ABC of Poisoning

JOHN HENRY
GLYN VOLANS

ANALGESICS: OPIOIDS

The opioid analgesics have long provided the medical profession with one of its most important assets: the power to relieve pain. Their effects are produced through the opioid receptor, and their analgesic potency varies from extremely powerful (drugs such as morphine, heroin, and pethidine) to mild (drugs such as codeine and dextropropoxyphene). They also possess psychotropic effects and cause euphoria and hallucinations. They slow the gut, constrict the pupil, and depress the central nervous system, causing sedation, suppression of the cough reflex, and depression of respiration. The more potent opioids, in particular, are prone to addiction and abuse, which is a major drawback to their use. Members of this group of drugs can be toxic in overdose, and this article deals with acute opioid toxicity and its management.

Opioids and products containing opioids

Heroin, morphine, pethidine, and papaveretum (Omnopon) are well known narcotic agents, but many of the drugs on this list may not be thought of as potent opioids. Pentazocine, dextromoramide, dihydrocodeine, and dextropropoxyphene are widely regarded as mild analgesics, but their effect in overdose may be just as lethal as an overdose of heroin. All these agents can cause fatal respiratory depression as little as one hour after ingestion, particularly if taken with alcohol. Diphenoxylate (combined with atropine as Lomotil) is used as an antidiarrhoeal agent but overdose can produce severe opioid effects. Many proprietary preparations available over the counter as cough mixtures, pain relievers, antidiarrhoeal agents, and sedatives contain small amounts of opioids, which when taken in overdose by an adult or administered to a young child may produce severe toxicity. Etorphine is a potent and rapidly acting opioid used as a tranquilliser and anaesthetic agent for animal use; it is provided with its own antidote, diprenorphine (Revivon). This agent or naloxone may be used as an antidote in an emergency.

Morphine	Buprenorphine	Dihydrocodeine
Heroin	Nalbuphine	Diphenoxylate
Pethidine	Meptazinol	Loperamide
Methadone	Dextropropoxyphene	Etorphine
Dipipanone	Codeine	etc
Pentazocine		

Presentation and immediate management

Opioid poisoning may be a life threatening emergency. It produces the classical triad of symptoms: pinpoint pupils, respiratory depression, and coma. The most immediate problem is respiratory depression, which may lead to respiratory and cardiac arrest. The cardinal feature of respiratory depression due to opioid toxicity is a slowing or irregularity of the respiratory rate due to a direct effect on the respiratory centre. Cyanosis is a late and serious sign.

Naloxone is a specific opioid antagonist, and respiratory depression due to suspected opioid overdose is an indication for its urgent administration. If, however, central cyanosis, respiratory arrest, convulsions, cardiac arrhythmias, or cardiac arrest have occurred, resuscitation, including assisted ventilation, takes precedence. Ventilation should be started at once using the mouth to mouth method or a Brook airway or Ambu bag.

If the patient is breathing spontaneously, or ventilation is supported, naloxone (0.8-2.0 mg) should be given intravenously and the patient observed for three minutes. Any change in the pupil size, respiratory rate, or state of consciousness should be regarded as a positive response. If recovery is minimal or only partial, a further dose of naloxone should be given. If the history or physical signs suggest opioid poisoning but the first bolus of naloxone produces no response further doses of 1.2-2.0 mg should be given until a response occurs or until 4-10 mg naloxone has been given.

Further management

Serial arterial PCO₂ estimations before and after 0.4 mg and 0.8 mg boluses of naloxone and during intravenous infusion

Naloxone has a plasma half life of one hour, but its peak effect after an intravenous bolus often lasts only about 10 minutes. Repeated doses should be administered at frequent intervals as required. In some cases an intravenous infusion may be required; doses of up to 5 mg/hour may be necessary. Prolonged infusions (for several days) may be required for overdoses of long acting opioids such as methadone. Intramuscular injections of naloxone may be used, particularly when the patient is in transit, but the patient must be closely monitored.

It should be clear from the above that there is no fixed dosage schedule. The dose of naloxone must be decided on the basis of the patient's clinical response in each case, and amounts far greater than the "usual" doses may need to be given. If naloxone is unavailable or the supply has run out supportive ventilation may be necessary.

Coma of unknown origin

Dilated pupils in opioid overdose

- 1 Hypoxia
- 2 Hypothermia
- 3 Hypoxic cerebral damage
- 4 Pethidine

Naloxone has both a diagnostic and a therapeutic role in coma of unknown origin when opioid overdose is a possibility. Small pupils, respiratory depression, and deep coma suggest that opioids may be responsible, but organophosphorus compounds may also cause a similar picture. The diagnosis should be reviewed if adequate doses of naloxone fail to produce a response. Hypoxia due to opioid poisoning can cause dilated pupils, which become small when oxygenation is adequate. If anoxic brain damage has occurred the pupils may remain dilated even after adequate oxygenation and dosage with naloxone. Hypothermia also causes dilated pupils even when due to opioids alone, and there may be no response to naloxone if hypothermia is profound. An absent or partial response may also occur if the patient has taken other central nervous system depressants or suffered hypoxic brain damage.

Opioid overdose in addicts

Narcotic addicts occasionally mistake the dose or the strength of their "fix." After intravenous administration there may be rapid onset of deep coma and respiratory depression. On examination there may be needle marks or "tracks" along veins in addition to the signs of opioid poisoning. Because addicts develop tolerance, and so take large doses of opioid, quite large amounts of naloxone are often needed. The patient may rapidly recover consciousness, may be violent, and usually wants to leave at once. If possible, however, the patient should be admitted and observed since coma and respiratory depression may recur. Naloxone not only reverses the symptoms of opioid poisoning in addicts but may also precipitate an acute withdrawal syndrome within minutes of administration. The symptoms may last for minutes or hours and include agitation, vomiting, abdominal cramps, nausea, diarrhoea, sweating, piloerection, vasoconstriction, and even convulsions.

The fact that the patient is known to be a narcotic addict is no contraindication to the use of naloxone, simply a note of caution. Further advice on the law relating to addicts and the notification of addicts may be found in the British National Formulary.

Complications

Pulmonary oedema in a narcotic addict. The patient had taken an overdose of heroin and was found lying on his left side.

Respiratory depression is the most important complication of opioid poisoning, but other complications may also cause difficulties in management.

Hypotension—may result from central nervous depression and opioid induced histamine release. The central venous pressure should be measured and fluids given to increase the pressure, after which inotropic agents should be given as required. Dextropropoxyphene also has a potent cardiodepressant effect which does not respond to naloxone.

Hypothermia—Muscle hypotonia and peripheral vasodilatation can accentuate body cooling due to exposure, causing severe hypothermia. The pupils will be dilated and the response to naloxone minimal or absent. The core temperature should be measured and appropriate treatment given. The prognosis is usually good.

Convulsions—Many opioids have convulsant properties, and cerebral hypoxia, as well as causing convulsions in its own right, can lower the convulsant threshold. The first step is to ensure adequate oxygenation and then to assess the effect of naloxone, after which conventional treatment can be given.

Non-cardiogenic pulmonary oedema—or the adult respiratory distress syndrome—is serious and potentially fatal; it is particularly seen with heroin and codeine overdose. It does not respond to diuretics or naloxone. Mechanical ventilation with positive end expiratory pressure is necessary.

Rhabdomyolysis—Pressure necrosis of muscle can occur in prolonged deep coma, but opioid induced rhabdomyolysis not due to pressure has also been described. Myoglobinuric renal failure may result, and if rhabdomyolysis has occurred adequate hydration is essential.

Combination analgesics

<u>Aspirin plus codeine:</u>	Aspirin and codeine tablets BP, Antoin*, Codis, Hypon*										
<u>Paracetamol plus codeine:</u>	Medocodene, Neurodyne, Panadeine, Paracodal, Para-Hypon*, Parake, Paralgin*, Pardale*, Pharnidone*†, Propain**†, Solpadeine*, Synda**										
<u>Aspirin plus paracetamol:</u>	Safapryn										
<u>Aspirin plus paracetamol plus codeine:</u>	Aspirin, paracetamol and codeine tablets BP, Myolgin*, Safapryn-Co										
<u>Dextropropoxyphene and paracetamol:</u>	Distalgic, Cosalgic										
<u>Dextropropoxyphene plus aspirin:</u>	Dolasan, Doloxene Compound*, Napsalgic										
Others:	<table> <tr> <td>Paracetamol plus dihydrocodeine</td><td>Paramol</td></tr> <tr> <td>Paracetamol plus morazone</td><td>Delimon</td></tr> <tr> <td>Paracetamol plus pentazocine</td><td>Fortagesic</td></tr> <tr> <td>Aspirin plus ethoheptazine</td><td>Zactrin</td></tr> <tr> <td>Aspirin plus ethoheptazine + meprobamate</td><td>Equagesic</td></tr> </table>	Paracetamol plus dihydrocodeine	Paramol	Paracetamol plus morazone	Delimon	Paracetamol plus pentazocine	Fortagesic	Aspirin plus ethoheptazine	Zactrin	Aspirin plus ethoheptazine + meprobamate	Equagesic
Paracetamol plus dihydrocodeine	Paramol										
Paracetamol plus morazone	Delimon										
Paracetamol plus pentazocine	Fortagesic										
Aspirin plus ethoheptazine	Zactrin										
Aspirin plus ethoheptazine + meprobamate	Equagesic										
Also contains caffeine *											
Contains diphenhydramine †											
Contains doxylamine ‡											

A number of formulations contain two analgesic drugs with the aim of combining the benefits of a centrally acting agent (usually an opioid) with those of a peripherally acting agent (aspirin, paracetamol, or a non-steroidal anti-inflammatory drug). When a combination analgesic is taken in overdose, the effects of the different constituents must be taken into account, so that the symptoms are understood and the appropriate treatment given. Many of these preparations contain very small amounts of opioid—for example, 10 mg or less of codeine per tablet. Thus, with these drugs most patients do not take a significant overdose of the opioid. Nevertheless, serious overdoses with combination analgesics do occur.

Centrally acting analgesics tend to produce drowsiness and coma in overdose, and in the case of opioids, naloxone should be given. The frequent use of compound analgesics is one of the reasons why plasma salicylate and paracetamol levels should be measured in every patient who is comatose due to suspected drug overdose. Compounds of salicylate plus an opioid may produce the signs of opioid overdose, but with rapid respiration due to salicylate toxicity. When the compound contains paracetamol, antidotal treatment for paracetamol poisoning should be given without delay. The constituents and trade names of the more commonly prescribed combination analgesics are listed.

Dr John Henry, MRCP, is consultant physician and Dr Glyn Volans, MD, FRCP, director, National Poisons Information Service, Guy's Poisons Unit, New Cross Hospital, London SE14 5ER.

The illustration of a naloxone infusion was reproduced, by permission, from Parker S G, Thomas D G, *Br Med J* 1983;287:1547.

What are the differences between British and American use of the terms "anaesthetist" and "anesthesiologist"? Is anesthesiology a recognised specialty in Britain and, if so, what is the specialist called? When was the specialty given official recognition?

Because the history, organisation, and practice of administering anaesthetics in Britain and America differ, precisely equivalent terms do not exist in all aspects of this specialty. The suffix -logy implies the study and practice of a learned discipline. Anesthesiology is thus the scientific and clinical basis of anaesthesia and related fields, including resuscitation, the respiratory and haemodynamic aspects of intensive care, and the relief of pain. The British term is anaesthetics, but "anaesthetics" is also used for the agents that induce anaesthesia. The context precludes ambiguity. Although "anesthesiology" would seem to be more appropriate etymologically, there is a strong British distaste for polysyllables.

In the United States an anesthesiologist is a qualified medical practitioner with specialised training in anesthesiology and is officially recognised as such if the training comprised a recognised course and if a certificate is obtained from the American Board of Anesthesiologists. In the United Kingdom the successful candidate, on passing the examination of the faculty of anaesthetists of the Royal College of Surgeons, is awarded the fellowship (FFARCS).

In the United Kingdom the generic term anaesthetist may be applied only to any medically or dentally qualified and registered practitioner who administers an anaesthetic. Usually the anaesthetist would be a FFARCS, and virtually always in hospital practice, except for those in training. Some dentists and a few family practitioners may anaesthetise for dental surgery and may be called anaesthetists when acting in that capacity. It is hoped to establish standards of proficiency in this area.¹ By contrast, the term anesthetist in the United States refers to physicians with a modest amount of training in anaesthesia who practise part time. They are mostly family

practitioners, usually in rural or otherwise isolated areas. A further difference exists in the nursing profession. In the United States a qualified nurse may take a two years' course in anaesthetics and may then legally administer anaesthetics under the supervision of a physician. They qualify as certified registered nurse anesthetists (CRNA) on passing an examination. In smaller hospitals in rural areas the nurse anesthetist would be supervised by the operating surgeon. In the United Kingdom nurses have never been allowed to administer general anaesthesia, though midwives may administer nitrous oxide 50% (Entonox) for analgesia.

No date can be given for the first official British recognition of anaesthetics as a specialty. Ever since Squire gave the first general anaesthetic at University College Hospital in 1846, administration of general anaesthetics has been the prerogative of qualified doctors and dentists. In the late 1920s and early '30s some anaesthetists at teaching hospitals were also part time physicians. By the mid-1930s they were all exclusively specialists at the university teaching hospitals, whereas at the smaller hospitals they might be family doctors or resident medical officers (interns). The Diploma in Anaesthetics, established in 1935 by the Conjoint Examining Board and later continued under the aegis of the Royal College of Surgeons, was granted after appropriate training and passing a qualifying examination. In 1948 the diploma became obligatory in obtaining a hospital appointment as consultant anaesthetist. Meanwhile the Royal College of Surgeons established a fellowship in a faculty of anaesthetists which was granted by election, and in 1952 the fellowship was obtainable by success in an examination. The FFARCS seems to be displacing the diploma as a requirement for senior posts.—B J FREEDMAN, consultant, London.

¹ Inter-faculty working party formed to consider implementation of the Wylie Report. Report. (Chairman Professor G R Seward, 1981.) Quoted by Sykes P. Dental anaesthesia—what next? *Dental Practice* 1984;22:10-2.