

## MORPHINE

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### Structure.

Morphine is obtained from opium, the juice secreted by the seeds of the poppy. It works on several types of receptors, widely found in nervous tissue. "Opioids" is a term used for all drugs that act on these receptors. These other opioids may be natural occurring substances, such as morphine, or made in the laboratory such as pethidine.

Morphine works on receptors in the cell membranes. These are protein-lipid molecules that alter their shape when stimulated to effect molecular changes within cells. There are thought to be three types of receptors that respond to opioids, mu, kappa and lambda. Morphine acts mainly on mu receptors to cause a wide variety of effects. The most important of these are relief of pain and respiratory depression. In anaesthesia morphine is used to relieve pain. This is an effect of its action on the spinal cord to decrease the transmission of painful stimuli from body to brain, and its action within the brain itself.

### Side Effects.

Morphine has many side effects. The most dangerous is respiratory depression. Minor degrees of respiratory depression may be detected following standard doses of morphine, but this is not clinically important. With higher doses or in frail patients, the respiratory rate decreases, the patient becomes increasingly sedated, and the pupils very small. Common side effects are nausea and vomiting due to a central action of morphine stimulating one of the centres in the brain concerned with vomiting called the chemotactic trigger zone. Other central nervous system side effects of morphine are cough suppression, sedation, and dependence leading to addiction. Addiction is not a problem when morphine is used to treat acute pain after surgery; sufficient morphine should always be given to relieve the pain.

Morphine also has an effect on the muscle of the bowel and urinary tract, causing the sphincter to contract and reduce the peristalsis (the wavelike movements of the bowel muscle that propel its contents forwards). This results in a delayed

emptying of the stomach, constipation, and may also lead to urinary retention.

Morphine can also cause histamine release, which causes itching of the skin and nose and a mild flushing of the skin. Morphine has little direct effect on the heart or blood pressure. However the blood pressure may fall slightly following the pain relief produced by morphine and also with the sedation which may be produced. Significant hypotension following morphine is usually due to other causes such as hypovolaemia. Occasionally patients with severe asthma may become wheezy. An unimportant, but early noticeable effect is that the pupils become small. This helps to differentiate respiratory depression caused by morphine from other causes.

### Precautions.

All patients who have been given morphine must be carefully observed for evidence of respiratory depression. This can be detected as a slow respiratory rate and a very sleepy patient with pin point pupils. Oxygen should be given by face mask, and positive pressure ventilation of the lungs started if necessary. Naloxone, 100-400 micrograms may be given intravenously if available.

### Dose and Uses

Morphine can be given orally, rectally, by intramuscular or intravenous injection, subcutaneously, sublingually, or injection into the epidural or subarachnoid space. The dose for analgesia by IM injection is 100-150mcg/kg, repeated 2 hourly as required. The dose used intravenously during anaesthesia depends on the nature and duration of the surgery. The usual dose given at the start of surgery when intermittent positive pressure ventilation is used is 100-200mcg/kg, followed by required additional doses of 1-2mg intravenously when required. After the patient has woken up further doses of 1-2mg may be given until the patient is free of pain. Much higher doses are sometimes used during specialist surgery such as cardiac or neurosurgery.

Morphine can be given to relieve chronic pain especially from cancer. Much higher doses are needed orally than by injection. The oral dose is very variable for individual patients; sufficient should be given to relieve the pain.

Morphine can be given into the epidural or subarachnoid space. This is to deliver the morphine close to one of its sites of action, the spinal cord. It is thought that pain relief of long duration can be obtained with very low doses of morphine. A single dose of epidural morphine may relieve pain for 12-24 hours. The usual adult dose for epidural morphine is 3-7 milligrams, and of subarachnoid morphine between 250mcg and 1mg. The main risk of this technique is that severe respiratory depression may occur up to 18 hours after the initial injection

because of the slow circulation of cerebral spinal fluid which carries the morphine up to the brain to act on the respiratory centre. It is vital that all those caring for a patient who has had this technique are aware of the potential side effects and watch out for them. This technique can only be used in specialist hospitals with intensive care facilities. In all other aspects the side effects of epidural and subarachnoid morphine are similar to morphine given by any other route.