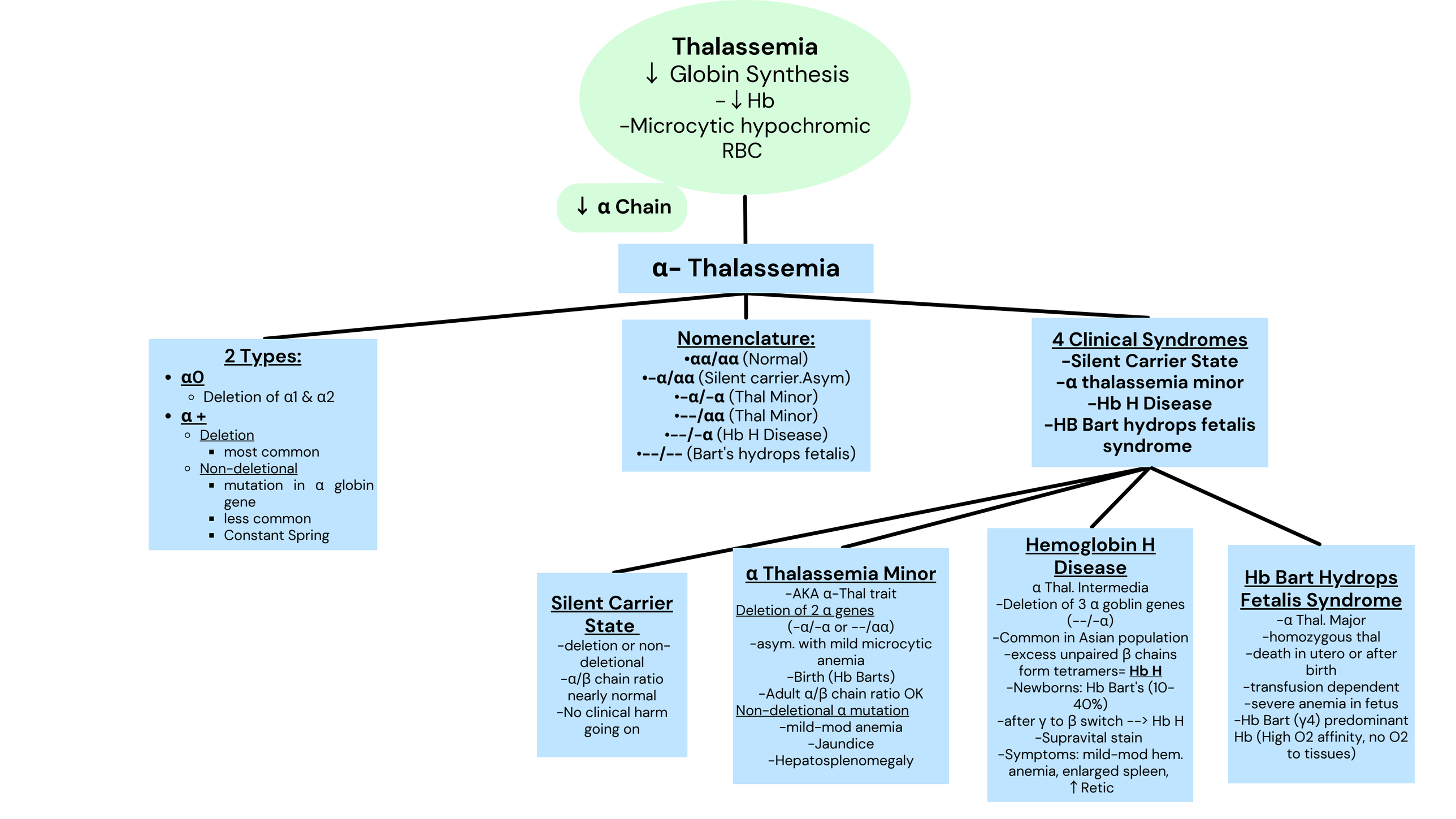
Thalassemia
↓ Globin Synthesis
- ↓ Hb
-Microcytic hypochromic RBC
↓ α Chain
α- Thalassemia
2 Types:
αO
Deletion of α1 & α2
α +
Deletion
most common
Non-deletional
mutation in α globin gene
less common
Constant Spring
Nomenclature:
•αα/αα (Normal)
•-α/αα (Silent carrier.Asym)
•-α/-α (Thal Minor)
•--/αα (Thal Minor)
•--/-α (Hb H Disease)
•--/-- (Bart's hydrops fetalis)
4 Clinical Syndromes
-Silent Carrier State
-α thalassemia minor
-Hb H Disease
-HB Bart hydrops fetalis syndrome
Silent Carrier State
-deletion or non-deletional
-α/β chain ratio nearly normal
-No clinical harm going on
α Thalassemia Minor
-AKA α-Thal trait
Deletion of 2 α genes
(-α/-α or --/αα)
-asym. with mild microcytic anemia
-Birth (Hb Barts)
-Adult α/β chain ratio OK
Non-deletional α mutation
-mild-mod anemia
-Jaundice
-Hepatosplenomegaly
Hemoglobin H Disease
α Thal. Intermedia
-Deletion of 3 α goblin genes (--/-α)
-Common in Asian population
-excess unpaired β chains form tetramers= Hb H
-Newborns: Hb Bart's (10-40%)
-after γ to β switch --> Hb H
-Supravital stain
-Symptoms: mild-mod hem. anemia, enlarged spleen, ↑ Retic
Hb Bart Hydrops Fetalis Syndrome
-α Thal. Major
-homozygous thal
-death in utero or after birth
-transfusion dependent
-severe anemia in fetus
-Hb Bart (γ4) predominant Hb (High O2 affinity, no O2 to tissues)

Thalassemia

↓ Globin Synthesis
- ↓ Hb
-Microcytic hypochromic RBC

↓ β Chain

β- Thalassemia

Types:
- **β0**: No β chain (Med. areas)
- **β+**: partial def. of β chains
- **βsilent**: silent carrier
- **δβ0**: mutations in δ or β genes in which no chains made
- **δβLepore**: Produce Hb Lepore.Fusion of the δ and β globin

Nomenclature:
- **β/β** (Normal)
- **βsilent/β** (Silent Carrier)
- **β+β or β0/β** (β Thal Minor)
- **β+/β+ or β+/β0 or β0/β0** (β Thal Major)
- **β Thal intermedia**

β- Thal Silent Carrier
-small ↓ in β chains production
Silent state (βsilent/β)
-nearly normal ratios
-no hem. abnormalities
Homozygous (βsilent/βsilent)
-mild β-thal intermedia phenotype
- ↑ Hb F and Hb A

β- Thalassemia Minor
-β thal trait (het. state)
-mild, asymptomatic anemia
-microcytic, hypochroic RBCs, target cells, elliptocytes, basophiilic stippling
-extra α chains combine with δ to form more Hb A2
- ↑ Italy and Greece

β - Thalassemia Major
-Homozy. or compound state
-severe anemia, microcytic and hypochromic RBCs, severe
-diagnosed 6 mon.-2 yr
-requires transfusions
-increased Hb F and Hb A2
-PB: micrycytosis, hypochromia, target cells, teardrop, inclusions, NRBCs, etc.
Without Treatment
-enlarged liver & spleen
-heatosplenomegaly
-prominence of forehead, cheek bones, upper jaw
-jaundice
-Fe accum. in various organs
With Treatment (regularly)
- hypertransfusion
-risk of iron overload
-Curable with HSCT

β - Thalassemia Intermedia
-symptoms fall between β thal major and minor
-non-transfusion depedent thalassemia
-Hb level between 7-10 g/dL
-May experience Iron Overload even though they do not receive transfusions

Thalassemias caused by defects in β -Globin Gene Clusters

Hereditary persistence fetal hemoglobin (HPFN)
- ↑ Hb F levels beyond infancy
-Deletion in δβ region or non-deletional mutations in γ-chain promoter region that lead to increase HbF
-asymptomatic except when see with another thalassemia

δβ0-Thalassemia
- ↑ Hb F levels beyond infancy
-Deletions of δ and β globin genes
- ↓ Hb A, normal/ ↓ Hb A2, 5-20% Hb F
- β thalassemia minor phenotype

Hb Lepore Thalassemia
-δβLepore
-Rare structural variant= fusion of δβ-globin genes
-Heterozygous Hb Lepore: similar clinical manifestations of β-thalassemia minor
-Homozygous Hb Lepore: similar clinical manifestations of β-thalassemia major