10.1 Common clinical features in endocrine disease

Symptom, sign or problem	Differential diagnoses
Tiredness	Hypothyroidism, hyperthyroidism, diabetes mellitus, hypopituitarism
Weight gain	Hypothyroidism, PCOS, Cushing's syndrome
Weight loss	Hyperthyroidism, diabetes mellitus, adrenal insufficiency
Diarrhoea	Hyperthyroidism, gastrin-producing tumour, carcinoid
Diffuse neck swelling	Simple goitre, Graves' disease, Hashimoto's thyroiditis
Polyuria and excessive thirst	Diabetes mellitus, diabetes insipidus, hyperparathyroidism, Conn's syndrome
Hirsutism	Idiopathic, PCOS, congenital adrenal hyperplasia, Cushing's syndrome
'Funny turns'	Hypoglycaemia, phaeochromocytoma, neuroendocrine tumour
Sweating	Hyperthyroidism, hypogonadism, acromegaly, phaeochromocytoma
Flushing	Hypogonadism (especially menopause), carcinoid syndrome
Resistant hypertension	Conn's syndrome, Cushing's syndrome, phaeochromocytoma, acromegaly
Amenorrhoea/oligomenorrhoea	PCOS, hyperprolactinaemia, thyroid dysfunction
Erectile dysfunction	Primary or secondary hypogonadism, diabetes mellitus, non-endocrine systemic disease, medication-induced (e.g. beta-blockers, opiates)
Muscle weakness	Cushing's syndrome, hyperthyroidism, hyperparathyroidism, osteomalacia
Bone fragility and fractures	Hypogonadism, hyperthyroidism, Cushing's syndrome, primary hyperparathyroidism

PCOS, Polycystic ovary syndrome.

10.2 Features suggestive of Graves' hyperthyroidism

History

- Female sex
- Family history of thyroid or other autoimmune disease
- Ocular symptoms ('grittiness', redness, pain, periorbital swelling)

Physical examination

- Vitiligo
- Thyroid acropachy
- Diffuse thyroid enlargement (can be nodular)
- Thyroid bruit
- Pretibial myxoedema
- Signs of Graves' ophthalmopathy (proptosis, redness, oedema)

10.3 Causes of thyroid enlargement

Type of enlargement	Associated clinical features
Diffuse goitre	
Simple/physiological (puberty, pregnancy)	Soft, symmetrical, non-tender
Graves' disease	Hyperthyroidism, ophthalmopathy, pretibial myxoedema
Thyroiditis (Hashimoto's, subacute)	Hypothyroidism with Hashimoto's, tender goitre with hypo- or hyperthyroidism in subacute
Drugs (lithium, amiodarone, iodine)	Relevant drug history
Iodine deficiency (endemic goitre)	Particularly in mountainous regions
Infiltrative (amyloidosis, sarcoidosis, tuberculosis)	May be tender, other features of systemic disease
Dyshormonogenesis (e.g. Pendred's syndrome)	Congenital hypothyroidism, sensorineural deafness (Pendred's)
Multinodular goitre	Multiple nodules palpable or on scan
Solitary nodule	
Dominant nodule in a multinodular goitre Colloid cyst Hyperplastic nodule Follicular adenoma	Distinguishing these may require ultrasound and/or fine needle aspiration
Thyroid carcinoma (papillary, follicular, medullary, anaplastic)	May be fixed, with vocal cord involvement and/or lymph nodes
Lymphoma	Lymphadenopathy
Metastasis	Other clinical evidence of malignancy

10.4 Investigations in thyroid disease

Investigation	Indication/comment
Biochemistry	
Thyroid function tests	To assess thyroid status
Immunology	
Antithyroid peroxidase (TPO) antibodies	Non-specific, high in autoimmune thyroid disease
Antithyroid stimulating hormone receptor antibodies (TRAbs)	Specific for Graves' disease
Imaging	
Ultrasound	Goitre, nodule
Thyroid scintigraphy (^{123}I, ^{99m}Tc)	To assess areas of hyper-/hypoactivity
Computed tomography	To assess goitre size and aid surgical planning
Invasive/other	
Fine-needle aspiration cytology	Thyroid nodule
Respiratory flow-volume loops	To assess tracheal compression from a large goitre

13.1 Common causes of arthralgia (joint pain)

Infective

- Viral (e.g. rubella, parvovirus B19, mumps, hepatitis B, chikungunya)
- Bacterial (e.g. staphylococci, Mycobacterium tuberculosis, Borrelia)
- Fungal

Postinfective

- Rheumatic fever
- Reactive arthritis

Inflammatory

- Rheumatoid Arthritis

Degenerative

- Osteoarthritis

Tumour

- Primary (e.g. osteosarcoma, chondrosarcoma)
- Metastatic (e.g. from lung, breast, prostate)
- Systemic tumour effects (e.g. hypertrophic pulmonary osteoarthropathy)

Crystal formation

- Gout, pseudogout

Trauma

- For example, Road traffic accidents

Others

- Chronic pain disorders (e.g. fibromyalgia (usually diffuse pain))
- Hypermobile Ehler's Danlos syndrome

13.2 Causes of muscle pain (myalgia)

Infective

- Viral: Coxsackie, cytomegalovirus, echovirus, dengue, SARS CoV2
- Bacterial: *Streptococcus pneumoniae*, *Mycoplasma*
- Parasitic: schistosomiasis, toxoplasmosis

Traumatic

- Tears
- Haematoma
- Rhabdomyolysis

Inflammatory

- Polymyalgia rheumatica
- Myositis
- Dermatomyositis

Drugs

- Alcohol withdrawal
- Statins
- Triptans

Metabolic

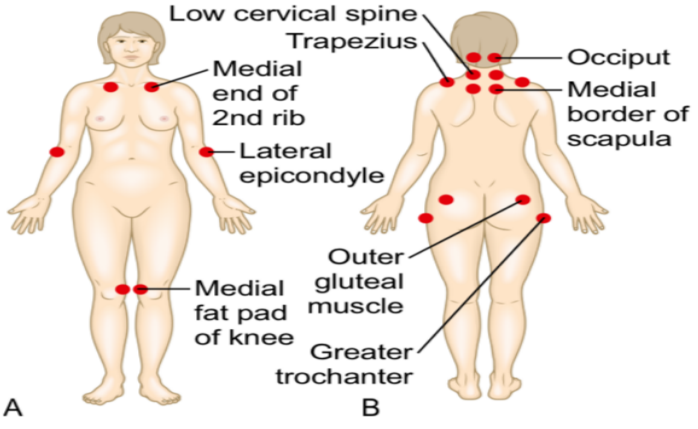
- Hypothyroidism
- Hyperthyroidism
- Addison's disease
- Vitamin D deficiency
- Neuropathic

13.3 Common patterns of referred and radicular musculoskeletal pain

Site where pain is perceived	Site of pathology
Occiput	C1, 2
Interscapular region	C3, 4
Tip of shoulder, upper outer aspect of arm	C5
Interscapular region or radial fingers and thumb	C6, 7
Ulnar side of forearm, ring and little fingers	C8
Medial aspect of upper arm	T1
Chest	Thoracic spine
Buttocks, knees, legs	Lumbar spine
Lateral aspect of upper arm	Shoulder
Forearm	Elbow
Anterior thigh, knee	Hip
Thigh, hip	Knee

13.4 Clinical vignette: arthralgia and fatigue

A 34-year-old mother-of-two presents to her General Practitioner (GP) with a 1-year history of gradually worsening pain and persistent fatigue. The pain moves around and involves the back, neck, shoulders, elbows, hands and knees. All joints are described as swollen, particularly her hands, which swell 'all over'. Further history reveals poor sleep, with the patient wakening every 2 hours and feeling unrefreshed in the morning. She has a difficult social background and a past history of depression and irritable bowel syndrome. Examination shows no skin or joint abnormality but there is widespread tenderness, particularly across her shoulders, in her neck and down her back (see figure). Blood tests are all normal. She is diagnosed with fibromyalgia.



Typical tender points in fibromyalgia. **A** Anterior view. **B** Posterior view.

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13.5 Extra-articular signs in rheumatic conditions

Condition	Extra-articular signs
Rheumatoid arthritis	Rheumatoid nodules, palmar erythema, episcleritis, dry eyes, interstitial lung disease, pleural ± pericardial effusion, small-vessel vasculitis, Raynaud's phenomenon, low-grade fever, weight loss, lymphadenopathy, splenomegaly, leg ulcers
Psoriatic arthritis	Psoriasis, nail pitting, onycholysis, enthesitis, dactylitis, episcleritis
Reactive arthritis	Urethritis, mouth and/or genital ulcers, conjunctivitis, iritis, enthesitis (inflammation of tendon or ligament attachments) (e.g. Achilles enthesitis/plantar fasciitis, rash (keratoderma blennorrhagica))
Axial spondyloarthritis	Inflammatory bowel disease, psoriasis, enthesitis, iritis, episcleritis, aortic regurgitation, apical interstitial fibrosis
Septic arthritis	Fever, malaise, source of sepsis (e.g. skin, throat, gut)
Gout	Tophi, signs of renal failure or alcoholic liver disease, obesity
Sjögren's syndrome	'Dry eyes' (keratoconjunctivitis sicca), xerostomia (reduced or absent saliva production), salivary gland enlargement, Raynaud's phenomenon, neuropathy
Systemic lupus erythematosus	Photosensitive rash, especially on face, mucocutaneous ulcers, alopecia, fever, pleural ± pericardial effusion, diaphragmatic paralysis, pulmonary fibrosis (rare), Raynaud's phenomenon, lymphopenia
Systemic sclerosis	Skin tightening (scleroderma, see Fig. 3.30C), telangiectasia, Raynaud's phenomenon, calcific deposits in fingers, dilated nail-fold capillaries, pulmonary fibrosis
Vasculitis	Rash, fever, malaise, neuropathy, tender cranial arteries in giant cell arteritis, nasal crusting and saddle nose in granulomatous polyangiitis
Auto-inflammatory Diseases	Rash, recurrent fever, serositis, aphthous ulceration, hepatomegaly, splenomegaly, deafness
Other	Erythema nodosum of shins in sarcoidosis and Behçet's disease, viral rashes, drug rashes, oral and genital ulceration in Behçet's disease

13.6 Clinical vignette: joint pain and rash

A 32-year-old woman is seen in the outpatient clinic with fatigue and intermittent pain and swelling in her hands, which she has had for the last year. She noticed a rash across her cheeks and on her arms while she was on holiday in Spain recently, and this seems to have sparked off painful mouth ulcers and worsening joint pain. She has no other relevant history. Examination shows a 'butterfly' rash across the cheeks and nose, several mouth ulcers and two swollen metacarpophalangeal joints. Blood tests reveal anaemia, lymphopenia, positive antinuclear antibody and raised anti-double-stranded deoxyribonucleic acid antibodies.
A diagnosis of systemic lupus erythematosus is made.

13.7 Drugs associated with adverse musculoskeletal effects

Drug	Possible adverse musculoskeletal effects
Glucocorticoids	Osteoporosis, myopathy, osteonecrosis, infection
Statins	Myalgia, myositis, myopathy
Angiotensin-converting enzyme inhibitors	Myalgia, arthralgia, positive antinuclear antibody
Antiepileptics	Osteomalacia, arthralgia
Immunosuppressants	Infections
Quinolones	Tendinopathy, tendon rupture

13.14 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis, 2010

Criteria	Score
Duration of symptoms (as reported by patient)	
<6 weeks	0
>6 weeks	1
Joint distribution (0–5)	
1 large joint[a]	0
2–10 large joints	1
1–3 small joints[b] (large joints not counted)	2
4–10 small joints (large joints not counted)	3
>10 joints (at least 1 small joint)	5
Serology (0–3)	
Negative RF and negative ACPA	0
Low positive RF or low positive ACPA	2
High positive RF or high positive ACPA	3
Acute-phase reactants	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1

Patients must have at least 1 swollen joint not better explained by another disease.
A score of ≥6 classifies the patient as having definite rheumatoid arthritis. A score of 4–5 is probable rheumatoid arthritis (i.e. a patient may have clinical rheumatoid arthritis but not fulfil all criteria).

[a]Large joints: shoulders, elbows, hips, knees and ankles
[b]Small joints: all metacarpophalangeal and proximal interphalangeal joints, thumb interphalangeal joint, wrists and 2nd–5th meta-tarsophalangeal joints.

ACPA, Anti-cyclic citrullinated peptide antibody; *CRP,* C-reactive protein; *ESR,* erythrocyte sedimentation rate; *RF,* rheumatoid factor.