Biochemistry #3 — Plasma Proteins

* Total protein Conc. = 6.0 - 8.0 g/dL
* Separation: 1) Salting Out → Fibrinogen / Albumin / Globulins (Na+ or NH4+ Sulfate)
  2) Electrophoresis → Albumin
  → α1 & α2 Globulins
  → β Globulins
  → γ Globulins.

* **Albumin** → Conc = 3.5-5.0 g/dL / 60% of total P.P.
  (60% in EC space; 40% in plasma)
  → mW = 69 kDa
  → $t_{1/2}$ = 20 days.
  → fastest in Electrophoresis @ Alkaline pH.
  → liver produces 12 g Albumin/day / 25% of total hepatic protein synthesis & 1/2 its secreted protein
  → preproprotein —(cisternae of RER)→ Signal peptide removed → Hexapeptide removed.
  → 1 pp chain; 585 AA, 17 S-S bonds.
  → Ellipsoidal shape.
  → Iso-electric pH = 4.7
  → functions: 1) colloidal osmotic pressure (75-80%)
  2) Transport function
  3) Nutritive function
  4) Buffering function (large # of Histidine residues).
  → hypoalbuminaemia → ↓ Serum Ca^{2+} (total); Ionic Ca^{2+} same
  ↓ 1 g/dL Albumin → ↓ 0.8 mg/dL Ca^{2+}

* **Globulins** (93-1193 kDa)
  → α → α_1 → α_1-Antitrypsin
  → α_1-Acid glycoprotein
  → α_1-Fetoprotein.
  → α_2 → haptoglobin
  → Ceruloplasmin
  → α_2-Macroglobulins
  → β → Transferrin
  → C-Reactive protein
  → Haemopexin
  → Complement C1q
  → β-lipoprotein (LDL)
  → γ → IgA
  → IgG
  → IgM
  → IgD
  → IgE

α_1-Antitrypsin (aka α_1-Antiprotease) / principal serine protease inhibitor of plasma
- 394 AA, 3 oligosaccharide chains.
- 790% of α_1
- inhibits: Trypsin, Elastase ...
- deficiency: Emphysema.
- Synthesised by: Hepatocytes & Macrophages.
- Smoking: oxidises Methionine (Active site) → Meth. Sulfoxide

α_1-Acid Glycoprotein → Plasma conc = 0.6-1.4 gm/dL / 41% Carb.
- progesterone transporter ; Carb. Transporter to injury sit
- Marker of Acute inflammation.

α_1-fetoprotein → foetal blood / Mid-pregnancy (highest conc.).
- Healthy Adult Normal conc: <1 Mg/100 mL
- ↑ in pregnancy
- Tumour Marker for Hepatocellular Carcinoma or Teratoblastoma

Haptoglobin → glycoprotein ; Hb-Hp (Non-covalent)
- 40-180 mg of Hb (Binding Capacity per dL).
- function: prevent loss of free Hb into kidney (too large to pass thru glomerulus)
- mW = 65 kDa. / Hb-Hp mW = 155 kDa.
- ↑ in inflam. conditions; ↓ in haemolytic Anaemias.
- $t_{1/2}$ = 5 days ; $t_{1/2}$ of Hb-Hp = 90 mins (80x faster clearance)
- (Free Hp level) or (Hp Binding Capacity) describe degree of Intravascular Haemolysis.

Ceruloplasmin → Blue colour (High Cu^{2+} content) (90% of plasma Cu^{2+})
- Cu^{2+} not readily exchangeable (6 atoms; very tightly).
- Activities: Ferroxidase, Copper Oxidase, Histaminase.
- Apoceruloplasmin + Cu^{2+} → Ceruloplasmin
  - synthesised in liver.
- Albumin carries 10% of plasma Cu^{2+} & binds less tightly therefore More imp in Cu^{2+} transport.
- Normal: 25-50 mg/dL
- Low levels: Wilson Disease (Hepatolenticular Degeneration) ↓ in liver Disease, Malnutrition, Nephrotic Syndrome

α_2 Macroglobulin → 8-10% of total plasma protein.
- tetrameric ; mW = 725,000
- synthesised by: Hepatocytes & Macrophages.
- in vivo Anticoagulant / carrier of Many GFs
- Normal Serum Level = 130-300 mg/dL.
- conc ↑ in Nephrotic Syndrome (other proteins are lost).

* CRP slide Missing *

Haemopexin → mW = 57,000 - 80,000
- Normal level = 0.5-1.0 gm/L
- @ birth: Low level / @ 1st year: Adult value.
- synthesised in: Liver.
- binds Haem (from Hb breakdown & other Haemoproteins).
- Low level in: Haemolytic Disorders, @Birth, drug induced
  High level in: pregnancy, DM, Malignancies, DMD (Duchenne Muscular Dystrophy)

Complement C1q → 1st complement factor to bind Ab.
- binds: Heparin, divalent Ions
- low levels: indicator for circulating Ag-Ab complex.
  high levels: Chronic infections

	IgG	IgA	IgM	IgD	IgE
fixes complement	✓	X	✓	—	X
cross placenta	✓	—	X	—	—
function	• secondary response • opsonisation • Neutralise Bacterial toxins & viri.	• prevent Attachment of Bacteria & Viri to Mucous Membranes	• primary response * Antigen Receptor on surface of B-cells	• uncertain * on surface of Many B-cells & serum	• Immediate hypersensitivity. • against worm infections.

Hypogammaglobulinaemia →
1) Losses from Body.
2) ↓ Synthesis.
3) Transient Neonatal.
4) primary genetic deficiency
5) Secondary → drug-induced (corticosteroid therapy)
   → Uraemia
   → Haematological Disorders.
6) AIDS.

Koshin Color

* Fibrinogen → aka Clotting factor 1.
  - 4-6% of total protein.
  - Large, asymmetric, 6 Pp, S-S, (-)ve Amino terminal (Glutamic Acid)
  - Maximum Viscosity to Blood.
  - Negative charge: 1) Solubility in plasma.
    2) Prevent Aggregation.

. < transport proteins >

Acute phase proteins:
1) CRP
2) Ceruloplasmin
3) α_1- Antitrypsin
4) α_1- Acid glycoprotein.
5) α_2- Macroglobulins.

Negative Acute phase proteins:
1) Albumin
2) Transthyretin (pre-Albumin)
3) Retinol Binding Protein
4) Transferrin.

Abnormal Proteins:
1) Bence Jones proteins ( )
   { Monoclonal Light chains;
   Urine in Multiple Myeloma;
   mW = 45,000;
   Identified by: Heat Coagulation Test;
   Detected by: Zone electrophoresis,
   Immunoelectrophoresis; }
2) Cryoglobulins ( )
   { Monoclonal IgM or IgG or Both;
   Coagulate when serum is cooled;
   ↑ in: RA, Multiple Myeloma, SLE,
   Lymphocytic leukaemia,
   Lymphosarcoma; }