# Endocrine

**Calcitonin:**

| | | |
|---|---|---|
| **A** | is a polypeptide hormone | (True) |
| **B** | is secreted by the thyroid epithelial cells | (False) |
| **C** | secretion is increased by a fall in serum calcium concentration | (False) |
| **D** | inhibits bone resorption | (True) |
| **E** | is secreted in excess in patients with medullary carcinoma of the thyroid. | (True) |

**Comments:**
Cacitonin is a peptide hormone released from the C cels of the thyroid in response to hypercalcaemia. It's hypocalcaemic effects are mediated by preventing bone resorption by osteoclasts

**Glucose-6-phosphate dehydrogenase deficiency:**

| | | |
|---|---|---|
| **A** | Is inherited as a sex-linked condition | (True) |
| **B** | is not clinically manifest in girls | (False) |
| **C** | Causes drug-induced haemolysis | (True) |
| **D** | Is an indication for splenectomy | (False) |
| **E** | Is more pronounced in mature red blood cells | (True) |

**Comments:**
G6PDH deficiency is x linked recessive. It can manifest in females if there are 2 copies of the abnormal gene. Drugs which cause haemolysis include aspirin, antimalarials, antibacterials and sulphonamides. Splenectomy is not helpful in the management of this condition. Young red blood cells have near normal enzymatic capacity.

**Longitudinal growth:**

| | | |
|---|---|---|
| **A** | Is relatively more affected than weight gain in hypothyroidism. | (True) |
| **B** | Is severely retarded in growth hormone deficiency in the first year of life. | (False) |
| **C** | Is equally dependent on maternal and paternal height. | (True) |
| **D** | Is greater in the mid trimester of pregnancy than in any period in postnatal life. | (False) |
| **E** | Is irreversibly damaged in intrauterine malnutrition. | (False) |

**Comments:**

Growth in children occurs in 3 phases. In the infant phase it is mainly determined by adequate nutrition, but insulin, insulin-like growth factors (especially 2) and thyroxine are also important. Full responsiveness to growth hormone only develops in late infancy. The infant phase of growth is characterised by extremely rapid growth, especially in the final trimester and the first 3 months postnatally. Inadequate weight gain or growth failure in this period is usually called failure to thrive. In the childhood phase,

normal thyroid and growth hormone activity are required in addition to adequate nutrition. Since it lasts longer than the other phases, this is the main determine to final height. The growth rate is however much slower. In the pubertal growth spurt, growth hormone and the sex steroids (especially testosterone and oestrodial) interact. Growth ceases when the growth plate disappears with the fusion of the epiphyses with the bone shaft of long bones.



**The following clinical features are commonly associated with congenital hypothyroidism in the neonatal period:**

| | | |
|---|---|---|
| **A** | hypothermia | (True) |
| **B** | Diarrhoea | (False) |
| **C** | Prolonged conjugated hyperbilirubinaemia | (False) |
| **D** | A small anterior fontanelle | (False) |
| **E** | Inguinal hernia | (False) |

**Comments:**
Hypothermia results from reduced metabolic rate. Constipation rather than diarrhoea is a common clinical feature. Prolonged conjugated hyperbilirubinaemia is a relatively uncommon sequelae. The anterior fontanelle would be tense. Umbilical rather than inguinal herniae are associated.

**The following are recognised features of Beckwith-Wiedemann Syndrome:**

| | | |
|---|---|---|
| **A** | Omphalocele | (True) |
| **B** | Macroglossia | (True) |
| **C** | Macrocephaly | (False) |
| **D** | Vertical ear lobe fissures | (False) |
| **E** | Hyperglycaemia | (False) |

**Comments:**

In about half of patients with Beckwith-Wiedemann Syndrome, hypoglycaemia is a feature due to hyperinsulinism. There is macrosomia, microcephaly, macroglossia, visceromegaly, and omphalocele. The ear lobe fissures are horizontal. There is an association with Wilm's tumour, hepatoblastoma, and retinoblastoma.



**A boy of 10 was operated upon for removal of a craniopharyngioma. In the six months following the operation he was noted to have gained an excessive amount of weight. Factors that might have contributed to this include:**

| | | |
|---|---|---|
| **A** | Growth hormone deficiency | (True) |
| **B** | Increased appetite | (True) |

| | | |
|---|---|---|
| **C** | Inappropriate ADH secretion | (False) |
| **D** | Secondary hypothyroidism | (True) |
| **E** | Adrenal insufficiency | (False) |

**Comments:**
Growth hormone deficiency is common following pituitary surgery and results in predominantly central obesity. Increased appetite may be the result of hypothalamic damage. Diabetes Insipidus rather than SIADH would be expected, though it would not cause weight gain. TSH deficiency would cause weight gain. Adrenal insufficiency would cause weight loss and fatigue.

**Congenital hypothyroidism:**

| | | |
|---|---|---|
| **A** | Cannot be diagnosed clinically before 3 months of age | (False) |
| **B** | May be associated with an ectopic thyroid gland | (True) |
| **C** | Needs life-long Thyroxine replacement | (True) |
| **D** | Can present in the newborn period with haemolytic jaundice | (False) |
| **E** | If undiagnosed causes short stature but with a normal bone age | (False) |

**Comments:**
Patients with congenital hypothyroidism may exhibit non specific clinical features e.g. jaundice and poor feeding however macroglossia is a fairly specific clinical finding aiding diagnosis. The commonest causes of congenital hypothyroidism are an absent or ectopic gland. The need for thyroxine is life long. The hyperbilirubinaemia is conjugated and 'haemolytic jaundice' would not occur. Short stature and delayed bone age occur.

**Precocious puberty:**

| | | |
|---|---|---|
| **A** | Is less common in girls | (False) |
| **B** | In boys it is usually idiopathic | (False) |
| **C** | Is a well recognised sequel to hydrocephalus | (True) |
| **D** | Is associated with a normal rate of skeletal maturation | (False) |
| **E** | Results in a reduction of final adult height | (True) |

**Comments:**
Precocious puberty is approximately five times more common in females. In females it is usually idiopathic, in males the commonest cause is a hypothalamic hamartoma. CNS disorders such as hydrocephalus, head trauma, cerebral palsy and meningitis are aetiological factors. Skeletal maturation is accelerated. The paradox of tall stature in childhood and short adult height results from premature epiphyseal fusion.

**Regarding hyperthyroidism in the adolescent:**

| | | |
|---|---|---|
| **A** | Usually resolves with 2 years of medical treatment. | (False) |
| **B** | Radioiodine treatment should be avoided because of the risk of genetic damage and neoplasia. | (False) |

| | | |
|---|---|---|
| **C** | May present with heart failure. | (True) |
| **D** | May be associated with increased stature and advanced bone age. | (True) |
| **E** | May present with chronic diarrhoea. | (True) |

**Comments:**

Neonatal hyperthyroidism is transient and is due to transferred thyroid stimulating immunoglobulins from mother. Juvenile hyperthyroidism is from Grave's Disease and is commonest in teenage girls.

Symptoms include:

- Systemic: anxiety, increased appetite, diarrhoea, weight loss; sweating, tremor, tachycardia, warm vasodilated peripheries; goitre; rapid growth with advanced bone age; behavioural problems.
- Eye signs (not in variable): exophthalmos, ophthalmoplegia, lid retraction, lid lag.

TREATMENT:

- Medical: carbimazole, propylthiouracil. Betablockers can be used for symptomatic relief, but not on their own. 50% relapse after 2 years when treatment is stopped.
- Surgical: sub-total thyroidectomy.
- Radioiodine: not considered to result in neoplasia or genetic damage. Follow-up, and subsequent thyroxine therapy, is often needed.



**The following are characteristic of Marfan's syndrome:**

| | | |
|---|---|---|
| **A** | Autosomal recessive inheritance | (False) |
| **B** | Pulmonary stenosis | (False) |
| **C** | Ectopia Lentis | (True) |
| **D** | Increased subischial height ratio: total height ratio | (False) |
| **E** | Pectus carinatum | (True) |

**Comments:**

Marfan's Syndrome is autosomal dominant. The characteristic features are tall stature, mainly due to increase in limb length, arachnodactyly, positive Steinburg's sign (thumb extends beyond the folded fist), hyperextensible joints, high arched palate, lens dislocation, severe myopia. Chest deformities and scoliosis are common. The major complication is cardiovascular because of medial degeneration. This results in aortic dissection, aortic and mitral valve prolapses with regurgitation. Echocardiographic monitoring is recommended. The subiscule height measures the sitting height, and the ratio between the sitting height and the total height is altered in disproportionate increased or short stature.



**Diabetes mellitus in children:**

| | | |
|---|---|---|
| **A** | always presents with keto acidosis | (False) |
| **B** | Can often be managed with oral hypoglycaemic agents | (False) |
| **C** | May be associated with prior mumps infection | (True) |
| **D** | Often remits for a variable period of time | (True) |
| **E** | Has a peak incidence at 10-12 years of age | (True) |

**Comments:**
Diabetes mellitus commonly presents with ketoacidosis in children, but not always. Though the incidence of type 2 diabetes in children is increasing, the most common cause is type 1 diabetes and insulin is required. The onset of type 1 Diabetes sometimes coincides with or follows a viral infection such as mumps, measles, rubella, CMV or influenza. The initial destruction of beta cells may temporarily halt and there may be a phase of islet cell regeneration which results in a 'honeymoon period' of remission. The peak incidence is at aged 10-12 years and most present around autumn and winter.

**The causes of true precocious puberty in a 7 year old may include:**

| | | |
|---|---|---|
| **A** | Thyrotoxicosis | (False) |
| **B** | Congenital adrenal hyperplasia | (False) |
| **C** | Craniopharyngioma | (False) |
| **D** | McCune-Albright Syndrome | (False) |
| **E** | Fragile X Syndrome | (False) |

**Comments:**

The development of secondary sexual characteristics before 8 years in females and 9 years in males is considered precocious. It may be of central origin (true), or due to excess sex steroid production (pseudo, false). In the former, gonadotrophins are increased, particularly FSH and LH, while in the latter they are low. In the latter, the normal sequence is therefore disrupted.

Causes of true precocious puberty include:

- Idiopathic or familial.
- CNS abnormalities (congenital such as hydrocephalus, acquired such as post-irradiation, infection or surgery, or tumours such as microscopic hamartomas).
- Hypothyroidism.

Causes of false precocious puberty include:

- McCune-Albright Syndrome.
- Adrenal disorders - tumours, CAH.
- Ovarian disorders - granulosa cell tumours.
- Testicular disorders - leydig cell tumours.
- Exogenous sex steroids.



**Hypergonadotrophic (primary) hypogonadism is seen in adolescents with:**

| | | |
|---|---|---|
| **A** | Congenital anorchia | (True) |
| **B** | 47, XXY karyotype (Klinefelter's syndrome) | (True) |
| **C** | 45, X karyotype (Turner's syndrome) | (True) |
| **D** | Untreated craniopharyngioma | (False) |
| **E** | Acute lymphoblastic leukaemia in remission | (False) |

**Comments:**
Congenital absence of the testes would result in low serum testosterone at puberty and compensatory rise in gonadotrophins. Individuals with Kleinfelter's syndrome have small firm testes, low serum testosterone and elevated gonadotrophins. 45X karyotype, causes streak ovaries, low serum oestrogen and hence increased gonadotrophins. Untreated craniopharyngioma causes defective gonadotrophin secretion. To induce remission in childhood ALL, the patients may have received cranio-spinal irradiation which causes hypothalamic and pituitary damage and hence gonadotrophins and other pituitary hormones may be low.

**Congenital adrenal hyperplasia due to 21 hydroxylase deficiency:**

| | | |
|---|---|---|
| **A** | Causes testicular enlargement | (False) |
| **B** | Results in delayed fusion of epiphyses | (False) |
| **C** | Produces increased aldosterone secretion | (False) |
| **D** | Has an autosomal recessive inheritance | (True) |
| **E** | Is more easily diagnosed in boys than girls | (False) |

**Comments:**
The condition causes virilisation in the female (male secondary sexual characteristics e.g. clitoromegaly, ambiguous genitalia) and in males sexual development may be entirely normal or precocious puberty develops. Delayed epiphyseal fusion is not a feature. Aldosterone deficiency causes salt wasting in this condition. The disease has an autosomal recessive inheritance. The disease is far more easily diagnosed in females who develop abnormal genitalia, than males who may have no clinical signs.

**Recognised features of Turner's syndrome include:**

| | | |
|---|---|---|
| **A** | Mental retardation | (False) |
| **B** | Cyanotic heart disease | (False) |
| **C** | Primary amenorrhoea | (True) |
| **D** | Accelerated bone age | (False) |
| **E** | Bilateral clinodactyly | (False) |

**Comments:**
Mental retardation is not a feature. Bicuspid aortic valve and coarctation rather than cyanotic heart disease are associated. Primary amenorrhoea occurs due to gonadal dysgenesis. Bone age may be delayed. Clinodactyly is not a feature.

**In Cushing's Syndrome secondary to adrenal carcinoma:**

| | | |
|---|---|---|
| **A** | There is increased skin pigmentation. | (False) |
| **B** | ACTH level is normal. | (False) |
| **C** | There is frequently an associated hypokalaemic alkalosis. | (True) |
| **D** | There is a loss of diurnal variation in serum cortisol. | (True) |
| **E** | The morning serum cortisol may be normal. | (True) |

---

**Comments:**

Cushing's Syndrome consists of a pattern of obesity with associated hypertension due to abnormally high levels of cortisol because of hyperfunction of the adrenal cortex. The syndrome may be dependent on ACTH or ACTH independent.

Aetiology

- a) Functioning adrenal cortical tumour: commonest in infants and usually a malignant carcinoma. 85% occur in children under the age of 7.
- b) Primary pigmented nodular adrenocorticol disease: ACTH independent, due to circulating immunoglobulins directed towards the ACTH receptor. Occurs as a component of the carnii complex (AD). ACTH independent Cushing's Syndrome also occurs in McCune-Albright Syndrome.
- c) Bilateral adrenal hyperplasia: In children older than 7 years, ACTH dependent Cushing's Syndrome is usually found secondary to a basophilic adenoma in the pituitary in about 20%. Microadenomas occur in most children.
- d) Ectopic production of ACTH: This may result in bilateral hyperplasia of the adrenals, e.g. islet cell carcinoma of the pancreas, neuroblastoma, ganglioneuroblastoma.

Clinical Features: Girls outnumber boys 3:1. Obesity (round face, prominent cheeks, buffalo hump, generalised obesity). Abnormal masculinisation with hypertrichosis, pubic hair, deep voice and acne with clitoral enlargement in girls. Growth impairment, hypertension. Increased susceptibility to infection. Occasional association with hemihypertrophy or other congenital defects. In older children striae on the hips, abdomen and the thighs, delayed pubertal development or amenorrhoea, deterioration in school work, emotional lability and renal stones may also occur. Cortisol levels in the normal child are elevated at 8.00am and decreased to <50% of this level by 8.00pm, except in children younger than 3 years in whom a diurnal rhythm is not always established. In Cushing's Syndrome, this rhythm is lost, and cortisol levels are usually elevated at night.

A single dose (short) Dexamethasone test may be helpful. A 2 day Dexamethasone test may be helpful in distinguishing between ACTH dependent or independent Cushing's Syndrome. Osteoporosis may be found on radiology, and the bone age may be moderately retarded. An MRI scan of the pituitary may be helpful in diagnosing pituitary adenomata.

Therapy:

- Benign corticol adenoma - unilateral adrenalectomy.
- Bilateral adenomata - sub-total adrenalectomy.
- Adrenocorticol carcinoma - excision.
- ACTH dependent Cushing's Syndrome - total adrenalectomy has fallen into disfavour, because the pituitary tumour may enlarge causing intense melanosis because of markedly increased levels of ACTH, and enlargement of the sella turcica may occur (Nelson Syndrome). External irradiation and transsphenoidal microsurgery may be used. Cyproheptadine is used in adults.



**The following are commonly used in confirming the diagnosis of insulin**

**dependent diabetes mellitus in a symptomatic child:**

| | | |
|---|---|---|
| **A** | A random plasma glucose of >7.5mmol/L | (False) |
| **B** | Finding of 3+ ketonuria | (False) |
| **C** | An HbA1c of 7.8% | (True) |
| **D** | A fasting plasma glucose of 6.5mmol/L | (False) |
| **E** | An abnormal glucose tolerance test | (False) |

**Comments:**

The diagnosis is usually relatively easy to confirm in a symptomatic child. A random glucose of >11.1mmol/L or a fasting glucose of >7.8mmol/L would be regarded as confirmatory. There is usually glycosuria in addition to ketonuria. Isolated ketonuria suggests fasting. A raised glycosolated haemoglobin (HbA1c) is also highly suggestive. A glucose tolerance test is rarely needed.



**A 3 year old child presents with a head circumference of 43cm. The following should be considered:**

| | | |
|---|---|---|
| **A** | Sotos Syndrome | (False) |
| **B** | Neurofibromatosis | (False) |
| **C** | Congenital rubella | (True) |
| **D** | Mucopolysacchardioses | (False) |
| **E** | Birth asphyxia | (True) |

**Comments:**

Microcephaly is defined as an OFC below the third centile with abnormally slow head growth.

**Causes include**: Familial (normal development), AR, severe developmental delay, congenital infection, brain insult (asphyxia, neonatal meningitis, infarction). In the majority of cases there is cerebral palsy, seizures or visual abnormalities. Sotos Syndrome, neurofibromatosis and mucopolysacchardioses may be associated with a large head.



**The findings of $K^+$ = 2.5 mmol and $HCO_3$ = 10.0 mmol are compatible with:**

| | | |
|---|---|---|
| **A** | Primary hyperaldosteronism | (False) |
| **B** | Renal tubular acidosis | (True) |
| **C** | Urinary diversion into the colon | (True) |
| **D** | Pancreatic fistula | (True) |
| **E** | Respiratory failure | (False) |

**Comments:**

Hypokalaemia, a decrease in the measured level of potassium in the serum, may be caused by:

1. Increased loss:
    - a) Renal: diuretic, Bartter Syndrome, hormonal (Cushing's, hyperaldosteronism, thyrotoxicosis), or renal tubular acidosis. The latter may be proximal (complete bicarbonate loss ± Fanconi's Syndrome), or distal (partial bicarbonate loss). Apart from renal tubular acidosis, all the others are associated with an alkalosis systematically.
    - b) Extra-renal loss: diarrhoea, laxative or enema abuse, vomiting, biliary drainage, or enterocutaneous fistulae. In addition, is the rare familial hypokalaemic periodic paralysis.
    - c) Fluid shift: diabetic ketoacidosis. Most of the latter groups are associated with acidosis.
2. Decreased Intake: a) Hypokalaemia can also result from decreased intake.



**In the Polycystic Ovary Syndrome:**

| | | |
|---|---|---|
| **A** | Hirsutism is common. | (True) |
| **B** | Androstenedione levels are lowered. | (False) |
| **C** | LH secretion is disturbed. | (True) |
| **D** | There is primary oligomenorrhoea. | (False) |
| **E** | There is an association with valproate therapy. | (True) |

**Comments:**

Polycystic Ovary Syndrome (Stein-Leventhal) is characterised by obesity, hirsutism, and secondary amenorrhoea, with bilaterally enlarged polycystic ovaries, but the manifestations are variable. The majority of patients have an increased LH to FSH level, with an abnormal rise in LH in the morning and an exaggerated response to gonadotrophin releasing hormones. A few patients have associated metabolic abnormalities such as 21-hydroxylase deficiency. Associations include insulin resistance hypoinsulinaemia, and acanthosis nigricans. Occasionally the syndrome may be caused by valproate therapy commencing before 20 years of age.



**Puberty in boys:**

| | | |
|---|---|---|
| **A** | Occurs on average two years later than in girls | (True) |
| **B** | Is first noticed when the testes first increase in size | (True) |
| **C** | may be associated with gynaecomastia | (True) |
| **D** | does not occur in the absence of growth hormone | (False) |
| **E** | May occur earlier if the child has been obese all his life | (True) |

**Comments:**

In girls breast development on average begins at 10.8 years and in males puberty begins around 13years(range 9-14 years). In boys puberty begins when testicular volume reaches 4mls, is followed by the development of pubic hair, then subsequently by phallic enlargement and the growth spurt occurs later. Gynaecomastia occurs as a result of the raised circulating testosterone levels being converted peripherally to oestrogen by aromatase. Puberty is dependent solely on gonadal maturation, adrenarche, hypothalamic GnRH and FSH/LH from the anterior pituitary. Obesity is frequently associated with early onset of puberty and rapid skeletal growth.

**A four year old boy presents in coma. For the previous few nights he has been enuretic, although previously dry. On admission he is dehydrated and his breath has a peculiar sweet smell. Blood gas analysis shows pH 7.12, pO2 95mmHg, pCO2 15mmHg, HCO3 10mmol/l.**

| | | |
|---|---|---|
| **A** | He is in diabetic ketoacidotic coma | (True) |
| **B** | He has metabolic alkalosis | (False) |
| **C** | Rehydration should be very slow in case of precipitating cardiac failure | (False) |
| **D** | The initial fluid of choice is 4% dextrose/0.18% saline solution | (False) |
| **E** | His breath has the characteristic small of ammonia | (False) |

**Comments:**
Features consistent with diabetic ketoacidosis include history of enuresis secondary to polyuria, dehydration and ketotic breath. He has a metabolic acidosis as bicarbonate levels are low. Rehydration should be relatively quickly, however over vigorous correction of the fluid deficit will precipitate cerebral oedema. The initial choice of fluid is 0.9% saline 'normal saline'

**The following findings suggest a diagnosis of 21-hydroxylase deficiency rather than congenital adrenal hypoplasia:**

| | | |
|---|---|---|
| **A** | Advanced bone age | (True) |
| **B** | Salt loss in the neonatal period | (False) |
| **C** | Pubic hair development | (True) |
| **D** | Hyperpigmentation | (False) |
| **E** | Raised ACTH levels | (False) |

**Comments:**

Congenital adrenal hypoplasia is X-linked, although milder autosomal recessive forms exist. There is decreased production of cortisol, so ACTH levels are elevated. Salt loss in the neonatal period may occur, and there may be hyperpigmentation. Puberty does not occur, and there may be associated bilateral cryptorchidism, because of a contiguous gene defect (hypogonadotrophic hypergonadism). 21-Hydroxylase deficiency accounts for 95% of congenital adrenal hyperplasia. This results in a decreased production of cortisol and aldosterone. ACTH is secondarily raised. Females usually present with an intersex condition in the neonatal period. Boys are at greater risk from salt loss, which occurs in two thirds of cases. This can lead to severe dehydration in the neonatal period. If they are not salt losers, then they may present with advance bone age, and dissociation (penile and pubic hair development while testes remain infantile) in later childhood.



**The following suggest McCune-Albright Syndrome rather than**

**neurofibromatosis as a cause of premature puberty:**

| | | |
|---|---|---|
| **A** | Male sex | (False) |
| **B** | Fibrous dysplasia of bone | (True) |
| **C** | Skin hypopigmentation | (False) |
| **D** | Skin hyperpigmentation | (True) |
| **E** | Nerve deafness | (False) |

**Comments:**

Precocious puberty may be primary or secondary. The latter are rare and are associated with dissonance (wrong sequence of puberty), rapid onset, and neurological signs and symptoms, which may suggest neurofibromatosis. McCune-Albright Syndrome occurs predominantly in females, and there is a mutation in a protein subunit controlling cAMP levels. It is characterised by skin hyperpigmentation, fibrous dysplasia of bone, which may result in pathological fractures, and endocrine overactivity (ovaries, thyroid, adrenal and pituitary). Ultrasound scan of ovaries and uterus revealing multicystic ovaries and an enlarging uterus suggests premature onset of a normal puberty, by far the commonest cause in females.



**A raised serum bicarbonate level is consistent with**

| | | |
|---|---|---|
| **A** | hypokalaemia | (True) |
| **B** | pyloric stenosis | (True) |
| **C** | diabetic ketoacidosis | (False) |
| **D** | chronic lung disease | (True) |
| **E** | chronic renal failure | (False) |

**Comments:**
a) Metabolic alkalosis usually accompanies hypokalaemia probably due to a shift of hydrogen ions from the extracellular to the intracellulr space. b) loss of acid from persistent vomiting c) bicarbonate low d) respiratory failure with $CO_2$ retention and high bicarbonate e) mild acidosis

**The following regarding Atrial Natriuretic Peptide are correct**

| | | |
|---|---|---|
| **A** | It is secreted in response to right atrial distension | (True) |
| **B** | It inhibits aldosterone release | (True) |
| **C** | It is a direct inotrope | (False) |
| **D** | It is a direct vasodilator | (True) |
| **E** | It is inactivated by endopeptidase | (True) |

**Comments:**
ANP is a 28 aa peptide that is synthesised and released by atrial myocytes in response to distension, angiotensin II and endothelin. It causes salt and hence water losses, is a vasodilator (through possible

direct and indirect mechanisms) and inhibits aldosterone release. Such actions reduce blood volume and cardiac output. ANP is degraded by neutral endopeptidase.

**Low serum magnesium can occur in the following:**

| | | |
|---|---|---|
| **A** | Spironolactone treatment | (False) |
| **B** | Alcoholism | (True) |
| **C** | Hypocalcaemia | (True) |
| **D** | Diabetic ketoacidosis | (True) |
| **E** | Polyuric acute tubular necrosis | (True) |

**Comments:**

Hypomagnesaemia is a feature of malabsorption syndromes, hypoparathyroidism, hypercalcaemia, hypocalcaemia, renal tubular acidosis, primary hyperaldosteronism, and alcoholism. It can occur because of prolonged diuretic therapy, through use of nephrotoxic agents, and because of prolonged intravenous therapy, particularly in infants, using non-magnesium containing fluids. It is often associated with tetany. The symptoms are predominantly of neuromuscular irritability, with tetany, fits and cardiac rhythm disturbances. Neonatal tetany may not resolve until hypomagneseamia has been treated.



**Antidiuretic hormone (ADH) secretion is inhibited by:**

| | | |
|---|---|---|
| **A** | cold | (True) |
| **B** | increased blood pressure | (True) |
| **C** | alcohol | (True) |
| **D** | decreased body fluid tonicity | (True) |
| **E** | barbiturates | (False) |

**Comments:**
ADH secretion is inhibited by dilution, cold, increased blood pressure, alcohol and tetracyclines. Barbiturates and SSRIs as well as sulphonylureas increase secretion.

**In congenital adrenal hyperplasia (CAH):**

| | | |
|---|---|---|
| **A** | 21-hydroxylase deficiency is the commonest variety | (True) |
| **B** | virilisation may be prevented by glucocorticoid treatment | (True) |
| **C** | adrenal crisis may occur within a few days of birth | (True) |
| **D** | blood 17-hydroxyprogesterone concentrations are greatly increased | (True) |
| **E** | severe hypoglycaemia may occur | (True) |

**Comments:**

CAH is due to 21 hydroxylase deficiency in over 90% of cases. Early treatment (in vivo treatment with steroids for the mother is used) may prevent virilisation of the female fetus. Salt losing adrenal crisis is well recognised in the classic variety of the disease with severe hyponatraemia, hypotension and hypoglycaemia from birth onwards. 21 hydroxylase is one of the enzyles responsible for the conversion of 17 OHP to cortisol and aldosterone. Consequently this metabolite is found in excess in CAH.

---

**Hyperprolactinaemia with hypogonadism is found in:**

| | | |
|---|---|---|
| **A** | Hyperthyroidism | (False) |
| **B** | Addison's disease | (False) |
| **C** | A chromophobe adenoma of the pituitary | (True) |
| **D** | Sheehan's syndrome | (False) |
| **E** | Post-cranial irradiation for acute lymphocytic leukaemia | (True) |

**Comments:**
Sheehan's syndrome is associated with a low prolactin concentration. A chromphobe adenoma (non-functioning) may cause hyperprolactinaemia through stalk compression and hypogonadism due to associated hypopituitarism. Cranial irradiation is associated with hyperprolactinaemia and hypogonadism may also be a consequence.

---

**Neonatal goitre may be caused by:**

| | | |
|---|---|---|
| **A** | antithyroid drugs given to the mother | (True) |
| **B** | prolonged use of iodide-containing medicines by the mother | (True) |
| **C** | maternal smoking | (False) |
| **D** | an inborn error of metabolism | (True) |
| **E** | thyroxine given to the mother | (False) |

**Comments:**
Neonatal goitre may be caused by the following:
Maternal drugs such as carbimazole, iodine containing compounds

Certain inborn errors of thyroid metabolism (such as Pendred's syndrome).

Maternal Graves disease due to the passage of TSH receptor antibodies across the placenta which will cause thyroid enlargement.

Giving thyroxine to the mother would not be expected to cause a goitre nor is maternal smoking associated with goitre.

---

**Which of the following is associated with a high serum thyroxine concentration?**

| | | |
|---|---|---|
| **A** | Normal newborns | (True) |

| | | |
|---|---|---|
| **B** | Hashimoto's syndrome | (False) |
| **C** | Thyrotoxicosis | (True) |
| **D** | Nephrotic syndrome | (False) |
| **E** | Cystic fibrosis | (False) |

**Comments:**
Shortly after delivery there is a rise in TSH thought to be a result of the abrupt change in environmental temperature and this returns to normal by 48h. The rise in TSH triggers a rise in thyroxine, which is in the hyperthyroid range by 24 hours. Hashimoto's syndrome results in low serum thyroxine. Nephrotic syndrome results in a low thyroid binding globulin and reduces total serum thyroxine. Cystic fibrosis may result in reduction in thyroxine concentration as a result of the reduced TSH secretion, which occurs in ill patients.

---

**Causes of delayed bone age include:**

| | | |
|---|---|---|
| **A** | Hypothyroidism | (True) |
| **B** | Familial short stature | (False) |
| **C** | Hypopituitarism | (True) |
| **D** | Coeliac disease | (True) |
| **E** | Congenital adrenal hyperplasia | (False) |

**Comments:**

Bone age correlates well with the stage of pubertal development, and can be helpful in predicting adult height in early or late maturing adolescence.

- Normal bone age: familial short stature.
- Delayed: constitutional maturational delay, endocrinologic short stature, under-nutrition. Standards include the Gruelich Pyle and the Tanner and Whitehouse Two Scores which can done on radiographs of the left wrist to look at ossification centres.
- Advanced: puberty, androgens. Also tend to be advanced in the obese child.



---

**A girl aged 5 years attending normal school presents to the outpatient clinic with bilateral enlargement of the breasts. Bone age is 5.8 years and height is on the 90th centile. There has been no vaginal bleeding:**

| | | |
|---|---|---|
| **A** | The diagnosis is unlikely to be precocious puberty | (True) |
| **B** | It is desirable to check her karyotype in making a diagnosis | (False) |
| **C** | Cranial ultrasoun should be requested | (False) |
| **D** | Menarche will likely take place in 3 years | (False) |
| **E** | She will need to be treated with Clomiphene | (False) |

**Comments:**

The diagnosis is unlikely to be precocious puberty as elevated gonadal steroid levels increase height velocity and the rate of skeletal maturation as well as causing feminisation and breast development.

The condition is more suggestive of premature thelarche. Karyotypic anomalies are not relevant. If central (LHRH dependent) precocious puberty is suspected then MRI would be of value rather than cranial ultrasound to identify hypothalamic lesions and other CNS lesions.

However pelvic ultrasound showing a normal uterine volume is the most sensitive discriminator between premature thelarche and true precocious puberty. Puberty and menarche should take place at the normally expected timing,( 11-13y). LHRH agonists are used in the treatment of precocious puberty of all types and not Clomiphene, an Estrogen antagonist.

**In the differential diagnosis of hypoglycaemia**

| | | |
|---|---|---|
| **A** | high C-peptide concentrations in the presence of hypoglycaemia suggest factitious insulin administration | (False) |
| **B** | a high ratio of proinsulin to insulin in a fasting blood sample is a feature of insulinoma | (True) |
| **C** | nesidioblastosis should be considered in the neonate or infant | (True) |
| **D** | the tolbutamide test is useful in the diagnosis of insulinoma | (False) |
| **E** | a 72hr fast fails to produce hypoglycaemia in up to 20% of insuliomas | (False) |

**Comments:**
nesidioblastosis is a diffuse b cell hyperplasia and a common cause of hypoglycaemia in children. High c-peptide in fasting hypoglycaemia argue against the factitious use of insulin as with this c-peptide would be suppressed.

**Children particularly at risk for rickets include:**

| | | |
|---|---|---|
| **A** | Those born small for gestational age | (False) |
| **B** | Asian infants living in Britain fed formula milk | (False) |
| **C** | Those with Hirschsprung's disease | (False) |
| **D** | Mentally handicapped children with epilepsy taking long-term anticonvulsants | (True) |
| **E** | Those with severe renal insufficiency | (True) |

**Comments:**
Small for gestational age infants are not at increased risk, of vitamin D deficiency, which is usually, the combined result of deficient sun exposure and decreased dietary intake. Breast fed Asian infants are at increased risk. Hirschprungs disease affects the large bowel and not small. Anti convulsants can cause osteomalacia by reducing 25 hydroxylation of vitamin D in the liver.

**A prepubertal boy of 16 who presents to clinic:**

| | | |
|---|---|---|
| **A** | Should have details of the onset of puberty in both parents and siblings recorded in the history. | (True) |
| **B** | Is most likely to have an endocrine disorder | (False) |
| **C** | Should be given a course of testosterone to initiate puberty | (False) |
| **D** | should have an immediate chromosome study | (False) |
| **E** | Is likely to have a bone age of 15 years | (False) |

**Comments:**

When health and nutrition are adequate, the onset of puberty is largely determined by genetic factors. The most likely diagnosis is constitutional delay in puberty secondary to a delay in activation of the LHRH pulse generator.

A family history may reveal that fathers and siblings entered puberty late (14-18y). Although testosterone may improve body image and start secondary sexual characteristics developing, there is no evidence that final height is improved. Chromosomal analysis would be indicated if there were small firm testes, gynaecomastia, and tall stature with eunochoid body habitus(arm span greater than height).

The bone age is likely to be considerably less in this individual, as all aspects of physiological maturation are delayed.

**Which of the following syndromes are associated with glucose intolerance?**

| | | |
|---|---|---|
| **A** | Ataxia telangiectasia | (True) |
| **B** | Cockayne Syndrome | (True) |
| **C** | Duchenne Muscular Dystrophy | (False) |
| **D** | Huntington's Chorea | (True) |
| **E** | Prader-Willi Syndrome | (True) |

**Comments:**

Glucose intolerance is relatively common in pregnancy, in the premature, and in the obese. Secondary diabetes can occur in chronic pancreatitis, acromegaly, phaeochromocytoma or Cushing's Disease. It is also associated with **ataxia telangiectasia**, Werner and Cockayne Syndromes (associated with premature aging) and insulin-resistance occurs in Prader-Willi Syndrome. It is also associated with familial combined hyperlipidaemia, and familial hypertriglyceridaemia.

**Hypoparathyroidism is associated with:**

| | | |
|---|---|---|
| **A** | increased incidence of Addison's disease | (True) |
| **B** | chronic mucocutaneous candidiasis | (True) |
| **C** | basal ganglia calcification, commonly causing Parkinsonism | (False) |
| **D** | short 4th + 5th metacarpals | (False) |
| **E** | good response of hypocalcaemia to calcium and vitamin D treatment | (True) |

**Comments:**
Hypoparathyroidism is associated with Addison's disease (autoimmune polyendocrine syndrome type 1 - mucocutaneous candidiasis) as well as other autoimmune conditions - T1DM, hypothyroidism. Short 4th and 5 th metacarpals are associated with pseudohypoparathyroidism. Basal ganglia calcification is common but does not usually cause parkinson's but more likely to cause chorea. The condition is treated with vitamin D.

**A six year old is admitted unconscious. His breath smells of Acetone. Blood gas estimation is pH 7.05, pCO2 24mmhg, standard bicarbonate 12mmol/l, blood glucose 47mmol/l. Which of the following may be expected?**

| | | |
|---|---|---|
| **A** | He has a respiratory acidosis | (False) |
| **B** | He has a metabolic acidosis | (True) |
| **C** | Treatment with insulin should be commenced | (True) |
| **D** | Is likely to have a raised blood urea | (True) |
| **E** | Large volumes of 0.9% sodium chloride IV are contraindicated because of the risk of precipitating cardiac failure | (True) |

**Comments:**
pCO2 and serum bicarbonate are low and this is consistent with metabolic acidosis and respiratory compensation. In respiratory acidosis the PCO2 would be high and bicarbonate levels would be higher to effect a ‘metabolic compensation’. In view of the fact that he has diabetic ketoacidosis, treatment with insulin should be commenced. As a result of osmotic diuresis and natriuresis mediated by glucose he will be dehydrated and sodium depleted. This will raise blood urea. Volume replacement with 0.9% saline must be adequate, however over vigorous rehydration could precipitate cerebral oedema.

**Regarding congenital hypothyroidism:**

| | | |
|---|---|---|
| **A** | It is much less common than phenylketonuria. | (False) |
| **B** | It is due to dyshormogenesis in about 10% of cases. | (True) |
| **C** | Hypothyroidism due to TSH deficiency is very rare. | (True) |
| **D** | Despite early treatment, a few patients have severe learning difficulties. | (False) |
| **E** | Neonatal screening detects about 95% of cases. | (False) |

**Comments:**

The neonatal screening programme for congenital hypothyroidism is a major recent triumph for Paediatrics. It is one of the most common of the metabolic defects, detection is virtually complete, and the long term outcome should be an IQ within the normal range. Causes of congenital hypothyroidism include:

- Athyrosis.
- Maldescent.
- Dyshormonogensis (10%).
- Iodine deficiency (commonest worldwide, but rare in the UK because of iodination of salt).
- TSH deficiency (usually associated with panhypopituitarism, very rare).

**The following suggest a diagnosis of familial combined hyperlipidaemia (FCHL) rather than heterozygous familial hypercholesterolaemia (FH):**

| | | |
|---|---|---|
| **A** | Tendon xanthomas | (False) |
| **B** | Presence of glucose intolerance | (True) |
| **C** | Strong family history of premature coronary artery disease | (False) |
| **D** | Presence of arcus senilus | (False) |
| **E** | Absence of hyperuricaemia | (False) |

**Comments:**

The genetic dislipidaemias occur in one third of patients who have suffered from their first myocardial infarction below the age of 50 years in men. The commonest is familial combined hyperlipidaemia (two thirds), with a fifth due to familial hypercholesterolaemia. The former can be diagnosed only on family studies, and there is elevation of fasting plasma tricglycerides not associated with hypercylomicronaemia. It is autosomal dominant, and some family members may have hypercylomicronaemia. Only 20% of children have elevated triglycerides before the age of 25. Obesity, insulin resistance, hyperinsulinaemia, glucose intolerance, and hyperuricaemia are associated. Heterozygous familial hypercholesterolaemia is dominantly inherited, and results from defects in the LDL receptor. The most important clinical manifestation is premature coronary artery disease, particularly with onset between the third or fourth decade. Tendon xanthomata and arcus cornea are rarely present in children, but are very important signs to identify.



**Nephrogenic diabetes insipidus is commonly associated with:**

| | | |
|---|---|---|
| **A** | Recurrent fevers | (True) |
| **B** | Craving for table salt | (False) |
| **C** | Abnormal growth | (True) |
| **D** | Urinary osmolality of 200 MOsmols/kg H20 or less | (True) |
| **E** | XY Karyotype | (True) |

**Comments:**
Clinical manifestations of nephrogenic DI include thirst, dehydration and hyperthermia. Patients crave water and ice cold drinks rather than salt. Inadequate caloric ingestion associated with incessant water intake can cause growth retardation and repeated bouts of hypernatraemia can cause mental impairment. Urine osmolarity of less than 200 mOsmols/kg H20, hypernatraemia and urine specific gravity of 1.005 or less are characteristic. Familial nephrogenic DI is commonly X linked and males present more often.

**Regarding the maintenance of diet in diabetes mellitus, the following are recommended:**

| | | |
|---|---|---|
| **A** | Six main meals per day. | (False) |
| **B** | A low fibre diet. | (False) |
| **C** | Use of highly refined sugars. | (False) |
| **D** | A high protein diet. | (False) |
| **E** | Increasing the medium chain fat contents of the diet. | (False) |

**Comments:**

The aim of dietary therapy is to match it to the insulin regimen to even out blood glucose concentrations as much as possible throughout the day. Three main meals and 3 snacks are given, and the diet is high in fibre and complex carbohydrates, and low in fat.



**Hypophosphataemia is associated with:**

| | | |
|---|---|---|
| **A** | Vitamin D therapy | (False) |
| **B** | Diabetic ketoacidosis | (True) |
| **C** | Metabolic alkalosis | (True) |
| **D** | Minimal change glomerulonephritis | (False) |
| **E** | Sucrose-isomaltase deficiency | (False) |

**Comments:**

Hypophosphataemia is associated with:

- Decreased intake: premature neonate, starvation or protein energy malnutrition, malabsorption.
- Fluid or electrolyte shifts: respiratory/metabolic alkalosis, diabetic ketoacidosis, steroid therapy.
- Increased losses: primary and tertiary hyperparathyroidism, renal tubular defects, diuretic therapy, post intravenous fluids.
- Combination: Vitamin D deficiency, Vitamin D resistant rickets.



**A grossly obese child age 13 years would have an increased likelihood of:**

| | | |
|---|---|---|
| **A** | Developing a slipped upper femoral epiphysis | (True) |
| **B** | Being prone to respiratory infections | (False) |
| **C** | Having fat parents | (True) |
| **D** | Having been weaned early | (False) |
| **E** | Elevated fasting blood sugar | (False) |

**Comments:**
Slipped upper femoral epiphyses is associated with obesity and growth hormone administration. Respiratory infections are not associated. The single greatest risk factor for childhood obesity is maternal

obesity. Weaning early is not a risk factor. Gross childhood obesity is associated with increased risk of type 2 diabetes, but this would manifest later.

**The following are true statements about female sexual development:**

| | | |
|---|---|---|
| **A** | Asymmetrical breast budding requires investigation | (False) |
| **B** | Peak height velocity occurs one year after beginning | (True) |
| **C** | The average span from breast stage 2 (B2) to menarche is 3 years | (False) |
| **D** | Most of the early menstrual cycles are anovulatory | (True) |
| **E** | Secondary amenorrhoea of 6 months or more merits investigation | (True) |

**Comments:**
Breast budding is often asymmetrical. Girls reach peak height velocity one year after the beginning of puberty and 1 year prior to menarche. The average span from breast stage 2 (11yrs) to menarche (12.9y) is 2 years. Most of the menstrual cycles in the first two years are anovulatory. All secondary amenorrhoea warrants investigation initially to rule out pregnancy.

**A 10 1/2 year old boy presents with delayed puberty. Investigations reveal low gonadotrophin secretion. The following are known causes:**

| | | |
|---|---|---|
| **A** | Klinefelter's Syndrome | (False) |
| **B** | Craniopharyngioma | (True) |
| **C** | Neonatal testicular torsion | (False) |
| **D** | Kallmann Syndrome | (True) |
| **E** | Crohn's Disease | (True) |

**Comments:**

Delayed puberty may be due to:

1. Low gonadotrophin secretion.
    - Constitutional: familial, sporadic.
    - Systemic disease: CF, severe asthma, Crohn's, excessive physical training.
    - Hypothalmopituitary disorders: acquired hypothyroidism, panhypopituitarism, isolated gonadotrophin or growth hormone deficiency, intracranial tumours (including craniopharyngioma), and an Kallmann's Syndrome (GNRH deficiency and inability to smell).
2. High gonadotrophin secretion:
    - Chromosomal: Klinefelter's, Turner's.
    - Steroid hormone enzyme deficiencies.
    - Acquired gonadal disease: post-surgery, chemotherapy/radiotherapy, trauma, torsion, autoimmune.



**The following statements have been made about early nutritional rickets:**

| | | |
|---|---|---|
| **A** | It can be prevented by a daily intake of 400 iu vitamin D | (True) |
| **B** | Serum calcium is reduced | (False) |
| **C** | Serum alkaline phosphatase is elevated | (True) |
| **D** | Bowing of legs is pathognomonic | (False) |
| **E** | Hypotonia is a clinical feature | (True) |

**Comments:**
400 iu Vitamin D is more than adequate to prevent rickets in children, Serum calcium is either normal or may be at the lower end of normal. Serum alkaline phosphatase is elevated because of increased osteoblastic activity. Bowing of the legs may be familial and is not necessarily always caused by rickets. Hypotonia can occur due to alterations in muscle phosphorus ratios.

**Testicular feminization syndrome**

| | | |
|---|---|---|
| **A** | is characterised by XXY chromosomal pattern | (False) |
| **B** | have a female phenotype | (True) |
| **C** | serum testosterone levels are low | (False) |
| **D** | serum oestrogen levels are high | (True) |
| **E** | is an X linked disorder | (True) |

**Comments:**
a-XY

**Causes of bilateral gynaecomastia in a male aged 44 who underwent normal puberty at 14 years of age includes:**

| | | |
|---|---|---|
| **A** | Prostatic carcinoma | (False) |
| **B** | Primary hypothyroidism | (False) |
| **C** | Ranitidine therapy | (False) |
| **D** | Testicular teratoma | (True) |
| **E** | Cannabis abuse | (True) |

**Comments:**
Gynaecomastia is caused by an imbalance between testosterone and oestrogen. This may occur with q teratoma and Cannabis is associated with alteration of sex hromone binding globulin. Unlike cimetidine, ranitidine does not produce gynaecomastia. Prostate carcinoma per se does not cause gynaecomastia but the induction of hypogonadism as treatment is. Hyperthyroidism not hypothyroidism is associated with gynaecomastia.

**The following are associated with skeletal dysplasias:**

| | | |
|---|---|---|
| **A** | ASD | (True) |

| | | |
|---|---|---|
| **B** | Multiple fractures | (True) |
| **C** | Hydrocephalus | (True) |
| **D** | Immune deficiency | (True) |
| **E** | Mental retardation | (True) |

**Comments:**
Skeletal dysplasias mean that all epiphyses, metaphyses, or diaphyses are involved. The vast majority have a genetic basis. There is a high rate of still borns and early postnatal death, so early correct diagnosis is necessary.

Complications:

- Ellis-van Creveld Syndrome: ASD or congenital heart disease.
- Osteogenesis imperfecta: multiple fractures.
- Achondroplasia: hydrocephalus.
- Cartilage hair hypoplasia: immune deficiency.
- Hypochondroplasia (some): mental retardation.

In addition, thanatophoric dwarfism is lethal, and achondroplasia is associated with Sudden Infant Death Syndrome. Many children with these dysplasias have poor body image.



---

**A 7 year old boy presents with tall stature. On investigation, his bone age is accelerated by one year. The following should be considered:**

| | | |
|---|---|---|
| **A** | Marfan's Syndrome | (False) |
| **B** | Hyperthyroidism | (True) |
| **C** | Congenital adrenal hyperplasia | (True) |
| **D** | Beckwith's Syndrome | (False) |
| **E** | Precocious puberty | (True) |

**Comments:**

The majority of tall children have a familial determinant for it. Other causes include:

- Hormonal: excess adrenal androgens, excess sex steroids, excess pituitary growth hormone (very rare), hyperthyroidism.
- Syndromes: Marfan's, homocystinuria, Klinefelter, Sotos, Beckwith.

In this case it would be unusual for congenital adrenal hyperplasia to present so late, but in boys who are not salt losers, a late presentation is possible. The accelerated bone age suggests a hormonal rather than syndromic cause.



---

**The following statements are true about congenital adrenal hyperplasia:**

| | | |
|---|---|---|
| **A** | It always presents shortly after birth | (False) |
| **B** | Boys more commonly present at an earlier age than girls | (False) |
| **C** | It is most frequently caused by 11-beta hydroxylase deficiency | (False) |
| **D** | It is commonly associated with genital pigmentation | (True) |
| **E** | It may be associated with hypertension | (True) |

**Comments:**
Congenital adrenal hyperplasia may present in teenagers with oligo/amenorrhoea and hirsuitism without significant virilisation and is termed late onset CAH. Girls present earlier because of virilisation and ambiguous genitalia, boys may present with precocious puberty. It is most commonly caused by 21 hydroxylase deficiency and genital pigmentation is due to high circulating ACTH 11 beta hydroxylase deficiency can cause virilisation with hypertension.

**The following are associated with poor diabetic control.**

| | | |
|---|---|---|
| **A** | Ingestion of complex carbohydrates | (False) |
| **B** | Associated ear infection | (True) |
| **C** | Onset of puberty | (True) |
| **D** | Overmonitioring | (False) |
| **E** | Inadequate exercise | (False) |

**Comments:**

Particular problems include:

- Refined sugars.
- Poor compliance with testing or insulin administration.
- Illnesses, especially infection.
- Exercise, especially vigorous or prolonged.
- Onset of puberty - this is partly physiological, but also relates to compliance.
- Family stress (divorce or separation).
- Poor family motivation or understanding.



**The following are recognised causes of post-neonatal hypoglycaemia:**

| | | |
|---|---|---|
| **A** | Tricyclic overdose | (False) |
| **B** | Urea cycle defects | (False) |
| **C** | Congenital adrenal hyperplasia | (True) |
| **D** | Medium chain asyle co-a deficiency | (True) |

| | | |
|---|---|---|
| **E** | Intravenous Salbutamol | (False) |

**Comments:**

The major causes are:

METABOLIC:

- a) Ketotic hypoglycaemia.
- b) Liver disease: Reye's Syndrome, acute liver failure.
- c) Inborn errors of metabolism (glycogen storage disease, galactosaemia, MCAD deficiency, organic acidaemia, tyrosinaemia, hereditary fructose intolerance).
- d) Poisoning: alcohol, aspirin.

HORMONAL:

- a) Growth hormone.
- b) ACTH: panhypopituitarism.
- c) Cortisol: Addison's Disease, congenital adrenal hyperplasia.
- d) Hyperinsulinsim: Nesidioblastosis, Beckwith's, insulinomas, exogenous insulin.



**The following findings suggest a diagnosis of Pompe's Disease rather than Von Gierke's Disease:**

| | | |
|---|---|---|
| **A** | 3cm liver | (False) |
| **B** | Infantile onset | (False) |
| **C** | Hypotonia | (True) |
| **D** | Hypertrophic cardiomyopathy | (True) |
| **E** | Absence of hypoglycaemia | (True) |

**Comments:**

Von Gierke's Disease (glucose-6 phosphatase deficiency) has infant onset, with liver enlargement, growth failure, and hypoglycaemia. It is treated with long-acting carbohydrates, and the prognosis is good. Pompe's Disease (lysosomal a-glucosidase deficiency), again has infant onset, with a lesser degree of liver enlargement than Von Gierke's Disease, but a predominant effect on muscle. This results in hypotonia, a hypertrophic cardiomyopathy, and death from heart failure.



**Sweating is a recognised feature of:**

| | | |
|---|---|---|
| **A** | Acromegaly | (True) |
| **B** | Ketoacidosis | (False) |

| | | |
|---|---|---|
| **C** | Adrenal insufficiency | (False) |
| **D** | Phaeochromocytoma | (True) |
| **E** | Insulinoma | (True) |

**Comments:**

Sweating is proportional to surface area, and increases with temperature, and sympathetic stimuli. There are thus a huge number of causes of hyperhidrosis. These include:

- Corticol: emotion, familial dysautonomia, congenital icthyosiform erythroderma.
- Hyperthalamic:
  - Drugs - antipyretics, emetics, insulin.
  - Exercise.
  - Infection - including defervescence.
  - Metabolic - including diabetes, hypopituitarism, hyperthyroidism, hypoglycaemia, obesity, pregnancy.
  - Cardiovascular - heart failure, shock.
  - Vasomotor - Cold injury, Raynaud's, rheumatoid arthritis.
  - Neurologic - post enchapalitic, tumour.
- Medullary: Encephalitis, syringomyelia, thoracic sympathetic trunk injury.
- Spinal: Cord transection.
- Changes in Blood Flow: AV fistula, Klippel-Trelaunay Syndrome.



**The following features are compatible with gonadal dysgenesis (Turner's syndrome):**

| | | |
|---|---|---|
| **A** | A baby girl presenting with oedema of the feet and hands at birth | (True) |
| **B** | Height at the age of 3 years is on the 10th centile | (True) |
| **C** | A greater incidence of pulmonary stenosis | (False) |
| **D** | A karyotype 45X/46XX | (True) |
| **E** | Delayed onset of secondary sexual characteristics | (True) |

**Comments:**
Lymphoedema and neck webbing are features. Varying degrees of short stature occur. Coarctation of the aorta and bicuspid aortic valve are features rather than pulmonary stenosis. 45X/46XX mosaicism may be present. Secondary sexual characteristics will be delayed due to the lack of oestrogen.

**In insulin-dependent diabetes mellitus:**

| | | |
|---|---|---|
| **A** | There is an association with HLA DR3 +DR4. | (True) |
| **B** | Patients are prone to ketosis. | (True) |
| **C** | There is a 2:1 male:female predominance. | (False) |
| **D** | It always follows the appearance of anti-islet cell antibodies. | (False) |

| | | |
|---|---|---|
| **E** | There is an association with mumps. | (True) |

**Comments:**

Both genetic and environmental factors play a role in the aetiology of diabetes. There is an increased twin incidence, and greatly increased chance if parents are affected. There is an association with HLA DR3 and DR4. The sex ratio is equal. The trigger, thought to be a viral infection with molecular mimicry for an antigen on the surface of beta cells of the pancreas. Autoantibodies are commonly found, but are not universal. Epidemics of mumps, rubella and Coxsackie virus infections have been associated with subsequent increases in the incidence of type 1 diabetes. It is possible that early exposure to cow's milk may be a factor in triggering it too.



**1, 25, dihydroxycholecalciferol:**

| | | |
|---|---|---|
| **A** | Causes suppression of parathyroid hormone (PTH) by direct action on the parathyroid gland. | (False) |
| **B** | Causes suppression of parathyroid hormone indirectly by increasing serum calcium. | (True) |
| **C** | Acts on cell surface receptors. | (True) |
| **D** | Is biologically more active than 25, dihydroxycholecalciferol. | (True) |
| **E** | Leads to increased osteoblast activity. | (False) |

**Comments:**

7, dihydrocholesterol is converted by sunlight into cholecalciferol (Vitamin D3). In the liver this is 25, hydroxylated, and in the kidney this is 1, 25 hydroxylated. Vitamin D is not abundant in natural foods except for fish liver oils, fatty fish and egg yolk. Ergocalciferol (Vitamin D2) is used to fortify margarine. 1, 25 dihydroxycholecalciferol is the most active form of the vitamin. It is produced following parathormone secretion in response to a low plasma calcium. The effect of 1, 25 (OH2D3) is to induce synthesis of a calcium binding protein (calbindin-D) in the intestinal mucosa with the resultant absorption of calcium. It also promotes bone dissolution and mineralisation. Thyroid hormones also mobilises calcium by directly enhancing bone resorption, an effect that requires 1, 25 dihydroxy Vitamin D. The effects of PTH on bone and kidney are mediated through binding to specific receptors on the membranes of target cells and through activation of the transduction pathway involving a G protein coupled with an adenelatecyclase system. Steroid hormones also work through binding to specific receptors on the cell surface and then influencing DNA transcription and translation in the cell nucleus.



**Raised serum inorganic phosphorous is found in**

| | | |
|---|---|---|
| **A** | acromegaly | (True) |
| **B** | renal tubular acidosis | (False) |
| **C** | dietary rickets | (False) |
| **D** | pseudo-hypoparathyroidism | (True) |
| **E** | chronic obstructive jaundice | (False) |

**Comments:**
Hyperphosphataemia is associated with Acromegaly as GH causes phosphate reabsorption. Pseudo-hypoPTH is also associated with hyperphosphataemia. b+c Phosphate is low.

**The following are recognised presentations of adrenal corticol insufficiency:**

| | | |
|---|---|---|
| **A** | Hyponatraemia | (True) |
| **B** | Hyperkalaemia | (True) |
| **C** | Hypercalcaemia | (True) |
| **D** | Hyperglycaemia | (False) |
| **E** | Metabolic alkalosis | (False) |

**Comments:**

Adrenal corticol insufficiency is rare.

Causes include: autoimmune: haemorrhage or infarction, adrenal leucodystrophy, TB.

Presentation may be:

- ACUTE: Hyponatraemia, hyperkalaemia, hypercalcaemia, hypoglycaemia, dehydration and hypotension and circulatory collapse.
- CHRONIC: Vomiting, lethargy, hyperpigmentation of the gums, scars and creases, growth failure.

An adrenal crisis requires urgent treatment with IV saline, glucose and hydrocortisone. Long term treatment is with glucocorticoid and mineralacorticoid replacement therapy. The steroids should be increased by 3-5 fold at times of insulin or operation. A medical bracelet is advisable.



**The following are known associations with phenylketonuria:**

| | | |
|---|---|---|
| **A** | Presentation in the second year of life with absence seizures. | (False) |
| **B** | The association of red hair and brown eyes. | (False) |
| **C** | Normal development. | (False) |
| **D** | Musty odour. | (True) |
| **E** | Response of some patients to piridoxine. | (False) |

**Comments:**

Phenylketonuria is a quarter as common as congenital hypothyroidism, with an incidence of 1:10,000 live births. It is due either to phenylalanine hydroxylase deficiency or problems with synthesis or recycling of the bioptrine co-factor. The presentation is with infantile spasms or developmental delay between 6 and

12 months of age. Patients may be musty smelling, fair haired and blue eyed and may develop eczema. Treatment is with restriction of dietary phenylalanine, while ensuring sufficient for physical and neurological growth. Co-factor defects are treated with a diet low in phenylalanine and high in neurotransmitter precursors.



---

**Regarding parathyroid hormone:**

| | | |
|---|---|---|
| **A** | It is composed of 84 amino acids. | (True) |
| **B** | Because of the high circulating serum levels, it can be detected by radio-immunoassay techniques. | (False) |
| **C** | Production is increased by a drop in serum phosphate. | (False) |
| **D** | PTH stimulates activity of 1-alpha hydroxylase in the kidney. | (False) |
| **E** | In pseudohypopararthyroidism, brachydactyly may be present. | (True) |

**Comments:**
Parathyroid hormone is an 84 amino acid chain protein produced by the parathyroid gland. The first 34 amino acid enterminal fragment possesses biological activity. Hypocalcaemia stimulates PTH production. This stimulates activity of 1-a-hydroxy in the kidney, and enhances the production of 1, 25 di(OH)2D3. The latter induces synthesis of a calcium binding protein (calbindin-D) in the intestinal mucosa with resultant absorption of calcium. PTH also mobilises calcium by directly enhancing bone resorption (with Vitamin D3). In the kidney it is a potent stimulus to the reabsorption of calcium in the loop of Henle. The effects of PTH on bone and kidney are mediated through specific membrane receptors.

---

**A 14 month old child is found to have a serum Ca concentration of 2.0mmol/L- phosphate of 0.68mmol/L- and alkaline phosphatase of 570. Which of the following conditions could explain these findings?**

| | | |
|---|---|---|
| **A** | Pseudohypoparathyroidism | (False) |
| **B** | Coeliac disease | (True) |
| **C** | Hypophosphatasia | (False) |
| **D** | Nutritional rickets | (True) |
| **E** | Renal failure | (False) |

**Comments:**

Causes of hypocalcaemia are:

- Parathyroid hormone deficiency:
  - a) aplasia or hypoplasia, e.g. Catch 22 Syndrome.
  - b) PTH gene mutations or receptor defects (latter includes pseudohyperparathyroidism).
  - c) Autoimmune disease.
  - d) Infiltrations.
- Vitamin D deficiency.
- Magnesium deficiency - primary hypomagnesaemia, renal tubular defects, aminoglycoside

therapy.

- Phosphate excess: laxatives. Hypophosphotasia is a defect due to decreased alkaline phosphatase activity. Renal failure usually results in a rise in phosphate, because of secondary hyperparathyroidism.



---

**Hirsutism is a recognised association of:**

| | | |
|---|---|---|
| **A** | treatment with minoxidil | (True) |
| **B** | arrhenoblastoma of the ovary | (True) |
| **C** | testicular feminisation syndrome | (False) |
| **D** | polycystic ovary syndrome | (True) |
| **E** | porphyria cutanea tarda | (True) |

**Comments:**
Hirsutes may be noted in PCOs, with minoxidil therapy, in PCT and with increased testosterone production as is ovarian tumours/arrhenoblastomas. Androgen insensitivity syndrome is associated with no response to testosterone.

---

**The following statements are true:**

| | | |
|---|---|---|
| **A** | Dyshormonogenesis is the commonest cause of congenital hypothyroidism | (False) |
| **B** | In patients with short stature (height below the 3rd centile) one should always screen for growth hormone efficiency | (False) |
| **C** | Congenital adrenal hyperplasia is a cause of ambiguous genitalia in the newborn | (True) |
| **D** | Children with diabetes mellitus always require treatment with insulin | (False) |
| **E** | Onset of puberty is usually earlier in boys than in girls | (False) |

**Comments:**
The commonest causes of congenital hypothyroidism are thyroid aplasia/hypoplasia or ectopic thyroid gland. Short stature may be the consequence of multiple factors and Growth hormone deficiency is identified in a minority of patients. Growth velocity, parental height, intercurrent illnesses and use of drugs such as steroids may be more relevant. In females with congenital adrenal hyperplasia, excessive adrenal androgens result in virilisation and ambiguous genitalia. The incidence of type 2 diabetes in children is rising, and children may be treated with weight loss/diet and or metformin. Also in the condition known as MODY (maturity onset diabetes of the young, autosomal dominant, defective insulin secretion) oral hypoglycaemics are used initially. The onset of puberty is delayed by approximately 2 years in males, when compared to females.

---

**The following are features of congenital adrenal hypoplasia:**

| | | |
|---|---|---|
| **A** | Low renin levels | (False) |

| | | |
|---|---|---|
| **B** | Exaggerated diurnal cortisol responses | (False) |
| **C** | Association with Duchenne Muscular Dystrophy | (True) |
| **D** | Association with vitiligo | (False) |
| **E** | Presentation with diarrhoea, vomiting and dehydration | (True) |

**Comments:**

Hypoadrenalism usually presents in the neonatal period with increasing pigmentation, salt loss and cryptorchidism in males. The disorder is due to a mutation in the DAX0 gene, a new nuclear hormone receptor family, located on Xp21. Hypogonadotrophic hypogonadism (HHG) is caused by the same gene mutation, and the cryptorchidism is explained by this. The disorder is located very close to the Duchenne muscular dystrophy gene and the glycerol kinase gene, so these are associations.



**Delayed puberty:**

| | | |
|---|---|---|
| **A** | Presenting as amenorrhoea in a girl with a bone age of 16 years is abnormal | (True) |
| **B** | Presenting as immature genitalia and short stature in a 15 year old boy indicates pathological gonadotrophin deficiency | (False) |
| **C** | Manifest by amenorrhoea in a 17 year old girl and associated with an elevated serum testosterone level suggests an androgen resistance disorder | (True) |
| **D** | In a short girl is an indication to perform chromosome analysis | (True) |
| **E** | Is more common in obese children | (False) |

**Comments:**
Normal bone age, with primary amenorrhoea may suggest gonadotrophin deficiency. Delayed puberty and short stature in a 15 year old could indicate either constitutional delay or pathological gonadotrophin deficiency. High serum testosterone, indicates androgen insensitivity which comprises abnormality of the androgen receptor, intrabdominal testes, XY karyotype, normal breasts but absent pubic hair. In a short female chromosome analysis should be performed to rule out Turner's syndrome. Delayed puberty is not common in obese children and requires investigation.

**Recognised features of distal RTA are:**

| | | |
|---|---|---|
| **A** | Hypokalaemia | (True) |
| **B** | Nephrocalcinosis | (True) |
| **C** | Inability to reduce urine below 7 | (False) |
| **D** | Inability to form ammonia in distal tubular cells | (False) |
| **E** | More severe manifestations than proximal RTA | (False) |

**Comments:**

Distal RTA results from a deficiency of hydrogen iron secretion by the distal tubular and collecting duct.

There is decreased formation of carbonic acid then carbon dioxide, resulting in a loss of bicarbonate of up to 10% of the filtered load. The pH of the urine cannot be reduced below 5.8, and there is secondary hyperchloraemia and hypokalaemia. Because less bicarbonate is wasted in distal and proximal RTA, the hypokalaemia is less severe. Nephrocalcinosis and nephrolithiasis may occur.

Aetiology:

1. Primary: Sporadic or AD or AR.
2. Secondary:
    - a) Intestinal nephritis (obstructive, pyelonephritis, transplant rejection, sickle cell disease, medullary sponge kidney).
    - b) Toxins (amphotericin, lithium, toluene)



---

**The following may be found in emotional deprivation:**

| | | |
|---|---|---|
| **A** | Low levels of growth hormone secretion. | (False) |
| **B** | Low levels of insulin-like growth factor-1. | (True) |
| **C** | Reduced growth hormone response to provocation. | (True) |
| **D** | Precocious puberty. | (False) |
| **E** | Low levels of insulin-like growth factor-2. | (False) |

**Comments:**

Emotional deprivation is an important cause of failure to thrive and mimics some aspects of hypopituitarism. The full details have not been worked out, but there are low levels of Insulin-like growth factor-1, and poor responses of growth hormone to provocation, and possibly delayed puberty. There may be evidence of poor mother/child relationship, with emotional and behavioural abnormalities. During catch-up, pseudotumour cerebri may occur.



---

**A child aged 10 days has ambiguous genitalia. Which of the following may be causative.**

| | | |
|---|---|---|
| **A** | if a buccal smear is chromatin negative there is a serious risk of an Addisonian crisis | (False) |
| **B** | a raised urinary output of pregnanetriol would confirm a diagnosis of congenital adrenal hyperplasia | (True) |
| **C** | the finding of the genotype 45 XO would reliably explain the anomaly | (False) |
| **D** | if testicles are present in the "labia" an acceptable explanation would be Klinefelter's syndrome | (False) |
| **E** | the most important factor in deciding the sex to which the child should be assigned is the genetic (chromosomal) sex | (False) |

---

**Comments:**
If buccal smear positive ie female then there would be at increased risk of salt crisis. Salt losers presenting in newborn period with crisis are more likely to be female. The commonest cause of ambiguous genitalia at birth is CAH, of which 95% are deficient in 21-hydroxylase. Less common enzyme defects involve 11B hydroxylase, and 3B hydroxysteroid dehydrogenase. About 2/3 of 21-hydroxylase are salt losers, and present with an hypoadrenal crisis. There is normal male genitalia in 47 XXY – Klinefelter's.

---

**Congenital hypothyroidism**

| | | |
|---|---|---|
| **A** | cannot confidently be diagnosed before the age of three months | (False) |
| **B** | is in some cases associated with a goitre | (True) |
| **C** | affects approximately 1 in 10,000 infants | (False) |
| **D** | may present with jaundice | (True) |
| **E** | requires thyroxine treatment throughout life | (True) |

**Comments:**
a-at aged 1 week, c-1:3,500

---

**Congenital hypothyroidism:**

| | | |
|---|---|---|
| **A** | Is normally treated using the L-isomer of Thyroxine | (True) |
| **B** | Has an incidence of 1 in 15,000 | (False) |
| **C** | Is a cause of bilateral inguinal herniae | (False) |
| **D** | Requires children to be placed in special schooling | (False) |
| **E** | Is best monitored by regular assessment of height velocity | (True) |

**Comments:**

Congenital hypothyroidism is treated using L thyroxine. The incidence is one in 4000. The condition is associated with umbilical herniae and not inguinal herniae.

Intellectual function and cognitive development may be impaired if the condition remains untreated or in cases of severe cretinism, which is rare. The rate of linear growth is retarded in this condition and always less than weight gain.

---

**Cretinism is characterised by**

| | | |
|---|---|---|
| **A** | premature fusion of epiphyses | (False) |
| **B** | persistance of jaundice in neonate | (True) |
| **C** | delayed dentition | (True) |
| **D** | paralytic ileus | (True) |

| | | |
|---|---|---|
| **E** | incidence about 1:200 | (False) |

**Comments:**
a-retarded bone age, e-1:5000. Also short stature, protruding tongue, broad flat nose, widely set eyes, sparse hair, dry skin, protruberant abdomen, umbilical hernia.

---

**Regarding calcitonin:**

| | | |
|---|---|---|
| **A** | A calcitonin producing medullary carcinoma of the thyroid can present with watery diarrhoea. | (True) |
| **B** | Calcitonin production can be a feature of multiple endocrine neoplasia's type 2B. | (True) |
| **C** | Calcitonin is produced from arachidonic acid. | (False) |
| **D** | High levels of calcitonin production causes hypercalcaemia in older children. | (False) |
| **E** | The main biological effect of calcitonin is to increase bone resorption. | (False) |

**Comments:**

Calcitonin is a polypeptide hormone produced by the C-cells (parafollicular) of the thyroid. It is of little consequence in children and adults, and even high levels produced by medullary carcinoma of thyroid do not cause hypercalcaemia. Medullary carcinoma can however, present as chronic watery diarrhoea. In the fetus, circulating levels are high and appear to augment bone metabolism and skeletal growth. In infants and children with congenital hypothyroidism (and hence presumed deficiency of C-cells) calcitonin levels are lower than normal. Its main biological effect is to inhibit bone resorption by decreasing osteoclastic activity. Calcitonin is also synthesised in other organs such as the GI tract, pancreas, brain and pituitary, and is thought to behave as a neurotransmitter imposing local inhibitory effect on cell function.



---

**Obesity is associated with a higher risk of developing**

| | | |
|---|---|---|
| **A** | Osteoarthritis | (True) |
| **B** | Diabetes mellitus | (True) |
| **C** | Renal carcinoma | (True) |
| **D** | Breast carcinoma | (True) |
| **E** | Osteoporosis | (False) |

**Comments:**
Obesity is associated with a higher risk of OA, carcinoma of the breast, kidney and prostate, hypertension, diabetes mellitus and psychiatric ocnditions such as depression. It is relatively protective for osteoporosis.

---

**Cause of hyperuricaemia include:**

| | | |
|---|---|---|
| **A** | Aspirin | (True) |

| | | |
|---|---|---|
| **B** | Lesch-Nyhan syndrome | (True) |
| **C** | Glycogen Storage Disease Type I | (True) |
| **D** | Polycythaemia rubra vera | (True) |
| **E** | Hereditary spherocytosis | (False) |

**Comments:**

Causes of hyperuricaemia include:

- Metabolic: gout, Glycogen Storage Disease Type I, fructose 160, phosphatase deficiency, Lesch-Nyhan Syndrome. The 2 mechanisms are either decreased activity of HGPT, or increased activity of PRPP.
- Increased cell destruction: particularly myeloproliferol diseases.
- Decreased renal clearance: diabetic ketoacidosis, aspirin, Down's Syndrome, Bartter's Syndrome, pyrozinamide therapy.

Management should be to decrease intake of high purine foods or to give allopurine (xanthine oxidase inhibitor).



---

**An 8 year old boy presents with bilateral 6ml testes, and some pubic hair. The following should be considered:**

| | | |
|---|---|---|
| **A** | Congenital adrenal hyperplasia | (False) |
| **B** | Hyperthyroidism | (False) |
| **C** | Gonadotrophin producing intracranial tumour | (True) |
| **D** | Gonadal tumour | (False) |
| **E** | Hypothalamic hemartoma | (True) |

**Comments:**

In males, precocious puberty is unusual, and is usually due to a brain tumour. Careful examination distinguishes true (synchronous) puberty from pseudopuberty. True precocious puberty, where testicular enlargement precedes pubic hair development and the growth spurt, usually results from excessive gonadotrophin release usually from an intracranial tumour. The testicular enlargement is bilateral. Pseudopuberty suggests an adrenal cause. Unilateral enlargement of the testes may be due to a tumour.



---

**The following are recognised causes of syndrome of inappropriate ADH secretion (SIADH):**

| | | |
|---|---|---|
| **A** | Guillian-Barre Syndrome. | (True) |
| **B** | Perinatal asphyxia. | (True) |

| | | |
|---|---|---|
| **C** | Use of positive pressure respirator | (True) |
| **D** | Renal infection | (False) |
| **E** | Benign intracranial hypertension | (False) |

**Comments:**
CNS causes - surgical or traumatic damage to the brain - encephalitis/ brain abscess - brain tumours - meningitis, Guillain-Barré syndrome/ bulbar poliomyelitis - cerebrovascular accidents, subdural haematomas - tumours of the fourth ventricle - neonatal hypoxia or hydrocephalus 2. Pulmonary disorders - pneumonia - tuberculosis - asthma

**Which of the following may be responsible for a hypokalaemic alkalosis?**

| | | |
|---|---|---|
| **A** | feeds that are too concentrated | (False) |
| **B** | congenital pyloric stenosis | (True) |
| **C** | cystic fibrosis | (True) |
| **D** | previous urinary diversion | (False) |
| **E** | renal failure | (False) |

**Comments:**
Metabolic alkalosis with hypokalemia is seen in pyloric stenosis because of the loss of stomach acid with K and HCl, and cystic fibrosis as in pseudo Bartter syndrome. Renal failure and urinary diversion cause metabolic acidosis. Bartter syndrome is a form of renal K wasting with elevated renin and aldosterone, the K is usually <2.5.

**A 3 year old boy was admitted in coma after a 2 day history of vomiting and abdominal pain.**

| | |
|---|---|
| **Hb** | 14 gm/dl |
| **WCC** | 17,000/cu mm |
| **Blood Glucose** | 25 mmol/l |
| **Sodium** | 150 mmol/l |
| **Potassium** | 3.7mmol/l |

| | | |
|---|---|---|
| **A** | The surgeon must be consulted to rule out an acute abdominal condition | (False) |
| **B** | Bedside urinalysis alone should make the diagnosis | (True) |
| **C** | 0.2% normal saline in 5% dextrose should be infused immediately | (False) |
| **D** | An injection of subcutaneous insulin will immediately reverse the comatose state | (False) |
| **E** | hypodermic injections of soluble insulin according to sliding scale of urine colour should be started immediately | (False) |

**Comments:**
This clinical picture of vomiting and abdominal pain is commonly seen with Diabetic ketoacidosis and can be mistaken for an acute abdomen. Urinalysis would be expected to show ketones, which would confirm the diagnosis of Diabetic Ketoacidosis. A solution containing dextrose should not be administered, however saline and potassium should be administered. Intravenous insulin and fluids would gradually

reverse the condition. Subcutaneous insulin is started only when the patient is fully awake, eating and drinking, and hyperglycaemia and ketonuria are controlled. Capillary glucose, plasma glucose and urine ketones are used to guide treatment.

---

**The following are true statements about male sexual development:**

| | | |
|---|---|---|
| **A** | The apex of the physical strength spurt antedotes the peak height velocity by six months | (False) |
| **B** | Sperm production begins in the early stages | (True) |
| **C** | The earliest detectable evidence is pubic hair growth | (False) |
| **D** | Breaking of the voice is dependent on testosterone | (True) |
| **E** | The average testicular volume in the adult is 15ml | (False) |

**Comments:**
The strength spurt occurs after the pubertal growth spurt. Spermatogenesis is commonly apparent from the age of 11 years and upwards, however motility, morphology and concentration do not reach adult levels till 17 years. The earliest detectable evidence of puberty in males is the increase in testicular size(length of 2.5cm and a volume of 4mls).The voice breaks at an average of 13.9y due to testosterone mediated growth of the laryngeal muscles, the cricothyroid cartillage and the larynx. The average testicular volume in the adult is around 20-25mls.

---

**Regarding the development of the fetal gonad:**

| | | |
|---|---|---|
| **A** | Mullerian hormone inhibits the development of male external genitalia. | (False) |
| **B** | Presence of the SRY gene determines development of the testes. | (True) |
| **C** | The female internal genitalia develop from the Wolffian ducts. | (False) |
| **D** | Leydig cells produce antimalarian hormone. | (False) |
| **E** | Dihydrotestosterone determines the development of male external genitalia. | (True) |

**Comments:**

The gonads in the fetus are initially undifferentiated. In the absence of the SRY gene, female ovaries and genitalia will develop. In the presence of it, testes will develop. The leydig cells are responsible for testosterone and dihydrotestosterone production. These respectively determine the development of the Wolffian ducts in to male internal genitalia, and the male external genitalia. Sertoli cells in the testes are responsible for the production of anti-mullerian hormone, which inhibits the development of female internal genitalia.



**Poorly controlled hypothyroidism in an 18 month old infant is associated with:**

| | | |
|---|---|---|
| **A** | High plasma TSH concentration | (True) |
| **B** | Delayed bone age | (True) |

| | | |
|---|---|---|
| **C** | Umbilical hernia | (True) |
| **D** | Diarrhoea | (False) |
| **E** | Normal development milestones | (False) |

**Comments:**
High plasma TSH concentration with low Free Thyroxine level would occur. Thyroid hormone is a prerequisite for normal growth and cognitive /psychomotor development so bone age and developmental milestones would be delayed. Constipation is associated as are umbilical herniae.

---

**A child presents at 18 months of age with hypoglycaemia and a convulsion.**
**The following suggest a diagnosis of ketotic hypoglycaemia:**

| | | |
|---|---|---|
| **A** | Macrosomia | (False) |
| **B** | Absence of ketones in the urine | (False) |
| **C** | 3cm liver | (False) |
| **D** | Elevated plasma insulin levels | (False) |
| **E** | Elevated serum allanene | (False) |

**Comments:**

Ketotic hypoglycaemia usually presents between 18 months and 5 years, improving spontaneously by 9 years. Hypoglycaemia occurs during intercurrent illness or when food intake is limited. The children tend to be small and have limited reserves for gluconeogenesis. There is ketonuria and ketonaemia, an appropriately low insulin level, and markedly reduced allanene levels (allanene is quantitatively the major gluconeogenic amino acid precursor).



---

**Hypernatraemic dehydration is commonly associated with the following:**

| | | |
|---|---|---|
| **A** | Cholera | (False) |
| **B** | Pyloric stenosis | (False) |
| **C** | Inappropriate ADH secretion | (False) |
| **D** | Diabetes insipidus | (True) |
| **E** | Diabetes mellitus | (False) |

**Comments:**
Cholera results in excessive water and sodium losses and hence hyponatraemia. Pyloric stenosis typically results in hypokalaemic, hypochloraemic, metabolic alkalosis and not cause hypernatraemia. Inappropriate ADH secretion causes hyponatraemia. In Diabetes insipidus failure to concentrate urine results in hypernatraemic dehydration with hyperosmolarity. Poorly controlled diabetes results in osmotic diuresis and renal sodium loss.

---

**Insulin-induced hypoglycaemia may present with:**

| | | |
|---|---|---|
| **A** | Hemiplegia | (False) |
| **B** | Aggressive behaviour | (True) |
| **C** | Foot drop | (False) |
| **D** | Night sweats | (False) |
| **E** | Light headedness | (True) |

**Comments:**

Hypoglycaemia occurs suddenly over a few minutes (DKA usually develops over hours or days). Symptoms are due to:

- Catecholamine response: pallor, sweating, fear, trembling, tachycardia.
- Cerebral glucopenia: hunger, drowsiness, mental confusion, seizures, coma. Mood and personality changes and individual physical responses may also occur.

The level of which symptoms occur may not meet the criteria of the hypoglycaemia in healthy subjects.



**Short Stature is a feature of:**

| | | |
|---|---|---|
| **A** | Down's syndrome | (True) |
| **B** | Achondroplasia | (True) |
| **C** | Untreated hypothyroidism | (True) |
| **D** | Obesity | (False) |
| **E** | Thyrotoxicosis | (False) |

**Comments:**
Short stature is a well known feature of Down's syndrome, Achondroplasia and untreated hypothyroidism. Obesity and nutrient excess is associated with tall stature. The presence of short stature in these children should alert clinicians to a co-existent endocrinopathy. Thyrotoxicosis is associated with tall stature.

**Diabetes in adolescence:**

| | | |
|---|---|---|
| **A** | Is usually associated with a decreased insulin requirement | (False) |
| **B** | Can unmask hypothyroidism | (True) |
| **C** | Causes a delayed menarche in girls | (False) |
| **D** | If poorly controlled causes reversible retinopathy | (False) |
| **E** | Is compatible with holding a full driving licence | (True) |

**Comments:**

Diabetes in adolescence is associated with insulin resistance and increased insulin requirement. Diabetes in adolescence may be poorly controlled and therefore if weight gain paradoxically develops then hypothyroidism should be suspected.

Delayed menarche occurs only if there is significant undernutrition as a consequence of poor control or an eating disorder. The retinopathy is not often reversible. There is no contraindication to holding a licence if hypoglycaemia without warning and major visual complications do not develop.

---

**In relation to Maple Syrup Urine Disease:**

| | | |
|---|---|---|
| **A** | It may present with prolonged jaundice. | (False) |
| **B** | It usually presents with severe metabolic acidosis, hypoglycaemia and seizures. | (True) |
| **C** | The urine has a characteristic fishy smell. | (False) |
| **D** | There is increased excretion of branch chain amino acids in the urine. | (True) |
| **E** | There is a high risk of early death during acute illnesses. | (True) |

**Comments:**

Maple Syrup Urine Disease usually presents with severe metabolic acidosis, hypoglycaemia, and seizures. There is increased excretion of the branch chain amino acids, leucine, isoleucine and valine, resulting in a characteristic maple syrup smell in the urine. Delayed diagnosis can result in learning difficulties and neurological dysfunction, and acute illnesses may precipitate a rapid decline.



---

**Microalbuminuria in diabetes mellitus:**

| | | |
|---|---|---|
| **A** | Improves with exercise. | (False) |
| **B** | Can be reversed with improved diabetic control. | (True) |
| **C** | Is a marker of renovascular disease. | (True) |
| **D** | Means the loss in urine of protein with a lower molecular weight than albumin. | (False) |
| **E** | Can be diagnosed on an early morning spot sample of urine. | (True) |

**Comments:**

A critical stage in the development of diabetic renal disease is the onset of microalbuminuria, defined as an albumin excretion rate of 30-300mg per day. Microalbuminuria predicts progression to renal failure and early cardiovascular mortality in both IDM and NIDDM patients. Microalbuminuria is associated with constellation of other risk factors for small and large vessel damage which includes raised blood pressure, poor glycaemic control, plasma lipid and clotting factor abnormalities, left ventricular hypertrophy, and insulin resistance. Treatment with ace inhibitors corrects albuminuria and prevents progression to persistent proteinuria. Blood glucose control significantly reduces the risk of progression from normal albuminuria to microalbuminuria. The treatment of microalbuminuria appears highly cost

beneficial and substantially increases life expectancy. All diabetic patients aged 12-70 years should be screened and the development of microalbuminuria should alert the physician to set in motion a programme of assessment, monitoring and correction of all risk factors for renal and cardiovascular disease.



**Thyrotoxicosis in childhood:**

| | | |
|---|---|---|
| **A** | Is more common in girls | (True) |
| **B** | Is often associated with tall stature | (True) |
| **C** | Unlike adults is not caused by an auto-immune process | (False) |
| **D** | Is treated in the first instance with anti-thyroid drugs such as Carbimazole | (True) |
| **E** | Is usually associated with a high TSH level | (False) |

**Comments:**
Thyrotoxicosis has a female preponderance in all age groups. Thyrotoxicosis in early life may cause delayed sexual maturation, although physical development is normal and skeletal growth may be accelerated. Thyrotoxicosis in this age group is mostly due to grave's disease. Anti thyroid drugs, are used initially and relapses can be treated with drugs or surgery. Radioactive iodine is generally not administered. TSH is suppressed.

**Primary hypothyroidism is associated with the following in childhood:**

| | | |
|---|---|---|
| **A** | Macrocytic anaemia | (True) |
| **B** | Alopecia areata | (True) |
| **C** | Cerebellar ataxia | (False) |
| **D** | Multiple serous effusions | (True) |
| **E** | Addison's disease | (True) |

**Comments:**

Hypothyroidism has the following clinical features:

- INFANTS: Feeding problems, prolonged jaundice, constipation, pale cold skin, course facies, large tongue, hoarse cry, occasional goitre, umbilical hernia, delayed development.
- CHILDREN: Cold intolerance, dry skin, cold peripheries, bradycardia, dry thin hair, pale puffy eyes with loss of eyebrows, goitre, slow relaxing reflexes, constipation, short stature, delayed puberty, obesity, deteriorating school work, learning difficulties, hyperprolactanaemia.

There is a known association with autoimmune diseases such as alopecia, vitiligo, pernicious anaemia, Addison's Disease.

**A 3 year old boy presents with polyuria and polydipsia. Serum osmolality is normal, and urine osmolality 200mmol/kg. The following suggest central rather than nephrogenic diabetes insipidus:**

| | | |
|---|---|---|
| **A** | Male sex | (False) |
| **B** | Affected preceding generation | (True) |
| **C** | Lack of correction of the dilute urine with desmopressin | (False) |
| **D** | Presence of optic atrophy | (True) |
| **E** | Presence of bitemporal hemianopia | (True) |

**Comments:**

Central diabetes insipidus has multiple causes including inherited (AD), pituitary tumour (especially craniopharyngioma), infiltration (especially Langerhan's cell histiocytosis), and syndromal (DIDMOAD = diabetes insipidus, diabetes mellitus, optic atrophy and deafness, autosomal recessive). Nephrogenic diabetes insipidus is X-linked, and is not corrected by desmopressin since the end organ is unresponsive.



**Puberty:**

| | | |
|---|---|---|
| **A** | In girls the first sign is the appearance of pubic hair | (False) |
| **B** | In boys the first sign is enlargement of the testes | (True) |
| **C** | Precocious puberty is more common in boys | (False) |
| **D** | Once the epiphyses of the long bones fuse with the metaphyses there is no further growth in stature | (False) |
| **E** | In girls menarche coincides with the peak of the growth spurt | (False) |

**Comments:**
The first sign of puberty in the female is breast development, termed thelarche. Enlargement of the testes of greater than 2.5cm in length or 4 mls in volume is a reliable indicator of puberty. Precocious puberty is approximately five times more common in females. Ossification centres appear in early life, and ultimately the epiphysis or growth plate will fuse with the shaft of the long bones and from then further growth will not occur. Most females have reached peak height velocity 1.3 years before menarche.

**The following are true of angiotensin II:**

| | | |
|---|---|---|
| **A** | It is 50 time more potent than angiotensin I as a renal arterial vasodilator. | (False) |
| **B** | It inhibits aldosterone secretion. | (False) |
| **C** | It reduces afterload in cardiac failure. | (False) |
| **D** | Angiotensin I is converted to angiotensin II in the kidney. | (False) |
| **E** | Secretion is increased by hypokalaemia. | (False) |

**Comments:**

Renin is produced by the juxtaglomerular apparatus of the kidney, and converts and alpha-2 globulin to angiotensin I. In the lung angiotensin I is activated to angiotensin II, which is 50 times more potent as a presser agent than noradrenaline. Angiotensin II acts directly on the adrenal cortex to stimulate secretion of aldosterone, a potent mineralocorticoid produced in the zona glomerulosa. Renin secretion is increased by sodium depravation, and aldosterone acts at the distal tubule to control sodium reabsorption (and indirectly, water reabsorption).



**In the management of a child with diabetes, it is true that:**

| | | |
|---|---|---|
| **A** | Children can treated with oral hypoglycaemic agents in most cases. | (False) |
| **B** | Most children require twice daily injections | (True) |
| **C** | Checking HbA1c values is a useful indicator of long term control. | (False) |
| **D** | The child should be encouraged to give his/her own injections from as early an age as possible | (True) |
| **E** | Routine urine tests are perfectly adequate for monitoring sugar values | (False) |

**Comments:**
Though the incidence of type 2 diabetes in children is increasing, the majority of children with the condition have type 1 insulin requiring diabetes. Most children require twice daily injections which are a mixture of short and long acting insulins. HbA1c gives an idea of` control during the previous 6-8 weeks. The child should be encouraged to self inject and self monitor. Capillary glucose testing is used to monitor glucose values.

**In normal puberty:**

| | | |
|---|---|---|
| **A** | Girls have breastbuds first. | (True) |
| **B** | Physiological gynaecomastia can occur in boys. | (True) |
| **C** | The growth spurt comes after the menarche. | (False) |
| **D** | Acne in girls is a reaction to androgens. | (True) |
| **E** | In boys the penis grows before the testes. | (False) |

**Comments:**

The normal sequence in girls is that breast buds and early pubic hair appear at around the same time. The height/growth spurt is maximal in the year prior to menarche. Average ages for onset of puberty 9.5 years, peak of growth spurt 12 years, menarche 13 years. With regard to male pubertal development, testicular volume precedes penile growth, which precedes the height/growth spurt. Testicular volume increase and early pubic hair at the earliest starts at 10.5 years, peaking at about 12 years, with maximal penile growth at 13.5 years and maximal growth spurt at 14 years.

**Hyperglycaemia (non-ketotic) in an established diabetic child:**

| | | |
|---|---|---|
| **A** | Is usually associated asymptomatic | (True) |
| **B** | Requires additional insulin immediately | (False) |
| **C** | May be seen following an untreated hypoglycaemic convulsion | (True) |
| **D** | Is a cause of recurrent urinary tract infections | (False) |
| **E** | Should be treated by reducing the number of daily carbohydrate exchanges | (False) |

**Comments:**
Non-ketotic hyperglycaemia is usually asymptomatic, or less frequently mild symptoms such as thirst and polyuria may develop. Additional 'stat' doses of insulin may cause hypoglycaemia later. Untreated hypoglycaemia may result in delayed hyperglycaemia through the influence of counter-regulatory hormones e.g catecholamines and growth hormone, which will raise blood glucose. Recurrent urinary infections are not associated, however furuncles are. The condition should be treated according to the cause. For example if the hyperglycaemia is reactive and preceded by severe hypoglycaemia, insulin dosage may have to be reduced and carbohydrates increased.

**The following suggest a diagnosis of homocysitinuria rather than Marfan's Syndrome:**

| | | |
|---|---|---|
| **A** | Mitral regurgitation | (False) |
| **B** | Progressive learning difficulty | (True) |
| **C** | Convulsions | (True) |
| **D** | Thromboembolic episodes | (True) |
| **E** | Response to piridoxine | (True) |

**Comments:**

Homocystinuria is due to cystothionesynthetase deficiency. Patients present with failure to thrive, developmental delay, and ectopia lentis. There is progressive learning difficulty, psychiatric disorders, and fits. Morphologically, patients resemble Marfan's Syndrome, although their complexion is usually fair with brittle hair. It may be complicated by thromboembolic episodes, about 50% respond to piridoxine, while the others are treated with a low methianine diet with cysteine supplements.



**An 18 month old boy investigated for failure to thrive and delayed development is found to have primary hypothyroidism:**

| | | |
|---|---|---|
| **A** | He is unlikely to achieve normal intelligence despite immediate commencement of appropriate treatment | (True) |
| **B** | If his bone age was 3 months the onset of his hypothyroid state is most likely to have occurred at 3 months of age | (False) |

| | | |
|---|---|---|
| **C** | Growth hormone deficiency is likely also to be associated | (False) |
| **D** | If untreated, he has a higher chance of developing atherosclerotic heart disease | (True) |
| **E** | He is more prone to develop parathyroid insufficiency | (False) |

**Comments:**
The diagnosis of congenital hypothyroidism has been delayed and hence thyroxine therapy will not restore mental function fully. The hypothyroidism is likely to have been present at birth. Growth hormone deficiency may be seen in association with secondary hypothyroidism if pituitary insufficiency exists, but not in primary hypothyroidism. Untreated hypothyroidism is associated with dyslipidaemia and cardiovascular disease. Hypoparathyroidism is unrelated.

**Presenting features of hypothyroidism include**

| | | |
|---|---|---|
| **A** | deafness | (True) |
| **B** | menorrhagia | (True) |
| **C** | hirsutism | (True) |
| **D** | enlarged thyroid gland | (True) |
| **E** | osteoporosis | (False) |

**Comments:**
Hirsutism is rarely reported in association with hypothyroidism although hair loss also features. Goitre is a frequent feature in both Hashimoto's thyroiditis and also iodine deficiency. Other presenting features include ataxia/neuronopathies particularly compression neuronopathies and the peaches and cream appearance due to hyper-betacarotinaemia. Cognitive impairment, macrocytic anaemia and pleural effusions also feature.

**Hypopituitarism is associated with:**

| | | |
|---|---|---|
| **A** | Normal long synacthen test | (True) |
| **B** | Abnormal short synacthen test | (True) |
| **C** | Less severe hyperkalaemia compared Addison's Disease | (True) |
| **D** | Normal cortisol in relation to insulin induced hypoglycaemia | (False) |
| **E** | Increased aldosterone secretion by ACTH | (False) |

**Comments:**

Causes of hypopituitarism are legion, but can be broken down into 5 groups:

- DEVELOPMENTAL DEFECTS: Anencephaly, holoprosencephaly, midfacial anomalies.
- GENETIC DEFECTS OF GROWTH HORMONE OR GROWTH HORMONE DEFICIENCY: Isolated, AR type I, AD type II, X-linked, multiple pituitary deficiencies.
- DESTRUCTIVE LESIONS: Trauma, infiltrative lesions (tumours, histiocytosis X, craniopharyngioma, sarcoid, TB, toxoplasmosis), irradiation, surgery, vascular lesions, autoimmune.
- UNRESPONSIVENESS TO GROWTH HORMONES: Insulin-like growth factor deficiency, Laron

dwarfism (GH receptor gene mutations).

- OTHER FUNCTIONAL DEFICIENCY: Hypothyroidism, psychosocial depravation.

The short synacthen test consists of a single dose of synthetic ACTH. Normally, there would be a prompt rise in cortisol production in response. If there is no effect, then a prolonged synacthen test should be done. This consists of administration of doses of successive days for 3 days. In centrally mediated (pituitary) defects, there is an increase in cortisol production over the course of 3 days. If there is a primary hypofunction of the adrenals, then no response occurs. The primary manifestations of hypopituitarism is growth failure, though microphallus, neonatal hypoglycaemia, apnoea or cyanosis may occur. Prolonged jaundice (conjugated and unconjugated) may occur. Peculiar facies may be noted, with prominent frontal bones, depressed saddle shaped nose, and well developed nasolabial folds, bulging eyes, and small chin. Genitalia are under-developed. Since the adrenals have been hypostimulated, cortrigenol responses in relation to hypoglycaemia will also be delayed. ACTH does not stimulate aldosterone secretion.



---

**A 13 year old girl, known to have diabetes, is controlled with insulin injections twice daily. She presents in coma, and on admission, a dextrostix estimation is less than 2mmol/l. The following observations may be relevant:**

| | | |
|---|---|---|
| **A** | She had taken part in a game of hockey at school that morning | (True) |
| **B** | She regularly had a mid-morning snack of two biscuits and a glass of milk | (True) |
| **C** | Menarche occurred two months ago | (False) |
| **D** | All her insulin is checked by her mother before the injection is given | (True) |
| **E** | She has recently changed over to mono component (MC) insulin | (False) |

**Comments:**
Hypoglycaemia may be the result of exercise. A slight alteration in the amount of food intake can be associated with hypoglycaemia and it is more prevalent in well monitored children with tighter glycaemic control. Hypoglycaemia A change from a mixed insulin containing short and intermediate acting insulin to monocomponent insulin without an additional change in dose will not be relevant. The history of menarche is irrelevant.

---

**Bone age:**

| | | |
|---|---|---|
| **A** | Is more advanced in girls than in boys of the same age | (True) |
| **B** | Is characteristically retarded in girls with untreated congenital adrenal hyperplasia | (False) |
| **C** | Is a better predictor of final adult height than height for age | (True) |
| **D** | May be retarded by emotional deprivation | (True) |
| **E** | May be retarded in chronic renal failure | (True) |

**Comments:**
Bone age and skeletal maturity are more advanced in females compared to males of the same age, and they reach peak height velocity earlier. Bone age is advanced in girls with untreated congenital adrenal hyperplasia due to the effects of the excessive androgens. Bone age (which can be measured with an x-

ray of the left wrist) determines the timing of puberty and can be used to predict how much additional growth is possible, therefore it is an excellent predictor of final adult height. Extreme emotional deprivation may retard growth by causing reversible hypothalamic-pituitary depression. Normal skeletal growth resumes rapidly after removal from the oppressive environment. Chronic renal failure is also a well known cause of growth failure and delayed skeletal maturation. Improved metabolic control, nutrition and growth hormone therapy improves growth in such patients.

---

**In a boy of 7 who was operated upon for a craniopharyngioma the following disorders can be expected to develop over the next couple of years:**

| | | |
|---|---|---|
| **A** | Poor growth | (True) |
| **B** | Hypothyroidism | (True) |
| **C** | Precocious puberty | (False) |
| **D** | Spastic diplegia | (False) |
| **E** | Diabetes mellitus | (False) |

**Comments:**
Pan hypopituitarism following surgical treatment would be expected, hence poor growth and secondary hypothyroidism. Delayed puberty would be expected rather than precocious puberty. Spastic diplegia would suggest extensive lateral expansion, which would not be expected. Diabetes mellitus is not a usual consequence.

---

**Associated biochemical and haematologial changes with diabetes include:**

| | | |
|---|---|---|
| **A** | increased fibrinogen | (True) |
| **B** | hyperaggregable platelets in patients with retinopathy | (True) |
| **C** | HbA1c is the only gylcosylated protein to reflect past control | (False) |
| **D** | hypertriglycerideaemia is the most frequent lipid abnormality in the untreated state | (True) |
| **E** | low HDL in type II diabetes is common | (True) |

**Comments:**

Diabetes is a major risk factor for atherosclerosis. The educated guesser could answer this question quite easily by just picking all the bad things and assuming they are associated with diabetes.

"Diabetes is associated with hypercoagulability and the predisposition for thromboembolic phenomena. Diabetics have increased fibrinogen, increased PAI-1 levels, and increased platelet aggregability; the latter is particularly a problem in the poorly controlled diabetic." **Read more ...**

For further reading on lipids in untreated diabetes see the UKPDS (U.K. Prospective Diabetes Study Group. U.K. Prospective Diabetes Study 27: plasma lipids and lipoproteins at diagnosis of NIDDM by age and sex. Diabetes Care 1997;20:1683-1687.)

---

**A 14 year old boy has an HbA1c of 11.7%. The following may be related to poor diabetic control:**

| | | |
|---|---|---|
| **A** | Haematuria | (False) |
| **B** | Snowflake opacities in the lens | (True) |
| **C** | Positive Rhombergism | (True) |
| **D** | Hyperacusis | (False) |
| **E** | Hypotriglycerideaemia | (False) |

**Comments:**

Good control of diabetes delays or prevents the microvascular complications of it, including retinopathy and nephropathy. The retinopathy results in deep haemorrhages, neovascularisation (retinitis proliferans), and occasional retinal detachment. In some ways these are similar to those that occur in retinopathy of prematurity. Cataract is characteristically snowflake, but can be of extremely rapid onset. Nephropathy is characteristically heralded by the onset of microalbuminuria. Positive Rhombergism suggests that peripheral neuropathy is present with loss of position sense. This can be compensated for by opening the eyes.



**Short stature is associated with:**

| | | |
|---|---|---|
| **A** | Down's syndrome | (True) |
| **B** | Homocystinuria | (False) |
| **C** | Prematurity | (False) |
| **D** | Turner 's syndrome | (True) |
| **E** | Pseudohypoparathyroidism | (True) |

**Comments:**
Short stature is a recognised feature of Down's syndrome and pseudohypoparathyroidism. Short stature in Turner's syndrome is the most common phenotypic feature and responds to Growth hormone administration. Homocystinuria is associated with tall stature and prematurity is not associated with short stature.

**Hyperprolactinaemia is associated with:**

| | | |
|---|---|---|
| **A** | Polycystic ovary syndrome | (False) |
| **B** | Depression | (False) |
| **C** | Acromegaly | (False) |
| **D** | Hyperthyroidism | (False) |
| **E** | Premature thelarche | (False) |

**Comments:**

Hyperprolactinaemia may be manifest by a milk discharge from the breasts. Causes include, prolactinoma, hypothyroidism (far increased TRH), and occasionally craniopharyngioma. Treatment consists primarily of Dopamine agonists such as bromocriptine, with a rare requirement for transsphenoidal surgery. Prolactin levels will also be increased in normal puberty. In premature thelarche (isolated breast development) plasma levels of LH and oestrodial are below the limits of normal assays, but basal levels of FSH and their responses to gonadotrophin releasing hormone stimulation are greater than those seen in normal controls. In contrast, children with true precocious puberty secrete predominately LH. Ultrasound examination of the ovaries reveals a normal size, but a few small cysts are not uncommon.



---

**A goitre in a neonate could be caused by the following conditions:**

| | | |
|---|---|---|
| **A** | Fetal alcohol syndrome | (False) |
| **B** | Maternal thyrotoxicosis | (True) |
| **C** | Maternal antithyroid medication | (True) |
| **D** | Maternal lithium treatment | (True) |
| **E** | Maternal thyroxine ingestion | (False) |

---

**Comments:**

Defective synthesis of T4 or defects of iodide uptake. Maternal iodides, antithyroid drugs, lithium, amiodarone Maternal iodine deficiency (endemic goitre) Maternal Graves disease (congenital hyperthyroidism) Thyroid teratoma Congenital goitre is usually sporadic and may result from the administration of antithyroid drugs or iodides during pregnancy for the treatment of thyrotoxicosis. Goitrogenic drugs and iodides cross the placenta and at high doses may interfere with synthesis of thyroid hormone, resulting in goitre and hypothyroidism in the fetus. The concomitant administration of thyroid hormone with the goitrogen does not prevent this effect, because insufficient amounts of thyroxine (T4) cross the placenta. Iodides are included in many proprietary preparations used to treat asthma; these preparations must be avoided during pregnancy, because they have often been a cause of unexpected congenital goitre. Amiodarone, an antiarrhythmic drug with a 37% iodine content, has also caused congenital goitre with hypothyroidism. Lithium carbonate also causes goitres; it is currently widely used as a psychotropic drug. Lithium competes with iodide; the mechanism producing the goitre or hypothyroidism is similar to that described earlier for iodide goitre. Lithium and iodide also act synergistically to produce goitre; their combined use should be avoided. Amiodarone, a drug used to treat cardiac arrhythmias, can cause thyroid dysfunction with goitre because it is rich in iodine. It is also a potent inhibitor of 5´- deiodinase, preventing conversion of T4 to T3. It can cause hypothyroidism, particularly in patients with underlying autoimmune disease; in other patients, it may cause hyperthyroidism.



---

**Periarticular calcification is a recognised consequence of:**

| | | |
|---|---|---|
| **A** | Chronic tophaceous gout | (True) |
| **B** | Haemochromatosis | (False) |

| | | |
|---|---|---|
| **C** | Rotator cuff lesions of the shoulder | (True) |
| **D** | Renal osteodystrophy | (True) |
| **E** | Mixed connective tissue disease | (True) |

**Comments:**

Metastatic calcification can occur for a variety of reasons, particularly post-inflammation, metabolic, or tumour. The pattern may be very helpful diagnostically. Examples include: renal osteodystrophy casing cutaneous vascular and visceral calcification. Tumours such as neuroblastoma, teratoma or Wilm's, thyroid medullary carcinoma, or retinoblastoma, osteosarcoma or enchondroma.

**Post-inflammation causes include**: dermatomyositis (tissue), constrictive pericarditis (pericardium), meconium peritonitis (peritoneum), chronic pancreatitis (pancreas).

**Infections**: TB, VZ pneumonia, parasitic infiltration of the liver, intracranial calcification from toxoplasma or CMV.

**Metabolic causes**: basal ganglia calcification (hypoparathryoidism), MELAS, pertelli (Zellweger), metastatic (chronic nephritis), hyperparathyroidism, idiopathic hypercalcaemia, hypervitaminosis D, adrenals (Addison's, post-haemorrhage, Wolman's), intracranial (osteopetrosis, Sturge-Weber).



**Congenital adrenal hyperplasia is associated with:**

| | | |
|---|---|---|
| **A** | X-linked inheritance | (False) |
| **B** | Over-production of ACTH | (True) |
| **C** | A low serum potassium | (False) |
| **D** | Undescended testes | (False) |
| **E** | Infertility in later life | (True) |

**Comments:**
Congenital Adrenal Hyperplasia has an autosomal recessive inheritance. Failure to synthesise cortisol by the adrenals leads to a feedback activation of ACTH production by the pituitary. Potassium retention occurs as a consequence of aldosterone deficiency. Undescended testes are not associated, however testicular adrenal rest tumours are associated. Undertreated patients may be infertile later due to the presence of high circulating androgens.

**The following conditions are generally transmitted by X-linked inheritance:**

| | | |
|---|---|---|
| **A** | Duchenne muscular dystrophy | (True) |
| **B** | Turner’s syndrome | (False) |
| **C** | Congenital adrenal hyperplasia (adrenogenital syndrome) | (False) |
| **D** | Haemophilia type A | (True) |
| **E** | Hypophosphataemia vitamin D resistant Rickets | (True) |

**Comments:**
The following disorders are X-linked: Duchenne muscular dystrophy, Haemophilia A, X-Linked vitamin D resistant rickets and Bruton's agammaglobulinaemia. Turner's syndrome is a chromosomal disorder, not a single gene disorder. Congenital adrenal hyperplasia is autosomal recessive.

---

**The feature of Turner's syndrome include:**

| | | |
|---|---|---|
| **A** | Short stature | (True) |
| **B** | Mental retardation | (False) |
| **C** | Karyotype XXY | (False) |
| **D** | Webbing of the neck | (True) |
| **E** | Increased incidence of coarctation of the aorta | (True) |

**Comments:**
Short stature (with height of >2.5 standard deviations below the mean height value for age) is an important phenotypic feature of the condition and it is not due to deficiency of growth hormone, thyroid hormone, adrenal or gonadal steroids but may improve following the administration of growth hormone. In general patients with gonadal dysgenesis do not differ from siblings in overall intelligence. The karyotype is XO or XO/XX in mosaics. Webbing of the neck, lymphoedema of the distal extremities, ascites and pleural effusions are features. Cardiovascular abnormalities other than coarctation include bicuspid aortic valve, mitral valve prolapse and aortic root dilatation.

---

**In Marfan's syndrome:**

| | | |
|---|---|---|
| **A** | The inheritance is dominant | (True) |
| **B** | The high-arched palate is pathognomic | (False) |
| **C** | Mental retardation is common | (False) |
| **D** | Glaucoma may be of one of the ocular signs | (True) |
| **E** | Generalised osteoporosis occurs | (False) |

**Comments:**
Marfan's syndrome is a dominantly inherited condition. A high arched palate may be seen in normal individuals. Mental retardation is seen in homocystinuria and not Marfan's syndrome. Subluxation of the lens is a feature and glaucoma. Osteoporosis occurs in homocystinuria.

---

**The following conditions can be inherited as an autosomal dominant:**

| | | |
|---|---|---|
| **A** | Neurofibromatosis | (True) |
| **B** | Achondroplasia | (True) |
| **C** | Prader-Willi syndrome | (False) |
| **D** | B-thalassaemia | (False) |
| **E** | Down's syndrome | (False) |

**Comments:**
Neurofibromatosis and achondroplasia are single gene Autosomal dominant disorders. B thalassaemia is recessively inherited. One copy of the abnormal gene is termed ‘thalassaemia minor’and if there are 2 copies of the abnormal gene the condition which develops is thalassaemia major. Prader Willi syndrome is a chromosomal disorder characterised by insatiable appetite, hyperglycaemia and short stature. Down’s syndrome is a chromosomal disorder.