Syringe drivers

A syringe driver should be considered in the palliative care setting when a patient is unable to take oral medication due to nausea, dysphagia, intestinal obstruction, weakness or coma. In the UK there are two main types of syringe driver:

- Graseby MS16A (blue): the delivery rate is given in mm per hour
- Graseby MS26 (green): the delivery rate is given in mm per 24 hours

The majority of drugs are compatible with water for injection although for the following drugs sodium chloride 0.9% is recommended:

- granisetron
- ketamine
- ketorolac
- octreotide
- ondansetron

Commonly used drugs

- nausea and vomiting: cyclizine, levomepromazine, haloperidol, metoclopramide
- respiratory secretions: hyoscine hydrobromide
- bowel colic: hyoscine butylbromide
- agitation/restlessness: midazolam, haloperidol, levomepromazine
- pain: diamorphine is the preferred opioid

Mixing and compatibility issues

- diamorphine (the most commonly used drug) is compatible with the majority of other drugs used including cyclizine*, dexamethasone, haloperidol, hyoscine butylbromide, hyoscine hydrobromide, levomepromazine, metoclopramide, midazolam
- cyclizine is incompatible with a number of drugs including clonidine, dexamethasone, hyoscine butylbromide (occasional), ketamine, ketorolac, metoclopramide, midazolam, octreotide, sodium chloride 0.9%

*precipitation may be seen at higher doses

Cyclizine may occasionally precipitate when mixed with hyoscine butylbromide but can be safely combined with hyoscine hydrobromide.

Palliative care prescribing: pain

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

Opioid side-effects

Usually transient	**Usually persistent**
Nausea	Constipation
Drowsiness	

Conversion between opioids

From	**To**
Oral codeine	Oral morphine Divide by 10
Oral tramadol	Oral morphine Divide by 5

From	**To**
Oral morphine	Oral oxycodone Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted. NICE give the following advice on conversion:

- a transdermal fentanyl 12 microgram patch equates to approximately 45 mg oral morphine daily

- a transdermal buprenorphine 20 microgram patch equates to approximately 30 mg oral morphine daily.

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

It is recommended that patients take **one-sixth of their total oral morphine** dose for breakthrough pain.

Colorectal cancer: referral guidelines

NICE recommend the following patients are referred urgently (i.e. within 2 weeks) to colorectal services for investigation:

- patients > 40 years old, reporting rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency persisting for 6 weeks or more
- patients > 60 years old, with rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without anal symptoms
- patients > 60 years old, with a change in bowel habit to looser stools and/or more frequent stools persisting for 6 weeks or more without rectal bleeding
- any patient presenting with a right lower abdominal mass consistent with involvement of the large bowel
- any patient with a palpable rectal mass
- unexplained iron deficiency anaemia in men or non-menstruating women (Hb < 11 g/dl in men, < 10 g/dl in women)

Spinal cord compression

Spinal cord compression is an oncological emergency and affects up to 5% of cancer patients. Extradural compression accounts for the majority of cases, usually due to vertebral body metastases. It is more common in patients with lung, breast and prostate cancer

Features

- back pain - the earliest and most common symptom - may be worse on lying down and coughing
- lower limb weakness
- sensory changes: sensory loss and numbness
- neurological signs depend on the level of the lesion. Lesions above L1 usually result in upper motor neuron signs in the legs and a sensory level. Lesions below L1 usually cause lower motor neuron signs in the legs and perianal numbness. Tendon reflexes tend to be increased below the level of the lesion and absent at the level of the lesion

Management

- high-dose oral dexamethasone

- urgent oncological assessment for consideration of radiotherapy or surgery

Testicular cancer

Testicular cancer is the most common malignancy in men aged 20-30 years. Around 95% of cases of testicular cancer are germ-cell tumours. Germ cell tumours may essentially be divided into:

- seminomas
- teratomas

Other type of germ cell tumours include yolk sac tumours. Non-germ cell tumours include Leydig cell tumours and sarcomas.

The peak incidence for teratomas is 25 years and seminomas is 35 years. Risk factors include:

- cryptorchidism
- infertility
- family history
- Klinefelter's syndrome
- mumps orchitis

Features

- a painless lump is the most common presenting symptom
- pain may also be present in a minority of men
- other possible features include hydrocele, gynaecomastia

Diagnosis

- ultrasound is first-line

Management

- orchidectomy
- chemotherapy and radiotherapy may be given depending on staging

Prognosis is generally excellent

- 5 year survival for seminomas is around 95% if Stage I
- 5 year survival for teratomas is around 85% if Stage I

Breast cancer: referral

NICE published referral guidelines for suspected breast cancer in 2005

Urgent referrals (i.e. within 2 weeks)

- any breast lump with features suggestive of cancer (hard, tethered etc)

- any breast lump in a post-menopausal woman, regardless of features suggestive of cancer
- any breast lump in a women more than 30 years old without features suggestive of cancer but which persists after her next period
- if there is past history of breast cancer any breast lump should warrant urgent referral
- spontaneous unilateral bloody nipple discharge
- unilateral eczematous skin or nipple change that does not respond to topical treatment, or with nipple distortion of recent onset

Non-urgent referrals

- women < 30 years old who present with a breast lump with no features suggestive of cancer, no relevant family history and no change in the size of the lump

NICE guidelines suggest a cut-off age of 30 years for a breast lump without features suggestive of cancer, but which persists after the next period.

Endometrial cancer

Endometrial cancer is classically seen in post-menopausal women but around 25% of cases occur before the menopause. It usually carries a good prognosis due to early detection

The risk factors for endometrial cancer are as follows*:

- obesity
- nulliparity
- late menopause
- unopposed oestrogen. The addition of a progestogen to oestrogen reduces this risk (e.g. In HRT). The BNF states that the additional risk is eliminated if a progestogen is given continuously
- diabetes mellitus
- tamoxifen
- polycystic ovarian syndrome

Features

- post-menopausal bleeding is the classic symptom
- pre-menopausal women may have a change intermenstrual bleeding
- pain and discharge are unusual features

Investigation

- first-line investigation is trans-vaginal ultrasound - a normal endometrial thickness (< 4 mm) has a high negative predictive value
- hysteroscopy with endometrial biopsy

Management

- localised disease is treated with total abdominal hysterectomy with bilateral salpingo-oophorectomy. Patients with high-risk disease may have post-operative radiotherapy
- progestogen therapy is sometimes used in frail elderly women not consider suitable for surgery

*the oral contraceptive pill is protective

Cancer in the UK

The most common causes of cancer in the UK are as follows*

- 1. Breast
- 2. Lung
- 3. Colorectal
- 4. Prostate
- 5. Bladder
- 6. Non-Hodgkin's lymphoma
- 7. Melanoma
- 8. Stomach
- 9. Oesophagus
- 10. Pancreas

The most common causes of death from cancer in the UK are as follows:

- 1. Lung
- 2. Colorectal
- 3. Breast
- 4. Prostate
- 5. Pancreas
- 6. Oesophagus
- 7. Stomach
- 8. Bladder
- 9. Non-Hodgkin's lymphoma
- 10. Ovarian

*excludes non-melanoma skin cancer

Superior vena cava obstruction

Superior vena cava (SVC) obstruction is an oncological emergency caused by compression of the SVC. It is most commonly associated with lung cancer.

Features

- dyspnoea is the most common symptom
- swelling of the face, neck and arms - conjunctival and periorbital oedema may be seen
- headache
- visual disturbance
- pulseless jugular venous distension

Causes

- common malignancies: small cell lung cancer, lymphoma
- other malignancies: metastatic seminoma, Kaposi's sarcoma, breast cancer
- aortic aneurysm
- mediastinal fibrosis
- goitre
- SVC thrombosis

Management

- general: dexamethasone, balloon venoplasty, stenting
- small cell: chemotherapy + radiotherapy
- non-small cell: radiotherapy

Prostate cancer: management

Localised prostate cancer (T1/T2)

Treatment depends on life expectancy and patient choice. Options include:

- conservative: active monitoring & watchful waiting
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

Localised advanced prostate cancer (T3/T4)

Options include:

- hormonal therapy: see below
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

Metastatic prostate cancer disease - hormonal therapy

Synthetic GnRH agonist

- e.g. Goserelin (Zoladex)
- cover initially with anti-androgen to prevent rise in testosterone

Anti-androgen

- cyproterone acetate prevents DHT binding from intracytoplasmic protein complexes

Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

Monoclonal antibodies

Tumour marker	**Association**
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

Tumour antigens

Tumour marker	**Association**
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	**Mechanism of action**	**Adverse effects**
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)

Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

Bone metastases

Most common tumour causing bone metastases (in descending order)

- prostate
- breast
- lung

Most common site (in descending order)

- spine
- pelvis
- ribs
- skull
- long bones

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- mediastinal fibrosis
- goitre
- SVC thrombosis

Management

- general: dexamethasone, balloon venoplasty, stenting
- small cell: chemotherapy + radiotherapy
- non-small cell: radiotherapy

Prostate cancer: prognosis

The Gleason score is used to predict prognosis in patients with prostatic cancer. The grading system is based on the glandular architecture seen on histology following hollow needle biopsy

The most prevalent and the second most prevalent pattern seen are added to obtain a Gleason score. The Gleason grade ranges from 1 to 5 meaning the Gleason score ranges from 2 to 10 (i.e. two values added)

The higher the Gleason score the worse the prognosis

Cervical cancer

The incidence of cervical cancer peaks around the 6th decade. It may be divided into

- squamous cell cancer (80%)
- adenocarcinoma (20%)

Features

- may be detected during routine cervical cancer screening
- abnormal vaginal bleeding: postcoital, intermenstrual or postmenopausal bleeding
- vaginal discharge

Risk factors

- human papilloma virus 16,18 & 33
- smoking
- human immunodeficiency virus

- early first intercourse, many sexual partners
- high parity
- lower socioeconomic status
- combined oral contraceptive pill*

Gastric cancer

Epidemiology

- overall incidence is decreasing, but incidence of tumours arising from the cardia is increasing
- peak age = 70-80 years
- more common in Japan, China, Finland and Colombia than the West
- more common in males, 2:1

Associations

- *H. pylori* infection
- blood group A: gAstric cAncer
- gastric adenomatous polyps
- pernicious anaemia
- smoking
- diet: salty, spicy, nitrates
- may be negatively associated with duodenal ulcer

Investigation

- diagnosis: endoscopy with biopsy
- staging: CT or endoscopic ultrasound - endoscopic ultrasound has recently been shown to be superior to CT

Lung cancer: risk factors

Smoking

- increases risk of lung ca by a factor of 10

Other factors

- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon

- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

Factors that are NOT related

- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a 10 * 5 = 50 times increased risk

Colorectal cancer: screening

Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screening programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligible patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cancer