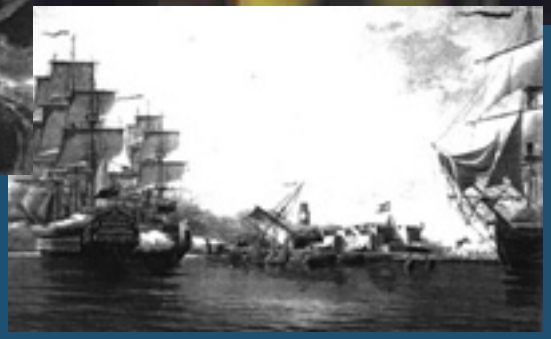
Pain Assessment and Pain Relief for Laboratory Animals



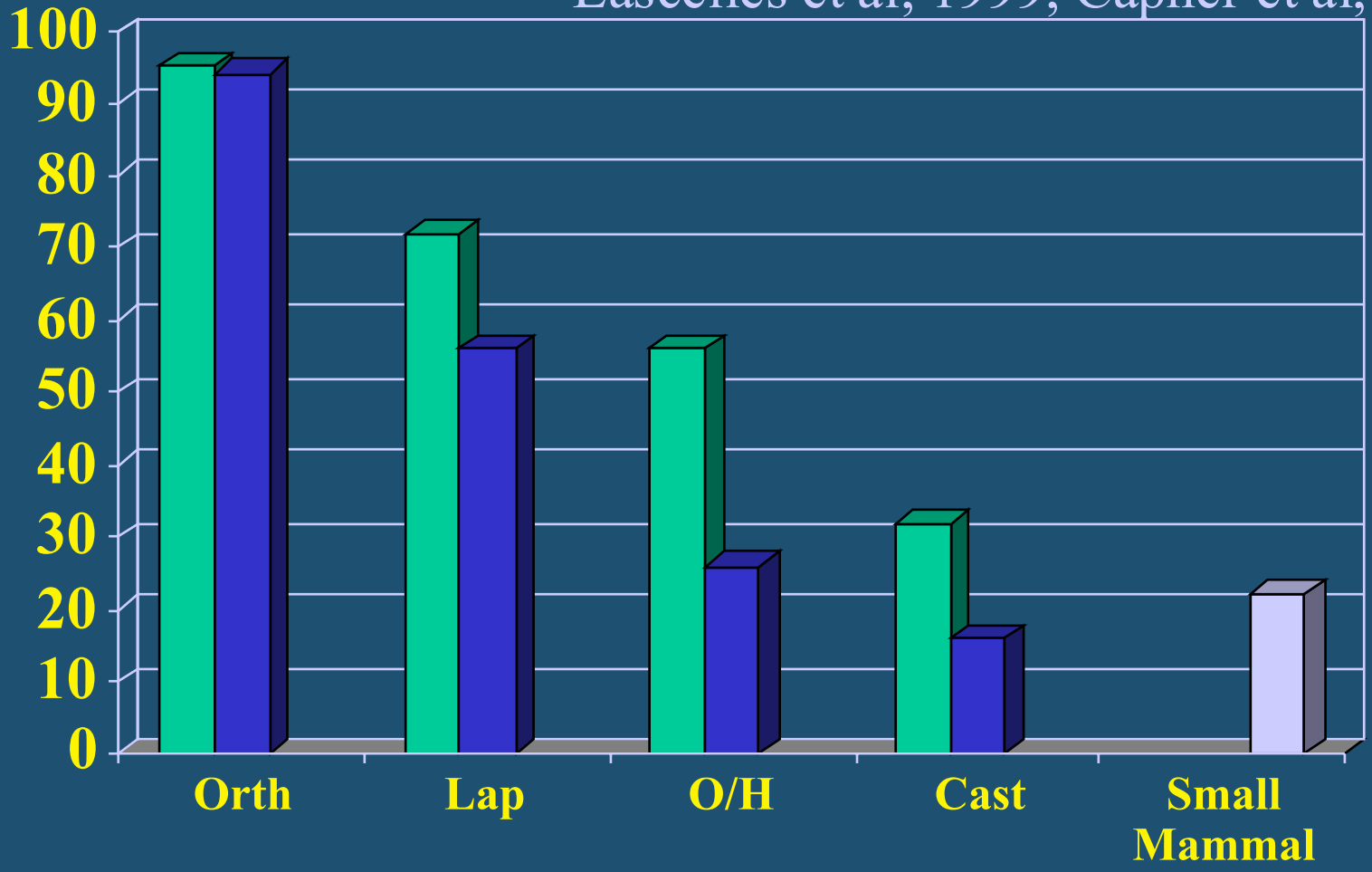
Nelson, Santa Cruz, 1797

Arm amputated - Rum was the anaesthetic, opium for post-operative pain relief

"…since that time, post-operative pain relief has developed very little" Alexander and Hill, Postoperative Pain Control, 1987

Percentage of animals receiving analgesics following surgery

Lascelles et al, 1999, Capner et al, 1999



Why so little progress with pain relief?

- Animals don't experience pain
- Animals don't experience as much pain as people

Uncritical anthropomorphism

"Animals are small furry people"

QuickTime™ and a
Video decompressor
are needed to see this picture.

…so we expect them to behave like people when they are in pain!

QuickTime™ and a
Video decompressor
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Pain Assessment

- Is an analgesic required?
- Opioid or NSAID?
- Is the dose given effective?
- Should the dose be repeated
  at what interval?
- Can therapy be discontinued

Why is Pain Assessment important?

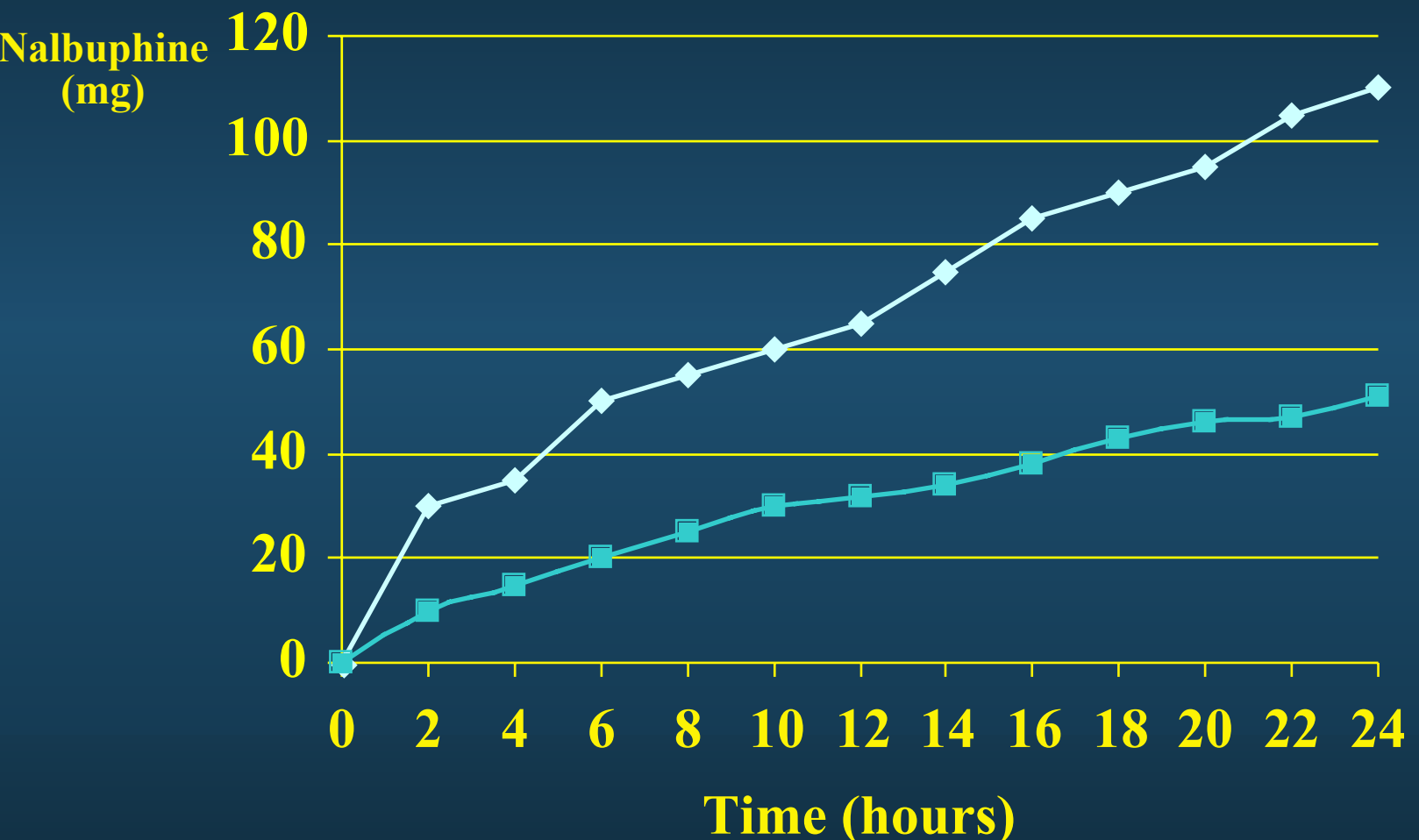
- Why not simply:
  "give the animal the benefit of the doubt"
  and give an analgesic, or take some other steps to alleviate pain ?

Variation in analgesic requirement

Data from people

- Type of surgical procedure
- Expertise of the surgeon
- Individual variation (sensitivity to analgesic)
- Individual variation (emotional state)

Cumulative nalbuphine consumption in man



How do we assess animal pain?

- ~~Uncritical anthropomorphism~~
- Clinical appearance
- Pain scoring (Behaviour, Physiological responses, Endocrine responses)

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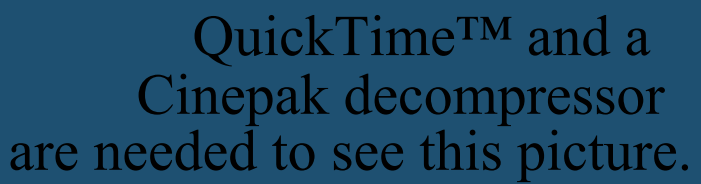
Clinical impression

9 yr old dog, thoracotomy previous day. Oxymorphone post-op and early today.

(Images from "Relieving Pain: assessment and managemen of post-operative pain in dogs and cats - interactive CD authored by Karol Mathews, available from CSAW, University of Guelph, Guelph, Ontario, Canada, N1G 2W1



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Ketorolac administered immediately after first video clip

QuickTime™ and a
Cinepak decompressor
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Pain scoring systems

- Numerical rating systems
- Verbal rating systems
- Colour scales
- Picture scales
- Visual analogue scales

Visual Analogue Scale

No Pain

Pain as Severe as Possible

Pain Scoring

- Posture 2
- External appearance 2
- Food intake 3
- Water intake 3
- Vocalisations 1
- Spontaneous Behaviour 2
- Provoked Behaviour 2

Total Score 15

Pain Scoring Problems

- Poor correlation of scores between observers
- Lack of predictive value of some clinical signs
- Lack of validation of factors used
- Lack of validation of scales used

Pain Scoring - Objective measures

- Pulse rate
- Skin conductance
- Blood pressure
- Corticosterone or cortisone concn.
- Catecholamine concn.
- Endorphin concn.

Endocrine responses

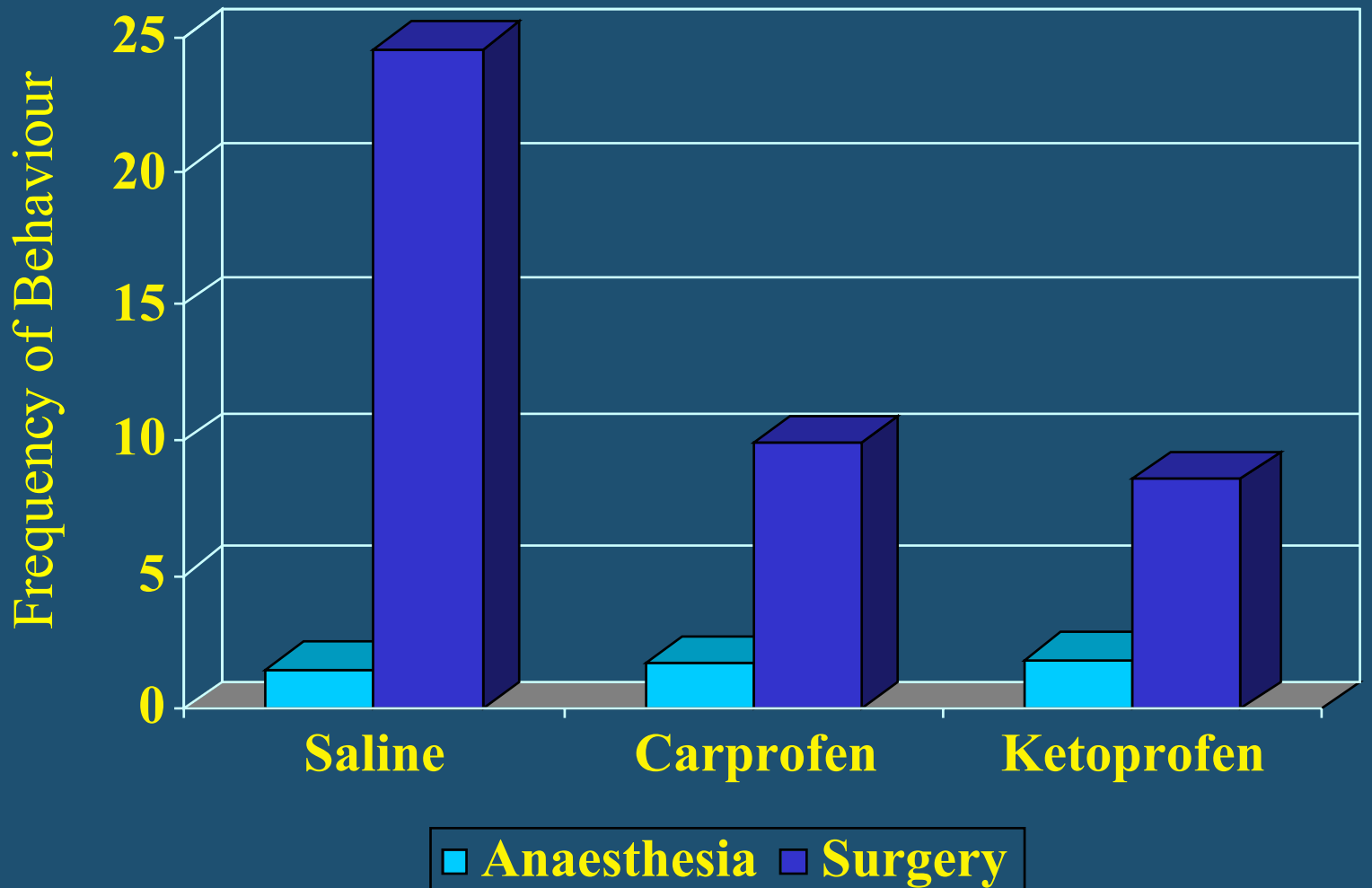
- Occur in response both to pain and to other stressors
- May be blocked by some analgesics
- Maximal response may occur after relatively moderate stress
- Reduction in response may not parallel reduction in pain

Assessment of Pain - Desirable features of pain-related behaviours

- Observation requires minimal training (must be easily recognised)
- Unaffected by drug administration alone
- Occur at an appropriate frequency or duration (either greatly increased or reduced)

Frequency of "back-arching" in rats after laparotomy or anaesthesia alone

Roughan and Flecknell, 2001



Pain alleviation - How?

Non-steroidal anti-inflammatory drugs

Opioids (morphine-like drugs)

Local anaesthetics

Analgesic drug

Opioids - Morphine-like drugs

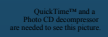
Analgesic agents- Opioids

Activity: Agonists (morphine), partial agonists (buprenorphine), antagonists (naloxone)

Receptor: mu, delta, kappa

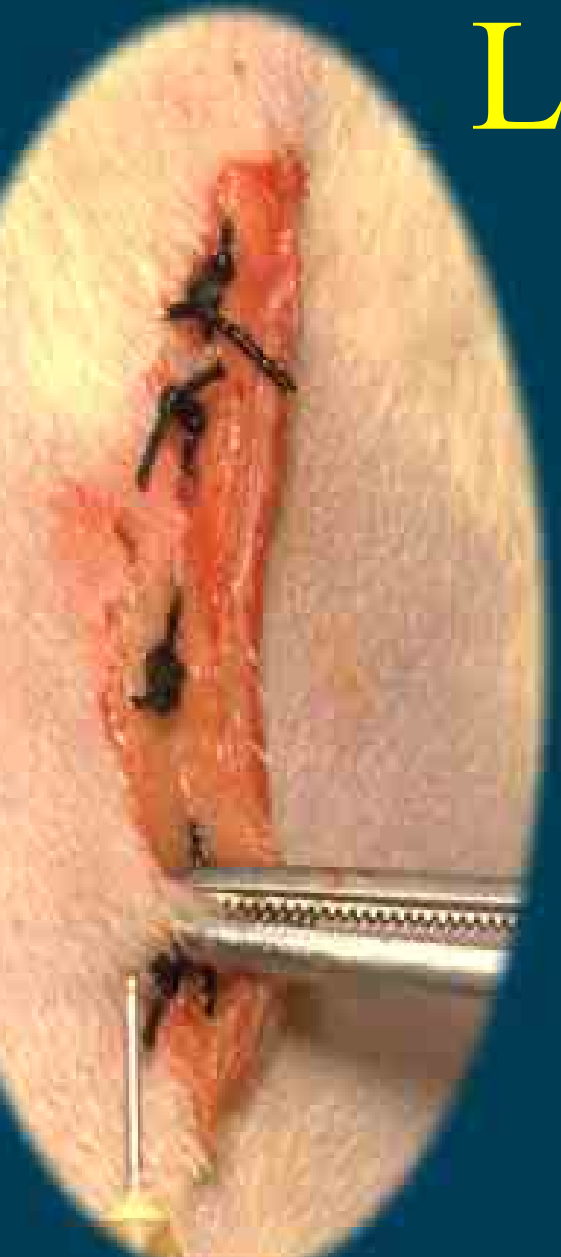
Duration of action: short (10-15 minutes - fentanyl); medium (2-4 hours - morphine), long (4-12 hours - buprenorphine)

Non-steroidal anti-inflammatory drugs



Non-steroidal anti-inflammatory drugs

- Historically, considered “mild” analgesics
- Newer compounds provide more effective analgesia (carprofen, ketoprofen)
- Act by suppressing one or more components of the inflammatory process



Local Anaesthetics

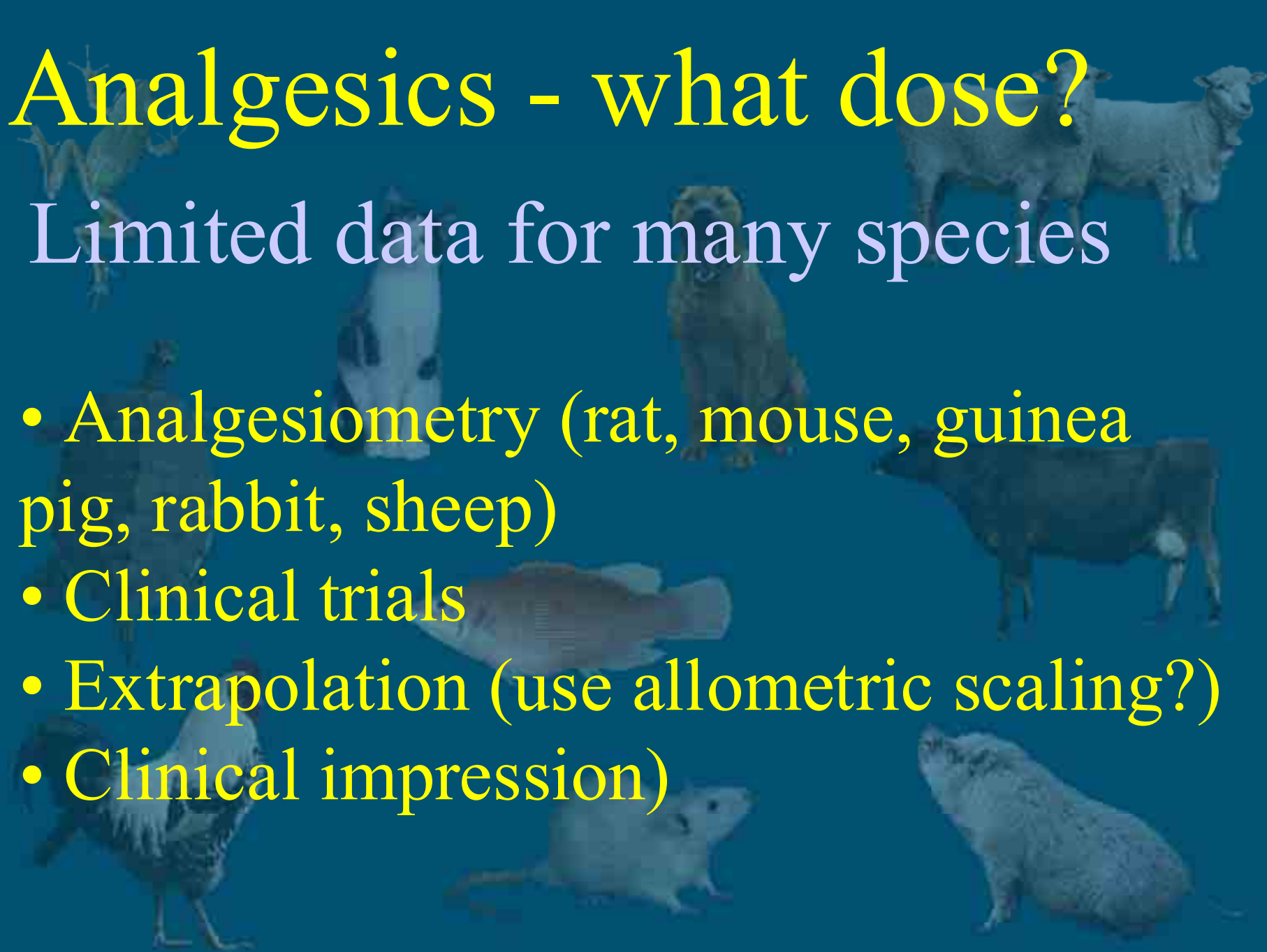
Lignocaine, Bupivacaine

- Block all nerve impulses
- Small fibres blocked first
- Can administer by a variety of routes - local infiltration, topical application, epidural or spinal

Analgesics - what dose?

Limited data for many species

- Analgesiometry (rat, mouse, guinea pig, rabbit, sheep)
- Clinical trials
- Extrapolation (use allometric scaling?)
- Clinical impression)



Multi-modal Pain therapy

Pain transmission involves several pathways and mechanisms

A single class of analgesic is unlikely to provide complete analgesia - even at high doses

Combining different classes of analgesics increases efficacy and may decrease dose rates

Administration of analgesics before noxious stimulation occurs

- Prevents central sensitisation (opioids, local anaesthetics)
- Reduces severity of inflammatory responses (NSAIDs) - so nociceptive imput reduced
- Integrate analgesic administration with anaesthetic protocol

Analgesic use in laboratory animals

- Always give at least one dose of analgesic
- Give pre-emptively if possible/practicable
- Use multi-modal analgesic protocols
- Try to use a method of pain assessment
- Adjust analgesic regimen according to animal's response

Pain control - Problems

Management of large numbers of animals

- Assessment of individual animal difficult and time-consuming
- Treatment labour-intensive
- Treatment may require staff to attend at all times (24 hours)

Pain control - Solutions

Management of large numbers of animals

- Assess small number, extrapolate to remainder
- Plan study carefully
- Use long-acting analgesics
- Administer analgesics in food or water
- Employ more staff!

Providing long term-analgesia (24h)

- Buprenorphine jelly (? Every 12 h)
- Fentanyl patches
- Epidural or spinal opioids
- NSAIDs - up to 72h in some species - ? 6-24 in many lab species
- New long acting analgesics?

Oral administration of opioids to rats

"Buprenorphine jelly"

- Familiarise for 2-3 days
- Buprenorphine 0.4mg/kg effective

Fentanyl patches

Reports of use in dog, cat and pig

Plasma levels not always adequate

Use as "background analgesia" and supplement as required


Continuous infusion
of opioids

Pain control - Problems

Analgesic side-effects:

- Toxicity (eg o/d of local anaesthetic)
- Respiratory depression, hypotension, vomiting (opioids)
- Renal dysfunction, gastro-intestinal irritation, platelet inhibition (NSAIDs)

Pain control - Solutions

Analgesic side-effects:

- Side-effects rarely have clinical significance
- Reduced by selecting appropriate dose rates and good anaesthetic protocols
- May interfere with specific research protocols - avoid by rational selection of analgesics

Analgesic side-effects

Place in relevant context

Anaesthetic drug effects

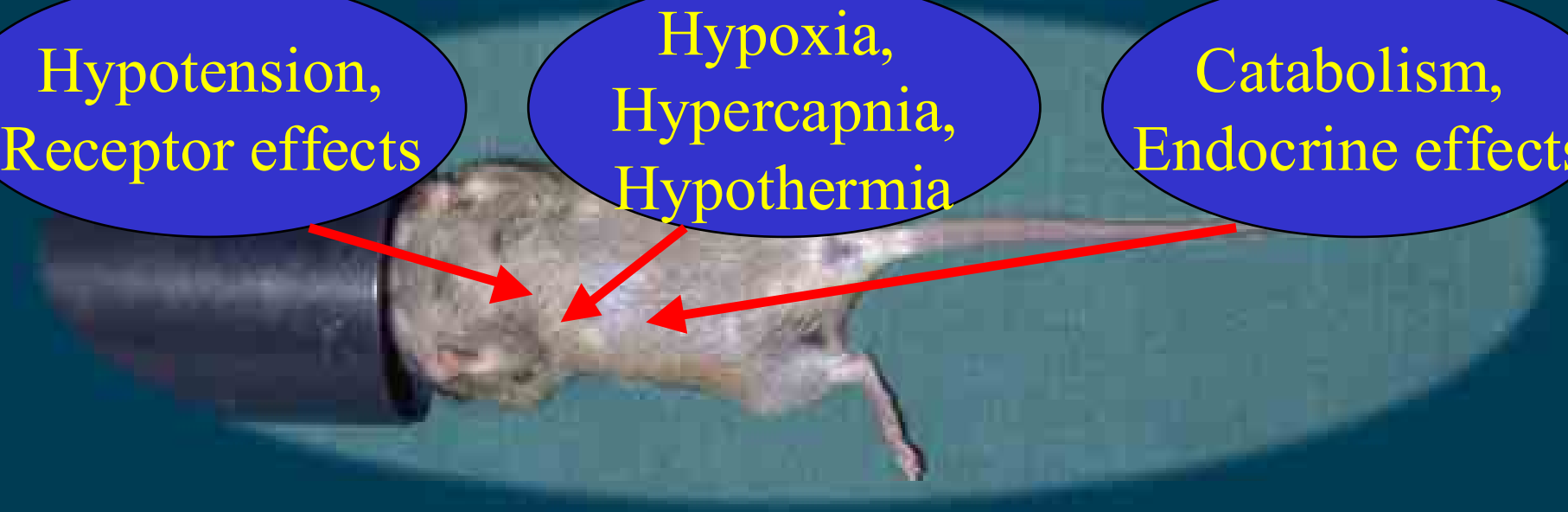
Non-specific Anaesthetic effects

Surgical stress response

Hypotension, Receptor effects

Hypoxia, Hypercapnia, Hypothermia

Catabolism, Endocrine effects



Pain control - Solutions

Analgesic side-effects:

- Consider research protocol and aims and objectives
- Consider potential interactions with anaesthesia, analgesia, and effects of surgery (and pain)
- Select analgesic regimen to minimise potential interactions

Pain control - Solutions

Analgesic side-effects:

- If uncertain, perform pilot study with control group
- Limit duration of treatment
- Be sure to consider consequences of unalleviated pain

Pain control - Problems

- We are slowly improving our management of post-surgical pain
- We have made very little progress dealing with chronic pain - we often do not even know if pain is present
- We have even less information concerning “distress”