy (eg. NSAIDs, acetaminophen, certain anticonvulsants and antidepressants). If opioid therapy is combined with nonpharmacologic and non-opioid therapy, as appropriate. Prior to initiation, known should be discussed and realistic treatment goals for pain/function should be established, incl discontinuation if benefits do not outweigh risks. Therapy should be continued only if clinically mea pain/function outweighs risks. Therapy should be initiated at the lowest effective dosage using imm (instead of extended-release/long-acting opioids). Risk associated with use increases with higher opi benefits should be re-evaluated when increasing dosage to ≥50 morphine milligram equivalents (MM ≥90 MME/day orally should be avoided unless carefully justified (Dowell [CDC 2016]).
- Dosage limit: Limit acetaminophen dose from all sources (prescription and OTC) to <4 g/day.
- Withdrawal: Concurrent use of agonist/antagonist analgesics may precipitate withdrawal symptoms an efficacy in patients following prolonged therapy with mu opioid agonists. Abrupt discontinuation follow also lead to withdrawal symptoms.

Metabolism/Transport Effects Refer to individual components.

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Onset of Action **Hydrocodone:** Opioid analgesic: 10-20 minutes

Duration of Action **Hydrocodone:** 4-8 hours

Metabolism **Hydrocodone:** Hepatic; O-demethylation via primarily CYP2D6 to hydromorphone (major, acti to 33-fold higher or as much as a >100-fold higher binding affinity for the mu-opioid receptor than hydrocodone); N CYP3A4 to norhydrocodone (major metabolite); and ~40% of metabolism/clearance occurs via other non-CYP pa 6-ketosteroid reduction to 6-alpha-hydrocol and 6-beta-hydrocol, and other elimination pathways (eg, fecal, biliary (Hutchinson, 2004; Volpe, 2011; Zhou, 2009)

Half-life Elimination **Hydrocodone:** 3.3-4.4 hours

Excretion **Hydrocodone:** Urine (26% of single dose in 72 hours, with ~12% as unchanged drug, 5% as norl conjugated hydrocodone, 3% as 6-hydrocodol, and 0.21% as conjugated 6-hydromorphol (Zhou, 2009)

Pharmacokinetic Note See Acetaminophen monograph.

Pregnancy Risk Factor C

Pregnancy Considerations Animal reproduction studies have not been conducted with this combina individual agents.

Breast-Feeding Considerations Acetaminophen and hydrocodone are excreted in breast milk. Du serious adverse reactions in the nursing infant, the manufacturer recommends a decision be made whether to dis discontinue the drug, taking into account the importance of treatment to the mother. See individual agents.

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult labeling. [DSC] = Discontinued product

Tablet, oral:

Hydrocodone bitartrate 2.5 mg and acetaminophen 325 mg

Hydrocodone bitartrate 2.5 mg and acetaminophen 500 mg [DSC]

Hydrocodone bitartrate 5 mg and acetaminophen 300 mg

Hydrocodone bitartrate 5 mg and acetaminophen 325 mg

Hydrocodone bitartrate 5 mg and acetaminophen 500 mg [DSC]

Hydrocodone bitartrate 7.5 mg and acetaminophen 300 mg

Hydrocodone bitartrate 7.5 mg and acetaminophen 325 mg

Hydrocodone bitartrate 7.5 mg and acetaminophen 500 mg [DSC]

Hydrocodone bitartrate 7.5 mg and acetaminophen 650 mg [DSC]

Hydrocodone bitartrate 7.5 mg and acetaminophen 750 mg [DSC]

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Name_____ Age____
Address_____ Date____

Rx

Hydrocodone7.5mg/Acetaminophen300mg

Disp: Twelve (12) tablets

Sig: Take one tablet every 4-6 hours as needed for pain.

Refills =0

Signature

DEA No. 613349072

Name_____ Age____
Address_____ Date____

Rx

Acetamin300mg/codeine30mg (Tylenol#3)

Disp: Twelve (12) tablets

Sig: Take one tablet every 4-6 hours as needed for pain.

Refills =0

Signature

DEA No. 613349072

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Name_____ Age___
Address_____ Date___

Rx

Oxycodone5mg/Acetaminophen325mg

Disp: Twelve (12) tablets

Sig: Take one tablet every 4-6 hours as needed for pain.

No Refills

Signature

DEA No. 613349072

Auxiliary Labels attached to an opioid/acetaminophen prescription when dispensed by the pharmacy

Label 1

CONTROLLED SUBSTANCE, DANGEROUS

UNLESS USED AS DIRECTED

Caution: Federal law prohibits the transfer of this drug to any

persons other than the patient for whom it was prescribed

Label 2

Contains acetaminophen. Do not take more than recommended.

Too much may cause liver damage. Discuss any questions with your doctor.

Label 3

Do not take other medicines that have acetaminophen,

(prescription or non-prescription) without checking with your doctor.

Label 4

ADDITONAL INFORMATION. DO NOT SHARE THIS MEDICINE with others

for whom it was not prescribed. CHECK WITH YOUR PHARMACIST about

how to dispose of unused medicine.

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Hydrocodone and Acetaminophen (Patient Education)

Pronunciation

(hye droe KOE done & a seet a MIN oh fen)

Brand Names: U.S.

hycet®; Lorcet® 10/650; Lorcet® Plus; Lortab®; Margesic® H; Maxidone®; Norco®; Stagesic™; Vicodin ES®; Vicodin HP®; Vicodin®; Xodol® 10/300; Xodol® 5/300; Xodol® 7.5/300; Zamicet™; Zolvit®; Zydone®

What are some things I need to know or do while I take this drug?

- .This drug may be habit-forming with long-term use.
- •If you have a history of a drug or drinking problem, talk with your doctor.
- •If you have liver disease, talk with your doctor.
- •If you have lung disease, talk with your doctor. You may be more sensitive to this drug.
- •If you have seizures, talk with your doctor.
- •Talk with your doctor before you use other drugs and natural products that slow your actions.
- •Avoid beer, wine, or mixed drinks.
- •Tell your doctor if you are pregnant or plan on getting pregnant. You will need to talk about the benefits and risks of using this drug while you are pregnant.
- •If you think there has been an overdose, call 1-800-222-1222 (the American Association of Poison Control Centers), your local poison control center (http://www.aapcc.org), or emergency room (ER) right away.

How do I store and/or throw out this drug?

- •Store at room temperature.
- •Store in a dry place. Do not store in a bathroom.
- •Keep all drugs out of the reach of children and pets.
- •Check with your pharmacist about how to throw out unused drugs.

General drug facts

- •If your symptoms or health problems do not get better or if they become worse, call your doctor.
- •Do not share your drugs with others and do not take anyone else's drugs.
- •Talk with the doctor before starting any new drug, including prescription or OTC, natural products, or vitamins.
- •If you have any questions about this drug, please talk with your doctor, pharmacist, or other health care provider.

Special Communication

CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016

Deborah Dowell, MD, MPH; Tamara M. Haegerich, PhD; Roger Chou, MD

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IMPORTANCE Primary care clinicians find managing chronic pain challenging. Evidence of long-term efficacy of opioids for chronic pain is limited. Opioid use is associated with serious risks, including opioid use disorder and overdose.

OBJECTIVE To provide recommendations about opioid prescribing for primary care clinicians treating adult patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life care.

PROCESS The Centers for Disease Control and Prevention (CDC) updated a 2014 systematic review on effectiveness and risks of opioids and conducted a supplemental review on benefits and harms, values and preferences, and costs. CDC used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework to assess evidence type and determine the recommendation category.

EVIDENCE SYNTHESIS Evidence consisted of observational studies or randomized clinical trials with notable limitations, characterized as low quality using GRADE methodology. Meta-analysis was not attempted due to the limited number of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of studies. No study evaluated long-term (≥1 year) benefit of opioids for chronic pain. Opioids were associated with increased risks, including opioid use disorder, overdose, and death, with dose-dependent effects.

RECOMMENDATIONS There are 12 recommendations. Of primary importance, nonopioid therapy is preferred for treatment of chronic pain. Opioids should be used only when benefits for pain and function are expected to outweigh risks. Before starting opioids, clinicians should establish treatment goals with patients and consider how opioids will be discontinued if benefits do not outweigh risks. When opioids are used, clinicians should prescribe the lowest effective dosage, carefully reassess benefits and risks when considering increasing dosage to 50 morphine milligram equivalents or more per day, and avoid concurrent opioids and benzodiazepines whenever possible. Clinicians should evaluate benefits and harms of continued opioid therapy with patients every 3 months or more frequently and review prescription drug monitoring program data, when available, for high-risk combinations or dosages. For patients with opioid use disorder, clinicians should offer or arrange evidence-based treatment, such as medication-assisted treatment with buprenorphine or methadone.