**COPD**

* COPD is defined by **two parameters** – symptomatology and airflow obstruction (AO):
* **Persistent** respiratory symptoms (as opposed to only **episodic** symptoms in asthma)
* AO: **not fully reversible and progressive**
* COPD includes three major subtypes (which **coexist** with each other in any given patient):
* Chronic bronchitis – clinically defined by chronic cough and sputum production
* Emphysema – pathologically defined by destruction of alveolar walls
* Small airway disease – reduced cross-sectional area of small bronchioles
* Emphysema is a pathological term that describes some structural changes a/w COPD
* **Types of emphysema:**

1. **Centrilobular**: a/w smoking; upper lobes and superior segments of lower lobes
2. **Panlobular:** a/w AAT deficiency; lower lobes
3. **Paraseptal:** centrilobular emphysema

* **Pathophysiology**
* Low FEV1 and low FEV1/FVC; not reversible with inhaled bronchodilators
* **V/Q (ventilation / perfusion) mismatch leads to hypoxemia**
* Increased RV (residual volume), or **air-trapping**
* **RV / TLC ratio increases**
* DLCO is reduced in emphysema
* **History and examination**
* **Triad of symptoms**: cough, sputum production and exertional dyspnea
* Recurrent acute exacerbations present with wheezing, cough, dyspnea
* Use of accessory muscles of respiration
* Tripod position
* Hoover’ sign
* Right heart failure (raised JVP and peripheral edema)
* **Digital clubbing is not a feature of uncomplicated COPD**
* Risk factors: Cigarette/ pollution/ chulla smoker/ AAT deficiency (‘Z’ allele- markedly reduced AAT)/ infections
* **Diagnosis**
* Compatible clinical feature
* Spirometry: FEV1 / FVC < 0.7
* CXR: Hyperinflation/ Flattening of diaphragm/ Tubular heart
* **Assessment of severity and staging:** ABCD assessment tool
* **Treatment of stable COPD**
* Smoking cessation: Nicotine replacement/Varenicline
* Inhaled bronchodilators (beta agonists and anticholinergics) given alone or in combination
* LTOT if PaO2 ≤55 mmHg
* LVRS: Indicated- Upper lobe emphysema; Contraindicated-FEV1 < 20%, DLCO < 20%, diffuse emphysema
* **Exacerbation of COPD**
* **Marked by worsening of dyspnea, cough, and wheezing**
* Noninvasive positive-pressure ventilation improves clinical outcomes

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**POLYMERASE CHAIN REACTION ( PCR )**

* The PCR allows the DNA in a single cell, hair follicle or spermatozoan to be amplified and analysed.
* Each cycle doubles the copy number of the amplified gene i.e. exponential increase
* **Requirements**
* Selected DNA strand- to be amplified
* **Four deoxyribonucleotides- dATP, dGTP, dCTP, and dTTP.**
* **Primers-** single-stranded oligonucleotides, 20-35 nucleotides long, complementary to the regions flanking target DNA.
* **MgCl2 and KCl**
* **Thermostable DNA polymerase**, which can withstand a temperature up to 95o C. Taq polymerase, isolated from Thermus aquaticus is heat-stable and does not get denatured at high temperatures.
* **Pfu is a thermostable enzyme having a proofreading activity (Taq polymerase doesn’t have proof reading activity) and is used for high fidelity DNA amplification.**
* **Procedure**

1. **Denaturation (96oC) -** the target DNA to be amplified is **heated to 95oC .**
2. **Annealing (50oC) -** the reaction mixture is cooled to 50oC, so the primers can bind to their complementary sequences on the single-stranded DNA templates.
3. **Extension (72oC) -** the temperature is raised to the optimal temperature for Taq polymerase to synthesize new strands complementary to the original DNA.

The new strand growth extends in 5’-3’ direction across the target DNA to make complimentary copies of the target.

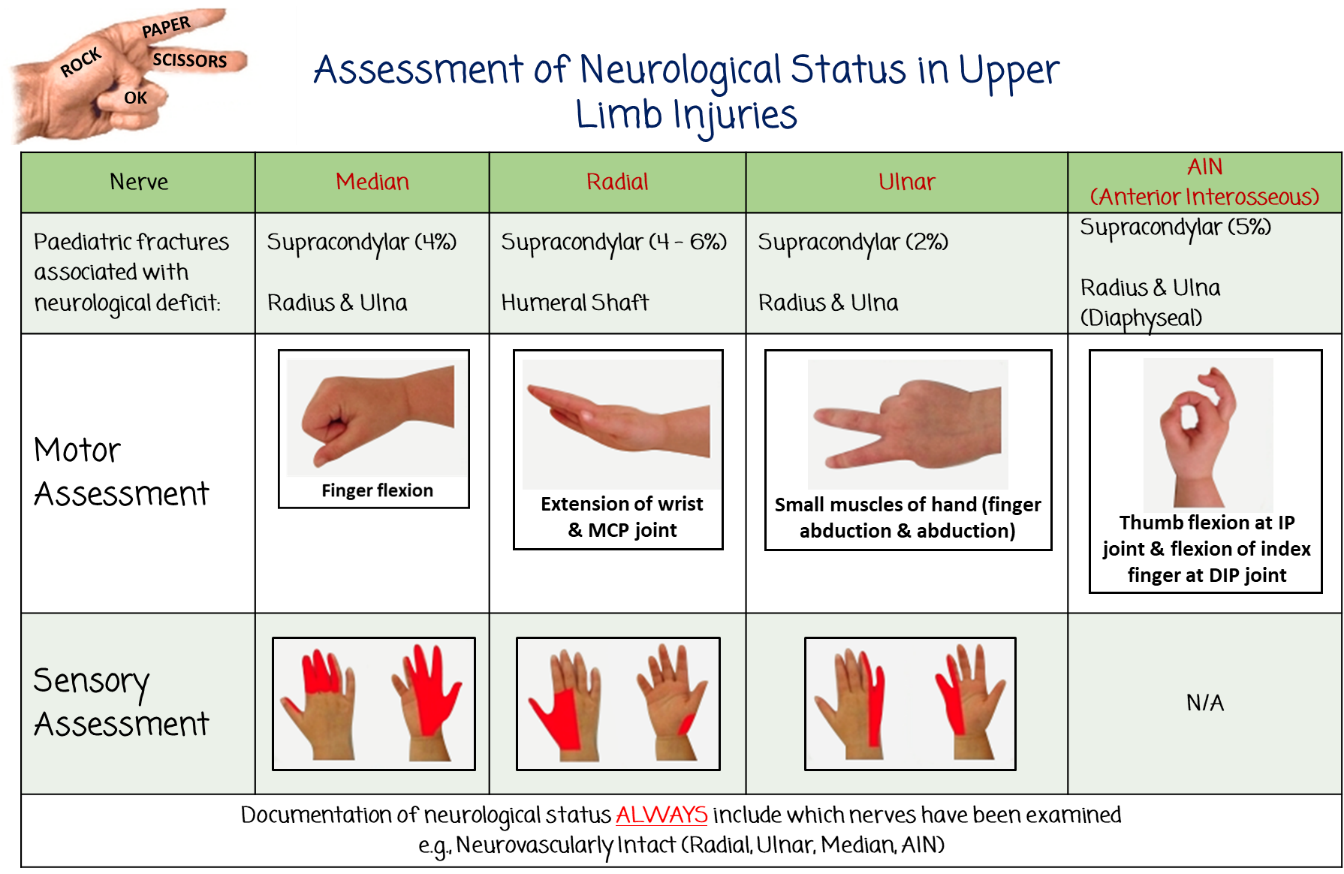
* **Applications**
  1. **Clinical diagnosis**-
* Detection of inherited disorders, viral & bacterial diseases.
* PCR allows quantification and helps in detection for early diagnosis.
* Cancers and bacterial infections like tuberculosis can be detected with PCR
  1. **Prenatal diagnosis-**
* For prenatal diagnosis of various disorders like sickle cell anemia, beta thalassemia, cystic fibrosis etc.
  1. **Comparison of a normal gene to its mutant form-**
* PCR amplifies mutant DNA so that it can be studied and later used in the diagnosis
  1. **Forensic analysis-**
* DNA isolated from single human hair, a tiny spot of blood, or a sample of semen is sufficient to determine whether the samples come from a specific individual.
  1. **Archaeology & Palaeontology-**
* **Types of PCR -**

|  |  |
| --- | --- |
| **Simple PCR** | * **Standard PCR process** |
| **Nested PCR** | * **When DNA is amplified by PCR in a very low concentration as compared to the total DNA in the sample.** * **In this process, two sets of primers are used to increase the sensitivity & specificity-**  1. **Outer primers - first DNA is amplified using outer primers.** 2. **Inner primers - it helps to amplify sequence inside the binding site of outer primers.** |
| **q- PCR (quantitative PCR) or Real-Time PCR** | * **In this DNA amplified is quantitated at the same time, not at the end of PCR as in conventional PCR.**   **Methods used are-**   * **Intercalating dyes- ethidium bromide & SYBR green (less toxic & more specific)** * **Sequence-specific probes-generate fluorescence when hybridize to the target sequence-Taqman, Molecular beacon & fluorescence resonance energy transfer (Fret) probes.** |
| **RT – PCR (Reverse transcriptase PCR)** | * **cDNA is generated from an mRNA template by reverse transcription. This cDNA is amplified by PCR, which can be used to synthesize useful proteins.** |
| **Multiplex PCR** | * **Simultaneous multiplication of many targets using different primers in one reaction.** |

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* COMMON NERVE INJURIES:

| INJURY | | NERVE INVOLVED | EFFECT | SPLINTAGE POSITION |
| --- | --- | --- | --- | --- |
| **Shoulder dislocation** | Axillary nerve | Deltoid paralysis | Initially anatomical position, followed by abduction till recovery |
| **Fracture shaft of humerus** | Radial nerve | **Wrist drop** | **Cock up splint** in wrist dorsiflexion |
| **Fracture medial condyle humerus** | Ulnar nerve | Mild claw hand | Knuckle bending position with **knuckle bender splint** |
| **Posterior dislocation of hip** | Sciatic nerve | Foot drop due to peroneal component involvement | **Foot drop splint**, keeping the foot in neutral position |
| **Knee dislocation, injury around neck of fibula** | Common peroneal nerve | Foot drop | **Foot drop splint** |
| **Monteggia fracture** | Posterior interosseous nerve (PIN) | Finger drop | **Cock up splint** |
| **Supracondylar fracture of humerus** | Anterior interosseous nerve (AIN) > median nerve | Pointing index finger | **Kiloh-Nevin sign (anterior interosseous) > pointing index (median nerve)** |



* Tests for ulnar nerve:

| TEST | MUSCLE AFFECTED |
| --- | --- |
| **Book test** | Adductor pollicis |
| **Card test** | Palmar interossei |
| **Igawa test** | Dorsal interossei |
| **Froment’s sign** | Compensatory flexion by flexor pollicis |

* Tests for median nerve:

| TEST | MUSCLE AFFECTED |
| --- | --- |
| Ape thumb deformity | Thenar muscles |
| Pen test | Adductor pollicis brevis |
| Kiloh Nevin sign | Flexor digitorum profundus (FDP) + Flexor pollicis longus |
| Benediction hand | Flexor digitorum superficialis + Lateral half of flexor digitorum profundus |

**NERVE ENTRAPMENT SYNDROMES-**

| Nerve | Entrapment syndromes | Part of nerve involved |
| --- | --- | --- |
| **Median nerve** | Carpal tunnel syndrome | **Median nerve (at wrist) (most common) –** superficial sensory branch is spared as it arises around 5 cm proximal to the carpal tunnel |
| Pronator syndrome | Median nerve (proximally compressed beneath ligament of Struthers, bicipital aponeurosis or origin of pronator teres or flexor digitorum superficialis) |
| **Ulnar nerve** | Cubital tunnel syndrome | Ulnar nerve **(between two heads of flexor carpi ulnaris)** |
| Guyon’s canal syndrome | Ulnar nerve **(at wrist)** |
| **Brachial plexus** | Thoracic outlet syndrome | **Lower trunk of brachial plexus (C8 and T1) and subclavian vessels** (between clavicle and first rib) |
| **Sciatic nerve** | Piriformis syndrome | Sciatic nerve |
| **Lateral cutaneous nerve of thigh** | Meralgia paresthetica | Lateral cutaneous nerve of thigh **(can also get involved In McRoberts’ obstetric maneuver)** |
| **Superficial radial nerve** | Cheiralgia paresthetica | Superficial radial nerve |
| **Posterior tibial nerve** | Tarsal tunnel syndrome | Posterior tibial nerve **(behind and below medial malleolus)** |
| **Interdigital nerve of 3rd and 4th toe** | Morton’s metatarsalgia | Interdigital nerve compression (usually of 3rd and 4th toe) |

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