INTRODUCTION
The Growth hormone (GH) assay has changed recently and is now reported in mcg/L rather than mU/L. An approximation for conversion of mU/L to mcg/L is to divide by 3.

CLINICAL ASSESSMENT OF EXCESS GROWTH HORMONE

FINGER SIZE ASSESSMENT
Finger size is an objective measure of soft tissue over-growth and can be used to follow the response to treatment. Measurement should be between 0900h and 1000h, prior to any intravenous cannulation. Ring size is assessed using the labelled rings and the fourth finger. The ring size is the one with the tightest fit. Record ring size from the non-dominant hand. If the finger is too large for size Z then use the fifth finger (and make a note of this).

SKIN-FOLD THICKNESS
The skin is measured using the skin-fold calliper on the dorsum of the hand over the mid point of the third metacarpal bone.
Set the scale on the callipers to zero. Place the patient’s hand flat on the table with the wrist in a neutral or extended position. A small skin-fold in the long axis of the hand is lifted up and placed between the blades of the calliper so the fold reaches exactly to the top of the jaw-blades.
Mean skin thickness in men is 2.8 mm when 20 yrs old decreasing to 1.75 mm when 70 yrs. Women's skin is approximately 0.2 mm thinner than similarly aged men. An abnormally thick skin is seen in 77% of acromegalics (mean + 2 s.d. in 40 year old males >3.4mm).

HEIGHT
Particularly important to assess in patients with gigantism (excess growth hormone secretion before epiphyseal closure). Accurate height measurement requires a true vertical surface, a firm horizontal surface, a tape measure and a movable block which is at right angles to the vertical surface. The patient should stand with the back as straight as possible, bare feet and with the heels together. The canthus of the eye should be in the same horizontal plane as the external acoustic meatus. The movable block is lowered to the crown of the head.

REFERENCES
DIAGNOSIS OF ACROMEGALY : ORAL GLUCOSE TOLERANCE TEST

INDICATION
Diagnosis of GH excess. Due to the pulsatile nature of GH secretion, random GH it of little use to diagnose or exclude acromegaly

CONTRAINDICATIONS
None.

PRECAUTIONS
None.

PREPARATION
Fasting from midnight.

PROCEDURE
- Basal blood sample for GH, IGF-1 and glucose at t = 0. The samples should be taken through an indwelling venous cannula to avoid the stress of repeated venepuncture.
- Administer 75 grams of oral glucose in 300 ml water over about 10 minutes. Alternatively give Lucozade 394ml (73kcal/100ml formulation) or 410 mls (70Kcal/100ml formulation). Take blood for GH and glucose at t=30, 60, 90, 120 minutes.
- Do the test supine as dumping can cause GH rise.

INTERPRETATION
In normal individuals, GH levels fall following oral glucose, and at least one of the samples during the test should have undetectable GH levels (ie less than 0.6mcg/L). Failure of suppression or a paradoxical rise in GH (in approximately 30% of cases) suggests acromegaly.

SENSITIVITY / SPECIFICITY
False positives can occur in chronic starvation, poorly controlled diabetes, chronic renal failure, liver disease, osmotic dumping of high glucose load, heroin addiction, adolescence, pregnancy or patients taking oestrogen therapy.
ASSESSMENT OF GH BURDEN: 5-POINT DAY CURVE FOR GH

INDICATIONS
Assessment of the biochemical severity of acromegaly, before, during or after treatment.

CONTRAINDICATIONS
None.

PRECAUTIONS
None.

PREPARATION
Eat and drink normally.
IV cannula (GH is a stress hormone).
Take medications at usual times.

PROCEDURE
Take blood samples for GH at 08:30, 11:00, 13:00, 17:00 and 19:00.
In addition take blood for basal pituitary function including IGF-1, (remember prolactin may be co-secreted with GH in up to a third of acromegaly patients).

INTERPRETATION
GH should normally be <1 mU/l on at least 2 of the samples
Mean GH should be <5 mU/L to suggest adequate control of GH if treated

REFERENCE
NEURO-OPHTHALMOLOGICAL ASSESSMENT

Visual acuity should be assessed with the use of Snellen charts and fundoscopy performed to exclude optic atrophy or papilloedema. Visual fields should be assessed by confrontation using a red pin. Formal assessment of visual fields with Goldmann perimetry should be performed in patients with any clinical or radiological evidence of optic chiasmal compression.

GHRH

Measure GHRH in the rare patient in whom a non-pituitary cause is suspected.

THERAPY IN ACROMEGALY

Therapeutic options include:
Somatostatin analogues (primary therapy or while awaiting surgery)
Dopamine agonists (particularly for prolactin cosecretion)
Pituitary Surgery
Post-operative radiotherapy
Stereotactic ‘gamma knife’ radiotherapy for recurrence
GH receptor agonists for recurrence

ASSESSMENT OF CURE / CONTROL

5-point GH day curve
IGF-1
Imaging results
SCREENING COLONOSCOPY IN ACROMEGALY

INDICATIONS
Patients with acromegaly should be offered regular colonoscopic screening due to increased risks of adenoma and malignancy. Total colonoscopy is required, not sigmoidoscopy.
Patients with acromegaly should be offered regular colonoscopic screening, starting at the age of 40 years.
The frequency of repeat colonoscopy should depend on the findings at the original screening and the activity of the underlying acromegaly.
Patients with an adenoma at first screening, or IGF-1 level above the maximum of the age-corrected normal range should be offered screening at three year intervals.
Patients with either a negative first colonoscopy or a hyperplastic polyp should be offered screening at five-year intervals I think the recent submission to JCEM relaxed this a little. Certainly I am much less 'enthusiastic' about colos than others. Often 10 years between exams and once over 60 if normal it seems improb to me that that patient will perish from Ca colon.

PREPARATION
These patients have increased colon length and circumference. Their colonic transit time is twice that of normal subjects..
Double bowel preparation is required, with admission to hospital 2 days before the procedure to ensure this occurs (4 sachets of klean prep per day for 2 days).

PROCEDURE
As per standard colonoscopy procedure; ensure adequacy of preparation.

INTERPRETATION
Macroscopic and histological findings determine management going forward.

REFERENCE
GROWTH HORMONE RECEPTOR ANTAGONISTS

INDICATIONS
- Pegvisomant is an analogue of human growth hormone that has been genetically modified to be a growth hormone receptor antagonist.
- It binds to growth receptors on cell surfaces, where it blocks growth hormone binding and decreases IGF-1.
- Licensed for use in patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-1 concentrations or was not tolerated.

CONTRAINDICATIONS
- The fall in IGF-1 levels induced by Pegvisomant is associated with an increase in growth hormone levels. Concerns have been raised about the relevance of this finding and the potential for tumour growth, although this has not been shown in the trials to date.
- Pregnancy, breastfeeding or plans to become pregnant.
- Hypersensitivity to pegvisomant or any of the excipients.

PRECAUTIONS
Side effects include injection site erythema and soreness (11%), sweating (7%), headache (6%) and asthenia (6%).
The development of isolated low-titre anti-growth hormone antibodies was observed in 16.9% of patients. The clinical significance of these antibodies is unknown.
Patients should be advised to use adequate contraception if necessary.
1-2% incidence of hepatitis.
Significant incidence of lipohypertrophy which can be bothersome, even with efficient rotation of sites.

PREPARATION
Baseline MRI pituitary
PROCEDURE

- Administer loading dose of 80mg/40mg pegvisomant subcutaneously.
- Following this, 10mg once daily by subcutaneous injection.
- Dose adjustments every 4-6 weeks. Increments of 5mg/day. Maximum dose 30mg/day.
- Based on IGF-1 levels appropriate dose changes should be made 4-6 weekly in increments of 5mg/day.
- Endocrine nurses are able to teach patients self-administration.
- Monitor ALT and AST at 4-6 week intervals for the first 6 months and thereafter every 6 months or as clinically indicated. Pegvisomant should be discontinued if signs of liver disease persist. The mechanism of the liver function disturbance is not understood, but available evidence suggests it resolves on discontinuation of the drug.
- Abnormalities of insulin sensitivity, lipids and bone turnover associated with active acromegaly resolve with pegvisomant treatment. Doses of insulin or hypoglycaemic agents may need to be decreased.
- MRI pituitary at 6 and 12 months and annually thereafter (or as clinically indicated).

REFERENCES


GROWTH HORMONE REPLACEMENT THERAPY

INDICATIONS
As per NICE guidelines:

- Peak growth hormone levels of < 9mU/l or < 3mcg/L, following an insulin tolerance test or glucagon test
- Severely depressed quality of life as measured by clinical interview, supported by the ‘Adult Growth Hormone Deficiency Assessment’ (AGHDA) questionnaire (Score should be 11 or more for the treatment to be started).

Nine months after initiation of therapy and ongoing monitoring, patients are reassessed and GH is only continued in those patients who demonstrate a QOL improvement of more than 7 points in the AGHDA score. If plans for continuation, initiate shared-care protocol with GP.

CONTRAINDICATIONS
Active growth of pituitary tumour
Other active malignancy
Critically ill patients
Patients with known hypersensitivity to GH or to any excipients of the product.
Pregnancy and lactation.

PRECAUTIONS
Caution in diabetes. Use lower starting doses. Warn patients with type I DM about changing insulin requirements: happens acutely.

Adverse effects may include headache, arthralgis, myalgia, fluid retention, mild hypertension and carpal tunnel syndrome. Most of these adverse effects were reported in earlier studies that used higher doses and are uncommon when the dose is titrated from a low starting dose. Benign cranial hypertension has rarely been reported, therefore persistent severe headaches will require investigation.

PREPARATION
Establish criteria for replacement.
Up-to-date MRI pituitary scan reviewed.
Document fundoscopy at baseline (no papilloedema).
Ensure deficiencies of other pituitary hormones adequately replaced (requirements may subsequently alter once established on GH replacement.)
PROCEDURE

Attend Frances Fraser ward to learn self-injection from specialist nursing staff.

The dose may range from 0.1mg–1.2mg daily.

The median maintenance dose is 0.4mg once a day (0.3mg males, 0.4mg females)

Dorothy Walker will oversee dose titration according to published departmental protocol.

Once established on appropriate dose, outpatient monitoring (arrange via Dorothy Walker) as follows:

- Clinical response and side-effects
- Pituitary imaging 1-3 yearly depending on type of pituitary pathology
- Regular serum IGF-1
- Weight and body mass index
- Waist:hip ratio
- Blood pressure
- ‘AGHDA’ questionnaire – 6 monthly
- Bone density yearly
- Thyroid function and serum biochemistry 6 monthly
- Glucose and HbA1c 6 monthly

REFERENCES

