DISORDERS OF HEMOSTASIS

Disorders of hemostasis are classified into two major groups:

1- Bleeding disorders

2- Hypercoagulopathy

Dental procedures are more concerned with bleeding disorders.

The approach to a patient with a bleeding disorder considers whether :

1- bleeding has been a lifelong issue (i.e., congenital) or has recently become a problem (i.e., acquired).

2- The approach should also consider the underlying pathophysiology, such as defects in the vasculature, platelets, or coagulation factor.

Bleeding disorders can be categorized into the following major types:

I- Bleeding caused by vascular disorders

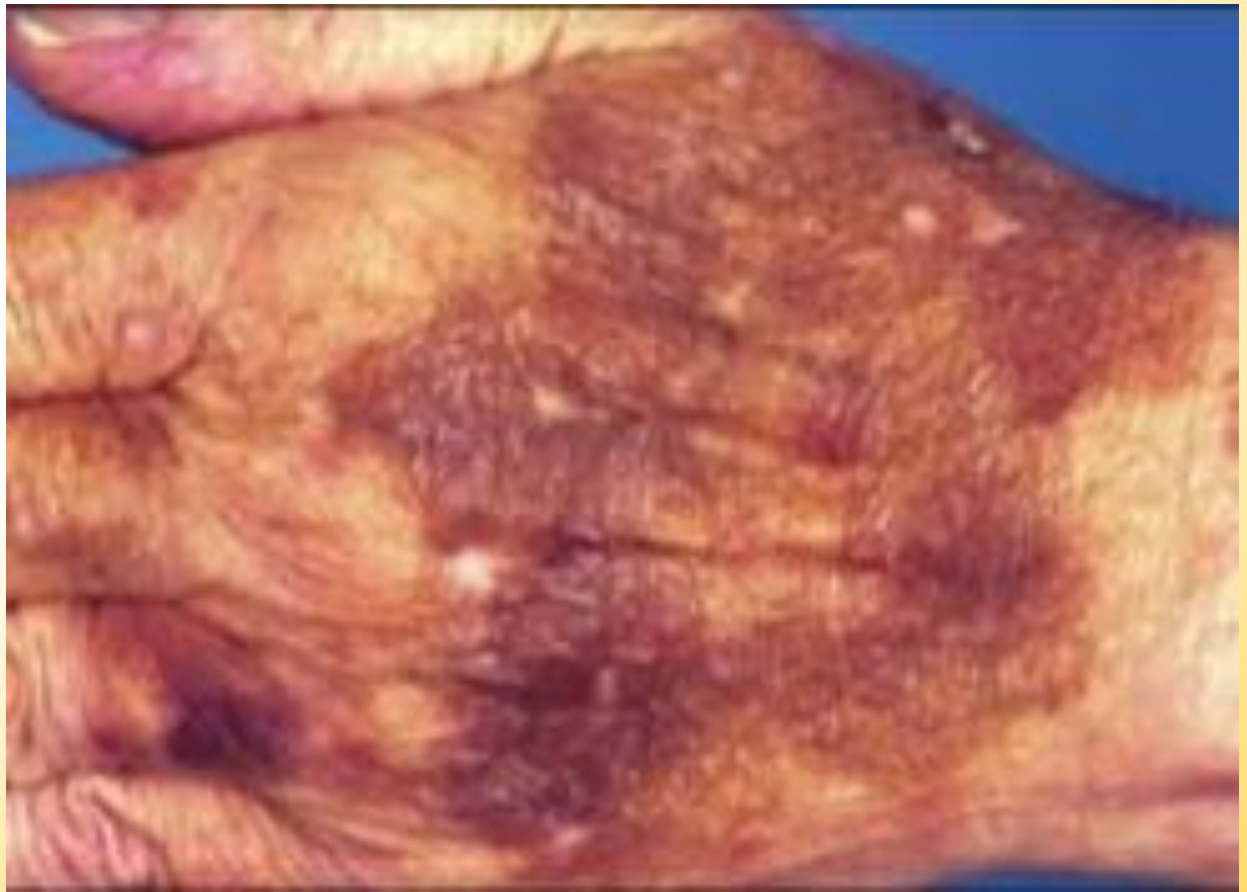
Vascular purpura (i.e., bruising) is defined as bleeding caused by intrinsic structural abnormalities of blood vessels or by inflammatory infiltration of blood vessels (i.e. vasculitis).

Vascular purpura usually causes bleeding in the setting of normal platelet counts and normal coagulation study results.

1- Senile purpura

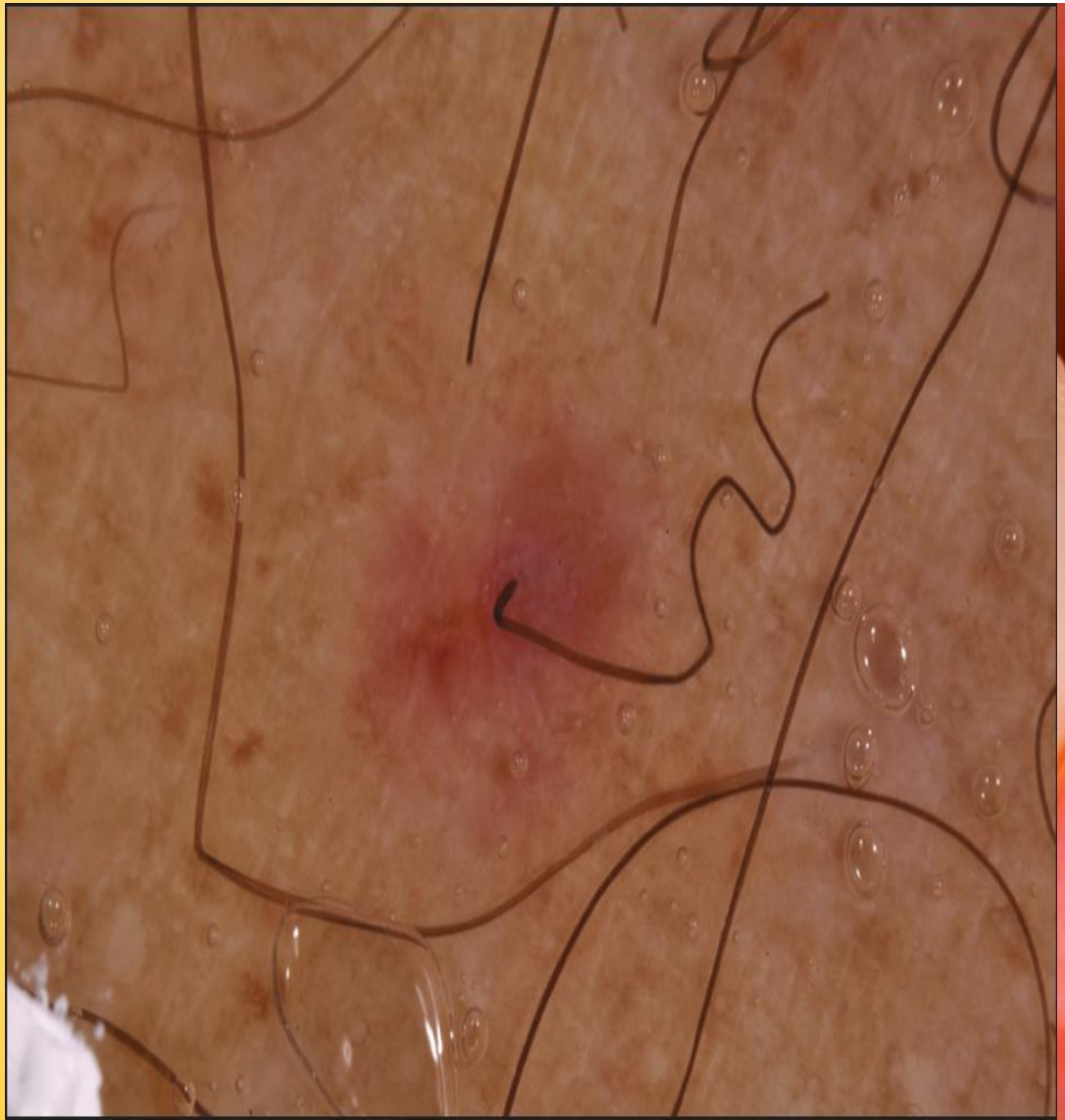
occurs in old age due to collagen breakdown and thinning of the subcutaneous tissue that overlies blood vessels.

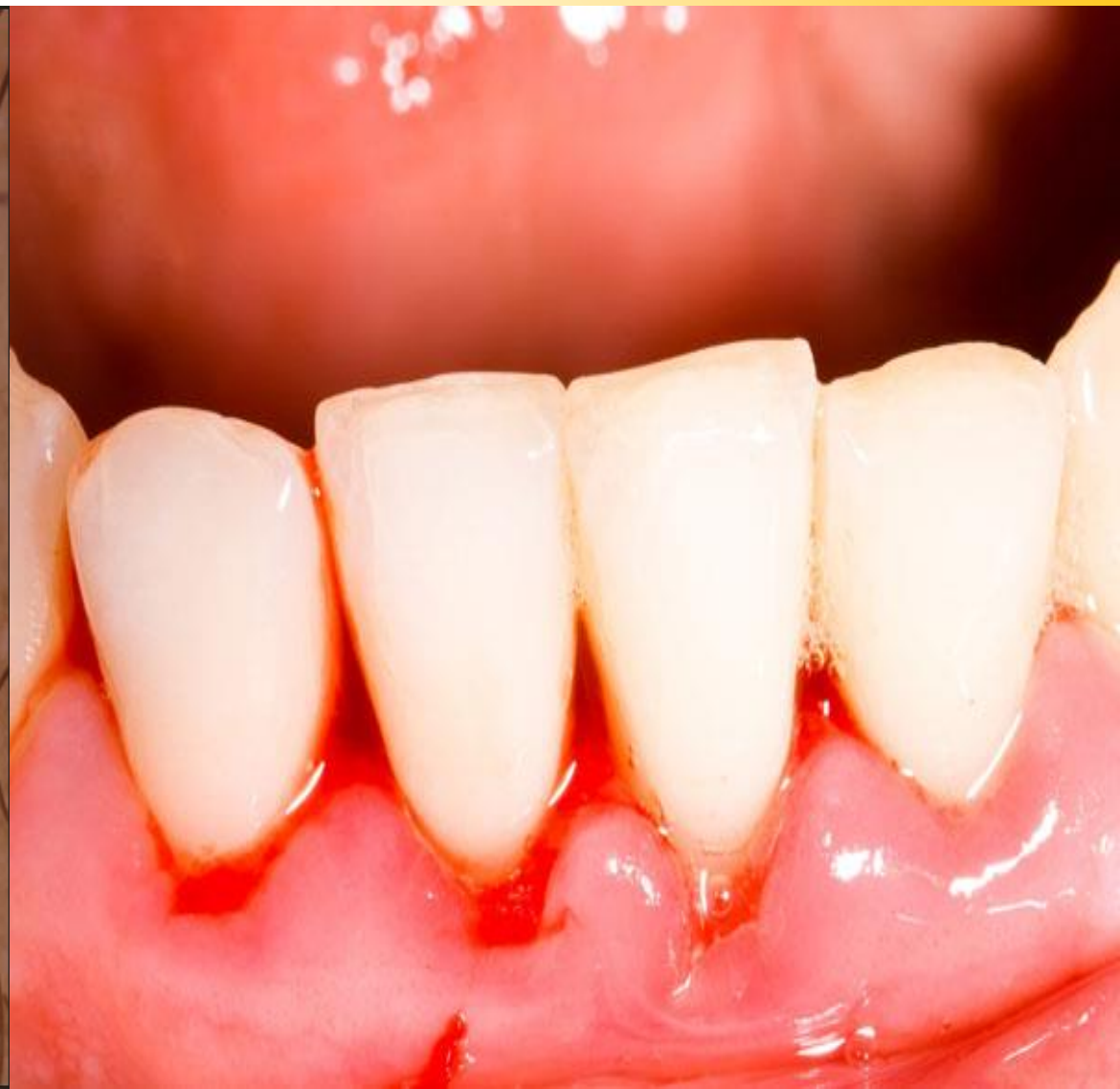
Similar effects are present in patient on steroid therapy.



2- Scurvy (deficiency of vitamin C)

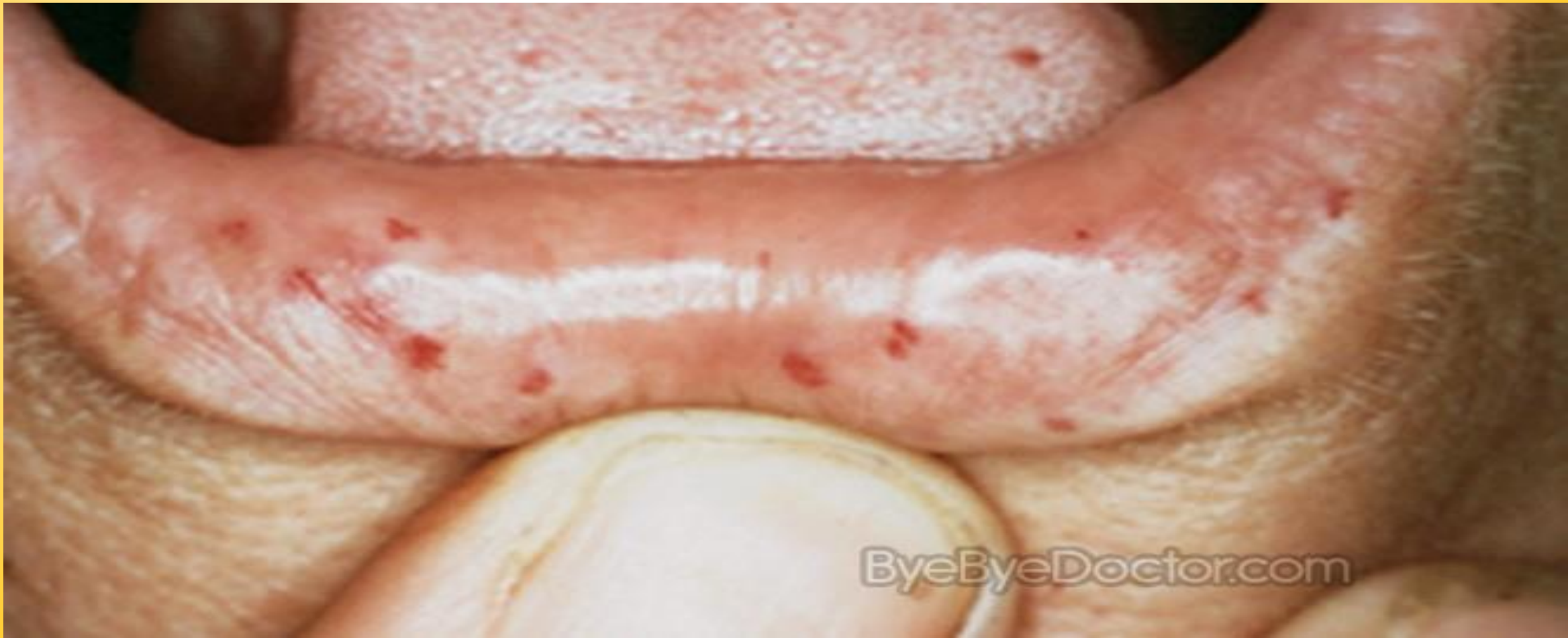
It is associated with perifollicular hemorrhage and gingival bleeding.





3- Hereditary hemorrhagic telangiectasia

An inherited disorder characterized by degeneration of the blood vessel wall that results in angiomatous lesions in the lips and GIT that might lead to significant bleeding.



II- Bleeding caused by thrombocytopenia

Thrombocytopenia is defined as platelets count of <150,000 platelets/µL.

The initial most important approach to a patient with thrombocytopenia is to decide whether this low platelet count is caused by:

1- decreased platelet production,

2-increased platelet sequestration, or

3- increased platelet destruction

Proper physical examination and specific laboratory findings can identify the exact cause of thrombocytopenia which is mandatory for correct treatment.

1- Decreased Marrow Production of Platelets

Decreased production of platelets in the bone marrow is characterized by decreased or absent megakaryocytes on the bone marrow aspirate and biopsy.

Causes include:

A- Destruction of bone marrow

Aplastic anemia, leukemia, miliary TB

B- Drugs

Usually associated with reversible thrombpcytopenia.

Examples include:

Chemotherapy, alcohol, estrogens, diuretics

C- Congenital Thrombocytopenia Syndromes

2- Platelet Sequestration

Up to 30% of circulating platelets are normally sequestered within the spleen at any time.

Causes include:

- **advanced liver disease**
- **myeloproliferative disorders accompanied by splenomegaly (e.g., chronic myeloid leukemia, chronic idiopathic myelofibrosis)**
- **malignant disease involving the spleen.**

- Splenectomy may be indicated to treat thrombocytopenia in some conditions such as myeloproliferative disease.

3- Platelet Destruction

Platelets destruction is usually occurring due to one of the following two mechanisms:

A- Immune-Mediated Platelet Destruction (antibody mediated platelet clearance)

B- Non–Immune-Mediated Platelet Destruction

Thrombocytopenia resulting from immune clearance may be severe, and platelet survival is often reduced from the normal 7 to 10 days to less than 1 day.

Despite severe thrombocytopenia, serious bleeding or hemorrhagic death is uncommon, partly because the function of young platelets is increased and partly because the number of circulating platelets required to maintain vascular integrity is relatively low, estimated at 7100/µL per day.

A- Immune Thrombocytopenic Purpura (ITP)

It is a clinical condition in which a decreased number of circulating platelets (thrombocytopenia) manifests as a bleeding tendency, due to the presence of antibodies against platelet leading to its destruction.

In children, acute ITP is often preceded by a viral infection such as varicella.

Patients with ITP exhibit petechial hemorrhage and mucosal bleeding and platelet counts are often lower than 20,000/μL.

Physical and laboratory findings are usually normal, so diagnosis is made by exclusion.

The patient may present with petechiae and ecchymoses, oozing from a venipuncture site, gingival bleeding, and hemorrhagic bullae.

More than 80% of children with acute ITP have a rapid remission, and ITP does not recur.

A subset of 10% to 20% of children eventually develops recurrent thrombocytopenia (i.e., chronic ITP); however, more than 70% of them respond completely to splenectomy.

B- Drug-Induced Platelet Destruction

Many drugs are associated with thrombocytopenia due to the development of antibodies against platelets, the most important examples of these drugs are:

- **penicillins**
- **cephalosporins**
- **Acetaminophen**
- **Ibuprofen**
- **Heparin**
- **Diuretics (chlorothiazide)**

III- Bleeding caused by platelet function defects

In these condition there is a defect in platelets function rather than number.

In other words, there is a qualitative not quantitative platelet dysfunction.These qualitative platelet disorders are most frequently encountered in individuals with normal or near-normal platelet counts.

These disorders could be congenital or acquired.

The use of aspirin and other antiplatelet drugs (clopidogrel) is most common cause of acquired platelet function defect.

As with aspirin, clopidogrel irreversibly inhibits platelet function and 7 days are required for full recovery of platelet function after discontinuation of this drug.

Fortunately, bleeding occurred as a side effect of antiplatelet drugs is usually mild, even if the patient underwent a surgical procedure including dental one.


Plavix® 75 mg
Clopidogrel
comprimés pelliculés
30 comprimés pelliculés


Plavix® 75 mg
Clopidogrel
Oral use
28 Film-coated tablets
Plavix® is a registered trademark.
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IV- Bleeding caused by von Willebrand disease

vWF is synthesized in endothelial cells and megakaryocytes and functions in plasma to mediate platelet adhesion to the damaged site.

It participates in:
1- platelets adhesion
2- binding to factor VIII and prevent its clearance from the body.

So, its deficiency will impair the function of both platelets and clotting factors.

The many mutations in the VWF gene have been phenotypically grouped into three major subtypes of vWD:

Type 1 von Willebrand Disease

- Most common type.
- Caused by a heterozygous mutation and has a dominant pattern of inheritance.
- Characterized by equivalent decreases in factor VIII, and vWF.
- Patients usually have mild to moderate bleeding, often only in relation to surgery or dental procedures.
- Both bleeding time and aPTT are elevated.
- Patients are treated with DDAVP (desmopressin, present as nasal spray), which stimulates endothelial cells to release stored vWF and leads to an increase in plasma vWF antigen.

La imagen podría no coincidir con el empaque actual del medicamento

Type 2 von Willebrand Disease

- Associated with a qualitative defect in the vWF molecule.
- Has 3 subtypes.
- Causes more severe bleeding than type 1.
- May produce a bleeding similar to hemophilia.
- It has variable response to DDAVP.

Type 3 von Willebrand Disease

- Very rare.
- Associated with complete deficiency of vWF.
- May lead to severe bleeding mimicking hemophilia.
- Treated with vWF concentrates as it does not respond to DDAVP.

V- Bleeding caused by coagulation factor disorders

In case of abnormalities of coagulation factors, the initial platelet plug is not solidified by secondary hemostasis.

The effects are clot breakdown and bleeding. This bleeding is different from platelet-type bleeding.

Coagulation factor deficiencies lead to bleeding in deep tissues and joints, and milder deficiencies result in bleeding in a delayed fashion after surgery.

So, delayed, deep seated, and severe bleeding.

Congenital Factor Deficiencies

The X-linked deficiencies of factor VIII (i.e., hemophilia A) and factor IX (i.e., hemophilia B) are the most common factor deficiencies after vWD.

Hemophilia A is about six times more common than hemophilia B.

Severity of hemophilia varies between patients from mild, moderate, to severe according to the degree of factor deficiency.

Symptoms and signs of severe hemophilia A and hemophilia B develop in childhood with bleeding into muscles, joints, and soft tissue.

Because they are X-linked disorders, they are observed primarily in male patients; the mother of an affected male patient is a carrier.

However, about 25% to 30% of cases of hemophilia result from new mutations and have no relevant family history.

Rarely, a female carrier can present with bleeding with factor level less than 30%.

Clinical features

- Spontaneous bleeding.

- Bleeding after any surgical procedure or minor trauma.

- Hemarthrosis (i.e., bleeding into joints)

- Intracranial bleeding.

The complications of hemophilia from chronic bleeding into joints and muscles, which leads to severe deformities, arthritis, muscle atrophy, and contractures.

Laboratory findings:

- PTT is prolonged

- PT is normal

- Bleeding time is normal

- Factor VIII, or IX are low.

Treatment

- Factor concentrate infusion

- **DDAVP is useful for mild to moderate hemophilia.**
- **It is used also to stop a bleeding episode or to prepare patients for dental or minor procedures.**
- **It is given intravenously and its peak effect is observed in 30-60 minutes.**
- **DDAVP can be used as an intranasal spray but its peak effect is at 60-90 minutes after administration.**
- **It is available in pharmacies in Iraq.**

Clinical tips

Dental extractions or mucosal procedures can be handled with a single preprocedure dose of FVIII, to achieve a peak level of approximately 30%, along with a single 20 mg/kg dose of EACA (an antifibrinolytic drug) .

Routine practice is to continue antifibrinolytic therapy in an outpatient setting for several days after the dental extraction, with a gradual tapering of the dosage over 5-7 days.

*** EACA: epsilom-aminocaproic acid**

Acquired causes of clotting factors deficiency include:

1- Vitamin K deficiency, as in prolonged post hepatic jaundice.

2- Severe impairment of liver function, whether acute or chronic (liver cirrhosis, acute fulminant hepatitis).

THANKS