

What is CGRP?

Carrie Dougherty MD

Associate Professor Neurology

MedStar Georgetown Headache Center



Disclosures

Research (no personal compensation): electroCore, Eli Lilly, Allergan, Amgen

Speaking honorarium: Amgen, Biohaven, electroCore, Eli Lilly, Novartis, Lundbeck, Teva

Consulting: Allergan, Biohaven, Clearview Health Partners, Guidepoint Consulting, GLG, Lundbeck, Magellan Rx Management, Novartis, Supernus and Theranica.



Outline



CGRP



Role in migraine



How medications act on CGRP



Q&A (definitely Q, maybe some A)



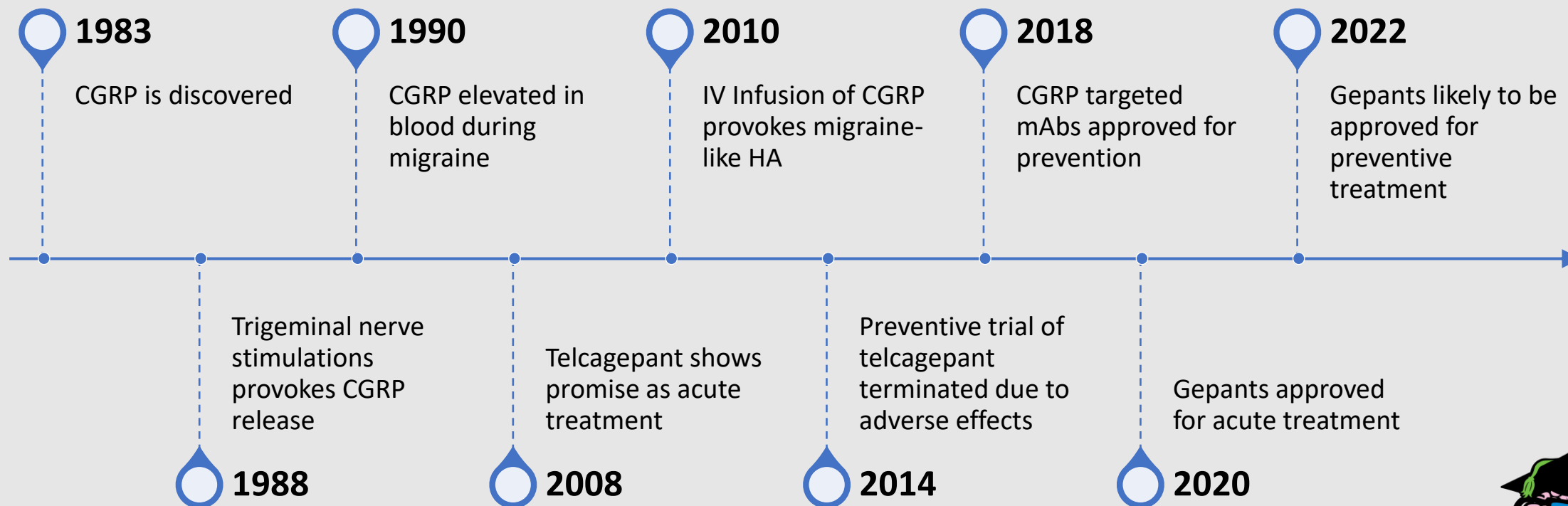
CGRP: Calcitonin Gene Related Peptide



- Neuropeptides: signaling molecules in the brain
- CGRP involved in regulating blood flow in the brain
- Acts to relax blood vessels



History of CGRP in Migraine



CGRP in Migraine

- CGRP levels increase during acute migraine
- Triptans reduce CGRP levels during acute migraine
 - Decrease corresponds with migraine relief
- CGRP increased between migraines in persons with CM
- Degree of CGRP elevation predicts positive response to onabotA

Cernuda-Morollón et al. Neurology 2013, 81 (14) 1191-1196

Goadsby PJ, et al. Ann Neurol. 1993; 33:48-56.

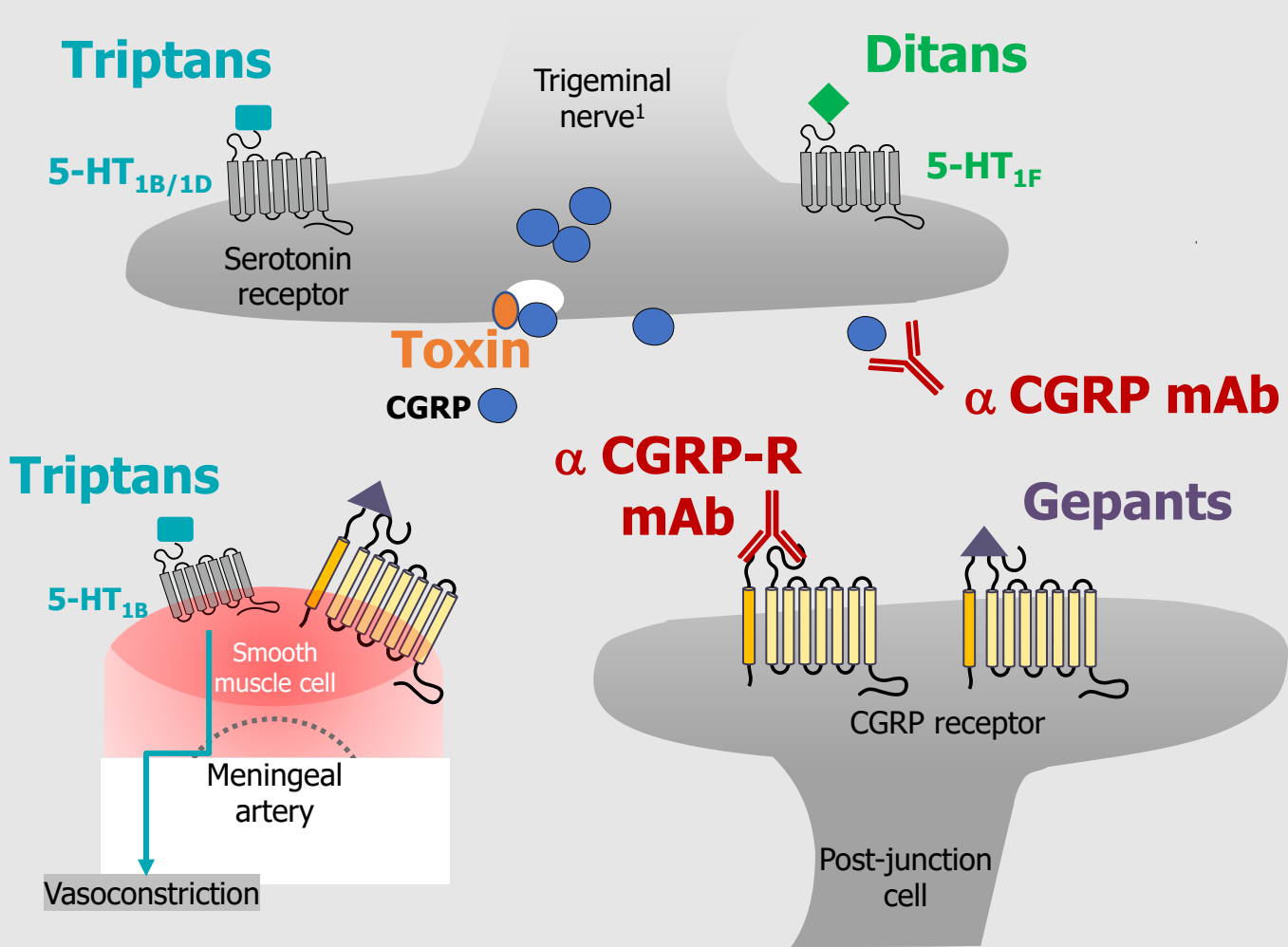
Cernuda-Morollón E, et al. Headache. 2014;54:987-95.

Cernuda-Morollón E, et al. Pain. 2015;156:820-4

Ashina M, et al. Neurology 2000;55:1335-40.



How do the meds work?



Triptans act on serotonin receptors 5HT1b/d

Ditans act on serotonin receptor 5HT1f

Gepants are small molecules that bind to and block the CGRP receptor, without causing any vasoconstrictive effects¹

Anti-CGRP monoclonal antibodies bind the CGRP receptor or CGRP itself¹





Onabotulinum toxin binds to docking proteins and inhibits vesicle release.

CGRP-R, calcitonin gene-related peptide-receptor; 5-HT, 5-hydroxytryptamine; mAb, monoclonal antibody.

1. Edvinsson L et al. *Nat Rev Neurol*. 2018;14(6):338-350.





CGRP Monoclonal Antibodies (mAbs)

	Erenumab (Aimovig) 	Galcanezumab (Emgality) 	Fremanezumab (Ajovy) 	Eptinezumab (Vypteti) 
Binding site	Receptor	Ligand	Ligand	Ligand
Administration	Subcutaneous injection	Subcutaneous injection	Subcutaneous injection	Intravenous infusion
Device	Autoinjector	Autoinjector Prefilled syringe	Autoinjector Prefilled syringe	
Dosing	70mg or 140mg monthly	240mg x1, then 120mg monthly	225mg monthly 675mg quarterly	100mg or 300mg monthly
Side effects	Injection site reaction Constipation Hypersensitivity reactions Constipation w complications* Hypertension*	Injection site reaction Hypersensitivity reactions	Injection site reaction	Nasopharyngitis Hypersensitivity reactions
*postmarket				



Gepants: Acute treatment

	Ubrogепant 	Rimegepant 
Dose	50, 100mg	75mg
Formulation	Oral tablet	Oral disintegrating tablet
Dosing regimen	1 tab at onset, can repeat in 2 hrs	1 tab at onset, can repeat in 24 hrs
Interactions	CYP3A4 inhibitors (antifungals, antibiotics, verapamil, barbiturates)	CYP3A4 inhibitors or inducers
Side effects	Nausea, sleepiness	Nausea



Q&A

- Can I just get my CGRP levels tested?
 - Oh, if it were only that easy
 - Half life is 7 minutes
 - No commercially available test
- What else does CGRP do in the body?



Q&A

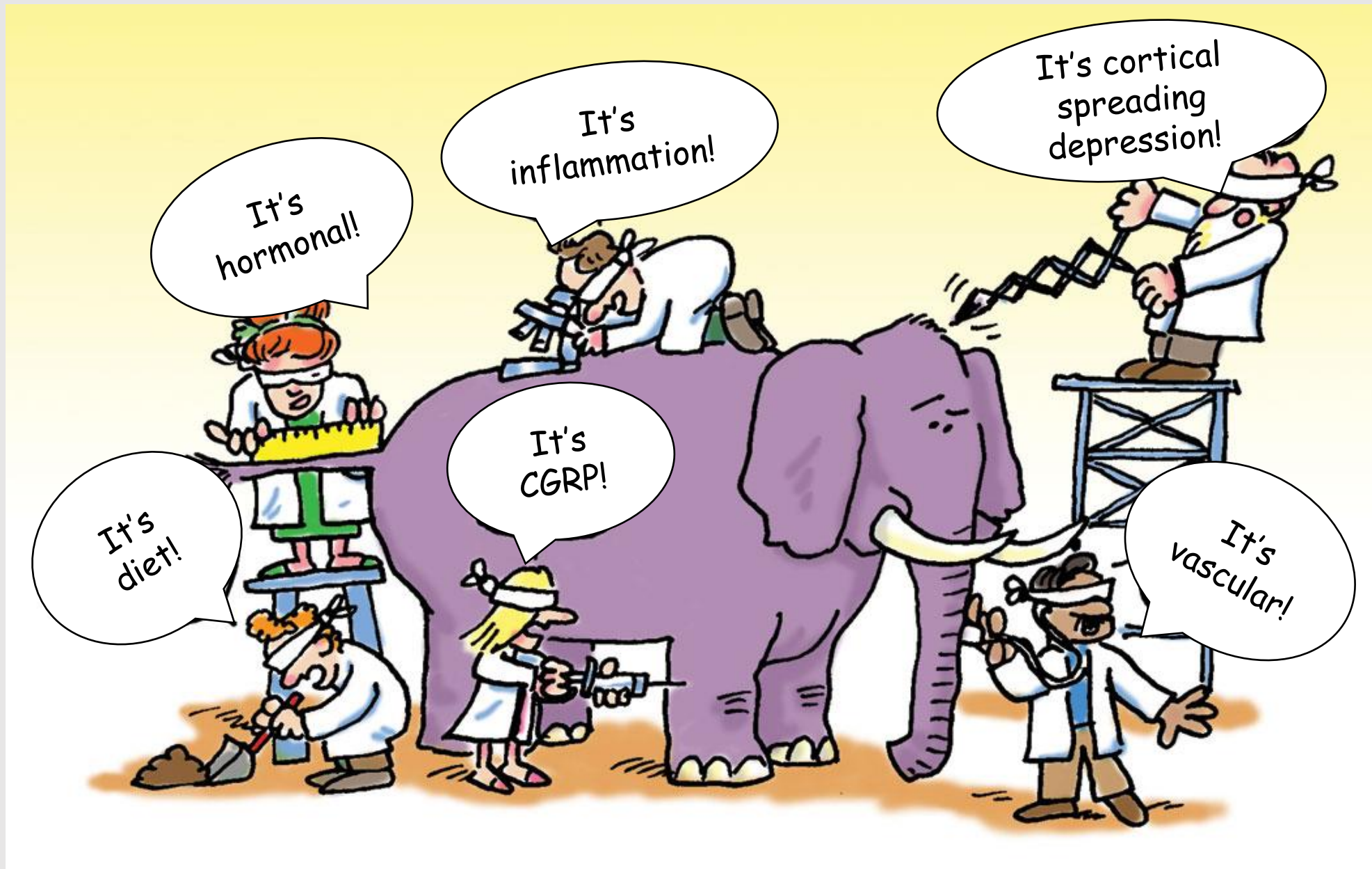
- Side effects
 - How are side effects determined?
 - On label
 - Postmarketing report
 - What if I have a side effect that's not listed?
 - Tell your doctor.
 - Report negative side effects of prescription drugs to the FDA www.fda.gov/medwatch or call 1-800-FDA-1088.



Q&A

- If I've tried one CGRP antibody, should I consider trying another?
 - Lack of benefit? Yes, the medications are different
 - Side effects? Maybe
- Why don't these medications help me?
 - Clinical trials often represent an "idealized" patient population
 - Migraine is complicated, CGRP is not the whole story.





Credit: Joe Sutliff



The future in bright!

