

MRI in Thalassemia

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Leading the Fight Against Thalassemia

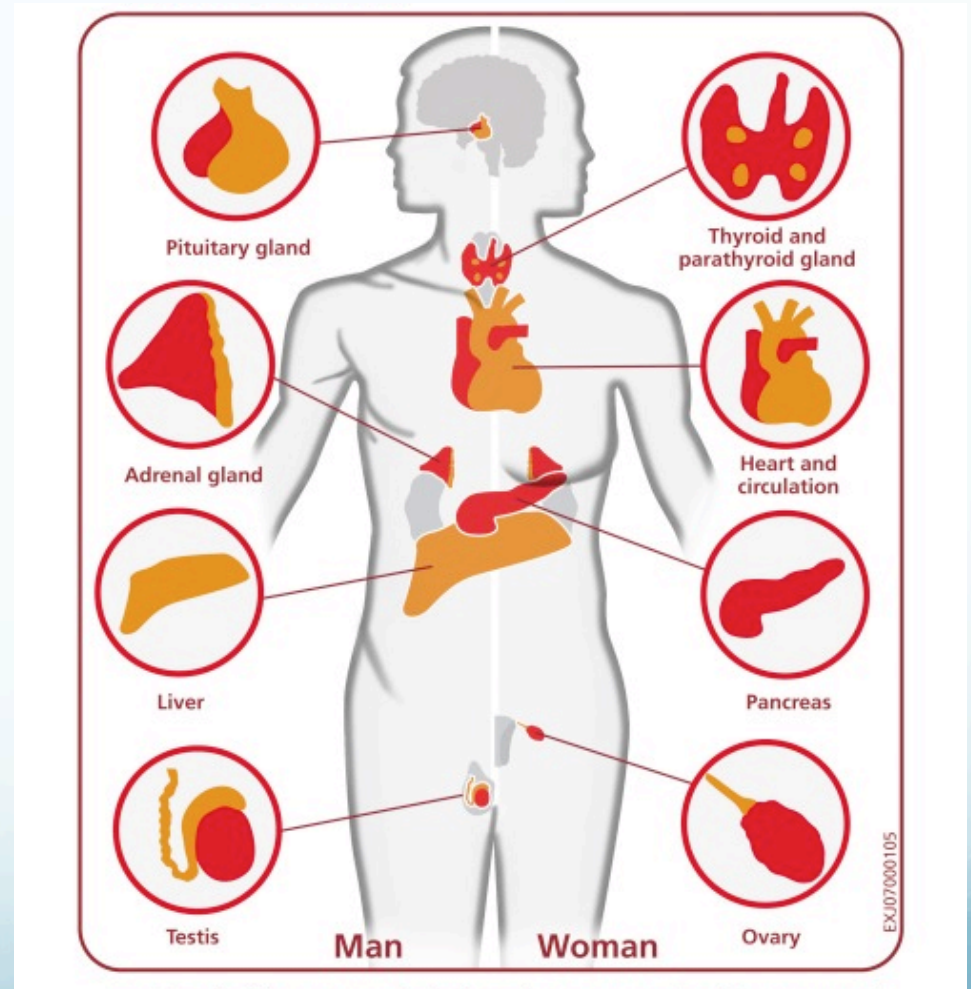
How Does Iron Overload Occur ?



- Patients with thalassemia require regular transfusions
 - Blood contains iron which cannot be removed because it carries oxygen to the tissues.
 - Each blood transfusions contains as much iron as a person would absorb in one year.
 - The body can only eliminate one transfusion per year.
- **Without iron chelation, dangerous levels of iron can build up in 1 year of transfusions.**

Organs Affected by Iron

- Liver
- Glands
 - Pituitary
 - Pancreas
 - Thyroid/Parathyroid
 - Adrenal
 - Ovary/Testis
- Heart & blood vessels

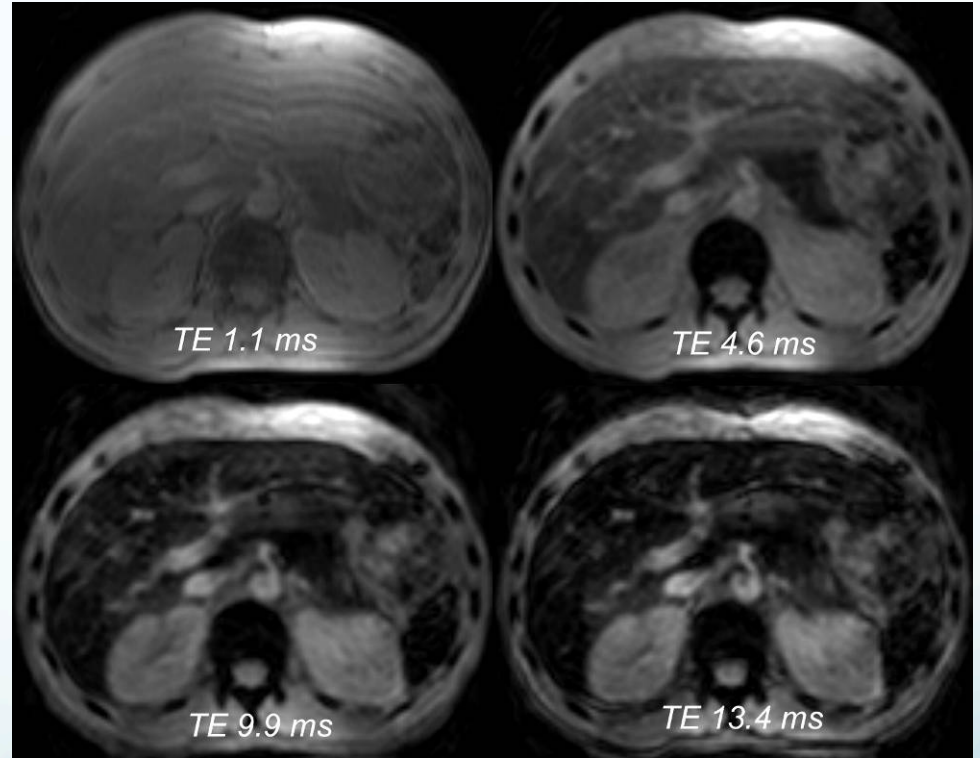


Why measure in each organ ?

- Iron loads and unloads at different rates in the different organs.
- While high ferritin and poor chelator compliance are always bad, iron can build up in gland and heart tissue even if ferritin values are low.
- Not all organs are equally sensitive to iron.
- Iron can accumulate silently for many years.

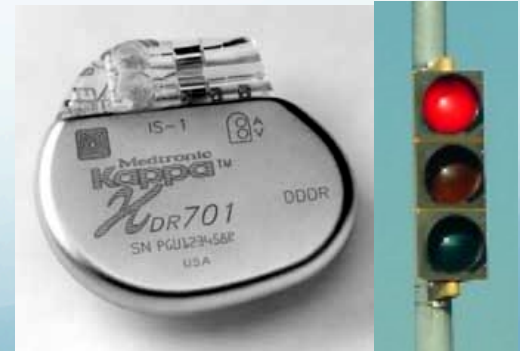
How does MRI measure iron?

- Iron in a magnet becomes a magnet.
- Iron darkens images.
- Rate of darkening is proportional to iron.
- We use computer programs to measure the darkening rate and relate it to iron.

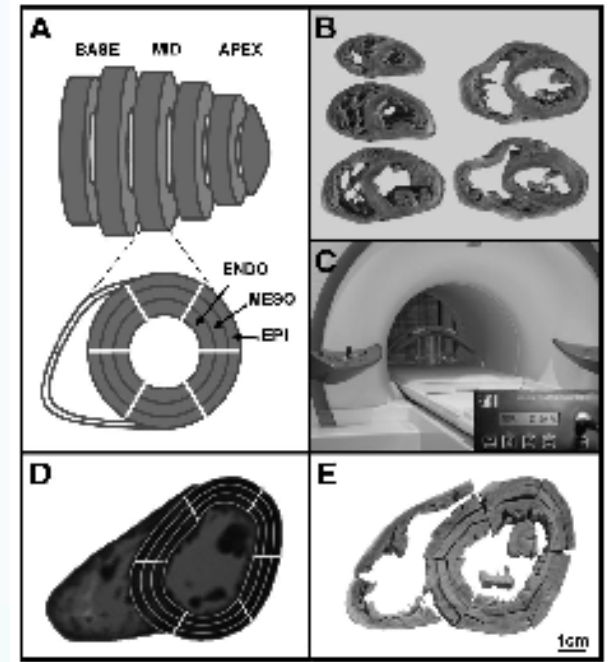
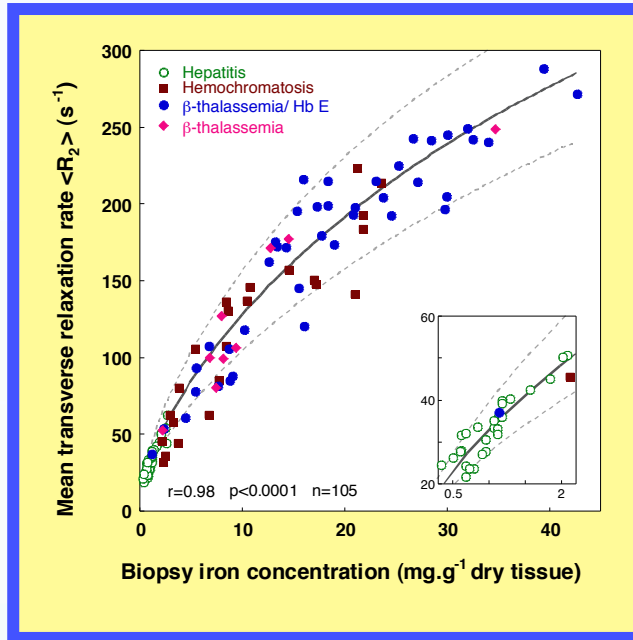


How is it done ?

- Patients lie quietly on a table for approximately an hour. They may be asked to hold their breath for 10-15 seconds. Scan of heart and liver is one hour.
- No IV's or medications are necessary.
- Porta-Caths and surgical clips are not a problem but patients with pacemakers can't be scanned

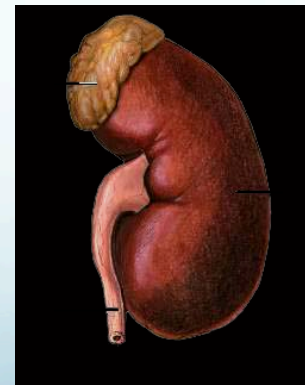
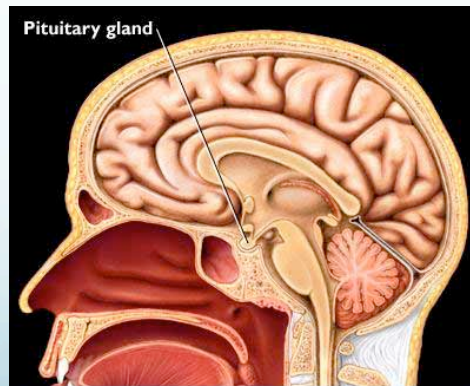
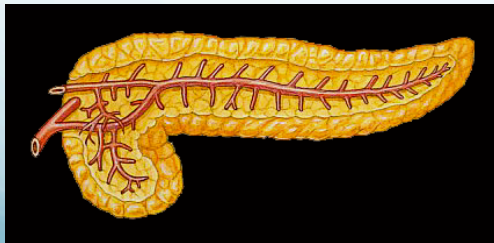
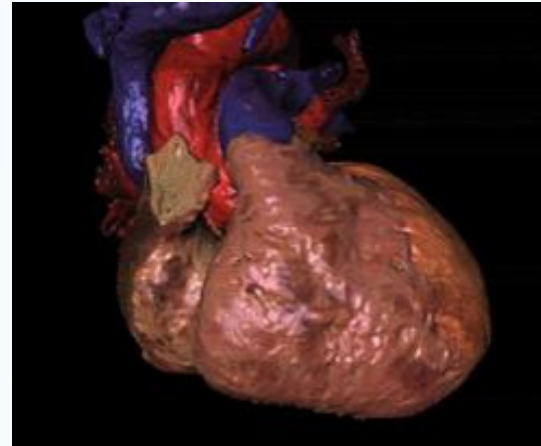
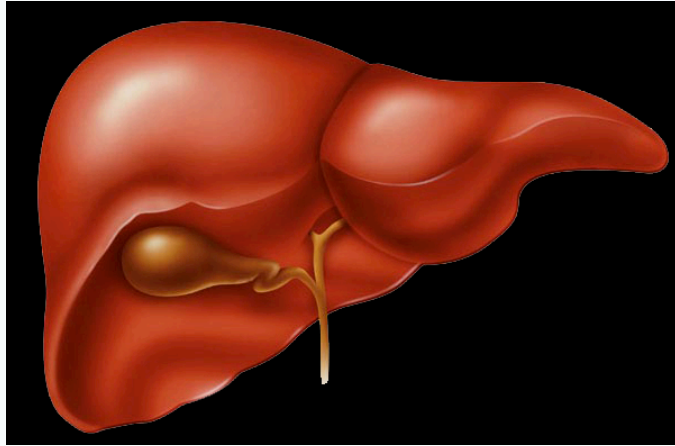


Does MRI measure iron ?



- We compare MRI results to direct iron measurements.

What organs can iron be measured?

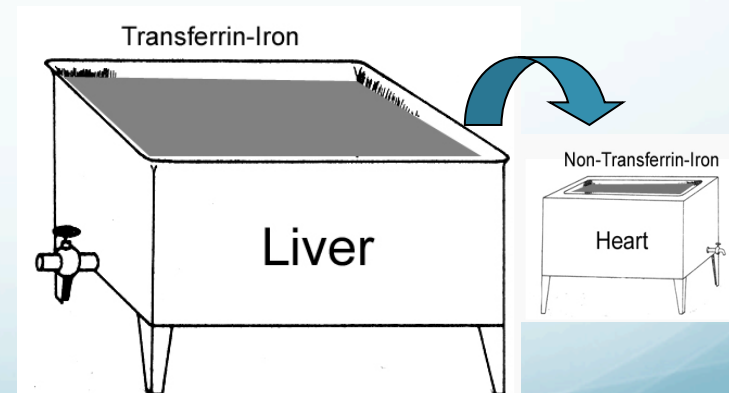


Liver Iron

- Liver iron levels are the best single marker of iron balance in the body.
 - Serum ferritin is a helpful number but liver iron is more accurate.
 - Liver iron levels help adjust chelation.
- High liver iron causes liver scarring and liver cancer.
- High liver iron also raises the risk that iron will build up elsewhere.

Iron In

Iron Out



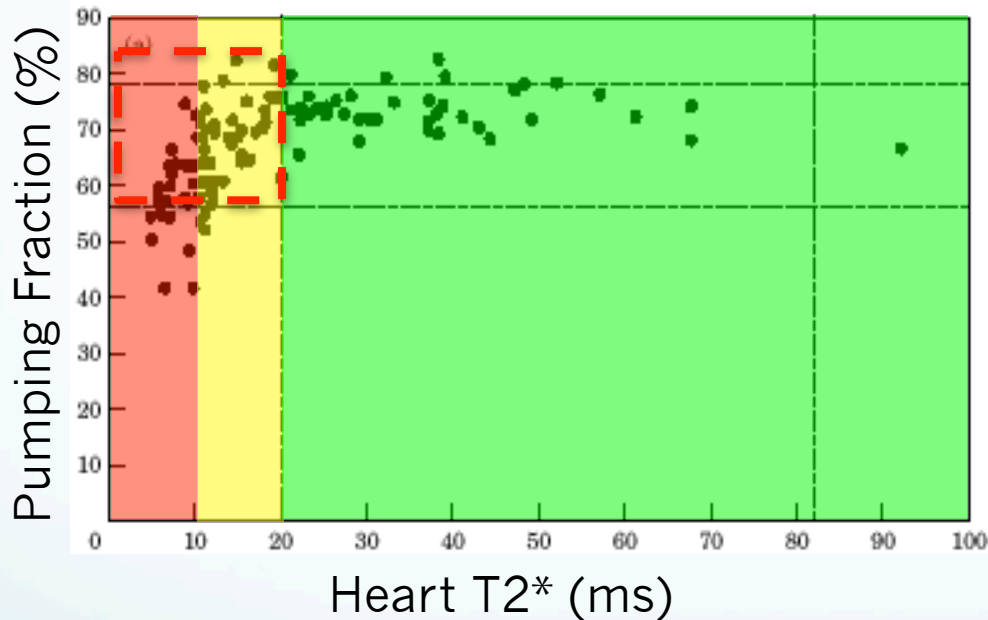
Levels of liver iron ?

- In the past, we thought that liver iron levels could be divided into low, intermediate and high risk, with < 7 mg/g being “safe” and > 15 mg/g being dangerous.
- Patients with liver iron levels greater than 15-20 mg/g dry weight still appear to be at much higher risk for liver, endocrine, and heart complications.
- However, there is really no “safe” level.
 - Missed chelator doses put the heart and glands at risk.
- We are now striving to normalize liver iron, with liver iron concentrations between 1 & 2 mg/g and ferritin values 200-400.

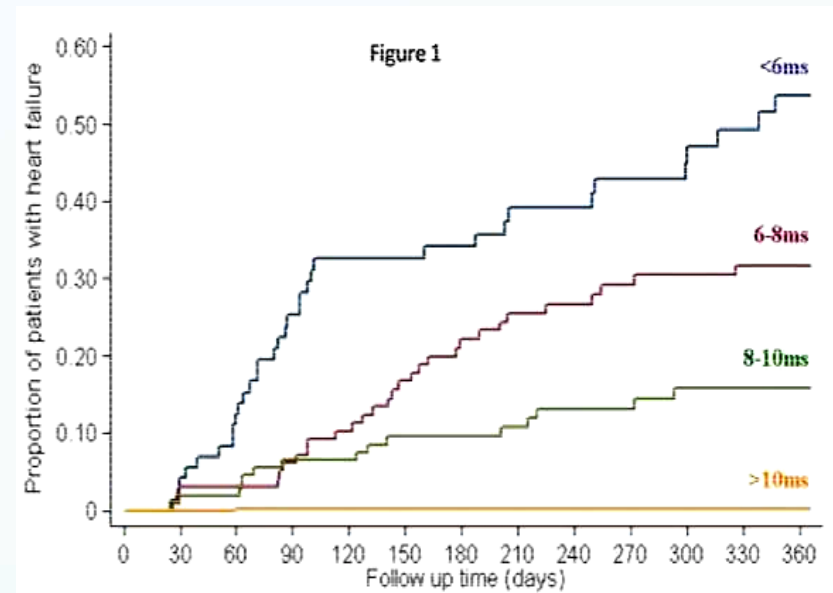
Heart Iron

- Heart iron is measured by a MRI value known as T2*.
- Low T2* means high iron and higher chance of heart problems.
- A heart T2* > 20 ms is normal
- A heart T2* between 10 & 20 ms is caution zone.
- A heart T2* < 10 ms represents higher danger.

Meaning of heart T2*



From Anderson et al, *Eur. J. Cardiology*, 2001



Kirk P, et al, *Circulation*, 2009

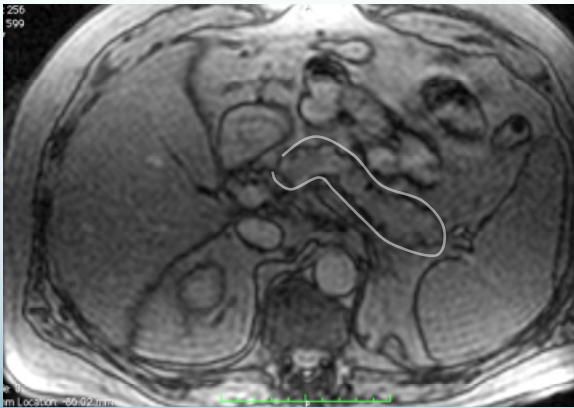
- Patients should try to get screened every 1 – 2 years, starting at around 8 years of age.
- Intensive chelation can prevent heart failure, even if the T2* is < 10 ms. But time is crucial.

Pancreas Iron

The pancreas makes insulin, a hormone that regulates sugar levels.

3 levels of pancreas problems

- Increased fasting level(100-126)
- Impaired response to sugar.
- Diabetes.



Older, no iron

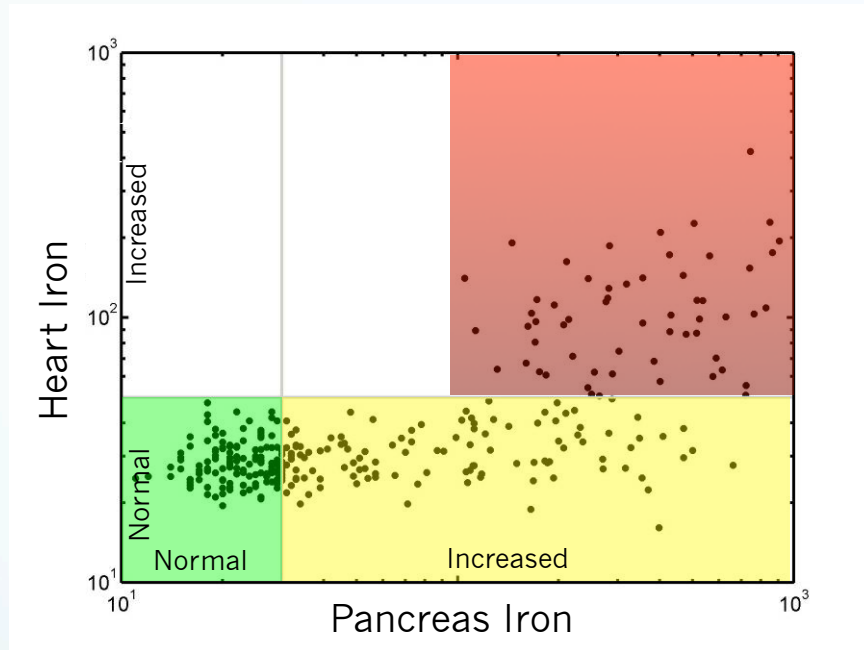


Older, iron, no diabetes



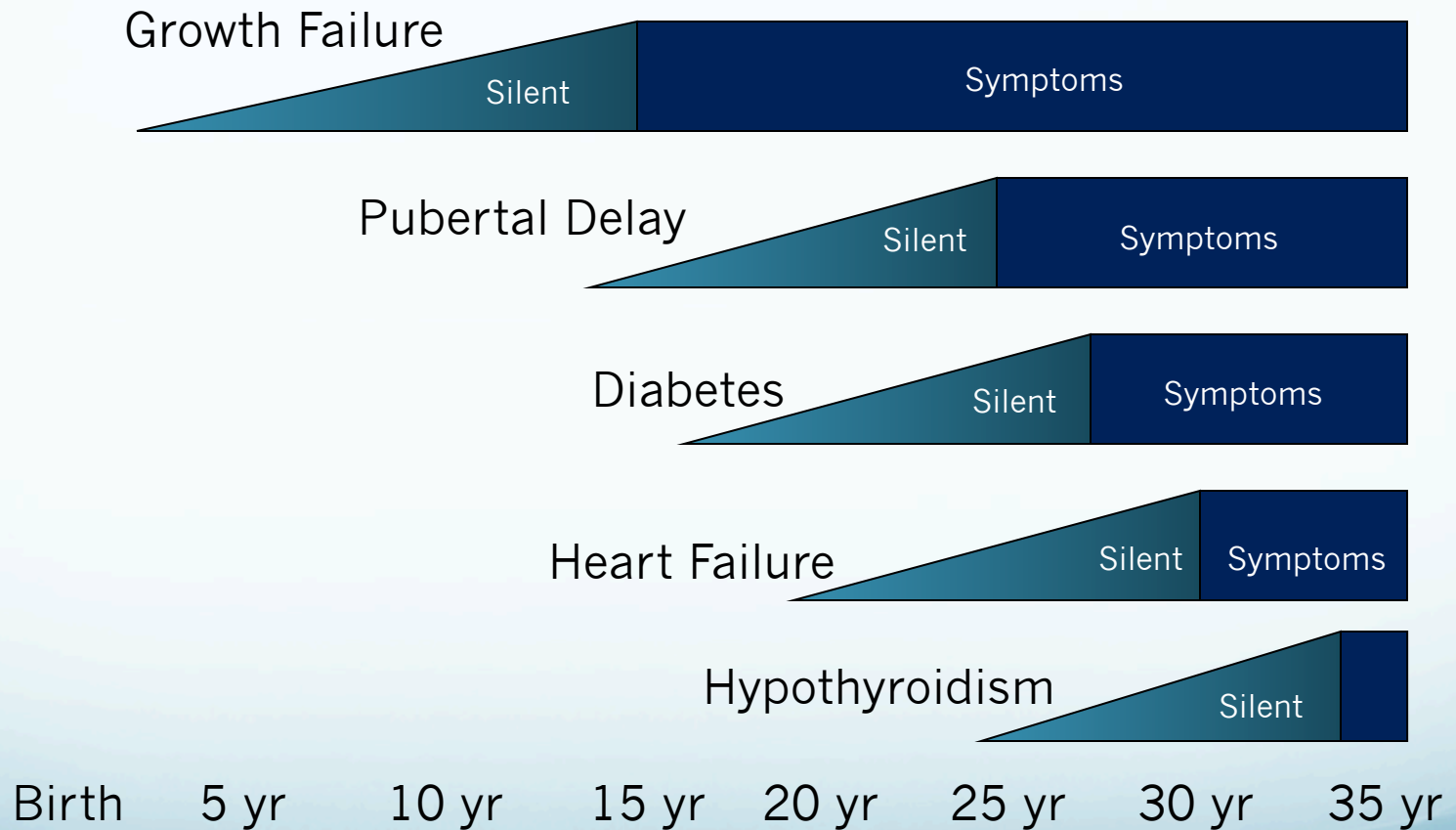
Older, iron, diabetes

Pancreas iron as early warning



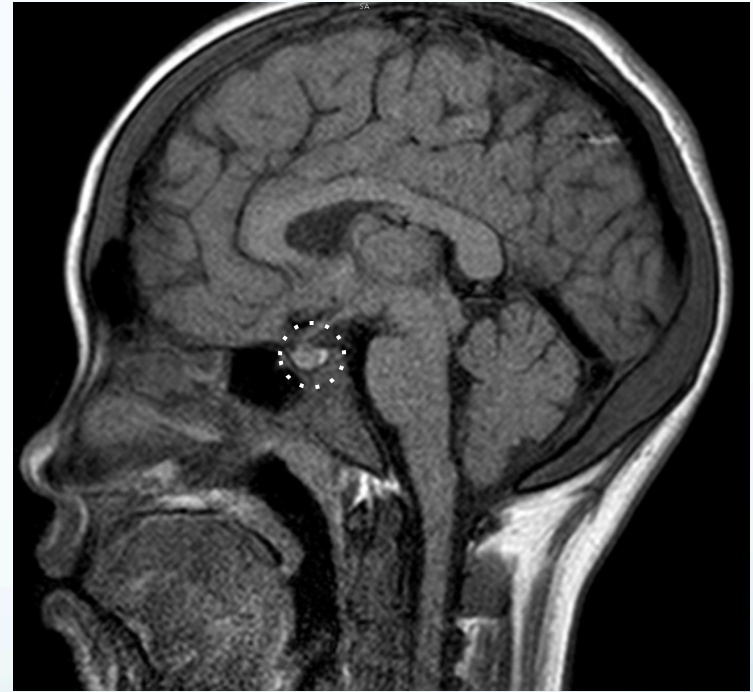
- The pancreas and heart load iron similarly.
- The pancreas loads before the heart.

Timing of Gland Problems

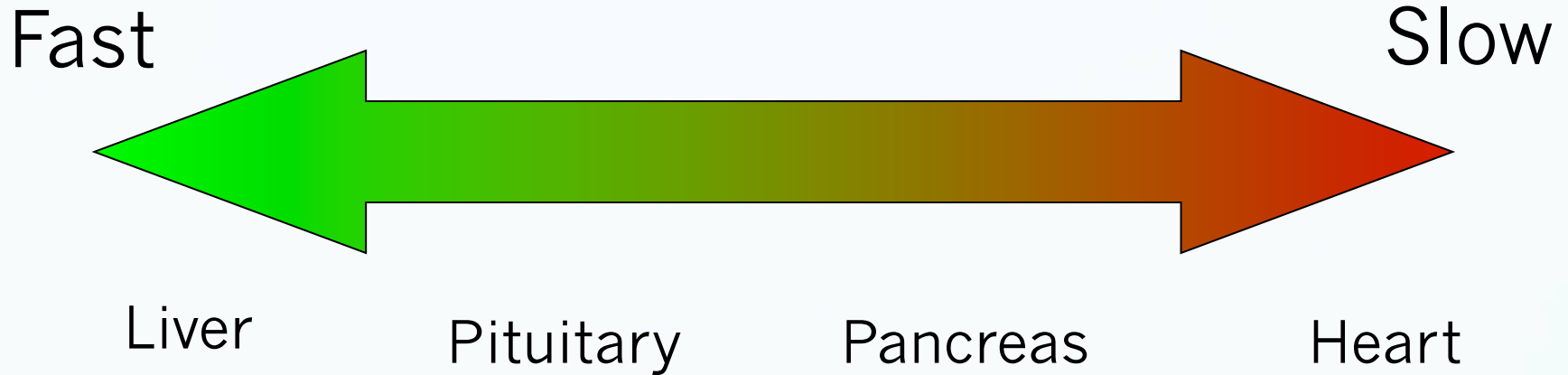


Pituitary Gland

- So-called “master” gland.
- Makes hormones that control other glands.
 - Sex hormones
 - Growth
 - Stress response
 - Thyroid function
- Pituitary iron causes hypogonadotropic hypogonadism (HH)



How do these organs relate ?



- The organs load and get rid of iron at different speeds.
- Chelation has to be taken nearly every day to protect the pituitary, pancreas, and heart.

Who can make the measurements ?

- Only Thalassemia centers can do the iron MRI's.
 - Experience matters. Most radiologists don't know how to make these measurements properly.
- Liver and heart represent standard of care.
- Pancreas is routine at CHLA but not yet at many other centers.
 - Not as easy as the liver/heart.
- Pituitary is performed at CHLA.

How can you help ?

- Ask your doctors to learn how to use MRI in their clinical practice if they are unfamiliar with it.
- Press your insurers to cover MRI for iron overload for routine clinical care if they do not.
- Participate in research validating MRI techniques.

Summary

- MRI measures the iron stored in the organs.
- Iron damage depends on how much and how long.
- MRI allows doctors to see the iron before damage occurs.
- Different organs load/unload at different rates.
- Regular MRI measurements of heart & liver are the standard of care.
- MRI of the pituitary and pancreas may help reduce iron toxicity in the future.