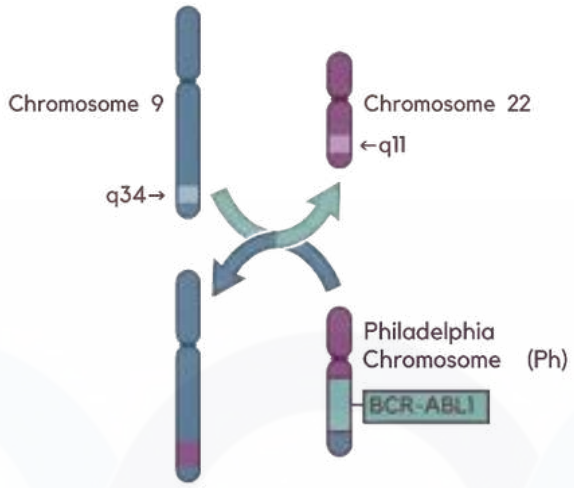
TUTORIALS

PG Residency
Hematology

Smart Notes. Better Scores.

Chronic Myeloid Leukemia (CML): Overview & Genetics

Module 1: Pathophysiology and Epidemiology



Constitutively active tyrosine kinase uncontrolled proliferation.

Definition

Clonal hematopoietic stem cell disorder characterized by uncontrolled proliferation.

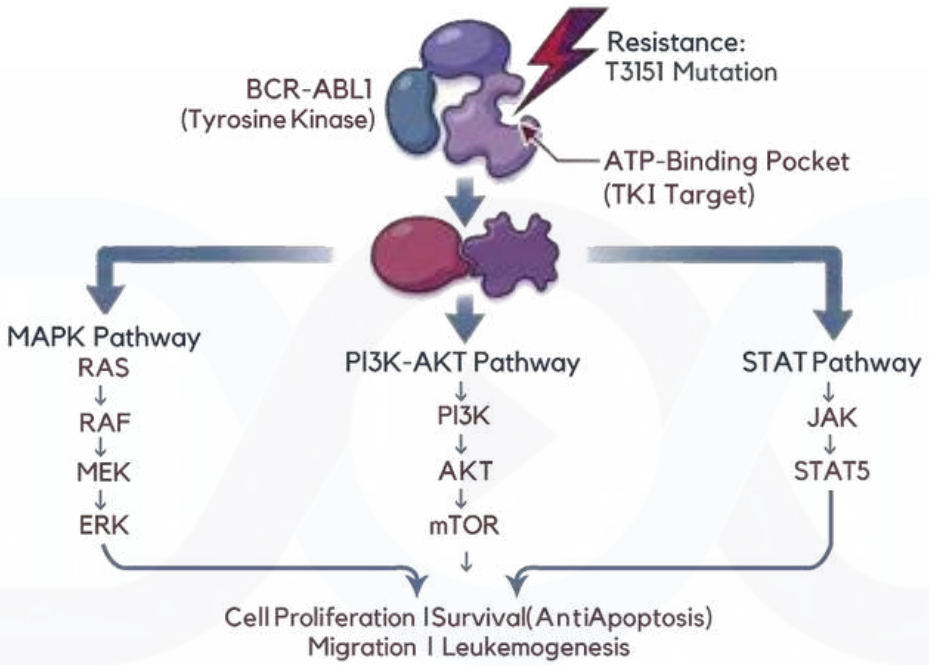
Epidemiology Sidebar
Incidence: 1.6 cases/ 100,000
Median Age: 55-65 years
Gender Ratio: Male 1.6: 1 Female
Pediatric: Rare (<3% of cases)

Pathogenesis

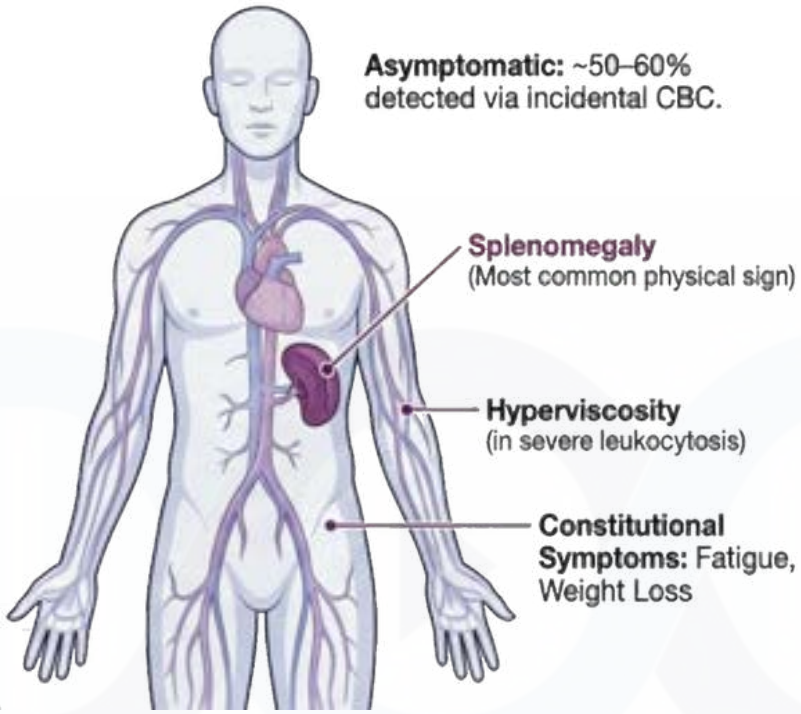
- **Driver:** t(9;22)(q34;q11)reciprocaltranslocation.
- **Mechanism:** BCR-ABL 1 fusion protein acts as an oncoprotein.

BCR-ABL1 Fusion Variants & Signaling

Fusion Protein (Size)	Breakpoint	Disease Association
Minor BCR (P190)	e1a2	**Ph+ ALL (Acute Lymphoblastic Leukemia)**
Major BCR (P210)	e13a2 / e14a2	**Classical CML**
Micro BCR (P230)	Telomeric breaks	**Indolent CML (Rare)**



Clinical Presentation & Hematological Findings



MOCK LAB REPORT

CBC PANEL

- WBC Count: >100,000/µL [HIGH] ↑
- Platelets: Elevated (Variable) [HIGH] ↑
- Basophils: Increased (Accelerated Phase if >20%)
- Hemoglobin: Variable Anemia

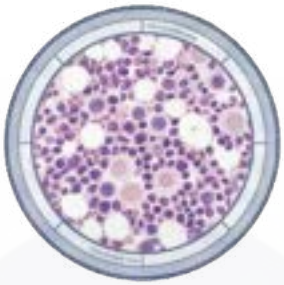
CHEMISTRY /SPECIAL

- Leukocyte Alkaline Phosphatase
- (LAP): **LOW** ↓
- Note: Differentiates from Leukemoid Rxn.
- Serum 812: ELEVATED

Diagnostic Investigations: Marrow & Genetics

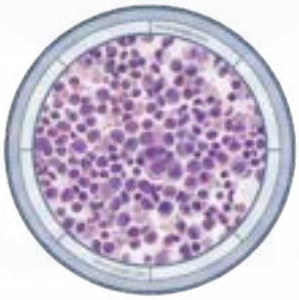
Normal Marrow

- Moderate cellularity, mix of hematopcilotic cells, fat spaces, a balanced 3:1 myeloid: erythroid ratio with fewer large- erythroid precursors erythroid precursors and numerous denser myeloid cells.



CML Marrow

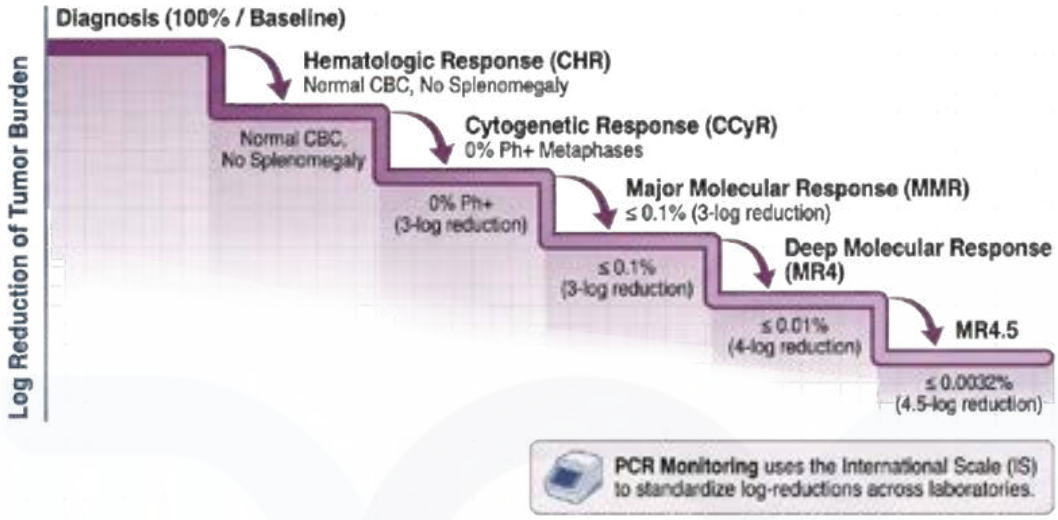
- Hypercellularity, with minimal fat spaces, vast expansion of myeloid cells at all stages of development, including many immature forms. Myeloid: Erythroid ratio: 20:1, very few erythroid islands.



Blast Criteria (Disease Phase by Blast Percentage)

Method	Scope	Clinical utility
Karyotyping	Chromosomalstructure	Detects t(9;22) & clonalevolution(additional abnormalities).
FISH	Interphase nuclei	Quantifies % of BCR-ABL 1 positive cells.
RT-PCR	mRNA Transcripts	Most sensitive; Quantitative monitoring (MMR/MR4).

Response Assessment & Molecular Milestones

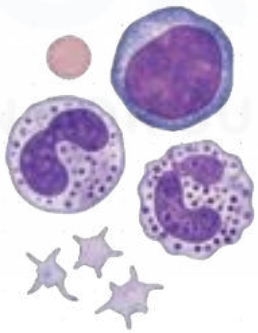


Advanced Phases & Prognostic Scoring

Phase Criteria

AcceleratedPhase (WHO 2016)

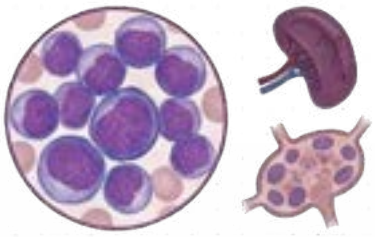
- Blasts 10-19°/o in blood or marrow.
- Basophils ≥20o/o.
- Persistent Thrombocytopenia (<100k) or Thrombocytosis (>1000k).
- Clonal Evolution (new cytogenetic abnormalities).



***[Note: Category removed in WHO 2022]**

Blast Crisis

- Blasts ≥20°/o in blood or marrow.
- Extramedullary blast proliferation.



Risk Stratification

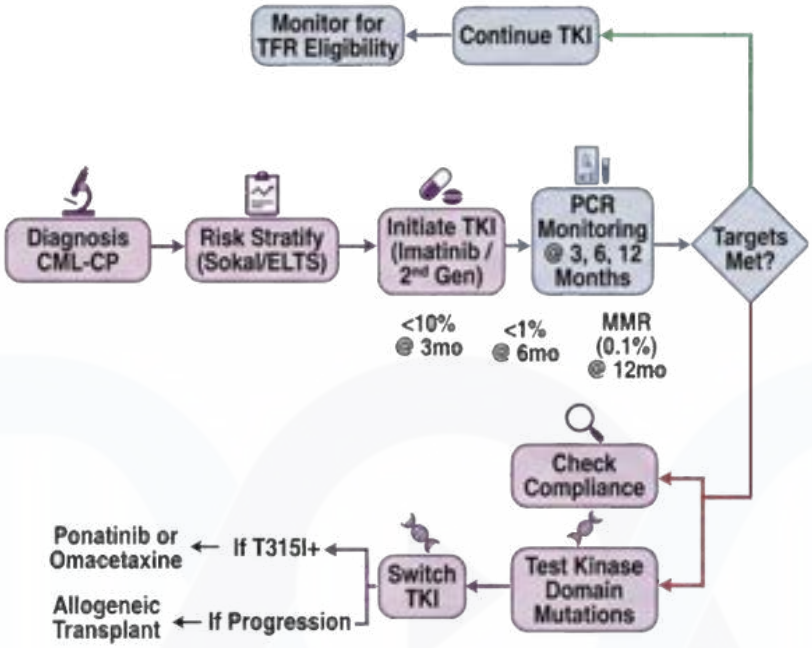
Score Name	Parameters Included
Sokal	Age, Spleen size, Platelets,Blasts
Hasford (Euro)	Sokal parameters+ Eosinophils
ELTS (EUTOS Long-Term)	Age, Spleen size, Blasts, Platelets

Scores are used to guide TKI selection and predict progression risk.

Tyrosine Kinase Inhibitors (TKIs): Pharmacology

Generation	Drug Agent	Key Side Effects / Toxicity	T3151 Activity
1st Gen	Imatinib	Fluid retention, Muscle cramps, GI upset. (Well tolerated).	Ineffective (X)
2nd Gen	Nilotinib	⚠ Vascular events (PAOD, Coronary), Metabolic syndrome.	Ineffective (X)
2nd Gen	Dasatinib	⚠ Pleural Effusion, Pulmonary HTN.	Ineffective (X)
2nd Gen	Bosutinib	GI Toxicity (Diarrhea), Liver enzyme elevation.	Ineffective (X)
3rd Gen	Ponatinib	⚠ Arterial occlusive events (High Risk).	Effective (✔)
3rd Gen	Omacetaxine	Myelosuppression. (Protein synthesis inhibitor).	Effective (✔)

Management Algorithm: CML Chronic Phase

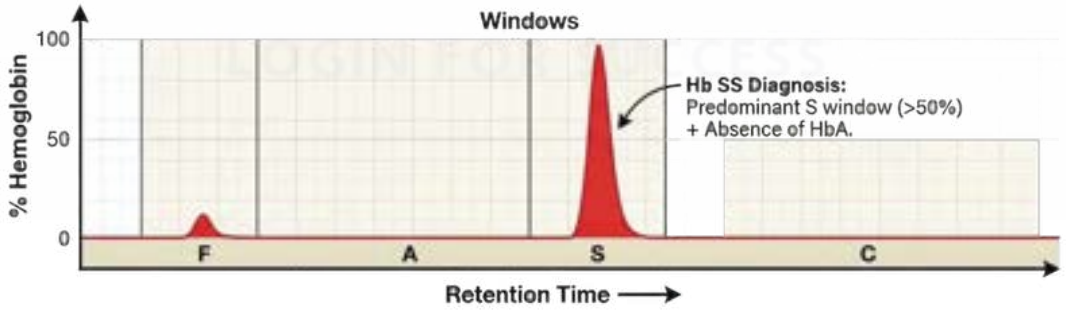


Treatment-Free Remission (TFR) Criteria

- Deep Remission (>MR4.5) sustained for ≥2 years.
- Protocol: Stop TKI with monthly PCR monitoring.
- Success Rate: ~50-60%.

Sickle Cell Anemia: Diagnosis via HPLC

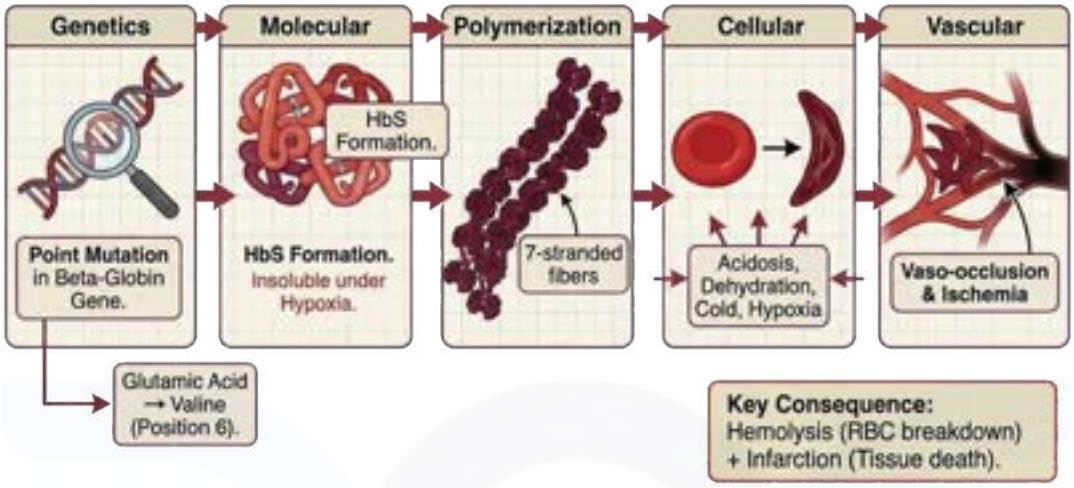
Module 2: HemoglobinElectrophoresis



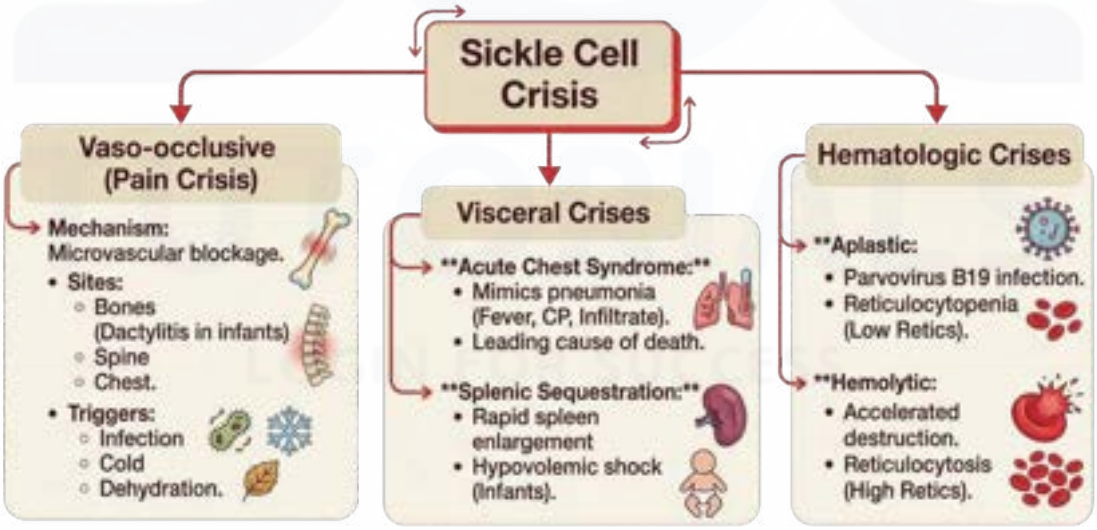
Separation based on globin chain weight and charge defect.

⚠ Clinical Note:
Transfusion Caveat: HPLC in recently transfused patients shows a mixed picture. Wait 3 months for washout or screen parents to distinguish Homozygote vs. Compound Heterozygote.

Pathophysiology: From Mutation to Vaso-occlusion

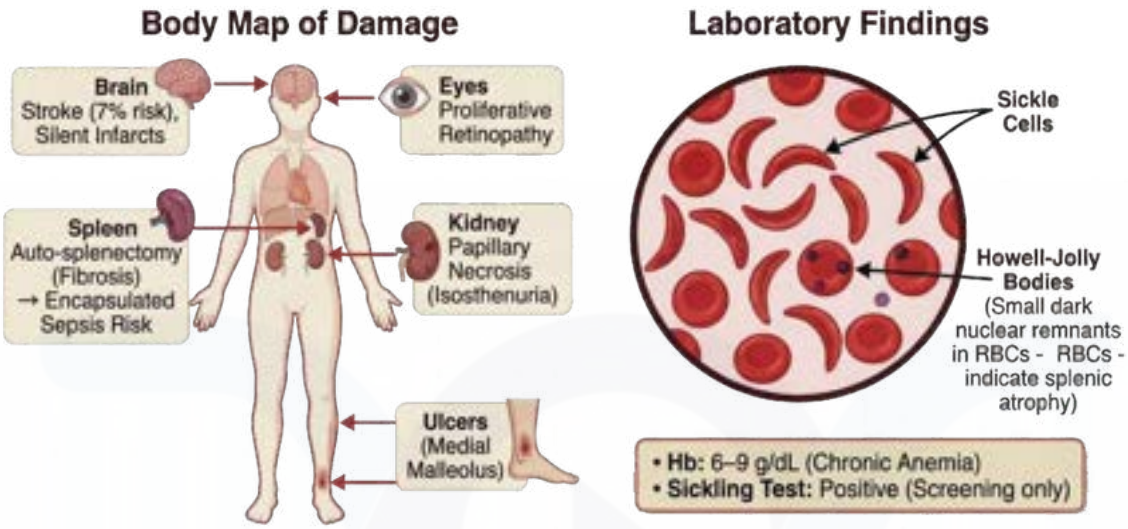


Clinical Crises in Hb SS

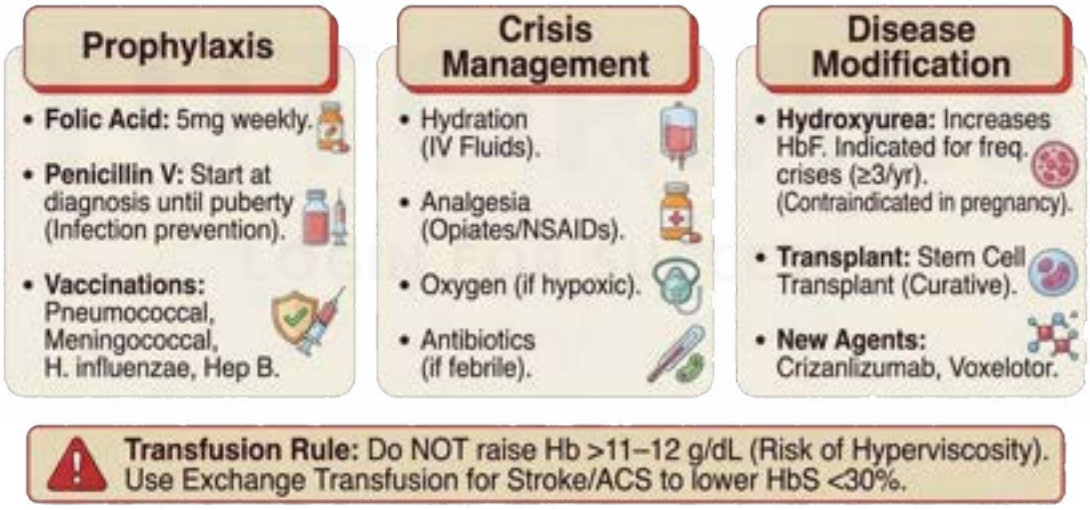


Chronic Complications & Laboratory Findings

Body Map of Damage



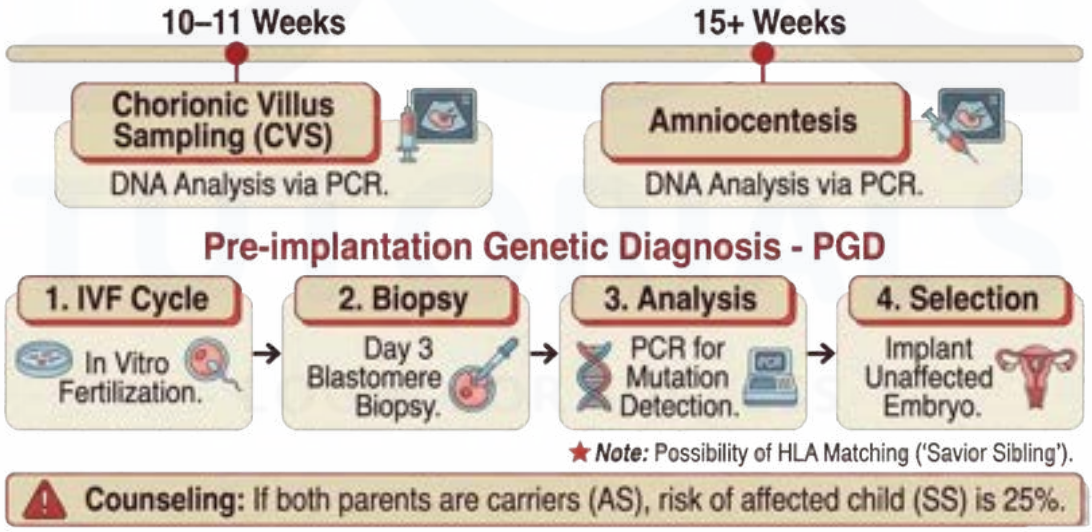
Principles of Management



Sickle Cell Variants & Differential

Genotype	Clinical Severity	Key Features/ Smear
HbAS (Trait)	Benign/ Asymptomatic	Protects against Malaria. Riskof Hematuria. Normal CBC.
Hb S-Beta Thal	Moderate to Severe	Resembles Hb SS but Low MCV + Splenomegaly (No auto-splenectomy).
HbSC Disease	Moderate (Better survival than SS)	Glu Lys mutation. Retinal issues, Thrombosis risk. Smear: Target Cells + Rhomboid Crystals.
HbE	Mild (Common in SE Asia)	Microcytic anemia.

Prenatal Diagnosis & Genetic Counseling



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