Paediatric Haem/Onc

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Learning Objectives

Haematology

- Age related changes in haemoglobin level: know approximate values in infants and young children.
- Iron deficiency anaemia: epidemiology, at risk groups, consequences to health (including neurodevelopment).
- Haemophilia: mode of inheritance, diagnosis and management.

Oncology

- Acute leukaemia: classification, presentation, diagnosis, management and prognosis.
- Wilms' tumour: presentation, management and prognosis.
- Neuroblastoma: presentation, management and prognosis.

Age related changes in Hb levels

- High at birth (14-20 g/dL)
- Falls to 9-13 g/dL at 2-3mo in term infants
- HbF decline postnatally to 2% by 1y
- >10 past infancy
- >11 in 2nd decade

Iron deficiency anaemia

- Microcytic, hypochromic anaemia.

ΔΔ

- β-thalassemia trait
- α-thalassemia trait
- anaemia of chronic disease.

Epidemiology

- Commonest cause of anaemia.
- Usually inadequate dietary intake rather than loss of iron.

Diagnosis of iron deficiency anaemia

- FBC
- blood film
- iron status
- Take detailed dietary Hx.

At risk groups for dietary iron deficiency

- Preterm infants
- Term infants: delayed mixed feeding or early introduction of unmodified cow's milk.
- Children
  - Poor diet associated with low socio-economic status or strict vegetarian diet.
  - Malabsorption
  - Blood loss: menstruation, hookworms, repeated venesection in babies, Meckel's diverticulum.

Consequences to health

MILD	May be asymptomatic
MODERATE	• irritability, lethargy, fatigue, anorexia • O/E pallor of skin and mucous membranes
SEVERE	• CCF • may need transfusion • in infancy/ early childhood is associated with developmental delay and poor growth (reversible with treatment)

Management

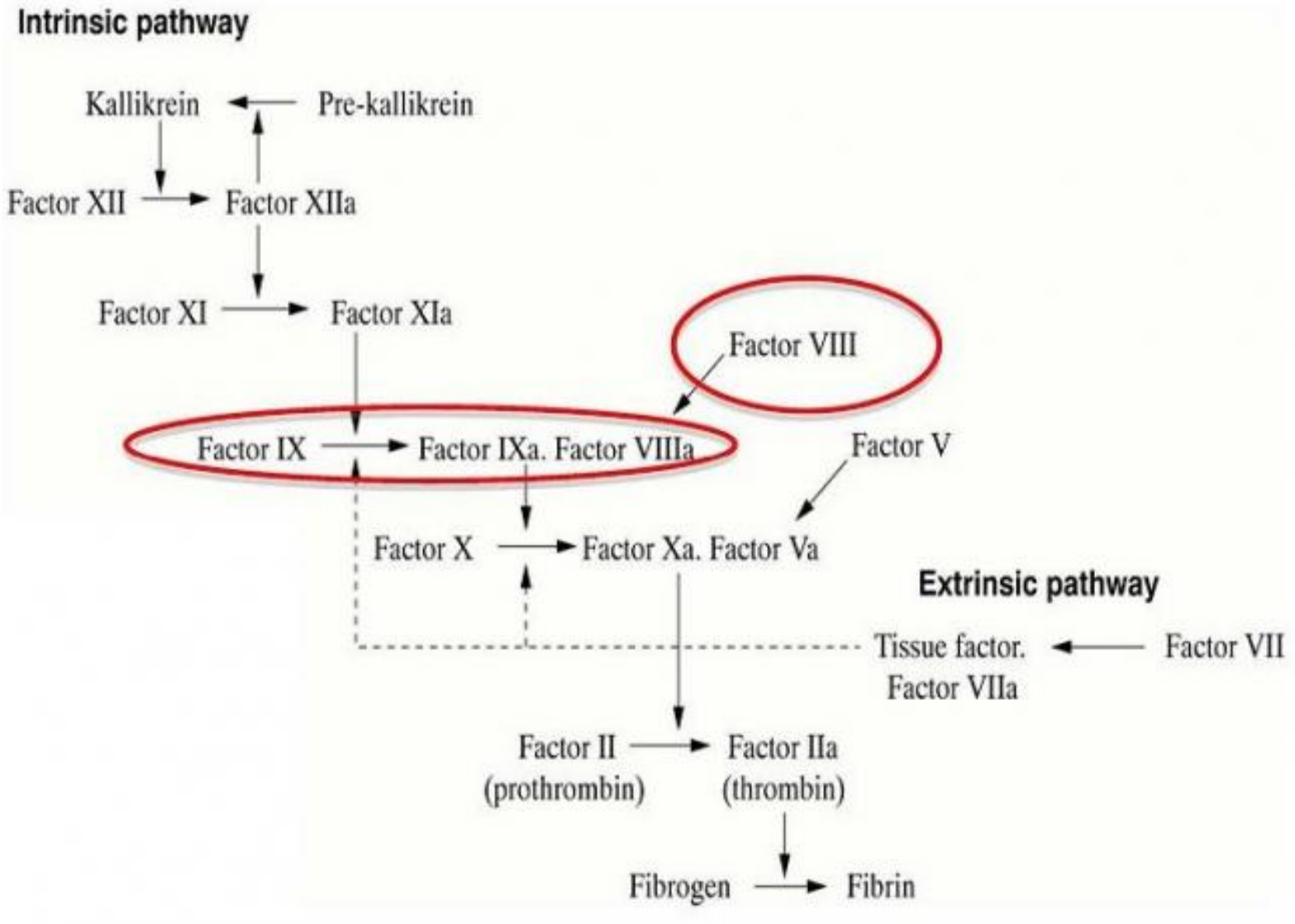
- Dietary advice, oral iron.

Genetic Disorders (Haem)

- **Haemophilia A (factor VIII deficiency)**
  - X-linked recessive disorder (affects boys)
  - 1/3rd new mutation

Diagnosis

- Prolonged APTT due to defect in intrinsic pathway.
- Factor VIII assay confirms diagnosis


Intrinsic pathway
Kallikrein
Pre-kallikrein
Factor XII
Factor XIIa
Factor XI
Factor XIa
Factor VIII
Factor IX
Factor IXa. Factor VIIIa
Factor V
Factor X
Factor Xa. Factor Va
Extrinsic pathway
Tissue factor.
Factor VIIa
Factor VII
Factor II
(prothrombin)
Factor IIa
(thrombin)
Fibrogen
Fibrin

Clinical Features

- Spontaneous, traumatic bleeding
  - subcutaneous
  - intramuscular
  - intra-articular

History

- Early bruising, abnormal bleeding from time begin to walk/fall over.

Management

- IV infusion of factor VIII concentrate
  - Treats and prevents bleeding
  - Prompt therapy reduces chronic arthropathy
  - Traumatic contact sports are forbidden.

- Mild haemophilia: desmopressin to release factor VIII from tissue stores.

Haemophilia B aka Christmas disease

- Factor IX deficiency
- Clinically similar to haemophilia A, but rarer.
- Prolonged APTT and reduced factor IX activity.
- *Treatment= prothrombin complex concentrate*

vWF deficiency

- AD inheritance: Affects girls and boys
- Combination of factor VIII deficiency and platelet dysfunction, but usually mild.

Acute Leukaemia

Classification

- Acute lymphocytic leukaemia (ALL)
  - Common subtype (75%) i.e. non-T, non-B cell.
    - Peak 3-6years
  - T-cell subtype (15%)
    - tendency for older children.
- Acute myeloid leukaemia (AML)
  - 80% associated with chromosomal abnormalities.

Presentation

- Often insidious, sometimes very rapid
  - Malaise
  - Pallor
  - Abnormal brusing
  - Lymphadenopathy
  - Bone pain
  - Hepatosplenomegaly
  - Infections

Diagnosis

- FBC: Low Hb and thrombocytopenia
- Blood film: Evidence of blast cells
- Bone marrow examination
  - essential to confirm & identify cytogenetic characteristics.

Management

- Initial treatment
  - blood transfusion
  - treat infection
  - protect kidneys against rapid cell lysis about to occur (with allopurinol)

1. Remission induction	• intensive regimen: 3-5 drugs to reduce tumour load and restore bone marrow function.
2. Intensification therapy	• blocks of chemo to consolidate remission.
3. Early CNS directed therapy	• intrathecal chemo to prevent CNS relapse
4. Maintenance therapy	• modest intensity over long period(2y for girls, 3y for boys) • Plus Co-trimoxazole to prevent Pnumocystis carnii
5. Treatment of relapse	• Relapse has poor prognosis. • High-dose chemo, total body irradiation and BM transplant may be considered

Prognosis

- ALL
  - 65% cured:
  - 75% remission
  - 75% survival beyond 5 years.

Prognostic factor	Good	Bad
Age (y)	2-9	<1
Sex	female	male
WCC (tumour load)	<50	>50
Tumour type	Common (non-T, non-B)	T or B cell types

- AML
  - Worse prognosis.

Wilms' Tumour

- From embryological renal tissue
- Susceptibility gene (WT1)

Presentation

- 80% < 5y, Rare >10 y.
- Abdominal pain (haemorrhage into tumour)
- Haematuria
- Hypertension: 25%. Compression or renin production.
- Usually unilateral, 5% bilateral

Diagnosis

- CT or USS (intrinsic renal mass) & biopsy.
- Search for distant metastases (lung, liver)

Management

- Surgical resection of primary
- Chemotherapy for all
- Radiotherapy for advanced disease

Prognosis

- 80% cure if no metastases
- 60% with metastases
- If relapse then poor prognosis

Neuroblastoma

- Malignant tumour arising SNS
- Commonly develops in adrenal gland or sympathetic chains

Presentation

- Abdominal mass (most common presentation; firm, non-tender; may not be primary)
- Systemic signs (pallor, weight loss, bone pain)
- Hepatomegaly or LN enlargement
- Eye metastasis = unilateral proptosis
- “Dancing eye”
- Watery diarrhoea
- Mediastinal mass on CXR

Diagnosis

- Raised urinary catecholamines. Used to monitor therapy response
- Confirmatory biopsy
- MIBG: scan with a radiolabelled tumour-specific marker
- Bone scan for mets

Management

- Surgical resection, chemotherapy, irradiation

Prognosis	Good	Bad
Age	<2y (In v. young may spontaneously regress)	>2y
Stage	Localised primary	Metastatic disease (30% survival)
N-myc status	Single copy	amplification

Any questions?