Subanaesthetic concentrations of ether, trichloroethylene, cyclopropane and nitrous oxide can provide analgesia (Dundee, Nicholl and Black, 1962). This property of ether (Artusio, 1955) and cyclopropane (Sheiner, 1958) has been applied to the production of analgesia for surgical procedures but only nitrous oxide and trichloroethylene have been used for postoperative analgesia.

Nitrous oxide has been used more widely. Two different methods have been employed. Low concentrations, 20–25 per cent, will produce moderate analgesia similar to, or greater than, that from narcotics (Chapman, Arrowood and Beecher, 1943; Parbrook, Rees and Robertson, 1964). Slight sedation may accompany the analgesia but other side effects are avoided. High concentrations, of about 50–70 per cent produce the somnolent state of “analgesic anaesthesia” (Petrovsky and Yefuni, 1960, 1962, 1965; Federmesser, 1962). This level is considered in greater detail later.

INDICATIONS FOR NITROUS OXIDE ANALGESIA

Nitrous oxide analgesia differs from that produced by narcotics in that its onset is rapid, the effect is sustained as long as inhalation continues, and the level of analgesia may be quickly controlled by modifying the inhaled gas percentage. There are three circumstances in which nitrous oxide has a special place.

Patients in whom narcotics alone prove inadequate.

The patient who needs to cough up sputum after an upper abdominal operation may find that conventional narcotic therapy gives inadequate relief. In such patients combined therapy with narcotic and low concentrations of nitrous oxide will provide better analgesia (Parbrook et al., 1964; Kaminski and Makowiecki, 1966; Parbrook, 1966). Alternatively, higher concentrations of nitrous oxide will give a state of “analgesic anaesthesia” with potent pain relief (Petrovsky and Yefuni, 1960, 1962, 1965; Federmesser, 1962).

Patients in whom narcotics are relatively contraindicated.

Narcotics carry a special risk of respiratory depression or hypotension. Although this matters little to the fit young patient it is an important consideration in frailer patients or after cardiac or similar major surgery. The respiratory depressant effect may be particularly dangerous in patients in hypovolaemic shock (Robson, 1964), or with chronic bronchitis (Murray and Grant, 1966), or who have received monoamine oxidase inhibitors within the preceding two weeks (Palmer, 1960; Taylor, 1962; Spencer and Smith, 1963).

Nitrous oxide can provide safer and more potent analgesia in these circumstances. Although several new analgesics are at present under assessment, none of them appears to have the freedom from toxic side effects to the circulatory or respiratory systems which characterizes nitrous oxide.

Patients in need of inhalational therapy.

The need for routine postoperative oxygen therapy has been emphasized by Stephen and Talton (1964). Should concurrent analgesia be required, nitrous oxide-oxygen mixtures may be administered without any added inconvenience to the patient.

TECHNIQUES OF ADMINISTRATION OF NITROUS OXIDE

Three techniques are possible: without air dilution, with air dilution, or inhalation of a limited number of deep breaths. With all techniques of continuous therapy humidification is desirable as in oxygen therapy (Wells, Perdva and Kinney, 1963; Rashad et al., 1967).
Without air dilution.

Where a patient has a tracheostomy or an indwelling endotracheal tube the administration of known percentages of nitrous oxide from an anesthetic machine presents no difficulty. Dammann and his co-workers (1963) used 20 per cent nitrous oxide as an analgesic and sedative to enable patients to tolerate an endotracheal tube after thoracic surgery. In a patient with a tracheostomy after cardiac surgery as little as 10 per cent nitrous oxide may suffice for analgesia and sedation (Parbrook, 1967a).

In other patients face masks are tolerated better than during oxygen therapy owing to the sedative effect of nitrous oxide. Standard anesthetic masks may be used with a semiclosed (Magill) circuit (Petrovsky and Yefuni, 1960, 1962, 1965; Pugachev and Kolygin, 1965). Alternatively, the modified airman’s mask illustrated (fig. 1A) may be more comfortable and provide a better fit (Parbrook, 1966).

A system without air dilution is necessary if “analgesic anaesthesia” is used or if the highest possible oxygen level is required.

With air dilution.

Many systems of oxygen therapy are now available which allow air dilution of the administered gas without risks of carbon dioxide build-up and hypoxia when the supply flow is reduced. Several recent reviews have been published (Flenley, Hutchison and Donald, 1963; Cotes, 1965; Winchell, 1965; Bethune and Collis, 1967; Catterall, Kazantis and Hodges 1967; Woods, 1967), and the Siebe Gorman (Cotes), M.C., or Edinburgh masks and nasal cannulae appear specially valuable.

If a premixed cylinder of 50 per cent nitrous oxide and oxygen is available, this is not only convenient but can be used without dilution after the gas flow has been reduced. With this system a modified airman’s mask illustrated (fig. 1B) may be more comfortable and provide a better fit (Parbrook, 1966).

A system without air dilution is necessary if “analgesic anaesthesia” is used or if the highest possible oxygen level is required.

With air dilution.

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oxide/50 per cent oxygen is substituted for the standard oxygen cylinder with such masks then one can administer nitrous oxide percentages in the region of 10–25 per cent, depending upon the mask system and flow rates in use (fig. 1B). The actual percentage will not be accurately known but can be altered according to the patient’s response by controlling the supply gas flow to the mask. The percentage of oxygen administered concurrently with the nitrous oxide will normally range from 27 to 35 per cent depending on the level of nitrous oxide needed.

Petrovsky and Yefuni (1965) describe the use of an air dilution technique with nasal catheters for postoperative pain. Analogous techniques using appropriate masks have been described by Ruben (1966) for dental anaesthesia and Tunstall (1966) for continuous analgesia in childbirth.

**Limited number of deep breaths.**

If only short-term analgesia is required then the appropriate level of analgesia may be obtained by limiting the number of breaths of nitrous oxide-oxygen mixture inhaled. This technique is of historical interest as it was introduced by Klikowitsch (1881) for analgesia in childbirth using an 80 per cent nitrous oxide/20 per cent oxygen mixture. The system is still used in midwifery but with premixed Entonox 50 per cent nitrous oxide/oxygen cylinders and demand valves (fig. 1c). Such a system may be applied to short-term pain relief postoperatively to enable a patient with abdominal pain to cough up retained secretions. The number of deep breaths of the nitrous oxide mixture may be regulated according to the patient’s needs and treatment repeated as required. Patients can be taught to self-administer the gas under supervision but the mask must be a reasonable fit and applied firmly to the face, otherwise air dilution of the inspired gas will occur.

**CHOICE OF TECHNIQUE**

Each of the above techniques has its own special advantages and the choice of technique will depend upon the individual circumstances. The first system (without air dilution) has the advantage that accurate percentages of nitrous oxide can be administered. The second system (with air dilution) allows the use of masks which are “disposable” and more comfortable for the patient. The third technique (Entonox demand valve) is specially suitable for short-term or intermittent analgesia.

The first and third systems were compared in a crossover trial in eighteen postoperative patients to indicate their relative merits for short-term analgesia (Parbrook, 1967b). The improvement of vital capacity from each treatment was used as an index of the degree of pain relief with the nitrous oxide system concerned. The results of this preliminary trial revealed no difference between continuous inhalation of 25 per cent nitrous oxide for 10 minutes, and the inhalation of ten deep breaths of 50 per cent nitrous oxide from a demand valve.

The latter system may have advantages in that the analgesia is induced more expeditiously and that the apparatus is readily available. It may be used to administer nitrous oxide (50 per cent) as an aid to physiotherapy after routine methadone therapy in the postoperative patient, in direct analogy to the use of the gas after pethidine in the patient in labour. The choice of the different narcotic in labour is dictated by the fact that pethidine is less depressant to respiration than other narcotics in the infant (Way et al., 1965) but may be more depressant in adults (Orkin et al., 1955; Foldes and Torda, 1965). In addition, pethidine gives little improvement of vital capacity in the postoperative patient as compared with methadone (Masson, 1962).

Nitrous oxide may benefit the pain arising on coughing, not only from upper abdominal wounds but also from thoracic, laminectomy and other wounds or from fractured ribs. It also warrants trial in other painful postoperative conditions (Nunn, 1966).

**SHORT-TERM USE OF “ANALGESIC ANAESTHESIA”**

Potent analgesia together with somnolence, marked amnesia and a tendency to dream characterize “analgesic anaesthesia”. High concentrations of nitrous oxide, generally between 50 and 70 per cent are used, but it is necessary to avoid too deep a level with loss of contact with the patient.

Federmesser (1962) and Barth and Lüder (1966) give full descriptions of the exacting techniques for application of these analgesic levels. The analgesia is adequate for painful dressings, incision of abscesses, and other minor surgical procedures, but Barth and Lüder advise against its
use for minor gynaecological procedures in view of the risk of dreams and consequent accusations of immorality against the surgeon.

The absence of any toxicity or after effects makes the technique ideal for a desperately ill postoperative patient who requires further minor surgery. As an example the author may quote an elderly frail patient with postoperative peritonitis and colovesical fistula after cancer surgery. He had electrolyte imbalance, productive cough and uraemia. He required immediate minor surgery to his colostomy even though it was felt he might not survive the procedure. “Analgesic anaesthesia” with a maintenance level of 60 per cent nitrous oxide/40 per cent oxygen proved satisfactory and obviated the risk of anaesthetic mortality.

LONG-TERM USE OF NITROUS OXIDE ANALGESIA
The duration of continuous long-term nitrous oxide analgesia is limited by the risk of leucopenia (Lassen et al., 1956; Green and Eastwood, 1963; Parbrook, 1967c). It may be wisest to limit the duration of such treatment to 24 hours, though there is evidence that even 48 hours may be safe (Petrovsky and Yefuni, 1965; Pugachev and Kolygin, 1965).

Russian workers have the greatest experience of long-term nitrous oxide. Petrovsky and Yefuni (1960, 1962, 1965) in their studies in adults, and Pugachev and Kolygin (1965) in their studies in children found nitrous oxide analgesia much better than alternative systems with narcotics after thoracic and other major surgical procedures.

Contraindications to nitrous oxide analgesia.
Apart from the leucopenic effect of nitrous oxide mentioned above, the gas is virtually non-toxic. Care is required in patients with abdominal distension, pneumothorax or after air encephalography as the gas will diffuse into such air pockets and increase their volume (Hunter, 1955; Saidman and Eger, 1965; Eger and Saidman, 1965). All these diffusion effects and the “diffusion anoxia” described by Fink (1955) are less with analgesic than with anaesthetic levels of nitrous oxide.

TRICHLOROETHYLENE ANALGESIA
Trichloroethylene, administered by Emotril inhaler has been found to give effective pain relief as an aid to physiotherapy (Ellis and Bryce-Smith, 1965). The patients, after abdominal surgery, inhaled several deep breaths of 0.5 per cent trichloroethylene prior to coughing.

A comparative study of nitrous oxide and trichloroethylene in the postoperative period (Parbrook, 1967b) indicated that nitrous oxide gave the greatest improvement of vital capacity but continuous trichloroethylene was not investigated. Hovell, Masson and Wilson (1967) assessed the analgesia from 10 minutes continuous inhalation of 0.5 per cent trichloroethylene in postoperative patients and found that 50 per cent of patients experienced moderate to good pain relief.

Although trichloroethylene is simple to administer, its analgesia has a slower onset than that of nitrous oxide and may be associated with unpleasant after-effects or “hangover” (Dundee and Moore, 1960).

There remains a possibility of other potent inhalational analgesics being discovered as a compound, tetrafluorobenzene, has been found to give excellent analgesia without loss of consciousness in mice (Neal and Robson, 1965).

CONCLUSIONS
Nitrous oxide-oxygen mixtures can be used to provide postoperative analgesia. They are of value when narcotics give inadequate analgesia or are contraindicated, and in patients receiving oxygen therapy. Low concentrations of nitrous oxide provide analgesia without side effects but, alternatively, high concentrations—“analgesic anaesthesia”—may be used.

The gas mixture may be administered without air dilution, with air dilution, or for a limited number of deep breaths. Ten deep breaths of 50/50 premixed gas are equivalent to continuous inhalation of 25 per cent nitrous oxide. Such a technique of deep breaths may be of value as an aid to postoperative physiotherapy.

Long-term nitrous oxide must be limited to 24 or 48 hours to avoid risk of leucopenia. Trichloroethylene has also been used as a postoperative analgesic.

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REFERENCES


INHALATIONAL ANALGESIA IN THE POSTOPERATIVE PERIOD


BOOK REVIEW


This number of the Postgraduate Medical Journal is devoted to publishing the proceedings of an international symposium on intensive therapy which was held in Liverpool in September last year.

The symposium starts with an account of monitoring during intensive patient care by Dr. Cliffe, while the problem of presenting the information derived from monitoring to the medical and nursing staff is imaginatively but too briefly discussed by Mr. Wolff. There follows a lucid account of the indications for oxygen therapy contributed by Dr. Howell in which, however, pulmonary oxygen toxicity is dismissed as a "theoretical danger".

Not everyone would agree with this, especially when 100 per cent oxygen is administered continuously by endotracheal or tracheostomy tube. Dr. McNichol's account of intensive care of patients following acute myocardial infarction is most informative. This is one field in which a quantitative assessment of the value of intensive care is available; the mortality rate is approximately halved.

Then follows a paper entitled "Cardiogenic shock treated with infusion of dextrose solution" by Dr. Nixon and co-workers, which is subjected to detailed appraisal in the ensuing discussion. Indeed, one of the best features of this symposium is the lively and informed discussion periods during which many topics of current interest to anaesthetists are covered, e.g. tissue oxygenation and the value of lactate/pyruvate ratios, renal perfusion during induced and haemorrhagic hypotension.

Next come two papers on status asthmaticus; the first, by Dr. Rees, is a general review of medical treatment, in which the considerable mortality from this oft-underplayed condition is emphasized. Drs. Riding and Ambiavagar then set out a very clear account of their therapeutic regime for dealing with these desperate cases, which includes bronchial lavage and IPPV with a fixed volume ventilator. An important point in this paper is the finding of large gastric residues in patients in status asthmaticus and this should engender caution in the use of IPPV by facemask as is suggested elsewhere in the symposium.

The place of IPPV in the management of chronic respiratory failure is considered by Dr. Kristensen and co-workers, who were, of course, one of the pioneer groups in this field. The question of long-term endotracheal intubation in place of tracheostomy in these patients is considered in the subsequent discussion. The place of IPPV following chest injuries is discussed by Dr. Ambiavagar who emphasizes the important lack of correlation between the extent of bony damage to the chest wall and the functional derangement of respiratory gas exchange.

There then follow two papers on intensive care of surgical patients, the first by Dr. Lawson and the second by Drs. Norlander and Norden. In the latter paper the possibility of ventilator sterilization with 70 per cent alcohol nebulized in the ultrasonic nebulizer is considered; this leads to an excellent discussion of the problems of cross-infection in intensive care units.

The two papers on renal problems by Drs. Luke and Kennedy and by Dr. Blagg present this complex subject most clearly and helpfully for the anaesthetist. The differential diagnosis of oliguria is dealt with in great depth and the relative indications for peritoneal or haemodialysis are given.

The often neglected subject of metabolic balance in severely ill patients is covered by papers by Drs. Hallberg and co-authors and by Dr. Peaston. The latter paper is especially rewarding, for it makes very clear the hopeless inadequacy of commonly employed intravenous therapy. As Dr. Peaston concludes, "the desperately ill should not be allowed to live on their own muscle protein by a process of endogenous cannibalism". After all, a good deal of muscle is required if the patient is ever to be weaned from his ventilator.

Dr. Sherwood Jones concludes the symposium, which he was largely responsible for organizing, with a discussion of the administration of intensive patient care.

This number of the Postgraduate Medical Journal will certainly be read by all engaged in this field of practice. It is, however, also recommended to those who are called upon only intermittently to deal with cases requiring intensive therapy, since it contains a mass of very practical advice. Finally the trainee preparing for the Final part of the F.F.A. will find it invaluable, especially if he has not the opportunity of himself working in an intensive care unit.

D. Gordon McDowall