Appendix

Appendix 1: Selected Genetic Mutations and Their Corresponding Endocrine States

Table A.1 Pituitary gland

Gene(s)	Endocrine condition
AIP	Familial isolated pituitary adenoma (FIPA) syndrome
KAL1, FGFR1	Kallmann syndrome
PROP1, POUF1F1	Combined pituitary hormone deficiency
Menin	Multiple endocrine neoplasia type 1
PRKAR1A	Carney complex
GnRH-1, KISS 1	Normosmic idiopathic hypogonadotropic hypogonadism (IHH)
DAX1	Normosmic IHH and adrenal insufficiency
LEP	Normosmic IHH and obesity

Table A.2 Thyroid gland

Gene(s)	Endocrine condition
SCN4A	Hypokalemic periodic paralysis
SLC26A4	Pendred's syndrome
PAX8, TSHR	Congenital hypothyroidism
THRB, THRA	Thyroid hormone resistance

Table A.3 Adrenal gland

Gene(s)	Endocrine condition
ALADIN	Triple A syndrome (primary adrenal insufficiency, alacrima, and achalasia)
RET	Multiple endocrine neoplasia types 2A and 2B
TSC1, TSC2	Tuberous sclerosis complex
VHL	Von Hippel-Lindau syndrome
ABCD1	X-linked adrenoleukodystrophy
MC2R	Familial glucocorticoid deficiency
SDHx	Hereditary pheochromocytoma-paraganglioma syndromes
TP53	Adrenocortical carcinoma
KCNJ5	Familial hyperaldosteronism

SDHx refers to SDHA, SDHB, SDHB, and SDHAF2

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Table A.4 Pancreatic gland

Gene(s)	Endocrine condition
GCK	Monogenic diabetes (uncomplicated course)
HNF1A	Monogenic diabetes (sulfonylurea responsive)
WFS1	Wolfram syndrome (DIDMOAD)
KCNJ11	Neonatal diabetes
ABCC8, KCNJ11	Congenital hyperinsulinism

Table A.5 Parathyroid gland, calcium, and bone metabolism

Gene(s)	Endocrine condition
CASR	Familial hypocalciuric hypercalcemia
ELN	Williams-Beuren syndrome
AIRE	Autoimmune polyglandular syndrome type 1
COL1A1, COL1A2	Osteogenesis imperfecta
GCM2, PTH	Familial isolated hypoparathyroidism
22q11.2	DiGeorge syndrome
PHEX	Hereditary hypophosphatemic rickets

Table A.6 Lipids and obesity

Gene(s)	Endocrine condition
CETP	CETP deficiency
ABCA1	Tangier disease
LEP	Congenital leptin deficiency
Apo C-II	Hypertriglyceridemia-related disorders
LPL	Hypertriglyceridemia-related disorders
LDL-R, PCSK-9	Familial hypercholesterolemia
LCAT	Familial LCAT deficiency
MTP	Abetalipoproteinemia
Apo E	Dysbetalipoproteinemia
ABCG5	Sitosterolemia

Appendix 2: Examination of the Thyroid Gland, an Endocrine Approach

Illustration of the optimal position of the palms and use of the second, third, and fourth digits in palpating the thyroid gland in the low anterior neck

Our approach involves sequentially inspecting, palpating, percussing (where relevant), and auscultating the thyroid.

Inspection of the Thyroid Gland

- A visible anterior neck mass, which is mobile on deglutition, implies an enlarged gland. Offer the patient a glass of water to drink. The normal thyroid gland cannot be visualized on inspection.
- Positive *Pemberton's sign* is suggestive of significant retrosternal extension of a goiter.

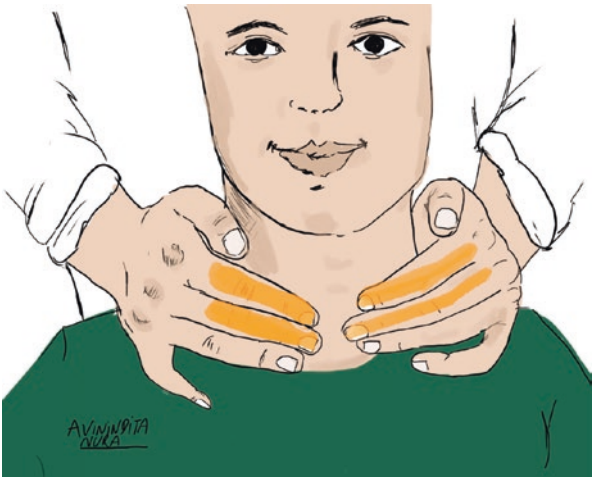

Fig. A.1 Examination of the thyroid gland

Palpation

- Optimal positioning of the neck will facilitate palpation of the gland. The patient's neck should be in a relaxed position, which prevents extensive nuchal extension or flexion. The sternocleidomastoid muscle should not be under tension, and there should be adequate room between the chin and the sternum to allow proper positioning of the hands.
- Sequentially palpate each thyroid lobe and isthmus. Occasionally there might be an accessory extension of the isthmus – the pyramidal lobe. Check for the consistency of the gland. Avoid deep palpation if the gland is tender, as might occur in De Quervain's thyroiditis. The normal thyroid has a mild firm consistency. The overlying skin is usually freely mobile over it. If the gland is attached to the overlying skin, it might be suggestive of either a malignancy or Riedel's thyroiditis.
- Attempt to feel for any discrete thyroid nodule. These are best appreciated using the pulp of your examining fingers (second, third, and fourth digits).
- Ask the patient to swallow during palpation, and check for any retrosternal extension of the thyroid gland.
- Grade thyromegaly with the WHO classification system (see Sect. 2.3.2).
- Palpate all regional lymph node groups (I to VI).

Percussion

- Percussion of the sternal manubrium may be required in patients with a suspected retrosternal goiter. The percussion note will be dull. This step is seldom warranted, especially if there is no palpable thyroid tissue extending below the proximal portion of the manubrium (thoracic aperture).

Auscultation

- In patients with hyperdynamic circulation, as might occur in overt Graves' disease, a bruit may be appreciated over the superior poles of the thyroid in the vicinity of the superior thyroid arteries.

Appendix 3: Mnemonics in Endocrinology

Pheochromocytomas (the 10 Percent Rule)
- 10% are familial
- 10% are malignant
- 10% are extra-adrenal

More recent evidence points to a genetic cause of pheochromocytomas in up to 30% of patients. This mnemonic provides an understanding of the general behavior of these tumors.

Pheochromocytomas (8Ps of Presentation)
- Pallor (*not* flushing)
- Perspiration
- Panic
- Pain (headache)
- Postural dizziness
- Panic attack
- Palpitations
- Paradoxical hypertension in the setting of beta-receptor blockers

Insulinoma (Rule of 10s)
- 10% are malignant
- 10% are multifocal
- 10% are due to multiple endocrine neoplasia type 1
- 10% are ectopic

Insulinomas are usually unifocal and benign.

Causes of Addison's disease (ADDISON)
- **A**utoimmune adrenalitis (primary adrenal insufficiency)
- **D**rugs (inhibitors of steroidogenesis, ketoconazole, mitotane)
- **D**iffuse amyloid deposition (amyloidosis)
- **I**nfectious agents (tuberculosis, human immunodeficiency virus)
- **S**econdary causes (hypopituitarism)
- **O**ther causes (adrenal hemorrhage)
- **N**eoplasia (usually metastases from primary tumors in the lung, breast, stomach, kidney, rectosigmoid colon or melanoma)

Causes of Diabetic Ketoacidosis (6 Is)
- **I**nfection (urinary or respiratory tract infections)
- **I**nsulinopenia (absolute in type 1 diabetes, relative in type 2 diabetes)
- **I**nfarction (silent myocardial infarction)
- **I**njury (significant trauma or stress)
- **I**ndex presentation (newly diagnosed type 1 diabetes)
- **I**ssues of adherence to insulin therapy

Cause of Hypercalcemia (SHIFT in calcium)
- **S**arcoidosis and other granulomatous diseases
- **H**yperparathyroidism, **h**yperthyroidism, **h**ypervitaminosis A and D
- **I**mmobilization (increased bone resorption)
- **F**amilial (familial hypocalciuric hypercalcemia)
- **T**umors, **t**hiazide diuretics, li**t**hium

Clinical features of Cushing's Syndrome (MOON FACIES)
- **M**enstrual disorders
- **O**steopenia or osteoporosis
- **O**besity (central distribution of fat)
- **N**eurosis (depression or psychosis)
- **F**ace (plethora, hirsutism, acne)
- **A**ltered muscle physiology (proximal muscle weakness)
- Supra**c**lavicular and dorso**c**ervical fat pads
- **I**nfection
- **E**levated blood pressure
- **S**kin (easy bruisability)

Causes of hypoglycemia, FEELING Dizzy
- **F**alse hypoglycemia (pseudohypoglycemia not meeting Whipple's criteria)
- **E**xogenous (insulin or insulin secretagogue)
- **E**thanol
- **L**iver failure
- **I**mmune dysfunction (stimulating anti-insulin antibodies)
- **N**eoplastic (insulinoma or sarcomas producing IGF-2)
- **G**landular dysfunction (pituitary insufficiency, adrenal insufficiency)
- **D**rugs (quinolones, pentamidine, beta-blockers, ACE inhibitors)

Multiple Endocrine Neoplasia *Type 1 (PPP)*
- Pituitary adenoma
- Pancreatic adenoma
- Parathyroid adenoma

Multiple Endocrine Neoplasia Type *2A (MPP)*
- Pheochromocytoma
- Medullary thyroid carcinoma
- Parathyroid adenoma

Multiple Endocrine Neoplasia Type 2B (MPM)
- Pheochromocytoma
- Medullary thyroid carcinoma.
- Mucosal neuromas and a marfanoid body habitus

Management of Osteoporosis (ABCDE)
- **A**ctivity (weight-bearing exercise)
- **B**isphosphonates
- **C**alcium supplementation
- **D** (vitamin D supplementation)
- **E**strogens (menopausal hormone therapy)

Causes of Gynecomastia (MAKE BREAST)
- **M**arijuana
- **A**lcohol
- **K**linefelter's syndrome
- **E**strogen excess
- **B**aby (circulating maternal estrogens)
- **R**eceptor blockers (ketoconazole, calcium channel blockers, and H2 blockers)
- **E**lderly
- **A**ntineoplastic agents (alkylating agents)
- **S**pironolactone
- **T**umors (adrenal or testicular)

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