Neurology
Internal Medicine Review

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Case #1

- A 65 year-old right handed man with history of DM, HBP and hypercholesteronemia developed acute onset slurred speech, difficulty in speech production and right sided hemiparesis. He immediately call 911.

STROKE BURDEN

- In US, 780,000 new or recurrent strokes per year
- 240,000 transient ischemic attacks (TIAs)
- 175,000 deaths/year=third leading cause
- One third of survivors (about 200,000) are permanently disabled=leading cause of disability
- >50% of neurologic hospital admissions
- >$50B annually for stroke and post-stroke care (>$60,000/stroke)

RISK FACTORS (NONMODIFIABLE)

- Age: Doubles per decade >55
- Sex: 24%-30% greater in men
- Race/ethnicity: 2.4 increase for African Americans
  2.0 increase in Hispanics
- Heredity: 1.9 increase in first degree relatives

CONTINUUM, Vol 11, No 4, August 2005, p. 19

RISK FACTORS (MODIFIABLE)

- MEDICAL
  - Hypertension
  - Atrial fibrillation
  - Carotid artery stenosis
  - Transient ischemic attack
  - Diabetes mellitus
  - Lipids
- LIFESTYLE
  - Smoking
  - Alcohol
  - Physical activity
  - Diet
  - Obesity

HYPERTENSION

- By far the most important modifiable risk factor
- Attributable risk for stroke is estimated at 40%
- Linear relationship to stroke at least to BP of 115/75
- For primary stroke prevention, 38% fewer strokes with mean decrease of 12 mm Hg systolic and 6 mm Hg diastolic

- *CONTINUUM,* Vol 11, No 4, 2005, p. 18-19

HYPERTENSION

- PROGRESS trial: 28% stroke reduction after minor stroke or TIA with perindopril (9/4 mm Hg BP drop)
- Possible benefit of ACE inhibitors beyond BP lowering effect
- HOPE trial: 32% reduction in stroke risk with ramipril vs placebo with 3/2 mm Hg drop in BP

HYPERTENSION

- LIFE trial: BP reduction equal between losartan and atenolol, but 25% reduction in stroke with losartan

- Recommendation: Combining a thiazide diuretic with ACE inhibitor is recommended for hypertensive patients with cerebrovascular disease

DIABETES

- Independent effect on stroke risk
- Frequently (60%) co-existent with HBP
- Risk Ratio for ischemic stroke=2.3 with FBS>140
- Although improvement in other vascular parameters has been shown with tight control, reduction in stroke risk has not yet been demonstrated

LIPIDS/STATINS

- No strong association between lipids and stroke
- BUT statin trials in patients with coronary artery disease show a reduction in stroke with statin use vs placebo
- Patients already on statins prior to stroke have better outcomes

LIPIDS/STATINS

- Third Report of National Cholesterol Education Program Expert Panel on Detection, Evaluation , and Treatment of High Blood Cholesterol in Adults recommends: Consideration of statins for high risk patients with coronary heart disease, diabetes, stroke, or TIA due to carotid stenosis, and asymptomatic carotid stenosis>50%
- Stroke Council of the American Stroke Association: "The vast majority of patients with a history of stroke or transient ischemic attack could benefit from statin use".

CASE CONTINUE

- Patient was immediately transfer to the closest stroke center where he was evaluated and tPA was administered

Features of a "Stroke Center"

- On call Stroke Team
- Neurologists (or other physicians) with special interest, training, and expertise in stroke care
- CT scans available at all times
- MRI capability
- Emergency access to cerebral angiography
- Neurosurgeon available on call
- Vascular neurosurgery or surgery expertise
- Clinical research program

Hospital Management

- TIME GOALS
  - Door to doctor - 10 minutes
  - Door to CT completion – 25 minutes
  - Door to CT read – 45 minutes
  - Door to treatment – 60 minutes
  - Neurology consult – 15 minutes
  - Neurosurgery – 2 hours
  - Admit to monitored bed – 3 hours

ER Stroke Evaluation Targets

- Rapid assessment of all symptomatic patients with onset < 24 hours
- CT scan started within 20 - 30 minutes of arrival
- Treatment initiated (if appropriate) within 45 - 60 minutes of arrival

tPA Indications in Acute Stroke

- First FDA approved acute stroke treatment
- CT negative for hemorrhage
- Treat within 3 hours of symptom onset
- Not used for patients with isolated, mild or rapidly improving deficits
- Contraindicated in patients with increased bleeding risks or uncontrolled high blood pressure

NINDS Trial Results

	Percentage with favorable outcome	
No.of patients: 312	t-PA 157	Placebo 145
Modified Rankin Scale	40 %	28 %
Glasgow Outcome Scale	43	32 %
NIHSS	34	20 %
Symptomatic ICH (within 36 hr)	6.4%	0.6 %
Death (by 90 days)	17%	21 %

NEJM 1995; 333:1581-7

NINDS NEJM Results

December 1995: NEJM article reported a positive treatment effect for the use of IV t-PA in the treatment of acute ischemic stroke patients within 3 hours of symptom onset.

- From Part 2, the adjusted t-PA to placebo global OR for favorable outcome was

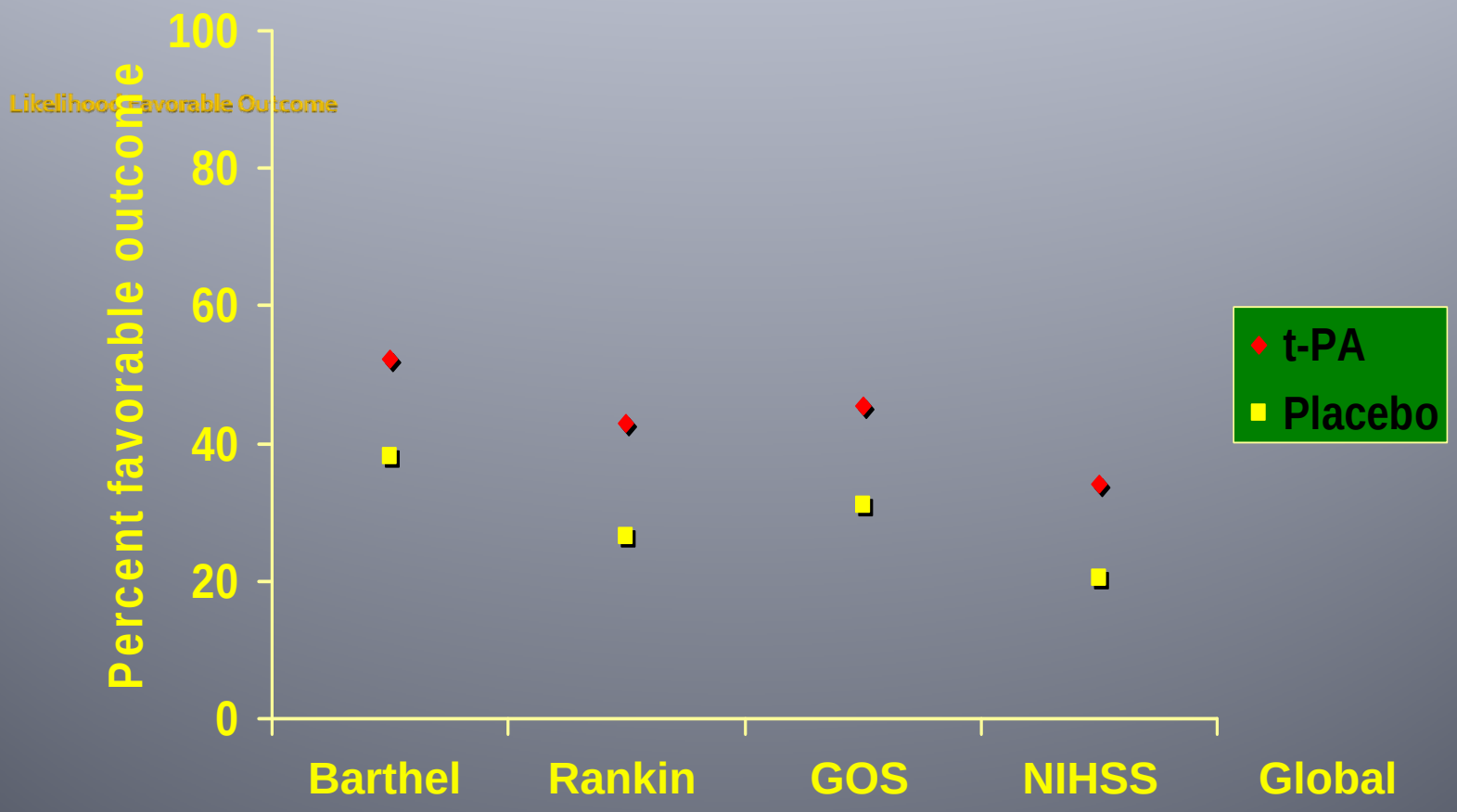
  1.7 (95%CI,1.2-2.6)

Reanalysis Findings

The committee concluded, despite an increased incidence of symptomatic intracerebral hemorrhage in t-PA treated patients, there was a statistically significant benefit of t-PA treatment measured by an adjusted t-PA to placebo global odds ratio of 2.1 (95% CI: 1.5-2.9) for a favorable clinical outcome at three months

The analysis was adjusted for center, time to treatment, study part, age, baseline NIHSS, diabetes, pre-existing disability, and the interaction between age and baseline NIHSS.

Likelihood of Favorable Outcome



Adjusted OR	2.2	2.4	2.1	2.2	2.1
95% CI	1.5-3.2	1.6-3.6	1.4-3.2	1.4-3.3	1.5-2.9

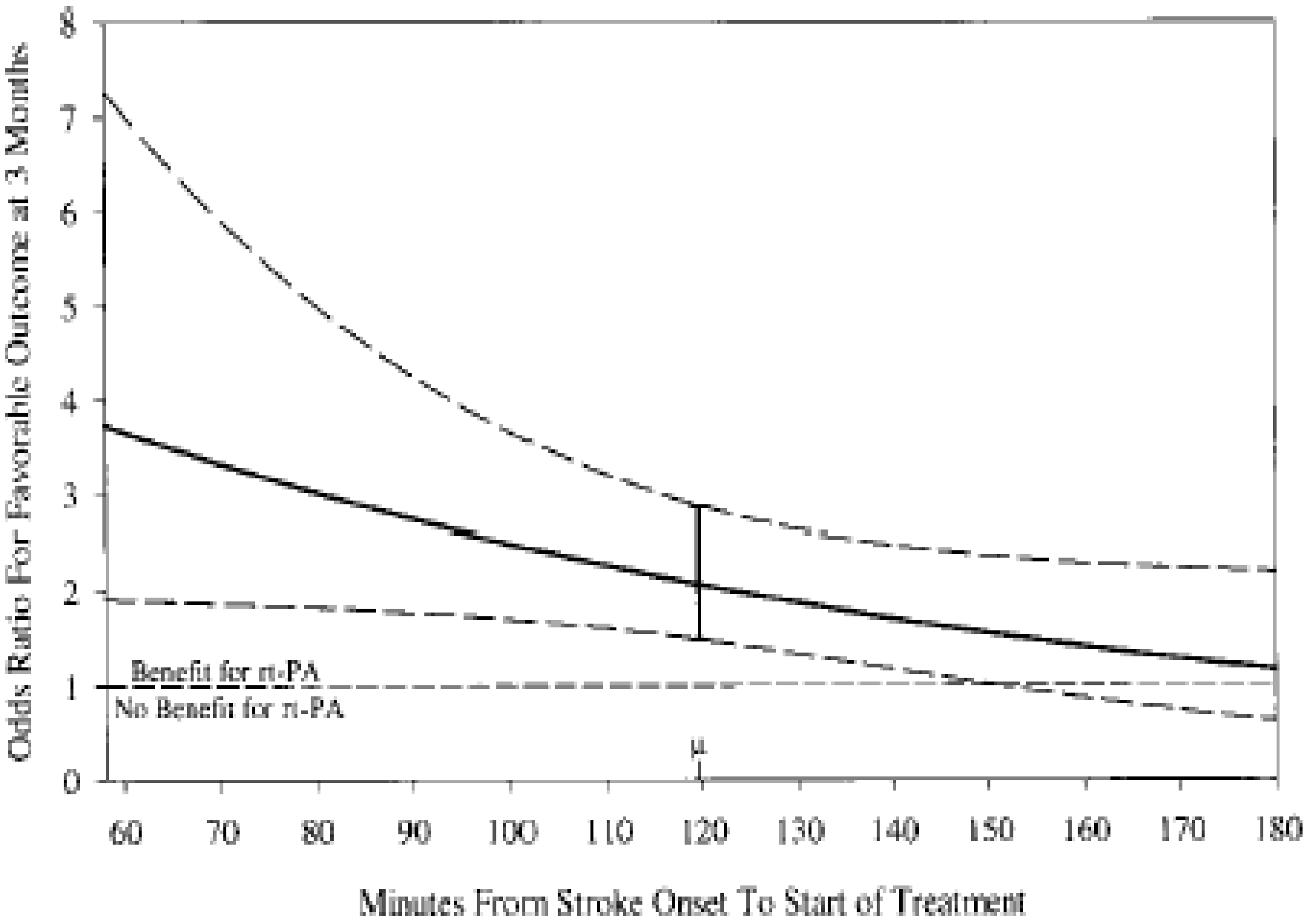
Early stroke treatment associated with better outcome

The NINDS rt-PA Stroke Study

J.R. Marler, MD; B.C. Tilley, PhD; M. Lu, PhD; T.G. Brott, MD; P.C. Lyden, MD; J.C. Grotta, MD; J.P. Broderick, MD; S.R. Levine, MD; M.P. Frankel, MD; S.H. Horowitz, MD; E.C. Haley, Jr., MD; C.A. Lewandowski; and T.P. Kwiatkowski, MD, for the NINDS rt-PA Stroke Study Group*

Article abstract—*Background:* The National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study showed a similar percentage of intracranial hemorrhage and good outcome in patients 3 months after stroke treatment given 0 to 90 minutes and 91 to 180 minutes after stroke onset. At 24 hours after stroke onset more patients treated 0 to 90 compared to 91 to 180 minutes after stroke onset had improved by four or more points on the NIH Stroke Scale (NIHSS). The authors performed further analyses to characterize the relationship of onset-to-treatment time (OTT) to outcome at 3 months, early improvement at 24 hours, and intracranial hemorrhage within 36 hours. *Methods:* Univariate analyses identified potentially confounding variables associated with OTT that could mask an OTT–treatment interaction. Tests for OTT–treatment interactions adjusting for potential masking confounders were performed. An OTT–treatment interaction was considered significant if $p \leq 0.10$, implying that treatment effectiveness was related to OTT. *Results:* For 24-hour improvement, there were no masking confounders identified and there was an OTT–treatment interaction ($p = 0.08$). For 3-month favorable outcome, the NIHSS met criteria for a masking confounder. After adjusting for NIHSS as a covariate, an OTT–treatment interaction was detected ($p = 0.09$): the adjusted OR (95% CI) for a favorable 3-month outcome associated with recombinant tissue-type plasminogen activator (rt-PA) was 2.11 (1.33 to 3.35) in the 0 to 90 minute stratum and 1.69 (1.09 to 2.62) in the 91 to 180 minute stratum. In the group treated with rt-PA, after adjusting for baseline NIHSS, an effect of OTT on the occurrence of intracranial hemorrhage was not detected. *Conclusions:* If the NINDS rt-PA Stroke Trial treatment protocol is followed, this analysis suggests that patients treated 0 to 90 minutes from stroke onset with rt-PA have an increased odds of improvement at 24 hours and favorable 3-month outcome compared to patients treated later than 90 minutes. No effect of OTT on intracranial hemorrhage was detected within the group treated with rt-PA, possibly due to low power.

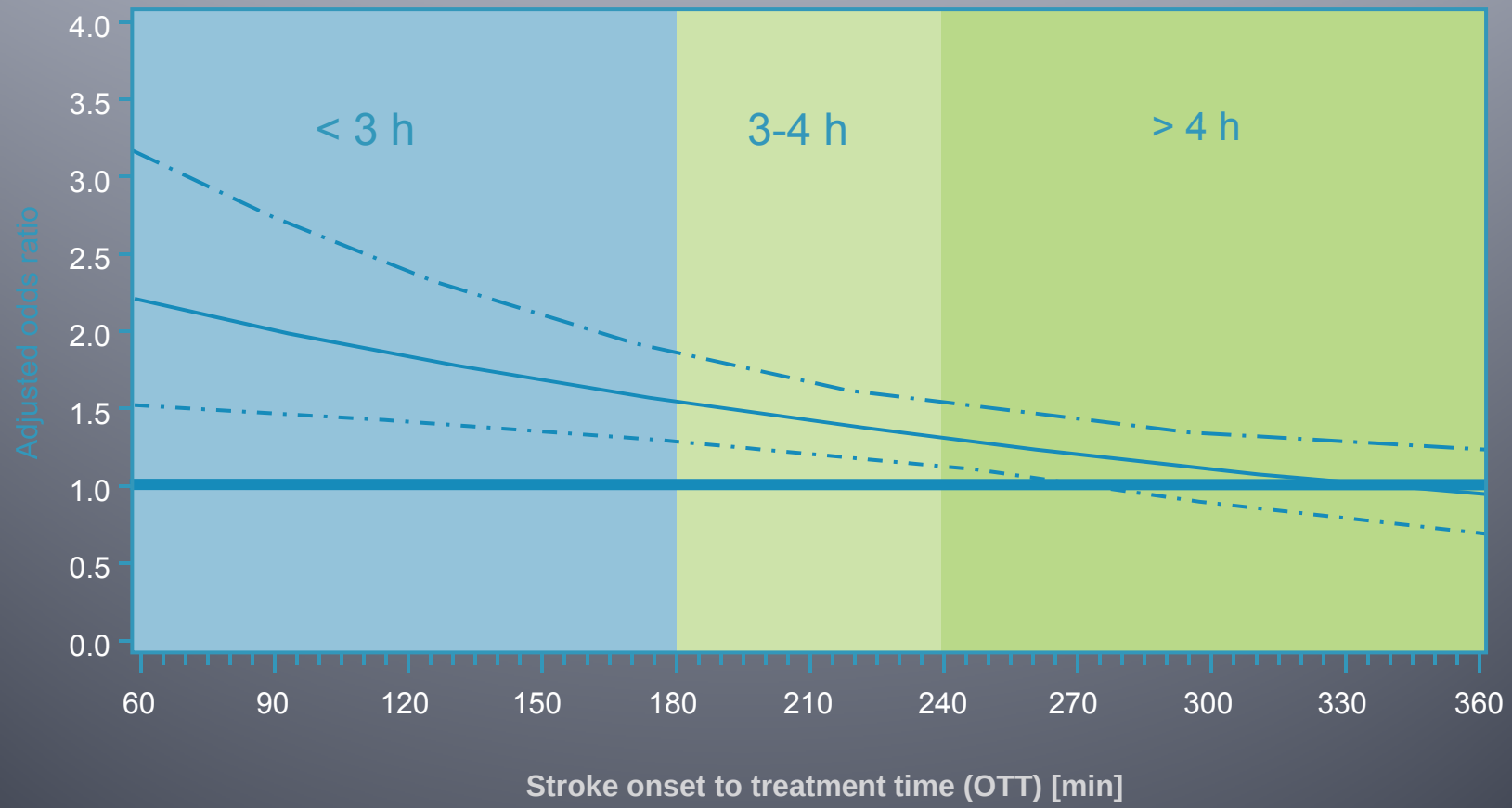
NEUROLOGY 2000;55:1649–1655


Odds Ratio For Favorable Outcome at 3 Months
8
7
6
5
4
3
2
1
0
Benefit for rt-PA
No Benefit for rt-PA
μ
60
70
80
90
100
110
120
130
140
150
160
170
180
Minutes From Stroke Onset To Start of Treatment

Time to Treatment and tPA Benefit

mRS 0-1 at day 90

Adjusted odds ratio with 95 % confidence interval by stroke onset to treatment time (OTT)



Case Continue

- Patient was succesfully treated with tPA with almost complete resolution of symptoms
- What is the next step?

WORKUP

- If carotid territory, duplex imaging, MRA, or CT angiography, ideally within 24 hours
- Benefit of surgery is time-dependent:

  -Within 2 weeks, NNT to prevent 1 stroke in 5 years is 5

  -After 12 weeks, NNT is 125

Postgrad Med 2005;117(1):9-14
Lancet 2004;363(9143):915-924

RECOMMENDATIONS IN SYMPTOMATIC PATIENTS

Use of Carotid Endarterectomy in Symptomatic Patients

Stenosis (%)	Recommendation
70-99%	CE is established as effective for recently symptomatic (within previous 6 months) patients with 70-99% ICA angiographic stenosis (**Level A**).
50-69%	•CE may be considered for patients with 50-69% symptomatic stenosis (**Level B**) but the clinician should consider additional clinical and angiographic variables (**Level C**). *See tables below.* •It is recommended that the patient have at least a five year life expectancy and that the peri-operative stroke/death rate should be <6% for symptomatic patients (**Level A).**
<50%	•CE should not be considered for symptomatic patients with <50% stenosis (**Level A**). •Medical management is preferred to CE for symptomatic patients with <50% stenosis (**Level A**).

RECOMMENDATIONS IN ASYMPTOMATIC PATIENTS

Use of Carotid Endarterectomy in Asymptomatic Patients	
Stenosis (%)	Recommendation
60-99%	It is reasonable to consider CE for patients between the ages of 40-75 years and with asymptomatic stenosis of 60-99% if the patient has an expected five year life expectancy and if the surgical stroke or death frequency can be reliably documented to be <3% (**Level A**). The five year life expectancy is important since peri-operative strokes pose an up front risk to the patient and the benefit from CE emerges only after a number of years.

SYMPTOMATIC INTRACRANIAL DISEASE

- WASID study: Compared ASA 1300 mg/day to warfarin INR 2-3
- No difference in stroke or vascular death, about 22% in both groups in 2 years
- Halted because of increased adverse events in warfarin group
- INR of 2-3 achieved only 67% of time (comparable to clinical practice)

ANTI-PLATELET THERAPY

- Aspirin approved by FDA for stroke prevention in patients with symptomatic cerebrovascular disease in doses of 50-325 mg/day
- Started within 48 hours of ischemic event produces modest benefit in reducing risk of early recurrent stroke

ANTI-PLATELET THERAPY

- Risk reduction after stroke/TIA
  -ASA: 13-25%
  -Dipyridamole: 16%
  -Ticlidipine: 20-23%
  -Clopidogrel: Equal to ASA
  -ASA+dypyridamole: 33%

ANTI-PLATELET THERAPY

- MATCH trial: ASA added to clopidogrel did not reduce recurrent vascular events, and increased major bleeding episodes
- Recommendation not to use for stroke prevention (although used for prevention of MI)
- BUT
  - Risk of hemorrhage not apparent for 3 months (highest risk for recurrent stroke)
  - MATCH had disproportionate number (52%) of patients with small vessel disease (those most prone to hemorrhage)
  - Only 34% with large artery disease, the group at highest risk for early recurrence
  - Possibility of short-term benefit, followed by long-term harm

TRANSIENT ISCHEMIC ATTACK (TIA)

- "Brief episode of neurological dysfunction caused by a focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour and without evidence of (radiographically defined) infarction".

- Albers, GW et al., NEJM 2002; 347:1713-1716

TIA

- 15-20% of strokes are preceded by TIA
- 90 day stroke risk after TIA is 10-20%
- One-half of these (i.e., 5-10%) will occur within 48 hours
- Higher risk of stroke after TIA associated with:
  - Motor deficit
  - Aphasia
  - Duration>10 min
  - Age>60
  - Diabetes

TIA

- Growing opinion that TIA and minor stroke need to be approached as aggressively as acute coronary syndromes
- Goals of early evaluation: Determine the mechanism and territory of ischemia to select appropriate preventive therapy
- Identify patients with symptomatic carotid artery disease who will benefit from early endarterectomy

- Gladstone, DJ. *Postgrad Med* 2005; 117(1):9-14

ANTI-THROMBOTIC WITHDRAWAL

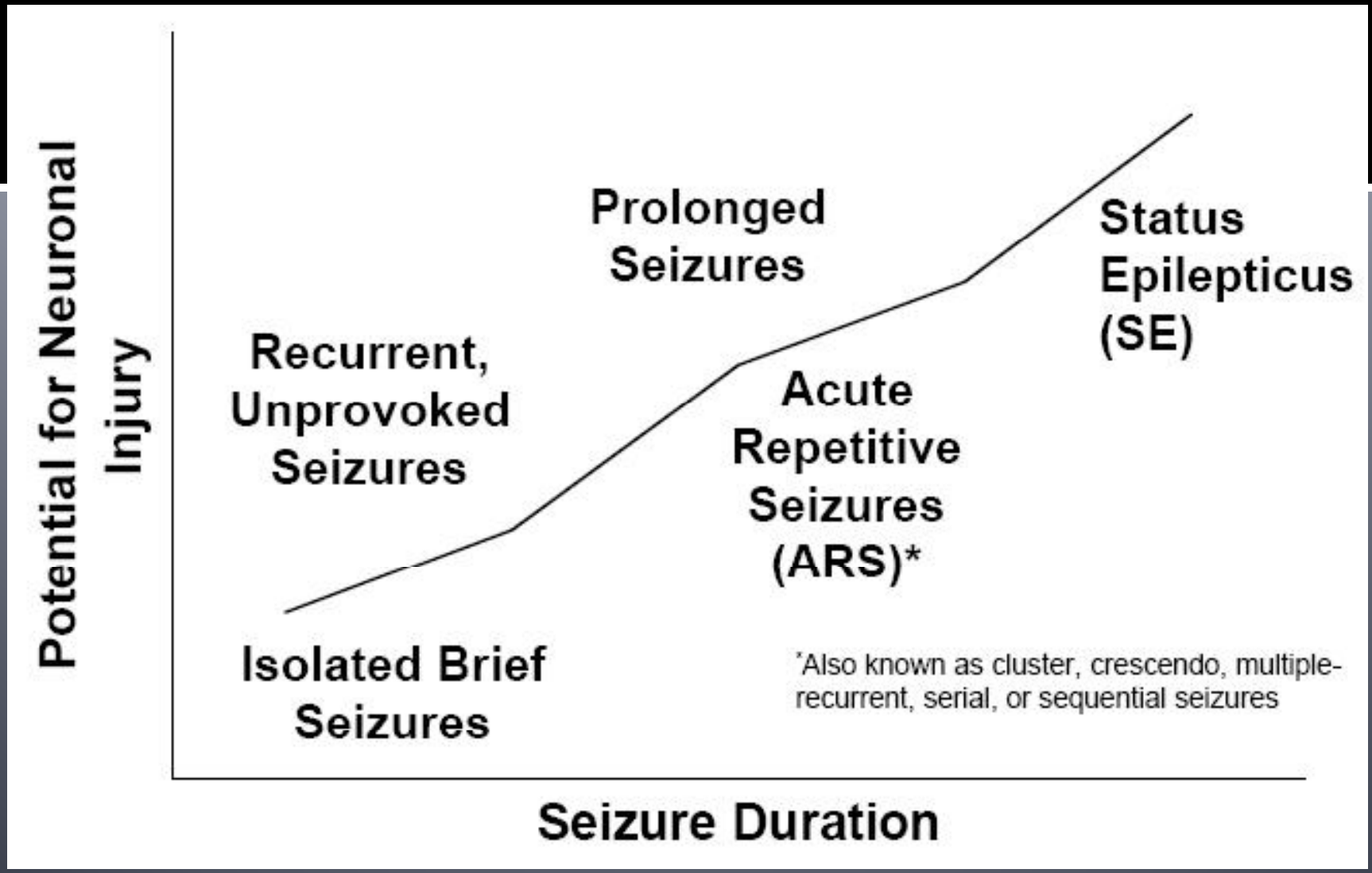
- Withdrawing ASA may significantly increase stroke risk
- Mean interval between infarction and ASA cessation was 9.5 days
- Odds ratio of ischemic stroke or TIA in 4 weeks after cessation of ASA was 3.4

- *Arch Neurol* 2005:1217-1220

Case #2

- A 35 year-old male patient with history of epilepsy using two medications at home ran out of medication one week ago and developed acute prolonged seizure. Patient was taken to the ER and upon arrival was still seizing

Spectrum of Seizures



Nature of the Beast

- Humans have very effective mechanisms to stop seizures
- After a single GTC "coma" often last several minutes during which seizure threshold are massively elevated
- Restore homeostasis and stop runaway excitation

Nature of the Beast

- During status these mechanisms fail
- Seizures occur in rapid succession or self-sustained
- Seizures and status are less likely to stop as time elapses

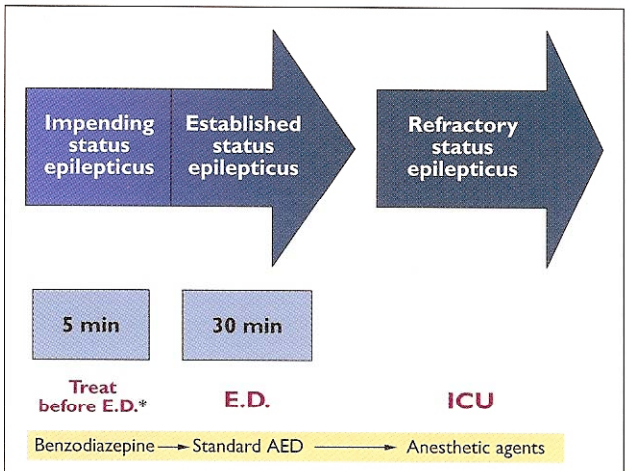
Clinical Definition

- 1983 – "fixed and enduring epileptic condition"
- 1993 – "duration of repetitive seizures was 30 min"
  - Based in time for neuronal injury and pharmacoresistance
- From then
  - 20 minutes — Bleck (1991)
  - 10 minutes — Treiman et al, VA Coop trial (early 1990's)
  - 5 minutes — Lowenstein et al (1997) , Wasterlian & Treiman 2006

Clinical Definition

- Average tonic clonic seizure is 59.9 sec
- Average partial complex seizure 2.5 min
- Once a seizure lasts >7 min, there is >95% chance that it will be a prolonged seizure

Phases of SE


Impending status epilepticus
Established status epilepticus
Refractory status epilepticus
5 min
30 min
Treat before E.D.*
E.D.
ICU
Benzodiazepine → Standard AED → Anesthetic agents

Physiological Changes Phase I

- Increase cerebral metabolism

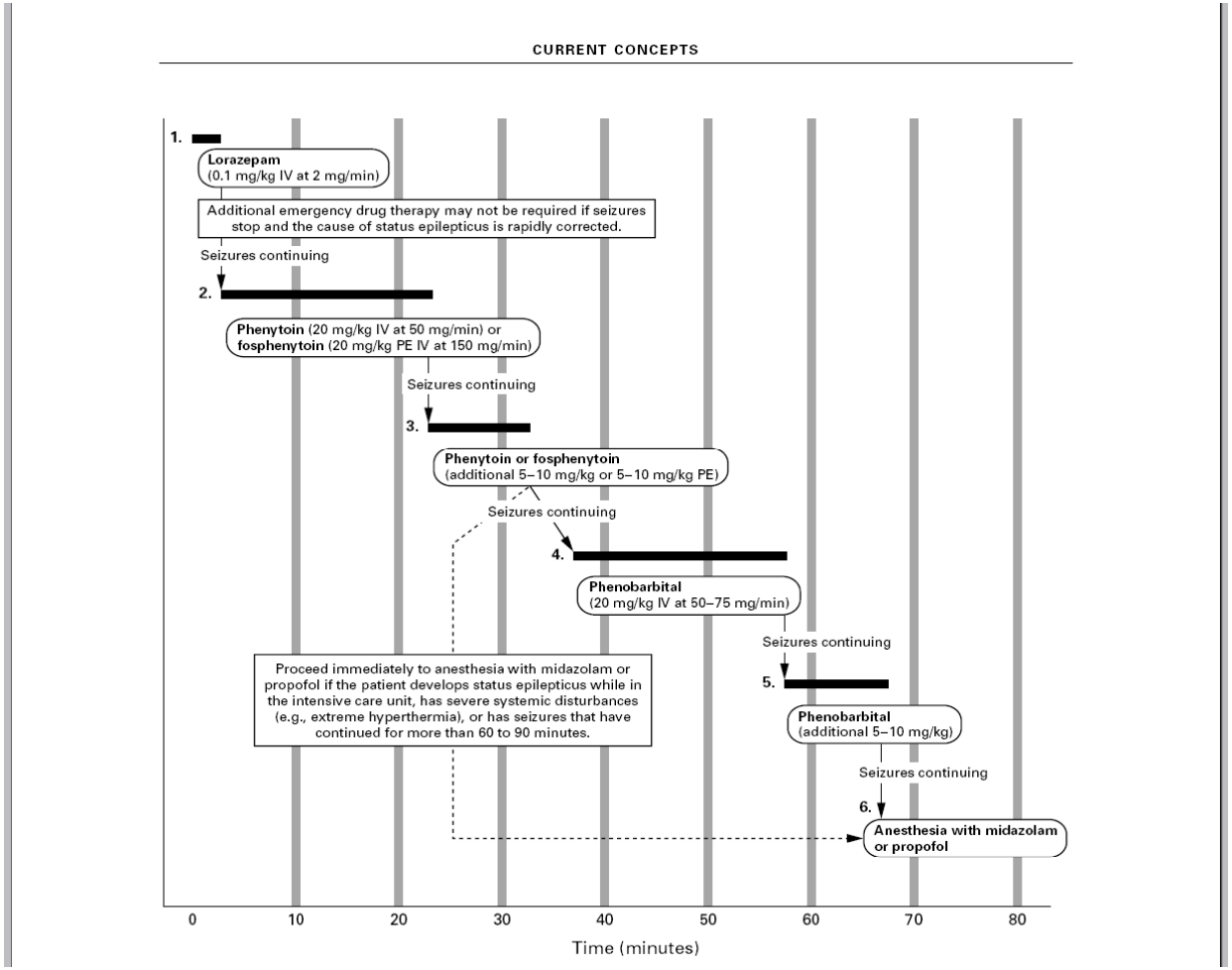
Cerebral Changes	Metabolic	Autonomic & Cardiovascular
Increased blood flow	Hyperglycemia	Hypertension
Increased metabolism	Lactic acidosis	Increased cardiac output and CVP
Energy requirements matched by supply of O2 and glucose		Massive catecholamine release
Increased lactate concentration		Tachycardia and cardiac arrhytmias
Increased glucose concentration		Salivation, Hyperpyrexia, Vomiting, Incontinence

Phase II

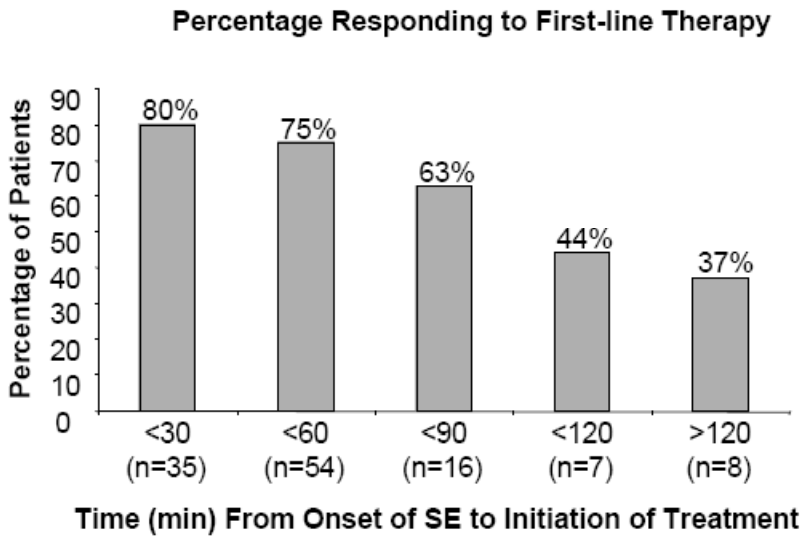
- Increased cerebral metabolic demands cannot be fully met

Cerebral Change	Metabolism	Autonomic & Cardiovascular
Failure of cerebral autoregulation	Hypoglycemia	Systemic hypoxia
Hypoxia	Hypo/Hyperkalemia	Falling blood pressure
Hypoglycemia	Metabolic and Respiratory acidosis	Falling cardiac output
Falling lactate concentrations	Hepatic and renal dysfunction	Respiratory and cardiac collapse
Falling energy state	Consumptive coagulopathy	Hyperpyrexia
Rising intracranial pressure and cerebral edema	Rhabdomyolysis, myoglobulinuria	
	Leukocytosis	

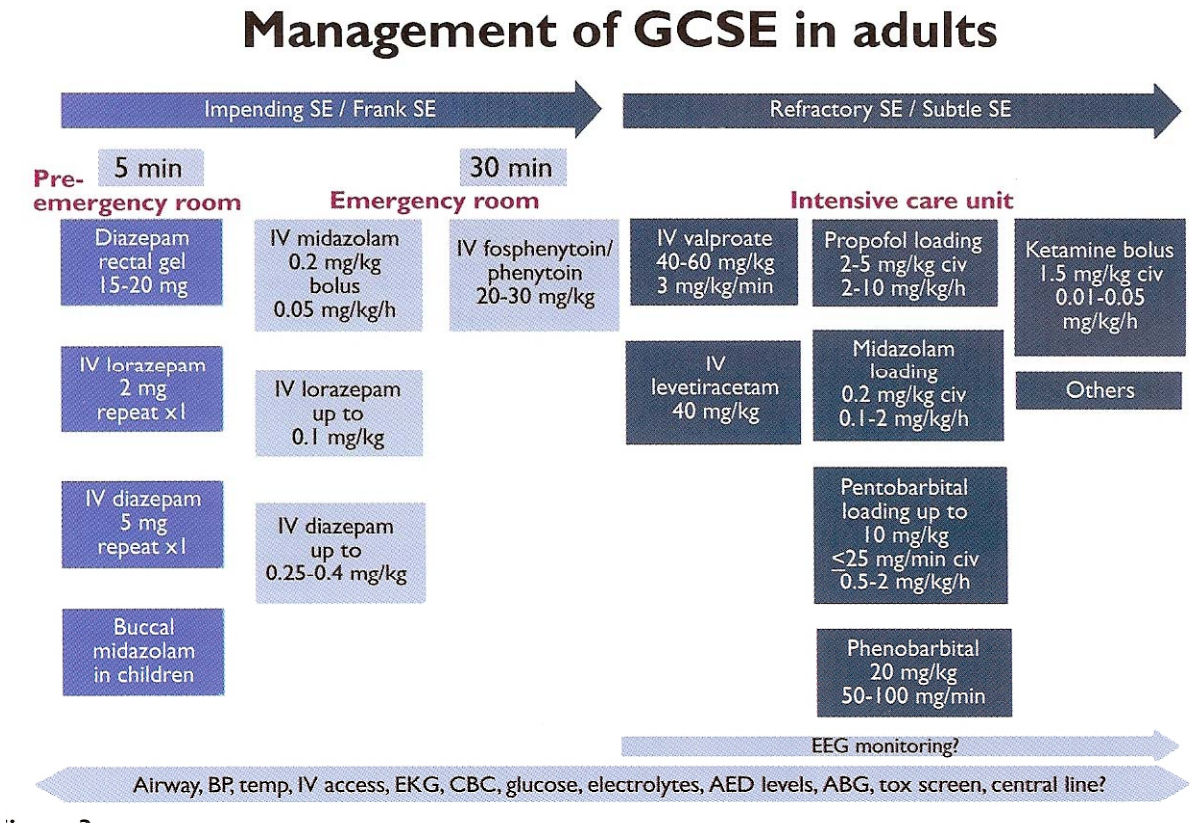
Management of GCSE



Early Treatment in Status Epilepticus



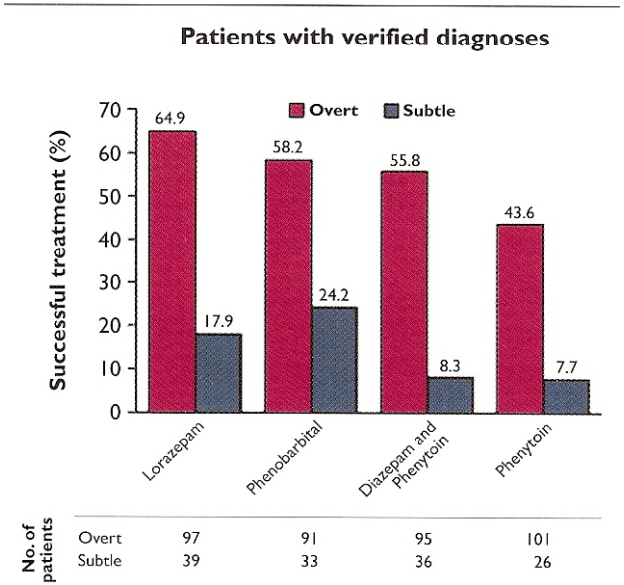
Management of GCSE



SE Treatment

- VA Cooperative Study of AED in SE
- First-line success
  - Lorazepam 64.9%
  - Phenobarbital 58.2%
  - Diazepam 55.8%
  - Phenytoin 43.6%
- Second-line success 7%
- Third-line agent 2.3%

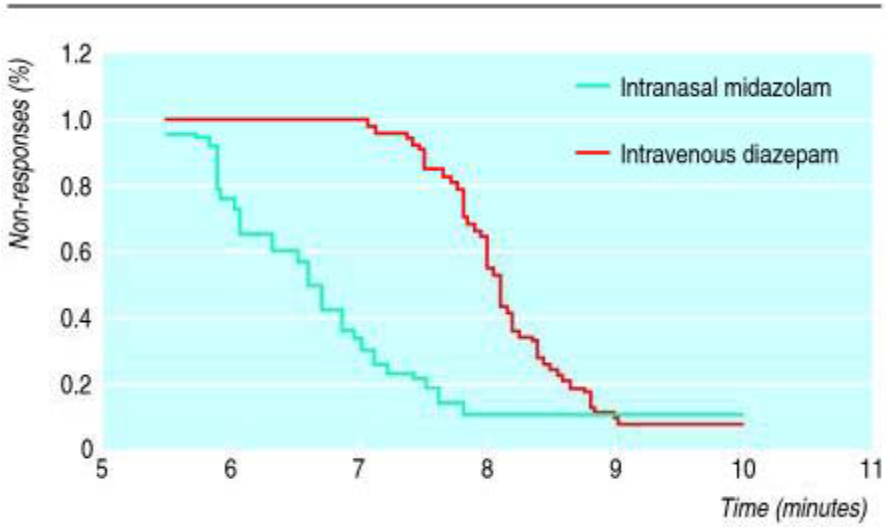
SE Treatment



Intranasal midazolam

- Non-FDA approved
- ER and possible out patient treatment
- 0.2 mg/Kg divided in both nostrils

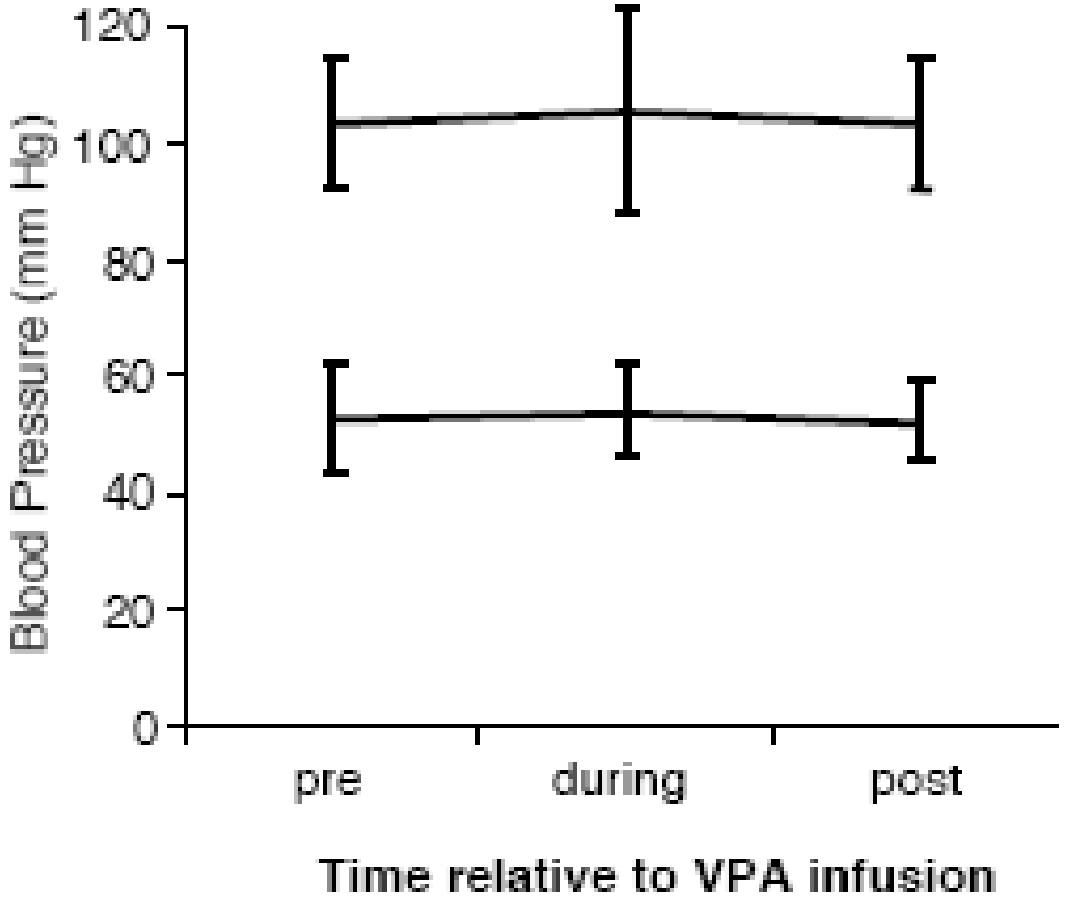
IN Midazolam vs IV Diazepam



Valproate

- Intravenous preparation approved in 1996
- Open label studies have shown efficacy for multiple types of SE
- IV Valproate was well tolerated with minor side effects
- Comparative with Phenytoin
- Incidence of side effect did not differ significantly

VPA loading effect in Blood Pressure



IV Valproate in Status Epilepticus

- Data limited to small series
- 23 adults with status > 30 min
  - Generalized n=12
  - Partial n=11
- Bolus of 15 mg/kg
- 20 min efficacy
  - GSE controlled in 11/12
  - Partial status controlled in 8/11
- No clinically relevant change in HR and BP

Levetiracetam

- Intravenous formulation available since 2006
- Favorable pharmacokinetics
- No controlled studies
- Multiple case reports
- Doses 500-7500 mg
- Control achieve 31-100%
- Few side effects

Ideal IV AED

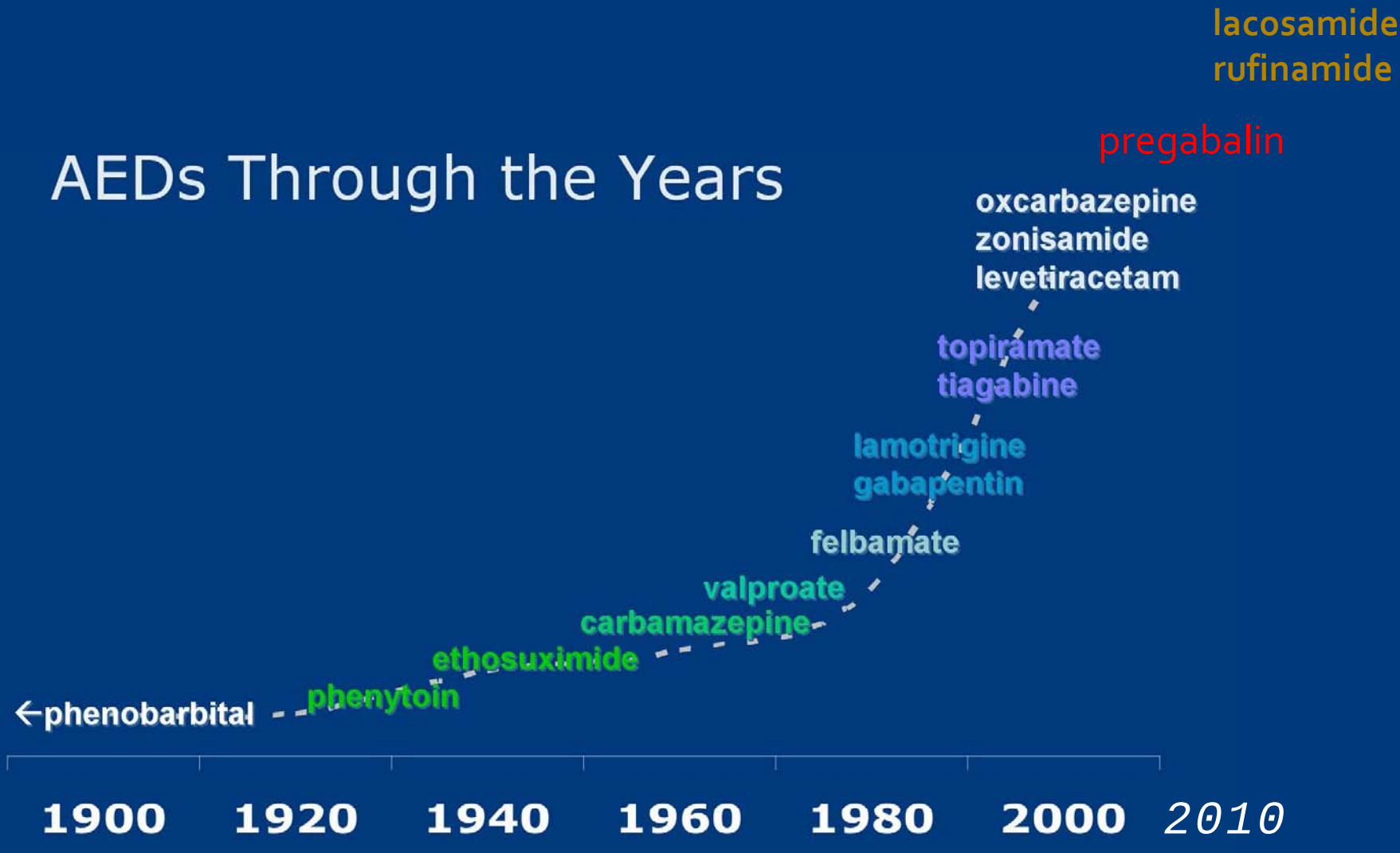
Table 1. Ideal intravenous antiepileptic drug (AED) characteristics

	DZP	LZP	PHT	FosPHT	PB	VPA	LEV
Ease of administration	X	X		X	X	X	X
Rapid onset of action	X	X	X	X		X[a]	?
Intermediate to long duration		X	X	X	X	X	X
Broad spectrum	X	X			X	X	X
Minimal morbidity				X		X	X
Useful as maintenance AED			X	X	X	X	X
i.v. solution compatibility				X		X	X

DZP, diazepam; FosPHT, fosphenytoin; i.v., intravenous; LEV, levetiracetam; LZP, lorazepam; PB, phenobarbital; PHT, phenytoin; VPA, valproate.

[a]Based on animal studies and limited clinical observations.

AEDs Through the Years



Graves N. *Am J Manag Care.* 1998;4(9 suppl):S463-S467; discussion S468-S474.

Case example #1

- This is a 67 y/o male patient with hypertension and Diabetes Mellitus type 2 who is referred to the neurologist because of nocturnal burning feet and pin and needle sensations distally in the legs in the last 6 months and getting worst causing now insomnia.
  - Type of pain? How do you describe his complains?
  - What do you think he may have?

Symptoms of Neuropathic Pain

Stimulus-Independent Symptoms (Symptoms Described by the Patient)

- Continuous burning pain
- Intermittent shooting, lancinating pain
- Electric shock–like pain
- Some paresthesias
  - Abnormal sensations that are not unpleasant
- Some dysesthesias
  - Abnormal sensations that are unpleasant

Signs of Neuropathic Pain

Stimulus-Evoked Pain (Elicited by the Physician on Examination)

Hyperalgesia

An increased response to a stimulus that is *normally painful*

Allodynia

Pain due to a stimulus that is *not normally painful*

Neuropathic Pain: Clinical Characteristics

- Burning, shooting, electrical-quality pain
- May be aching, throbbing, sharp
- Neuropathic sensations: dysesthesias, paresthesias

Common Neuropathic Pain Syndromes

- Diabetic neuropathy
- Post-herpetic Neuralgia (PHN)
- Phantom Limb pain
- Trigeminal Neuralgia

The most common cause of chronic neuropathic pain are the peripheral neuropathies

Peripheral neuropathies

- Is one of the most common neurologic conditions that affect the peripheral nerves (motor, sensory and autonomic)
- 2 broad groups: hereditary and acquired

Classification of neuropathies

- Axonal type
  - Injury to the axon or cell body results in axonal or Wallerian degeneration
    - Length dependent process affecting first the distal part and progressing proximally
    - Wallerian degeneration indicates focal nerve injury with degeneration of the axon distal to the site of injury

Axonal neuropathies

- Most common causes are toxic-metabolic
  - Diabetes, uremia, alcohol, thyroid, nutritional, paraneoplasic. HIV collagen vascular diseases
    - Large fiber – loss of position and vibration, hyporeflexia, hypotonia and weakness
    - Small fiber – diminished pain and temperature sensation, spontaneous pain and autonomic involvement

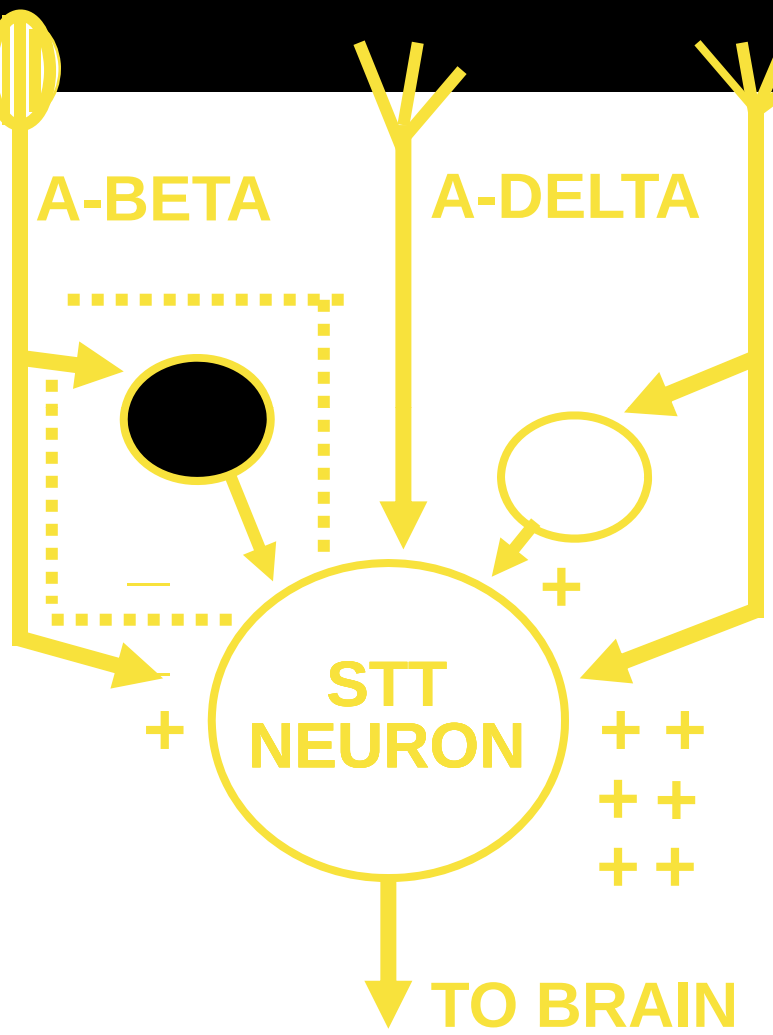
Neuropathies

- Demyelinating neuropathies
  - Injury to the Schwann cell or myelin results in demyelination (focal, multifocal or diffuse)
  - Demyelination usually follows by Schwann cell proliferation and remyelination

General symptoms and signs in neuropathy (the prototypic syndrome)

- Distal, symmetric weakness
- Atrophy
- Decreased or absent DTR's
- Dista sensory loss, positive sensory signs
- Autonomic symptoms

Loss of Inhibitory Interneuron Function



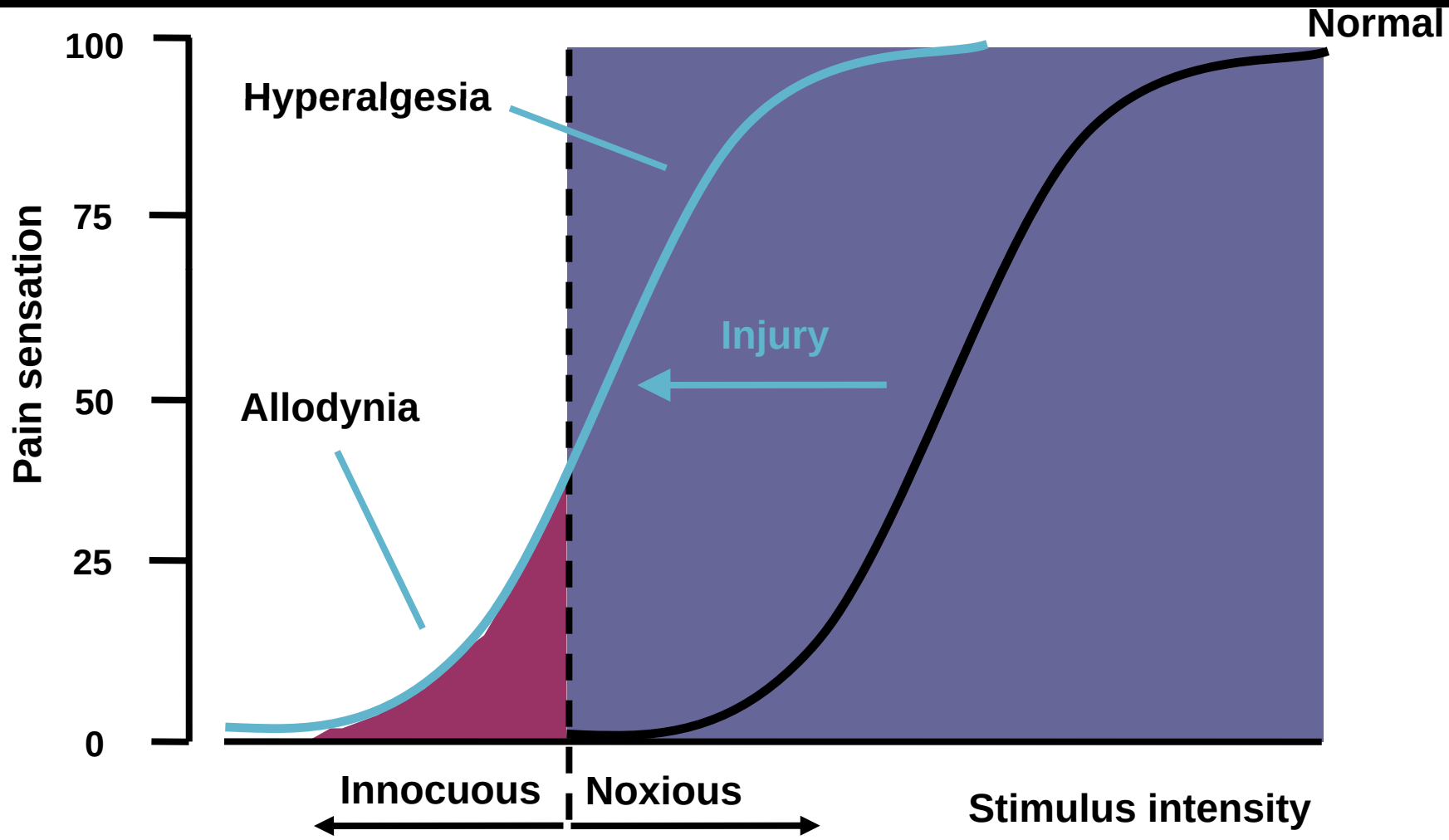
Tonic activity in C nociceptors

Enhanced postsynaptic effects by NMDA-receptor sensitization

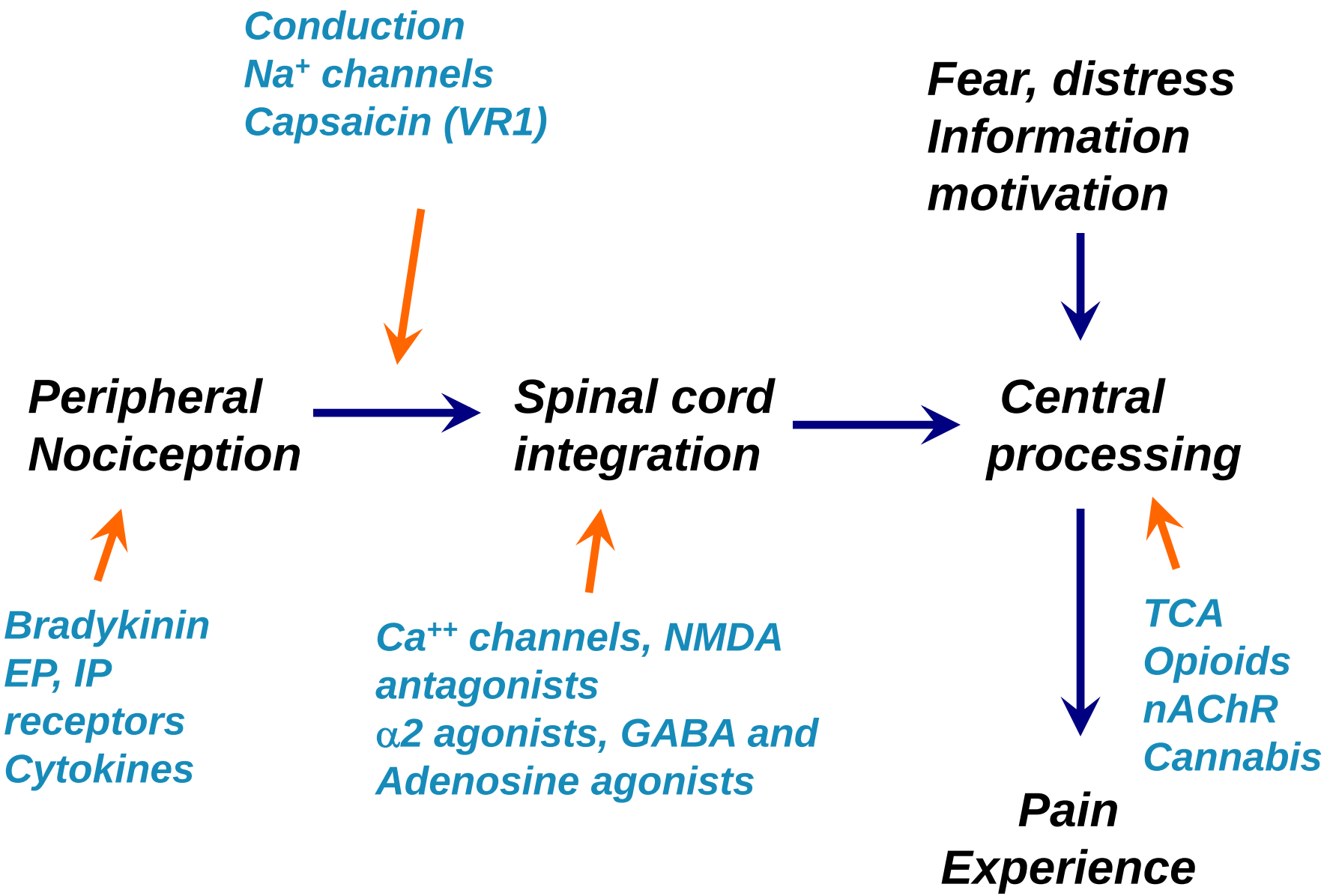
Expressions of Sensitization

- Hyperalgesia – heightened pain perception to a noxious stimulus resulting from abnormal processing of nociceptor inputs in the PNS or CNS
- Allodynia – sensation of pain evoked by a non-noxious stimulus

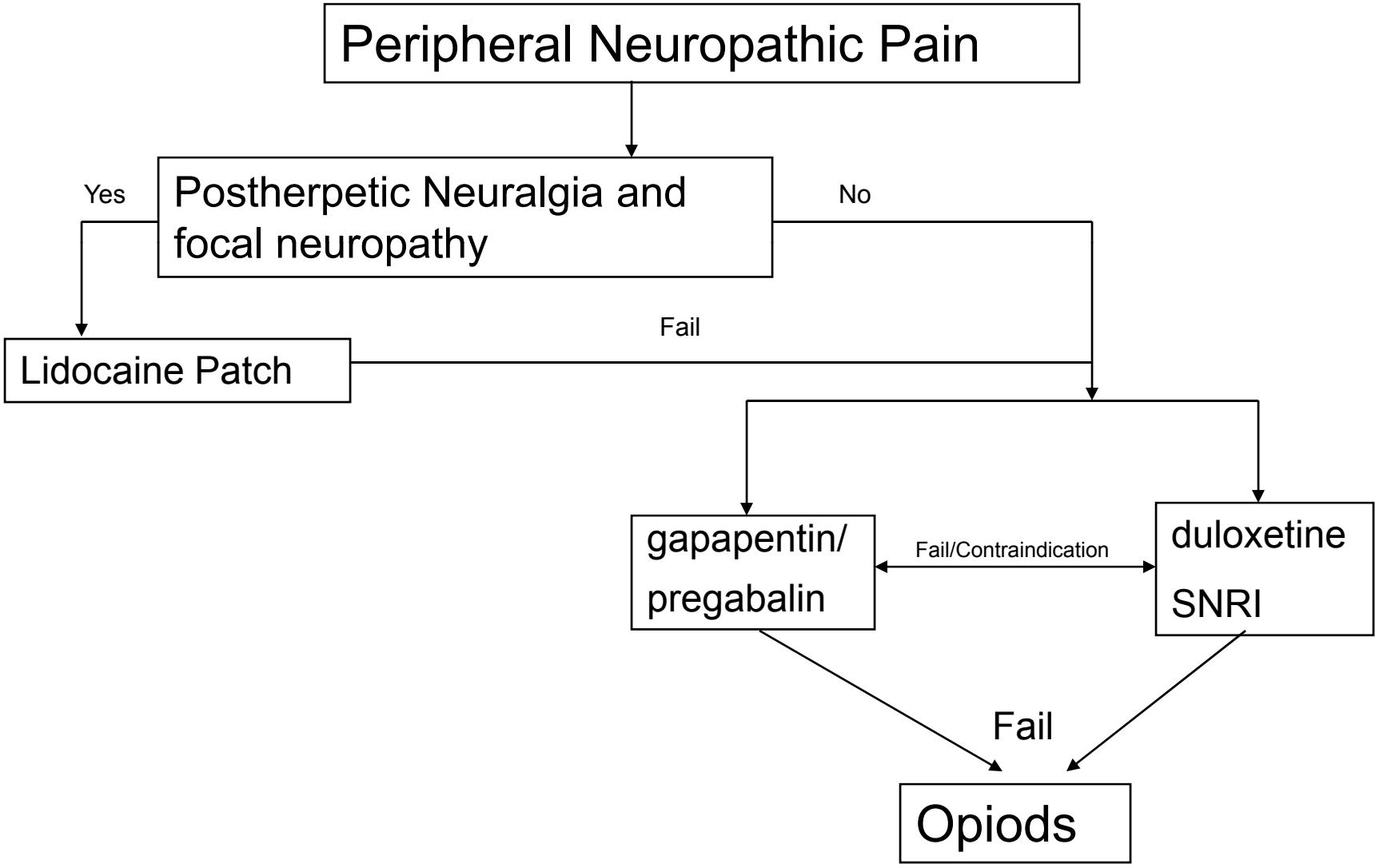
Allodynia and Hyperalgesia



Cervero and Laird. *Pain.* 1996;68:13-23.


Conduction
Na+ channels
Capsaicin (VR1)
Fear, distress
Information
motivation
Peripheral
Nociception
Spinal cord
integration
Central
processing
Bradykinin
EP, IP
receptors
Cytokines
Ca++ channels, NMDA
antagonists
α2 agonists, GABA and
Adenosine agonists
TCA
Opioids
nAChR
Cannabis
Pain
Experience

Neuropathic Pain Treatment



Case #4

- A 24 year-old female presents with recurrent episodes of unilateral headaches associated to nausea and vomiting. In addition she complains that both light and noises worsen the headaches.

How Common is Migraine?

- 30,000,000 Americans
- 20% of women
- 7% of men at any given time
- Most of us have some migraine manifestations occasionally

Recognizing Migraine

- Pounding unilateral headache
- Preceded by visual or other aura
- Nausea, vomiting
- Light and sound sensitivity

What is migraine?

Migraine without aura (MO)

At least five attacks fulfilling these criteria:

- Headache lasting 4–72 h (2–48 h in children)
  - With at least two of:
    - unilateral location
    - pulsating quality
    - moderate/severe intensity
    - aggravated by activity
- Accompanied by at least one of:
  - nausea
  - vomiting
  - photophobia and/or phonophobia
- No evidence of organic disease

Migraine with aura (MA)

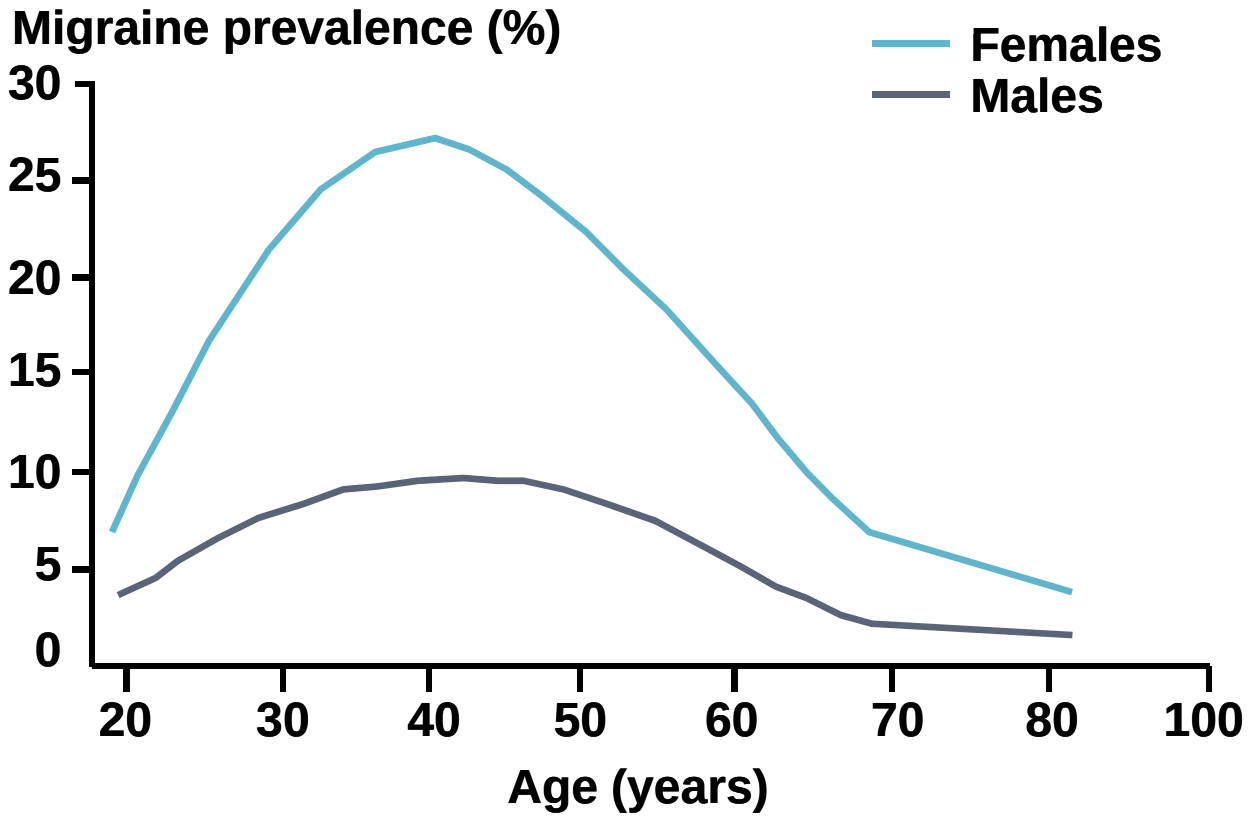
At least two attacks fulfilling these criteria:

- At least three of the following:
  - one or more fully reversible aura symptoms
  - gradually developing or sequential aura symptoms
  - no one aura symptom lasts longer than 1 h
  - headache shortly follows or accompanies aura
- No evidence of organic disease

Diagnosis of migraine

- Diagnosis depends on patient history
- No specific tests or clinical markers
  - Positive diagnosis if attack history fulfils IHS criteria for migraine
  - Other pointers include:
    - family history of migraine
    - age of onset <45
    - presence of aura
    - menstrual association
  - Organic disease must be excluded

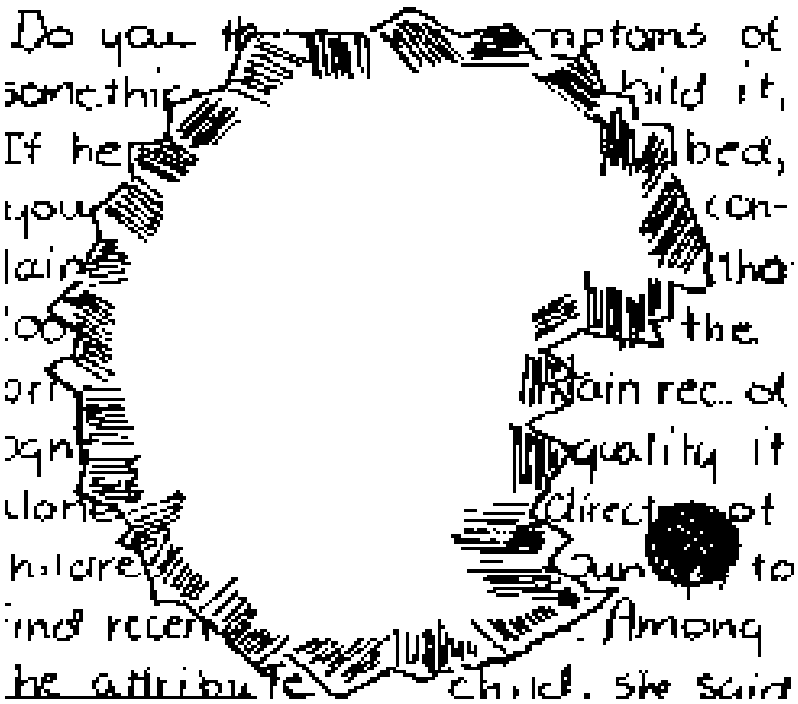
Prevalence of migraine by sex and age



The American Migraine Study (*n*=2479 migraine sufferers) Lipton and Stewart (1993)

Phases of Migraine

- Vague Prodrome: psychic change, cravings, not feeling well
- Aura: Focal symptoms and vision
- Headache: Throbbing unilateral pain
- Inflammation: Prolonged phase
- Postdrome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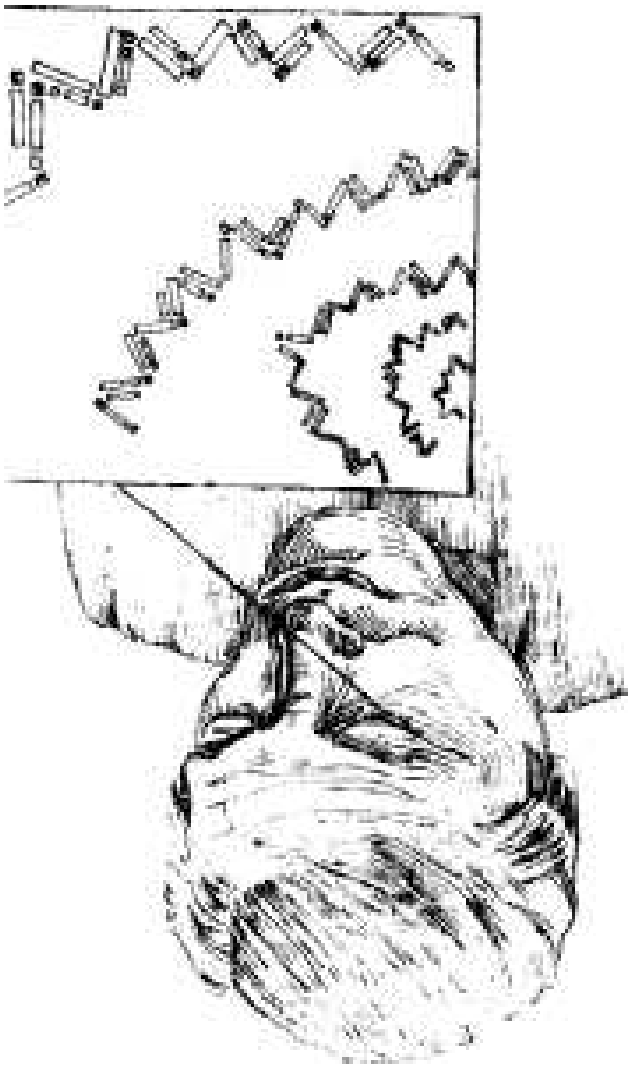
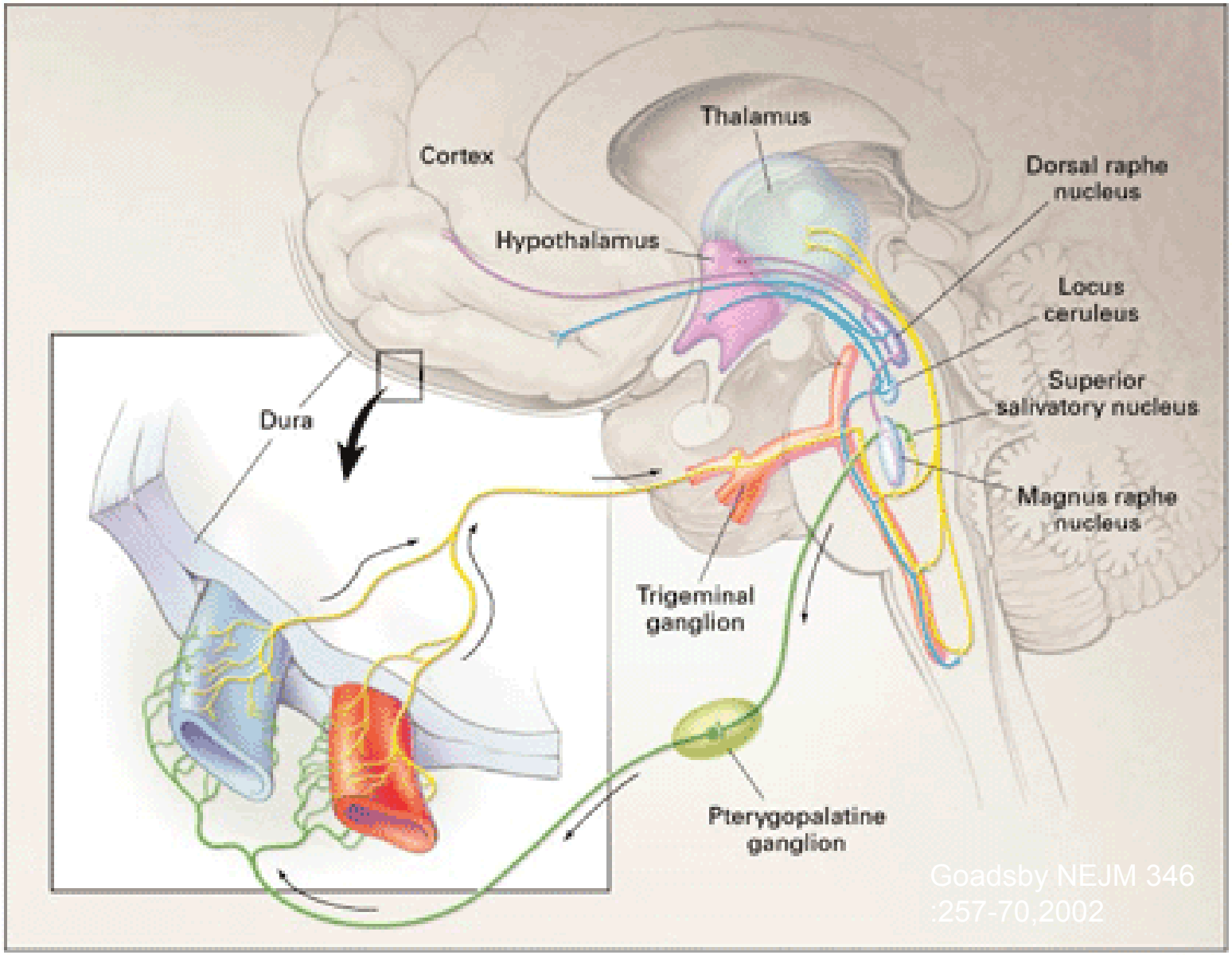


Trigeminal Theory

- Serotonin
- Trigeminal Afferents: sensory function of face and meninges
- Trigeminal efferents to vessels
- Cause vessel spasm and sensitivity
- This theory primarily explains action of Triptans: 5-$HT_{1b,d}$ agonists

Migraine Pathophysiology



Allodynia Theory

- Migraine is a state of hypersensitivity
- Light, sounds, smells, touch (head in headache)
- Need for dark room
- Best preventives decrease sensitivity.
- Anticonvulsants, tricyclics, beta and calcium channel blockers

What is Central Sensitization?

- Central Sensitization is a time-dependent physiological event
- During a migraine attack, neuronal pathways become sensitized in stages
  - Peripheral neurons are activated early in the attack (mild pain phase throbbing)
  - Central neurons are activated later in the attack (full-blown migraine)

Cutaneous allodynia

- Phenomenon later in migraine attack
- Once it develops pts less likely to respond to triptans
- In small sample 15% of pts with and 93% of pts without CA responded to triptan (Burstein et al)

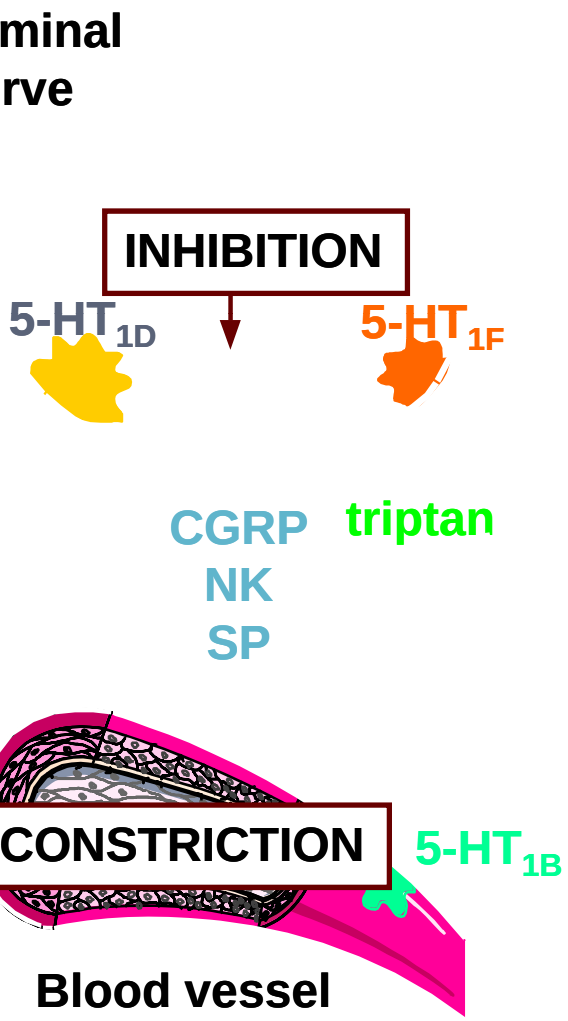
Migraine Phenomena

- Focal and paroxysmal onset of symptoms
- Specific visual phenomena
- Spreading numbness and moving visual phenomena and sensory distortions.
- Nausea, vomiting “sick” headache
- Pounding unilateral or bilateral pain
- Psychic changes
- Light and sound sensitivity even between attacks
- Effectiveness of triptans
- Effect of anticonvulants
- Role of serotonin

Treatment

- Effective treatment of attack
- Prevention
- Address comorbidities

Mechanisms for treatment



CGRP	calcitonin gene related peptide
NK	neurokinin A
SP	substance P

Adapted from Goadsby (1997)

Acute Attack

- Triptans:
  - sumatriptan, zolmitriptan, almotriptan, naratriptan, frovatriptan, elitriptriptan, riaztriptan
- NSAID's
- Fioricet
- Midrin (isometheptane, chlorphenoxazone, apap
- OTC: Caffeine, apap, phenacitin, asa
- Ergots: Caffergot, DHE nasal, injected
- Narcotics
- Depacon

TRIPTANS: TREATMENT CHOICES

- Sumatriptan
  - Tablet (25, 50, 100 mg)
  - Injection (6 mg)
  - Nasal spray (5, 20 mg*)
  - Combination with naproxen
- Zolmitriptan
  - Tablet (2.5, 5 mg)
  - Nasal spray (5 mg)
- Naratriptan
  - Tablet (1, 2.5 mg)
- Rizatriptan
  - Tablet (5, 10 mg)
- Almotriptan
  - Tablet (6.25, 12.5 mg)
- Frovatriptan
  - Tablet (2.5 mg)
- Eletriptan
  - Tablet (20, 40 mg)

Question and Answer

- Are there differences between the triptans?
- If one triptan fails, will another triptan work?

* Pediatric efficacy shown

Ferrari MD et al. *Lancet*. 2001.

Triptan worries

- Not released under age 18
- If you even suspect CAD don't use or get proper exclusionary tests.
  - Man or woman of a certain age
  - Smoker or other risk factors
- Cerebrovascular disease or complicated migraine - contraindicated
- Watch for overuse. These are rescue medicines

Consider Combinations

- Triptan + NSAID
- Triptan + anti-nausea
- Unconventional agents
- Phenergan, Compazine alone or in combination.
- Steroids

Prophylaxis

- Anticonvulsants: topiramate, valproate, gabapentin??
- Tricyclics
  - Amitriptylene, nortriptylene, trazodone
- Beta Blockers
  - Timolol, propranolol, nadolol
- Calcium channel blocker – verapamil
- SNRI's - duloxetine ??

MIGRAINE CHECKLIST

- Caffeine
  - Coffee
  - Soft drinks
  - MEDICINES
- Sleep
- Depression
- Meals
- Stress
- Menstrual Periods

Plea

- Listen to patients
- Migraine is mixed up with a lot of things
  - Emotional factors: husbands, kids, bosses, general dissatisfaction with life
  - Sleep disturbances
  - Hormonal changes
- If you do not address these you will not be treating your patients and headache will persist