1628: William Harvey demonstrated continuous circulation using valves in brachial veins. (Showed by expressing blood distally, then releasing to fill veins towards the heart.)

**COMPOSITION OF BLOOD:**

Blood, when centrifuged (as with hematocrit) separates (p 654) into
- **plasma** (55%) Liquid portion of blood, contains 9% protein
- **formed elements** (45%) Erythrocytes,
  - "Buffy coat" Leukocytes (5 kinds) & platelets

**Clotting:** forms (analogous to coagulation of milk in cheese formation):
- **serum** ("whey") lacks clotting factors
- **clot** consists of RBC entrapped in insoluble fibrin fibers

**PLASMA:** Contains clotting factors, contains Four types of proteins (but not fibrinogen):

<table>
<thead>
<tr>
<th>protein</th>
<th>% total</th>
<th>function</th>
</tr>
</thead>
<tbody>
<tr>
<td>albumin</td>
<td>54%</td>
<td>maintains osmotic pressure</td>
</tr>
<tr>
<td>globulin</td>
<td>38%</td>
<td>14% α, 13% β, 11% γ. (electrophoresis)</td>
</tr>
<tr>
<td>fibrinogen</td>
<td>7%</td>
<td>precursor to fibrin, lacking in serum</td>
</tr>
<tr>
<td>prothrombin</td>
<td>1%</td>
<td>precursor to thrombin which activates fibrinogen, serum lacks</td>
</tr>
</tbody>
</table>

**ERYTHROCYTES:** (p 658) biconcave disc. incrs by emotional, physical in spleen and liver
- Shape increases surface area of RBC to 3200 sq meters, 1500x area of body
- 7 micrometer diameter, increases as pH drops: therefore larger in veins
  - Males: 5,400,000 / cmm; 15 g Hb
  - Females 4,700,000 / cmm; 13-14 g H
  - Life span of 80-120 days

**HEMOGLOBIN:** (p 659) each RBC about 280 mil mol.
- Adult: two α (α) (141 AA) two β (β) (146 AA)
- Fetus: two α chains two γ chains

**Reticuloendothelial system** (RES) phagocytic macrophages removes effete (inelastic) RBCs
- Occurs in spleen esp, also connective tissue, liver and bone marrow

**Heme catabolism:** Draw porphyrin, snipped to release Fe++ (see right)
- p 662 Fe++ is salvaged and may be stored in liver as ferritin, or in bone marrow
- Waste: protoporphyrin converted to bilirubin, giving bile its golden-yellow color

**HEMATOPOIESIS:** (p 663)
- all blood cells formed from pluripotent stem cells: hemocytoblasts in several sites:
  1) earliest embryo mesenchyme of yolk sac
  2) late embryo liver
  3) fetus then spleen
  4) adults red marrow, esp of ribs, skull, vertebrae, pelvis.

**REGULATION:** ERYTHROPOIESIS, proliferation of stem cell progeny, stimulated by erythropoietin (EPN), activated in blood by renal erythropoietic factor (REF)
- REF cleaves a plasma protein to yield EPN.
- EPN increased by hypoxia.
- antiEPN abolishes synthesis of RBC

**ANEMIAS:**
- aplastic anemia: esp due to radiation etc.
- pernicious anemia: B₁₂ lack, may be due to lack of intrinsic factor
- hemolytic anemia: sickle cell anemia (p 660)
- thalassemia: decreased synth of one or more globulin chains, Hb precipitates—cells destroyed
  - alpha thalassemia = reduced alpha chains
  - beta = reduced B chains