Hemoglobin Evolution Pathway

Oxyhemoglobin → Deoxyhemoglobin → Intracellular Methemoglobin → Extracellular Methemoglobin → Hemosiderin

- **Fe^{2+}** (ferrous iron): Oxyhemoglobin → Deoxyhemoglobin
- **Fe^{3+}** (ferric iron): Methemoglobin → Hemosiderin formation
- Location matters: Intracellular vs extracellular compartmentalization

MRI Sequences

- T1:
  - Best for identifying methemoglobin (subacute hemorrhage) via T1 shortening; less sensitive for early deoxyhemoglobin or tiny chronic deposits.
- T2:
  - Shows the classic transition from bright (hyperacute) to dark (acute/early subacute) back to bright (late subacute/chronic), but can be nonspecific and influenced by edema and CSF.
- GRE (2D T2*):
  - Sensitive to susceptibility from deoxyhemoglobin, methemoglobin, and hemosiderin, but less sensitive and lower spatial resolution than SWI for microbleeds.
- SWI (3D T2* with phase):
  - Maximally sensitive to susceptibility; detects more and larger hemorrhagic foci than GRE and shows characteristic mixed high/low signal due to both T2* and T1 “shine-through.”

Stages and hemoglobin forms

Acute/Hyperacute

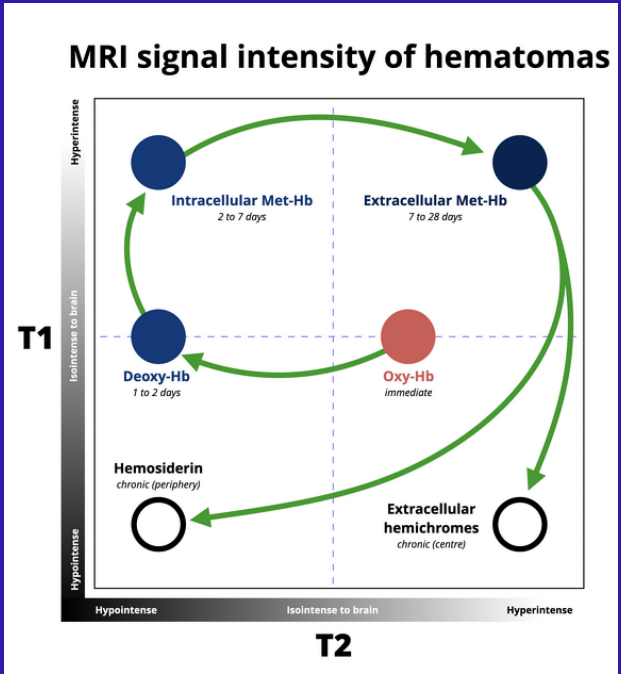
- **Hyperacute** (< 24 h): Predominantly intracellular oxyhemoglobin; blood is still intravascular or just extravasated, with high water content and minimal deoxyhemoglobin. This yields near-normal T1 and bright T2, often with surrounding vasogenic edema that is hyperintense on T2/FLAIR.
- **Acute** (≈ 1–3 days): Intracellular deoxyhemoglobin forms as oxygen tension falls, producing strong T2* susceptibility effects. T2 signal drops, while T1 remains iso–hypointense, and GRE/SWI show marked hypointensity.

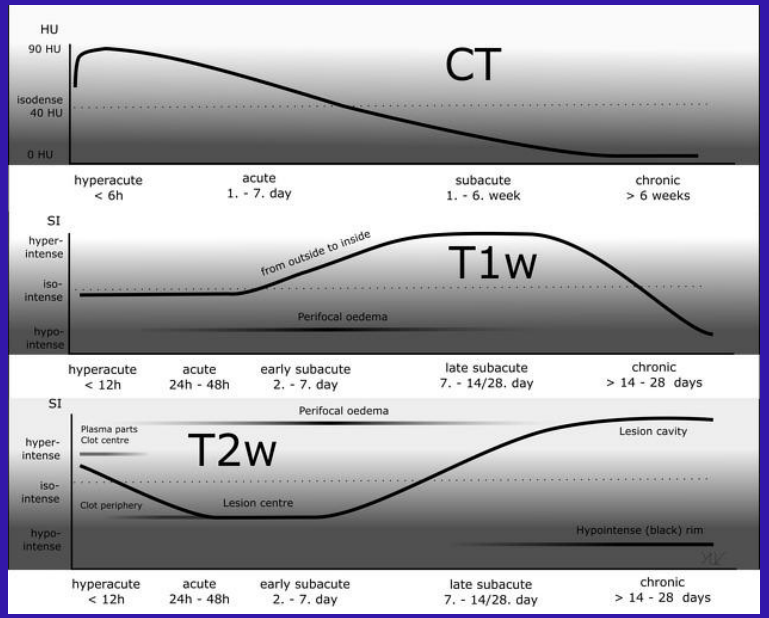
Subacute phases

- **Early subacute** (≈ 3–7 days): Hemoglobin is converted to intracellular methemoglobin, which has pronounced T1 shortening. The hematoma becomes T1 bright but remains T2 dark because RBC membranes are intact and susceptibility effects persist.
- **Late subacute** (≈ 7–28 days): RBC membranes lyse, releasing extracellular methemoglobin, which reduces susceptibility effects and increases both T1 and T2 signal. The hematoma appears hyperintense on T1 and T2, often with a developing hypointense hemosiderin rim on GRE/SWI.

Chronic stage

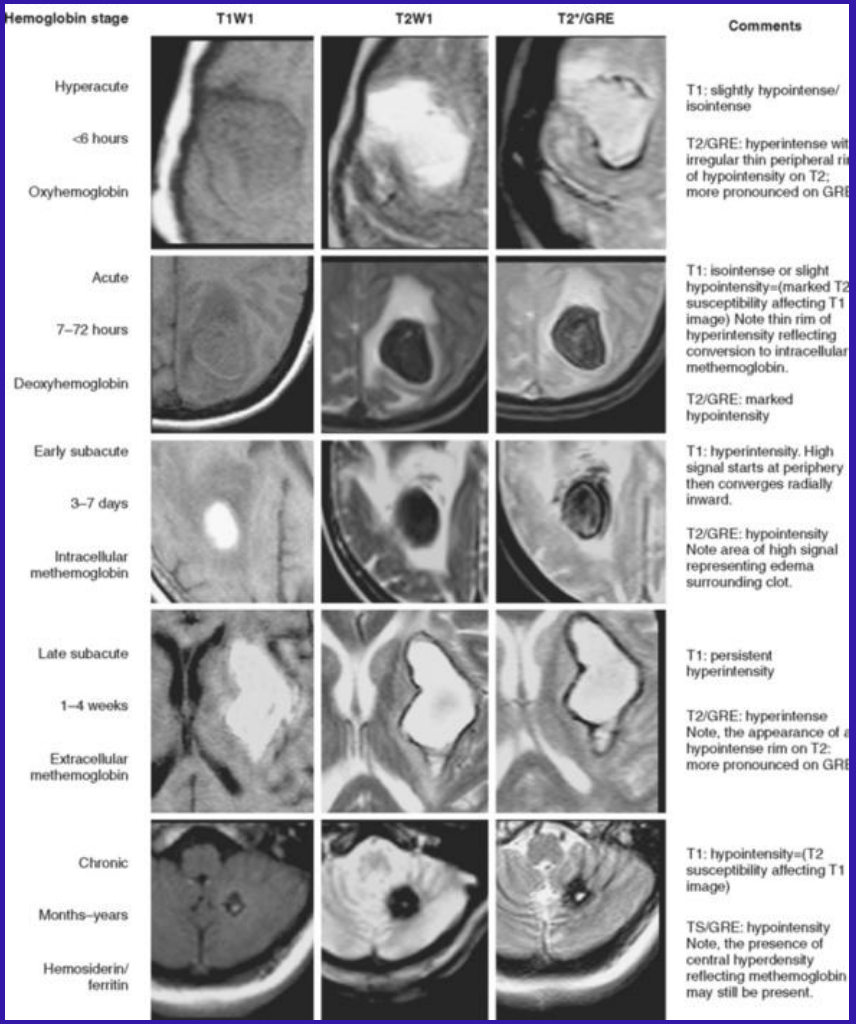
- **Chronic** (> 1 month): Methemoglobin is further degraded to hemosiderin and ferritin within macrophages at the margins of the cavity. This yields a dark hemosiderin rim (blooming on GRE/SWI) surrounding a region of encephalomalacia/CSF-like signal that is T1 hypointense and T2 hyperintense





Mnemonic	Abnormal	T1	T2
It Be	Hyperacute	I	B
IdDy	Acute	I	D
BiDdy	Early Subacute	B	D
BaBy	Late Subacute	B	B
DooDoo	Chronic	D	D

Stage	Age	Compartment	Hemoglobin
Hyperacute	<24 Hours	Intracellular	Oxyhemoglobin
Acute	1-3 Days	Intracellular	Deoxyhemoglobin
Early Subacute	>3 Days	Intracellular	Methemoglobin
Late Subacute	>7 Days	Extracellular	Methemoglobin
Chronic	>14 Days	Extracellular	Hemosiderin



INTRACRANIAL HEMORRHAGE	T1 WI	T2 WI	T2 GRE
Hyperacute	Hypo o isointense	Hyperintenso	Hypointense Rim
Acute (12-48 h)	hyperintense Halo Isointense Center	hyperintense Halo Isointense Center	Hypointense
Early Subacute(72 h)	Hyperintense	Hypointense	Diffusely hypointense
Late Subacute (3-20 d)	Hyperintense	Hyperintense	Hypointense rim
Chronic (9 sem)	Hypontense	Hyperintense Cavity Hypointense Halo	Hypointense periphery

Stage	Approx age	Dominant blood product	T1 signal	T2/FLAIR signal	GRE/SWI signal	Notes
Hyperacute	< 24 h	Intracellular oxyhemoglobin	Isointense to mildly hyperintensepmc.ncbi.nlm.nih+1	Hyperintense relative to brain, with surrounding hyperintense edemapmc.ncbi.nlm.nih+2	Variable; may show thin hypointense rim if deoxyhemoglobin starts to formpmc.ncbi.nlm.nih+2	High water content; clot not fully formed; CT may still be isodense early.pmc.ncbi.nlm.nih+1
Acute	~1–3 days (often 12 h–2–3 d)	Intracellular deoxyhemoglobin	Isointense to hypointensepmc.ncbi.nlm.nih+2	Hypointense core with hyperintense vasogenic edema rimpmc.ncbi.nlm.nih+2	Markedly hypointense (blooming)mriquestions+2	Strong T2* susceptibility; GRE/SWI very sensitive for detection.mriquestions+1
Early subacute	~3–7 days	Intracellular methemoglobin	Hyperintense (T1 shortening)pmc.ncbi.nlm.nih+2	Hypointense or mixed, often with peripheral hyperintense edemastroke-manual+2	Hypointense (persistent susceptibility from intracellular methemoglobin)thieme-connect+1	Classic T1-bright, T2-dark pattern for early subacute parenchymal hematoma.stroke-manual+1
Late subacute	~7–28 days	Extracellular methemoglobin	Hyperintensepmc.ncbi.nlm.nih+1	Hyperintense; may be heterogeneous with surrounding edemapmc.ncbi.nlm.nih+2	Variable; can be iso- to hyperintense centrally with hypointense rim as hemosiderin developsstroke-manual+2	RBC lysis releases methemoglobin; susceptibility less in center, more at rim.pmc.ncbi.nlm.nih+1
Chronic (early)	> 1 month to ~2 months	Peripheral hemosiderin/ferritin with central serum/CSFpmc.ncbi.nlm.nih+2	Center iso- to hypointense (encephalomalacia/CSF-like); rim hypointensestroke-manual+1	Center hyperintense (gliosis/CSF); dark hypointense rimstroke-manual+1	Prominent hypointense rim with blooming; microbleeds appear as small dark focithieme-connect+2	Volume loss and gliosis; SWI best for detecting small chronic hemosiderin deposits.thieme-connect+2
Chronic (late)	Months–years	Residual nonparamagnetic hemochromes, encephalomalaciastroke-manual+1	Hypointense parenchymal loss, often similar to CSF; rim persistsstroke-manual+1	Hyperintense encephalomalacia with persistent dark rimstroke-manual+1	Stable hypointense rim or scattered microbleedsthieme-connect+2	Represents final stage with parenchymal atrophy and stable hemosiderin staining.stroke-manual+1

Hyperacute Stage (< 24 hours)

Intracellular Oxyhemoglobin (Fe^{2+})

- **Biochemistry:** RBCs intact with normal oxygenated hemoglobin
- **Mechanism:** High local O_2 tension maintains Fe^{2+}; antioxidant systems prevent oxidation
- **MRI:** T1 iso/mildly bright | T2 bright (high water) | GRE variable
- **Clinical:** Clot forming; hyperintense edema rim on T2/FLAIR

Acute Stage (1–3 days)

Intracellular Deoxyhemoglobin (Fe^{2+})

- **Biochemistry:** O_2 dissociates; Fe^{2+} remains but hemoglobin conformation changes
- **Mechanism:** RBC membranes intact; paramagnetic centers exposed, causing strong T2* effects
- **MRI:** T1 iso/dark | **T2 markedly dark** | **GRE/SWI blooming**
- **Best sequence:** GRE or SWI for acute blood detection

Early Subacute Stage (3–7 days)

Intracellular Methemoglobin (Fe^{3+}, RBCs intact)

- **Biochemistry:** Deoxyhemoglobin auto-oxidizes to Fe^{3+} methemoglobin
- **Mechanism:** Methemoglobin reductase overwhelmed; Fe^{3+} causes T1 shortening
- **MRI:** **T1 bright** | T2 dark (intracellular) | GRE dark (blooming)
- **Classic pattern:** T1 hyperintense, T2 hypointense = parenchymal hematoma

Late Subacute Stage (7–28 days)

Extracellular Methemoglobin (Fe^{3+}, RBCs lysed)

- **Biochemistry:** RBC membranes break down; methemoglobin released into fluid
- **Mechanism:** Water access increases, reduces field inhomogeneity → T2 lengthens
- **MRI:** **T1 bright** | **T2 bright** | GRE variable (iso to mildly dark)
- **Developing rim:** Hemosiderin deposits at periphery (dark on GRE/SWI)

Chronic Stage (> 1 month)

Hemosiderin & Ferritin (Fe^{3+} storage); Encephalomalacia

- **Biochemistry:** Microglia/macrophages phagocytose debris; iron stored in ferritin/hemosiderin
- **Mechanism:** Clustered Fe^{3+} creates strong local susceptibility; parenchymal loss evident
- **MRI:** T1 iso/dark center | T2 bright center | **Dark hemosiderin rim on GRE/SWI**
- **SWI advantage:** Best for detecting microbleeds and chronic hemosiderin

Biochemistry Summary

Stage	Iron State	RBC Integrity	Paramagnetism
Hyperacute	Fe^{2+}	Intact	Minimal
Acute	Fe^{2+}	Intact	Strong T2*
Early Subacute	Fe^{3+}	Intact	Strong T1 + T2*
Late Subacute	Fe^{3+}	Lysed	Dispersed Fe^{3+}
Chronic	Fe^{3+}	Ingested	Storage foci