



## **Lost in Translation: Making Sense of Clinical Treatment Guidelines**

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### **Disclosures: Charles Argoff**

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▪ **Drug/Product Off-Label Use Disclosure**

- Off-label use of a drug and/or product will be addressed in this presentation. This information will be verbally disclosed both at the beginning of the presentation and at the time of drug/product discussion.



## Lost in Translation: Making Sense of Clinical Treatment Guidelines

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- Multiple clinical treatment guidelines have been published regarding headache and pain management
- However, many have questioned the benefit of such clinical guidelines for the treatment of individual patients
- This course will review key published treatment guidelines for migraine, interventional pain management, chronic opioid use, neuropathic pain, and chronic low back pain
- The faculty will review the relevant guidelines and discuss their strengths and critical weaknesses when using such guidelines to actually treat people



## Evidence Based Medicine

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- Evidence-based medicine (EBM) has been defined as "the conscientious, explicit and judicious use of current best evidence in **making decisions about the care of individual patients**"  
*Sackett, D. Evidence-based Medicine - What it is and what it isn't. BMJ 1996; 312:71-72*
- EBM: The judicious use of the best current available scientific research in making decisions about the care of patients. EBM is intended to **integrate clinical expertise** with the research evidence and patient value

<http://www.medterms.com/script/main/art.asp?articlekey=33300>



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## **Do Published Migraine Guidelines Improve Patient Outcomes?**



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### **Learning Objectives**

- Using published American Academy of Neurology guidelines for the treatment of certain headache conditions as an example of such guidelines upon attending this symposium, the participant will be able to:
  1. Identify pharmacologic therapies which have strong evidence for their use in the prevention of episodic migraine.
  2. Identify the notable limitations of such recommendations.



## Real Patients – Do Current Treatment Guidelines Help?

- 32 yo female experiencing 2 migraine headaches each week: known FH, worsens around the time of her menstrual cycle, has never been treated
- 18 yo male experiencing postconcussion syndrome and posttraumatic migraine presents to your office
- 28 yo female experiencing 15 headaches monthly, 10 clearly migraine, lasts more than 4 hours, experiencing for more than 3 consecutive months—no response to multiple prophylactic approaches
- 40 yo female experiencing chronic daily headache using OTC analgesics daily

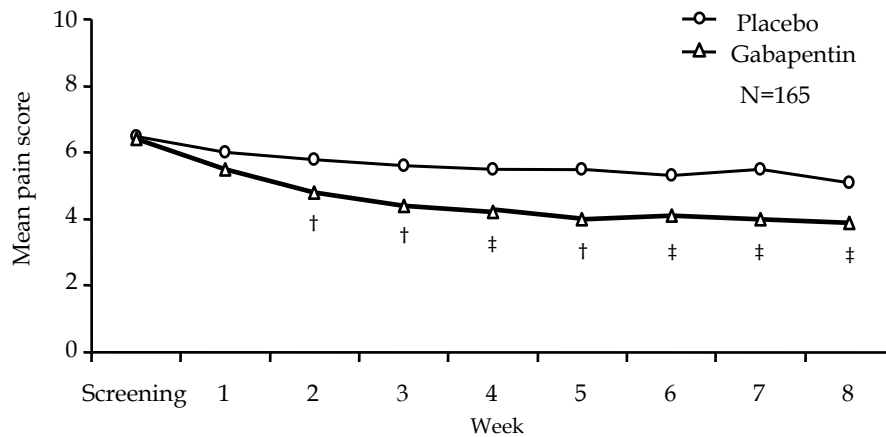
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*"Discouraging Data on the Antidepressant"*

## Gabapentin in the treatment of painful diabetic neuropathy\*



\*Not approved by FDA for this use

†  $P < 0.01$ ; ‡  $P < 0.05$

Adapted from Backonja M, et al. *JAMA*. 1998;280(21):1831-1836.

## Interventional Therapies for Chronic Pain

- Trigger point injections/botulinum toxin
- Epidural steroid injection
- Sacroiliac joint injection and RFA
- Facet joint injection and RFA
- Discography
- IDET, nucleoplasty, disc RFA
- Spinal cord stimulation
- Spinal drug delivery

RFA, radiofrequency ablation; IDET, intradiscal electrothermal therapy.

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## How Good is the Evidence?

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## EBM Must Be about EBP

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### Steps in the EBP Process:

- **ASSESS** the patient: Start with the patient—a clinical problem or question arises from the care of the patient
- **ASK** the question:  
Construct a well built clinical question derived from the case
- **ACQUIRE** the evidence:  
Select the appropriate resource(s) and conduct a search
- **APPRAISE** the evidence: Appraise that evidence for its validity (closeness to the truth) and applicability (usefulness in clinical practice)
- **APPLY**: talk with the patient, integrate that evidence with clinical expertise, patient preferences and apply it to practice
- **SELF-EVALUATION**: Evaluate your performance with this patient

What is EBP? Introduction to **Evidence-Based Practice**  
[www.hsl.unc.edu/services/tutorials/ebm/whatis.htm](http://www.hsl.unc.edu/services/tutorials/ebm/whatis.htm)



## AAN Guidelines: Pharmacologic treatment for episodic migraine in adults

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- Authors analyzed published studies from June 1999 through May 2009 using a structured review process developed/published by the AAN
- Recommendations are divided into Level A, Level B, Level C, Level U



## **AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont'd)**

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- Level A: established as effective and should be offered
- Level B: probably effective and should be considered
- Level C: possibly effective and may be considered
- Level U: evidence is conflicting or inadequate to support or refute the specific treatment



## **AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont'd)**

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- Level A (established as effective and should be offered for migraine prevention):
  1. Anticonvulsants: divalproex sodium, sodium valproate, topiramate
  2. B-blockers: metoprolol, propranolol, timolol
  3. Triptan: frovatriptan for short-term menstrual associated migraine prevention





## **AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont'd)**

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- Level B (probably effective and should be considered for migraine prevention):
  1. Antidepressants: amitriptyline, venlafaxine
  2. B-blockers: atenolol, nadolol
  3. Triptans: naratriptan, zolmitriptan for short-term menstrual associated migraine prevention



## **AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont'd)**

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- Level C (possibly effective and may be considered for migraine prevention):
  1. ACE inhibitors: lisinopril
  2. Angiotensin receptor blockers: candesartan
  3. A-agonists: clonidine, guanfacine
  4. Anticonvulsant: carbamazepine
  5. B-blockers: nebivolol, pindolol



## AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont'd)

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- Level U (evidence is conflicting or inadequate to support or refute the use of the medication for migraine prevention):
  1. Anticonvulsant: gabapentin
  2. Antidepressants: SSRI/SNRI, protriptyline
  3. Antithrombotics: acenocoumarol, warfarin, picotamide
  4. B-blocker: bisoprolol
  5. Calcium channel blockers: nicardipine, nifedipine, nimodipine, verapamil
  6. Acetazolamide
  7. Cyclandelate



## AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont'd)

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- Level A NEGATIVE (established as ineffective and should not be offered for migraine prevention): Anticonvulsant: lamotrigine
- Level B NEGATIVE (probably ineffective and should not be considered for migraine prevention): clomipramine
- Level C NEGATIVE (possibly ineffective and may not be considered for migraine prevention): acebutolol, clonazepam, nabumetone, oxcarbazepine, telmisartan



### **AAN: NSAIDS and other complementary treatments for episodic migraine prevention in adults**

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- Level A (established as effective and should be offered for migraine prevention): Petasites (butterbur)
- Level B (probably effective and should be considered for migraine prevention): fenoprofen, ibuprofen, ketoprofen, naproxen, naproxen sodium, MIG-99 (feverfew), magnesium, riboflavin, subcutaneous histamine



### **AAN: NSAIDS and other complementary treatments for episodic migraine prevention in adults (cont'd)**

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- Level C (possibly effective and may be considered for migraine prevention): cyproheptadine, Co-Q10, estrogen, mefenamic acid, flurbiprofen
- Level U (evidence is conflicting or inadequate to support or refute the use of the medication for migraine prevention): aspirin, indomethacin, omega-3, hyperbaric oxygen
- Level B NEGATIVE (probably ineffective for migraine prevention): montelukast



## **AAN: Botulinum neurotoxin in the treatment of migraine**

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- “There is presently no consistent or strong evidence to permit drawing conclusions on the efficacy of BoNT in chronic daily headache (mainly transformed migraine) Level U
- In October 2010, approximately 2 years after that statement was published, the FDA approved onabotulinum toxin A for the treatment of chronic migraine!

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## **“Real” Clinical Considerations NOT Addressed**

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- No available evidence is sufficient to establish how to choose an optimal therapy for an individual person
- Evidence is NOT available to help the practitioner to choose one treatment over another
- Treatment must be individualized
- No evidence exists for making comparisons among multiple agents within the same class
- For all Level A recommended treatments a large percentage of patients FAILED to benefit

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## References

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**Are the CDC Chronic Opioid Guidelines Improving Patient Outcomes?**

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## **APS/AAPM Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain (2009)**

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- Patient selection and risk stratification
- Informed consent and opioid management plans
- Initiation and titration of COT
- Methadone
- Monitoring
- High-risk patients
- Dose escalations, high-dose opioid therapy, opioid rotation, indications for discontinuations of therapy

APS, American Pain Society; AAPM, American Academy Of Pain Medicine; COT, chronic opioid therapy  
Chou R, et al. *J Pain*. 2009;10(2):113-130.



## **APS/AAPM Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain (2009) (cont'd)**

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- Opioid-related adverse effects
- Use of psychotherapeutic cointerventions
- Driving and work safety
- Identifying a medical home and when to obtain consultation
- Breakthrough pain
- Opioids in pregnancy
- Opioid policies

APS, American Pain Society; AAPM, American Academy Of Pain Medicine  
Chou R, et al. *J Pain*. 2009;10(2):113-130.



## CDC Guidelines-1

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- Determining when to initiate or continue opioids for chronic pain outside end-of-life care
- Selection of opioid therapy, nonpharmacologic therapy, nonopioid pharmacologic therapy
- Establishment of treatment goals
- Discussion of risks and benefits of therapy with patients

<http://www.cdc.gov/drugoverdose/prescribing/guideline.html>- accessed 11/1/15



## CDC Guidelines-2

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- Opioid selection, dosage, duration, follow-up, and discontinuation
- Selection of extended-release and long-acting opioids
- Dosage considerations
- Duration of treatment for acute pain and chronic opioid use
- Considerations for follow-up and discontinuation of opioid therapy

<http://www.cdc.gov/drugoverdose/prescribing/guideline.html>- accessed 11/1/15



## CDC Guidelines-3

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- Assessing risk and addressing harms of opioid use
- Evaluation of risk factors for opioid-related harms and integration into the management plan
- Review of prescription drug monitoring program data
- Use of urine drug testing
- Considerations for concurrent use of opioids and benzodiazepines
- Arrangement of treatment for opioid use disorder

<http://www.cdc.gov/drugoverdose/prescribing/guideline.html>- accessed 11/1/15

