Analgesia

Hot Plat Test

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Yes we are visit Analgesia

That's Hot Plat test

One of analgesic test in lab animals

Pain is the most common symptom for which patients see a doctor. Different types of drugs are used for treatment of pain. In general, they include:

1. Drugs, relieving pain due to multiple causes (analgesics)

- **narcotic analgesics** (morphine, fentanyl, etc): act chiefly in the CNS
- **non-narcotic analgesics** (paracetamol, metamizole): act chiefly peripherally

2. Drugs relieving pain due to a single cause or specific pain syndrome only

They are not classified as analgesics:

- naratriptan (migraine),
- carbamazepine (neuralgias)
- glyceryl trinitrate (angina pectoris)
- adrenal steroids (inflammatory pain)
- butylscopolamine (spasm of visceral smooth muscles)
- baclofen (spasm of striated muscles).

3. Adjuvant drugs (anxyolitics, neuroleptics, antidepressants) may modify the perception of pain and remove the concomitants of pain such as anxiety, fear, depression. Placebo gives relief in 3%.

4. Anaesthetics (general and local) are used during surgical operations, some diagnostic, and other painful procedures.

Nociception is a consequence of tissue injury (trauma, inflammation). It causes the release of chemical mediators (ACh, PGE, NA, 5-HT, glutamate, bradykinin, endogenous opioids, adenosine). They have neuronal or non-neuronal origin. These mediators activate nociceptors.

Nociceptors are pain-receptors. Nociceptors transmit information by thin myelin (A-delta) and non-myelin (C) fibers to the spinal cord and brain.

Pain perception has a complex mechanism.
It is a result of nociceptive impulses reaching the brain (thalamus, cortex), *plus* impulses from other peripheral receptors, e.g. heat and mechanoceptors, whose threshold of response is reduced by the same chemical mediators.
These are processed in the brain hence modulated inhibitory impulses pass down to regulate the continuing afferent input.
But pain can occur without nociception (e.g. some neuralgias). ***Pain is a psychological state,*** though most types of pain have a physical cause.

MAIN TYPES OF PAIN

Acute pain (defined as < 3 months duration) transmitted principally by fast conducting myelin A-delta fibers. It has major nociceptive input (physical trauma, pleurisy, myocardial infarction, perforated peptic ulcer).
The narcotic (opioid) and sometimes non-narcotic analgesics are used for treatment of acute pain.

Chronic pain (defined as > 3 months duration) is transmitted principally by slow conducting non-myelinated C fibers. It is better regarded as a syndrome rather than a symptom. It is depressing to the patient who sees no prospect for relieving the suffering. Analgesics alone are often insufficient and adjuvant drugs (antidepressants or neuroleptics) as well as non-drug therapy (including psychotherapy) have increasing importance.

Neuropathic pain follows *damage of the nervous system*. Acute pain without nociceptive (afferent) input (e.g. some neuralgias) is less susceptible to analgesics. The suitable drugs are some antidepressants and carbamazepine.

Transient pain is provoked by activation of nociceptors in the skin and other tissues in the absence of tissue damage. It protects humans from physical damage coming from the environment or excessive stressing of the tissue. It is a part of normal life and does not need treatment.

- suppose that a specific dose of analgesic drug (x mg) produced analgesia in 35 out of 100 animals, then the % response is 35% response.
- if we increase the dose of the analgesic drug to (2x mg); the % of animals responding would also increased (for example to 65%). this is a graded % response

i.e. increasing the dose in a population will result in an increase of the % of individuals responding although for each animal it is either all (analgesia) or none (no analgesia).

Objective

- to determine the RP of a test analgesic drug using multiple point (2x2) assay
- method of inducing pain: thermal method


HOT PLATE
model-DS37
sorrel
TEMPERATURE CAL.
TEMPERATURE °C
TIMER
2 23:43


Sorel
TEMPERATURE °C
TIMER
2 23:43


HOT PLATE
model-DS37
sorel
TEMPERATURE CAL.
55.2
TEMPERATURE °C
000.0
TIMER
3 0:31


HOT PLATE
model-DS37
sorrel
55.1
TEMPERATURE °C
3 0:31


HOT PLATE
model-DS37
sorrel
TEMPERATURE CAL.
55.1
TEMPERATURE °C
000.0
TIMER
3 0:32

Procedures:

1. mice are divided into 4 groups (3 groups for test drug and 1 group for control); n=5.

- group A treated with codein (20mg/kg Bw. Sc.) dose of the test drug
- group B with Aspire (120mg/kg Bw. Po.) dose of the test drug
- group C with Diclofenac (5mg/kg Bw. Po.) dose of the standard drug respectively.
- group D with normal saline served as control

2. mice are placed on hot plate at 55±1°C and observed for max 30 sec.

- ❑ the reaction time to the nociceptive stimulus is recorded by determining the time between the placing of the mouse on the hot plate and the mouse licking its forelimb or hind limb or jumping out of the hot plate.

3. the reaction time is recorded twice; before drug administration and 30 minutes after drug injection

dose drug	reaction time before drug admnistration				
	M 1	M 2	M 3	M 4	M 5
A					
B					
C					
D					

- The analgesic effect for each dose is calculated as the % of the Maximal Possible Effect (% MPE) using the following formula:

$$\% \text{ MPE} = \frac{(T-C)}{20-C} \times 100$$

$$\% \text{ AE (analgesic effect)} = \frac{T-C}{C} \times 100$$

where

C = mean reaction times before drug administration

T = mean reaction time after drug administration

- Dose-effect curves are constructed by plotting % MPE vs. log dose or % AE vs. log dose

RP = anti log M

Drug Dose	Reaction time before drug admnistration (sec.)					Reaction time after drug admnistration (sec.)			
	M 1	M 2	M 3	M 4	M 5				
A 10	12	14	10	13	13				
B 20	13	14	10	11	12				
C 10	14	12	10	11	13				
D 20	12	13	14	15	13				

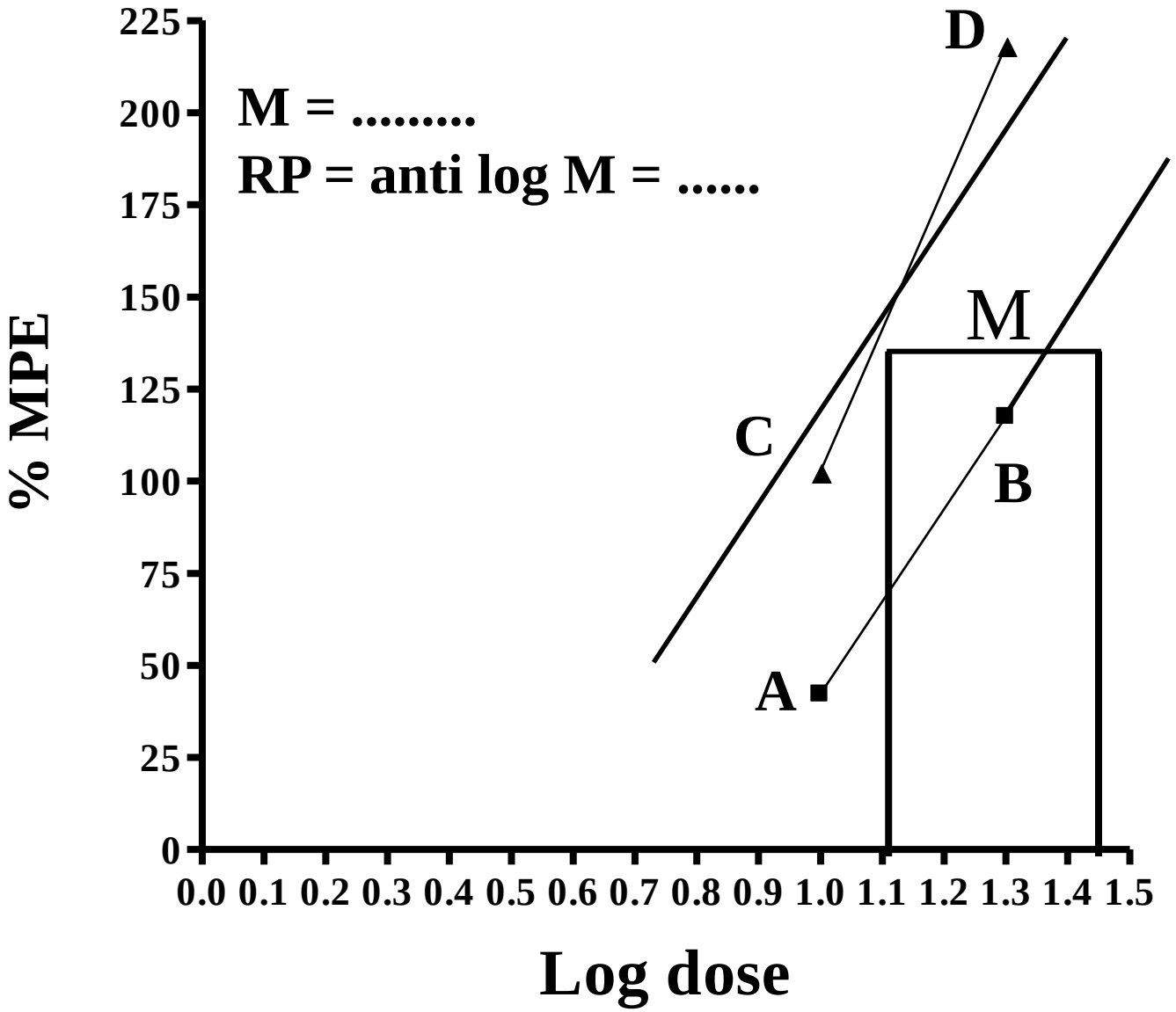
$$\% \text{ MPE} = \frac{15.6 - 12.4}{20 - 12.4} \times 100$$

$$= 42.11$$

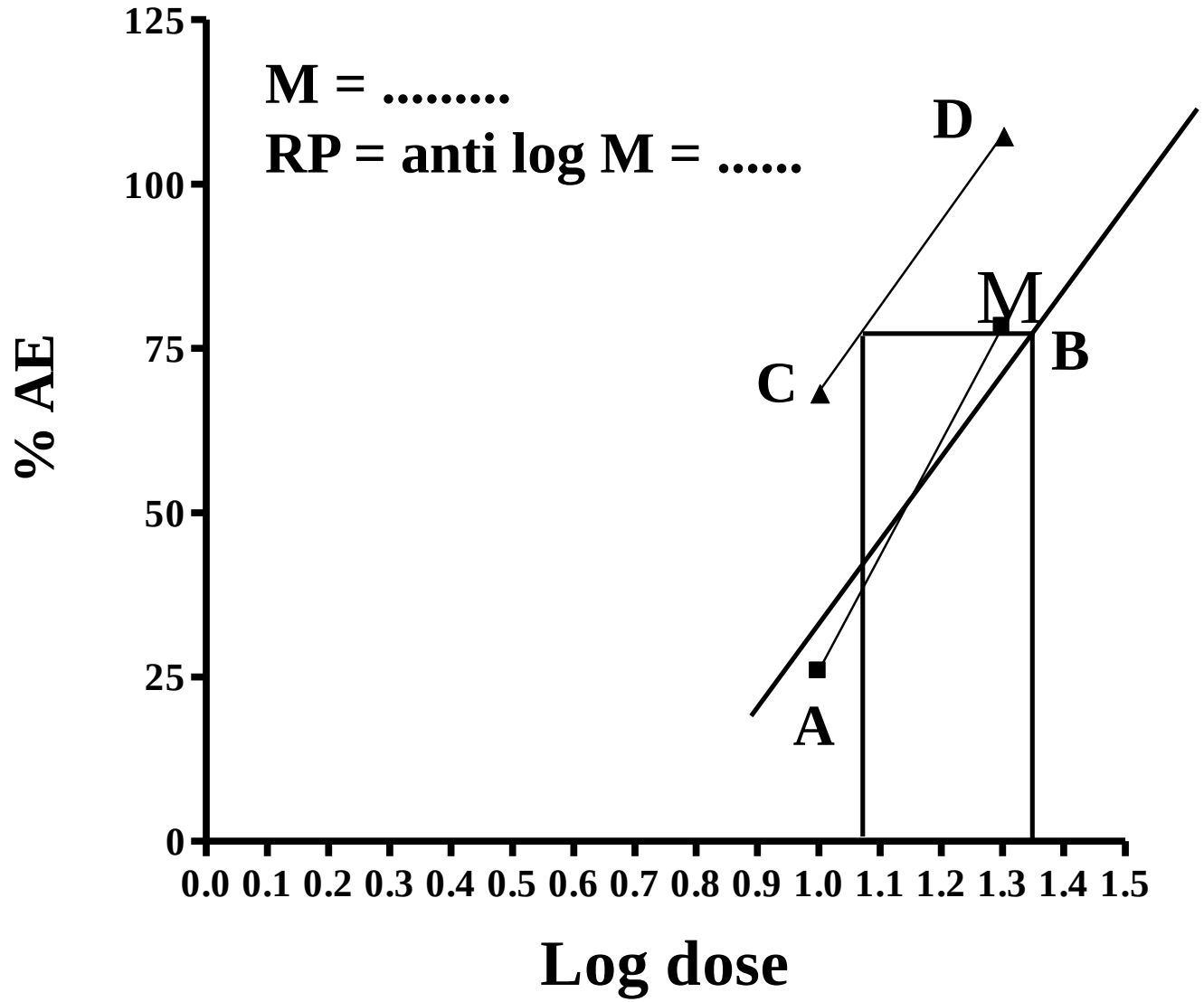
$$\% \text{ AE} = \frac{15.6 - 12.4}{12.4} \times 100$$

$$= 25.88$$

dose	Log dose	% MPE
A 10	1	42.11
B 20	1.3	117.5
C 10	1	102.18
D 20	1.3	218.18


M = ...
RP = anti log M = ...
% MPE
225
200
175
150
125
100
75
50
25
0
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4 1.5
Log dose
D
M
C
B
A

dose	Log dose	% AE
A 10	1	25.88
B 20	1.3	78.3
C 10	1	68.3
D 20	1.3	107.5


M = ...
RP = anti log M = ...
D
M
C
B
A
125
100
75
50
25
0
% AE
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4 1.5
Log dose

❑ Using hot-plate method, for screening of analgesic effect of a test solution, the following are responses (reactions time) showed by mice before and after i.p. codeine (30 μg/ml; C and D) and test drug (A and B) injections. Calculate the % MPE and % AE for each dose. Calculate the RP and the concentration of test solution.

dose	Reaction time (before injection)					Reaction time (after injection)				
	m1	m2	m3	m4	m5	m1	m2	m3	m4	m5
A	9	10	12	9	10	17	18	18	24	18
B	10	9	14	14	13	19	22	25	26	28
C	11	13	12	12	15	16	19	22	20	18
D	14	13	11	13	12	25	22	24	19	27