Section I

Basic Immunology

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CHAPTER

1

History of Pediatric Immunology

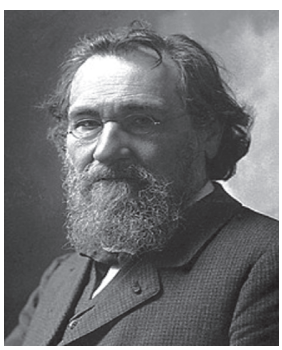
Sunil Natha Mhaske, Prajakta Ghatge

In ancient period, disease occurrence was thought that it is due to punishment from God or witches curse. Some people thought it is due to an imbalance in the energy channels within the body. Pathogens, organisms and immunology were undiscovered field.

Immunology is a branch of biology that covers the study of immune systems in all organisms. Immunology has many applications in the disciplines of medicine like organ transplantation, oncology, rheumatology, virology, bacteriology, parasitology, psychiatry, and dermatology.

Following are the pioneering scientists involved in immunology:

Ilya Ilyich Mechnikov (Elie Metchnikoff)



- Born on 3 May 1845–died on 15 July 1916.
- Father of natural immunity.
- Russian zoologist.
- Done pioneering research in immunology.
- He first coined the term "immunology."
- 1882—discovery of phagocytes (macrophages).
- 1908—with Paul Ehrlich were jointly awarded Nobel Prize.
- 1903—coined the term "gerontology".
- Established the concept of cell-mediated immunity.

Antonie Philips van Leeuwenhoek

- Born on 24 October 1632–died on 26 August 1723.
- Dutch businessman and scientist.
- Father of microbiology.
- One of the first microscopists and microbiologists.
- He was first to document microscopic observations of muscle fibers, bacteria, spermatozoa, red blood cells, crystals in gouty tophi, and blood flow in capillaries.
- Made more than 500 optical lenses and 25 single-lens microscopes.

Edward Jenner

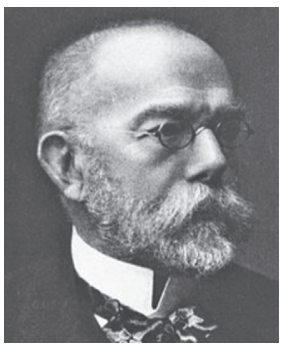
- Born on 17 May 1749–died on 26 January 1823.
- English physician and scientist.
- Pioneer of smallpox vaccine—world's first vaccine.

- Described protective effect of cowpox against smallpox.
- His work saved more lives than work of any other human.
- Was first to describe the brood parasitism of cuckoo.
- 1788—elected as fellow of the Royal Society.

Louis Pasteur

- Born on 27 December 1822–died on 28 September 1895.
- French biologist, microbiologist and chemist.
- Discoveries of the principles of vaccination, microbial fermentation and pasteurization.
- Created the first vaccines for rabies and anthrax.
- Discoveries provided direct support for the germ theory of disease.
- Best known for his invention of treating milk and wine to stop bacterial contamination (pasteurization).
- His work led the understanding of a fundamental principle in the structure of organic compounds.

Robert Koch



- Born on 11 December 1843–died on 27 May 1910.
- German physician and microbiologist.
- Founder of modern bacteriology.
- Identified specific causative agents of tuberculosis, cholera, and anthrax.
- Creation of Koch's postulates.
- 1905—received the Nobel Prize in Physiology or Medicine.

Emil von Behring

- Born on 15 March 1854–died on 31 March 1917.
- German physiologist.
- 1901—awarded Nobel Prize in Physiology or Medicine for his discovery of a diphtheria antitoxin.
- 1890—published an article with Kitasato Shibasaburo reporting "antitoxins" against both diphtheria and tetanus.

Paul Ehrlich

- Born on 14 March 1854–died on 20 August 1915.
- German–Jewish physician and scientist.
- Fields—hematology, immunology, and antimicrobial chemotherapy.
- Credited with finding a cure for syphilis in 1909.
- Invented precursor technique to Gram staining bacteria.
- Developed for staining tissue capability to diagnose numerous blood diseases.
- Received the Nobel Prize in Physiology or Medicine for his contributions to immunology.

Frank Macfarlane Burnet

- Born on 3 September 1899–died on 31 August 1985.
- Australian virologist.
- Known for his contributions to immunology.

- 1960—won Nobel Prize for predicting acquired immune tolerance.
- Developed theory of clonal selection.
- Discovered causative agents of Q-fever and psittacosis.
- 1960—honored with first Australian of the Year.
- 1978—honored with a Knight of the Order of Australia.
- Also received the Lasker Award.

Susumu Tonegawa

- Born on 5th September 1939.
- Japanese scientist.
- 1987—awarded Nobel Prize for Physiology or Medicine. For his discovery of the genetic mechanism that produces antibody diversity.
- Studied the molecular, cellular and neuronal basis of memory formation and retrieval.
- Discovery of immunity diversity—elucidated the genetic mechanism of the adaptive immune system, which had been the central question of immunology for over 100 years.
- Pioneered introductory transgenic and gene-knockout technologies in mammalian systems.

Indira Nath

- Born in 14 January 1938.
- Indian immunologist.
- Contribution—immune unresponsiveness in man, reactions and nerve damage in leprosy and a search for markers for viability of the leprosy bacillus.

- Research is focused on the cellular immune responses in human leprosy.
- Had 120 publications.
- Her pioneering work is a significant step towards the development of treatment and vaccines for leprosy.
- 1999—Awarded the Padma Shree by Government of India.
- 2002—L'Oréal-UNESCO awards for Women in Science.

Kitasato Shibasaburo

- Born on 29 January 1853–died on 13 June 1931.
- Japanese physician and bacteriologist.
- 1894—co-discoverer of the infectious agent of bubonic plague in Hong Kong.
- 1901—was nominated for the first annual Nobel Prize in Physiology or Medicine.
- Discovery of diphtheria antitoxin serum.

Gerhard Domagk

- Born on 30 October 1895–died on 24 April 1964.
- German pathologist and bacteriologist.
- Discovered Sulfonamidochrysoidine—first commercially available antibiotic.
- 1939—received Nobel Prize in Physiology or Medicine.

- He researched infections caused by bacteria.
- 1951—was one of seven Nobel Laureates who attended 1st Lindau Nobel Laureate Meeting.

Jules Bordet

- Born on 13 June 1870–died on 6 April 1961.
- Belgian immunologist and microbiologist.
- Bacterial genus Bordetella is named after him.
- Discovered phagocytosis of bacteria by white blood cells, an expression of cellular immunity.
- 1895—Bordet made his discovery on bacteriolytic effect of acquired specific antibody.
- 1906—isolated *Bordetella pertussis* in pure culture and posited it as the cause of whooping cough.
- 1919—Nobel Prize in Physiology or Medicine for his discoveries relating to immunity.

Milestones in the History of Immunology

1798 Edward Jenner: Smallpox vaccination.

1877 Paul Erlich: Recognized mast cells.

1879 Louis Pasteur: Developed an attenuated chicken cholera vaccine.

1883 Elie Metchnikoff: Developed cellular theory of vaccination.

1885 Louis Pasteur: Developed rabies vaccine.

1891 Robert Koch: Explored delayed type hypersensitivity.

List of Scientists Awarded Nobel Prize for their Work in Immunology

Year	Scientist	Country	Contribution
1901	E von Behring	Germany	Serum antitoxins as basis of immunity
1905	Robert Koch	Germany	Demonstrated cellular immunity to tuberculosis
1908	E Metchnikoff	Russia	Roles of phagocytosis (by Metchnikoff) and of
	Paul Ehrlich	Germany	antitoxins (by Ehrlich) in acquired immunity
1913	C Richet	France	Anaphylaxis in response to toxin from a jelly fish
1919	J Border	Belgium	Complement-mediated bacteriolysis
1930	K Landsteiner	United States	Discovery of human ABO blood groups
1951	Max Theiler	South Africa	Development of yellow fever vaccine
1957	D Bovet	Switzerland	Discovery of antihistamines
1960	FM Burnet	Austraila	Discovery of acquired immunological tolerance
	Peter Medawar	Great Britain	
1972	RR Porter	Great Britain	Chemical structure of antibodies
1977	RR Yalow	United States	Development of radioimmunoassay
1980	G Snell	United States	Dicovery of major histocompatibility complex
	J Dausset	France	
	B Benacerraf	United States	
1984	C Milstein	Great Britain	Monoclonal antibody production from hybridoma
	GE Kohler	Germany	
	Niels K Jeme	Denmark	Immune regulatory theories
1987	S Tongeawa	Japan	Gene rearrangement in antibody production
1991	ED Thomas	United States	Contributions to transplantation immunology
	J Murray	United States	
1996	PC Doherty	Australia	Role of major histocompatibility complex in
	RM Zinkernagel	Switzerland	antigen recognition by T cells

1900 Paul Erlich: Theorized specific antibody formation.

1906 Clemens von Pirquet: Coined the word allergy.

1938 John Marrack: Formulated antigen-antibody binding hypothesis.

1942 Jules Freund and Katherine McDermott: Researched adjuvants.

1949 Macfarlane Burnet and Frank Fenner: Formulated immunological tolerance hypothesis.

1959 Niels Jerne, David Talmage, Macfarlane Burnet: Developed clonal selection theory.

1957 Alick Isaacs and Jean Lindemann: Discovered interferon (cytokine).

1962 Rodney Porter and team: Discovered the structure of antibodies.

1962 Jaques Miller and team: Discovered thymus involvement in cellular immunity.

1962 Noel Warner and team: Distinguished between cellular and humoral immune responses.

1968 Anthony Davis and team: Discovered T cell and B cell cooperation in immune response.

1974 Rolf Zinkernagel and Peter Doherty: Explored major histocompatibility complex restriction.

1985 Susumu Tonegawa, Leroy Hood, and team: Identified immunoglobulin genes.

1987 Leroy Hood and team: Identified genes for the T cell receptor.

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CHAPTER

2

Examination of the Pediatric Musculoskeletal System

Aritra Guha, Shankha Subhra Nag, Pinaki Ranjan Debnath

The pediatric musculoskeletal examination is an important part of the pediatric clinical examination.

In a pediatric setting, the musculoskeletal system examination should be conducted in 2 steps:

1. An initial screening examination
2. A focused examination of the affected joint or limb.

As children seldom report their complaints, we need to specifically look for certain signs, symptoms and pointers in them in order to identify a particular disease.

SCREENING EVALUATION

a. Infants and Neonates

i. The infant is usually examined on a table or on the mother's lap.
ii. We need to observe the general body contour, symmetry and proportion and record anthropometry.
iii. We need to assess the patients tone and reflexes.
iv. We must observe for any spontaneous movement or any evidence of paralysis or pseudoparalysis.
v. We should screen the child for congenital deformities like clubfoot, spina bifida, DDH.

b. Children and Adolescents

i. The child should be examined in minimal clothing and preferably in presence of a parent.
ii. Assess for scoliosis: Forward bending test.
iii. Assess for joint mobility.
iv. Assess the gait: Normal, short limb, Trendelenburg, antalgic
v. Assess for clubfoot and flatfoot: Toe walking.
vi. Assess for limb length discrepancy: Coleman block test.
vii. Assess for any evidence of osteomyelitis: Any scar, sinus, signs of inflammation.

Alternatively, we can use a screening tool that has been developed and presented by Professor Helen Foster. The pGALS (pediatric gait, arms, legs and spine) is a validated, simple and quick musculoskeletal screening tool for the use in the school-aged child. It has been formulated from the adult GALS, through consultation with the members from the British Society for Paediatric and Adolescent Rheumatology (BSPAR). pGALS is available for basic clinical examination and help to facilitate screening of pediatric population with musculoskeletal problems.

What is pGALS?

It is an evidence-based protocol for elementary pediatric musculoskeletal assessment

which can also help the non-specialist to differentiate normal from abnormal. The pGALS has an excellent practical aspect and it is a very simple technique which can be successfully performed in younger children. pGALS is performed when there is a suspicion of a musculoskeletal disease on clinical grounds. It comprises a few questions, observations and commands to perform some simple tasks.

pGALS: An elementary musculoskeletal assessment for school-aged children

- **Screening questions:**
  - Do you feel any pain or stiffness in your joints, muscles or your back?
  - Do you have any difficulty while getting yourself dressed without any help?
  - Do you have any difficulty while going up and down stairs?
- **Gait:**
  - Observation of the child during walking.
  - "Walk on your tip-toes and walk on your heels".
- **Arms:**
  - "Put your hands out in front of you".
  - "Turn your hands over and then make a fist".
  - "Pinch your index finger and thumb together".
  - "Touch the tips of your fingers with your thumb".
  - Squeeze gently the metacarpophalangeal joints.
  - "Put your hands together and put your hands back to back".
  - "Reach up and touch the sky with your arms".
  - "Look at the ceiling".
  - "Put your hands behind your neck".
- **Legs:**
  - Feel for the effusion at the knee joints: "Bend and then straighten your knee" (active movement of knees and examiner feels for crepitus).
  - Passive flexion (up to 90°) with internal rotation of hip.
- **Spine:**
  - "Open your mouth and put 3 of your (child's own) fingers in your mouth".
  - Lateral flexion of cervical spine: "Try and touch your shoulder with your ear".
  - Observation of the spine from behind: "Can you bend and touch your toes?" Observe curve of the spine both from the side and behind.

Practical tips while performing the pGALS examination

- Ensure the child feels comfortable, built rapport, ask about pain, and explain what you intend to explore.
- Observe the child while walking in the room, getting undressed and at play.
- Ensure the child is appropriately exposed (socks, shoes, and exposure of limbs).
- Get the child to copy you doing the maneuvers.
- Search for the verbal and non-verbal clues of discomfort (e.g. facial expression, withdrawal) while following the commands.
- Conduct the full screen, as the extent of joint involvement may not be clear from the history.
- Look for any asymmetry (e.g. muscle bulk, swelling of the joints, range of the joint movement).
- Observe the clinical patterns (e.g. non-benign hypermobility and marfanoid habitus or elasticity of the skin, and any relation existing between leg length discrepancy and scoliosis).

When to perform pGALS in the assessment

- Child with muscle, joint, or bone pain.
- Unwell child with pyrexia.
- Child with limp.
- Delay or regression of motor milestones.
- The clumsy child in the absence of neurological disease.
- Child with chronic disease and known association with musculoskeletal presentations.

Pediatric Regional Examination of the Musculoskeletal System (pREMS)

Preceded by pGALS which is an elementary musculoskeletal assessment, the examiner is directed to a focused examination of the relevant area(s). A consensus approach to pediatric regional examination of the musculoskeletal system known as pREMS, has been developed from the observations of the doctors and allied health professionals working in pediatric musculoskeletal (pMSK) medicine.

pREMS is basically based on the look, feel, move, function principle similar to that of adult REMS 28 according to the particular joint or anatomical region. Although it may differ by anatomical region, reflecting different pathologies from those observed in adults. pREMS involves active movements that is being performed first and then passively by the examiner and also includes the addition of measure for some joints and areas depending upon the clinical scenario. Details of the examination techniques for each joint are beyond the scope of this chapter and the reader is directed to go through concerned sections.

General Principles

Introduction:

- Introduce yourself to child and parent/accompanying guardian.
- Elaborate what you want to examine, gain verbal consent to examine.
- Normal variants in leg alignment, joint range, gait, developmental milestones must be kept in view.

Look for:

- Swellings, rashes (e.g. psoriasis or vasculitis), muscle wasting, scars, leg length discrepancy.
- Deformity or dysmorphism or disproportions or discomfort (nonverbal clues).

Feel for: Temperature, swelling, tenderness (including joint lines).

Move for:

- Full range of movement active and passive (observe for any asymmetry).
- Restriction of movement grading as per mild, moderate or severe.

Function and measure:

- Functional assessment of a joint or anatomic region must include power of muscles and stability.
- Measurement of the height/leg length.

pREMS—Examination Schedules according to Anatomical Regions

The options refer to additional maneuvers suggested for common clinical scenarios.

1. *Examination of the Hand and Wrist*

- Inspection of hands for muscle wasting, skin and nail changes—check for both dorsum and palms. Observe any asymmetry.
- Feel for the arterial pulse, tendon thickening and bulk of the thenar and hypothenar eminences.
- Feel for skin temperature, nodules or crepitations which may be more prominent with movements.
- Squeeze metacarpophalangeal (MCP) joints followed by the proximal and distal interphalangeal joints.
- Bimanually palpate the swollen or painful joints (including wrists).
- Look and feel along the ulnar border.
- Assess full finger extension and flexion—active and passive.
- Assess wrist flexion and extension, abduction and adduction—active and passive.
- Assess function: Grip and pinch, picking up small object, writing or drawing (developmental stage of the child is to be taken into consideration in this case).
- Special conditions—assess for hypermobility syndromes, muscle power, carpal tunnel syndrome with Tinels test, peripheral neuropathy and pulses, nail fold capillaroscopy where connective tissue disorder is suspected.

Points to note

Range of movement (ROM)

Normal:

1. 80° of flexion (flexor carpi ulnaris, flexor carpi radialis, with assistance from flexor digitorum superficialis).

2. 70° of extension (extensor carpi ulnaris, extensor carpi radialis brevis and longus, along with assistance from extensor digitorum).
3. 20° of radial deviation (abductor policis longus, flexor carpi radialis, extensor carpi radialis longus and brevis).
4. 30° of ulnar deviation (extensor carpi ulnaris and flexor carpi ulnaris).

2. Examination of the Elbow

- Look for the carrying angle, scars, swellings or rashes, any deformities.
- Feel for the skin temperature.
- Palpate over head of radius, joint line, medial and lateral epicondyles.
- Assess for the full flexion and extension, pronation and supination movements—active and passive.
- Assess coordination of movement, e.g. hand to nose or mouth, hands behind head.
- Special conditions—assess for hypermobility syndromes, muscle power, joint instability tests, and enthesitis.

3. Examination of the Shoulder

With the patient standing or in sitting posture:

- Inspect shoulders, clavicles and sternoclavicular joints from the front, side and behind, and assess shoulder level on both sides.
- Inspect skin in axillae and palpate for lymphadenopathy.
- Assess the skin temperature.
- Palpate the bony landmarks and adjacent muscles.
- Assess movement and function: Hands behind head, hands behind back.
- Assess external rotation, flexion, extension and abduction movements—active and passive.
- Observe the scapular movement.
- Special conditions assess for hypermobility syndromes, muscle power, joint instability.

4. Examination of the Hip

With the child in supine posture while lying on a couch:

- Look for the flexion deformity and leg length discrepancy.
- Search for scars, rashes on the overlying skin.
- Feel the greater trochanter for tenderness.
- Assess full hip flexion, internal and external rotation, abduction and adduction movements—active and passive.
- Assess hip abduction movement (lying on side)—active and passive.
- Perform Thomas test.

With the child lying in prone posture on couch:

- Perform sacroiliac joint palpation.
- Assess for internal and external rotation movements.

With the child in standing position:

- Assess posture and leg alignment.
- Observe gluteal muscle bulk of both sides.
- Perform the Trendelenburg test on both sides.
- Assess function (gait with turning, running and ancillary movements).
- Special conditions assess for hypermobility, muscle power, enthesitis, thigh-foot angle (with in-toeing).

5. Examination of the Knee

***With the child in standing position*:**

- Look for varus or valgus deformity, hyperextension and popliteal swellings.
- Look for scars and rashes on the overlying skin.
- Assess the gait (see hip examination).

***With the child lying supine on the couch*:**

- Look from the end of the couch for varus or valgus deformity, muscle wasting, scars and swellings.
- Look from the side for fixed flexion deformity.
- Look for passive hyperextension and leg length discrepancy.
- Feel the skin temperature.
- With the knee slightly flexed, palpate the joint line and the borders of the patella.
- Palpate the popliteal fossa.
- Perform a patellar tap and cross fluctuation (bulge sign).

- Assess full flexion and extension movement—active and passive.
- Special conditions: Assess stability of the knee ligaments like medial and lateral collateral ligaments (anterior and posterior Drawer test), tests for anterior knee pain, patellar maltracking, assess for hypermobility, enthesitis, hamstring tightness, iliotibial band tightness and thigh-foot angle (with in-toeing).

6. Examination of the Foot and Ankle

With the child lying in supine posture on couch:

- Look at the dorsal and plantar surfaces of the foot.
- Feel the skin temperature.
- Palpate for peripheral arterial pulses.
- Gently squeeze the metatarsophalangeal joints.
- Palpate the mid-foot, ankle joint line and subtalar joints.
- Assess movements at the ankle joint (dorsiflexion and plantar flexion), subtalar joint (inversion and eversion), mid-tarsal joints (passive rotation), and of the great toe (dorsiflexion and plantar flexion)—active and passive
- Look at the patient's footwear.
- Special conditions—assess for hypermobility, thigh-foot angle (with in-toeing), enthesitis, muscle power, nail fold capillaroscopy.

With the child in standing posture:

- Look at the forefoot, mid-foot (arch of the foot) and the hindfoot.
- Assess gait cycle (heel strike, stance, toe off), running and turning, and ancillary movements.
- Assess muscle bulk of the calves.

7. Examination of the Spine

With the child in standing position:

- Inspect from the side and behind.
- Inspect skin and gluteal cleft.
- Assess the limb/trunk proportion.
- Inspect the facial and jaw profile.
- Palpate the spinal processes and paraspinal muscles.
- Assess for the lumbar flexion and extension, lateral flexion, cervical flexion and extension, cervical rotation and lateral flexion, thoracic rotation—active and passive.
- Assess temporomandibular joints and opening of the mouth with interdental distance measurement.
- Special conditions: Schobers test, Stork test (standing on one leg while extension of spine elicits pain).

With the child in sitting posture on couch (standing in younger child):

- Assess the thoracic rotation.

With the child lying supine on couch:

- Perform straight leg raising test and dorsiflexion of the greate toe.
- Assess the deep tendon reflexes of the limbs.
- Special conditions—assess leg length discrepancy, hypermobility, sacroiliac joint tenderness on palpation.

Suggested Readings

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CHAPTER

3

Applied Anatomy of Joints and Musculoskeletal Pain

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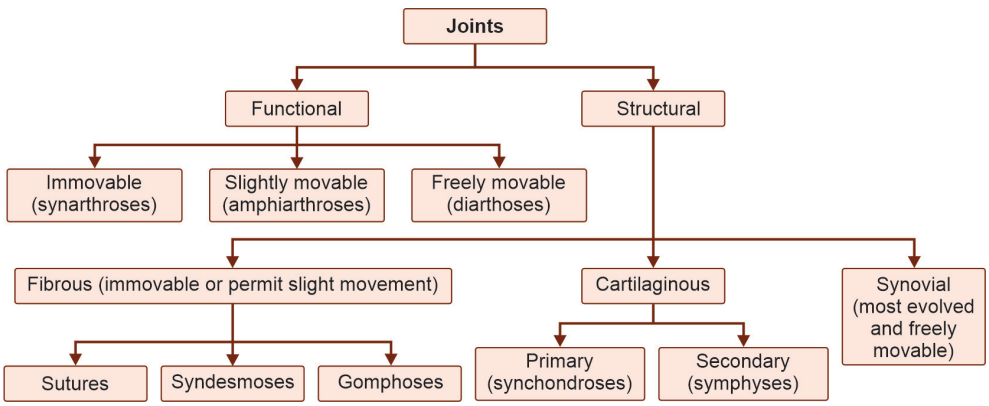
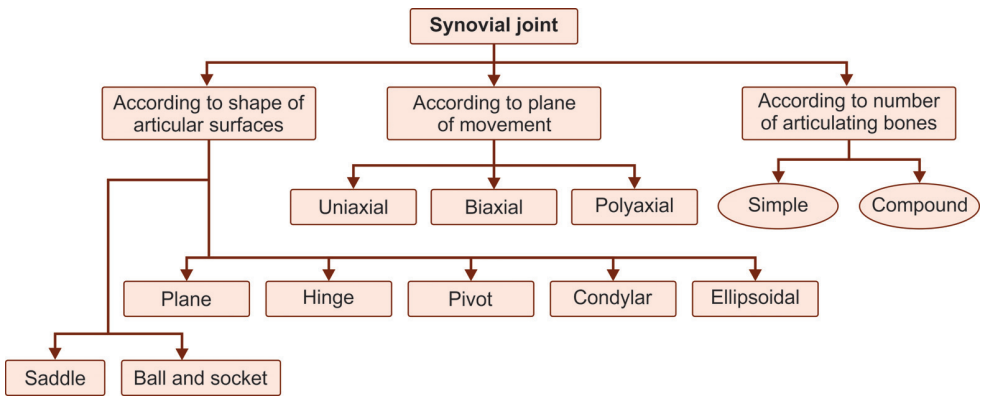
Introduction

Joints are the union between two or more bones or rigid parts of the skeleton.

Classification of Joints



Classification of Synovial Joints



MUSCULOSKELETAL PAIN

Introduction: Musculoskeletal pain usually affects the bones, muscles, ligaments, tendons and nerves. It can be acute (having a rapid onset with severe symptoms) or chronic. It can be localized to one region, or widespread.

Types of Musculoskeletal Pain

1. **Bone pain:** It is deep, dull or penetrating in nature. It most commonly results from an injury or trauma. It is important to differentiate that the pain is not related to a fracture or tumor.
2. **Muscle pain:** It is often lesser in intensity than bone pain, but it can still be debilitating. Muscle pain can be caused by an injury, reduced blood flow to the muscle, infection, malignancy or connective tissue disease. The pain can present with muscle spasms or even muscle cramps only.
3. **Tendon and ligament pain:** Pain in the tendon or ligament is often caused by the injuries, including trivial sprains. This type of musculoskeletal pain often becomes worse with stretching or moving the affected area.
4. **Fibromyalgia:** It is a condition that may present with pain in the muscles, tendons or ligaments. The pain is usually in multiple locations and can be even difficult to describe. Fibromyalgia is usually accompanied by other systemic vague symptoms and various motor, sensory and autonomic symptoms.
5. **Joint pain:** Joint injuries and diseases usually produce a stiff, aching joint called as "arthritic pain". The pain may range from mild to severe and worsens with joint movement. Joint inflammation or arthritis is a common cause of joint pain which can be accompanied by swelling of the corresponding joint.
6. **Tunnel syndromes:** These clinical entities refer to musculoskeletal disorders that cause pain due to nerve compression. These disorders include carpal tunnel syndrome, cubital tunnel syndrome, and tarsal tunnel syndrome. The pain tends to spread along the course supplied by the nerve and may present like burning sensation. These disorders are often caused by overuse of the corresponding joints or muscles.

APPLIED ANATOMY OF JOINTS

Applied Anatomy of Sternoclavicular Joint

1. **Anterior dislocation of sternoclavicular joint:** It results into forward projection of the medial end of clavicle beneath the skin. It may also be pulled upward by sternocleidomastoid muscle.
2. **Posterior dislocation of sternoclavicular joint:** It usually follows a direct trauma applied to the front of the joint which drives the clavicle backward. This type is more serious because the displaced clavicle may press onto the trachea, oesophagus, and/or major blood vessels at the root of the neck.

Applied Anatomy of Shoulder (Glenohumeral) Joint

1. **Adhesive capsulitis of shoulder joint:** Adhesive fibrosis and scarring between the inflamed joint capsule of the glenohumeral joint with the subacromial bursa, rotator cuff and deltoid muscle often cause **frozen shoulder**. It is a condition observed in individuals within the range of 40–60 years of age. A person with this condition has difficulty in abducting the arm and can achieve an apparent abduction of up to 45° by elevation and rotation of the scapula.
2. **Dislocations of the shoulder joint:** The shoulder joint is the most commonly dislocated large joint.
   i. *Anteroinferior dislocation*: Sudden violence applied to the humerus with the joint fully abducted causes tilting of the humeral head downward on to the inferior weak part of the glenohumeral joint capsule. This results into disruption and tear of the joint capsule which is followed by inferior displacement of the humeral head below the glenoid fossa.

ii. *Posterior dislocation*: It is rare and is usually caused by direct violence onto the front of the joint.

3. **Shoulder pain:** Injury to the shoulder joint results into pain, limitation of movement, and muscle atrophy owing to disuse of the corresponding muscles.

However, pain in the shoulder region can be caused by disease elsewhere and the shoulder joint may be anatomically and functionally normal. For example:

i. The pressure of the cervical rib can cause shoulder pain.
ii. Irritation of the diaphragmatic pleura or peritoneum can produce referred pain via the phrenic and supraclavicular nerves.

Applied Anatomy of Elbow Joint

1. **Bursitis of elbow joint:** The subcutaneous olecranon bursa is exposed to injury during fall on the elbow and infection from abrasions of the overlying skin.

   The bursa may become inflamed and swollen which is known as **student's elbow** or **miner's elbow**.
2. **Subluxation and dislocation of radial head:** Preschool children, particularly girls, are vulnerable to transient subluxation or incomplete dislocation of the head of the radius, also known as **nursemaid elbow** or **pulled elbow**.

   The history to these cases is almost similar. The child is suddenly lifted by the upper limb while the forearm is pronated. The child may cry out, refuse to use the limb, and protect the limb by holding it with the elbow flexed and the forearm pronated.
3. **Dislocations of the elbow joint:** Elbow joint dislocations are common, and mostly posterior type. Posterior dislocation occurs after falling on the outstretched hand.
4. **Damage to the ulnar nerve with elbow injuries:** The close relationship of the ulnar nerve with the medial side of the elbow joint makes the nerve vulnerable to injury following dislocation and/or fracture. Ulnar nerve can become stretched owing to lateral deviation of the forearm in a poorly reduced supracondylar fracture of the humerus. This can lead to ulnar nerve palsy.

Applied Anatomy of the Wrist Joint

1. **Rheumatoid arthritis:** It commonly affects the wrist and hands and considered amongst the major causes of serious loss of function and deformities. Affected joints are swollen accompanied by synovial thickening and movements are restricted. In the latter stage, articular cartilage and the underlying bones are eroded and the fingers tend to deviate medially known as ulnar deviation.
2. **Madelung's deformity:** It is the congenital subluxation or dislocation of the lower end of ulna due to malformed bones. The deformity varies in degree from a slight prominence of lower end of ulna at the back of the wrist to complete dislocation of the inferior radioulnar joint with marked lateral deviation of the hand known as radial deviation.
3. **Bull rider's thumb:** It refers to a sprain of the radial collateral ligament and avulsion fracture of the lateral part of the proximal phalanx of the thumb. The injury is common in individuals who ride mechanical bulls.

Fall on Outstretched Hand

If forces are excessive, different parts of the upper limb may give away under the strain. The area affected seems to be related to the age.

1. In a young child, for example, there may be a posterior displacement of the distal radial epiphysis.
2. In the teenager, the clavicle might fracture.
3. In the young adult, the scaphoid is commonly fractured; and
4. In the elderly, the distal end of the radius is fractured about 2.5 cm proximal to the wrist joint known as **Colle's fracture**.

Applied Anatomy of Hip Joint

1. **Dislocation of the hip joint:** It can be of two types:
   i. *Congenital dislocation:* It is common, occurring in approximately 1.5 per 1000 live births; it is bilateral in approximately half of the cases. Girls are affected at least 8 times more frequently than the boys. Dislocation occurs when the femoral head is not located within the acetabulum appropriately. Inability to abduct the thigh is characteristic of congenital dislocation. In addition, affected limb appears to be shorter, resulting in a positive **Trendelenburg sign**.
   ii. *Acquired dislocation:* According to the type of dislocation (Figs 3.1 and 3.2):
      a. Posterior dislocation: **Commonest**. A head on collision that causes the knee to strike the dashboard may dislocate the hip when the femoral head is forced out of the acetabulum.
      b. Anterior dislocation: Uncommon; because this articulation is very strong and stable.
      c. Central dislocation: Fall on the side or a blow over the greater trochanter may thrust the femoral head into the floor of the acetabulum and may cause fracture of the pelvis.
2. **Osteoarthritis of the hip:** It is a common cause of severe morbidity especially in elderly. It also affects young persons, when there has been a previous damage from an injury or disease.
3. **Coxa vara and coxa valga:** The angle of inclination varies with age, sex and development of femur. It also may change with any pathological process that weakens the neck of the femur (e.g. rickets). When the angle of inclination is decreased, the condition is called coxa vara, and when it is increased, the condition is called coxa valga. The latter may cause only a slight abduction deformity of the hip which often goes unnoticed.

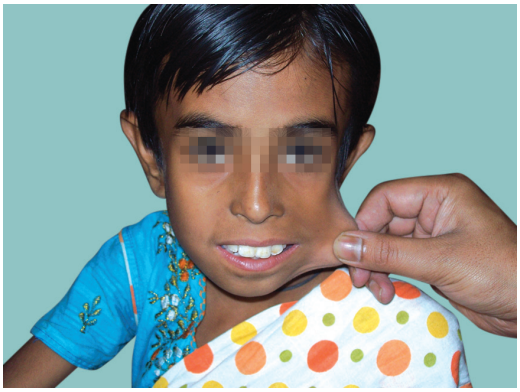


Fig. 3.1: Ehlers-Danlos syndrome with hyperelasticity

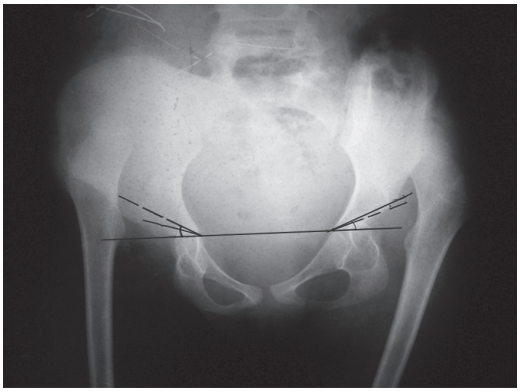


Fig. 3.2: EDS with bilateral hip dislocation

Applied Anatomy of Knee Joint

1. **Knee joint injuries:**
   i. *Ligament sprains:* The most common knee injuries often reported in contact sports and these occur when the foot is fixed to the ground. The firm attachment of the tibial collateral ligament (TCL) to the medial meniscus has considerable significance because disruption of this ligament frequently results in concomitant tearing of the medial meniscus.
   ii. *Unhappy triad of O'Donoghue:* This injury is frequently caused by blow to the lateral side of the extended knee or excessive lateral twisting of the flexed knee that disrupts the tibial collateral ligament and tears the medial meniscus from the joint

capsule. The anterior cruciate ligament (ACL) becomes taut during knee flexion and it serves as a pivot for rotator movements of the knee. If it also tears alongside the rupture of the TCL and medial meniscus, an **unhappy triad of knee** injuries is caused.

2. **Patellar dislocation:** When patella is dislocated, it nearly always dislocates laterally. Patellar dislocation is more common in women, presumably because of their greater Q-angle which represents the oblique placement of the femur relative to tibia. In addition, it indicates the angle of pull of quadriceps relative to the axis of the patella and tibia.
3. **Bursitis in knee region:**
   i. *Prepatellar bursitis:* It is caused by friction between the patella and overlying skin. If the inflammation is chronic, the bursa becomes distended with fluid and forms a swelling anterior to the knee. This condition is known as **housemaid's knee.**
   ii. *Subcutaneous infrapatellar bursitis:* It is caused by excessive friction between the tibial tuberosity and overlying skin; the edema occurs over the proximal end of the tibia. This condition was formerly known as **clergyman's knee**.
4. **Popliteal cysts:** Popliteal cysts or **Baker cysts** are abnormal fluid-filled sacs of synovial membrane in the region of the popliteal fossa. Popliteal cyst is almost always a complication of chronic knee joint effusion. The cyst may be a herniation of the gastrocnemius or semimembranosus bursa through the fibrous layer of the joint capsule into the popliteal fossa and has communication with the synovial cavity of the knee joint by a narrow stalk.

Applied Anatomy of Ankle Joint

1. **Ankle injuries:** The ankle is the most frequently injured major joint in the body. Ankle sprains are most common type. A sprained ankle is nearly always an inversion injury, involving twisting of the weight-bearing foot in plantar flexion position. Lateral ligamental sprains occur in the sports where running and jumping are required, particularly basketball. The lateral ligament or talofibular ligament is injured commonly because it is much weaker than the medial ligament or deltoid ligament. The talofibular ligament that resists inversion at the talocrural joint.
2. **Pott's fracture:** This occurs when the foot is forcibly everted and causes dislocation of the ankle. This action pulls the extremely strong deltoid ligament attached to medial malleolus causing fracture at the lower end of tibia. The talus then moves laterally, shearing off the lateral malleolus or, more commonly cause fracture of the fibula superior to the tibiofibular syndesmosis joint.

Applied Anatomy of Joints of the Foot

1. **Hallux valgus:** It is a foot deformity caused by pressure from the footwear and degenerative joint diseases. It is characterized by the lateral deviation of the great toe. Often the surrounding tissues swell and the resultant pressure and friction against the shoe causes a subcutaneous bursa to form. When this bursa gets tender and inflamed, it is called **bunion.**
2. **Pes planus (flat foot):** The flat appearance of the foot before three years of age is normal and results from the thick subcutaneous fat pad in the sole. As children get older, the fat is lost, and a normal medial longitudinal arch becomes visible.

   Flat feet can be of following types:

   (i) Flexible (flat, lacking a medial arch, when weight bearing but normal in appearance when not bearing the body weight.), and (ii) Rigid (flat even when not bearing body weight.) Flexible flat foot is common in child but usually resolves with age as the ligaments mature and become taut. The condition occasionally persists into adulthood and may or may not be symptomatic.

Rigid flat feet with a history that goes back to the childhood are likely to have underlying bony deformity.

3. **Club foot (talipes equinovarus):** It refers to foot that is twisted out of position. Incidence of common type of talipes equinovarus is 2/1000 live births and it involves the subtalar joints. Boys are affected twice as often as girls. The hindfoot is inverted, the ankle is plantar flexed, and the forefoot is adducted. The foot assumes the position of a horse's hoof, hence the prefix, "**equino**". In half of those affected, both feet are malformed. A person with an uncorrected club foot cannot put the heel and sole flat and must bear the weight on the lateral surface of the forefoot. Consequently, walking becomes painful.

Applied Anatomy of Axial Joints

1. **Fracture and dislocation of axis:** Fractures of the vertebral arch of the axis is one of the most common injuries of the cervical vertebrae. Usually the fracture occurs in the bony column formed by the superior and inferior articular processes of the axis. A fracture in this location is called **traumatic spondylosis of second cervical vertebra.** It usually occurs as a result of hyperextension of the neck, rather than the combined hyperextension of the head and neck, which causes **whiplash injury**. Such hyperextension of the head was used to execute criminals by hanging, in which a knot was placed under the chin before the body was suddenly dropped its length through the gallows floor; often this fracture has been known as **hangman's fracture**.
2. **Injury of the coccyx:** An abrupt fall onto the buttocks may cause a painful subperiosteal bruising or fracture of the coccyx, or fracture and dislocation of the sacrococcygeal joint. Displacement is common, and surgical removal of the fractured bone often required to relieve pain.
3. **Abnormal fusion of vertebrae:** In approximately 5% of people, L5 is partly or completely fused with the sacrum. This is known as **hemi-sacralization** and **sacralization of fifth lumbar vertebra,** respectively. In others conditions, first sacral vertebra (S1) is separated from the sacrum and is partly or completely fused with fifth lumbar vertebra (L5), which is called **lumbarization of first sacral vertebra**. When L5 is sacralized, the L5-S1 level become distinct and the L4-L5 level degenerates causing painful symptoms.
4. **Disc prolapse:** Flexion of the vertebral column produces compression anteriorly and stretching or tension posteriorly while squeezing the nucleus pulposus further posteriorly towards the thinnest part of annulus fibrosus. If annulus fibrosus has degenerated, the nucleus pulposus may herniate into the vertebral canal and compress the spinal cord or the nerve roots of the cauda equina, e.g. **sciatica:** It is the pain in the lower back radiating down the back of the thigh into the leg, which is often caused by a herniated lumbar intervertebral disc that compresses the L5 or S1 component of the sciatic nerve.

Suggested Readings

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CHAPTER

4

Rational Use of Laboratory Investigations in Pediatric Immunology

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Introduction

Diagnosis of a rheumatological disorder is mostly clinical, based on symptoms, signs and relevant clinical examination. Laboratory investigations are needed for diagnosis in some situations, classification, extent of disease, disease activity, monitoring response to treatment, adverse effects of drugs and prognosis. As most of the rheumatological disorders affect multiple systems, they often present with symptoms similar to infectious, endocrine, metabolic or infiltrative diseases. Laboratory investigations are also helpful in excluding such disorders. It must be kept in mind that no investigation can rule out or confirm any rheumatological disorder. The aim of this chapter is to familiarize the readers with rational use of investigations in pediatric rheumatology.

CBC

Although not diagnostic per se, they are an essential part of work-up of any suspected rheumatological disorder in a child. They generally tells us about degree of inflammation, adverse effects of drugs or sometimes points towards any alternative diagnostic possibilities.

Anemia

Anemia is normocytic normochromic as in most other chronic inflammatory disorders. The degree of anemia correlates with extent of disease activity. Conversely, if anemia is out of proportion to disease activity, leukemia should be suspected. However, possibility of co-existing nutritional anemia should be kept in mind. A hemoglobin level <7 gm% is unusual for a systemic inflammatory disorder and may be suggestive of hemolysis (AIHA in SLE) or infiltrative disorder (e.g. leukemia). Sickle cell anemia may have some bony manifestation and may mimic a rheumatological disorder, although it is not the presenting symptom.

Leukocytosis/penia

Leukocytosis is seen in active rheumatological disorder, infective arthritis, septic arthritis, osteomyelitis or leukemia. Leukopenia is found in SLE, bone marrow infiltrative disorders and also as adverse reaction to some drugs like methotrexate, azathioprine, etc.

Thrombocytosis/penia

In acute inflammatory states, platelet count is high due to stimulation of megakaryocytes by proinflammatory cytokines. Very high platelet count is seen in subacute phase of Kawasaki disease, in the 2nd week. Similar to leukopenia, low platelet count is seen in SLE, bone marrow infiltrative disorders and also as adverse reaction to some drugs like methotrexate, azathioprine, etc.