MEDICINE PAPER II

TIPS CLASS

- Cardiology - 15
- Endocrinology and Metabolic disorders- 15
- Clinical Nutrition - 3
- Toxicology/Poisoning- 3
- Dermatology - 4
- Psychiatry - 5
- Medical Statistics -5

CARDIOLOGY- PHYSIOLOGY

- **Functional anatomy and physiology (Davidson)**
- **Coronary circulation**
- **Conduction system**
- **Cardiac Biomarkers**

CARDIOLOGY- PHYSIOLOGY

- Lecture Sheet

❑Junctional tissue
❑Action Potential
❑Haemodynamics (CO, VR, SV)
❑Cardiac Cycle
❑JVP
❑Heart Sound
❑BP regulation

- Which event/s correspond/s to Isovolemetric Relaxation?

A. C wave in JVP
B. AV valve open
C. Ventricular pressure falls below atrial pressure
D. It ends by opening of mitral valve
E. Produces 3rd heart sound

FFFTF

CARDIOLOGY- CLINICAL

- Murmur- SBA- MS, AS
- Heart Failure **
- Atrial Fibrillation
- AV block
- CABG p- 491
- MI- Detail Management & Complications ** P-495,496,
- Accelerated Hypertension
- Acute Rheumatic fever
- Infective endocarditis **
- Congenital heart disease- Cyanotic, Acyanotic**, VSD
- Cardiomyopathy- DCM, HOCM ** (AS vs HOCM)
- Acute pericarditis
- Pericardial effusion
- Cardiac tamponade**

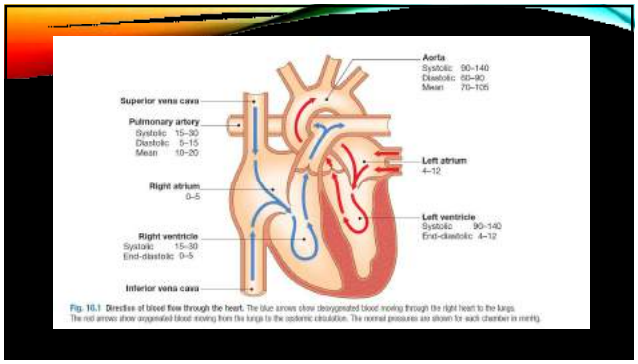


Fig. 16.1 Direction of blood flow through the heart. The blue arrows show deoxygenated blood moving through the right heart to the lungs. The red arrows show oxygenated blood moving from the lungs to the systemic circulation. The normal pressures are shown for each chamber in mmHg.

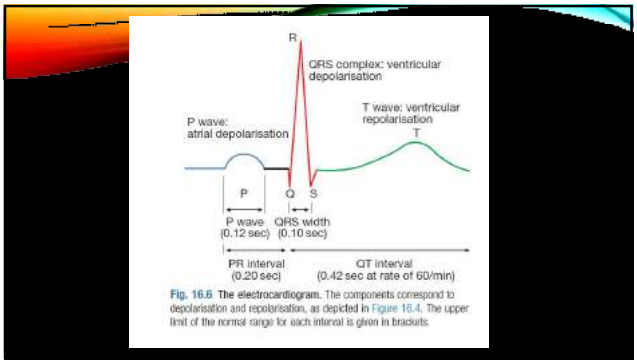
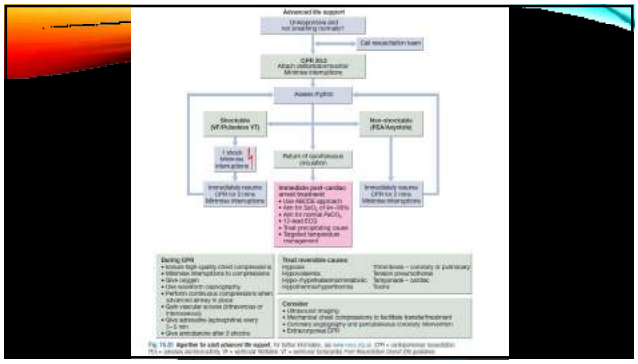
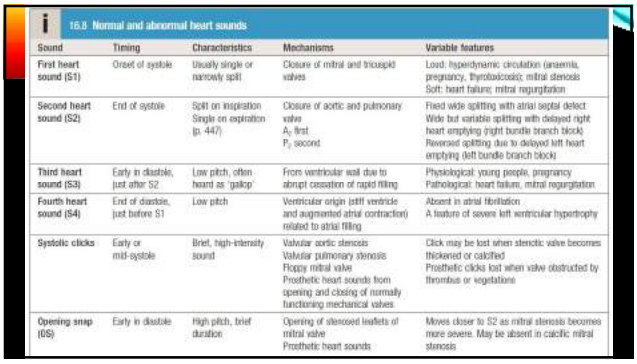


Fig. 16.6 The electrocardiogram. The components correspond to depolarisation and repolarisation, as depicted in Figure 16.4. The upper limit of the normal range for each interval is given in brackets.





16.8 Normal and abnormal heart sounds

Sound	Timing	Characteristics	Mechanisms	Variable features
First heart sound (S1)	Onset of systole	Usually single or narrowly split	Closure of mitral and tricuspid valves	Loud: hyperdynamic circulation (anaemia, pregnancy, thyrotoxicosis); mitral stenosis Soft: heart failure; mitral regurgitation
Second heart sound (S2)	End of systole	Split on inspiration Single on expiration (p. 447)	Closure of aortic and pulmonary valve A_2 first P_2 second	Fixed wide splitting with atrial septal defect Wide but variable splitting with delayed right heart emptying (right bundle branch block) Reversed splitting due to delayed left heart emptying (left bundle branch block)
Third heart sound (S3)	Early in diastole, just after S2	Low pitch, often heard as 'gallop'	From ventricular wall due to abrupt cessation of rapid filling	Physiological: young people, pregnancy Pathological: heart failure, mitral regurgitation
Fourth heart sound (S4)	End of diastole, just before S1	Low pitch	Ventricular origin (stiff ventricle and augmented atrial contraction) related to atrial filling	Absent in atrial fibrillation A feature of severe left ventricular hypertrophy
Systolic clicks	Early or mid-systole	Brief, high-intensity sound	Valvular aortic stenosis Valvular pulmonary stenosis Floppy mitral valve Prosthetic heart sounds from opening and closing of normally functioning mechanical valves	Click may be lost when stenotic valve becomes thickened or calcified Prosthetic clicks lost when valve obstructed by thrombus or vegetations
Opening snap (OS)	Early in diastole	High pitch, brief duration	Opening of stenosed leaflets of mitral valve Prosthetic heart sounds	Moves closer to S2 as mitral stenosis becomes more severe. May be absent in calcific mitral stenosis

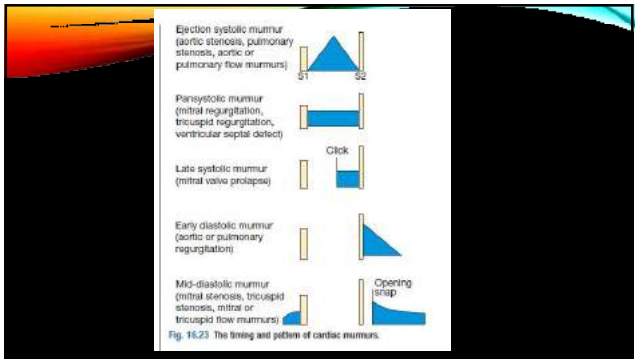


Fig. 16.23 The timing and pattern of cardiac murmurs.

16.9 Features of a benign or innocent heart murmur

- Soft
- Mid-systolic
- Heard at left sternal edge
- No radiation
- No other cardiac abnormalities

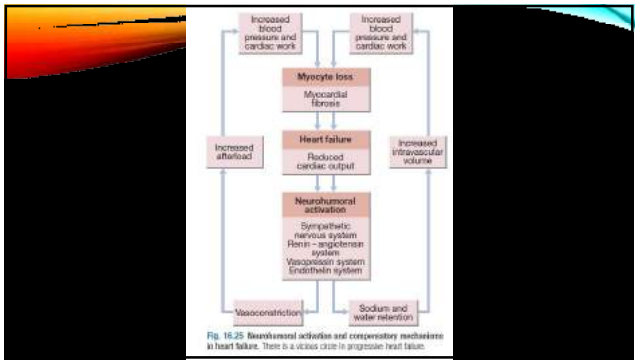


Fig. 16.25 Neurohumoral activation and compensatory mechanisms in heart failure. There is a vicious circle in progressive heart failure.

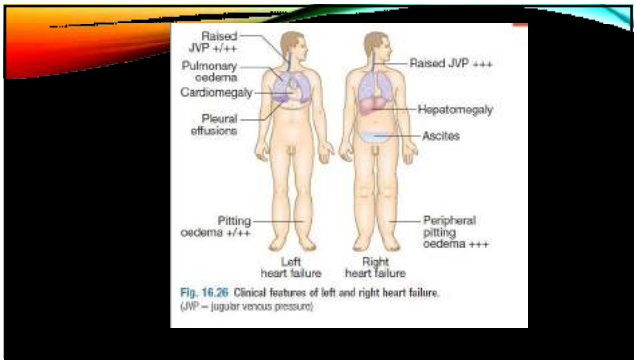
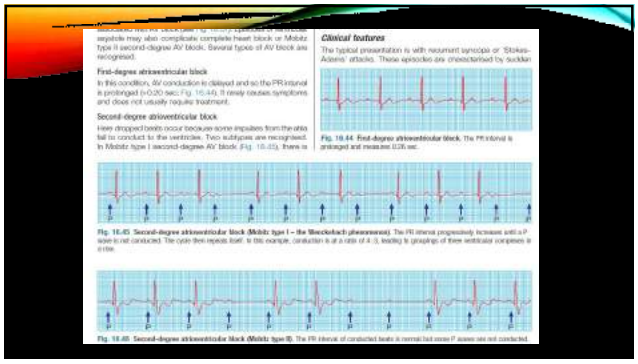


Fig. 16.26 Clinical features of left and right heart failure. (JVP – jugular venous pressure)



Clinical features

First-degree atrioventricular block

Second-degree atrioventricular block

Fig. 16.44 First-degree atrioventricular block. The PR interval is prolonged and measures 0.36 sec.

Fig. 16.45 Second-degree atrioventricular block (Mobitz type I – the Wenckebach phenomenon). The PR interval progressively increases until a P wave is not conducted. The cycle then repeats itself. In this example, conduction is at a ratio of 4:3, leading to groupings of three ventricular complexes in a row.

Fig. 16.46 Second-degree atrioventricular block (Mobitz type II). The PR interval of conducted beats is normal but some P waves are not conducted.

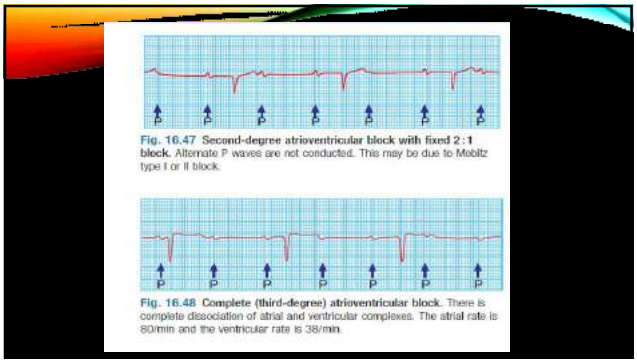
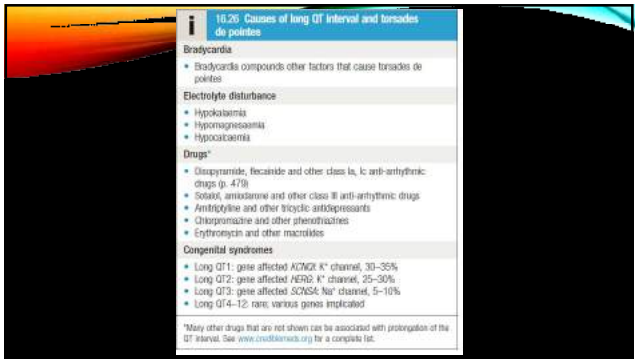


Fig. 16.47 Second-degree atrioventricular block with fixed 2 : 1 block. Alternate P waves are not conducted. This may be due to Mobitz type I or II block.

Fig. 16.48 Complete (third-degree) atrioventricular block. There is complete dissociation of atrial and ventricular complexes. The atrial rate is 80/min and the ventricular rate is 38/min.



i 16.26 Causes of long QT interval and torsades de pointes

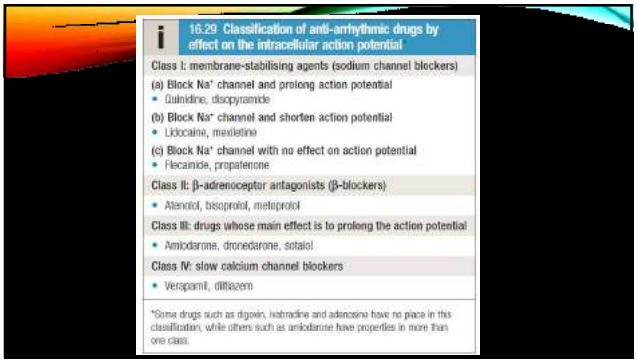
Bradycardia
- Bradycardia compounds other factors that cause torsades de pointes

Electrolyte disturbance
- Hypokalaemia
- Hypomagnesaemia
- Hypocalcaemia

Drugs*
- Disopyramide, flecainide and other class Ia, Ic anti-arrhythmic drugs (p. 479)
- Sotalol, amiodarone and other class III anti-arrhythmic drugs
- Amitriptyline and other tricyclic antidepressants
- Chlorpromazine and other phenothiazines
- Erythromycin and other macrolides

Congenital syndromes
- Long QT1: gene affected *KCNQ1* K^+ channel, 30–35%
- Long QT2: gene affected *HERG* K^+ channel, 25–30%
- Long QT3: gene affected *SCN5A* Na^+ channel, 5–10%
- Long QT4–12: rare; various genes implicated

*Many other drugs that are not shown can be associated with prolongation of the QT interval. See www.crediblemeds.org for a complete list.



i 16.29 Classification of anti-arrhythmic drugs by effect on the intracellular action potential

Class I: membrane-stabilising agents (sodium channel blockers)

(a) Block Na^+ channel and prolong action potential
- Quinidine, disopyramide

(b) Block Na^+ channel and shorten action potential
- Lidocaine, mexiletine

(c) Block Na^+ channel with no effect on action potential
- Flecainide, propafenone

Class II: β-adrenoceptor antagonists (β-blockers)
- Atenolol, bisoprolol, metoprolol

Class III: drugs whose main effect is to prolong the action potential
- Amiodarone, dronedarone, sotalol

Class IV: slow calcium channel blockers
- Verapamil, diltiazem

*Some drugs such as digoxin, ivabradine and adenosine have no place in this classification, while others such as amiodarone have properties in more than one class.

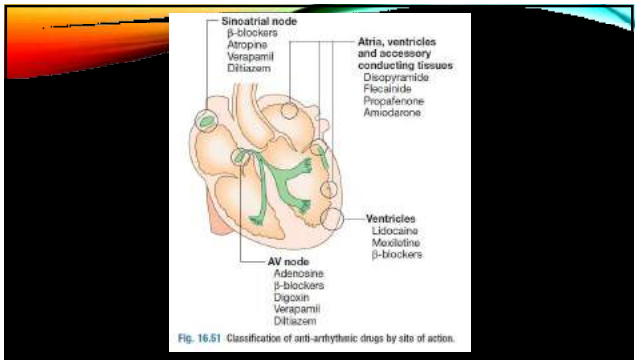
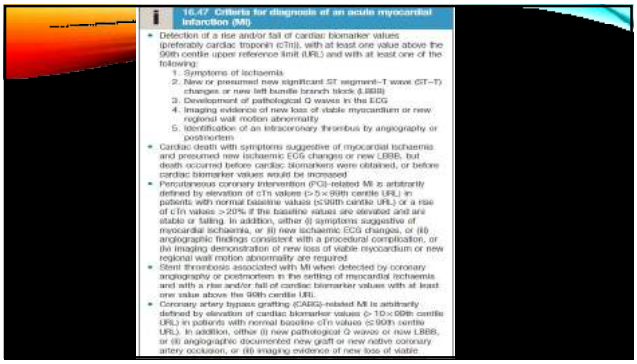
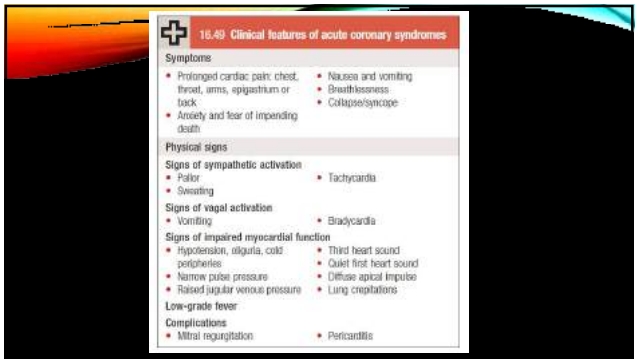
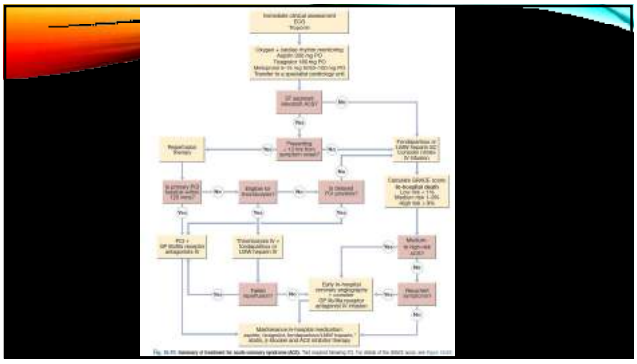
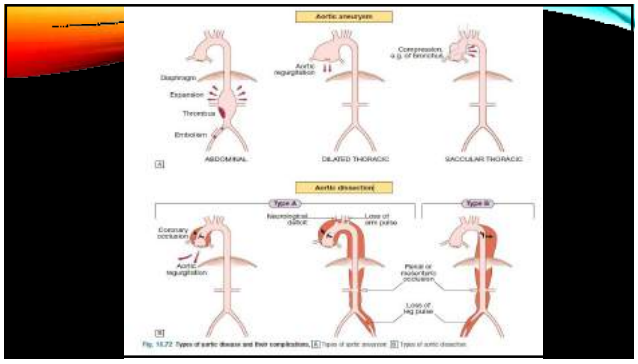


Fig. 16.51 Classification of anti-arrhythmic drugs by site of action.









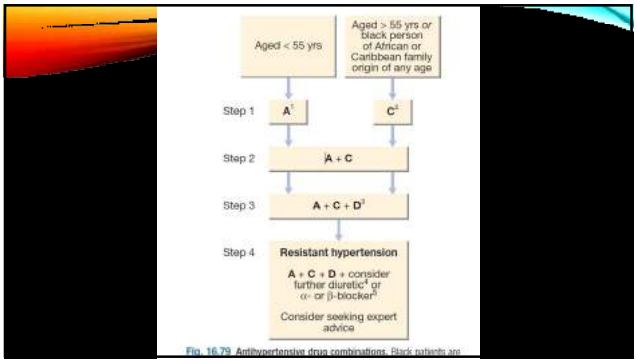


Fig. 16.79 Antihypertensive drug combinations. Black patients are

i 16.72 The influence of comorbidity on choice of antihypertensive drug therapy

Class of drug	Compelling indications	Possible indications	Caution	Compelling contraindications
α-blockers	Benign prostatic hypertrophy	–	Postural hypotension, heart failure[1]	Urinary incontinence
ACE inhibitors	Heart failure Left ventricular dysfunction, post MI or established CAD Type 1 diabetic nephropathy Secondary stroke prevention[1]	Chronic renal disease[1] Type 2 diabetic nephropathy	Renal impairment[2] PAD[1]	Pregnancy Renovascular disease[2]
Angiotensin II receptor blockers	ACE inhibitor intolerance Type 2 diabetic nephropathy hypertension with left ventricular hypertrophy Heart failure in ACE-intolerant patients, after MI	Left ventricular dysfunction after MI intolerance of other antihypertensive drugs Proteinuric or chronic renal disease[1] Heart failure	Renal impairment[2] PAD[1]	Pregnancy
β-blockers	MI, angina Heart failure[1]	–	Heart failure[1] PAD Diabetes (except with CAD)	Asthma or chronic obstructive pulmonary disease Heart block
Calcium channel blockers (dihydropyridine)	Older patients, isolated systolic hypertension	Angina	–	–
Calcium channel blockers (rate-limiting)	Angina	Older patients	Combination with β-blockade	Atrioventricular block, heart failure
Thiazides or thiazide-like diuretics	Older patients, isolated systolic hypertension, heart failure, secondary stroke prevention	–	–	Gout[1]

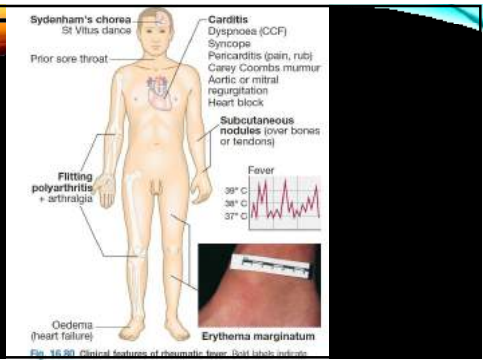
i 16.66 Hypertensive retinopathy

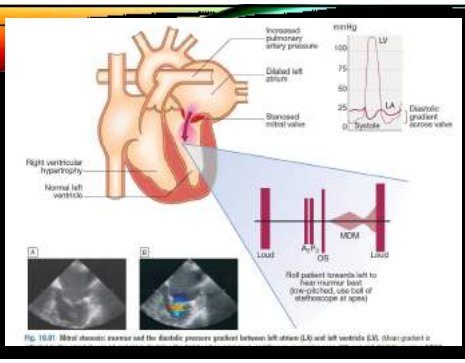
Grade 1
- Arteriolar thickening, tortuosity and increased reflectiveness ('silver wiring')

Grade 2
- Grade 1 plus constriction of veins at arterial crossings ('arteriovenous nipping')

Grade 3
- Grade 2 plus evidence of retinal ischaemia (flame-shaped or blot haemorrhages and 'cotton wool' exudates)

Grade 4
- Grade 3 plus papilloedema





i 16.69 Clinical features of aortic regurgitation

Symptoms

Mild to moderate aortic regurgitation
- Often asymptomatic
- Palpitations

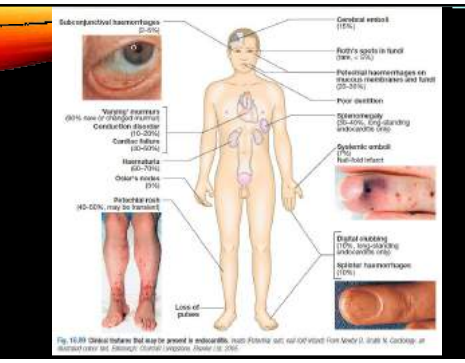
Severe aortic regurgitation
- Breathlessness
- Angina

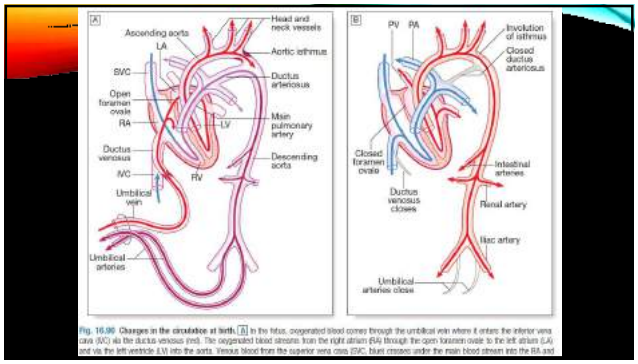
Signs

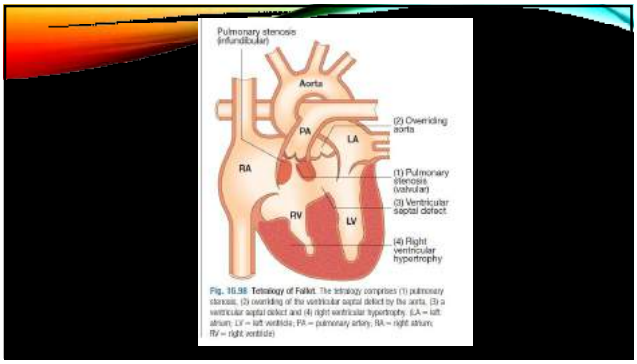
Pulses
- Large-volume or 'collapsing' pulse
- Low diastolic and increased pulse pressure
- Bounding peripheral pulses
- Capillary pulsation in nail beds: Quincke's sign
- Femoral bruit ('pistol shot'): Durozíez's sign
- Head nodding with pulse: de Musset's sign

Murmurs
- Early diastolic murmur
- Systolic murmur (increased stroke volume)
- Austin Flint murmur (soft mid-diastolic)

Other signs
- Displaced, heaving apex beat (volume overload)
- Pre-systolic impulse
- Fourth heart sound
- Crepitations (pulmonary venous congestion)







ENDOCRINOLOGY

ENDOCRINE PHYSIOLOGY

- **Sheet**
  - **Types & Classification of Hormones**
  - **Sites of Mechanism**
  - **Mechanism of Action (All Hormones)**

CLINICAL ENDOCRINOLOGY

- Thyroid gland functional anatomy and physiology
- Thyroid function test
- Thyrotoxicosis **
- Hypothyroidism
- Asymptomatic abnormal thyroid function test
- Grave's disease **
- Hashimoto's thyroiditis **
- Subacute thyroiditis

CLINICAL ENDOCRINOLOGY

- Turner syndrome
- Klinefelter syndrome
- Hypercalcemia
- Familial hypocalciuric hypercalcemia ***
- Adrenal gland functional anatomy and physiology
- Cushing syndrome
- Addison's disease **
- Pheocromocytoma **
- Acromegaly

18.5 How to interpret thyroid function test results

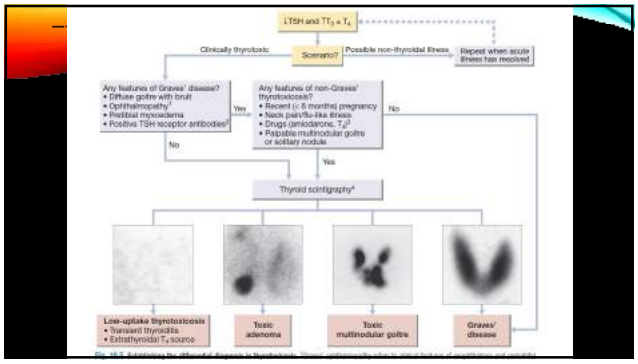
TSH	T_4	T_3	Most likely interpretation(s)
U.D.	Raised	Raised	Primary thyrotoxicosis
U.D. or low	Raised	Normal	Over-treatment of hypothyroidism with levothyroxine Factitious thyrotoxicosis
U.D.	Normal[1]	Raised	Primary T_3 toxicosis
U.D.	Normal[1]	Normal[1]	Subclinical thyrotoxicosis
U.D. or low	Raised	Low or normal	Non-thyroidal illness Amiodarone therapy
U.D. or low	Low	Raised	Over-treatment of hypothyroidism with liothyronine (T_3)
U.D.	Low	Low	Secondary hypothyroidism[2] Transient thyroiditis in evolution
Normal	Low	Low[1]	Secondary hypothyroidism[2]
Mildly elevated 5–20 mIU/L	Low	Low[1]	Primary hypothyroidism Secondary hypothyroidism[2]
Elevated >20 mIU/L	Low	Low[1]	Primary hypothyroidism
Mildly elevated 5–20 mIU/L	Normal[1]	Normal[1]	Subclinical hypothyroidism
Elevated 20–500 mIU/L	Normal	Normal	Artifact Heterophilic antibodies (host antibodies with affinity to the animal antibodies used in TSH assays)
Elevated	Raised	Raised	Non-adherence to levothyroxine replacement – recent 'loading' dose Thyroid hormone resistance

[1]Usually upper part of reference range. [2]T_4 is not a sensitive indicator of hypothyroidism and should not be requested. [3]Usually lower part of reference range. [4]i.e. Secondary to pituitary or hypothalamic disease. Note that TSH assays may report detectable TSH.
iTSH = thyroid-stimulating hormone; U.D. = undetectable

18.7 Clinical features of thyroid dysfunction

Thyrotoxicosis		Hypothyroidism	
Symptoms	Signs	Symptoms	Signs
Common			
Weight loss despite normal or increased appetite Heat intolerance, sweating Palpitations, tremor Dyspnoea, fatigue Irritability, emotional lability	Weight loss Tremor Palmar erythema Sinus tachycardia Lid retraction, lid lag	Weight gain Cold intolerance Fatigue, somnolence Dry skin Dry hair Menorrhagia	Weight gain
Less common			
Osteoporosis (fracture, loss of height) Diarrhoea, steatorrhoea Angina Ankle swelling Anxiety, psychosis Muscle weakness Periodic paralysis (predominantly in Chinese and other Asian groups) Pruritus, alopecia Amenorrhoea/oligomenorrhoea Infertility, spontaneous abortion Loss of libido, impotence Excessive sweating	Goitre with bruit[1] Atrial fibrillation[1] Systolic hypertension/increased pulse pressure Cardiac failure[1] Hyperreflexia Ill-sustained clonus Proximal myopathy Bulbar myopathy[1]	Constipation Hoarseness Carpal tunnel syndrome Alopecia Aches and pains Muscle stiffness Deafness Depression Infertility	Hoarse voice Facial features: Purplish lips Malar flush Periorbital oedema Loss of lateral eyebrows Anaemia Carotenaemia Erythema ab igne Bradycardia, hypertension Delayed relaxation of reflexes Dermal myxoedema
Rare			
Vomiting Apathy Anorexia Exacerbation of asthma	Gynaecomastia Spider naevi Onycholysis Pigmentation	Psychosis (myxoedema madness) Galactorrhoea Impotence	Ileus, ascites Pericardial and pleural effusions Cerebellar ataxia Myotonia

[1]In Graves' disease only. [2]Features found particularly in elderly patients.



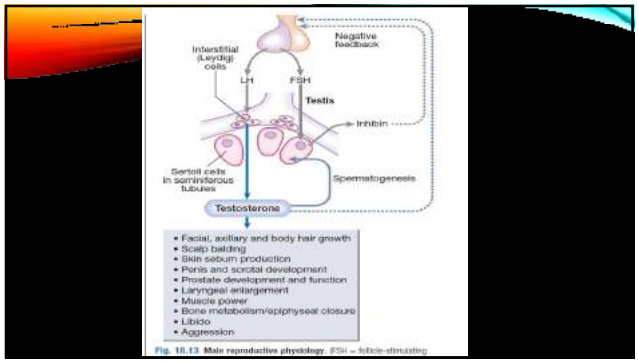


Fig. 18.13 Male reproductive physiology. (FSH – follicle-stimulating

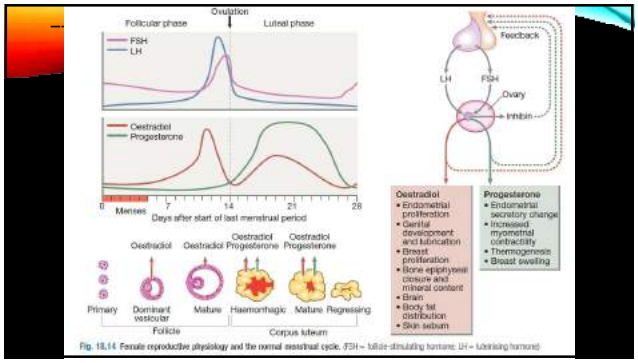


Fig. 18.14 Female reproductive physiology and the normal menstrual cycle. (FSH – follicle-stimulating hormone; LH – luteinising hormone)

18.20 Causes of delayed puberty and hypogonadism

Constitutional delay

Hypogonadotrophic hypogonadism
- Structural hypothalamic/pituitary disease (see Box 18.5A, p. 681)
- Functional gonadotrophin deficiency:
  - Chronic systemic illness (e.g. asthma, malabsorption, coeliac disease, cystic fibrosis, renal failure)
  - Psychological stress
  - Anorexia nervosa
  - Excessive physical exercise
  - Hyperprolactinaemia
  - Other endocrine disease (e.g. Cushing's syndrome, primary hypothyroidism)
- Isolated gonadotrophin deficiency (Kallmann's syndrome)

Hypergonadotrophic hypogonadism
- Acquired gonadal damage:
  - Chemotherapy/radiotherapy to gonads
  - Trauma/surgery to gonads
  - Autoimmune gonadal failure
  - Mumps orchitis
  - Tuberculosis
  - Haemochromatosis
- Developmental/congenital gonadal disorders:
  - Steroid biosynthetic defects
  - Anorchidism/cryptorchidism in males
  - Klinefelter's syndrome (47XXY, male phenotype)
  - Turner's syndrome (45XO, female phenotype)

18.25 Causes of infertility

Female factor (35–40%)

- Ovulatory dysfunction:
  - Polycystic ovarian syndrome
  - Hypogonadotrophic hypogonadism (see Box 18.20)
  - Hypergonadotrophic hypogonadism (see Box 18.20)
- Tubular dysfunction:
  - Pelvic inflammatory disease (chlamydia, gonorrhoea)
  - Endometriosis
  - Previous sterilisation
  - Previous pelvic or abdominal surgery
- Cervical and/or uterine dysfunction:
  - Congenital abnormalities
  - Fibroids
  - Treatment for cervical carcinoma
  - Asherman's syndrome

Male factor (35–40%)

- Reduced sperm quality or production:
  - Y chromosome microdeletions
  - Varicocele
  - Hypergonadotrophic hypogonadism (see Box 18.20)
  - Hypogonadotrophic hypogonadism (see Box 18.20)
- Tubular dysfunction:
  - Varicocele
  - Congenital abnormality of vas deferens/epididymis
  - Previous sexually transmitted infection (chlamydia, gonorrhoea)
  - Previous vasectomy

Unexplained or mixed factor (20–35%)

18.26 Causes of gynaecomastia

Idiopathic

Physiological

Drug-induced

- Cimetidine
- Digoxin
- Anti-androgens (cyproterone acetate, spironolactone)
- Some exogenous anabolic steroids (diethylstilbestrol)
- Cannabis

Hypogonadism (see Box 18.20)

Androgen resistance syndromes

Oestrogen excess

- Liver failure (impaired steroid metabolism)
- Oestrogen-secreting tumour (e.g. of testis)
- Human chorionic gonadotrophin-secreting tumour (e.g. of testis or lung)

18.27 Causes of hirsutism

Cause	Clinical features	Investigation findings	Treatment
Idiopathic	Often familial Mediterranean or Asian background	Normal	Cosmetic measures Anti-androgens
Polycystic ovarian syndrome	Obesity Oligomenorrhoea or secondary amenorrhoea Infertility	LH:FSH ratio > 2:1 Minor elevation of androgens* Mild hyperprolactinaemia	Weight loss Cosmetic measures Anti-androgens (Metformin, glitazones may be useful)
Congenital adrenal hyperplasia (95% 21-hydroxylase deficiency)	Pigmentation History of salt-wasting in childhood, ambiguous genitalia, or adrenal crisis when stressed Jewish background	Elevated androgens* that suppress with dexamethasone Abnormal rise in 17-OH-progesterone with ACTH	Glucocorticoid replacement administered in reverse rhythm to suppress early morning ACTH
Exogenous androgen administration	Athletes Virilisation	Low LH and FSH Analysis of urinary androgens may detect drug of misuse	Stop steroid misuse
Androgen-secreting tumour of ovary or adrenal cortex	Rapid onset Virilisation: clitoromegaly, deep voice, balding, breast atrophy	High androgens* that do not suppress with dexamethasone Low LH and FSH CT or MRI usually demonstrates a tumour	Surgical excision
Cushing's syndrome	Clinical features of Cushing's syndrome (p. 667)	Normal or mild elevation of adrenal androgens* See Investigations (p. 667)	Treat the cause (p. 667)

*e.g. Serum testosterone levels in women: < 2 nmol/L (< 58 ng/dL) is normal; 2–5 nmol/L (58–144 ng/dL) is minor elevation; > 5 nmol/L (> 144 ng/dL) is high and requires further investigation.
(ACTH = adrenocorticotrophic hormone; CT = computed tomography; FH = follicle-stimulating hormone; LH = luteinising hormone; MRI = magnetic resonance imaging)

18.28 Features of polycystic ovarian syndrome

Mechanisms*	Manifestations
Pituitary dysfunction	High serum LH High serum prolactin
Anovulatory menstrual cycles	Oligomenorrhoea Secondary amenorrhoea Cystic ovaries Infertility
Androgen excess	Hirsutism Acne
Obesity	Hyperglycaemia Elevated oestrogens
Insulin resistance	Dyslipidaemia Hypertension

*These mechanisms are interrelated; it is not known which, if any, is primary. PCOS probably represents the common endpoint of several different pathologies.
(LH = luteinising hormone)

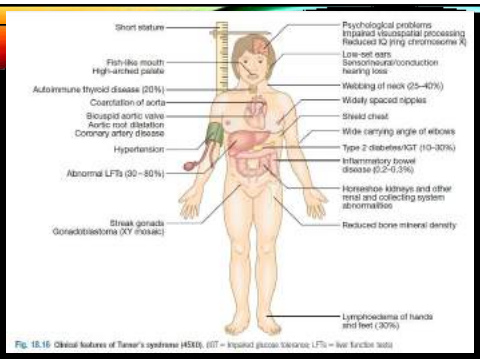
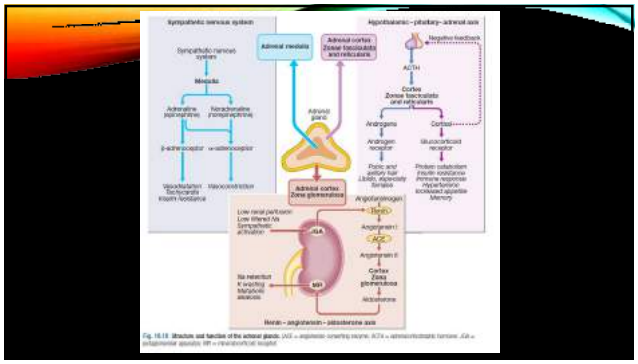


Fig. 18.16 Clinical features of Turner's syndrome (45X0). (IGT = impaired glucose tolerance; LFTs = liver function tests)

18.33 Differential diagnosis of hypocalcaemia

	Total serum calcium	Ionised serum calcium	Serum phosphate	Serum PTH	Comments
Hypoalbuminaemia	↓	↔	↔	↔	Adjust calcium upwards by 0.02 mmol/L (0.1 mg/dL) for every 1 g/L reduction in albumin below 40 g/L
Alkalosis	↔	↓	↔	↔ or ↑	p. 368
Vitamin D deficiency	↓	↓	↓	↑	p. 1049
Chronic renal failure	↓	↓	↑	↑	Due to impaired vitamin D hydroxylation Serum creatinine ↑
Hypoparathyroidism	↓	↓	↑	↓	See text
Pseudohypoparathyroidism	↓	↓	↑	↑	Characteristic phenotype (see text)
Acute pancreatitis	↓	↓	↔ or ↓	↑	Usually clinically obvious Serum amylase ↑
Hypomagnesaemia	↓	↓	Variable	↓ or ↔	Treatment of hypomagnesaemia may correct hypocalcaemia

(↑ = levels increased; ↓ = levels reduced; ↔ = levels normal)



18.38 Classification of endogenous Cushing's syndrome

ACTH-dependent – 80%

- Pituitary adenoma secreting ACTH (Cushing's disease) – 70%
- Ectopic ACTH syndrome (bronchial carcinoid, small-cell lung carcinoma, other neuro-endocrine tumour) – 10%

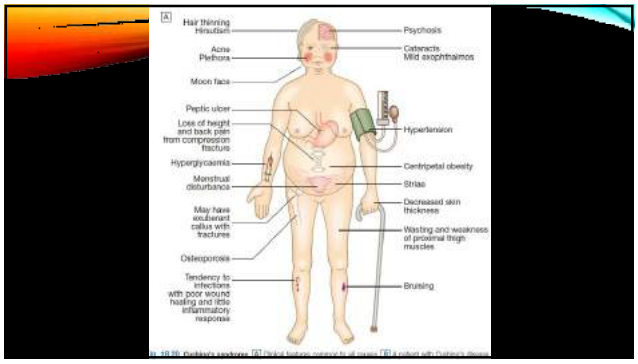
Non-ACTH-dependent – 20%

- Adrenal adenoma – 15%
- Adrenal carcinoma – 5%
- ACTH-independent macronodular hyperplasia; primary pigmented nodular adrenal disease; McCune–Albright syndrome (together < 1%)

Hypercortisolism due to other causes (also referred to as pseudo-Cushing's syndrome)

- Alcohol excess (biochemical and clinical features)
- Major depressive illness (biochemical features only, some clinical overlap)
- Primary obesity (mild biochemical features, some clinical overlap)

(ACTH = adrenocorticotrophic hormone)



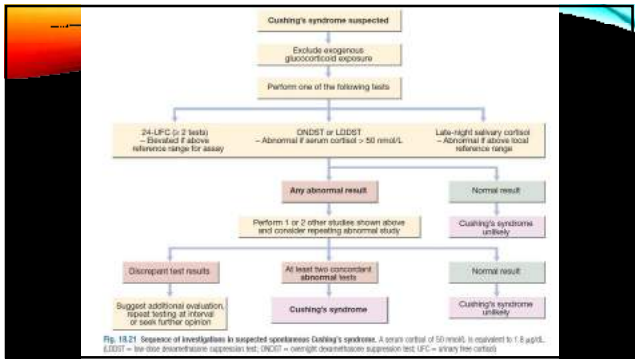
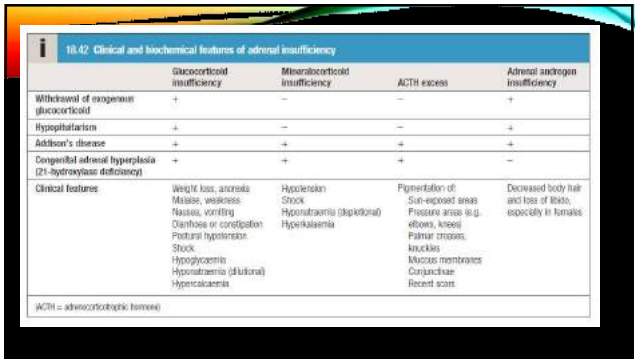


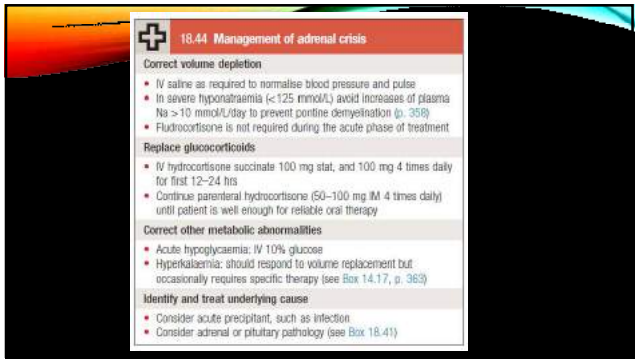
Fig. 18.21 Sequence of investigations in suspected spontaneous Cushing's syndrome. A serum cortisol of 50 nmol/L is equivalent to 1.8 μg/dL. (LDDST = low-dose dexamethasone suppression test; ONDST = overnight dexamethasone suppression test; UFC = urinary free cortisol)



18.42 Clinical and biochemical features of adrenal insufficiency

	Glucocorticoid insufficiency	Mineralocorticoid insufficiency	ACTH excess	Adrenal androgen insufficiency
Withdrawal of exogenous glucocorticoid	+	–	–	+
Hypopituitarism	+	–	–	+
Addison's disease	+	+	+	+
Congenital adrenal hyperplasia (21-hydroxylase deficiency)	+	+	+	–
Clinical features	Weight loss, anorexia Malaise, weakness Nausea, vomiting Diarrhoea or constipation Postural hypotension Shock Hypoglycaemia Hyponatraemia (dilutional) Hypercalcaemia	Hypotension Shock Hyponatraemia (dipsketional) Hyperkalaemia	Pigmentation of: Sun-exposed areas Pressure areas (e.g. elbows, knees) Palmar creases, knuckles Mucous membranes Conjunctivae Recent scars	Decreased body hair and loss of libido, especially in females

(ACTH = adrenocorticotrophic hormone)



18.44 Management of adrenal crisis

Correct volume depletion

- IV saline as required to normalise blood pressure and pulse
- In severe hyponatraemia (< 125 mmol/L) avoid increases of plasma Na > 10 mmol/L/day to prevent pontine demyelination (p. 358)
- Fludrocortisone is not required during the acute phase of treatment

Replace glucocorticoids

- IV hydrocortisone succinate 100 mg stat, and 100 mg 4 times daily for first 12–24 hrs
- Continue parenteral hydrocortisone (50–100 mg IM 4 times daily) until patient is well enough for reliable oral therapy

Correct other metabolic abnormalities

- Acute hypoglycaemia: IV 10% glucose
- Hyperkalaemia: should respond to volume replacement but occasionally requires specific therapy (see Box 14.17, p. 363)

Identify and treat underlying cause

- Consider acute precipitant, such as infection
- Consider adrenal or pituitary pathology (see Box 18.41)

18.50 Pancreatic neuro-endocrine tumours

Tumour	Hormone	Effects
Gastrinoma	Gastrin	Peptic ulcer and steatorrhoea (Zollinger–Ellison syndrome, p. 902)
Insulinoma	Insulin	Recurrent hypoglycaemia (see above)
VIPoma	Vasoactive intestinal peptide (VIP)	Watery diarrhoea and hypokalaemia
Glucagonoma	Glucagon	Diabetes mellitus, necrolytic migratory erythema
Somatostatinoma	Somatostatin	Diabetes mellitus and steatorrhoea

18.51 Clinical features of the carcinoid syndrome

- Episodic flushing, wheezing and diarrhoea
- Facial telangiectasia
- Cardiac involvement (tricuspid regurgitation, pulmonary stenosis, right ventricular endocardial plaques) leading to heart failure

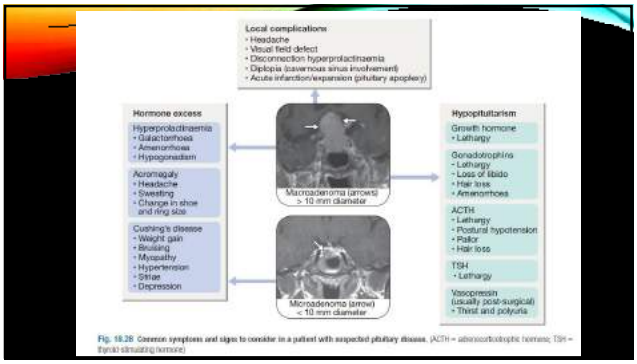


Fig. 18.28 Common symptoms and signs to consider in a patient with suspected pituitary disease. (ACTH = adrenocorticotrophic hormone; TSH = thyroid stimulating hormone)

18.61 How and when to do a water deprivation test

Use
- To establish a diagnosis of diabetes insipidus and to differentiate cranial from nephrogenic causes

Protocol
- No coffee, tea or smoking on the test day
- Free fluids until 0730 hrs on the morning of the test, but discourage patients from 'stocking up' with extra fluid in anticipation of fluid deprivation
- No fluids from 0730 hrs
- Attend at 0830 hrs for measurement of body weight and plasma and urine osmolality
- Record body weight, urine volume, urine and plasma osmolality and thirst score on a visual analogue scale every 2 hrs for up to 8 hrs
- Stop the test if the patient loses 3% of body weight
- If plasma osmolality reaches >300 mOsmol/kg and urine osmolality <600 mOsmol/kg, then administer DDAVP (see tests) 2 µg IM

Interpretation
- Diabetes insipidus is confirmed by a plasma osmolality >300 mOsmol/kg with a urine osmolality <600 mOsmol/kg
- Cranial diabetes insipidus is confirmed if urine osmolality rises by at least 50% after DDAVP
- Nephrogenic diabetes insipidus is confirmed if DDAVP does not concentrate the urine
- Primary polydipsia is suggested by low plasma osmolality at the start of the test

18.60 Causes of diabetes insipidus

Cranial

Structural hypothalamic or high stalk lesion
- See Box 18.54

Idiopathic

Genetic defect
- Dominant (AVP gene mutation)
- Recessive (DIDMOAD syndrome – association of diabetes insipidus with diabetes mellitus, optic atrophy, deafness)

Nephrogenic

Genetic defect
- V2 receptor mutation
- Aquaporin-2 mutation
- Cystinosis

Metabolic abnormality
- Hypokalaemia
- Hypercalcaemia

Drug therapy
- Lithium
- Demeclocycline

Poisoning
- Heavy metals

Chronic kidney disease
- Polycystic kidney disease
- Sickle-cell anaemia
- Infiltrative disease

18.63 Multiple endocrine neoplasia (MEN) syndromes

MEN 1 (Wermer's syndrome)
- Primary hyperparathyroidism
- Pituitary tumours
- Pancreatic neuro-endocrine tumours (e.g. non-functioning, insulinoma, gastrinoma)
- Bronchial and thymic carcinoids
- Adrenal tumours
- Cutaneous lesions (e.g. lipomas, collagenomas, angiofibromas)

MEN 2 (also known as MEN 2a or Sipple's syndrome)
- Primary hyperparathyroidism
- Medullary carcinoma of thyroid
- Phaeochromocytoma

MEN 3 (also known as MEN 2b)
- As for MEN 2 above (though medullary thyroid cancer occurs earlier, even within the first year of life)
- Marfanoid habitus
- Skeletal abnormalities (e.g. cranial deformities)
- Abnormal dental enamel
- Multiple mucosal neuromas

MEN 4
- Primary hyperparathyroidism
- Pituitary tumours
- Possible tumours in the adrenals, reproductive organs, kidneys
- Possible pancreatic, gastric, bronchial and cervical neuro-endocrine tumours

18.64 Autoimmune polyendocrine syndromes (APS)*

Type 1 (APECED)
- Addison's disease
- Hypoparathyroidism
- Type 1 diabetes
- Primary hypothyroidism
- Chronic mucocutaneous candidiasis
- Nail dystrophy
- Dental enamel hypoplasia

Type 2 (Schmidt's syndrome)
- Addison's disease
- Primary hypothyroidism
- Graves' disease
- Pernicious anaemia
- Primary hypogonadism
- Type 1 diabetes
- Vitiligo
- Coeliac disease
- Myasthenia gravis

*In both types of APS, the precise pattern of disease varies between affected individuals.
(APECED = autoimmune poly-endocrinopathy–candidiasis–ectodermal dystrophy)

dystrophy (APECED). This is inherited in an autosomal recessive fashion and is caused by loss-of-function mutations in the autoimmune regulator gene *AIRE*, which is responsible for the presentation of self-antigens to thymocytes in utero. This is essential for the deletion of thymocyte clones that react against self-antigens and hence for the development of immune tolerance (p. 82). The most common clinical features are described in Box 18.64, although the pattern of presentation is variable and other

DIABETES

Boxes
- 20.1, 20.2,20.3, 20.4, 20.9, 20.10, 20.11, 20.12, 20.13, 20.14, 20.15, 20.18,
- 20.23** 20.26*****, 20.27, 20.29, 20.35, 20.36, 20.38,
- 20.39 **,
- 20.40**,
- 20.41** 20.43, 20.44, 20.45

Figures
- 20.2, 20.3, 20.4, 20.5, 20.6, 20.7, 20.8, 20.9, 20.12, 20.23***

- Function anatomy and physiology ******
- DKA cardinal features *****and management
- HHS

CLINICAL NUTRITION

- Disorders of altered energy balance
  - Obesity *
  - Under-nutrition

Micronutrients, minerals and their diseases
  - Vitamins ****
  - Inorganic micronutrients ****

POISONING & ENVENOMATION

- Figure 7.1 causes and treatment
- Box 7.4 and 7.5 ****

Box 7.7, 7.8, 7.9*****,7.10,
- 7.14*** 7.17 (specially increased risk of malignancy)

Figure 7.3----
Gastric lavage, Urinary alkalization, Paracetamol poisoning management, TCA poisoning management, OPC poisoning features and management, Ethanol and Methanol poisoning
Bedside test in envenomed patient/ 20 minutes whole blood clotting test
Box 8.1, 8.3, Clinical effect **, Box 8.7

PSYCHIATRY

- The mental state examination (Reading)
- Functional anatomy and physiology (Reading)
- Delusion
- Hallucination
- Principles of management of psychiatric disorder (different types এর নাম ও Indication)
- Dementia
- Alzheimer's disease
- Fronto- temporal dementia
- Lewy body dementia
- Wernicke - Korsakoff syndrome
- Schizophrenia
- Anxiety disorder
- OCD
- PTSD
- Somatoform disorder
- Eating disorder
- Puerperal psychiatric disorder

Boxes
- 28.6
- 28.16
- 28.23
- 28.26
- 28.31
- 28.32

Figure

DERMATOLOGY

****
- Eczema
- Psoriasis
- Lichen planus
- Acne

***
- Rosacea
- Scabies
- Basal Cell Carcinoma
- Squamous Cell Carcinoma
- Malignant Melanoma

- Toxic epidermal necrosis
- Dermatitis herpetiformis (associated with Coeliac disease)
- Causes of decreased pigmentation
- Causes of increased pigmentation
- Causes of Nail disease
- Pyoderma gangrenosum causes
- Necrobiosis lipodica causes
- Erythema multiforme
- Erythema nodosum
- Acanthosis nigricans causes

BIOSTATISTICS

1.5 Predictive values: 'What is the probability that a person with a positive test actually has the disease?'

	Disease	No disease
Positive test	A (True positive)	B (False positive)
Negative test	C (False negative)	D (True negative)

Positive predictive value = A/(A+B) × 100
Negative predictive value = D/(D+C) × 100

1.6 Type 1 and type 2 thinking

Type 1	Type 2
Intuitive, heuristic (pattern recognition)	Analytical, systematic
Automatic, subconscious	Deliberate, conscious
Fast, effortless	Slow, effortful
Low/variable reliability	High/consistent reliability
Vulnerable to error	Less prone to error
Highly affected by context	Less affected by context
High emotional involvement	Low emotional involvement
Low scientific rigour	High scientific rigour

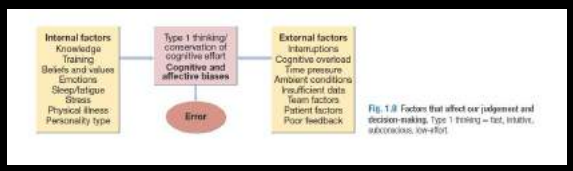


Fig. 1.8 Factors that affect our judgement and decision-making. Type 1 thinking – fast, intuitive, subconscious, low-effort.

5.5 Calculation of risk using descriptive epidemiology

Prevalence
- The ratio of the number of people with a longer-term disease or condition, at a specified time, to the number of people in the population

Incidence
- The number of events (new cases or episodes) occurring in the population at risk during a defined period of time

Attributable risk
- The difference between the risk (or incidence) of disease in exposed and non-exposed populations

Attributable fraction
- The ratio of the attributable risk to the incidence

Relative risk
- The ratio of the risk (or incidence) in the exposed population to the risk (or incidence) in the non-exposed population

5.6 Epidemiological study designs

Design	Description	Example
Clinical trial	Enrols a sample from a population and compares outcomes after randomly allocating patients to an intervention	Medical Research Council (MRC) Streptomycin Trial – demonstrated effectiveness of streptomycin in tuberculosis
Cohort	Enrols a sample from a population and compares outcomes according to exposures	Framingham Study – identified risk factors for cardiovascular disease
Case–control	Enrols cases with an outcome of interest and controls without that outcome and compares exposures between the groups	Doll R, Hill AB. Smoking and carcinoma of the lung. British Medical Journal 1950 – demonstrated that smoking caused lung cancer
Cross-sectional	Enrols a cross-section (sample) of people from the population of interest; obtains data on exposures and outcomes	World Health Organisation Demographic and Health Survey – captures risk factor data in a uniform way across many countries