

Chronic (non-overt) DIC in Patients with breast cancer

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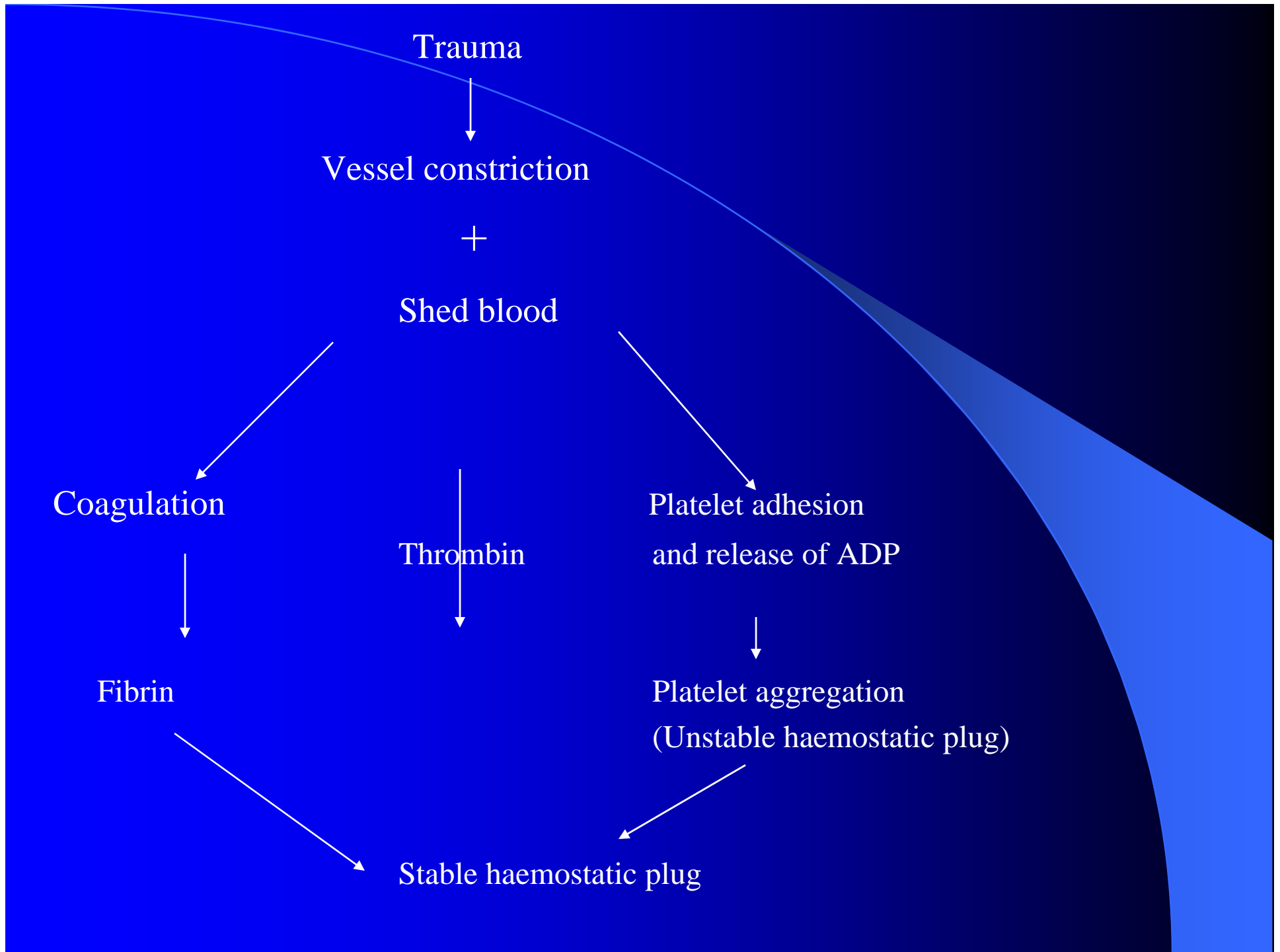
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Normal Haemotasis.

- The Haemostatic system has five major components,
blood vessels , Platelets, coagulation factors,coagulation inhibitors and fibrinolytic elements.

Function

- The functions of the normal haemostatic process are to prevent blood loss from intact vessels , to arrest bleeding from injured vessels and to keep vessels patent for continuous blood flow.
- A simplified scheme of normal haemostasis is shown here.



Coagulation Cascade.

- The main function of the coagulation system is in the event of injury, to produce thrombin which causes
 1. Activation of platelets in haemostasis
 2. Forms a stable fibrin network from circulating fibrinogen
 3. Stimulates coagulation inactivating mechanisms, thus limiting the process to the vicinity of the injury.

Coagulation Pathways

1. Extrinsic Pathway
2. Intrinsic Pathway
3. Common pathway .

Coagulation Components

1. Coagulation Protein
2. Inhibitors of coagulation
3. Fibrinolytic system

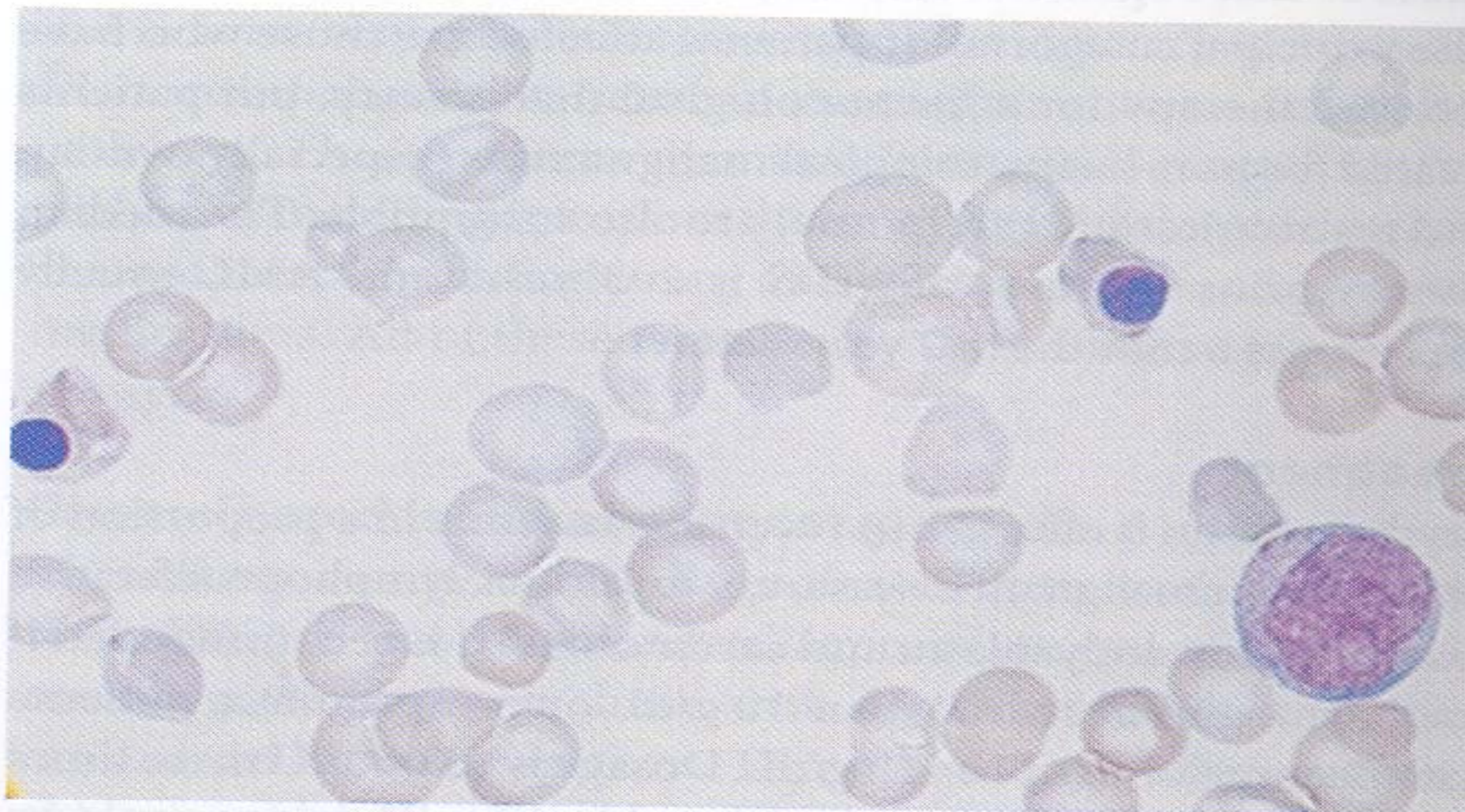


Figure 59.1 Nucleated red cells and an immature myeloid precursor in the peripheral blood film of a patient with a leucoerythroblastic anaemia.

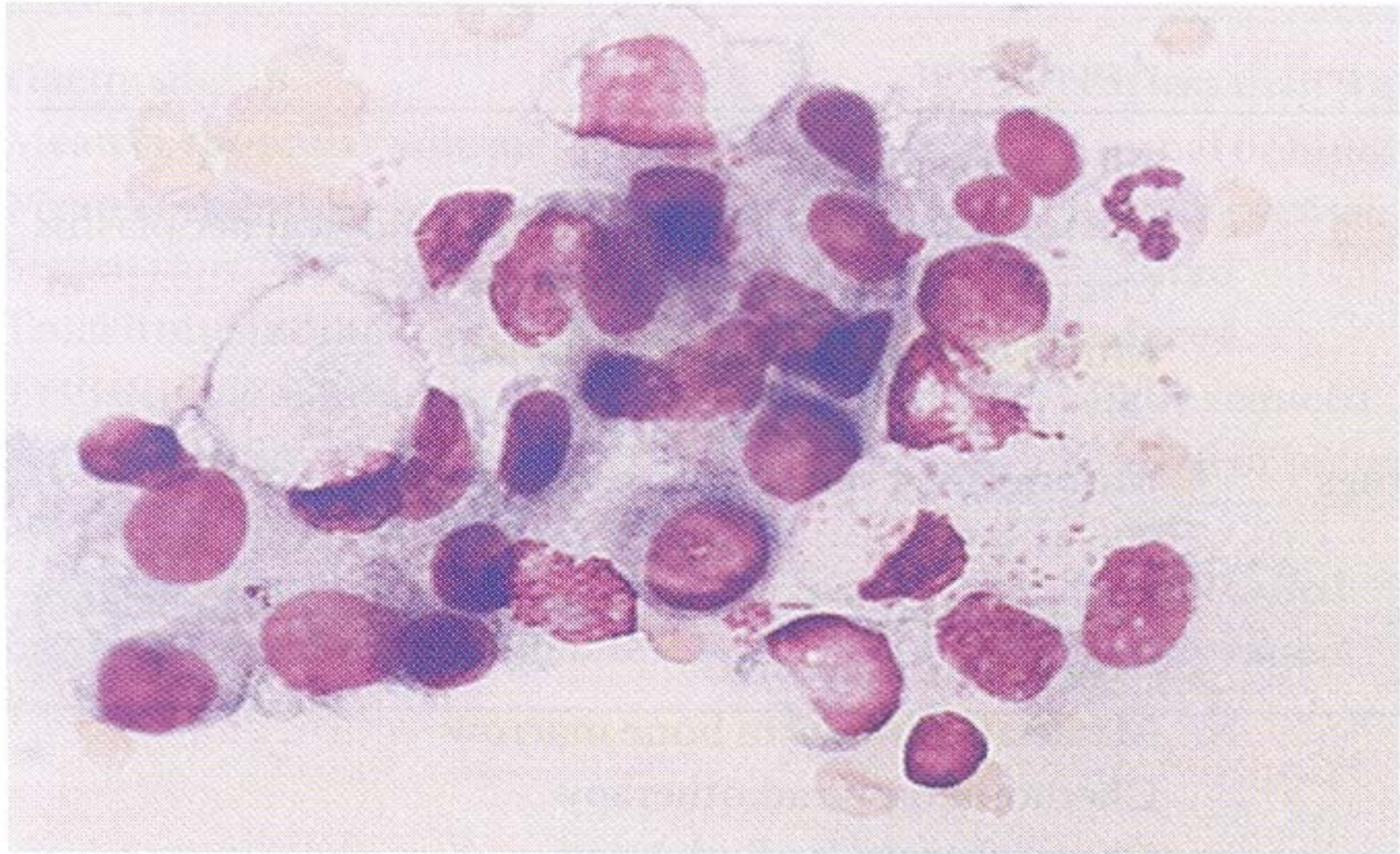


Figure 59.2 Bone marrow aspirate showing infiltration by metastatic breast carcinoma.

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

- **Chronic or compensated DIC (Non Overt)**
- **Acute or uncompensated DIC (Overt)**

CONDITIONS ASSOCIATED WITH DIC

Malignancies

- **Acute DIC:** AML-M3., acute myelomonocytic or monocytic, leukemia, disseminated prostatic carcinoma.
- **Chronic DIC.** Lung, breast, gastrointestinal malignancy.

SURGICAL OPERATIONS

- Acute DIC.
- Heart and Lungs surgery

INFECTIONS.

- **Acute DIC.** Bacteria and their toxins, fungi, viruses, rickettsiae.
- **Chronic DIC.** Any chronic infection (eg tuberculosis, abscesses, osteomyelitis)
- **Noninfectious inflammatory disease.**
- **Inflammatory bowel disease, Crohn's disease and similar disorders..**

OBSTETRICAL COMPLICATIONS

- **Acute DIC** Abruptio placentae, abortions (especially therapeutic abortions)
Aminotic fluid embolism, hemorrhagic shock
- **CHRONIC DIC**: Dead fetus syndrome.

VASCULAR DISEASE

- Acute DIC Brain infarction or hemorrhage
- Chronic DIC. Aortic aneurysm, giant hemangioma

VENOMS, Trauma & OTHERS

- VENOMS

Acute DIC: Snake, spider (rare)

- Trauma

- Acute DIC : Massive tissue destruction, brain damage.

- OTHERS

Acute DIC: Heparin-induced thrombocytopenia with thrombosis (HITT), Purpura fulminans in newborns (Homozygous protein C deficiency)

Heamolytic transfussion reaction.

Pulmonary embolism

Hypersensitiviity reactions

Heat stroke.

Pathogenesis of DIC

- DIC occurs when monocytes and endothelial cells are activated or injured by toxic substances elaborated in the course of certain diseases. The response of monocytes and endothelial cells to injury is to generate tissue factor on the cell surface, activating the coagulation cascade.
- In acute DIC an explosive generation of thrombin depletes clotting factors and platelets and activates the fibrinolytic system.

- Bleeding into the subcutaneous tissues, skin and mucous membrane occurs along with occlusion of blood vessels caused by fibrin in the microcirculation.
- In chronic DIC, the process is the same, but it is less explosive. Usually there is time for compensatory responses to take place which diminish the likelihood of bleeding but gives rise to a **hyper coagulation state leading to thrombosis**.

PATHOGENESIS OF DIC

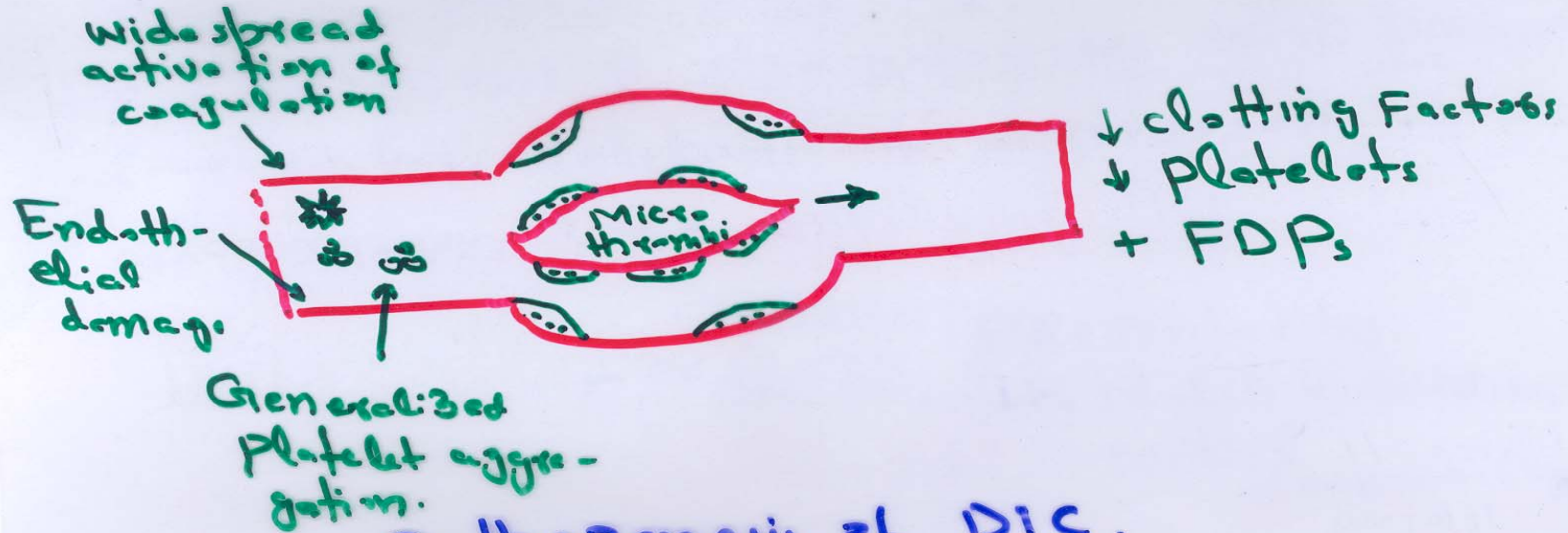
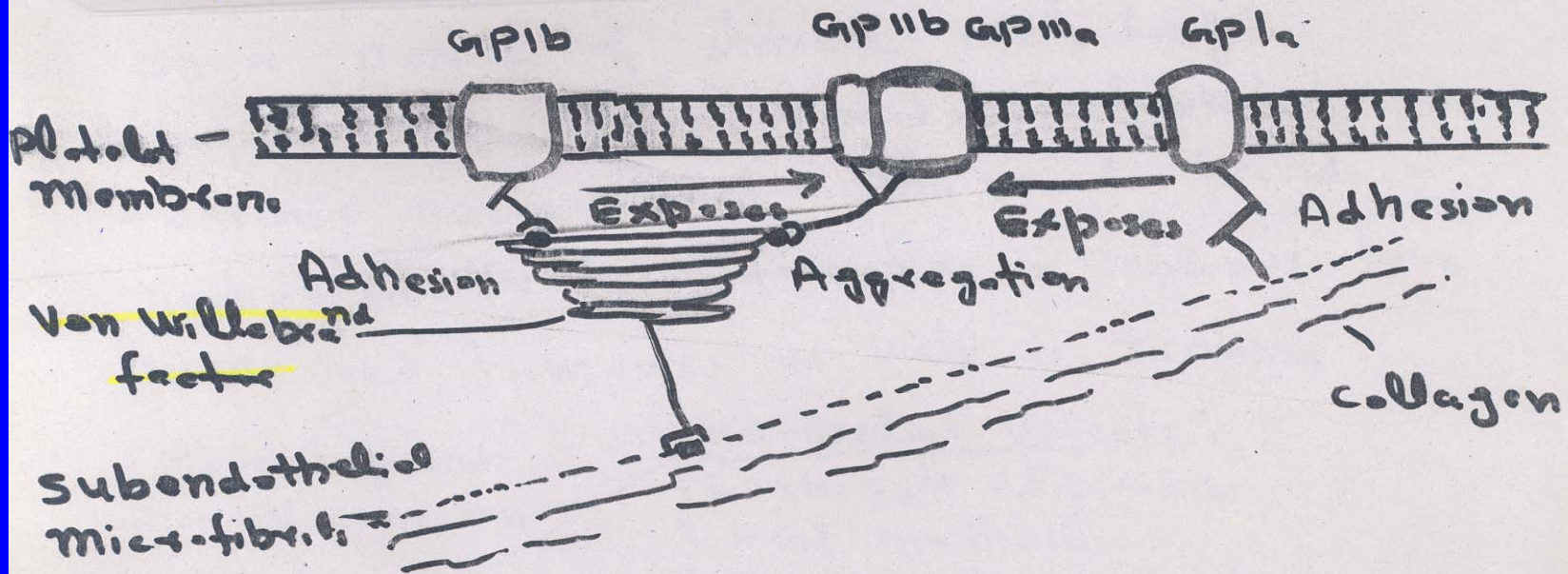


Fig. 1.7 Pathogenesis of DIC.



Clinical Features and Diagnosis of chronic DIC

- ● Signs of DVT or Arterial thrombosis or embolism
- ● Superficial venous thrombosis
- ● Multiple thrombotic sites.
- ● Serial thrombotic episodes.

Laboratory diagnosis.

- Normal, increased or decreased PT,APTT,TT
- High,normal or low fibrinogen level.
- High,normal or low platelet counts.
- Increased level of FDPs and D-dimers.

MANAGEMENT OF DIC.

- Treat the underlying disease
- Avoid delay.
- Treat vigorously e.g shock,sepsis
- Manage the DIC (Acute DIC).

With bleeding

- Blood components as needed.
- Fresh frozen plasma
- Cryoprecipitate.
- Platelet transfusion

WITH ISCHEMIA

- Anticoagulant after bleeding risk is corrected with blood products

CRONIC DIC.

WITHOUT THROMBOEMBOLISM

- No specific therapy needed but prophylactic drugs (e.g. low dose heparin, low-molecular weight heparin) may be used for patients at high risk of thrombosis.

WITH THROMBOEMBOLISM

Heparin or low molecular weight heparin, trial of warfarin sodium (Coumedin)(if warfarin is unsuccessful long term use of low-molecular weight heparin may be helpful.

Study

- Selection of the subjects:

Total 75 subjects.

Group I ---- 50 Breast Cancer patients

Group II ---- 25 Normal control

- Study Universe

Two Teaching Hospitals of Peshawar.

- Duration of study: one year

Laboratory Investigations

- **General**

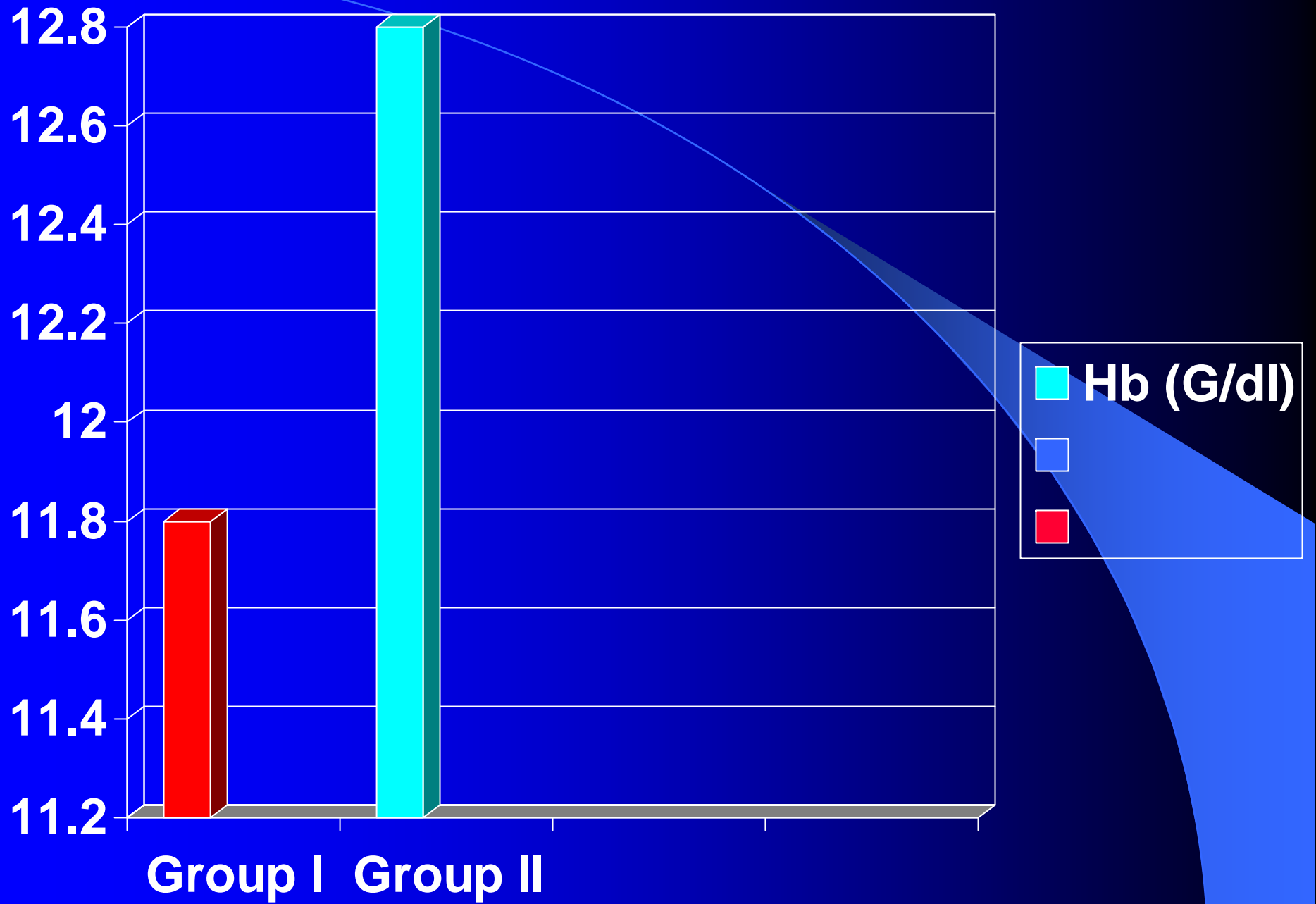
Hemoglobin ,TLC, DLC and Platelet counts

- **Specific**

- Prothrombin Time
- Activated Partial Thromboplastin Time
- Thrombin Time (Fibrinogen Assay)
- Fibrinogen Degradation Products (FDPs)
- D-dimer detection

Hemoglobin Level in Control (II) and Cancer Patients (I)

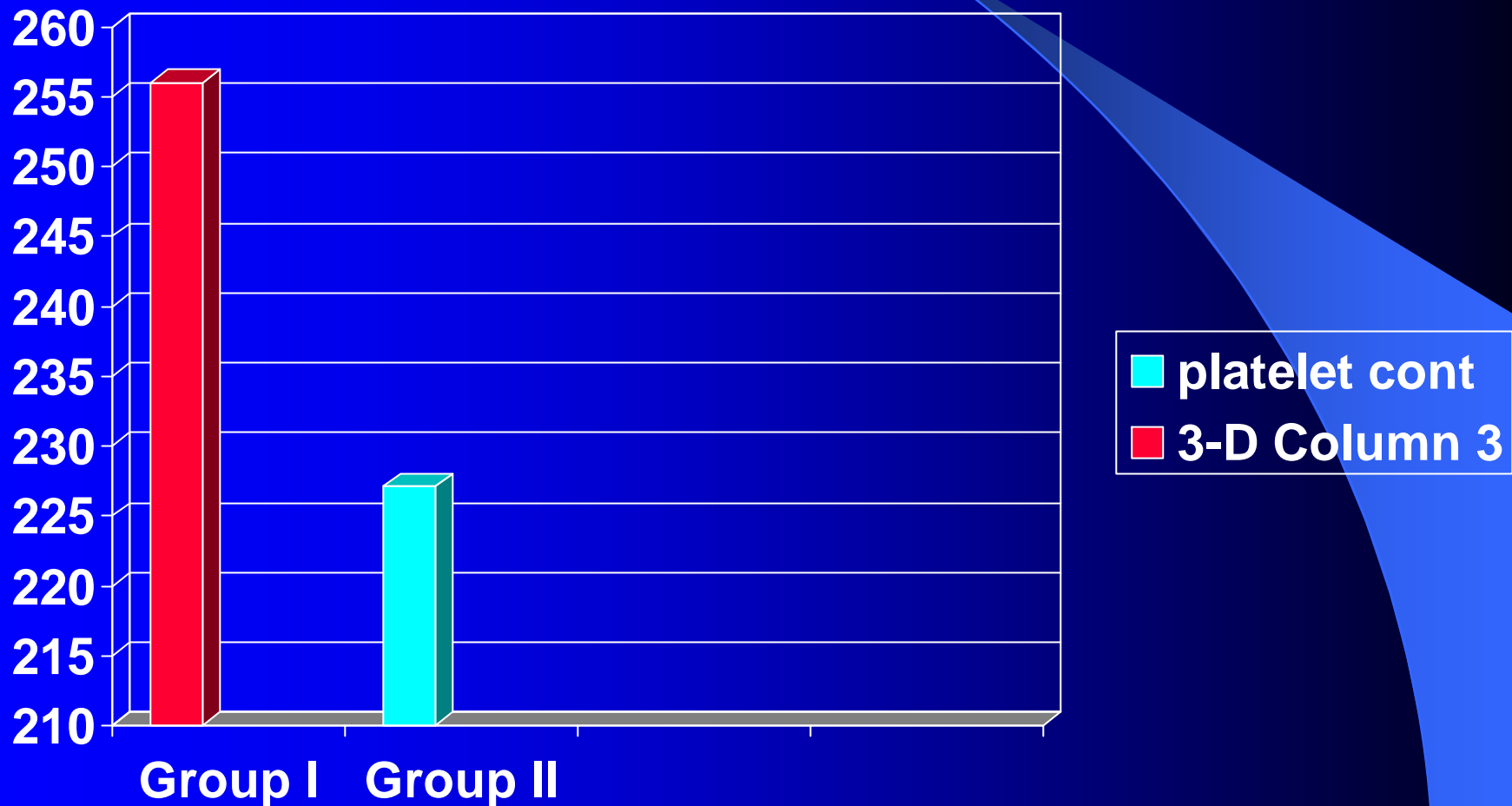
Hb (G/dl)	Group II (Control)	Group I (Cancer Patients)
Mean \pm SD	12.8 \pm 0.99	10.8 \pm 1.7
Range	11.5 – 14.3	5.2 – 11.8
TOTAL SUBJECTS	25	50



Platelets count in Control and Cancer Patients.

Platelet count ($10^9 / L$)	Group II (Control)	Group I (Cancer Patient)
Mean \pm SD	227.1 \pm 49.9	256.0 \pm 91.6
Range	154-329	138 -529
TOTAL SUBJECTS	25	50

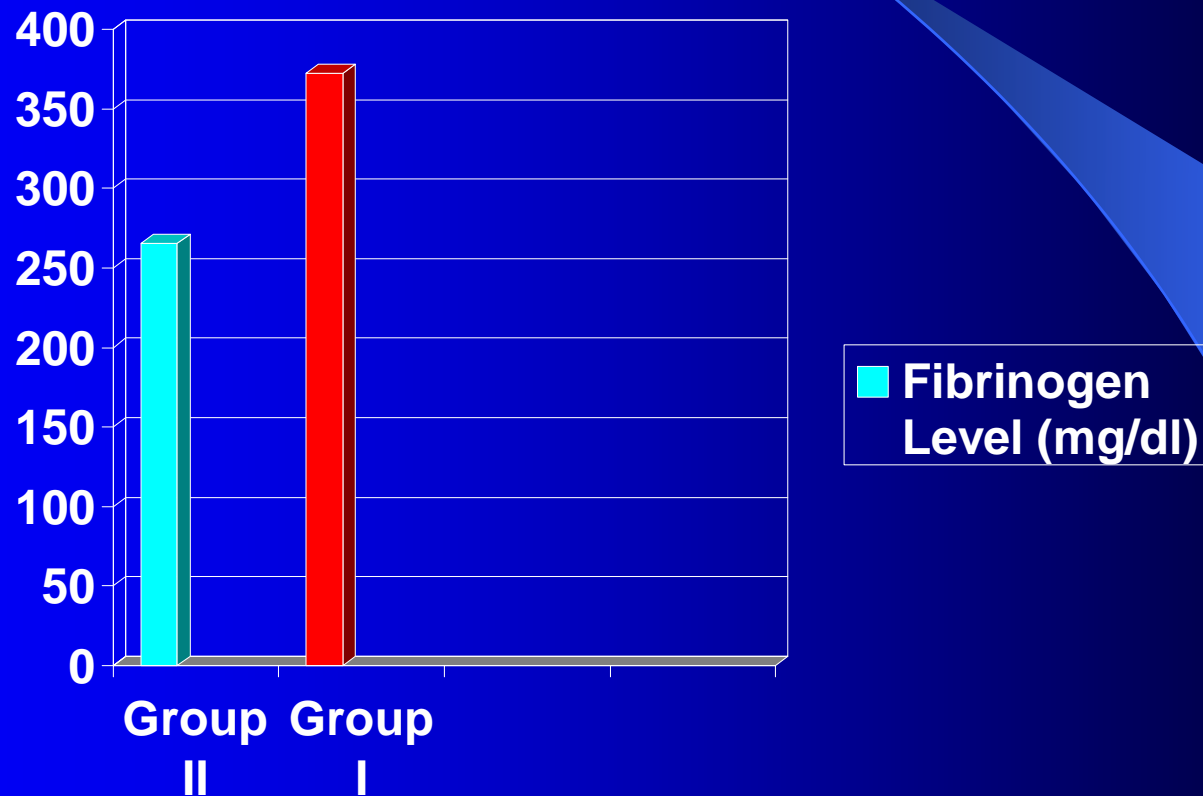
Platelets count in Control and Cancer Patients.



Fibrinogen Level in Control and Cancer Patients

FIBRINOGEN (mg/dl)	Group II (Control)	Group I (Cancer Patient)
Mean \pm SD	265.6 \pm 44.9	372.4 \pm 116.03
Range	210 – 350	140 - 520
TOTAL SUBJECTS	25	50

Fibrinogen Level in Control and Cancer Patients



PT in Control Group (II) and Breast Cancer Patients).

PT (Sec)	Group II (Control)	Group I (Subjects with Breast Cancer)
Mean \pm SD	12.8 \pm 1.27	12.2 \pm 2.17
Range	11-15	12-16
Total Subjects	25	50

The results are expressed as mean \pm SD Value.
Statistical Analysis

II Vs I

P>0.05

(NS)

APTT in Control group (II) and Subjects with Breast Cancer (I)

The results are expressed as mean \pm SD Value.

APTT (Sec)	Group II (Control)	Group I (Subjects with Breast Cancer)
Mean \pm SD	25.2 \pm 2.5	25.9 \pm 2.3
Range	21-27	21-32
Total Subjects	25	50

Statistical Analysis

II Vs I

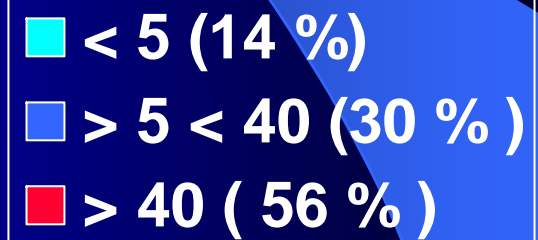
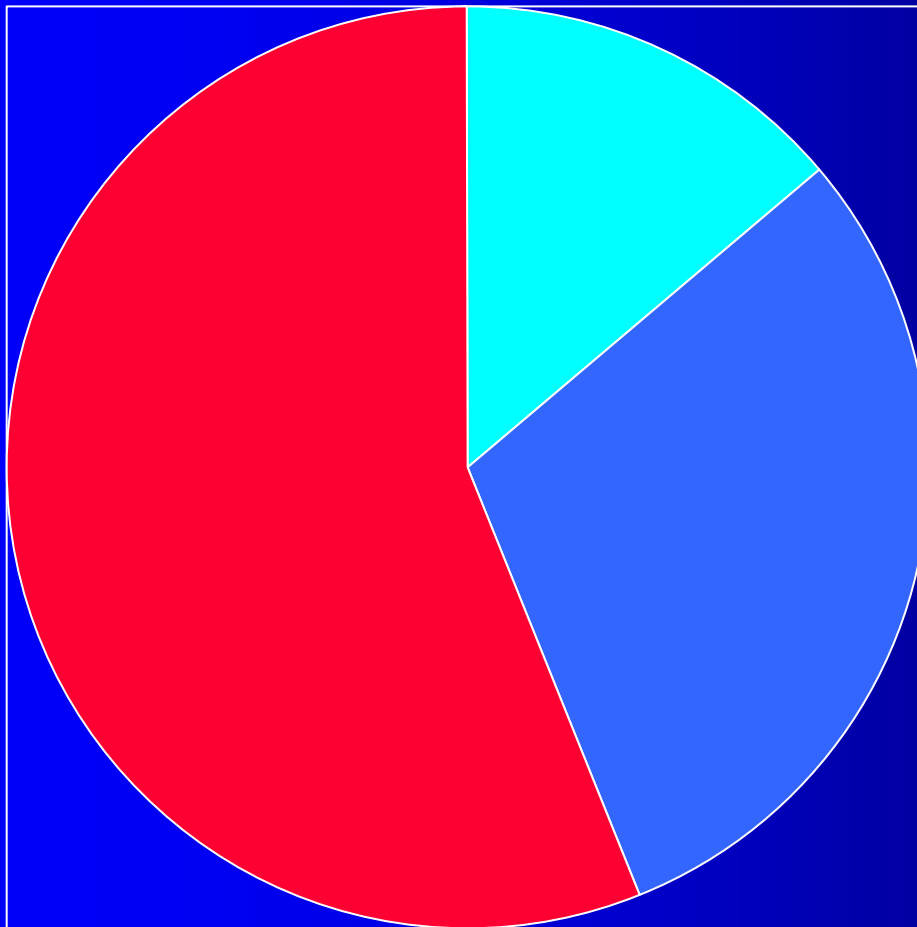
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FDPs in Control and Cancer Patients

FDPs (ug/ml)	Group II (Control)	Group I (Cancer Patient)
< 5	25	07 (14 %)
> 5 < 40	--	15 (30 %)
> 40	--	28 (56 %)
TOTAL SUBJECTS	25	50

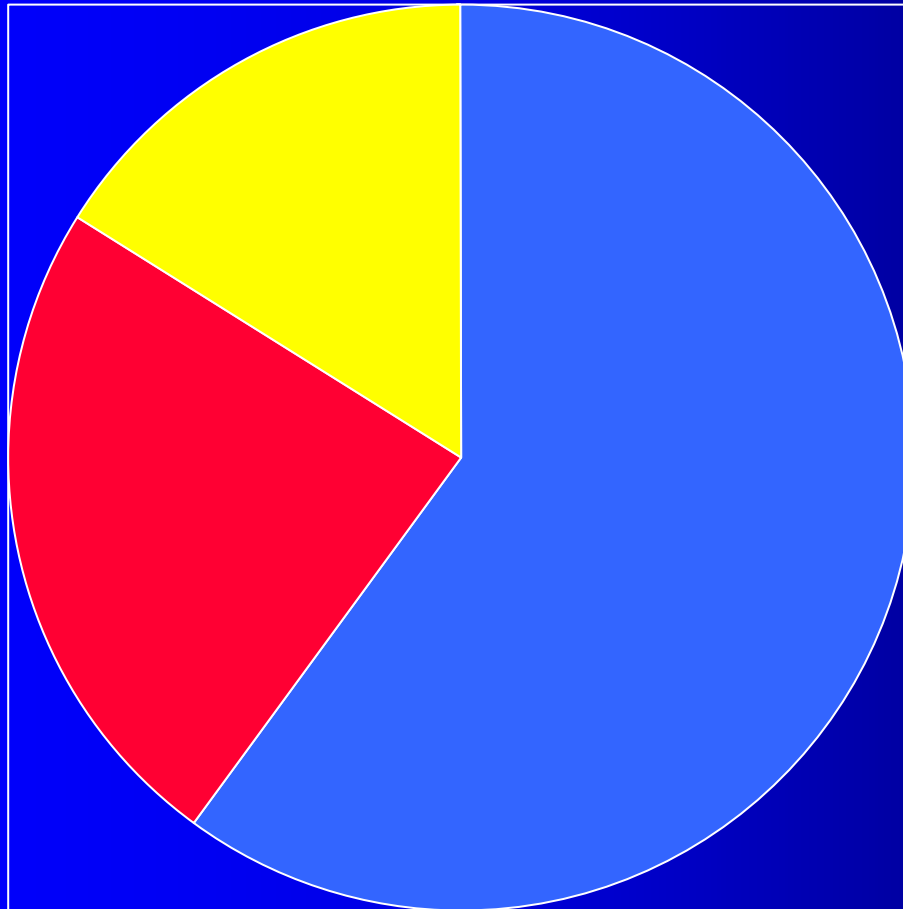
FDPs in Cancer Patients



D-dimers in Control and Cancer Patients

D-dimers (ng/ml)	Group II (Control)	Group I (Cancer Patient)
< 250	25	---
250 – 500	--	30 (60 %)
500 – 1000	--	12 (24 %)
1000 – 2000	--	08 (16 %)
TOTAL SUBJECTS	25	50

D-dimers in Control and Cancer Patients



FIBRINOGENOLYSIS

FIBRINOLYSIS

● Platelet Count. Normal.

Decreased

● FDPs. +++

++

● D-Dimers. --

++

● Treatment.

● Anti-fibrinolytic Agents.
(e.g EACA, Tranexamic acid)

Replacement Therapy

Fresh whole blood

Heparin ±

* EACA: Epsilon Amino Caproic Acid.

Conclusion

- This study reveals that patients with Breast Cancer are associated with
- **Chronic or non-overt DIC** state with normal coagulation profile , Increased levels of FDPs , D-dimers, Fibrinogen and Platelet count as compared to control.
- **Hypercoagulable state** in Breast Cancer makes cancer perhaps the best example of **acquired Thrombophilia**.
- **D-Dimer** is more sensitive marker for detecting chronic DIC in patients having breast cancer as compared to FDP's

THANK YOU

