DRUGS USED IN ENDODONTICS

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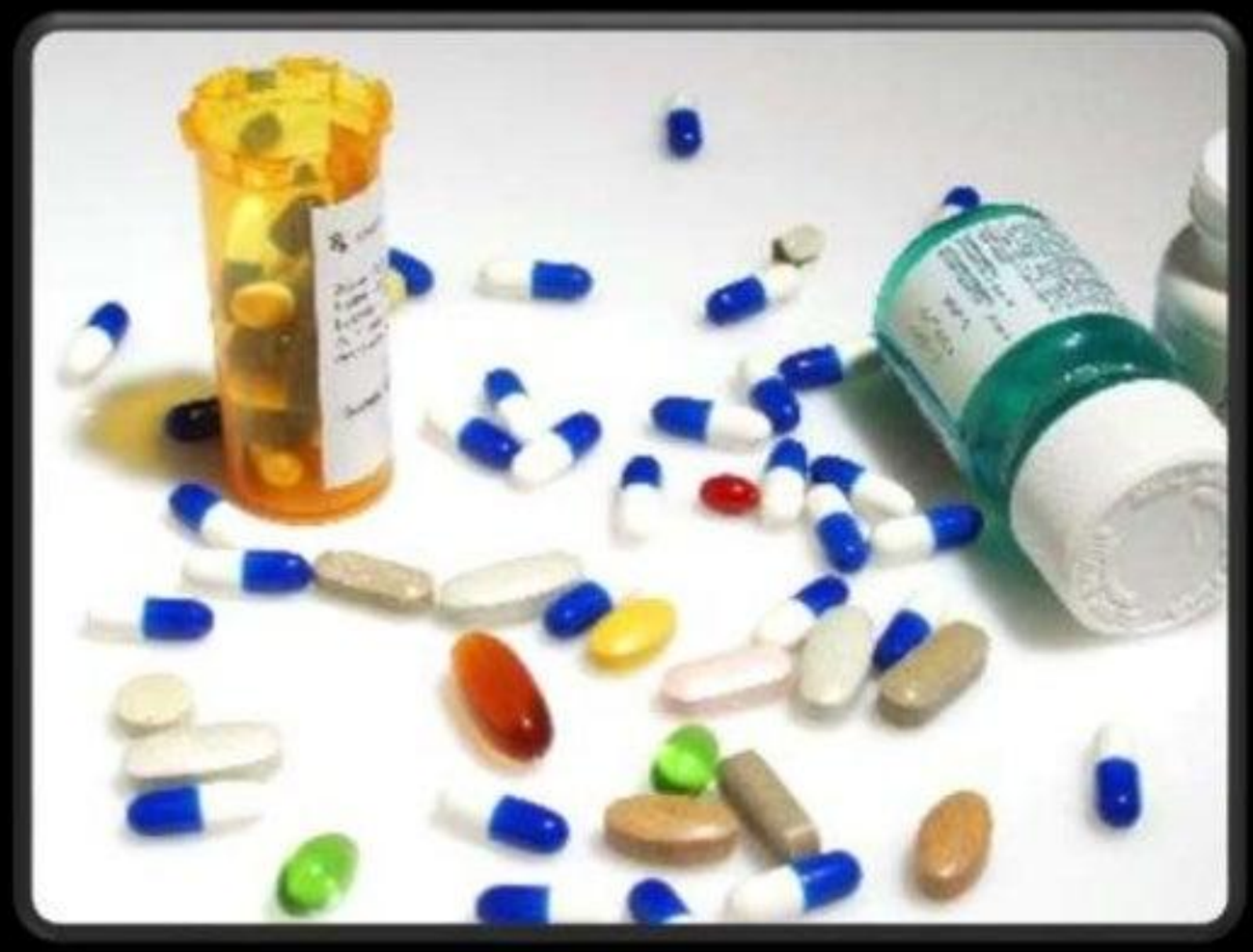


Definitions

- A medicine or other substance which has a physiological effect when ingested or otherwise introduced into the body

-Oxford dictionary

- A ***pharmaceutical drug***, also referred to as a ***medicine*** or (loosely) ***medication***, officially called ***medicinal product***, can be loosely defined as any chemical substance — or product comprising such — intended for use in the medical diagnosis, cure, treatment, or prevention of disease.
- The word pharmaceutical comes from the Greek word *Pharmakeia*.
- *According to the* ***Food, Drug, and Cosmetic Act,***

(1) : a substance recognized in an official pharmacopoeia or formulary

(2) : a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease

(3) : a substance other than food intended to affect the structure or function of the body

(4) : a substance intended for use as a component of a medicine but not a device or a component, part, or accessory of a device

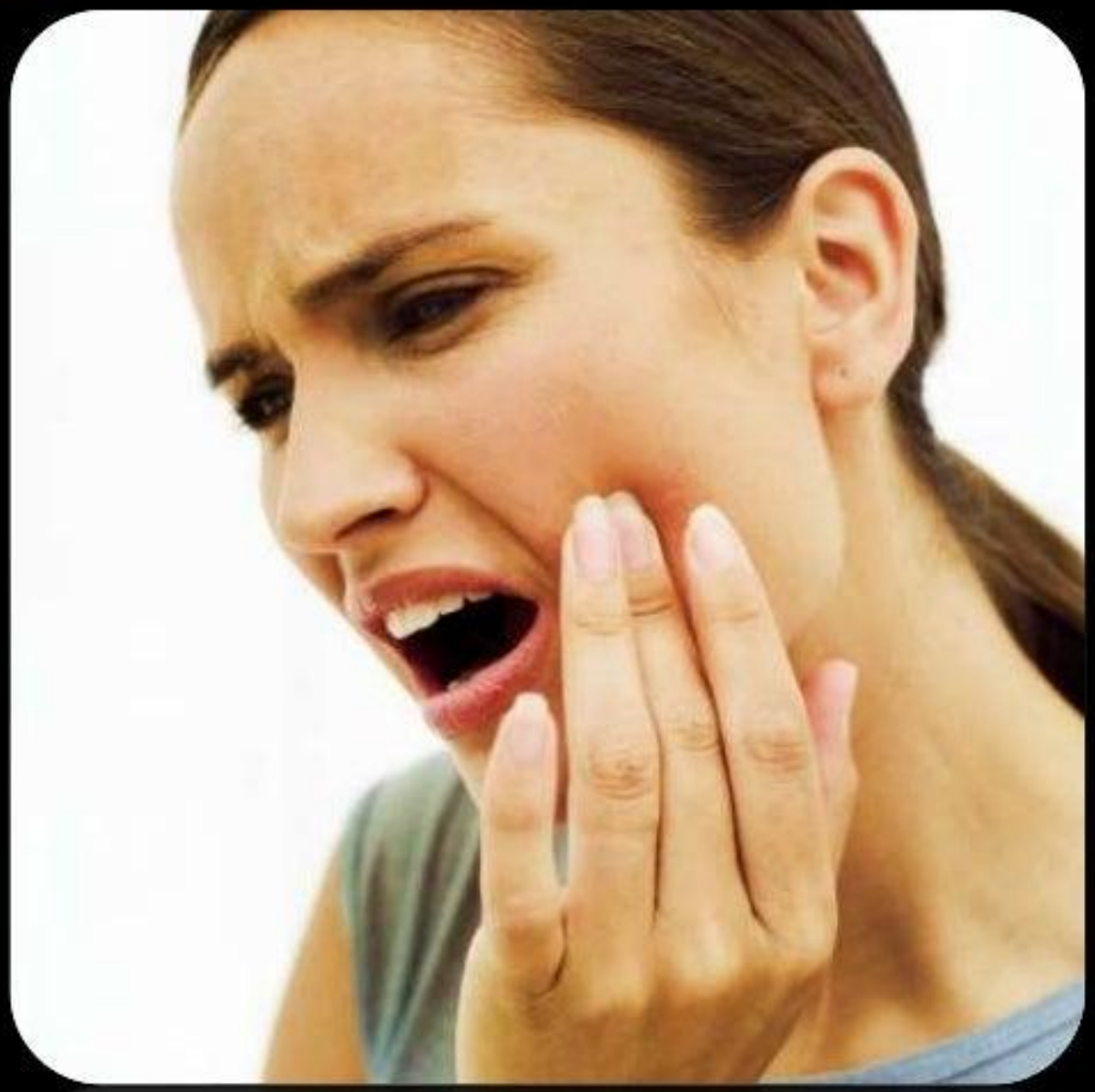
CLASSIFICATIONS

Based on when the drug is administered-

- **Pre treatment-** analgesics, antibiotics, anti-anxiety
- **Treatment**- corticosteroids, antibiotics, anti-microbials, local anaesthesia
- **Post treatment-** antibiotics, corticosteroids, analgesics

Based on route of administration-

- **Local**- topical antibiotics, anti-microbials, topical anaesthetics
- **Systemic**- oral- antibiotics, analgesics, anti anxiety
  - injectable- im/iv- antibiotics, analgesics, sedatives
- **Inhalation**- sedatives, anaesthesia

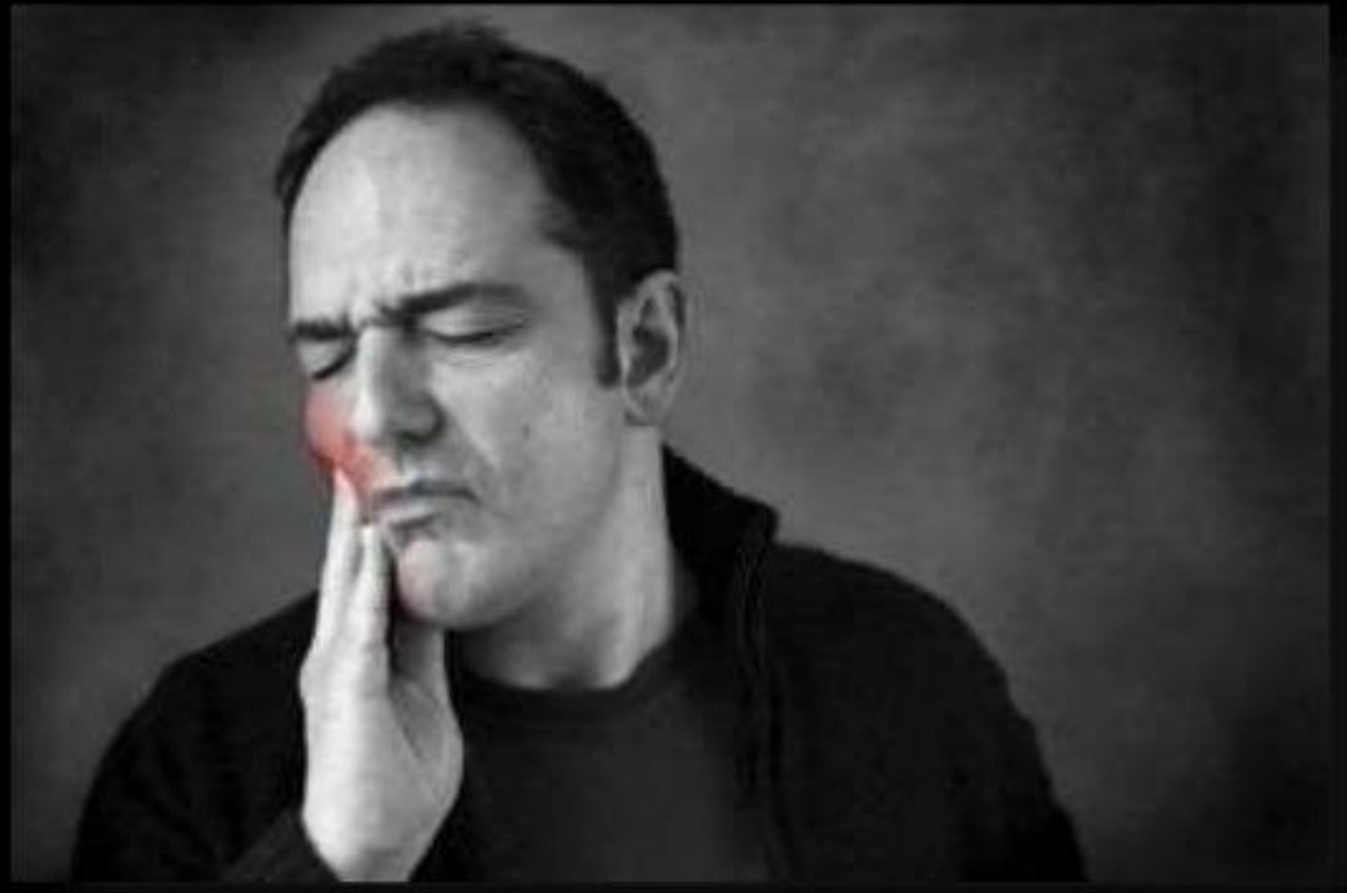


PART I

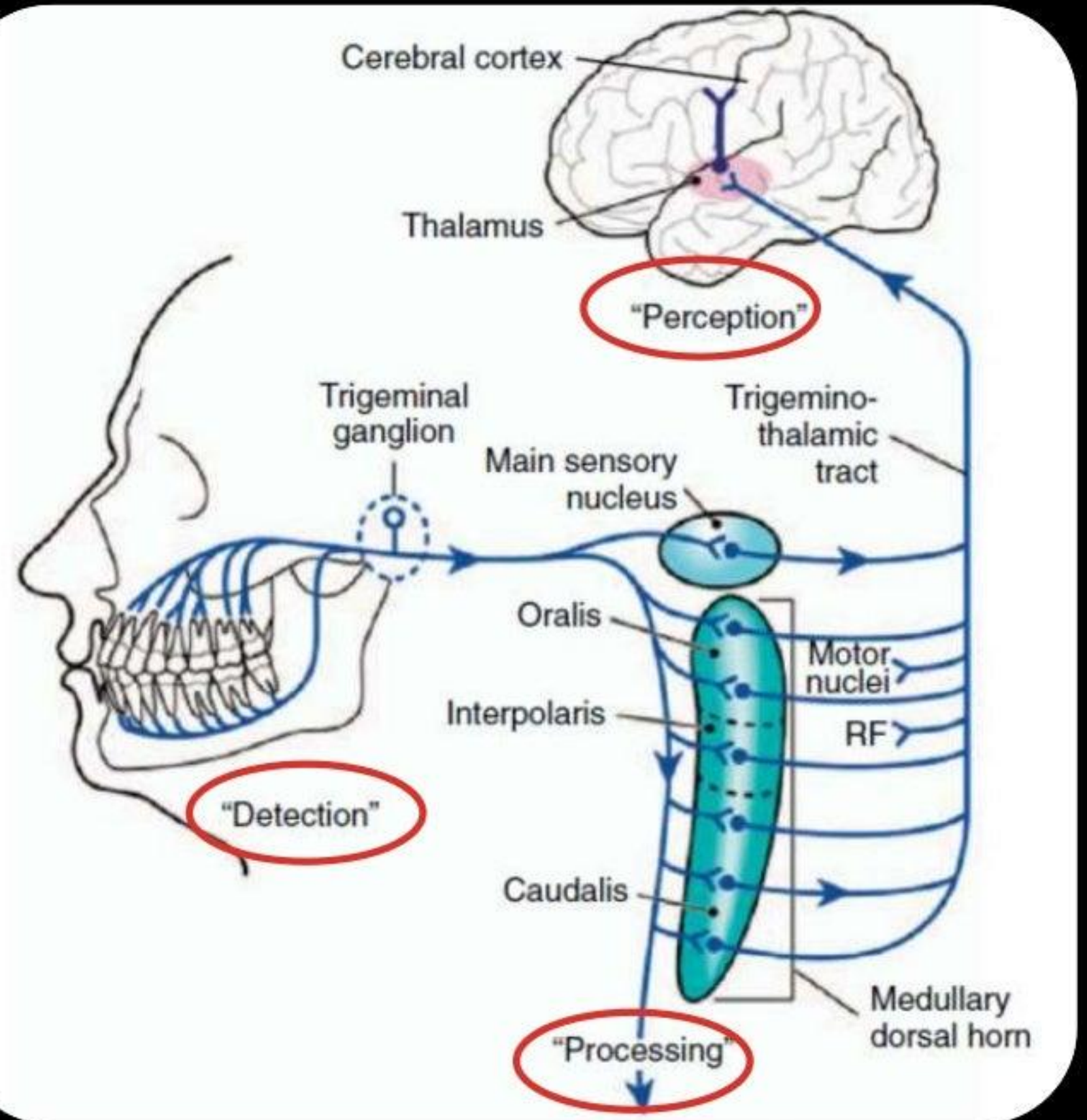
PAIN AND ANALGESICS IN ENDODONTICS

- *The skill of the clinician is often judged primarily by their success or failure of pain control.*

-Cohen, Pathways of the Pulp



The Trigeminal Pain System



ANALGESICS- NONNARCOTIC

Management of endodontic pain is **multifactorial** and directed at reducing the peripheral and central components of hyperalgesia through combined endodontic procedures and pharmacotherapy.

2 classes mainly-

NSAIDS

Acetaminophen

NSAIDS

- Very effective in managing pain of inflammatory origin- binds to plasma proteins- exhibit increased delivery to inflamed tissue via extravasation of plasma proteins.
- Less studies done comparing NSAIDS on endodontic pain in particular
- Ibuprofen- considered the prototype of contemporary NSAIDs and has a well-documented efficacy and safety profile.
- Etodolac (i.e., Lodine) has minimal gastrointestinal (GI) irritation.
- Ketoprofen (i.e., Orudis) has been shown in some studies to be somewhat more analgesic than ibuprofen

- They act primarily through the inhibition of cyclooxygenase (COX) enzymes 1 and2.
- COX-1 is expressed throughout the body and has a role in protection of stomach mucosa, kidney function and platelet action.
- COX-2 is induced by various endogenous compounds such as cytokines, mitogens and endotoxins in inflammatory cells and is responsible for the elevated production of prostaglandins during inflammation.
- Nakanishi et al demonstrated high levels of expression of COX-2 in samples of human dental pulps with a diagnosis of irreversible pulpitis.
- These two proteins share a 60% homology and catalyze the conversion of arachidonic acid into prostaglandin E2.
- PGE2 is subsequently metabolized by a variety of syntheses into PGH2, PFI2, PGD2, PGF2 and thromboxane A2.
- Inhibiting COX-2 blocks prostaglandin formation and ultimately prevents inflammation and sensitization of the peripheral nociceptors.

Pharmacological Strategies to Control Post-operative Endodontic Pain
Zahed Mohammad, Alireza Farhad, Meisam Khalesi
Dent Res J 2007; 4(2): 61-68

- **NSAIDS combined with other drugs** (e.g., flurbiprofen with tramadol) or pretreatment and posttreatment application of NSAIDs provides effective pain control.

- The introduction of selective inhibitors of COX-2 offered the potential for both analgesic and antiinflammatory benefits and reduced GI irritation.

- Oral surgery pain studies evaluating COX-2 inhibitors have indicated that Rofecoxib (i.e.,Vioxx) has significant analgesic efficacy.

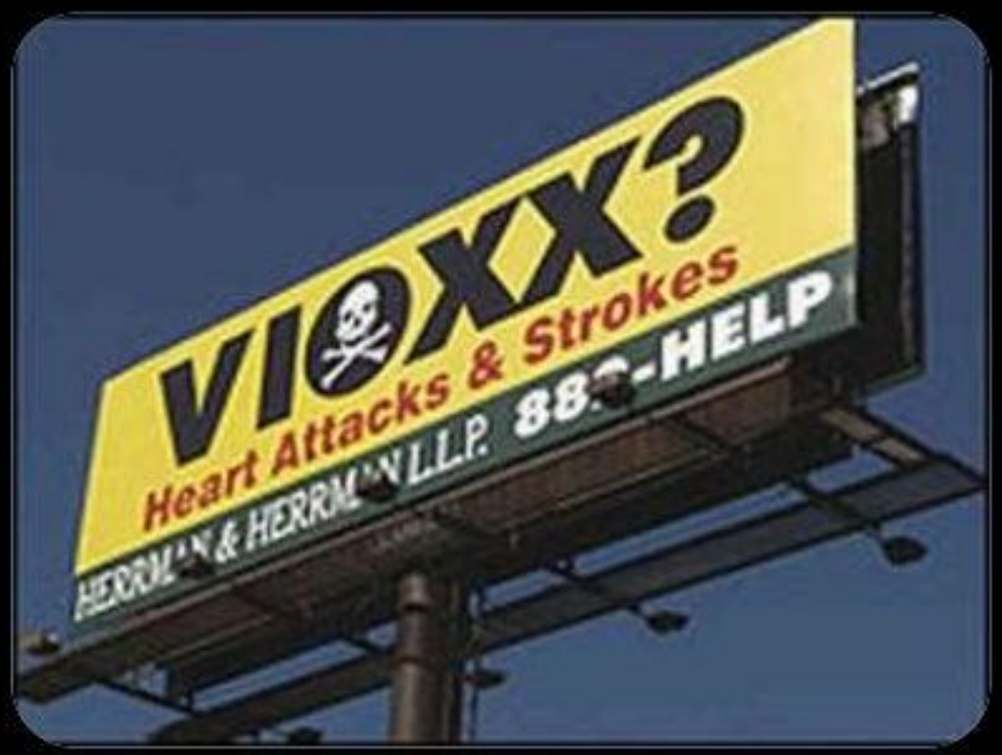
- COX-2 levels are increased in inflamed human dental pulp, and a COX-2 inhibitor (rofecoxib) is analgesic in patients with endodontic pain.
- Concern has been raised that the COX-2 inhibitors may also display at least some GI irritation in patients with preexisting GI disease

- Increased risk for prothrombic events following long-term administration of rofecoxib (**VIOXX**), which led to the withdrawal of this drug from the market in 2004.

- Diclofenac (Voltaren) is a relatively COX-2-selective drug and seems to have a similar degree of COX-2 selectivity as celecoxib.

- Diclofenac was associated with increased CV events.

- In the randomized trial analysis, there was an increase in CV risk with high-dose ibuprofen.



The News Tuesday, 27th September 2005

NZ woman joins suit against Vioxx

As soon as she had a heart attack New Zealand woman Helen Barns says she knew that the discomfort pain relievers Vioxx was to blame.

Increasingly worried health support worker Barns, 58, is one of more than 200 New Zealanders who have contacted United States law firm Kenneth B. Moll & Associates saying they have had a heart attack after taking Vioxx.

The firm has now filed a class action in Louisiana on behalf of six New Zealanders who have suffered heart attacks after taking Vioxx.

Barns has been contact along with Christchurch man Ian Thorne Gee in the court documents as a representative of the New Zealanders.

Vioxx manufacturers Merck & Co pulled Vioxx from the market in September last year after studies showed the drug increased the risk of heart attacks and strokes.

In August this year, a Texas jury found Merck & Co liable for the death of a man after he took Vioxx and awarded $US253.5 million ($NZ380 million) to his widow.

Barns said that on August 17, 2001, after taking Vioxx for two weeks for her arthritis, she had a heart attack.

"I was given an injection into the top of my hand and I remember the doctor saying 'This will do one of three things — it will kill you, it will cause you to have a stroke or it will dissolve the clot'.

"That was very scary. Even though I was only semi-conscious I remember them saying that."

After 10 minutes, Barns felt the pressure easing and knew she would pull through but she was in no doubt as to what caused the heart attack.

"I told the ambulance men when they came it was the Vioxx.

"Every time I took it I got a really heavy chest but I thought that maybe that was just it getting into my system and thought 'well, I've got to persevere with this if I want relief from the arthritis'."

But on the final morning she took the Vioxx, the pain had got worse and Barns said it felt like she was "in a vice".

> "I was given an injection into the top of my hand and I remember the doctor saying 'this will do one of three things — it will kill you, it will cause you to have a stroke or it will dissolve the clot'."
>
> Helen Barns

Lawyer Kenneth Moll said he supported the New Zealand claim to be successful, and hoped such awards could be into the millions of dollars.

Mr Moll said as many as 45,000 New Zealanders had taken Vioxx.

He said although New Zealanders were protected by accident compensation legislation from suing for injury in New Zealand, there was nothing to stop them doing so in the US.

Merck is appealing against the Texas verdict. It has also pledged to fight any further cases. —NZPA

Based on the available data, the FDA has requested that manufacturers of all prescription products containing nonselective NSAIDs revise their product labeling to include

(1) a boxed warning regarding the potential serious adverse CV events and the serious, potentially life-threatening GI adverse events associated with the use of this class of drugs

(2) a contraindication for use in patients who have recently undergone coronary artery bypass surgery

(3) a medication guide for patients, regarding the potential for CV and GI adverse events associated with the use of this class of drugs.

Given this situation and reasonable alternative NSAIDs, its recommended not considering COX-2 inhibitors for treating routine endodontic pain patients.

Limitations and Drug Interactions

- NSAIDs exhibit an analgesic ceiling that limits the maximal level of analgesia and induces side effects, including those affecting the GI system (3% to 11% incidence) and the CNS (1% to 9% incidenc of dizziness and headache).

- NSAIDs are contraindicated in patients with ulcers and aspirin hypersensitivity.

- Also associated with severe GI complications

- Risk of adverse effects increases with increasing lifetime accumulated dose of these drugs.

- Acetaminophen and opioid combination drugs represent alternatives for those patients unable to take NSAIDs

Acetaminophen

- one of the most commonly used drugs
- found in Combination products for the relief of pain and symptoms of cold or flu.
- considered safe when taken at normal doses, but in higher doses causes liver toxicity and has become the most common cause of acute liver failure
- conjugated in the liver to form inactive metabolites.

- A small portion is metabolized by the cytochrome P450 system to form *N*-acetyl-*p*-benzoquinone imine (NAPQI), which is very toxic but is generally detoxified by glutathione and converted into nontoxic compounds.

- Large doses of acetaminophen saturate the main route of metabolism, causing more acetaminophen to be converted to NAPQI.

- Liver injury occurs once glutathione becomes depleted and NAPQI is allowed to accumulate.

- Healthy adults should not take more than 4 g (4000 mg) of acetaminophen in a 24-hour period.

Summary of Selected Nonnarcotic Analgesics

Analgesic	Trade Name	Dose Range (mg)	Daily Dose (mg)
Acetaminophen	Tylenol et al.	325-1000	4000
Aspirin	Many	325-1000	4000
Diflunisal	Dolobid	250-1000	1500
Diclofenac potassium	Cataflam	50-100	150-200
Etodolac	Lodine	200-400	1200
Fenoprofen	Nalfon	200	1200
Flurbiprofen	Ansaid	50-100	200-300
Ibuprofen	Motrin et al.	200-800	2400 (Rx)
Ketorolac*	Toradol	30-60 (oral)	60
Naproxen Na	Anaprox et al.	220-550	1650 (Rx)
Naproxen	Naprosyn	250-500	1500
Ketoprofen	Orudis	25-75	300 (Rx)

Opioid Analgesics

- potent analgesics
- used in dentistry in combination with acetaminophen, aspirin, or ibuprofen
- activate mu opioid receptors located at several important sites in the brain
- Activation of these receptors inhibits the transmission of nociceptive signals from the trigeminal nucleus to higher brain regions
- opioids also activate peripheral opioid receptors located in dental pulp
- Intraligamentary injection of morphine has been shown to significantly reduce pain in endodontic patients and other inflammatory pain states
- *Adverse side effects*, which can include nausea, emesis, dizziness, drowsiness, and the potential for respiratory depression and constipation.

A combination formulation is preferred because it permits a lower dose of the opioid, thereby reducing side effects

Selected Opioid Combination Analgesic Drugs

Formulation	Trade Name*	Possible Rx
APAP 300 mg and codeine 30 mg	Tylenol with codeine no. 3	2 tabs q4h
APAP 500 mg and hydrocodone 5 mg	Vicodin, Lortab 5/500	1-2 tabs q6h
APAP 325 mg and oxycodone 5 mg	Percocet	1 tab q6h
APAP 500 mg and oxycodone 5 mg	Tylox	1 tab q6h
ASA 325 mg and codeine 30 mg	Empirin with codeine no. 3	2 tabs q4h
ASA 325 mg and oxycodone 5 mg	Percodan	1 tab q6h

- Codeine is often considered the prototype opioid for orally available combination drugs.
- 60-mg dose of codeine produces less analgesia than either aspirin 650 mg or acetaminophen 600 mg

Analgesic Doses of Representative Opioids

Opioid	Dose Equivalent to Codeine 60 mg
Codeine	60 mg
Oxycodone	5-6 mg
Hydrocodone	10 mg
Dihydrocodeine	60 mg
Propoxyphene HCl	102 mg
Propoxyphene-N	146 mg
Meperidine	90 mg
Tramadol	50 mg