Dissertation for Masters Thesis

M.Phil (Emergency Medicine)
University of Cape Town
South Africa

PAEDIATRIC ANALGESIA AND SEDATION IN THE EMERGENCY DEPARTMENT

Treatment methods: An overview

Special reference: The use of ketamine for procedural sedation, intranasal midazolam for treatment of persistent seizure activity, and intranasal diamorphine to treat severe pain.

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I started my career as medical practitioner in 1979, and have since worked in many different Emergency Departments in South Africa, Namibia and the United Kingdom.

In most Emergency Departments, medical personnel find it difficult to deal effectively and appropriately with pain and anxiety in the ill and injured child.

This perennial problem has been the motivation behind my study. I wanted to find out what the nature of the problem was, how pain and anxiety can be recognised and measured, and what methods, pharmacological and non- pharmacological, are available to deal with pain and anxiety, especially in children, in the Emergency Department.

I specifically investigated certain methods that are completely acceptable to patients, and that have the potential for effective, expedient and well tolerated (needle-free) analgesia and sedation.

During 2004, I worked for 5 months as a locum consultant in the Accident and Emergency Department of the Royal Lancaster Infirmary in Lancaster, United Kingdom.

This Department has done intensive research in the use of intramuscular ketamine for procedural sedation under the leadership of Mr (Dr) RG McGlone. This is an ongoing clinical trial in which I have also actively participated: I have used the method on many occasions, and collected data for clinical research, as described in this dissertation. I also assisted middle grade doctors in the Department by teaching them the technique.

At the Royal Lancaster Infirmary Accident and Emergency Department, it is standard protocol to use intranasal diamorphine by method of a mucosal atomized device (MAD) in all children suffering from severe pain after injury or illness, and also using the same device for intranasal midazolam in children with persistent seizure activity.

Apart from my own involvement and research into these effective methods of treatment, I have done a formal review study on the use of intramuscular ketamine for procedural sedation, and the intranasal administering of drugs such as midazolam and diamorphine in children, by using a mucosal atomized device (MAD).

Information was obtained from official publications and medical records.

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12 May 2005

TO WHOM IT MAY CONCERN

This is to testify that I have read through the M.Phil. (Emerg. Med.) thesis of **Dr VG Loftie-Eaton** for language editing purposes. I made several corrections and adjustments, but was obviously not in a position to comment on the technical and/or medical terminology.

I remain available for consultation and may be contacted at any of the above numbers or addresses.

Signed

Dr Edwin Hees
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PAEDIATRIC ANALGESIA AND SEDATION IN THE EMERGENCY DEPARTMENT

Introduction:

PAIN:

"Bodily suffering; a distressing sensation of soreness, (usually in a particular part of the body)" (*Oxford English Dictionary*).

"Any unpleasant sensation occurring in varying degrees of severity as a consequence of injury, disease, or emotional disorder / the acutely unpleasant physical discomfort experienced by somebody who is violently struck, injured or ill in certain ways" *(American Heritage Dictionary / Encarta Dictionary)*.

ANXIETY:

"A state of intense apprehension, often to a degree that the normal physical and psychological function of the affected individual is disrupted / A state of abnormal and intense apprehension or fear of real or imagined danger, manifested physiologically, as increased heart rate, sweating, trembling, weakness, and stomach or intestinal discomfort" (*American Heritage Dictionary / Encarta Dictionary*).

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Just as in adults, in infants and children pain, anxiety and fear are often associated. All concerned with the care and treatment of children (and adults) have a duty to anticipate and avoid, as well as relieve, pain and anxiety and the psychological and emotional threats of illness and injury as soon as possible. Although pain is a common reason for patients to attend the emergency department of a hospital, it is often poorly dealt with, especially in children. Some physicians still assume that the lower the mental capacity of a patient, the less ability to perceive pain.

Oral analgesia in children with acute pain may be inadequate due to limited drug choice or delayed gastric emptying. Intramuscular and intravenous administration can distress the child, and the rectal route suffers from limited acceptability and the problems of slow and variable onset and of consent.

Certain drugs administered trans-mucosally via the nasal route may offer the potential for effective, expedient and well-tolerated analgesia that is acceptable to patients, and administration is not delayed by the need for a doctor to give an intravenous injection, but this method also has its limitations.

AWARENESS OF PAIN

It is now accepted practice to provide analgesia for all children and infants, including those at less than 26 weeks gestation. Until recently, (10-15 years ago), children and especially neonates were felt to have less capacity than adults to feel and remember

pain and therefore to require less analgesia (1-3). This led to inadequate treatment of sick children and of children in pain and thus unnecessary suffering in this particularly vulnerable group of patients (4).

The main reasons for this belief were that children were less able to feel pain as their nervous system is immature and incompletely myelinated (5-6), and also that young children have no experience of pain and thus cannot understand or perceive nociception as adults do.

Pain occurs after stimulation of specific nerve endings or nociceptors lying in the skin and musculoskeletal tissues. There are two types of afferent nociceptive fibres; fast A-delta fibres and slow C fibres. Thin myelinated fast A-delta fibres have a conduction velocity of 10-20 m/s and result in immediate sharp, well-localised pain.

Unmyelinated C fibres have slower conduction velocity of 1 m/s and result in dull aching, diffuse pain. Both A-delta and C fibres enter the spinal cord via the dorsal root, terminating in the dorsal horn. The ascending fibres of the spinothalamic tract transmit the impulses to the cerebral cortex mainly by the neurotransmitter peptide, substance P (7).

Pain transmission can be modified at several points. At a spinal level large diameter A-beta fibres transmit impulses from low-threshold impulses sensitive to touch, pressure and vibration, which inhibit nociceptive transmission.

This explains the analgesic effect of massage by means of trans-coetaneous nerve stimulation. Pain can also be modified centrally by descending inhibitory fibres, which may explain why people in intensely emotional situations, such as a fight, do not feel pain.

The modification of pain transmission by inhibitory neurones is the gate theory of pain (8). There is now clear evidence that the coetaneous receptors, neural pathways, neurotransmitters and the cortical senses required for pain perception are present by mid-gestation and are fully organised in infancy (9-10). The nociceptive nerve tracts in the spinal cord and central nervous system undergo myelination during the second and third trimesters of gestation.

In adults, the nociceptive impulses in the peripheral nerves are carried through unmyelinated C fibres and thinly myelinated A-delta fibres. It would appear that complete myelination is not necessary for pain perception and therefore newborn babies, who have partial myelination, are capable of experiencing pain (10).

Although infant neurons are incompletely myelinated, this will not result in lack of function, but only in slightly lower conduction. In infants slower conduction velocity is also compensated for by shorter inter-neural distances (11).

Children and infants respond to painful stimuli with changes in heart rate, blood pressure, palm sweating, facial expressions and crying, as well as complex behavioural changes in sleep cycles, REM sleep and feeding patterns.

Work by Anand *et al.* demonstrated that infants undergoing surgery with little or no analgesia mounted a significant stress response with increased release of catecholamines, growth hormone, glucagons and corticosteroids, and insulin suppression, resulting in prolonged hyperglycaemia, and increases in blood lactate and ketones (12-13).

Infants who receive potent analgesia have been shown to have significantly fewer complications postoperatively (14).

There is, therefore, comprehensive evidence that infants and children can and do perceive pain and should not be denied pain relief. It is our role as medical staff to recognise the emergency situation in which a child may be when he or she is stressed and in pain, and thus to quantify and treat the pain and anxiety appropriately.

REASONS FOR POOR PROVISION OF ANALGESIA AND SEDATION FOR CHILDREN IN THE EMERGENCY DEPARTMENT

Poor Communication:

Children may attend hospital with preconceived negative ideas learnt from parents or other children.

Parents may unintentionally condition their children into believing a hospital is a place to be feared and where painful procedures are performed, rather than a place where pain and illness are relieved.

Sometimes the parent's own fear and anxiety of the hospital environment may upset or distress the child. Poor communication between staff may also lead to delay in providing adequate analgesia.

Poor pain and anxiety assessment:

Objective pain and anxiety assessment in children is notoriously difficult and often not made, partly because of their difficulty in communicating pain and also medical staff may underestimate the degree of pain (15).

The lack of a universal assessment method and/or technique may also foster under-treatment of children's pain and anxiety.

Once assessment has been made and analgesia provided, pain levels should be reassessed periodically to determine the continuing adequacy of pain relief and the need for further analgesia.

Staff inexperience:

The medical and nursing school curriculum and training of junior doctors and nurses does not always prepare staff adequately to provide sufficient and adequate analgesia and /or sedation to children.

Inexperienced staff members may have a poor ability to recognise, assess and understand pain and anxiety.

They also generally lack the ability to examine a young child properly and to make a speedy diagnosis.

Inexperienced clinicians also sometimes lack an understanding of how analgesia and sedative drugs work, and of the techniques available to treat pain and anxiety effectively.

PAIN ASSESSMENT

To treat children's pain effectively, medical staff must become familiar with the pain-assessment tools available, although in some emergency conditions these may be impractical.

Pain is a parameter of clinical need and deserves attention sooner rather than later.

According to a study by Maurice *et al.*, these pain assessment tools include (15):

Observation of behaviour:

A child's behaviour such as crying, holding an injured body part protectively, and verbalisation of pain should be recognised and documented. The parent's knowledge of and comments on the child's usual pain behaviour can also be useful.

Inference:

The type of injury sustained or illness presented can give clues to the degree of pain the child is experiencing. Clinical evaluation and common sense will result in a child receiving prompt and effective analgesia and/or sedation.

Objective pain tools:

Accurate and objective assessment of a child's clinical condition and associated pain allows selection of appropriate analgesia.

Assessment should be performed as soon as possible after a child arrives at the emergency unit, preferably as part of the triage procedure.

The use of pain tools has largely been restricted to research in the past and there is no evidence that their use improves patient outcome.

They take time and patience to explain to the patient and sometimes generate increased and unnecessary paper work (15).

However, establishing the routine use of appropriate pain and anxiety scales is likely to help standardise and improve pain and anxiety management in an emergency department.

Various pain tools have been devised, including visual analogue scales, numerical scales and "Happy face / Sad face" scales (Wong-Baker faces scale) (16, 17).

Children aged over 4 years can usually understand and cooperate with these scales and pain tools.

The ***visual analogue*** scale consists of a straight line with verbal anchors of '*no pain*' and '*very severe pain*' at each end. The child picks a point along the line that describes the degree of pain they feel.

The visual analogue scale can also have ***numerical anchors*** in which the child chooses a number from 1 to 10, with 1 signifying 'no pain' and up to 10 signifying 'unbearable pain'.

The ***Happy face / Sad face*** tool consists of a row of faces ranging from a happy, smiling face to an unhappy, crying face. The child picks the face that best describes his or her pain (18).

For children younger than 4 years who cannot understand the pain tools described above, a physiological measure of their pain can be made, using indicators such as increased pulse rate, raised blood pressure, sweating, pallor and dilated pupils (15).

If the child is too distressed to communicate his or her pain level adequately, the doctor or nurse should make a quantitative estimate of the pain and anxiety level with the aid of the child's parent or carer and also by using clinical skill, observation and common sense.

A simple *pain score system (P = Pain)* can be used on a scale: P0 to P3, where P 0 = '*no pain*', P 1 = '*mild pain*', P 2 = '*moderate pain*' and P 3 = '*severe pain*'.

The pain score and time should be recorded and repeated periodically to assess the efficacy of analgesia given, and the need for further pain relief.

A prompt and accurate diagnosis is essential to treat the underlying cause as soon as possible and thereby also relieve the child's pain and anxiety.

One can also add a simple *anxiety score system (A = Anxiety)*, on a scale: A0 to A3; where A 0 = '*no anxiety*', A 1 = '*mild anxiety*', A 2= '*moderate anxiety*' and A 3= '*severe anxiety*'. (Classification explained in later text).

It is important for the clinician to decide which problem is the most prominent, pain or anxiety, or both, and to make a correct decision on appropriate treatment to gain optimal effect.

PAIN MANAGEMENT

All staff concerned should be adequately trained in pain management.

They should know how to recognise, assess and score pain, anxiety and fear. Young children cannot describe their experience, although they can show their feelings. Older children may mask or deny their feelings or suffering.

Staff must decide when and how to tell a child about a forthcoming procedure, why it is necessary, whether it will be painful or not, and how any pain will be eased.

Probably the most common sedative-analgesic and biggest lie is to tell the child is "almost done" or "only a sharp scratch".

When decisions on care are made, not only parents but also the child, as far as understanding allows, should participate. It is often possible to remove most pain and anxiety by means of a simple, friendly and good explanation.

The child and parents should never be misled.

The treatment environment should be as child-friendly and as peaceful as possible.

Ideally pain relief should be given as soon as possible. Therefore an emergency unit should have very specific protocols in place on how to deal with the injured or ill child with pain.

Protocols should have specific elements, for example:

- Training of medical and nursing staff: Immediate medical review and assessment of children and decisions on appropriate and effective analgesia and/or sedation for specific cases. Triage should be based on the ABC protocols of emergency medicine and on the vital signs of the patient. Incident to analgesia time should be specific;
- Assessment of pain in children by using a specific system or assessment tools in age groups;
- There should be a specific pain management protocol in place: The choice of analgesia and sedation available, or the use of alternative methods, for example, immobilisation, elevation, cooling and reassurance;
- The correct and full use of monitors and resuscitation facilities during the use of stronger forms of analgesia and sedation (for example, ketamine, opioids or benzodiazepines), for procedural sedation;
- The correct and specific use of different medications and methods of administration. An in-depth knowledge and understanding of analgesia and sedation, the compatibility of drugs and specific treatment plans for individual cases;
- Rapid reduction of stress factors in the patient. Setting up a standard check list.

Stress Responses

Illness, injury and tissue-damaging procedures have physiological, hormonal, metabolic and immunological consequences.

'Stress responses' appear to aid survival in the face of adverse circumstances, but they are not always commensurate with the threat and may be harmful.

Stress factors in patients:

- Anxiety and fear of physical harm, bodily injury and death
- Pain
- Tiredness
- Hunger and, or thirst
- Hypothermia
- Fever
- Tubes, catheters, intravenous lines
- Spinal board, cervical collars, splints, masks and bandages
- Poor communication, language
- Monitor noises, alarms, general noise level in the emergency department
- Strange and unfamiliar environment and procedures
- Medical personnel
- Separation from parents
- Fear of loss of control, autonomy and competence
- Uncertainty about expected acceptable behaviour.

REDUCING FEAR AND ANXIETY IN CHILDREN IN THE EMERGENCY UNIT

Many children present to the emergency unit with injuries or illness that will require brief, but often painful, procedures. Despite analgesia, however, fear and anxiety often causes the child to become uncooperative, making treatment difficult.

Children who are very anxious will experience more pain during painful procedures, thereby reducing their ability to comply and increasing the time taken to complete the procedure, as well as increasing the stress levels of everyone involved.

It is important to reduce any adverse psychological effect that an injured child may experience as a result of an emergency unit attendance. Failure to recognise and understand the fear and anxiety of the child, or what is more likely to be acceptable for the child may result in long-lasting negative psychological effects.

Where possible, parents should be encouraged to remain with the child throughout the procedure, because separation from parents is beyond the child's coping mechanism and is viewed as abandonment and punishment by the child.

Despite measures to put both the child and parents at ease, some children are so overwhelmed by fear that they cannot be consoled or convinced that care is needed. In such cases the use of an appropriate anxiolytic or sedative as additional support of sedation can be very useful.

The clinician cannot properly examine or treat a child suffering from extreme anxiety and fear, and it is therefore important to decide on the score of anxiety and treat accordingly.

Anxiety score: A0 – A3:

A1 = Mild anxiety: The child may cry and withdraw initially from physical touch or examination, but will respond positively after a short while as a result of reassurance and/or play from the parent, nurse and/or clinician.

A2 = Moderate anxiety: The patient may cry, scream, kick, fight and refuse any physical touch or examination. After a while of reassurance and distraction the child may calm down, but as soon as the clinician starts to work on him, he will start to scream and withdraw again, which makes examination extremely difficult, stressful, uncomfortable, and time consuming.

A3 = Severe anxiety: A total uncooperative child who will not allow any physical touch or examination.

PAEDIATRIC PRESCRIBING

For various reasons children often react differently from adults to the administration of drugs. The younger and smaller the child, the greater the caution is needed in prescribing and administering medications.

The hepatic and renal immaturity which characterises the first month of life results in very slow clearance and inadequate detoxification of certain drugs, and this is even more marked in pre-term infants.

For many agents the half-life (T1/2) is shorter in children than in adults, due to the greater relative activity of the microsomal enzyme system. The activity declines to normal adult levels after puberty.

The body compartments in neonates and infants have a different size compared to those in children and adults. A larger apparent volume of distribution (Vd) is found for most of the agents used in infants and young children.

Protein binding for some agents appears to be diminished in infants and neonates, compared to binding in adults.

Competition by agents for albumin-binding sites is also a danger as the unbinding of bilirubin may result in brain damage (kernicterus).

Problem agents in some analgesia and drugs sometimes used for anxiety or sedation include:

Phenotiazine antiemetics – e.g. prochlorperazine is likely to produce extrapyramidal effects, even at low doses.

Salicylates – may have a toxic effect in young children, especially if they are dehydrated and acidotic, and aspirin has been associated with Reye's syndrome.

Antihistamines – may produce paradoxical excitation, even at low dosage.

Dose calculation

- It is most important never to guess or roughly estimate dosage.
- Doses should be adjusted according to body weight; the upper limit is reached when the appropriate adult dose is reached.
- Since many physical phenomena are more closely related to body surface than to body weight, body surface estimates are more accurate for calculations of paediatric doses. This may be particularly relevant for drugs in which exact dosage is critical.
- Catzel's formula, based on surface area, may be useful when the paediatric dose of a drug (mg/kg) or the child's weight is not known (see Table 1).
- Dosages should, however, always be individualised for medication, patient and disease treated.
- Reduced doses are indicated in renal disease, liver disease, the dehydrated child and obese children.
- Special caution is needed in the severely malnourished child.

Paediatric doses according to Catzel's formula (Table 1) (19):

Table 1:

Age:	Percentage of adult dose:
Birth	10
2 months	15
4 months	20
12 months	25
18 months	30
3 years	33 ½
5 years	40
7 years	50
10 years	60
11 years	70
12 years	75
14 years	80
16 years	90
20 years	100

Routes of administration

Oral:
This is usually the method of choice unless there are other specific indications. Liquid preparations are most suitable for children; however, many contain sucrose which encourages dental decay. Sugar-free tablets and liquid preparations should be used whenever possible, when prolonged therapy is needed.

- When a prescription for a liquid oral preparation is written and the dose ordered is smaller than 5 ml, generally the preparation should be diluted with a suitable vehicle so that the required dose is contained in 5 ml, or special dosing measures should be used.
- It is best not to prescribe teaspoon doses, as teaspoons vary greatly in size; a standard 5 ml measure should be used.
- Medicines should not be added to the contents of infants' feeding bottles. The ingested dose may be reduced if the child does not drink all of the contents of the bottle. Also, the medication may interact with the milk or other contents of the bottle.

Rectal:
Absorption from suppositories is erratic, with resultant under-dosage or toxicity. This route is usually not recommended and is seldom used.

Topical:
Drugs may be absorbed through the skin in significant quantities, particularly when applied to skin which has been burned or excoriated (e.g. nappy rash). Examples are corticosteroids, hexachlorophene and borates. Topical antibiotics are best avoided because of the dangers of sensitisation.

Parenteral:
Preparations may be given by intra-dermal, hypodermic, intramuscular or intravenous injection.

- The intramuscular route is not suitable for paediatric analgesia in the emergency department: They are painful, absorption is unpredictable and onset of action is slow.
- If essential, however, the outer aspect of the thigh is the preferred site for intramuscular injection in young infants. Injections in the buttock carry a special danger of sciatic nerve injury. If the buttock is used, the injection must be given in the outer part of the outer upper quadrant.
- The syringe should be prepared out of the child's sight to minimise the fear-provoking experience.
- When an intramuscular or intravenous injection is given to a child, a second person should be present to hold the patient to ensure safe administration.
- The administrator should always be prepared for the development of anaphylactic or other untoward reactions.
- A sterile technique is essential.

- If alcohol is used for cleaning the skin, it should be allowed to dry before inserting the needle to prevent a possible burning pain.
- Intramuscular injections should be given deeply, so as to prevent abscess formation, but not so deeply as to be near bone periosteum.
- If repeated injections are required, a different injection site should be used each time.
- The intravenous route provides the most reliable and controllable method for relief of pain, despite the need for cannula insertion. Intravenous administration allows for careful titration of the analgesic agent against response to provide effective pain relief, minimise toxic effects, and allow top-up doses as required.

Intranasal:

Drugs administered intranasally are more reliably absorbed than those given orally. Nasal administration also obviates such problems as hepatic metabolism or local gastric effects.

The large surface area, uniform temperature, high permeability and extensive vascular area of the nasal mucosa and its ease of access facilitate rapid systemic absorption of intranasal administered drugs, such as opioids.

The rate and extent of absorption, and plasma concentrations, are comparable to intravenous drug administration.

Good nasal bioavailability can be reached with drugs with molecular weights as high as 6000 Daltons.

The mucosal atomization device (MAD) is currently the best nasal delivery system available, due to good mucosal distribution of the drug.

Example: The bioavailability of midazolam with an MAD is 83%, compared with that of a dropper, which is 50%.

Furthermore, intranasal delivery represents a "needle free" and patient-friendly route for various drugs.

Limiting factors of intranasal use are blocked, infected, traumatised, painful or bleeding nose.

Prescription writing

- Prescriptions should state the age and bodyweight of the child, the dose, frequency and route of administration, and the recommended duration of treatment.
- It is particularly important to state the strengths of tablets and capsules, and the concentration per volume of oral liquids.
- It is also important to note the batch numbers and expiry date of each drug.
- Allergies, sensitivity to specific medication and use of chronic medication, should be documented.

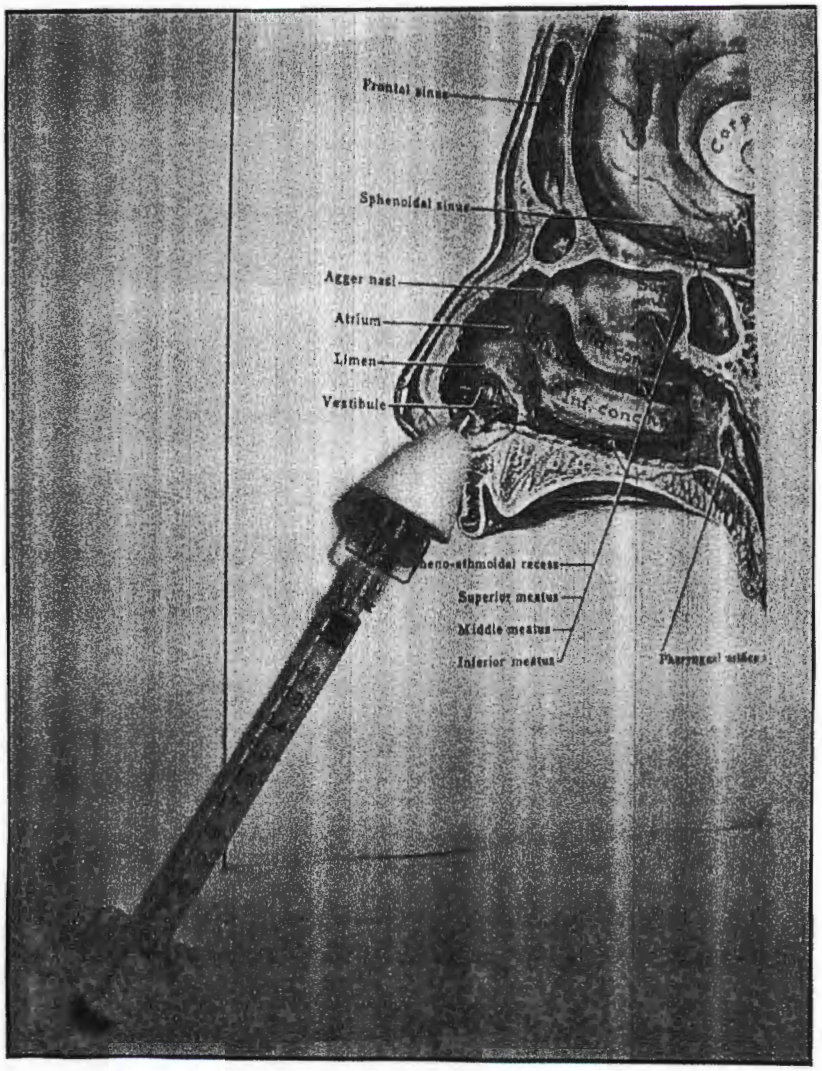
USING THE MUCOSAL ATOMIZATION DEVICE (MAD):

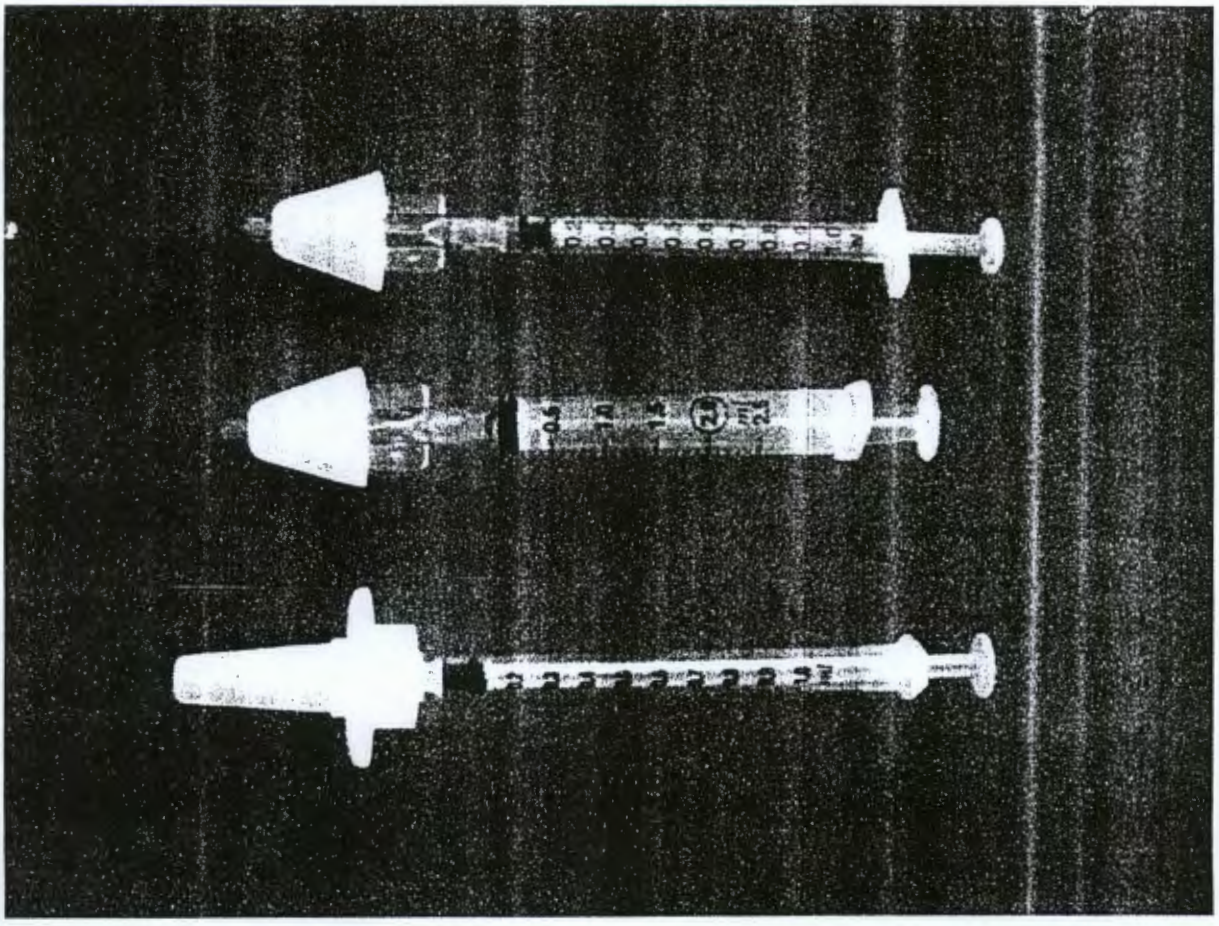
- 1st: Draw up a practice solution of saline or water
- Be aware of the volume and what dose will be equal
- 2nd: Expel air from syringe
- 3rd: Attach the MAD device via luer lock.
- 4th: Briskly compress the syringe plunger:
  - Brisk brief compression results in controlled atomization.
  - Gently pushing the plunger will not result in atomization.
  - With practice you can give an exact volume down to 1/10 of a millilitre.

Inspect nostrils for mucus, blood or other problems, which might inhibit absorption.

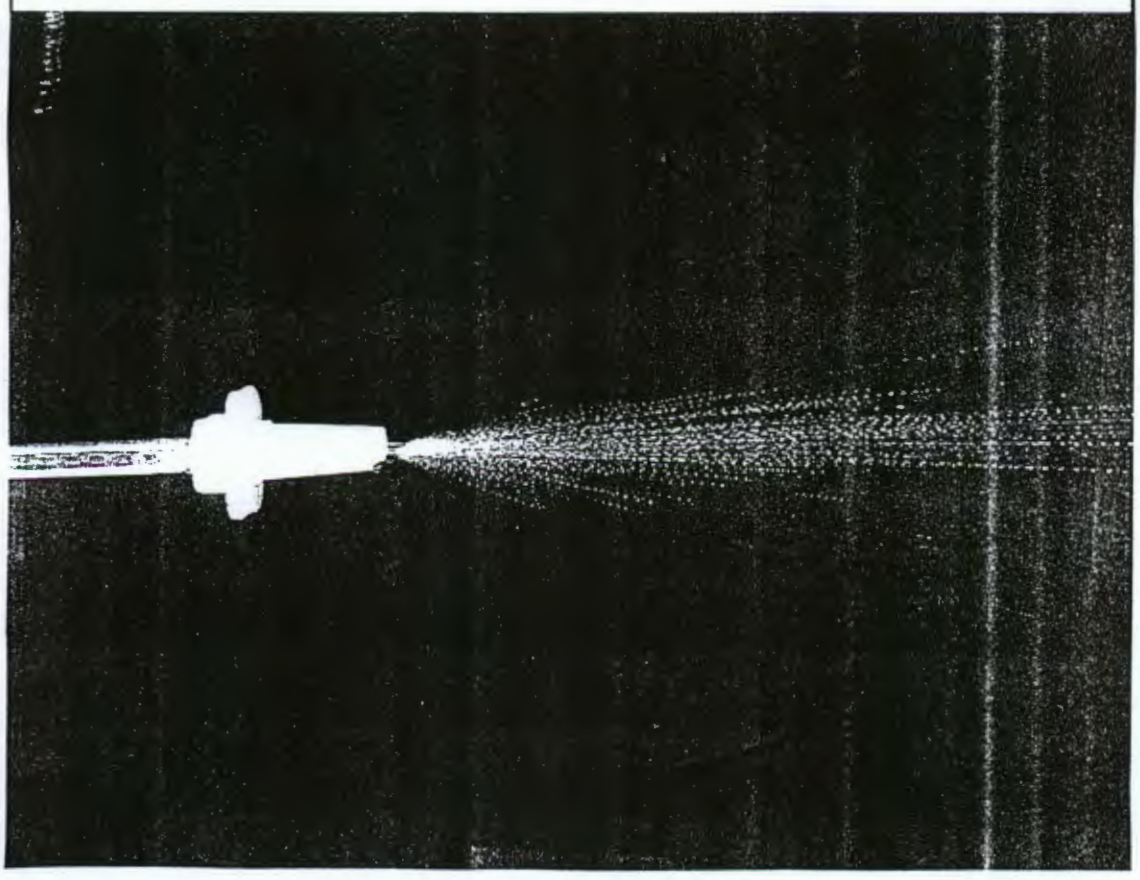
To administer the medication:

1. Assure correct medication, dosage, concentration and volume to be used.
2. Patient should be in the supine position.
3. Angle the mucosal atomization device (MAD) towards the atrium of the nose.
4. Assure that the tip of the MAD is well placed inside the nostril.
5. Briskly compress the syringe to administer the full dose of the medication.





The following picture demonstrates a 1ml syringe being used with an atomizer.



ENG

INDICATIONS FOR USE: for atomizing topical solutions across the naso and oropharyngeal mucous membranes.

INSTRUCTIONS FOR USE:

1. Disconnect MAD® from included syringe (MAD100 only).
2. Fill syringe with desired volume of solution and eliminate remaining air.
3. Connect the MAD® to the syringe.
4. Place the MAD® tip in the nostril or oropharyngeal cavity.
5. Compress the syringe plunger to spray atomized solution into the nasal or oropharyngeal cavity.
6. Re-use the MAD® on the same patient as needed, then discard.

EU Authorised Representative:

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NON-PHARMACOLOGICAL MEASURES TO RELIEVE PAIN AND ANXIETY

Certain non-pharmacological measures that, when used in conjunction with drug therapies, act cumulatively to provide analgesia and anxiolysis to the child in the emergency unit (20).

Medical personnel involved with child care should know these measures and use them appropriately.

The emergency room environment:
Much can be done to alleviate stressors by *creating a reassuring environment* aimed at meeting children's needs.

- Children should be seen in a designated paediatric area, which is audio-visually separate from the areas in which adults are treated, but should be visible from the nurses' station.
- The designated area should be 'child-friendly' and safe, with colourful wall murals, toys, story books, colouring books and crayons, music and television equipment, and play material available to provide distraction for children.
- Toys and equipment should be regularly checked for specific safety standards and must be regularly cleaned, washed or replaced.
- Potentially frightening medical equipment and instruments should be hidden from sight or camouflaged where possible.
- At least one parent should be encouraged to stay with the child to reassure them in the emergency department. Parents should not be bullied into staying with the child, however, if they are anxious or squeamish.
- If possible, seriously injured or sick children should be allocated a dedicated liaison nurse, who stays with the patient throughout the planned procedures. She can explain what is happening and reassures the child, but plays little part in the physical care of the child. This allows the child to form a bond with one person in the unfamiliar environment.

Physiological methods of pain relief:

Various techniques are available including distraction, guided imagery, relaxation, hypnosis and cognitive behavioural therapy.

Before a procedure, prepare age-appropriate information about the procedure, including an explanation of what the child is likely to feel. This should increase the understanding of children and parents, and reduce stress and anxiety (20).

The child should be permitted to make an age-appropriate choice in treatment method to give a sense of control after a procedure has been explained, that is, as far as essential treatment methods allows.

1. **Distraction:**

This is the most frequently used behavioural therapy and puts the pain at the periphery of awareness. It is especially useful in relatively short painful procedures.

Distraction strategies must be appropriate for the child's age:

Infants (up to 1 year): Music, cuddling, rocking and using a soothing, quiet tone of voice.

Preschool, (1-5 years): Allow the child to have a sense of control by 'helping', for example to open a dressing pack or bandage. Singing, picture books, puppets and stories can be very useful.

School age (6-12 years): Use creative imaginary figures/toys or playing with a kaleidoscope or 3D viewer.

Adolescent: Use a cassette or CD player with their favourite music and encourage them to tap out or sing with it.

2. **Guided imagery:**

This involves the use of imagination to modify the response to pain.

A child can imagine himself in his favourite place or with his favourite character. It allows the child to have some degree of control of the situation.

3. **Relaxation:**

This reduces autonomic activity and, as a patient cannot be relaxed and anxious simultaneously, pain tolerance should be increased if the patient is relaxed.

4. **Hypnosis:**

This has also been found to be useful in the management of patients with both acute and chronic pain and has been defined as focused attention, an altered state of consciousness or a trance, often accompanied by relaxation that decreases the child's perception of pain (21).

5. **Cognitive behaviour therapy:**

This entails desensitising the child to anxiety-provoking stimuli and rewarding the child when he or she exhibits positive coping behaviour.

To be effective, this therapy requires time and planning and thus its use is often limited in the emergency setting.

Coetaneous stimulation methods of pain relief:

These would include hot or cold applications, superficial massage, acupuncture and trans-coetaneous electrical nerve stimulation (*TENS*).

- The use of acupuncture may be limited in the emergency department as children are often afraid of needles.
- *TENS* delivers controlled low-voltage electricity to the body via electrodes and has been found to be useful in the management of localised pain.
- Cold therapy provides rapid relief from symptoms by reducing swelling, relieving pain and alleviating inflammation. Cold application reduces bruising and the throbbing sensation often associated with injury. Ideal for use are, for example, Mobil-Ice compression packs.

Physical methods of pain relief:

These include the use of splints, elevation, cooling, and different types of dressings.

- Splinting provides immobilisation. Elevation reduces swelling of an affected limb and thus relief of pain.
- Dressings can relieve both pain and anxiety. An example of this would be the application of a burn dressing, which will sooth the affected area and also has the psychological benefit of covering the wound, the sight of which may be distressing to both child and parent.

PHARMACOLOGICAL AGENTS AVAILABLE FOR LOCAL AND SYSTEMIC ADMINISTRATION IN THE MANAGEMENT OF CHILDREN'S ANXIETY AND PAIN

ANXIOLYTIC AND SEDATIVE AGENTS:

Sometimes it may be necessary to provide sedation without administering analgesia.

The indication for this would be on the basis of anxiety, fear and stress-related traumatic experiences.

Procedural sedation of children in the emergency unit

The terminology surrounding sedation in the emergency environment may be confusing and inappropriate. '*Conscious sedation*', '*Monitored Anaesthetic Care*', and '*Dissociate Anaesthesia*' are all anaesthetic terms. A more appropriate term '*Procedural Sedation*', has been recommended by the American College of Emergency Physicians for the use in the emergency environment.

The definition of '*Conscious sedation*' is generally accepted and may be used to describe '*Procedural sedation*'; it refers to a state of pharmacologically induced depression of the central nervous system, where the airway is maintained, verbal contact (if appropriate) can be maintained with the patient and the patient is roused by gentle physical stimulation (22). No interventions are required to maintain a patent

airway, and spontaneous ventilation is adequate. Cardiovascular function is maintained. If left undisturbed, the patient may simply fall asleep.

The drugs most commonly used to induce such a state by instilling variable levels of sedation include midazolam, diazepam, nitrous oxide, chloral hydrate and ketamine.

Benzodiazepines:

There are three drugs in this group that should be well understood:

- Short acting: Midazolam (*Dormicum*).
- Intermediate acting: Lorazepam (*Ativan*).
- Long acting: Diazepam (*Valium*).

These drugs have *no analgesic effect*, so additional or added analgesia may sometimes be required for pain relief.

Midazolam (*Dormicum*):

Midazolam is a short-acting imidazo-benzodiazepine derivate with hypnotic, anxiolytic, anti-convulsion, sedative, muscle-relaxant and amnesic properties. It has a rapid onset and may be used for procedural sedation, pre-operative sedation and induction of general anaesthesia.

Benzodiazepines facilitate neurotransmission at gamma aminobutyric acid (GABA) synapses. GABA is a potent neurotransmitter and it is thought that approximately one third of all synapses within the brain use it as their transmitter, therefore depressing excitable neurones.

The central nervous system effects of midazolam follow the serum levels closely, thus the serum concentration is relevant to the level of sedation required (23). The sedated child becomes compliant, but does not lose consciousness (when recommended doses are used) (24).

Various studies have been undertaken to examine the oral dose required to achieve an adequate serum level to produce the desired sedative effect without undesirable side effects.

It is found that 0,45 mg/kg – 0,5 mg/kg produce safe and effective sedation (23), (25).

Midazolam synopsis: (24)

Table 2		
Administration	Oral Sublingual Nasal Intravenous Intramuscular Rectal	0.5 mg/kg (0.25-0.75mg/kg) 0.25-0.3 mg/kg 0.2-0.4 mg/kg 0.05-0.15 mg/kg (titrate to effect) 0.05-0.15 mg/kg (painful and not recommended) 0.5 mg/kg
Time to peak effect	Oral	10-30 min

	Sublingual Nasal Intravenous Rectal	10-15 min 10-15 min 3-5 min 10-20 min
Duration of action	Intravenous Oral and rectal Nasal	20-60 min (dose related) 60 min (dose related) 20-40 min
Adverse reactions	Respiratory depression Ataxia, diplopia Paradoxical excitation Hypotension Nasal burning, bitter after-taste (for 2 days)	Dose related; common with opiates, reduce dose by 25 – 30% In rapid administration, especially in hypovolaemia, neonates If used intranasal
Drug interactions	Opiates, barbiturates CNS depressants Erythromycin Calcium channel blockers Protease inhibitors	Respiratory depression; apnoea; prolonged sedation Prolongs recovery Delay metabolism (inhibit cytochrome p450) Delay metabolism (inhibit cytochrome p450) Inhibit cytochrome p450 enzyme; titrate slowly in HIV patients on antiretroviral drugs.
Special concerns	Decrease dose in high-risk debilitated patients	
Antagonist	Flumazenil	10micro/kg i.v.i given slowly over 15 seconds, repeat every 2 – 3min – up to max 1mg/kg

When used in combination with opiates, midazolam can produce a 'super-additive effect' (i.e. the total effect of the combination is greater than the sum of the anticipated effect of the individual drugs).

Midazolam should therefore be used with caution in compromised children or those with upper airway obstruction (tonsil hypertrophy, for example).

Although many children initially act disinhibitedly after small doses, some may have a true paradoxical response and become more agitated with higher doses. In such an event it is wiser to switch to an alternative sedative, since increasing the dose may lead to severe agitation followed by unconsciousness and respiratory compromise. Diplopia is the most distressing effect for the child (24).

The **oral route** has become increasingly popular and is well tolerated. A cherry-flavoured syrup is available, but the intravenous preparation can be mixed with more palatable juices (apple, orange, grape) or drinks (Coke, Fanta, lemonade) or even analgesics (Panado, Stopayne, Ponstan) in order to disguise the bitter after-taste (24).

Rectal administration is also usually well tolerated in children who have not been toilet trained (< 1yr), but absorption may be irregular.

In some United Kingdom A&E departments **intranasal** midazolam is used as the preferred method of administration of the drug to treat children with *status epilepticus*. This method is mostly used where IV access is not immediately obtainable. (*See attachment: Royal Lancaster Infirmary Protocol*).

The effects of midazolam can be reversed by flumazenil.

The use of intranasal midazolam to treat persistent seizure activity:

Protocol:

-The administration of the drug may be performed only by well-trained and experienced medical staff, who will be able to recognise any adverse effects of the drug and can effectively deal with it.

- Always and continuously assess ABCs: **A**irway, **B**reathing and **C**irculation.
- Double check the dosage, concentration and volume to be used.
- Ensure the correct environment and equipment, and obtain written consent.

Use age/weight-based table to determine proper volume and dose of intranasal midazolam for atomization:

Patient age (Years)	**Weight (Kg)**	**Intranasal volume (ml)* Concentration: 5mg/ml**	**Dose (mg): 0,2 mg/kg**
Neonate	3 kg	0,3 ml (Use 1 ml syringe)	0,6 mg
< 1 yr	6 kg	0,4 ml	1,2 mg
1 yr	10 kg	0,5 ml	2,0 mg
2 yr	14 kg	0,7 ml	2,8 mg
3 yr	16 kg	0,8 ml	3,2 mg
4 yr	18 kg	0,9 ml	3,6 mg
5 yr	20 kg	1,0 ml	4,0 mg
6 yr	22 kg	1,0 ml	4,4 mg
7 yr	24 kg	1,1 ml (Use 2 ml syringe)	4,8 mg
8 yr	26 kg	1,2 ml	5,2 mg
9 yr	28 kg	1,3 ml	5,6 mg
10 yr	30 kg	1,4 ml	6.0 mg
11 yr	32 kg	1,4 ml	6,4 mg
12 yr	34 kg	1,5 ml	6,8 mg
Small teenager	40 kg	1,8 ml	8,0 mg

- * This volume is based on the calculated dose plus 0,12 ml MAD dead space and rounded off to the next highest 0,1 ml.

- **Calculation formula**:

  Assess weight in kg. **[(Age + 4) x 2 = Wt in kg]**

  Calculate the appropriate dose of midazolam, using the following formula:

  Children: Total wt (kg) x 0,2 mg = Total dose of midazolam. (Maximum dose: 10 mg).

  Total volume in millilitres of midazolam (5mg/ml concentration) = Total mg dose, divided by 5 mg/ml + 0,12 ml for dead space of MAD device.

  [Information supplied by Perry Hill International Pharmaceutical Company, with compliments]

  How to administer the intranasal medication:

- Inspect nostrils for mucous, blood, or other problems, which might inhibit absorption.
- Load 1-ml or 2-ml syringe (depending on volume needed) with appropriate millilitre volume of midazolam (use only 5 mg/ml concentration) and attach to the MAD nasal atomizer.
- Place atomizer within the anterior antrum of the nostril and briskly compress the syringe to administer ½ of the volume into each nostril, so that all the medication is administered.
- Supply oxygen if and as needed and ensure ABCs.

A reduced dose / volume of intranasal midazolam can be used *to treat severe anxiety* during *procedural sedation*.

More research, however, is necessary to determine the exact dose, volume, efficacy and outcome.

Intranasal pre-medication of infants and children with midazolam has been studied by Karl HW as to efficacy and outcome (26).

It has been recommended as an intranasally administered pre-medicate; however, the potential for life-threatening complications has limited its use.

It has been associated with significant respiratory depression and oxyhaemoglobin desaturation (26).

Intranasally administered midazolam has a pungent odour, tastes bad and can cause topical irritation from its benzyl alcohol preservative.

Lorazepam (*Ativan*):

This is an intermediate-acting benzodiazepine, which has no metabolites.

It is more potent than diazepam. It is useful in acute anxiety states.

Pharmacokinetics:

- Well absorbed orally with about 90% bioavailability;
- Vd = 1.3 L/kg;
- T1/2 = 10-20 hours; protein binding 85%;
- No active metabolites formed; after glucuronide conjugation in the liver, it is excreted renally.

The intravenous dose for children is 0.1 mg/kg; however, if administered after an opioid has been given, this dose should be halved.

Diazepam (*Valium*):

This is a long-acting benzodiazepine derivate.

It has active metabolites and has a sclerosing effect on veins.

Pharmacokinetics:

- Oral absorption and bioavailability is complete. Tmax = 0.5 – 2 hours;
- Vd = 1.1 L/kg; protein binding, 98%;
- T1/2 = 20 – 70 hours; desmethyldiazepam, 2-5 days;
- Extensively metabolised in the liver where active metabolites (desmethyldiazepam, temazepam, oxazepam) are formed and conjugated before slow renal excretion.

Indications: Used pre-operatively and during minor procedures, such as endoscopy, to relieve anxiety and to produce sedation, muscle relaxation and anterograde amnesia.

Dosage: *Oral*: 0.1-1.0 mg/kg/day in divided doses every 3-4 hours, largely dependent upon individual response and concomitant medication.

Intravenous: 0.1 mg/kg, administered slowly over 3-5 minutes;
Intramuscular injection should be avoided since absorption is slow and erratic;
Rectal administration: 0.5 mg/kg. IV solutions can be given rectally in same doses as for oral, when IV route is inaccessible.

[*For status epilepticus*: Children up to 3 years: 5 mg; over 3 years: 10 mg. A special rectal applicator with Diazepam 5mg per applicator is also available for easy, quick and safe administration.]

Side-effects: Respiratory depression, apnoea, hypotension, bradycardia and cardiac arrest.

The Benzodiazepine anagonist: Flumazenil (*Anexate*).

Flumazenil binds competitively to benzodiazepine receptors; in this way it reverses the central sedative effects of the benzodiazepines.

The *adult dose* IV, is 0.2 mg over 15 seconds (Ampule: 0.1 mg/mL); if a response is not achieved within 60 seconds, 0,1 mg may be given at 60-second intervals up to a maximum total dose of 1 mg.

If there is no response, aetiology should be questioned.

Other sedative drugs:

a. The Barbiturates: Phenobarbitone (*Gardenal*) and Phenytoin (*Epanutin*).

Phenobarb and Phenytoin are regarded as 'second-line' drugs for *status epilepticus* in patients who have not responded to a second dose of a Benzodiazepine.

They are also used prophylactically in head-injury patients who are at high risk of fitting.

Details concerning these drugs is considered to be beyond the scope of this paper.

b. Haloperidol (Serenace)

Details concerning this drug is considered to be beyond the scope of this article.

c. Dexmedetomidine (*Precedex*)

This is a new drug to be released in South Africa soon.

It has both anxiolytic and analgesic properties, which makes it a potentially useful drug. It does not cause respiratory depression, patients maintain cognition and are easily rousable.

Nitrous oxide (*Entonox*):

Nitrous oxide is inhaled as a mixture with oxygen usually at 50/50 ratio causing analgesia, amnesia and a dissociative state.

Pharmacokinetics:

- Solubility in blood is low, and a change in the concentration inhaled results in a rapid change in anaesthetic and analgesic effects;
- MAC = > 100%;
- Minimally metabolised; excreted unchanged by exhalation. Small amounts may be eliminated by the skin.

It has a good analgesic effect within 3-4 minutes, wearing off approximately 5 minutes after inhalation of the gas has stopped. Self-administration by patients is facilitated by way of a 'demand valve', which is triggered by the patient forcefully inhaling.

Nitrous oxide in a 70% mixture with 30% oxygen has shown to be more effective than EMLA application in providing analgesia for paediatric venous cannulation (27).

Administration is painless and children as young as 3-4 years can control administration themselves. The use of a mouthpiece to inhale the *Entonox* can encourage children who are frightened of using a face mask to inhale the gas.

Nitrous oxide must be delivered by a failsafe system which shuts off if oxygen flow is obstructed. A precaution to be borne in mind is that at -6°C, the nitrous oxide and oxygen 'separate'; as a result an anoxic mixture of gas may be delivered to the patient.

It is valuable for use in short procedures such as the application or changing of dressings, splint application, draining an abscess, removing a splinter, or cannula insertion.

It is generally an under-used and under-rated method of analgesia in children in the emergency environment.

Nitrous oxide has a *disadvantage* that it is absorbed into and causes expansion of gas filled spaces, so it is *contraindicated* when a pneumothorax, bowel obstruction or head injury (raises intracranial pressure) is suspected (28).

Chloral hydrate:

Research during a nine-month retrospective study (29) has shown that chloral hydrate failed to sedate 23% of children on whom the drug was used.

It induces post-administration vomiting in many patients and also causes prolonged sedation.

This drug is not commercially available in South Africa. According to the SA Drug Information Centre, it can only be made up for special cases in certain hospitals.

Ketamine:

The use of ketamine for procedural sedation:

An article was recently published in the *Emergency Medical Journal* (UK) by McGlone *et al.* from the Royal Lancaster Infirmary, Lancaster, United Kingdom, on 501 consecutive cases that received intramuscular ketamine, 2.0 or 2.5 mg/kg, as procedural sedation, for the treatment of minor painful procedures in children in the emergency department.

The study was done to demonstrate the safety and acceptability of ketamine and to determine if the incidence of adverse effects is related to dose or other variables (30).

This report is the largest case series published on the use ketamine for procedural sedation of children in the United Kingdom to date.

The method of the study was a prospective data collection and analysis using Stats-direct and SPSS software (UK).

501 consecutive cases were collected from August 1996 to April 2002. A total of 310 children received 2.0 mg/kg and 191 received 2.5 mg/kg. 26 Children received a second dose. In 7 cases oxygen saturation fell below 93%; 3 of these fell below 90%. There was 1 case of laryngospasm. 8 cases received airway suctioning, 5 of these were lip or mouth wounds. 17% vomited in recovery or at home, for which one child required admission. Muscle hypertonicity was observed in 6.8%, disturbed sleep or nightmares in 2%. The median time of discharge was 85 minutes.

97% of parents reported the experience "the same as" or "better than" expected.

No children suffered any lasting or troublesome complications.

The conclusion of the study was that 2.0-2.5 mg/kg intramuscular ketamine sedation is a safe and acceptable technique, when used within a defined protocol, by trained and experienced staff, with appropriate monitoring and correct equipment available. (30).

The use of lower-dose ketamine (2 mg/kg), warrants further study in view of potentially fewer airway complications and quicker discharge times.

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist with opiod receptor activity. It effectively produces analgesia, anaesthesia and a dissociative state (28). Controlled studies and case reports on ketamine demonstrate efficacy in neuropathic and nociceptive pain. Because ketamine is a phencyclidine analogue, it has some of the adverse psychological effects found with hallucinogen, especially in adults.

Pharmacokinetics:

- Ketamine is rapidly absorbed from IM injection sites and distributed to perfused tissues, including the CSF;
- Vd = 3-5 L/kg; protein binding, 20-50 %;
- T1/2 = about 80 minutes;
- Anaesthesia is produced within 30-60 seconds (IV) and 12-25 minutes (IM);
- Analgesia will persist longer than anaesthesia;
- 90% is excreted renally after extensive metabolism in the liver. Hepatic dysfunction may elevate plasma levels and delay elimination. Norketamine, a major metabolite, has about one sixth the activity of the parent ketamine.

Ketamine can be a very useful drug in the emergency department, especially when you need to keep a child calm and relatively motionless to perform short but painful procedures, for example, suturing of lacerations.

By using ketamine in the correct environment and by appropriately trained personnel, more minor procedures can be dealt with in the emergency unit, thus being cost effective and also saving valuable theatre and other medical personnel time.

A specific protocol should exist to ensure safe use of the drug:

- The procedure must be undertaken by a well-trained senior or middle-grade doctors only, and the doctor must always be assisted by a trained emergency department nurse.
- Set up and follow a procedure and equipment check list to ensure correct actions by all involved.
- The child and parent must be fully informed about the procedure and the specific use of ketamine in a manner appropriate to the child's age and the child's and parent's understanding.
- Ensure that a consent form is completed and signed.
- Ensure that an anaesthetic cream (EMLA) is applied over the injection site to the child's upper leg, 45 min before the procedure.
- Ensure the patient is nil per mouth for at least 3 hours prior to the procedure.
- Ensure that a fully equipped resuscitation trolley, suction apparatus, oxygen supply, blood pressure and pulse monitor and pulse oximetry are available in theatre.
- Check ketamine expiry date on the vial and make available an atropine 0.6 mg ampule and a 1 ml syringe plus orange needle.
- Document the child's weight and double check and document the doses of ketamine and atropine that should be administered: Ketamine 2.5 mg/kg [100 mg/ml vial] and atropine 0.01 mg/kg [0.6 mg/ml or 600 microgr/ml ampule].
- Prepare all instruments and equipment to be used for the procedure before administering the injection.
- Ensure that the theatre is quiet and check time.
- Document specific times: Injection administration, start and finish of procedure. Also document any adverse effects.
- Ensure parents are given a vomit bowl after the procedure and when discharged.
- Observe the child in the unit until 100% awake (60-90 minutes) and ensure no adverse effects before discharge. Advise the parent that the child should not walk unaided for at least 2 hours after the procedure.

Contraindications for the use of ketamine:

- When a planned procedure is complicated by a more serious underlying injury, for example, closed fractures or a head injury with loss of consciousness.
- Raised intra-cranial pressure.
- A current respiratory tract infection or active asthma.
- Patients with severe cognitive and/or motor delay or severe behavioural problems.
- Hypertension, glaucoma or porphyria.
- Prior adverse reaction to ketamine

- Full meal within 3 hours prior to procedure.

Adverse effects of ketamine: (24).

- Increased salivation, secretions (<10%) (reduced by atropine use).
- Laryngospasm, coughing (especially with URTI and infants < 3 months of age).
- Respiratory depression is rare. (Increased risk with bolus administration, neonates and premature babies).
- Hypertension, tachycardia.
- Emergence phenomena, hallucinations.
- Rigidity or hypotonicity.
- Ataxia.
- Random movements of head and extremities (<5%).
- Nystagmus.
- Vomiting (10%).
- Increases intra-ocular pressure.
- Elevates intracranial pressure and cerebral metabolic rate.
- May loose protective reflexes: Increase risk of aspiration (full stomach).

Drug interactions:

- Benzodiazepines, opiates.
- Drugs metabolised by the liver.

During procedural sedation:

Start the theatre clock upon administration of the ketamine and atropine injection.

Within 5 minutes the drug will take effect. The child's eyes may become glazed.

If the desired degree of sedation is not achieved, a second lower dose of ketamine can be given.

The child will not be aware of his/her surroundings and will not recognise parents. The drug effect will last approximately 30 minutes.

Ensure that a local anaesthetic is also used in the laceration area when a wound is to be sutured, or foreign body to be removed, as the ketamine alone will not give sufficient analgesic effect.

Ensure that the monitors and oximeter are correctly placed on the patient and check vital signs throughout the procedure.

Oxygen and suction should be immediately available.

An emergency trolley with all appropriate emergency drugs and intubation equipment should be immediately available, should the need arise to use any of it.

Always maintain a safe environment for the whole period, until the child is fully awake.

Provide the child with a vomit bowl, should the need arise to use it.

Document the time, drugs and dosages used, procedure done and any adverse effects.

Dosage of intramuscular ketamine and atropine (Table 3)

(Dosage chart as used in the A&E department of the Royal Lancaster Infirmary, Lancaster, United Kingdom, with compliments).

Table 3:

ATROPINE				KETAMINE		
Weight in kg	**Dose**	**600 microgram/ml**	**500 microgram/ml**	**Weight in kg**	**Dose 2.5mg/kg**	**Dose 2mg/kg**
	mg	ml	ml			
10	0.10	0.16	0.2	**10**	25	20
11	0.11	0.18	0.22	**11**	27.5	22
12	0.12	0.2	0.24	**12**	30	24
13	0.13	0.21	0.26	**13**	32.5	26
14	0.14	0.23	0.28	**14**	35	28
15	0.15	0.25	0.30	**15**	37.5	30
16	0.16	0.26	0.32	**16**	40	32
17	0.17	0.28	0.34	**17**	42.5	34
18	0.18	0.30	0.36	**18**	45	36
19	0.19	0.31	0.38	**19**	47.5	38
20	0.20	0.33	0.40	**20**	50	40
21	0.21	0.35	0.42	**21**	52.5	42
22	0.22	0.36	0.44	**22**	55	44
23	0.23	0.38	0.46	**23**	57.5	46
24	0.24	0.4	0.48	**24**	60	48
25	0.25	0.41	0.50	**25**	62.5	50
26	0.26	0.43	0.52	**26**	65	52
27	0.27	0.45	0.54	**27**	67.5	54
28	0.28	0.46	0.56	**28**	70	56
29	0.29	0.48	0.58	**29**	72.5	58
30	0.30	0.5	0.60	**30**	75	60

An anti-sialogogue (Atropine) is often used to help reduce the incidence of hypersalivation seen with the use of ketamine, and many authors recommend its use.

In the Lancaster study an incidence of 12% of hypersalivation was reported, but in another study by Green *et al.* an incidence of 1.7% was reported.

There seems to be little difference in clinical effect between the 2 doses of ketamine used, although the 2.0 mg/kg may offer a lower incidence of airway problems and salivation (30).

Ketamine has been described as the ideal agent for paediatric sedation in emergency departments in the UK, USA, Australia, Europe, Japan, Mexico, the Middle East and Singapore, using the technique regularly.

However, despite the enthusiasm of many authors and practitioners, ketamine may not be the ideal agent.

Emergence reactions, sub-anaesthetic conditions and airway problems do occur and it is generally recommended that only physicians skilled in airway management and resuscitation are involved in the care of sedated children (31).

In a literature search study done by Howes MC, he describes several adverse effects: Apnoea: "extremely rare", laryngospasma: very rare (0.017% - where intubation was required), emergence phenomena: 0 – 10%; less common with IM administration and rarely upsetting for children under 10 years old, vomiting: 8.5%, other reactions: nystagmus, ataxia, myoclonus, random limb movements, opisthotonus and flushing. Doses investigated by Howes, was in a range 0.5 – 16 mg/kg.

The modern and acceptable trend by emergency department practitioners is to use doses: 2 – 5 mg/kg IM, or 0.5 – 2 mg/kg IV. (31).

In a recent study done by Treston at the Royal Darwin Hospital in Australia to address the relationship between pre-procedure fasting time and intra-procedure vomiting in children aged 1 – 12 years undergoing procedural sedation with intravenous ketamine in the emergency department, it was found that prolonged pre-procedure fasting time did not reduce the incidence of post-procedure vomiting.

Fasting times were accurately recorded in 257 consecutive cases.

Overall rate of post-procedure vomiting was 13.9%. No vomiting occurred during any procedures. It was found that there was a trend towards increased vomiting with increased fasting time.

It was found that those children whocfasted 3 hours or more pre-procedure had a vomiting rate of 15.8% and those who fasted less than 1 hour had a rate of only 6.6%.

Increase of vomiting was associated with increase in age.

No clinical evidence of aspiration pneumonitis occurred (32).

These results should be viewed in comparison to the expected rate of post-general anaesthesia vomiting for paediatric ambulatory, or day surgery.

Various rates of post-general anaesthesia vomiting have been recorded, from 4% - 50%, although it is noted that the reference study with low rate of post-general

anaesthesia vomiting excluded vomiting in the recovery room (occurring in 15%) as a complication.

Two large studies involving paediatric anaesthesia were noted to report rates of postoperative vomiting of 35% of 989 day-surgery patients (33) and 30% of 29 220 patients (34).

The use of intranasal ketamine as an analgesic:

Different studies showed promising results by using intranasal ketamine as an analgesic agent, but more research in this specific field is necessary.

Malinovsky (1996) used intranasal ketamine in a random, open label, not controlled study in 8 patients (age 2 – 7 years), at a dose of 9 mg/kg, for anaesthesia. No adverse reactions were reported. (35).

Weksler (1993) used intranasal ketamine in a random, double-blind study, actively controlled in 86 patients for anaesthetic pre-medication. (Age: 2 – 5 years and dose 6 mg/kg). No adverse effects were reported.

Kaube (2000) used intranasal ketamine in an older group (11 Patients, age: 18 – 47 years and a dose of 25 mg) to treat migraine. It was a non-randomised, open label, not controlled study. Significant adverse reactions were reported of ataxia and alienation feelings.

Carr (2003) did a randomized, double-blind, placebo-controlled, multi-centre, crossover study on 20 adult patients of the treatment of breakthrough pain in chronic pain patients and demonstrated a significant analgesic efficacy of intranasal ketamine in comparison to intranasal placebo (36).

Although study medication was administered intra-nasally, nasal signs and symptoms were few and inconsequential.

A distinctive taste, however, was reported more often following treatment with ketamine than following treatment with placebo.

Innovative Drug Delivery Systems, Inc. (IDDS) is conducting phase I/II clinical trials on a trans-nasal ketamine formulation. Institutional Review Board permission was granted at New England Medical Center (Boston), Johns Hopkins University Medical Center (Baltimore) and the Methodist Comprehensive Pain Institute (Memphis). (37).

Sedation for intubation:

So-called '*rapid sequence intubation*' should be a controlled procedure done under the best conditions that circumstances permit.

This will be aided by a good understanding of the equipment, assistance and the drugs that should be available.

Induction agents:

The induction agent of choice in the emergency environment is **Etomidate** (*Hypnomidate*).

Pharmacokinetics:

- Following IV injection, etomidate is rapidly distributed to the brain and other body tissues;
- Anaesthesia is produced within 60 seconds, lasting 3-5 minutes;
- Vd = 4 L/kg; 76% bound to plasma proteins;
- T1/2 = 75 minutes;
- Metabolised mainly in the liver by ester hydrolysis; metabolites are excreted renally.

It has minimal respiratory and cardiovascular depressant properties.

Dose:
An IV dose of 0.3 mg/kg over 30 seconds is effective in 60 seconds, and has a duration of action of 4 minutes.

Involuntary muscle movements and a brief period of apnoea should be anticipated.

Other drugs used as induction agents for intubation are: **Propofol** (*Diprivan*), **Thiopentone,** and **Midazolam.** All of them have disadvantages compared to Etomidate in the emergency environment.

Paralysing agents:

The drug of choice, a depolarizing (non-competitive) agent with a rapid onset of action, **Suxamethonium chloride** (*Scoline)*, should be used unless a contraindication exists, in which case the non-depolarizing agent, **Atracurium** (*Tracrium*), is an alternative.

The paralysing agent should be administered only once the induction agent has started to take effect.

Pharmacokinetics of suxamethonium chloride:

- Muscle fasciculation is followed by rapid and complete muscle relaxation, occurring within 30-60 seconds and lasting for 3-5 minutes, after which it gradually and spontaneously dissipates within 10 minutes;
- Suxamethonium is rapidly hydrolysed in the plasma and tissues by pseudocholinesterase and only 10% is excreted unchanged;
- Continuous infusion or repeated doses may lead to tachyphylaxis. Excessive dosage (> 500 mg), may cause a dual block which has features of a non-depolarising block.

Suxamethonium dose: 1 mg/kg: Duration of action, approximately 4 minutes.

Caution: Most problems associated with the use of Suxamethonium are related to hyperkalaemia, e.g. in burns, major trauma, crush injuries and severe sepsis.

The drug should be used with caution in patients with penetrating eye injuries, because it can cause raised intra-ocular pressure.

Malignant hyperthermia is demonstrated by the masseter muscles not relaxing after the effect of the drug should have worn off.

Atracurium dose: 0.3 mg/kg, the onset of action is 2 minutes, and the duration of action is 15 – 30 minutes.

These drugs should be used only by doctors well trained in anaesthetic procedures.

Patient safety during sedation

The safety of the patient during procedures, when using sedation, is at all times a high priority and it is therefore important that emergency department personnel should work in close relationship with the anaesthetist's department of the hospital.

The issue is whether clinicians giving intravenous or any other route of sedation can manage the potential complications, especially airway obstruction and hypoventilation.

The requirements of a sedation regimen in children undergoing noxious procedures could be listed as rapid onset, adequate depth of sedation to allow for stimulation of the child during the procedure, the maintenance of spontaneous respiration, immobility, rapid recovery and minimal side effects.

The safe and effective use of ketamine for procedural sedation in children undergoing painful procedures in the emergency department has been described.

Whatever methods or drugs are used to sedate children, there may always be a failure rate.

Individuals have varying responses to the same dose of sedative and, because of the requirement to err on the side of caution in dosing, a significant minority of children will not be adequately sedated with sensible drug dosing and a small number may demonstrate paradoxical hyper-excitement or disinhibition (22).

The possibility of unsuccessful sedation should be made clear to the parents before the procedure. A failure rate of 10-20% has been suggested as reasonable (22).

An **effective protocol** to ensure the ***safety of patients during any procedure***, when making use of drugs causing sedation, (sedatives or analgesia), in the emergency department, should be on the same high level as for general anaesthesia, and **should include**:

- Complete medical clerking and patient consent;
- Medical assessment of patients before sedation and the specific exclusion of high-risk cases;
- The cardiovascular and respiratory systems should be examined and baseline observations made and documented;
- The child should be fasted for an appropriate length of time;
- A trained assistant should be available;
- A dedicated area equipped to deal with most of the possible complications;
- Sufficient cardiovascular and respiratory monitor equipment available;
- A dedicated recovery area with appropriately trained nursing staff.

A trouble-free series of several hundred sedations does not demonstrate equivalent to general anaesthesia, even if a serious adverse event occurs only once in several thousand cases, whichever technique is used (22).

In the United States, an assessment of adverse drug reports between 1967 and 1994 was submitted to the FDA, and the survey revealed at least 52 deaths and 27 episodes of serious morbidity, including 6 episodes of permanent neurological damage and 15 prolonged hospitalisations attributed to sedation.

The causes of these events were mainly overdose, inadequate monitoring, inadequate training of personnel involved, or premature discharge (22).

Groups of patients who are likely to present problems during sedation are largely predictable and include neonates and children aged less than 6 months, those with renal or hepatic impairment, respiratory distress, abnormalities of the airway, CNS disease and patients on multiple drug therapies.

The medical and nursing staff involved in giving sedation to children will require adequate training; probably the minimum requirement should be current PALS, ACLS and ATLS provider certificates.

Guidelines should be in place on how frequently staff should perform sedation to remain competent, and the frequency of mandatory updates on paediatric sedation and resuscitation.

EMERGENCY LOCAL AND TOPICAL ANALGESIA

Local Anaesthetic:

Local anaesthesia provides a simple, cheap, and relatively safe adjunct to manage children's pain in the emergency unit. It has the advantage that with appropriate

training and supervision, most techniques can be performed by junior emergency department doctors.

Local anaesthetics produce a reversible block of conduction in nerve fibres. The rate, duration and extent of action depend on the type, calibre and site of the nerve fibre, as well as its degree of myelination and state of activity. Not only sensation but various autonomic and motor activities may be lost.

They may be divided into two main groups:

- **Ester-type agents**, such as amethocaine, cocaine, procaine, benzocaine, oxybuprocaine are hydrolysed in the plasma and, to a lesser extent, in the liver by cholinesterases. Several representatives are for topical application.
- **Amide-type agents** include lidocaine, mepivacaine, bupivacaine, prilocaine. These are metabolised in the liver by microsomal enzymes with variable, small amounts excreted unchanged in the urine. They may be more inclined to accumulate after multiple administrations.

The principal clinical implication is that the ester group is associated with higher incidence of hypersensitivity (allergic) reactions than the amide group; the amide group enjoys preference for parenteral and local use.

Special prescribe points:

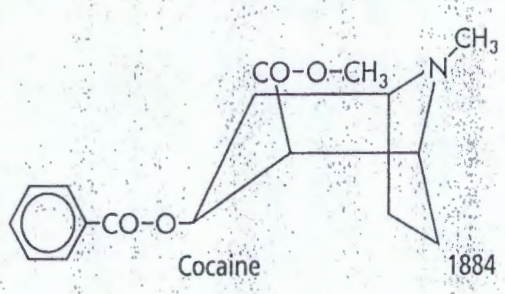
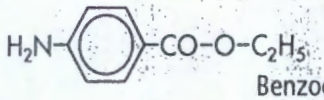
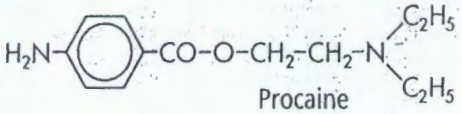
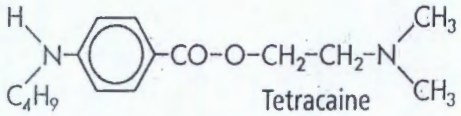
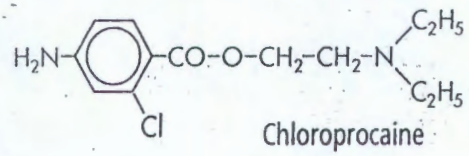
- The patient should be closely monitored for the duration of the clinical action of the drug (30 – 45 minutes) following parenteral administration.
- Avoid in infected or inflamed tissues.
- Resuscitation equipment and drugs for the management of potential complications should always be available.
- Toxicity results from accumulation with repeated doses.
- Seizures should be treated with an intravenous benzodiazepine or a short-acting barbiturate.
- Severe cardiovascular complications may result from inadvertent intravascular administration.
- A vasoconstrictor should never be used in the local anaesthesia of digits, nose, ears or penis, and should not be injected into an area with reduced blood flow due to peripheral vascular disease.

Topical anaesthesia:

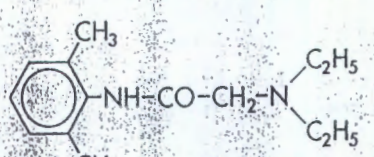
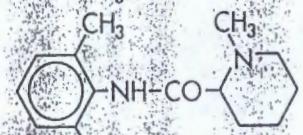
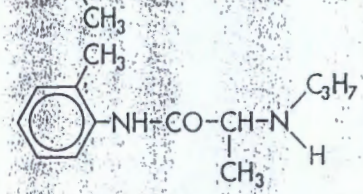
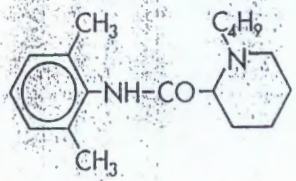
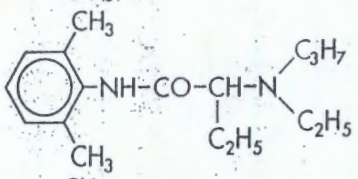
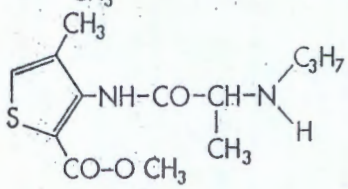
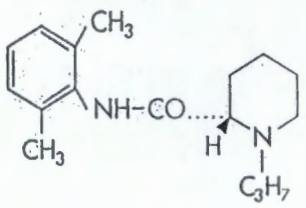
Local anaesthetic cream can be applied to the skin before venepuncture or cannulation, if the child's condition allows time for this (28).

- **EMLA**: (Eutectic Mixture of Local Anaesthetics) contains 2.5% lignocaine and 2.5% prilocaine. It is applied in a thick layer and sealed under an occlusive dressing for 45 - 60 minutes. It is contraindicated for infants under the age of 1 year.

Local anesthetics with an ester bond

Aromatic residue	Inter-mediate chain	Substituted amino group	Year intro-duced
 Cocaine			1884
 Benzocaine			1900
 Procaine			1905
 Tetracaine			1930
 Chloroprocaine			1955

Local anesthetics with an amide bond

Aromatic residue	Inter-mediate chain	Substituted amino group	Year intro-duced
		Lignocaine	1944
		Mepivacaine	1957
		Prilocaine	1960
		Bupivacaine	1963
		Etidocaine	1972
		Carticaine	1974
		Ropivacaine	1996

The principal clinical implication is that the ester group is associated with higher incidence of hypersensitivity (allergic) reactions than the amide group; the amide group enjoy preference for parenteral and local use.

- **Ametop**: Contains 4% amethocaine. It has a faster rate of onset than EMLA (30 - 40 min), a longer duration of action and causes vasodilatation, which may aid cannulation. (This preparation is not available in South Africa).

Topical agents do not provide pain relief for intra-muscular injections in children.

Topical creams should not be applied to mucous membranes or open wounds as rapid absorption may result in systemic toxicity.

- **TAC**: This is a mixture of tetracaine 1% (10 mg/ml), adrenaline 1:4000 (250 mcg/ml) and cocaine 4% (40 mg/ml), and is often used in the USA (28). It can be used to anaesthetise open wounds for cleaning and suturing. It can be applied to the wound on gauze. It can be prepared in several formulations; however, the maximum dose of 1.5 ml of TAC per kg of body weight should not be exceeded. It should not be used on mucous membranes or where there is a risk of distal ischemia, because of the vasoconstrictor properties of adrenaline.

Topical spray / jelly:

Xylocaine pump spray for the larynx: Lidocaine 10 mg, 95% alcohol 32% m/v per metered spray. Also: Adco-Ethyl Chloride spray; 100ml.

Remicaine jelly is available as a 2% in 20 ml tube (400 mg/20ml). It can be used to insert tubes and catheters. The maximum recommended *adult* dose is 200 mg.

Ophthalmologic local anaesthetics:

These are used principally for examination and for minor optical procedures such as the removal of corneal foreign bodies; they should never be given for relief of symptoms.

Care should be taken to protect the anaesthetised eye from foreign body contamination and trauma.

Home and self-instillation of topical eye anaesthetics may lead to repeated and prolonged exposure and should be discouraged.

- **Tetracaine**: Minims Amethocaine HCl drops; 0.5% & 1%. One drop takes effect within 15 seconds and lasts about 15 minutes. Also: Covostet 0.5%.
- **Oxybuprocaine**: Novecin Wander 0.4%. It also has bactericidal properties. It may be less irritating than tetracaine, and the onset and duration of action are similar to tetracaine. It is also available in combination with fluorescein, for detection of abrasions and the removal of foreign bodies from the cornea. Also: Minims Benoxinate HCl 0.4%.
- **Proxymetacaine**: Opthetic 0.5%. It has similar potency to tetracaine.
- **Lidocaine / fluorescein**: Lignocaine & fluorescein drops, 4%.

Local infiltration:

Local infiltration is the anaesthetic technique most commonly used in the emergency department to provide anaesthesia for suturing children's wounds.

Lidocaine (Lignocaine):

It is most commonly used in the emergency environment.

Paediatric dose: By infiltration: Maximum dose 3 mg/kg without a vasoconstrictor and 6.5 mg/kg with a vasoconstrictor.

Pharmacokinetics:

- It is injected subcutaneously, takes effect in 2-4 minutes and lasts approximately 30 minutes – 2 hours;
- Vd = +/- 1 L/kg;
- It is effectively absorbed from mucous membranes;
- Distribution is extensive;
- T1/2 = 1-2 hours;
- Protein binding: 70%;
- 90 % metabolised in the liver; 10% is excreted unchanged in the urine, the rest as metabolites.

1% Lignocaine = 10 mg/ml, max adult dose = 20 ml
2% Lignocaine = 20 mg/ml, max adult dose = 10 ml
Dental cartridges do not permit aspiration, and contain 1.8 ml of 2% lignocaine. Therefore 6 cartridges contain 216 mg.

Contraindications:

- Absolute: Heart block or other conduction disturbances, hypovolaemia and myasthenia gravis.
- Relative: Hepatic impairment, epilepsy.

Inhaled nitrous oxide during infiltration can make the procedure more acceptable to children.

Preparations include: *Peterkaien* 1%, 2%; *Remicaine* 1%, 2%; *Xylotox* 2% (1,8ml dental cartridge); *Carbocaine Dental* 3%, 54mg/1.8ml; *Citanest 3%-Octapressin*.

Field block:

A field block may be used to drain a small abscess or clean an infected wound.

The anaesthetic is injected at a point slightly distant from the infected tissues based on the principle that branches of sensory nerves run parallel to the skin surface in the subcutaneous tissues.

The anaesthetic is injected around the perimeter of the wound or abscess approximately 1cm away from its edge using a maximum dose of 3 mg/kg of Lignocaine.

The block may take 2-3 minutes longer to take effect than local infiltration. A field block is also useful in areas difficult to infiltrate anatomically, such as the ear.

Peripheral nerve block / Regional block:

This technique involves injection of local anaesthetic in the region of a peripheral nerve to provide anaesthesia to the area supplied to the nerve.

Bupivacaine is a longer-acting anaesthetic than lignocaine and is often used for nerve blocks at a concentration of 0.25% (2.5mg/ml) with an upper limit of 2 mg/kg in children (28). These techniques are best used in older children and adolescents.

Regional blocks will give good anaesthesia without distorting local landmarks for laceration repairs.

Many patients will find regional blocks more comfortable than local wound injections.

Complications of local anaesthesia:

These include systemic toxicity, anaphylactic reactions, local damage with bruising, haematoma formation, nerve injury and needle breakage.

Systemic toxicity occurs when the blood concentration of local anaesthetic exceeds the toxic level, leading to significant amounts reaching the brain and myocardium.

Early symptoms of toxicity are tingling around the mouth, tinnitus, slurred speech, and dizziness. These symptoms may progress to confusion, convulsions, coma, hypotension and arrhythmias.

If toxicity is suspected, the anaesthetic should be stopped immediately.

The patient must be moved to the resuscitation area and treated according to the ABCs of emergency medicine.

Convulsions can be treated with small, incremental doses of diazepam.

Hypotension should be treated by laying the patient flat, gaining secure intravenous access and giving fluid resuscitation.

Cardiac arrhythmias usually resolve spontaneously, but bradycardia may require treatment with atropine.

Anaphylactic reactions to local anaesthetics are rare, but must be treated as an emergency for anaphylactic reactions.

Caution during injection of local anaesthetic:

- Carry out an aspiration test before and during the injection.
- Administration of a test dose is necessary in most blocks.
- Always inject local anaesthetics in incremental doses (several test doses).
- Maintain verbal contact with the patient.
- Keep careful notes of the block procedure.

ANALGESIC AGENTS

The ideal analgesic should have the following features:

- Easy, acceptable and painless administration.
- Rapid onset of action.
- Predictable and effective analgesic properties.
- No side effects.
- Affordable.
- Safe.

Superficial and musculoskeletal pain responds most favourably to mild analgesia like paracetamol and aspirin and non-steroidal anti-inflammatory agents (example: Ibuprofen), whereas the opioids may be more suitable for visceral pain.

Mild analgesics:

1. Paracetamol:

Paracetamol is an excellent analgesic for mild to moderate pain. It can be given orally in a dose of 10-15 mg/kg 4-6 hourly, to a maximum of 4 doses per 24 hours. A rectal preparation is also available. It has analgesia and antipyretic effect but has no anti-inflammatory properties. It acts centrally as a cyclo-oxygenase inhibitor.

- Oral bioavailability is 73-93%. Vd = 0.8-1 L/kg. Plasma protein bindings are negligible at therapeutic levels;
- T1/2 = 1-4 hours;
- 90-95% of a dose is conjugated in the liver and excreted renally as glucuronide and sulphate metabolites, with < 3% unchanged drug;
- The potentially toxic intermediate metabolites formed by the P450 cytochrome oxidative enzyme system are usually detoxified by glutathione. Toxic effects on the liver and / or kidneys may occur if glutathione stores are depleted, such as in overdose or prolonged use of excessive doses;
- Contraindications: Hepatic or renal disease, anaemia and other disorders of the haemopoietic system.

2. Aspirin:

Aspirin is a cheaper drug than paracetamol and is as an effective analgesic, reducing pain through prostaglandin inhibition.

It has been associated with Reye's syndrome in children with acute febrile illness and should therefore be avoided in children under the age of 12 years.

Aspirin can also cause gastrointestinal irritation, bronchospasm and reduced platelet function with increased risk of haemorrhage.

Pharmacokinetics of aspirin:

- Oral bioavailability is about 68%. It is rapidly hydrolysed to the active metabolite salicylate which is 90% bound to albumin in serum;
- Vd = 0.1-0.2 L/kg;
- T1/2 aspirin = 15-20 minutes;
- T1/2 salicylate = 2-20 hours (dependent on dose and urinary pH);
- 1% is renally excreted as unchanged aspirin, the remainder as salicylate and its conjugated metabolites that are formed in the liver;
- Therapeutic levels of salicylate: analgesic and antipyretic effect, 25-50 mcg/mL; anti-inflammatory effect, 150-300 mcg/mL.

Non-steroidal anti-inflammatory analgesia

In general NSAIDs should be avoided in compromised patients, as they have the tendency to impair renal perfusion, and cause retention of sodium and fluid in the body.
The administration of NSAIDs in an under-hydrated patient increases the risk of renal damage.

3. Ibuprofen:

Ibuprofen is widely used in the United Kingdom and is considered as a safe and effective drug in children over the age of one year.

Pharmacokinetics:

- Oral absorption is rapid, but rate is reduced by food. 99% is bound to plasma, mainly albumin;
- T1/2 = 1.8-2 hours;
- Metabolised in the liver and excreted in the urine, mainly as inactive metabolites. Accumulation is uncommon since elimination from the plasma is rapid.

It acts by peripheral inhibition of prostaglandins. It has analgesic, antipyretic and anti-inflammatory properties, and has the advantage of a longer duration of action than paracetamol or aspirin.

It can induce bronchospasm in children with asthma and is contraindicated if there is a history of asthma, gastrointestinal bleeding or renal impairment.

It is not recommended for children under 1 year of age, or weighing less than 7 kg.

Oral dose: 5 mg/kg, given 6-8 hourly.

Also available are:
* **Mefenamic acid** (*Ponstan*); Oral dose: 6.5 mg/kg/dose given 8 hourly and,
* **Diclofenac** in suppository form, which can be useful in children who are vomiting. Dosage: 1 mg/kg given 8-12 hourly.

Ophthalmic use:
NSAIDs eye drops are particularly useful for pain relief in post-examination of eye injuries, corneal abrasions, superficial corneal and scleral lacerations, and post-corneal foreign body removal.

Diclofenac (*Naclof*): 1 mg/mL: Apply 3-5 drops, as needed as a single dose, then 1 drop 3-4 times per day.

Also available: **Flurbiprofen** (*Ocufen*) and **Indometacin** (*Indocid*).

Moderate / strong analgesics:

Opioids

1. Codeine:

Pharmacokinetics:

- Oral bioavailability is about 50%; analgesia effects may be expected within 15-30 minutes;
- Vd = 2.6 L/kg; protein binding, 7%;
- T1/2 = 2.5-4 hours, the analgesic effect lasting 4-6 hours;
- Metabolised in the liver, where about 10% is converted to morphine. Excreted renally, 5-15% unchanged and the remainder chiefly as conjugated metabolites;
- Contraindications: Respiratory depression, head injuries and acute asthma.

This is a mild opioid drug useful even in young children to control mild to moderate pain. The oral dose is 0.5-1 mg/kg given every 4-6 hours.

Intravenous administration is not recommended as it can cause profound hypotension, probably because of histamine release.

Combined with paracetamol, codeine has a small additive effect and can be used when stronger pain relief is needed.

Like other opioids, codeine can cause nausea, vomiting, respiratory depression and constipation, but these side effects are rare when used appropriately (28).

2. Tilidine (*Valoron*):

This opioid is indicated for severe pain. Concentration: 50 mg/0.5ml (= 20 drops).

Paediatric dose:
Oral: 1-9 years, 1 drop for each year of age plus 2 drops, 6-8 hourly; 10-14 years, a maximum of 10 drops (25 mg); monitor carefully.

According to the SA Drug Information Centre, there is no reference for this drug to be prescribed or administered as per kg body weight, but rather by age. [Tilidine is not registered for paediatric use in the UK or the USA]

Pharmacokinetics:

- It is absorbed from the GI tract, metabolised and excreted in urine, mainly as metabolites;
- Tilidine is a prodrug; the metabolite, nortilidine is responsible for its analgesic activity.

An overdose may cause convulsions.

Contraindications:
Absolute: Head injuries or increased intra cranial pressure, bronchial asthma, respiratory infection and cardiac failure.
Relative: Hypothyrodism and impaired liver function.

3. Morphine:

Morphine is an excellent drug for the treatment of severe pain resulting from burns, fractures and other severe or multiple injuries.

It produces analgesia by inhibiting synaptic transmission of opioid receptors to the brain.

Intravenous morphine is the gold standard in pain relief during acute conditions.

Pain scores should be noted before, during and after use, and children should be closely monitored at all times.

Pharmacokinetics:

- Oral bioavailability, 12-36%;
- Vd = 3-4 L/kg;
- Protein binding, 35%, mainly to albumin;
- T1/2 = 2-3 hours;
- Analgesic effects occur within 10-30 minutes (parenterally), lasting 4-5 hours;
- Metabolised in the liver, chiefly by conjugation, where 5-10% is converted to the active metabolite normorphine. Glucuronide metabolites and a small amount of unchanged drug are excreted in the urine. About 10 % appears in bile and undergoes enterohepatic recirculation.

Contraindications:
Absolute: Head injury or intracranial lesions with raised intracranial pressure, diarrhoea caused by poisons and acute abdominal conditions.

Relative: Hypothyrodism, Addison's disease, hepatic and renal function impairment, and acute asthma.

Side effects of respiratory depression, hypotension and nausea are rare.

Anti-emetics are rarely needed in combination with opioids in children.

Paediatric dosage:
Intravenously; 0.1-0.2 mg/kg titrated over 2-3 minutes. It can also be administered *IM or subcutaneously*; 0.1-0.2 mg/kg, with 3-4 doses per 24 hour period.

Oramorph:
Oral dose; 0.2-0.4 mg/kg is often more acceptable to children.

However, morphine is unreliably absorbed from the gastrointestinal tract because of high first pass metabolism resulting in delayed, unpredictable onset of action.

In a study done by Illum *et al.* (2002) they tested the absorption of nasally administered morphine by using it in combination with chitosan as an absorption-promoting agent (38).

Morphine administered intra-nasally to humans as a simple solution is only absorbed in a limited degree, with a bioavailability of the order of 10% compared to intravenous administration.

The chitosan-morphine nasal formulations have been tested in healthy volunteers in comparison with slow intravenous infusion (over 30 min) of morphine.

The results show that the nasal formulation was rapidly absorbed with a T-max of 15 min or less and a bioavailability of nearly 60%.

The shape of the plasma profile for nasal delivery of the chitosan-morphine formulation was similar to the one obtained for slow intravenous administration of morphine (38).

In the management of acute and breakthrough pain, it is important to use a drug and a route of administration that will provide a time-action profile characterized by rapid onset and early peak effect and duration commensurate with the span of most breakthrough pain situations.

Hence, a pure micro-opioid agonist such as morphine, with relative short plasma half-life, administered nasally with an adequate delivery system, would be a suitable choice.

Very few studies on nasal delivery of morphine to humans have been published.

Chast *et al.* (1992) administered 20 mg of morphine acetate to six postoperative patients by the nasal and oral routes and reported a peak plasma concentration 15 min after nasal and 30 min after oral administration.

The plasma profile after nasal administration was very similar to that seen after parenteral administration.

Very few studies have been carried out on the transport of morphine from the nose to the brain.

Illum's study supports the view that nasal morphine is absorbed directly from the nose into the systemic circulation and bypasses the gut wall and the liver and thereby first pass metabolism.

The tolerability of the formulations as experienced by the volunteers was generally good.

The main central effect recorded was that of sedation.

More research and study are necessary on the use of intranasal morphine, as well as on the use of different delivery systems, especially in children.

Diamorphine: (*Heroin*)

This is an alternative to morphine, used in the United Kingdom, at a dose of 0.04-0.08 mg/kg **intravenously.**

It is a powerful opioid analgesic.

It may cause less nausea and hypotension than morphine.

Recent trials using **intranasal** diamorphine at 0.1 mg/kg have been shown to be effective, safe and acceptable in children suffering with acute pain from illness and injuries (28).

The use of intranasal diamorphine for paediatric pain relief:

The nasal mucosa aids absorption, as it is richly vascularised, and the sub-epithelial cells are lined by fenestrated epithelium.

Diamorphine is rapidly and well absorbed across the nasal mucosa, as it is lipophilic.

Administration can be in a small volume due to its high water solubility and it has low irritancy.

It has a potency twice that of morphine with a similar duration of action.

The bioavailability via the nasal route is 50% and peak blood levels are attained within 5 minutes of administration.

Pain scores should be used before and after analgesia.

Children should be supervised and monitored carefully for any signs of respiratory depression, vomiting, hypotension or any other adverse reactions.

Dosage:
Diamorphine: 5 mg /1ml ampule.
Dosage calculated by patient weight: 0.1 mg/kg, where weight equals:
(Age + 4) x 2 = Weight in kg.
The volume (0.2 ml), is administered via a MAD attached to the syringe, and should be split between both nostrils.

Example: A 6-year-old child of 20 kg would receive 0.2 ml of correct concentration.

Stages to be followed in administering intranasal diamorphine:

Stage 1	Stage 2	Stage 3	Stage 4

Weight (kg)	Age	Dose (mg): 0.1 mg/kg	Volume of water (ml)	Amount to be given (ml)
10	1-2	1 mg	1 ml	0.2 ml
15	2-4	1.5	0.65	0.2
20	4-6	2	0.5	0.2
25	6-8	2.5	0.4	0.2
30	8-10	3	0.35	0.2
35	10-12	3.5	0.3	0.2

Stage 1: Obtain weight of child to nearest 5 kg, or by using the following formula if weighing is not possible:

(Age + 4) x 2 = Wt in kg

Stage 2: Ensure the correct dose is prescribed: @ 0.1 mg/kg.
Stage 3: Use a 1 ml syringe, and add the appropriate volume of water to a 5 mg ampule of diamorphine.
Stage 4: Draw up 0.2 ml of mixture made in stage 3 and administer intranasally, using an atomiser (MAD) attached to the syringe.

For children < 10kg (1 year), calculate at 0.1 mg/kg.

Diamorphine administered trans-mucosally, via the nasal route, offers the potential for effective, expedient and well-tolerated analgesia that is acceptable to patients.

Cone *et al.* (1993) evaluated the pharmaco-dynamic properties of intranasal compared with intramuscular diamorphine. Established scales were used to evaluate drug effects and psychomotor performance.

Intranasal diamorphine appeared to produce physiological and behavioural effects over a similar time course to those produced by intramuscular administration. No statistically significant differences were reported between 6 mg intranasal and 6 mg intramuscular administration in terms of drug effects. (39).

There have been four published clinical evaluations of intranasal diamorphine; two of these were evaluations of intranasal diamorphine as an analgesic agent in children, (40, 41), and the other two were evaluations of patient-controlled intranasal diamorphine for postoperative pain in adults, (42, 43).

Kendall *et al.*(2001) reported the only published randomised controlled clinical trial evaluating intranasal diamorphine as an analgesic agent; this was preceded by a published pilot study (40).

The pilot study consisted of children aged between 3 and 16 years with clinically suspected limb fractures (i.e. in acute moderate to severe pain) presenting to the Emergency Department.

They were randomized to receive either a conventional dose of intramuscular morphine sulphate 0.2 mg/kg or intranasal diamorphine hydrochloride 0.1 mg/kg.

This exploratory dose was selected because diamorphine was generally thought to be twice as potent as morphine.

The intranasal morphine was administered as drops in a solution from a syringe in a total volume of 0.2 ml. This was a small pilot study (data were available from 51 children), but it appeared that the dose of intranasal diamorphine provided adequate and expedient analgesia, was well tolerated and without significant adverse events.

The findings of this pilot study further evaluated in a much larger multi-centre randomized control trial, which was designed and carried out in accordance with the International Conference for Good Clinical Practice.

The patient population and drug doses were the same as in the pilot study, but the methodological design, quality assurance and subsequent statistical analysis were far more rigorous.

The intranasal morphine was administered as an aerosolised spray in a total volume of 0.1 ml, in order to minimise any dose being swallowed and because experimental evidence had shown that the aerosolised spray in midazolam was more effective than nasal drops (44).

The primary outcome measure was reduction in pain score over time, as measured either using a Wong Baker face pain scale or a visual analogue scale. Pain scores were measured at baseline, and then at 5, 10, 20 and 30 minutes after drug administration.

Multiple observers of pain (including the children, staff and parents) were employed. Other outcome measures included the tolerance to drug administration, the acceptability of the treatment and adverse event recording. All children had continuous monitoring of their pulse, respiration rate, oxygen saturation and Glasgow Coma Scale.

There were 404 eligible patients who completed the trial (204 having received intranasal diamorphine, and 200 having received intramuscular morphine).

Onset of pain relief was faster in the intranasal diamorphine group, with lower pain scores at 5 ($p = 0.04$), 10 ($p = 0.003$), and 20 ($p = 0.002$) minutes after treatment, but no difference between groups ($p = 0.20$) after 30 minutes.

Intranasal diamorphine was significantly better tolerated, with 80% of children showing no obvious discomfort compared with 9% showing no discomfort in the intramuscular morphine group.

Treatment administration was judged to be acceptable in a significantly higher proportion of children receiving intranasal diamorphine than intramuscular morphine sulphate.

No serious adverse effects were observed in the intranasal diamorphine group. The frequency of minor adverse events was similar in both groups.

The authors concluded that intranasal diamorphine provides the same overall degree of pain relief as intramuscular morphine, but that intranasal diamorphine provides quicker onset of analgesia.

Intranasal diamorphine was found to be well tolerated and to have an acceptable safety profile in the 204 patients in this study group.

Ward *et al.* (2002), evaluated intranasal diamorphine in a similar setting with adults, comparing it with intravenous diamorphine, in a randomised controlled trial (43).

52 consecutive patients undergoing lower limb joint surgery were randomized to receive diamorphine as patient-controlled analgesia postoperatively either by the intranasal (1.0 mg bolus, 3 minute lockout) or intravenous (0.5 mg bolus, 3 minute lockout) route.

Pain was assessed during the first 24 hours postoperatively, both at rest and upon movement.

Patients in the intranasal group had significantly higher pain scores than the intravenous group, both at rest (intranasal median 35.5 vs intravenous median 20; $p = 0.03$) and upon movement (64 vs 50; $p = 0.016$). However, significantly fewer patients in the intranasal group experienced episodes of vomiting (intranasal 0/24 vs intravenous 6/24 patients).

The authors acknowledged that their study was not blinded and that bias may have been introduced by patient expectations. Patients in the intranasal group were also significantly heavier than those in the intravenous group (90.8kg vs 80.8kg) and it may have lowered the reported analgesic effect due to lower bioavailability of the drug.

The intranasal bottle used to administer the drug had to be held in the upright position and greater physical effort was required to use the device (43).

There would not appear to be any physiological reason why intranasal diamorphine should work any less well in adults than in children, although its major advantage over other forms of parenterally administered diamorphine is its tolerability (i.e. it is needle-free). This advantage is particularly applicable to a paediatric population.

More studies need to be done on the use of *intranasal morphine sulphate* by using the mucosal atomized device (MAD).

The *volumes and concentration* to gain optimal effect, possible adverse effects and safety profile of *morphine sulphate versus diamorphine*, using the MAD, also need investigation.

A survey was done over a period of 12 months (March 2001 to March 2002) in the United Kingdom in five large emergency departments on the use of intranasal diamorphine:

* North Bristol NHS Trust (333 patients);
* Bristol Children's Hospital (650 patients);
* The Royal United Hospital in Bath (350 patients);
* Gloucester Royal Hospital (250 patients);
* Cheltenham Royal Hospital (250 patients).

It would appear that intranasal diamorphine is being adopted as an effective, rapidly acting, safe and well-tolerated analgesic agent, particularly in children (45).

4. Pethedine

Pethedine has a shorter duration of action than morphine and less sedative effects.

Pharmacokinetics:

- Oral bioavailability, 50-60-%;
- Vd = 3-4 L/kg; protein binding, 60%;
- Onset of analgesia is within 1 minute after IV and 10-15 minutes after IM or subcutaneous administration, lasting 2-4 hours;
- Metabolised in the liver to active norpethidine and inactive metabilites. Norpethedine, with a long half-life (8-21 hours), may increase excitatory effects in the event of cumulation;
- Excreted in the urine, about 5% unchanged and up to 33% as norpethedine.

Dosage: 0.5-1.0 mg/kg intravenously.
Disadvantage: It can cause nausea, vomiting, anxiety, tremors, disorientation and even convulsions in some patients.

5. Fentanyl

Fentanyl is a new and potent synthetic opioid analgesic, with pharmacological actions similar to morphine and pethedine, except for its shorter duration of action.

It has a rapid onset of action and duration of 30-40 minutes.

It is used intra-operatively for its analgesic effect, as a supplement to general anaesthesia, or to produce neuroleptanalgesia if combined with an appropriate neuroleptic such as droperidol.

Paediatric dose:

Over 2 years with spontaneous respiration: 3-5 mcg/kg IV over 3-5 minutes, followed by supplements of 1 mcg/kg as required.

It can also be given intra-nasally (28).

Disadvantage: It may cause respiratory depression, which lasts longer than the analgesic effect especially in combination with other sedatives and analgesia.

It rarely causes hypotension, possibly because it causes less histamine release than morphine.

Fentanyl should only be used by doctors with anaesthetic training because of its rare side effect of causing severe thoracic and abdominal muscle rigidity which may make ventilation difficult.

This effect may occur when high doses or rapid infusion are used (> 15 mcg/kg).

Naloxone may reverse this effect (28).

6. Tramadol (*Tramal*)

PDR (USA) information: Tramadol is available as Ultracet (35,5 mg Tramadol HCl / 325 mg Acetaminophen tablets, and Ultram (50 mg Tramadol HCl), tablets.

Tramadol is a centrally acting synthetic opioid analgesic. Although its mode of action is not fully understood, from animal tests at least two complementary mechanisms appear applicable: binding of parent and M1 metabolite to micro-opioid receptors and weak inhibition of re-uptake of nor-epinephrine and serotonin. Opioid activity is due to both low affinity binding to the parent compound and higher affinity binding of the O-demethylated metabolite M1 to micro-opioid receptors.

Acetaminophen is a non-opiate, non-salisilate analgesic.

Indication for usage:

It is used for the short term, 5 days or less, management of acute pain.

According to the PDR, the safety and effectiveness of Ultracet has not been studied in the paediatric population; however, recent studies have suggested that it can be useful as dental analgesia and in pre-medication for elective surgery.

Serious potential consequences of Tramadol overdose are respiratory depression, lethargy, coma, seizure, cardiac arrest and death.

[Adult dose: Ultracet: 2 tablets every 4-6 hours as needed for pain relief. Maximum dose: 8 tablets per day].

7. Nalbuphine (*Nubain*)

This opioid (morphinan derivate) is used largely in the pre-hospital setting by paramedics.

It acts as a partial opioid antagonist.

When a patient received *Nubain*, and subsequent doses of morphine are required, larger doses of morphine will be needed to achieve the same desired analgesic effect; it is for this reason that emergency unit doctors should be aware of this drug.

Paediatric dose: Usually 0.1-0.2 mg/kg, 3-6 hourly as needed.
[Adult dose: IM, s/c or IV, 10-20 mg (70 kg adult), repeated 3-6 hourly as required].

It is registered in South Africa, but presently not commercially available.

8. Ketamine

Ketamine is a phencyclidine derivate that binds to opioid receptors. Its properties were discussed in detail earlier in this paper under: '*Procedural sedation of children in the emergency unit*'.

Monitoring and discharge

All children given analgesic drugs ***with potentially sedating effects*** should undergo a brief assessment before drug administration.

Base line observations should include: level of consciousness (GCS score), heart rate, oxygen saturation, respiratory rate, blood pressure, body weight, pain score and anxiety score.

It is inadvisable to give sedating analgesic drugs to children who have an altered conscious level, unless a full anaesthetic is required and is given by appropriately trained staff (28).

All drugs given should be well documented with dosage, time given, time intervals, route of administration and any adverse effects.

After administration of any sedative analgesic, vital signs observations should be repeated at least every 30 minutes, until the child has fully recovered from the drug effect.

Discharge criteria for children who received analgesic drugs with potentially sedating effects (28):

If the child is to be sent home, he or she should fulfil the following criteria before discharge to the care of a parent or responsible adult:

- An infant must be able to sit unaided and to hold his / her head up, and a child must be able to walk unaided;
- The child has regained pre-analgesia observations of respiratory rate, conscious level and oxygen saturation;
- The child remains in the emergency department for at least one hour after administration of the sedative analgesic;
- The supervising adult receives a full explanation and advice sheet and understands it. Ideally this should be signed and countersigned;
- The child has been prescribed appropriate non-sedating analgesia to take home.

Only when all five criteria are met can the child safely be discharged to go home.

Summary

Children and infants exposed to noxious stimulus feel pain to the same extent as adults.

For a child the unfamiliar and sometimes frightening environment of the emergency department can compound and heighten their experience of pain and anxiety.

Provision of analgesia and sedation to children in the emergency unit is currently often inadequate because of poor pain and anxiety recognition and assessment, poor availability of specific protocols, insufficient training of emergency unit personnel and staff inexperience.

Children's pain and anxiety should be assessed and quantified using objective pain and anxiety tools and relief methods.

Effective analgesic and anxiolytic agents should be given in adequate doses and appropriate routes for the type and level of pain and/or anxiety suffered.

Physical methods of pain relief can be used such as splints, cooling, elevation and dressings.

Psychological methods of pain relief and anxiolysis range from play therapy and guided imagery to providing a department decorated in a 'child-friendly' style, with children seen in an area audio-visually separate from adult patients where possible.

Drug administration should be highly tolerable and as pain free as possible. More use should be made of intranasal administration of drugs when and where appropriate.

The use of ketamine for procedural sedation, intranasal midazolam for treatment of persistent seizure activity, and intranasal diamorphine to treat severe pain, should be introduced as useful and safe treatment options in the emergency department, but only in the hands of experienced and well-trained staff with appropriate facilities, equipment and specific treatment protocols in place.

Real commitment from all staff members involved in the emergency department to recognise pain, fear and anxiety in children, and to make sure to deal with each situation at hand appropriately, promptly and correctly can solve many of the current problems.

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PAIN AND ANXIETY SCORE LEVELS:

-MANAGEMENT BY USING CLINICAL JUDGEMENT AND DIAGNOSIS-

A good clinical and age related history (from patient, carer or parent), clinical observation, examination and diagnosis, properly documented, is necessary:

History:

Document the time and mechanism of injury, onset and profile of disease, treatment to date, underlying pathology, allergies and chronic medication.

Observations:

Pulse rate, respiratory rate, blood pressure, temperature, oxygen saturation, blood glucose value and conscious level: Document all observations.

Physical examination:

- Quick overview according to the ABC-principals of emergency medicine, and treat accordingly if and when necessary.
- Quick, but thorough general examination. Document body mass. Estimate: *(Age+4) x 2 = Weight (kg)*
- Specific and thorough examination of injured or diseased area.
- Make a proper and correct diagnosis as soon as possible, using clinical skills and special investigations when appropriate, but do not delay giving sufficient analgesia and or sedation.

Pain score:

A young child cannot communicate his or her extent of injury or the degree of pain that they experience, and therefore the clinician has to decide what the pain score should be by using his clinical skills and common sense: A proper pain score will lead to a decision on appropriate analgesia to be administered.

'0'= No pain, 'P1'= Mild pain, 'P2'= Moderate pain, 'P3'= Severe pain.

Anxiety score:

Associated with pain, a child will experience anxiety and fear, which will and can lead to a total uncooperative patient.

The clinician will often find it extremely difficult to examine or treat the anxious child and therefore it is important to firstly decide on the degree of associated anxiety and fear experienced by the child, and then secondly on appropriate treatment.

The anxiety and fear levels may often be much higher than the underlying injury or disease would allow.

'0'= No anxiety, 'A1'= Mild anxiety, 'A2'= Moderate anxiety, 'A3'= Severe anxiety

PAIN SCORE TABLE: CLINICAL EVALUATION

'0'= NO PAIN	'P1'= MILD PAIN	'P2'= MODERATE PAIN	'P3'= SEVERE PAIN
	Sprain	Multiple sprains	Torn ligaments
	Abrasion	Multiple abrasions	Multiple abrasions, sensitive areas
	Contusion	Multiple contusions	Multiple contusions with possible extensive underlying soft tissue injury, ex: crush injury
	Minor burns, ex. single minor blister	Burns: Multiple / sensitive area, ex. Hot water, sun	Compartment syndrome
	Minor infection / with or without inflammation	Infection with moderate inflammation	Extensive burns, ex. chemical, oil etc
	Foreign body: ex. Bead or stone in nose or ear; Splinter in foot, etc	Foreign body: ex. grit in eye, fish hook, thorn, glass splinter etc	Infection with extensive swelling and inflammation.
	Puncture wound	Minor laceration, sensitive area	Foreign body: ex. on cornea, large thorns, grit or splinters etc
	Sting, bites: ex. Mosquito, fly, flea etc	Sting, bites: ex. Bee sting, spider bite etc	Large or multiple lacerations
	Minor laceration, insensitive area	Greenstick fracture	Fracture, open fracture, multiple fractures
		Dislocation: ex. Finger digit (ball injury), patella	Fracture / dislocation, ex. of the ankle
		Haematoma	Neuralgic pain/ nerve compression
		Post surgical complication, ex. reopening of sutured wound	Stings, bites: ex. scorpion, snake, bee, dog bites
		Systemic infection causing pain, ex. head ache and muscle pain associated with tick bite fever or lower abdominal pain during cystits	Dislocation of larger joints, ex. shoulder, elbow
			Large effusion or haematoma following injury

			Combination of injuries associated with possible underlying pathology
			Acute systemic disease causing extreme pain, ex. head ache in meningitis, malaria etc.
			Acute abdomen
			Acute obstruction
			Penetrating wounds, multiple open wounds, Multiple trauma

SUGGESTED MANAGEMENT AND ANALGESIA FOR SPECIFIC PAIN SCORE LEVELS.

PAIN SCORE

'0'= No Pain	'P1'= Mild Pain	'P2'= Moderate Pain	'P3'= Severe pain
Good communication and explanation necessary and usually sufficiant. No specific analgesia required	Simple, accurate and friendly communication & explanation of injury and/ or disease and treatment plan (Age related) Reassurance Distraction with relatively short procedures Guided imagery Relaxation Eliminate stress factors **Physical methods**: • Cooling • Dressing • Elevation • Strapping • Splint **Mild analgesia**: (Decide on appropriate medication, specific dose, and route of administration.) **Paracetamol** **Asperin** **Codeine** **Topical/ Surface anaesthetic** cream, drops or spray	Simple, accurate and friendly communication. (Age related). Explain to patient and parent the specific injury and/ or disease. Make sure they understand necessary procedures, risks involved and expected outcome. Reassurance Distraction, guided imagery & relaxation may help Eliminate stress factors **Physical methods:** • Cooling • Dressing • Elevation • Strapping • Splint Decide on specific and appropriate analgesia, dose and route of administration. **Nitrous Oxide** **Local anaesthetic** infiltration, field block, regional block	Simple, accurate and friendly communication (Age related) Explain to patient and parent the specific injury and/ or disease. Make sure they understand necessary procedures, risks involved and expected outcome. Sign informed consent if applicable Reassurance Distraction, guided imagery & relaxation may help Eliminate stress factors as far as clinically safe and possible **Physical methods:** • Cooling • Dressing • Elevation • Strapping • Splint Decide on specific and appropriate analgesia, dose and route of administration.

		(Ex: *Carbocaine, Lignocaine HCl max safe dose: 3mg/kg; Bupivicaine max dose of 2mg/kg; Prilocaine*) **Topical/ Surface anaesthetic:** (Ex: *Adco-Ethyl Chloride, Amethocaine, Ametop, EMLA 5%, Remicaine, Xylocaine)* **Paracetamol** (*Panado*) **Mefenamic acid** (*Ponstan*) **Asperin** **Codeine** (Combination drugs useful: Ex. *Stopayne*) **Pethedine** **Tilidine** **NSAID**: Where inflammation plays a part of pain (Ex. *Nurofen*) **Re-assess and monitor effect of analgesia**	**Nitrous Oxide** **Local anaesthetic** infiltration, field block, regional block (Ex: *Carbocaine, Lignocaine HCl*) **Topical/ Surface anaesthetic:** (Ex*: Adco-Ethyl Chloride, Amethocaine, Ametop, EMLA 5%, Remicaine, Xylocaine*): For use on skin & mucous membranes, IV cannula insertion, NG tube, urinary catheter, etc. **Opioid agonist:** • **Codeine** • **Tilidine** • **Morphine** • **Tramadol** • **Pethedine** • **Fentanyl** **Check specific dosages for specific route of administration** **Re-assess and monitor effect of analgesia.**

Mild analgesics:

	Dose/ route	Analgesic	Anti-pyretic	Anti-Inflammatory	Approximate cost	Comments
Paracetamol	< 3/12 age , 10 mg/kg. > 3/12 age, 10-15 mg/kg; 4-6 hrly; Max 4 doses/ 24h00. Oral or rectal	Yes	Yes	No	100ml @ R32,13	Avoid in liver disease
Ibuprofen	20 mg/kg in 3-4 divided doses. Oral	Yes	Yes	Yes	200 ml @ R99.23	Avoid in asthma and under 12 months of age or under 10 kg.

Opioid analgesia:

	Route	Dose	Analgesic potency	Respiratory depression	Approxi-mate cost	Comments
Codeine	Oral	1 mg/kg; 4-6 hrly	Mild – moderate pain	+	500ml @ R101.17	Not advised IV: risk of histamine release and anaphylaxis.
Morphine* *(IV: Gold standard for severe pain)*	Oral / rectal/ intra-nasal IV	0.2-0.4 mg/kg prn 4 hrly 0.1-0.2 mg/kg prn, 4 hrly.	Severe pain	++	10mg amp @ R18.75 15mg amp @ R20.69	Poor oral bioavailability; nausea; anxiolytic. Give slow IV bolus, titrate against response.

Diamorphine (In UK)	IV Oral/ intra-Nasal	0.08 mg/kg prn 4 hrly 0.1-0.2 mg/kg 4 hrly	Severe pain	++	IV: £1.10 12p	Shorter duration of action than morphine; less nausea. <u>Intranasal:</u> Volume 0.2 ml / Dose: 0.1 mg/kg: Attach MAD
Fentanyl (Sublimaze)	IV	3-5 mcg/kg	Severe pain	+++	R70.11	Rapid onset, short acting
Pethedine	IV	0.5-1.0 mg/kg	Moderate pain	++	25mg @ R17.73 50mg @ R19.44 100mg @ R20.92	Nausea, dry mouth, constipation.
Tramadol HCl	IV, IM, SC, Oral	50-100mg	Moderate – severe pain	+	100 mg amp @ R38.30 50mg caps @ R7.75	Nausea, constipation. Not recommended under 14 years of age.
Tilidine HCl	Oral	Drops: (1 drop= 2.5 mg). Max: single dose of 1 mg/kg	Moderate – severe pain	++	10ml drops @ R227.40	Nausea, confusion, dry mouth. Overdose may cause convulsions. Not for child under 1 year of age.

Patients who need / receive opioid analgesia, should be carefully selected, adhering to the following guide lines:

- Assess opioid sensitivity
- Monitor dose and effect regularly
- Prescribing to be by a single team as far as possible with proper documentation: Dose, time and complete drug register.
- Patient or guardian must sign informed consent
- Provide additional doses for breakthrough pain.

Opiates can be used even in young infants, provided great care is taken in calculating the dose which should be checked with a second qualified staff member.

***IV Morphine:**

1-3 months: 0.025 mg/kg
3-6 months: 0.05 mg/kg
6-12 months: 0.1 mg/kg
1-12 years: 0.1-0.2 mg/kg,

Administer ***slowly*** over 10 minutes in a ***dilute solution*** (e.g. 1 mg/ml) and titrated against response.

Monitor: Blood pressure, pulse, respiration rate, SaO2, & ECG.

If analgesia is inadequate and there is no sign of respiratory depression, a further, lower dose may be given after not less than 5-10 minutes.

If intravenous access cannot be rapidly achieved, consider intranasal route, if appropriate.

Nerve block: Maximum safe dose of lignicaine 3 mg/kg not to be repeated more than every 4 hours and the maximum dose for bupivacaine is 2 mg/kg.

Splintage: It provides good analgesic support, e.g. Thomas splint or POP back slabs before X-ray.

Entenox: It is a very good interim measure, e.g. while achieving IV access, performing a nerve block, change burns dressings, or move a fractured limb to splint or at x-ray.

ANXIETY SCORE TABLE:

'0'= No anxiety	'A1'= Mild anxiety	'A2'= Moderate anxiety	'A3'= Severe anxiety
	The patient may cry initially and withdraw from any physical touch or examination, but will respond positively after a short while, by using reassurance and/ or play from the parent, nurse, and/ or clinician. The clinician can examine and treat the patient without much difficulty.	The patient may cry, scream, kick, fight and, refuse any physical touch or examination. Clinical examination may be very difficult, but the child will respond positively after a while to reassurance, play or distraction by parent, nurse, or clinician. As soon as the clinician starts to deal with the physical problem again, the patient will start crying and withdraw, which make examination and treatment, difficult, stressful, time consuming and uncomfortable.	A total uncooperative patient who will not allow any physical touch or examination. The child cannot be consoled or convinced that care is needed by using play, reason or distraction. Physical examination and treatment is often impossible. The state of anxiety and fear is often much higher than the physical injury or disease would normally cause. The degree of fear and anxiety can compromise the underlying illness or injury.

ANXIETY SCORE LEVELS AND MANAGEMENT

'0'= No anxiety	'A1'= Mild anxiety	'A2'= Moderate anxiety	'A3'= Severe anxiety
Reassurance No specific medication	Reassurance Distraction, explanation (Age appropriate)	Reassurance Distraction, Explanation (Age appropriate) Patient may need anxiolytic drug **Benzodiasepines:** **Lorazepam** (*Ativan*) Intravenous: 0.1mg/kg [Use ½ dose after opioid has been given] Sublingual: 0.1mg/kg **Diazepam** (*Valium*) Intravenous: 0.1mg/kg Rectal: 0.5mg/kg **May consider for procedural sedation**: (Assure sign of consent form & patient information on drug use) **Ketamine**: *Intramuscular: 2.5mg/kg (With Atropine 0.1mg/kg) *Intranasal: 5mg/kg [When used in combination with a benzodiazepine, 3mg/kg intranasal] *Oral: 3mg/kg *Intravenous: 1mg/kg	Reassurance Distraction, Explanation (Age appropriate) Anxiolytic drug recommended **Benzodiazepines:** **Midazolam** (*Dormicum*) Intranasal: 0.4mg/kg Oral/rectal: 0.5mg/kg Intravenous: 0.1mg/kg **Lorazepam** (*Ativan*) Intravenous: 0.1mg/kg [Use ½ dose after opioid has been given] **Diazepam** (*Valium*) Intravenous: 0.1mg/kg Rectal: 0.5mg/kg **Consider for procedural sedation:** (Assure sign of consent form) **Ketamine** *Intramuscular: 2.5mg/kg (With Atropine 0.1mg/kg) *Intranasal: 5mg/kg [In combination with a benzodiazepine, 3mg/kg intranasal] *Oral: 3mg/kg *Intravenous: 1mg/kg Ketamine may be used in combination with **Midazolam**** (See *advised dosages*)

Cost of midazolam:

- 15mg/3ml @ R86.47
- 50mg/10ml @ R227.92
- 5mg/5ml @ R46.80
- 7,5mg tab @ R8.72

Cost of ketamine:

- 50mg/ml @ R190.00
- 10mg/ml @ R94.00

****For paediatric procedural sedation:**

Advised dosages when **midazolam** and **ketamine** are used in combination:

Intravenous route: Ketamine 1mg/kg + midazolam 0.01mg/kg
Oral route: Ketamine 3mg/kg + midazolam 0.5mg/kg (In flavoured cooldrink)
Intranasal route: Ketamine 2,5mg/kg + midazolam 0,2mg/kg via mucosal atomization device (MAD).

Drug administration:

The **intranasal route** is convenient and safe and can be considered as the route of choice for administering diamorphine in children with acute pain.

Midazolam may have a bitter after taste, while ketamine sometimes causes a mild burning sensation and unpleasant taste, when administered intranasally.

The rich vascular plexus within the nasal cavity, allows drugs that cross the mucous membrane, greater bioavailability than the rectal and oral routes, and avoids the hepatic first metabolism of oral drug administration.

The rate and extent of absorption, and plasma concentrations, are comparable to intravenous drug administration. Good nasal bioavailability can be reached with drugs with molecular weights as high as 6000 Daltons.

The mucosal atomized device (MAD) is the best nasal delivery system, due to good mucosal distribution of the drug. The bioavailability of midazolam via an atomizer is 83%, compared with that of a dropper, which is 50%.

The bioavailability of opioids and ketamine with an atomizer is approximately 50%.

Limiting factors of intranasal use are a blocked, infected, traumatised, painful or bleeding nose.

The **rectal route** can be effective for the administration of benzodiazepines, especially in uncooperative paediatric patients. The drug is absorbed via the inferior rectal vein and also bypass the liver.

DR VG LOFTIE-EATON
[MBChB, DCH, BScMedSc.Hons(O&G)]

CONSENT FORM

For medical or dental investigation, treatment or operation

Hospital .....
Unit Number .....

Patient's Surname .....
Other Names .....
Date of Birth .....
Sex: *(please tick)* Male ☐ Female ☐

DOCTORS OR DENTISTS *(This part to be completed by doctor or dentist. See notes on the reverse)*

TYPE OF OPERATION INVESTIGATION OR TREATMENT

I confirm that I have explained the operation investigation or treatment, and such appropriate options as are available and the type of anaesthetic, if any (general/regional/sedation) proposed, to the patient in terms which in my judgement are suited to the understanding of the patient and/or to one of the parents or guardians of the patient

Signature..... Date .../.../.....

Name of doctor or dentist .....

PATIENT/PARENT/GUARDIAN

1. Please read this form and the notes overleaf very carefully.
2. If there is anything that you don't understand about the explanation, or if you want more information, you should ask the doctor or dentist.
3. Please check that all the information on the form is correct. If it is, and you understand the explanation, then sign the form.

I am the patient/parent/guardian *(delete as necessary)*

I agree
- to what is proposed which has been explained to me by the doctor/dentist named on this form.
- to the use of the type of anaesthetic that I have been told about.

I understand
- that the procedure may not be done by the doctor/dentist who has been treating me so far.
- that any procedure in addition to the investigation or treatment described on this form will only be carried out if it is necessary and in my best interests and can be justified for medical reasons.

I have told
- the doctor or dentist about any additional procedures I would not wish to be carried out straightaway without my having the opportunity to consider them first.

Signature .....

Name .....

Address .....

(if not the patient) .....

.....

NOTES TO:

Doctors, Dentists

A patient has a legal right to grant or withhold consent prior to examination or treatment. Patients should be given sufficient information, in a way they can understand, about the proposed treatment and the possible alternatives. Patients must be allowed to decide whether they will agree to the treatment and they may refuse or withdraw consent to treatment at any time. The patient's consent to treatment should be recorded on this form (further guidance is given in HC(90)22 *(A Guide to Consent for Examination or Treatment.)*

Patients

- The doctor or dentist is here to help you. He or she will explain the proposed treatment and what the alternatives are. You can ask any questions and seek further information. You can refuse the treatment.
- You may ask for a relative, or friend, or a nurse to be present.
- Training health professionals is essential to the continuation of the health service and improving the quality of care. Your treatment may provide an important opportunity for such training, where necessary under the careful supervision of a senior doctor or dentist. You may refuse any involvement in a formal training programme without this adversely affecting your care and treatment.

STATUS EPILEPTICUS IN CHILDREN

Common causes 'Febrile status' (see Febrile convulsions)

- Acute cerebral trauma
- Idiopathic epilepsy
- Bacterial meningitis
- Encephalopathy
- Poisoning

Management:

- **INVOLVE SENIOR STAFF AND PAEDIATRICIANS EARLY**
- High flow Oxygen
- Support the airway and ventilation with adjuncts if necessary