1. **Constipation:** this common side effect may cause nausea, vomiting and abdominal cramps and if extreme, may produce overflow diarrhoea. A useful definition of constipation is: a decrease in the frequency of bowel movements, passage of hard stools that may be difficult to pass.

As well as delaying gastric emptying, and stool transit through the small bowel, opioids decrease propulsive peristalsis, dry out the stool and may also affect the urge to defaecate.

Prevention strategies include: (a) increased dietary fibre(e.g. high fibre cereal, apple sauce, prune juice, rhubarb); (b) increased fluid intake (c) adequate exercise if possible (d) adequate time and privacy for toileting.

Several options are available to treat constipation:

(a) **osmotic laxatives** (disaccharides and saline cathartics) Disaccharides exert an osmotic effect as they are not absorbed by the bowel, thereby increasing bulk, but they may cause cramps, abdominal distension and flatulence. Milk of magnesia, a saline cathartic, uses osmotic forces to pull fluid into the bowel to increase the weight of the stool and soften it.

(b) **emollient or lubricant laxatives** : e.g. docusate sodium, glycerin suppositories.

(c) **bulk cathartics:** increase the mass and soften stool e.g psyllium (Metamucil)

(d) **stimulant cathartics**: these promote intestinal motility and may be given orally or rectally: e.g. senokot. They may cause painful cramping, but this can be minimised by giving small doses with each meal and a slightly larger dose at bedtime.

(e) **naloxone**: has been found to be useful in opiate-induced constipation.. but it causes withdrawal symptoms as it is an opiate antagonist, so is not recommended.

(f) **combination preparations** : e.g senna-S which is docusate+senna, a useful combination in narcotic-induced constipation.

(g) **enemas:** may be necessary: breaks up and washes out impacted faecal matter. Should only be used sparingly.

(h) **Mestinon** 60mg half-1 tablet 3-4 times a day may help : this drug is usually used to treat a condition called Myasthenia gravis and may also relieve dry mouth.

2. **Sedation:**

(a) eliminate contributory factors such as non-essential drugs and metabolic disturbance;

(b) reduce opiate dose if possible

(c) add in an adjuvant such as an antidepressant in order to be able to reduce the opiate dose required

(d) switch to a different opioid

(e) consider more invasive methods

3. **Mental clouding:** cognitive impairment may be managed in a similar way to sedation. Confusional state may require low dose haloperidol.

4. **Nausea and vomiting:** persistent nausea is uncommon. Transient problems can be relieved by using agents such as promethazine, prochlorperazine, metoclopramide or hydroxyzine. A typical prescription might be phenergan 25mg every 4-6 hours.

Stemetil can be taken buccally which allows rapid absorption if vomiting precludes usual oral administration. Hydromorphone and levorphanol seem to cause less nausea than other opioids. Severe nausea and vomiting may require rehydration with intravenous fluids and other causes need to be excluded. Treatment of constipation as a contributory factor may be required.

5. **Fluid retention:** swelling in the feet and lower legs is quite common. It may be due to fluid retention or to vascular dilatation caused by opioids. A low salt diet, restriction of fluid intake and possibly administration of mild diuretics such as Lasix may assist. (these may cause some loss of potassium which might slightly increase symptoms such as muscle weakness, but can be avoided by eating plenty of fruit and vegetables, especially bananas)

6. **Headache:** opioids taken regularly may cause a daily low-grade headache known as "rebound headache." They are of a vascular type, generally throbbing in the back of the head or forehead and temple region. In susceptible patients, migraine headaches may be triggered. Simple headaches may respond to mild analgesics such as paracetamol (acetaminophen) or aspirin whilst migraines may be prevented or aborted by ritalin.

7. **Insomnia:** this is a paradoxical effect of opioids. Using an opioid that causes sedation may overcome this: a sustained-release formula can be used at night. Some patients have benefited from using melatonin, which is a hormone involved in induction of sleep.

Failure of these strategies may be addressed by adding in an anti-depressant medication at

night such as trazadone(50-100mg) or nortriptyline(25-50mg). Use of benzodiazepines such as oxazepam, temazepam or diazepam should be restricted to short-term use (up to 2 weeks) only due to the high risk of dependence and tolerance.

Use of caffeine early in the day to boost energy and promote daytime activity may help to encourage sleepiness at night.

8. **Myoclonus**: it is not a common clinical problem and is benign, but may be distressing for the patient. Measures such as clonazepam or valproate may alleviate the symptoms. If myoclonus is persistent it may be worthwhile changing to a different opiate. Of course, myoclonus may be a part of the underlying condition.

9. **Pruritus:** (itching): this rarely persists chronically and can be relieved by diphenydramine if it occurs during the initial treatment phase. Itching associated with a rash suggests an allergic problem and may indicate the need to change to a different opioid preparation.

10. **Urinary retention:** this is rare as a chronic problem due to opioid therapy and may be treated using bethanecol. Underlying neurological or urological problems are more likely to be the cause of this symptom if it is persistent.

11. **Decreased libido:** men may experience decreased libido and potency that can be relieved by supplemental testosterone administered orally or by injection.

12. **Respiratory depression:** generally not a significant problem as pain itself antagonises the respiratory depressive effect of opiates; however, if the dose is too high, it may occur. The least possible efficacious dose of naloxone is given in order to preserve analgesia and avoid withdrawal.

13. **Withdrawal syndrome:** if the medication is abruptly discontinued, anyone who has been taking opioids regularly is likely to suffer from : increased pain (plus hypersensitivity), generalised aches, cold sweats, restlessness, tremor, involuntary movements, dizziness, nausea, vomiting, diarrhoea, sneezing and yawning. Heart rate and blood pressure may rise.

These symptoms usually occur within 8-12 hours of the last dose and are likely to peak at 48-72 hours. If it is proposed to discontinue opiate medication, reducing the dose gradually by 10-20% every 3-6 days may reduce the severity of any withdrawal symptoms.

Clonidine 0.1-0.3 mg (1-2 tablets) every 6-8 hours may alleviate the symptoms (or it can be administered as a patch). Tranquillisers such as diazepam (valium) 5-10mg every 6 hours may reduce agitation and tremors.