



No MUs is good MUs

Opioid-free analgesia in the addicted (or recovering addict) patient

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outline

- ***Introduction - why this topic?***
- Review of addiction.
- Case study.
- Pathophysiology & Rx options.
- What does the evidence support?
- Conclusions.
- Questions ... from you!



51,000 admissions for opiate (non-heroin) abuse in 2003 (U.S. Dept. of Health and Human Services)

non-heroin: Dilaudid, Demerol, codeine, opium, oxycodone ... remember “MU receptors.”

Physical changes (plasticity) with disease.

Technician vs. Clinician.

Bring together things from the class.

introduction



addiction

Introduction - why this topic?

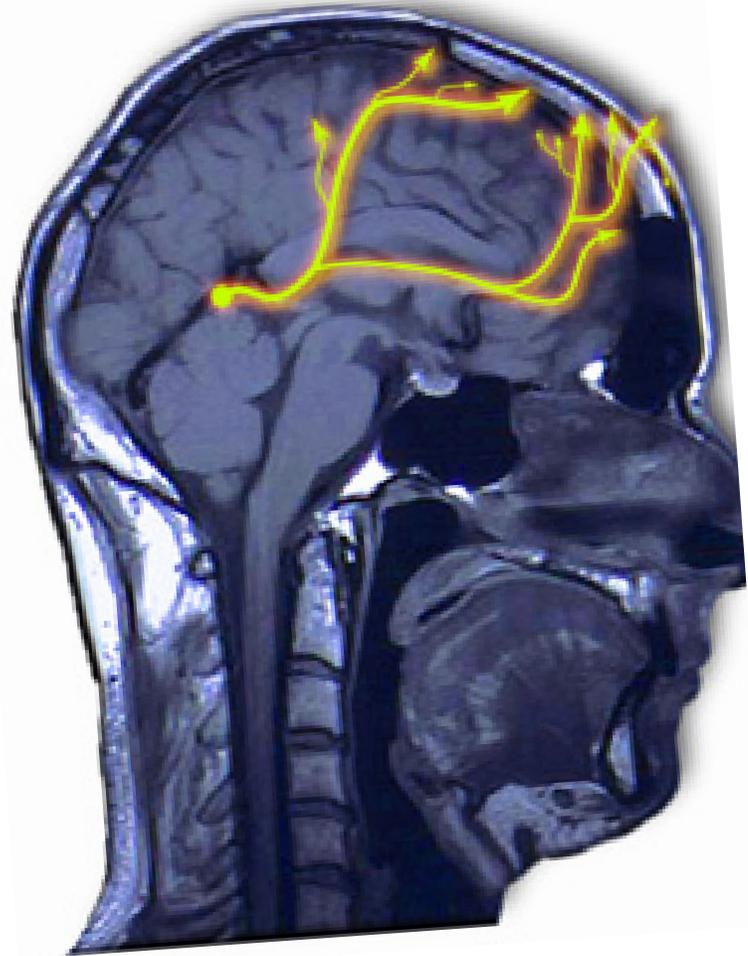
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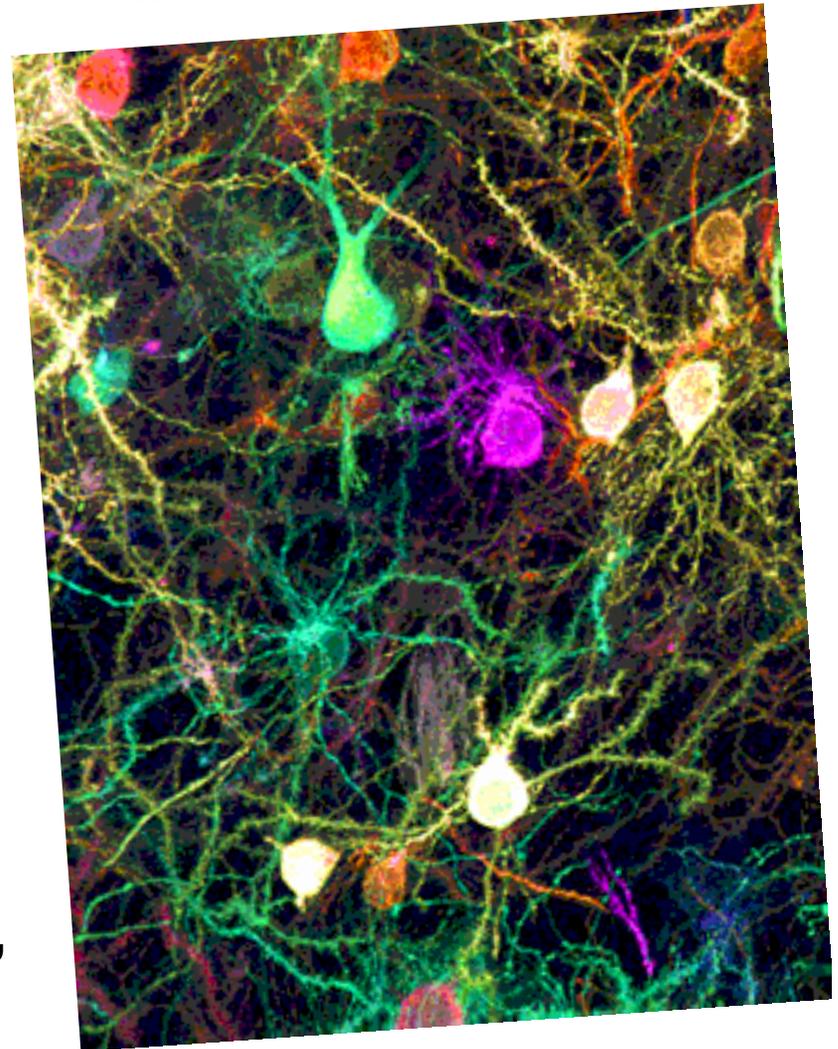
addiction

- DSM-IV criteria
- long term disease (HTN, DM-II, CRPS)
- Reward pathway ---
“everything comes together in the limbic system.” Dr. Cheatle
- Increasing # of D2 receptors in CNS.



addiction

- Predisposing factors: (Ives et al 2004)
 - family history
 - psychiatric history
 - **personal history**
- Dysregulation of pathway to/from hypothalamus.
- This change is permanent, so the risk never goes away.



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Case study ... J.M.

54-year-old women

- Scheduled for elective total right knee arthroplasty.
- H/O:
 - HTN
 - anxiety
 - polysubstance (ETOH & opioid) abuse.
- Having been clean for 20 years
PT requests no opioids for analgesia.



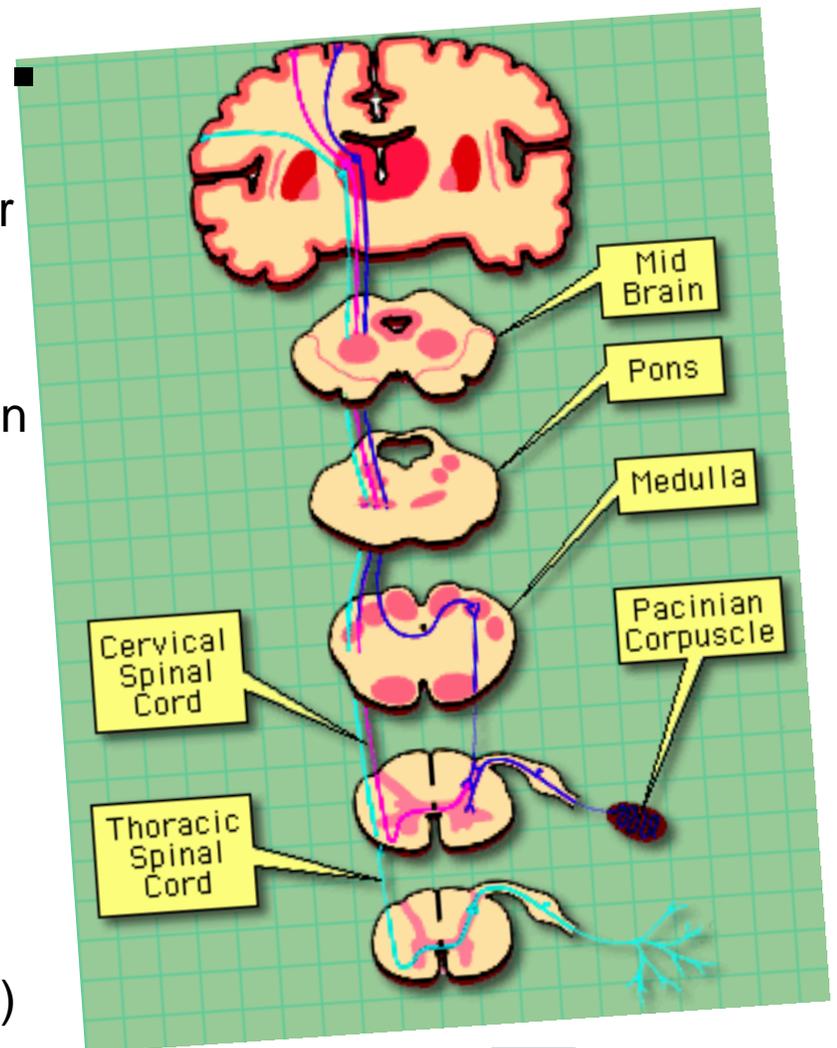
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What's happening here.

- The nerve root is the primary site of action for epidural and spinal analgesia.
- LA injected into the subarachnoid or epidural space, bathes the nerve roots achieving a sensory and possibly motor blockade. (Morgan et al., 2006)
- Blockade is thru action at the dorsal horn which blocks sodium channels in the inactive closed state.
- Also blockade of potassium and calcium channels.
- This inhibits generation and propagation of nociceptive electrical activity.
- Also inhibits post-synaptic depolarization driven by substance P, further decreasing nociceptive transmission. (Barash et al., 2001)



Rx for success



 Precedex®
(dexmedetomidine HCl Injection)

- **Dexmedetomidine (Precedex)**
- provides analgesia (and sedation) via central agonist action on alpha-2 receptors.
- 8x more selective than clonidine.
- sedative and anxiolytic properties through the locus coeruleus in the CNS.
- analgesic effects through activation of the alpha-2c receptor subtype by accentuating the action of opioids (Szumita et al., 2007).

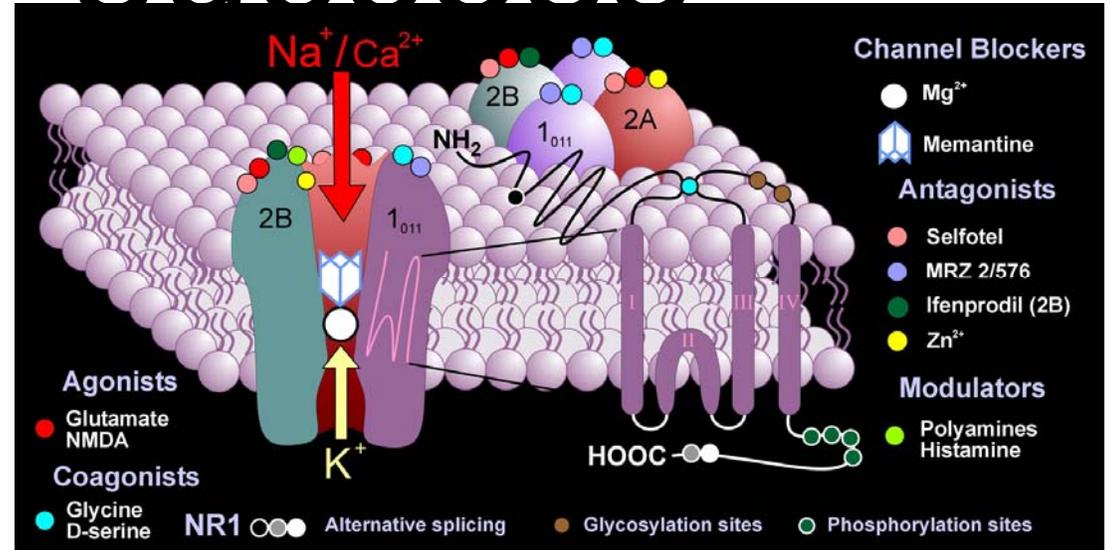


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and Critical Care Medicine



Rx for success

● Ketamine



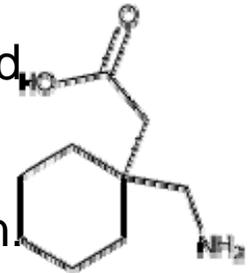
- Binds noncompetitively to N-methyl-D-aspartate (NMDA) receptors.
- May exert effects at other sites including opioid receptors, muscarinic receptors, as well as voltage-sensitive sodium and and calcium L-type channels.
- In a review article published in *Pain*, (studies that were randomized, prospective, controlled, double-blind and reported pain scores); intravenous low dose ketamine found to reduce pain significantly.
- At doses necessary to provide intense analgesia, an increased risk for psychotomimetic adverse effects (Schmid et al., 1999).



Neurontin



- Important Dynamics: works via binding presynaptic Ca⁺⁺ receptors.
- Reduction in release of nociceptive neurotransmitters (Substance P, CRGP)
- Decrease excitation in the dorsal horn combats allodynia and hyperalgesia.
- May be useful in acute pain by inhibiting central sensitization.
- Important Kinetics: GI absorption is saturable at usual doses.
- Results in an inverse relationship between dose and bioavailability.
- This is not the case for pregabalin.



Chemical Formula: C₉H₁₇NO₂



Clonidine



- Analgesic dynamics:
 - stimulates alpha-2 receptors in the substantia gelatinosa to release norepinephrine causing hyper-polarization of afferent pathways.
 - Intraarticular injection with 0.25% Bupivacaine provided analgesia for 600 minutes following outpatient knee arthroscopy.
 - Adverse events: bradycardia and hypotension.
 - Average Percocet use was 3 tablets in 1st 24 hours.
 - No support for additional to peripheral nerve block.





Dynamics – selectively inhibits cyclooxygenase II at therapeutic dosages

Cox II expression increased 10-20 times in inflammatory states & may contribute to central sensitization

Kinetics - Requires 5 days to reach a steady state

CV effects r/t renal regulation of blood pressure resulting in sodium and water retention and 20 mmhg increase in blood pressure

Analgesia:

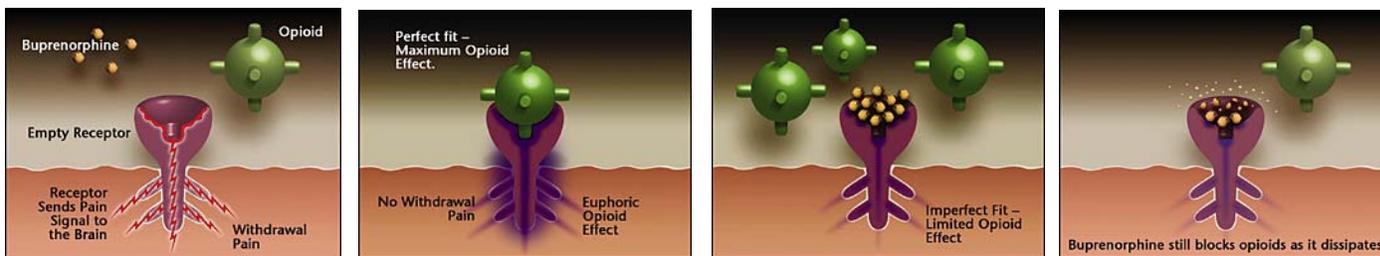
More effective than Percocet (10/1000) in relieving pain post knee arthroscopy

Perioperative advantages: lack of platelet inhibition, diminished GI AE, long duration of action



Buprenorphine

- Semisynthetic derivative of morphine indicated for maintenance therapy with the addicted patient or moderate to severe pain.
- Partial Mu & Kappa agonist/antagonist.
- Mu supra-spinal analgesia, respiratory depression, and myosis.
- Kappa spinal analgesia, dysphoria, psychomimetic effects.
- High affinity and slow dissociation from opioid receptors associated with more mild withdrawal.
- May be abused but at higher doses exhibits an antagonistic effect resulting in a safer profile.



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Evidence Based Practice

● Isn't Precedex really just snake oil?

- A study published in the *Canadian Journal of Anesthesia*(2006) focused on whether intraoperative infusion of dexmedetomidine provided effective postoperative analgesia.
- 50 women undergoing total abdominal hysterectomy. The subjects were computer randomized into two groups of 25; group D (those receiving precedex) and group P (placebo).
- Group D received a bolus dose over 30 minutes prior to induction, followed by a continuous infusion which was discontinued at the end of surgery. Group P received that same volumes in the form of .9% NS.
- After extubation, both groups were given a Morphine bolus of 3 mg followed by an IV PCA at 1 mg boluses with a lockout interval of 5 minutes, continued for 48 hours.
- The average morphine consumption for group P was 65.8 +/- 20.6mg v.s. Group D used 28.6 +/- 10.7mg. This much lower consumption of morphine indicates the significant analgesic effect of intraoperative precedex (Gurbet et al., 2006).



Evidence Based

Practice

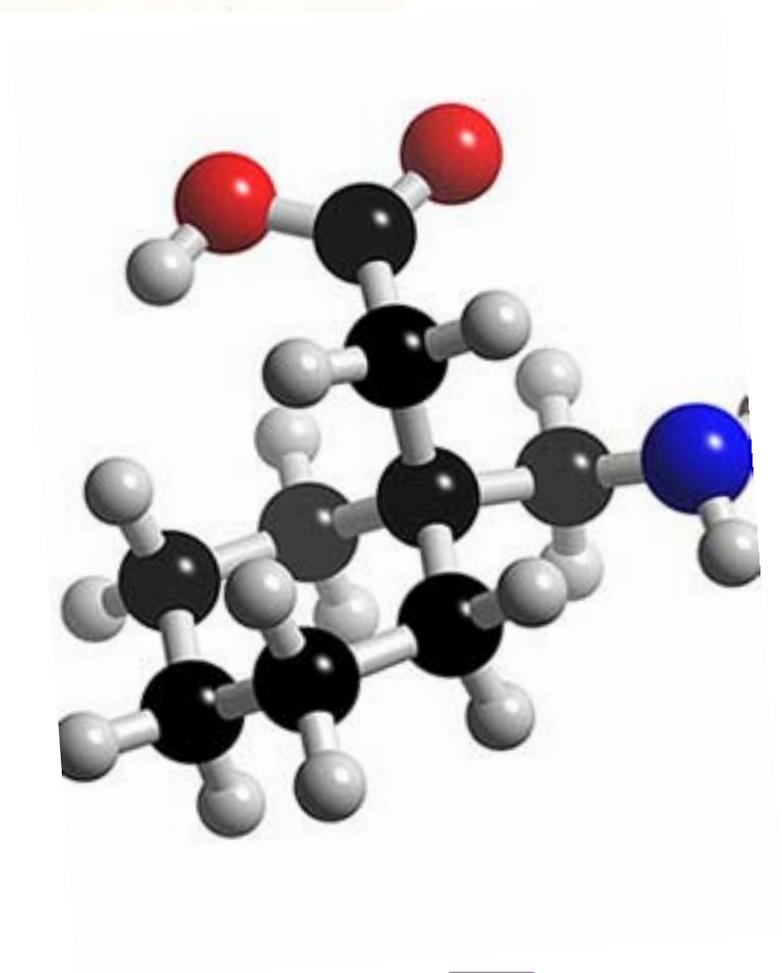
- No, really. Isn't Precedex just snake oil?
- Findings published in *Anesthesia & Analgesia*(2004). 34 patients scheduled for elective inpatient procedures were included in a study comparing precedex to morphine for postoperative analgesia.
- In this case precedex was started 30 minutes prior to the end of surgery and continued in PACU.
- The level of sedation was similar for both groups in the PACU.
- However, patients receiving precedex for postsurgical pain had a significantly slower postoperative heart rate and required 66% less morphine in the PACU compared to the control group who received only morphine (Arain et al, 2004).



Neurontin



- Research Review:
- 22 randomized, double blind, controlled clinical trials.
- 1909 participants.
- Opioid sparing effect 30mg +/- 4mg in 1st 24 hours.
- Diminished pain & less use of pain medications at 1 and 3 months.
- Effect not significantly related to dose.



Remember our case study?

- Is her request appropriate?
- Good. So, is this doable?
- Fine, right answer, but how?



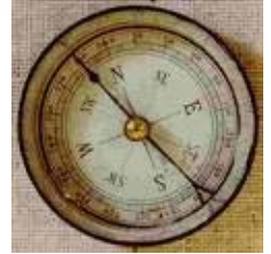
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Actual

Conclusions



- Addiction changes neural pathways ... permanently.
- You may encounter a PT who requests no opioids.
- Then again you may never ... that's not the point.
- By staying informed you can best care for your PTs.
- There is more than one path to relief of pain



Sources

- Arain, R.S., Ruehlow, M.R., Uhrich, D.T., & Ebert, J.T. (2004). Anesthesia & Analgesia, 98, 153-158.
- Barash, G. P., Cullen, F. B., & Stoelting, K. R. (2001). Clinical Anesthesia. Philadelphia: Lipincott Williams & Wilkins.
- Brill, S., & Plaza, M. (2004). Non-narcotic adjuvants may improve the duration and quality of analgesia after knee arthroscopy: a brief review. *Canadian Journal of Anesthesia*, 51(10), p 975-978.
- Cheadle, M.D., Gallagher, R. M. (2006). Chronic pain and comorbid mood and substance use disorders: a biopsychosocial treatment approach. *Current Psychiatry Reports*. Oct;8(5):371-6.
- Department of Health and Human Services. retrieved on 06 April 2008 from <http://www.drugabusestatistics.samhsa.gov/2k6/opiatesTX/opiatesTX.cfm>
- Frampton, J. E. & Keating, G. m. (2007). Celecoxib a review of its use in the management of arthritis and acute pain. *Drugs*: 67(16) 2432-2472.



Sources and More

- Gurbet, A., Basagan-Mogol, E., Turker, G., Ugun, F., Kaya, N., & Ozcan, B. (2006). Intraoperative infusion of dexmedetomidine reduces perioperative analgesia requirements. *Canadian Journal of Anesthesia*, 53:7, 646-652.
- Heit, H. A., & Gourlay, D. L. (2008). Buprenorphine new tricks with an old molecule for pain management. *Clinical Journal of Pain*, 24(2), 93-98.
- Ives, T.J., Chelminski, P.R., Hammett-Stabler, C.A., Malone, R.M., Perhac, J.S., Potisek, N.M., Shilliday, B.B., DeWalt, D.A., Pignone, M.P. (2006) Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. *BMC Health Services Research*. April 4;6:46.
- Johnson, R. E., Fudala, P. J., & Payne, R. (2005). Buprenorphine: considerations for pain management. *Journal of pain and symptom management*, 29(3), 297-307.
- Joshi, W., Reuben, S. S., Kilaru, P. R., Slar, J., & Maciolek, H. (2000). Postoperative analgesia for outpatient arthroscopic knee surgery with intraarticular clonidine. *Ambulatory Anesthesia*, 90(5), 1102-1106.



Sources and More Galore

- McCartney, C. J., Duggan, E., & Apatu, E. (2007). Should we add clonidine to local anesthetic for peripheral nerve blockade? A qualitative systematic review of the literature. *Regional anesthesia and pain medicine*, 32(4), 330-338.
- Morgan, E.G., Mikhail, S. M., & Murray, J.M. (2006). *Clinical Anesthesiology*. New York: McGraw-Hill Companies, Inc.
- Schmid, L.R., Sandler, N.A., & Katz, J. (1999). Use and efficacy of low dose ketamine in the management of acute postoperative pain: A review of current techniques and outcomes. *Pain*, 82, 111-125.
- Szumita, M.P., Baroletti, A.S., Anger, E.K., & Wechsler, E.M. (2007). Sedation and analgesia in the intensive care unit. Evaluating the role of dexmedetomidine. *American Society of Health-System Pharmacologists*, 64, 37-44.
- Tippana, E. M., Hamunen, K., Kontinen, V. K., Kalso, E. (2007). Do surgical patients benefit from perioperative gabapentin/pregabalin? A systematic review of efficacy and safety. *Anesthesia & Analgesia* 104(6) 1545-1557.

