Endocrine disorders

Contents:

For full information on treatment side effects, cautions and contraindications, see electronic British National Formulary (www.bnf.org) or the relevant summary of product characteristics (www.medicines.org.uk).

For information on preparing intravenous medicines for administration, see Medusa Injectable Medicines Guide for the NHS (see Clinical Guidance home page)

1. Diabetes mellitus

Treatment aims to minimise the risk of long-term complications associated with diabetes (e.g. nephropathy, retinopathy, neuropathy). Diabetes is a strong risk factor for cardiovascular disease; adjunctive treatment such as ACE inhibitors, low-dose aspirin or lipid-regulating drugs may be beneficial for diabetic patients with significant cardiovascular risk.

In practice, treatment should be adjusted to the individual's target blood glucose and glycosylated haemoglobin. Suggested general targets:

- Glycosylated haemoglobin (HbA1c) < 7.0% (53mmol/mol)
- Pre-meal capillary blood glucose level = 4 to 10mmol/L

NOTE: Targets will vary depending on patient-specific circumstances (eg, for patients who are pregnant, see diabetes team care plan for patient).

There are two types of diabetes. They are:

i) Type 1 diabetes
ii) Type 2 diabetes

i) Type 1 diabetes

Patients with type 1 diabetes are treated with regular injections of subcutaneous insulin.
NOTE: All doses of insulin should be measured and administered using a commercial insulin pen device or an insulin syringe.

The Diabetes Nurse Specialists should be contacted to review all patients who are prescribed subcutaneous insulin therapy for the first time (at APH, bleep 2705, at CGH, bleep 4332).

There are three insulin regimes usually utilised:

a) Biphasic insulin administered twice daily
b) Short acting insulin administered three times daily with long acting insulin at bedtime
c) Intermediate or long acting insulin administered once daily
d) Insulin dosing

a) Biphasic insulin administered twice a day

Suitable for:
Patients newly started on insulin therapy and patients with regular lifestyles

This usually involves a biphasic insulin mixture being administered before breakfast and evening meals.

b) Short-acting insulin administered three times daily with long-acting insulin at bedtime ("basal-bolus regimen")

Suitable for:
Patients who want a flexible lifestyle and are able to self-manage their diabetes effectively

This regimen can give good blood glucose control.

c) Intermediate- or long-acting insulin administered once daily

Suitable for:
Patients with type 2 diabetes who require insulin therapy in addition to dietary control and/or oral antidiabetic treatment. They are also useful for patients who rely on district nursing services.

d) Insulin dosing

Starting doses of insulin vary depending on a number of factors. For patients newly diagnosed with type 1 diabetes, insulin requirements over the previous 24 hours are useful

for estimating future requirements. For patients with type 2 diabetes uncontrolled on maximal oral therapy, a suggested starting dose is 10 units twice daily of biphasic insulin.
NOTE: The term "units" must be used at all times (ie, in case notes and on medicines reconciliation forms). Abbreviations (eg, "U" or "IU") must NEVER be used.

Insulin doses should not be altered as a result of a single raised blood glucose; it is wise to observe for patterns and alter insulin accordingly. Alterations of 10% (increases or decreases) are appropriate if blood glucose is persistently high (>10mmol/L) or low (<4mmol/L).
NOTE: Do not omit insulin in a patient with low blood glucose. If a patient's blood glucose falls below 4mmol/L, treat as per hypoglycaemia guidelines (see section 2 — "Hypoglycaemia") then refer the patient to the diabetes team for a review of treatment.

The following insulin preparations are available:

Short-acting soluble insulin (inject immediately before meals)
- Actrapid®
- Humulin S
- Hypurin porcine neutral

Short-acting human insulin analogue (inject immediately before meals)
- NovoRapid® (Insulin aspart)
- Humalog® (Insulin lispro) 100units/mL & 200units/mL
- Apidra® (Insulin glulisine)

Intermediate-acting insulin (inject 20 to 30 minutes before meals)
- Insulatard®
- Humulin I®

Long-acting insulin (inject 20 to 30 minutes before meals)
- Lantus® (Insulin glargine 100units/mL)
- Toujeo® (Insulin glargine 300units/mL)
- Levemir® (Insulin detemir)
- Tresiba® (Insulin degludec) 100units/mL & 200units/mL
  NOTE: Can be used in children and adults
  For Consultant/Associate Specialist in Diabetes initiation ONLY.

  See Tresiba® - Selecting Appropriate Patients (Adults) for Treatment

Biphasic insulin (soluble and isophane mix) (inject immediately before meals)
- Humulin M3®
- Hypurin porcine 30/70 mix

Biphasic analogue mix (inject immediately before meals)
- NovoMix 30®
- Humalog Mix25®
- Humalog Mix50®

The Diabetes Specialist Nurses can provide further information on which administration devices are available for each type of insulin (this information can also be found in the BNF). They will supply all new patients with the pen devices for use with insulin cartridges.

ii) Type 2 diabetes

Patients with type 2 diabetes can be treated, at first, by dietary or lifestyle interventions. However, many also require oral antidiabetic medicines or insulin to maintain satisfactory control.
For more information on when to prescribe each medicine (using HbA1c and body mass index), see **Type 2 diabetes — clinical management (adults).**

MHRA Safety alerts:
SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis

Canagliflozin: signal of increased risk of lower extremity amputations observed in trial in high cardiovascular risk patients

2. Hypoglycaemia

Hypoglycaemia is defined as a blood glucose level that is less than 4mmol/L and associated with symptoms including feeling clammy, pallor, tachycardia, confusion or slurred speech. Severe hypoglycaemia is defined as a blood glucose level that is less than 2.2mmol/L.
The course of treatment should be determined according to the patient's presenting features. These will fall into various categories:

i) Patients who are unconscious, having seizures or very aggressive
ii) Conscious patients who are able to swallow but are disorientated, uncooperative or aggressive
iii) Conscious and oriented patients who are able to swallow
iv) Long acting carbohydrate requirement

3. Diabetic ketoacidosis

When a patient is diagnosed with diabetic ketoacidosis, always inform the appropriate medical registrar and the Diabetes Specialist Nurse team.

4. Surgery — managing blood glucose for diabetic patients

Information on managing patients with diabetes who are undergoing surgery, and when a GKI infusion should be considered, can be found in **Diabetes management during surgery (adults).** This guideline includes instructions on whether or not doses of insulins or other antidiabetic medicines should be withheld on the day of surgery.

If a GKI infusion is required, it should be prescribed using the "Glucose-Potassium-Insulin Infusion Prescription and Administration Chart", which is available on all wards.

Ward guidelines for GKI regimens

- For advice regarding GKI infusions contact the Diabetes Team / Specialist Nurses
- Notify Theatre / Anaesthetist / Endoscopist that the patient is diabetic at the earliest opportunity prior to the procedure.
- Check blood glucose every two hours on the day of a surgical procedure
- If a GKI infusion is required, it should be commenced before the patient is taken to theatre
- The infusion should be continued until after regular insulin / oral antidiabetic drugs and normal diet have been restarted and tolerated.
- Continue monitoring blood glucose as directed.
- In an emergency contact the Medical Team on Call.

DO NOT administer insulin via a separate syringe pump. It is inappropriate and potentially dangerous.
DO NOT alter the rate of the GKI infusion (from 100mL per hour) in response to fluctuating blood glucose. This is ineffective.
DO NOT prescribe consecutive GKI infusions in advance (e.g. overnight) by use of a sliding scale. This may result in consistently high or low blood glucose levels.

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5. Hypothyroidism

Hypothyroidism is is managed in various ways, they include:

i) Use of levothyroxine (T_4)
ii) Use of liothyronine sodium (T_3)
iii) Sub-clinical hypothyroidism
iv) Use of testosterone to treat hypothyroidism associated hypogonadism

i) Levothyroxine

Typically, plasma levothyroxine (T_4) levels will be decreased and thyroid stimulating hormone (TSH) levels increased in hypothyroidism. However TSH may be slightly decreased or normal if the hypothyroidism is secondary to pituitary failure.

Elderly patients or those with pre-existing heart disease
Levothyroxine 25 micrograms, orally, once daily for at least 4 weeks;
increase by 25 micrograms daily every 4 weeks according to thyroid function tests (TFTs) and clinical status (may take several weeks to establish correct dose).

Other patients

Levothyroxine 50 micrograms, orally, once daily for at least 4 weeks;
increase by 50 micrograms every 4 weeks according to TFTs and clinical status (may take up to 3 months).

Usual maintenance dose
100 to 150 micrograms once daily.

The maximum dose of levothyroxine is unlikely to be higher than 150 micrograms daily, therefore suspect poor compliance if doses of 200 micrograms or more are required.
In patients stable on levothyroxine, check TFTs at least annually.
Irregular intake of high doses may lead to TFTs being normal due to the long half-life and pharmacological properties of high doses of levothyroxine. Therefore, caution is needed if the patient subsequently receives regular high doses (eg, during a hospital admission).

ii) Liothyronine sodium
Liothyronine is more potent than levothyroxine, and has a rapid onset but shorter duration of action. It is used when rapid control is required (e.g. for patients in a severe hypothyroid state or a hypothyroid coma).

Liothyronine 5 to 20 micrograms by slow IV injection every 12 hours or every 4 hours (if necessary)
Or
50 micrograms stat then 25 micrograms every 8 hours
reducing to
25 micrograms twice daily

Once the patient is conscious, switch to: **Liothyronine** 10 to 20 micrograms, orally, daily; increase dose gradually to 60 micrograms daily in divided doses. Reduce dose in elderly patients.
20 micrograms liothyronine ≡ 100 micrograms of levothyroxine.

Patients should be switched from oral liothyronine to oral levothyroxine for long term maintenance therapy as soon as clinically practical. Switching guidelines can be found here.

Some patients with confirmed T3/T4 conversion failure may require long term liothyronine supplementation.

iii) Sub-clinical hypothyroidism
The management of patients with sub-clinical hypothyroidism (a high level of thyroid-stimulating hormone [TSH] in the presence of normal T_4 and T_3 levels) remains controversial. The benefits of replacement therapy should be weighed against potential problems that can accompany the excessive use of levothyroxine (e.g. osteoporosis). If treatment is initiated, the aim is to normalise TSH.

iv) Use of testosterone to treat hypothyroidism associated hypogonadism
Testosterone undecanoate (Nebido®) 1000mg IM every 12 weeks may be required by some patients with hypothyroid associated hypogonadism.

6. Hyperthyroidism

In patients with hyperthyroidism, plasma thyroid stimulating hormone (TSH) levels are reduced (and can be virtually undetectable) whereas free levothyroxine (T_4) and liothyronine (T_3) levels are increased.

There are several ways in which hyperthyroidism is treated:

i) Titration regimen
ii) Block-replace regimen
iii) Sympathomimetic symptom management

Carbimazole and propylthiouracil are similarly effective (carbimazole 5mg orally is equivalent to propylthiouracil 50mg orally) but carbimazole tends to be used more often, with propylthiouracil being reserved for patients who experience a sensitivity reaction or adverse effect to carbimazole, or those who are pregnant.

Treatment is usually continued for 12 to 18 months, after which patients should be monitored closely for the subsequent 12 months and every 6 months thereafter.

i) Titration regimen

First choice
Carbimazole Give 15 to 40mg, orally, per day in divided doses until the patient is euthyroid (may take 4 to 8 weeks).
Maintenance: 5 to 15mg daily (treatment to continue for 12 to 18 months).
NOTE:
Prescribers are reminded of the importance of recognising bone marrow suppression induced by carbimazole and to discontinue treatment immediately if suspected. Clinicians are advised to:

- **Ask patients to report symptoms and signs of infection, especially sore throat, mouth ulcers, bruising, bleeding, fever**
- **Perform a white blood cell count if there is any clinical evidence of infection (regular full blood count monitoring does not predict this reaction)**
- **Stop treatment promptly if there is any clinical or laboratory evidence of neutropenia (this condition is reversible**

Second choice
Propylthiouracil 200 to 400mg, orally, per day in divided doses until the patient is euthyroid (may take 4 to 8 weeks).
Maintenance: 50 to 150mg daily (treatment to continue for 12 to 18 months).

ii) Block-replace regimen

Carbimazole 40-60mg, orally, daily in divided doses until TFTs near normal levels (usually takes 4 weeks). Then maintain **carbimazole** at 40mg daily and initiate **levothyroxine** 50 micrograms daily and titrate levothyroxine dose every 4 weeks according to TFTs.
Continue combination treatment for 18 months.
Usual maintenance dose: Carbimazole 40mg daily, levothyroxine 100 micrograms daily.

iv) Sympathomimetic symptom management

Propranolol 20 to 40mg, orally, three times daily for 2 to 6 weeks.

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7. Adrenal insufficiency – treatment

There are several facets to treatment of adrenal insufficiency. They include:

i) Acute adrenocortical insufficiency
ii) Replacement therapy
iii) Withdrawal of corticosteroids

i) Acute adrenocortical insufficiency

Hydrocortisone sodium succinate 100mg, by IV injection, every 6–8 hours for 24–48 hours (then commence replacement therapy).

ii) Replacement therapy

The adrenal cortex normally secretes cortisol, which has glucocorticoid and weak mineralocorticoid activity, and the mineralocorticoid aldosterone. In deficient states, replacement therapy is best achieved using hydrocortisone and the mineralocorticoid fludrocortisone.

First choice
Hydrocortisone 20 to 30mg, orally, each day in two or three divided doses.
A larger dose should be given in the morning and a smaller dose(s) in the afternoon or early evening. The dose should be doubled if the patient experiences inter-current illness
And,
if the patient is exhibiting mineralocorticoid deficiency
Fludrocortisone 50 to 300micrograms, orally, daily.
NOTE: If patient develops hypertension, reduce dose or stop fludrocortisone

iii) Withdrawal of corticosteroids

NOTE: The Committee on Safety of Medicines (CSM) has recommended that gradual withdrawal of corticosteroids should be considered in those patients whose disease is unlikely to relapse and have:

- Recently received repeat courses (particularly if taken for longer than three weeks)
- Taken a short course within a year of stopping long-term therapy
- Other possible causes of adrenal suppression
- Received more than 40mg prednisolone daily (or equivalent)
- Been given repeat doses in the evening
- Received more than 3 weeks treatment

If the patient's disease is unlikely to relapse and they have received corticosteroid therapy for less than three weeks and are not included in the categories outlined above, then

treatment can be stopped abruptly. During withdrawal of corticosteroids, the dose can be reduced relatively rapidly down to physiological doses (equivalent to 7.5mg of prednisolone) and then reduced more slowly.

All patients who are taking (or are likely to take) oral glucocorticoids (eg, prednisolone, hydrocortisone, dexamethasone) at any dose for 3 months or longer should be assessed for prophylactic treatment for osteoporosis — see **Osteoporosis — Management**

8. Assessing adrenal failure (Synacthen® tests)

The two tests used to assess adrenal failure are:

i) Short Synacthen® test
ii) Prolonged Synacthen® test

See **Synacthen tests® for assessment of adrenal failure (adults)** for details of which to use and how to perform and interpret these tests.

9. Diabetes insipidus

Desmopressin, an analogue of antidiuretic hormone, is used to treat pituitary diabetes insipidus. In nephrogenic diabetes insipidus, benefit may be obtained from the paradoxical antidiuretic effect of thiazide diuretics (e.g. bendroflumethiazide 5mg daily). For further information, contact a consultant endocrinologist.

Desmopressin tablets 100 micrograms, orally, twice or three times a day;
Maintenance: 200micrograms to 1.2mg daily;
Usual dose: 100 to 200 micrograms twice or three times a day.
Or
Desmopressin nasal spray 10 to 20 micrograms (1 to 2 sprays), intranasally, once or twice daily. Adjust dose to achieve slight diuresis once a day.
NOTE: Desmopressin is contraindicated in cardiac insufficiency and in patients treated with diuretics.
Serum and urine osmolarity should be monitored to avoid excess therapy.

Patients should also have their fluid intake restricted. Treatment without concomitant fluid restriction may lead to water retention and hyponatraemia.

10. SIADH (syndrome of inappropriate secretion of antidiuretic hormone)

All patients with SIADH should be subjected to strict fluid restrictions (ie, <1L fluid intake per day).

The tetracycline demeclocycline can be used to treat hyponatraemia induced by resistant inappropriate secretion of antidiuretic hormone.

Demeclocycline 300mg, orally, three or four times daily; reduced to a maintenance dose of 600 to 900mg daily.
NOTE: Demeclocycline is contraindicated in patients with renal impairment.

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11. Growth hormone deficiency

Somatropin is recommended in adults only if the following 2 criteria are fulfilled:

- The patient is suffering from severe growth hormone deficiency, established by dynamic growth hormone testing and reduced IGF-1 (insulin-like growth factor-1) levels
- The patient is experiencing impaired quality of life measured using a specific questionnaire

Treatment must be initiated and managed by a physician with expertise in growth hormone disorders.
For further information, see **NICE technology appraisal on "Growth Hormone Deficiency (adults) — Human Growth Hormone"**

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12. Osteoporosis (prevention and treatment)

For information on when to prescribe medicines to treat or prevent osteoporosis, see **Osteoporosis — Management**

For all patients with inadequate dietary consumption
Adcal D3, Calcichew D3 Forte, Natecal D3 or **Calceos** one tablet, orally, twice daily (this provides 1 to 1.2g of calcium and 800 units of vitamin D3 per day)
Or,
for patients who cannot tolerate the tablets
Calfovit D3 one sachet, orally, once daily
And,
if additional treatment is indicated (see guidelines)

First choice
Alendronate 70mg, orally, once weekly

Second choice (if patients intolerant of alendronate)
Risedronate 35mg, orally, once weekly
Or
Ibandronate 150mg, orally, once a month

MHRA Drug safety alerts:
Bisphosphonates: very rare reports of osteonecrosis of the external auditory canal
Bisphosphonates: atypical femoral fractures
Bisphosphonates: osteonecrosis of the jaw

If unable to tolerate a bisphosphonate:
Strontium ranelate 2g orally once daily (preferably at bedtime). Avoid food and milk for 2 hours before and after taking; and avoid antacids for 2 hours after taking.

MHRA Drug safety alert- Strontium ranelate: cardiovascular risk

If unsuitable for strontium and female:
Raloxifene 60mg, orally, once daily
(Hormone Replacement Therapy (HRT) is an additional treatment option for women with menopausal symptoms and/or intolerant of other treatments.)

Third choice
Zoledronic acid 5mg, by IV infusion, once a year. Product is made ready to infuse and should be given over at least 15 minutes.

MHRA Drug safety alerts:
Bisphosphonates: very rare reports of osteonecrosis of the external auditory canal
Bisphosphonates: atypical femoral fractures
Bisphosphonates: osteonecrosis of the jaw
Intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk

If failed on, or contraindicated for, all other formulary treatments
Etidronate Administered as part of Didronel PMO®. See product information for dosing.
NOTE: To be initiated by an orthogeriatric or rheumatology consultant ONLY, as per NICE technology appraisal 161 (www.nice.org.uk/ta161). For more information, see the trust guideline on Osteoporosis — Management.
Or
Denosumab 60mg, by SC injection, once every 6 months.
NOTE: To be initiated by an orthogeriatric or rheumatology consultant ONLY, as per NICE technology appraisal 204 (www.nice.org.uk/ta204) or technology appaisal 194 (www.nice.org.uk/ta194)

MHRA Drug safety alert-Denosumab (Xgeva▼, Prolia); intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk

13. Hypercalcaemia of malignancy, Paget's disease and osteolytic lesions (other uses for bisphosphonates)

i) Hypercalcaemia of malignancy

Aggressive rehydration with sodium chloride 0.9% may be sufficient to lower serum calcium. Disodium pamidronate is effective in hypercalcaemia of malignancy. Patients should be rehydrated with sodium chloride 0.9% solution before or during treatment.

Disodium pamidronate Give 15 to 90mg as a single IV infusion or in divided doses over 2 to 4 days according to serum calcium levels. Infuse at a rate not exceeding 60mg/hour.

Initial serum calcium (mmol/L) – corrected or uncorrected	**Dose of disodium pamidronate**
< 3	15 to 30mg
3 to 3.5	30 to 60mg
3.5 to 4	60 to 90mg
> 4	90mg

A decrease in serum calcium can be observed within 24 to 48 hours, however it may take 4 to 5 days to be fully effective. If normocalcaemia is not achieved within this time, a further dose of disodium pamidronate may be given.

Maximum dose: 90mg per treatment course.
NOTE: Patients should be advised not to drive or operate machinery immediately after treatment.

ii) Paget's disease

Disodium pamidronate Give 90mg by intravenous infusion at a rate of 45mg per hour. This dose can be repeated on two occasions within a two-week period. For patients with severe renal impairment, the dose and infusion rate should be reduced (see The Renal Drug Handbook for further information or contact the pharmacy department).
NOTE: This regimen is unlicensed.
Contact a consultant rheumatologist for further information.
Then
Alendronate 70mg, orally, once weekly for three months

Oral **calcium** and **vitamin D** supplements are recommended for patients with Paget's disease to prevent the development of hypocalcaemia.

iii) Osteolytic lesions and bone pain

Disodium pamidronate Give 90mg by slow IV infusion every 4 weeks (or every 3 weeks if this coincides with chemotherapy). Infuse at a rate not exceeding 60mg/hour.

MHRA Drug safety alerts:
Bisphosphonates: very rare reports of osteonecrosis of the external auditory canal
Bisphosphonates: atypical femoral fractures

Bisphosphonates: osteonecrosis of the jaw
Intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk

14. Hyperprolactinaemia

Hyperprolactinaemia can be induced by drugs such as the phenothiazines and metoclopramide, as well as some diseases (eg, pituitary adenoma or pregnancy).

First choice
Cabergoline 500 micrograms, orally, weekly (as a single dose or as two separate doses on different days); increased at monthly intervals in steps of 500 micrograms according to response.

Maintenance: 1mg weekly (range: 250 micrograms to 2mg weekly). Doses over 1mg should be given as divided doses.
NOTE: Exclude pregnancy before starting treatment with cabergoline and discontinue if pregnancy occurs during treatment.

Cabergoline is contraindicated for patients with a history of puerperal psychosis.

NOTE: Routine screening for cardiac valvular diseases may be needed if cabergoline is used at high doses (ie, above 1mg/week) and the CSM advises that it may be appropriate to measure the patient's erythrocyte sedimentation rate, serum creatinine level, and to obtain a chest X-ray, before commencing treatment.

15. Testosterone deficiency

Replacement therapy with testosterone can be prescribed for male patients with hypogonadism once testosterone deficiency has been confirmed by clinical symptoms and laboratory analysis.

Sustanon 250® Give 1mL, by deep IM injection, usually every 3 weeks.
Or
Testosterone 2% gel (Tostran®) Apply 3g (60mg testosterone) of gel to clean, dry, intact skin of the abdomen or both inner thighs, once a day. Adjust dose to response; maximum: 4g/day. Do not wash application site for 2 hours.

NOTE: It is essential to monitor PSA (prostate specific antigen) annually for all patients receiving testosterone therapy (more frequently if the PSA is raised or rising).