Example1:
MCH= 22
MCHC= 32
*Notice that the normal range for MCH is (28-32).
If we consider only MCH we will consider the cell to be hypochromic, but we must use the MCHC value & since MCHC value is within the normal range →the cell is **Normochromic** – we consider MCHC NOT MCH -.

Example2:
MCH= 38
MCHC= 33
→the cell is **Normochromic** (according to MCHC value although MCH is too much above the normal level).

So:
MCHC → indicates the amount of Hb in the whole RBCs, so it determines whether the cell is normo-,hyper-,or hypo- chromic.
MCH → indicates the amount or the weight of Hb in ONE RBC, but doesn't indicate whether the cell has below normal, normal or above normal levels/ amounts of Hg.
Also we have to relate MCH to the volume (MCV).

Hemostasis

Hemostasis: stopping of blood loss through the affected (injured) blood vessels.

Three reactions take place when the injury occurs:
1-Vasoconstriction →to reduce blood flow→ reduce blood loss.
Some factors play a role in vasoconstriction:
A) Myogenic stimulus (smooth muscle contraction) due to the injury
B) Release of Serotonin
C) Release of Adrenaline from the blood or from the platelets
D) Release of Endothelin-1 from the damaged endothelial cells

2-Platelet plug formation
Steps: (Platelet Adhesion) Platelets adhere to the surface of the injured blood vessel & upon adhesion, platelets are stimulated → **(The Release Reaction)** platelets rupture and release substances → **(Platelets Aggregation)** they accumulate above each other → **(Procoagulant Activity)** platelet factor 3 is produced forming a proper medium for coagulation & then fibrin threads are formed → **(platelets fusion)**.

So in vascular injury, factor 3 which is a phospholipid is produced to activate the extrinsic pathway of the clotting mechanism & also there is activation of factor 12 for the intrinsic pathway

3-Then at the end, thrombin is produced to activate fibrinogen→ **Fibrin is formed**

*clotting factors are from 1-13 - & also there is the platelet factor -3 -, you have to know the factors numbers as well as the names of the clotting factors, note that there is no clotting factor -6.

*To remember from the previous lecture the figure about the intrinsic pathway:
It begins with the activation of factor XII then activation of factor XI which activates factor IX, now, IXa with VIIIa, phospholipid and Ca form a complex called the TENASE complex.
TENASE complex= {activated factor9 + activated factor8 +PL +Ca} acts as an enzyme to activate factor X.

For the extrinsic pathway:
During the injury, factor III is produced → activated factor VII along with factor III & Ca form the 2nd complex.
2nd complex= {activated factor7 + factor 3 + Ca} also activates factor X.
SO, both pathways activate factor X.

Now the common pathway begins:
Activated factor X with activated factor V, phospholipid and Ca form a complex called thrombokinase.
ThromboKinase complex = { act.factor10 + act.factor5 + PL + Ca } activates prothrombin to become **Thrombin** → which functions on fibrinogen to become **Fibrin →** fibrin threads are formed & are stabilized under the effect of factor XIII in the presence of thrombin and Ca.

So, these are the 3 pathways (intrinsic, extrinsic & common) of the clotting mechanism.

**-platelets can activate factor XI directly without the need of factor XII.
So factor XII can activate factor XI & also factor XII is important in the activation of prekallikrein to become kallikrein.

**-What is the most important pathway?? The extrinsic pathway
Explanation: the formation of clots in the blood is abnormal, usually because of inflammation or infection → this attracts monocytes which can produce a factor similar to the tissue factor – factor III - and this activates the extrinsic pathway.

***Calcium role in hemostasis:**
If we remove calcium from the blood, the blood will not clot, because Ca is really important & is needed in **every step** of coagulation mechanism except the first two steps of the intrinsic pathway.

-The functions of **Ca** in the platelets:
1- Activation of phospholipase.
2- Activation of secretion.
3- Contraction of Actomyosin (actin & myosin filaments).

- don't forget that factors {II, VII, IX, X} are **Vitamin K-dependent factors.
**-factor 12 activates the intrinsic pathway and fibrinolytic system→ this mean that there is a balance between coagulation and fibrinolysis (dissolving the coagulation).

-The doctor mentioned notes about the table of "blood coagulation factors"-:
Factor V→ for both pathways
Factor IV→ the Dr said that he talked about it
Factor VII→ for the extrinsic pathway along with the tissue factor
Factor VIII→ for the intrinsic pathway, don't forget its three parts (VWF, FVIII – C, FVIIIR:AG)
Factor X→ for the extrinsic, intrinsic, and the beginning of the common pathways
Factor XII→ for the intrinsic pathway
Factor XIII→ for both + the common pathway as it stabilizes the fibrin threads

-Functions of thrombin**:
1- Activation of factors VIII, V, XIII and fibrinogen
2- It has a role in the aggregation of platelets along with ADP and collagen
3- Thrombomodulin binds to thrombin to activate protein C which (prot C) requires protein S to function

-Blood neither clots nor bleeds → Blood circulates normally (It has a **Normal Fluidity)
**-Factors that cause the normal fluidity of the blood:

- **Heparin** from basophiles and mast cells.
- **Clotting factors**, mainly prothrombin and fibrinogen: present in the blood in the inactive form and during the circulation, they are removed (some of them) by the liver.
- In everybody there are **minor clottings** that occur normally and dissolve immediately. From this process there are 2 advantages; first, the clotting factors are used up in these minor clotting & so are reduced. Second, the end products of degradation of the minor clottings –fibrin/ fibrinogen degradation products- function as Anti-coagulants.
- The **lining of the blood vessel**s is very smooth and not sticky to the platelets, also it's negatively charged & so repels the platelets.
- There is a protein (anti-coagulant) in blood called **Anti-thrombin III,** it inhibits the action of thrombin as well as factors IXa, Xa, XIa , and XIIa (a means activated).
- We mentioned that thrombomodulin binds to thrombin to activate **protein C**, and protein C doesn't function unless there is **protein S** (prot. S is a cofactor for prot. C), this **complex** functions as an anti-coagulant; inactivates factor V in the presence of Ca as well as factor VIII.
- 2 other proteins **α2-macroglubulin** and **α1-antitrypsin** contribute to the anti-thrombin effect of the plasma.

If all these factors don't function, then fibrinolytic system begins.

Fibrinolytic system

**- we mentioned that factor XII activates the intrinsic pathway of coagulation as well as the fibrinolytic system, and also it produces Bradykinin vasodilator.

**-Fibrinolytic system is a physiological response to the vascular injury similar to coagulation.
Fibrinolysis means the **production of Plasmin**

There are plasminogen activators:
#endogenous →tissue plasminogen activators and contact phase of coagulation

#exogenous →urokinase (this enzyme is present in the plasma) and streptokinase (from streptococcus) >>> this (streptokinase) is called { The **LIFE INJECTION** } which immediately dissolves the thrombus.

→These activators produce Plasmin <<>> Also note that there is α2-antiplasmin, so there is balance in the fibrinolytic system too.
- PLASMIN lyses the fibrinogen, fibrin, factors V & VIII >> formation of fibrin/ fibrinogen degradation products will take place which in turn inhibits fibrin threads formation + platelet aggregation.

Clot retraction

-If the blood is left in the lab in tubes→ **clot retraction** will happen
There's partial retraction that occurs either because of time or abnormality in the blood

Clot retraction time: measures the ability of the blood clot to retract, it takes 1-2 hours to have a partial clot retraction, whereas to have a complete clot retraction, the time needed exceeds 2 hours.

Two major factors (there are other factors) play a role in clot retraction:

1. Platelets
2. Calcium

In thrombocytopenia, the clot retraction is deficient because platelets # is low.

-The following series of steps are mentioned by the dr., however, the info between brackets **{}** are the correct & accurate ones according to dr. Faraj's lectures, I kept dr. Salim's notes, because his Qs will be according to the info HE gives us:

1. Sometimes, unwanted clots are formed in the blood vessels & they don't move forming→ **Thrombus**.
{Don't forget that any thrombus isn't composed only from one clot, instead, it's composed of several clots separated by platelet masses**}**
2. Now, this thrombus is either dissolved or sometimes under the effects of the circulation, it's pushed & removed from its attachment and circulates in the blood vessels.
{The thrombus is highly dry & firm & so can never be pushed away from their site as a one unit under the effect of the circulation only, however, **parts** of the thrombus may be pushed away from it by the circulation**}**
Note by the dr.: The circulating thrombus is called an **Embolus.
{The embolus isn't the circulating thrombus; it's the circulating **part** that has detached from the thrombus**}**
3. Then, the embolus reaches narrow areas & if this embolus reached the heart or the brain, then this is a serious condition.

**-Most heart attacks are caused by either:

- **Atherosclerosis**: the accumulation of lipids inside the blood vessels, so become relatively narrow.
- **Arteriosclerosis**: losing the flexibility of the arteries especially in old age, BUT if it happens during adulthood, there will be a disease, whereas in old age, it's considered to be normal to some extent to have arteriosclerosis, BUT still, it depends on the degree, if arteriosclerosis is too much even in old age, then for sure, there's a high risk for death.

The end ☺

Please refer to the slides ...
Sorry for any mistake & good luck

Done by: Ala`a al Addasi