



Diamond Blackfan Anemia: Treatment & Remission

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Remission

- 568 patients enrolled in the DBAR
- 79 patients experienced a remission
- 71 patients were available for analysis
 - Male: female ratio for remission patients is 0.97:1
 - Median age at diagnosis: 3 m (range, 0 to 23.3 yrs)

Lee et al. Remission in Patients with Diamond Blackfan Anemia Appears to be Unrestricted by Phenotype of Genotype. *Blood* 112(11):3092, 2008

Results

- 73% entered remission while on steroid therapy
- 16% in remission while receiving both steroid and transfusion
- 8% in remission from chronic transfusion therapy

Results

- Median age of remission for all pts:
 - 5.7 years (range, 0.3 to 46.6 years)
 - males 5.8 years (range, 0.3 to 46.6 years)
 - females 4.8 years (range, 0.9 to 26 years)

Results

- Median duration of treatment to remission:
3.1 years (range, 1 month to 37.6 years)
- Median duration of remission:
11.5 years (range, 6 months to 48.1 years)
- The actuarial likelihood of entering remission is approximately 20% by 25 years of age

Results

- Remissions were observed in DBA patients or in affected family members with any RP mutation and in those with no known mutation

Conclusions

- Remission in patients with DBA is not an uncommon event.
- 55/71 of patients have durable remissions (median 11.5 years).
- The actuarial likelihood of entering remission is approximately 20% by 25 years of age.
- Steroid responsiveness is not a prerequisite for remission.
- The expression of a remission phenotype within multiplex families is quite variable.

- **Be on the lookout: New remission study through DBAR to update clinical characteristics and biology (blood samples) of remission in DBA this fall**

Treatments for DBA

- Transfusion therapy
 - Chronic red cell transfusion regimen
 - Start when Hb is less than 8 gm/dL
 - Transfuse 10-15 ml/kg every 3-4 weeks
 - Ideally transfuse until live vaccinations given (age 1)
 - May need to end earlier if venous access difficulty
 - If needs Port, please ask for a plastic one
 - **Goal: maintain adequate quality of life while maintaining growth**

Treatments for DBA

- Corticosteroid trial
 - Start after live vaccinations complete or sooner if venous access difficult
 - Prednisone equivalent of 2 mg/kg/day, usually given twice daily
 - Give Prednisone with Zantac or Prevacid to protect stomach
 - Begin ~2 weeks after a transfusion and continue for no more than 4 weeks if no response
 - Start Bactrim or Septra to prevent Pneumocystis pneumonia once response obtained

Treatments for DBA

- Corticosteroid therapy
 - If response noted then wean to 1 mg/kg/day over 2 months and then to 0.5 mg/kg/day or 1 mg/kg/every other day or lower

Goal: Best response at the lowest dose possible

- May need 3x/week or 2x/week
- Must be brave enough to wean, as patient might be in remission

Treatments for DBA

- Corticosteroid therapy
 - Watch growth!!!!
 - If falling off growth curve, or having pathologic fractures, need to consider a steroid hiatus
 - Consult endocrine for all patients, sooner if having growth issues

Treatments for DBA

- If no response to steroids then discontinue – do NOT increase dose
- Resume transfusion therapy
- Maintain growth

Goal:

- Hb 10 for <1 year of age
 - Hb 9-10 for ages 2-16 yrs
 - Hb 10 for adults
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- At 10-15 transfusions, begin chelation therapy

Treatments for DBA

- Chelation therapy
 - After age 2, begin Exjade at 20-40 mg/kg/day
 - When able, begin Jadenu at 14-28 mg/kg/day
 - If ferritin not decreasing, may need to consider Desferal therapy
 - Once able, obtain MRI T2* to check heart and liver iron load
 - Consider liver biopsy if liver iron concentration is high or possible SCT
 - If iron overload high, start Desferal at 50-60 mg/kg/day over 10-12 hours/day subcutaneously
 - If too high, need to give Desferal 24 hrs/day intravenously
 - More with Dr. Wolfe tomorrow

Iron overload in a patient with Diamond Blackfan anemia

Prior to death

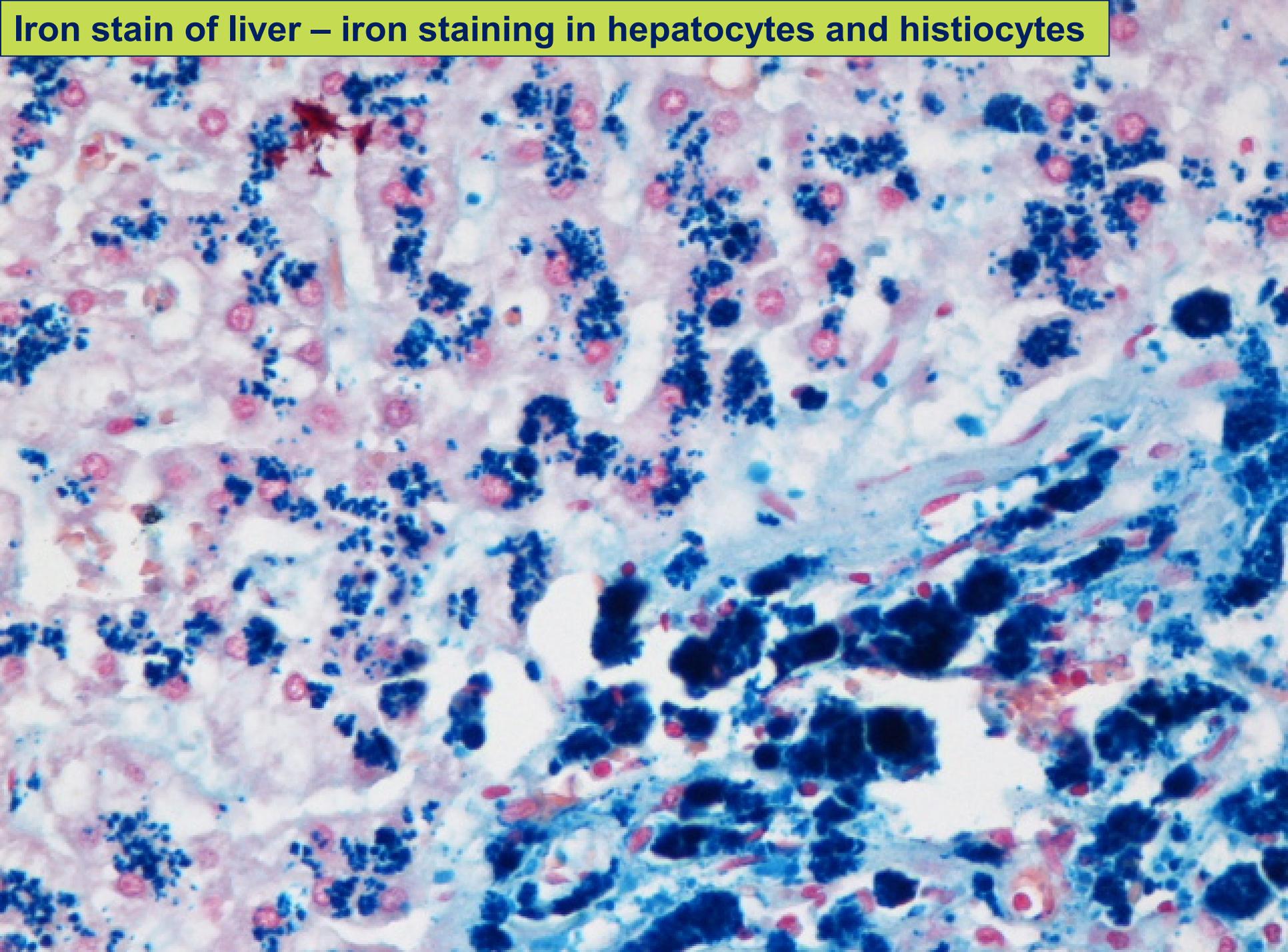
Autopsy

- Ferritin 4100 $\mu\text{g/L}$
(acceptable <1000-1500)
 - LIC – 9.7 mg/gram dry weight
(acceptable 3-7)
 - T2* 12 milliseconds
weight
(acceptable 20-25)
- 30.34 mg/gram dry
- 9.24 mg/gram dry

Liver with iron overload

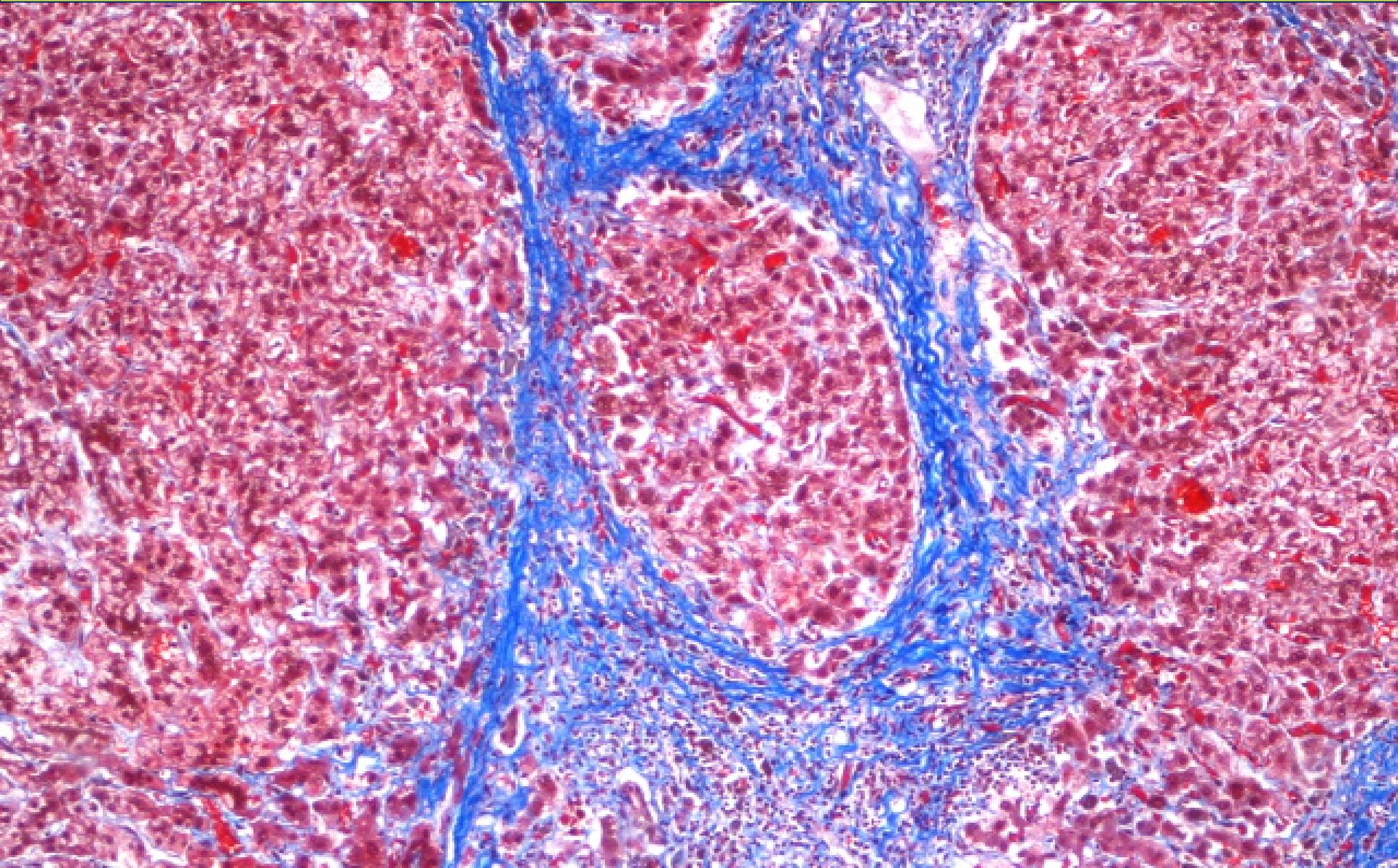


Normal liver



Iron stain of liver – iron staining in hepatocytes and histiocytes

Trichrome stain of liver – medium magnification to show liver cirrhosis with fibrosis and nodules in a patient with hepatic iron overload (no iron stain)



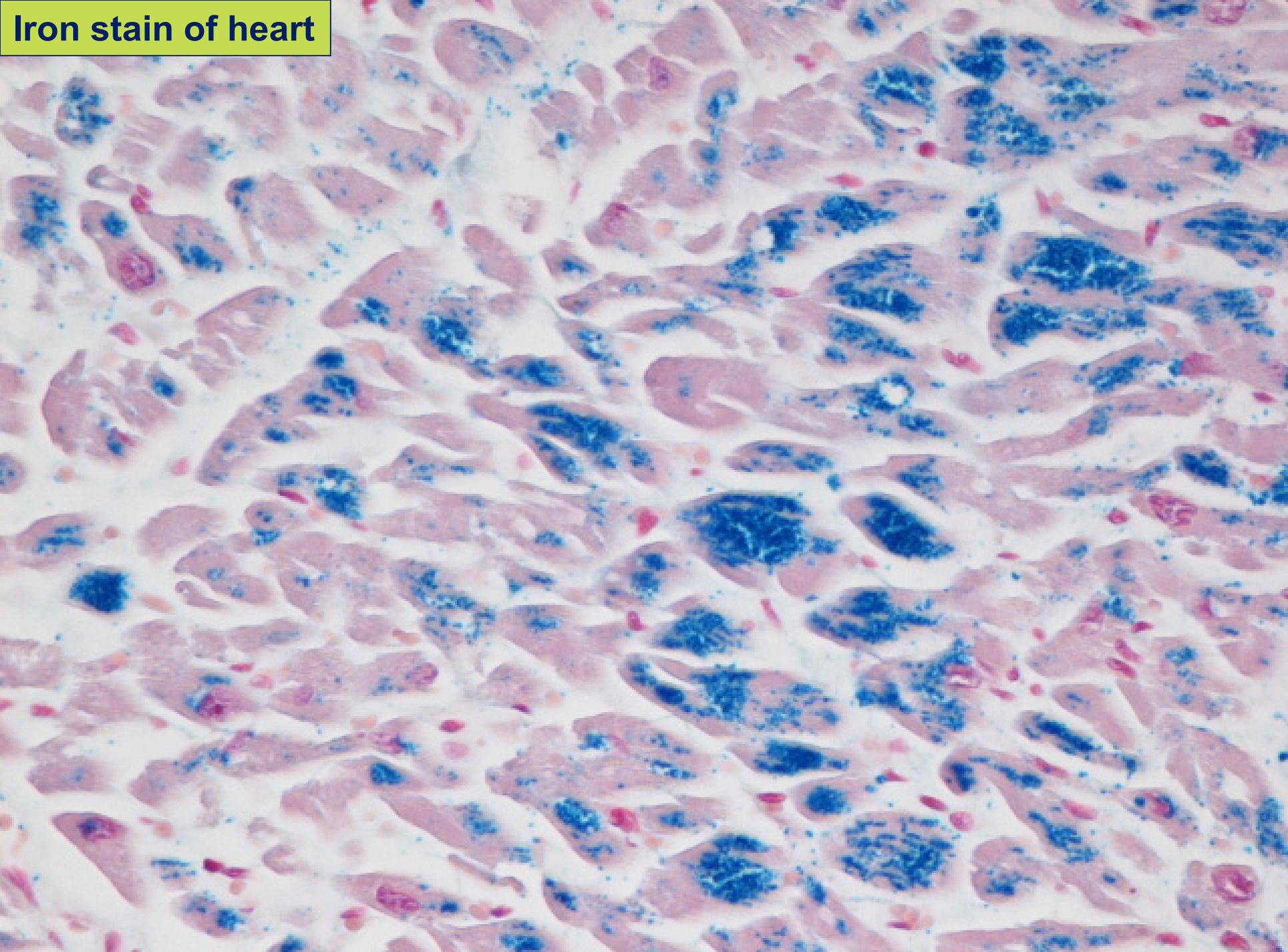


Dilated cardiomyopathy with iron overload

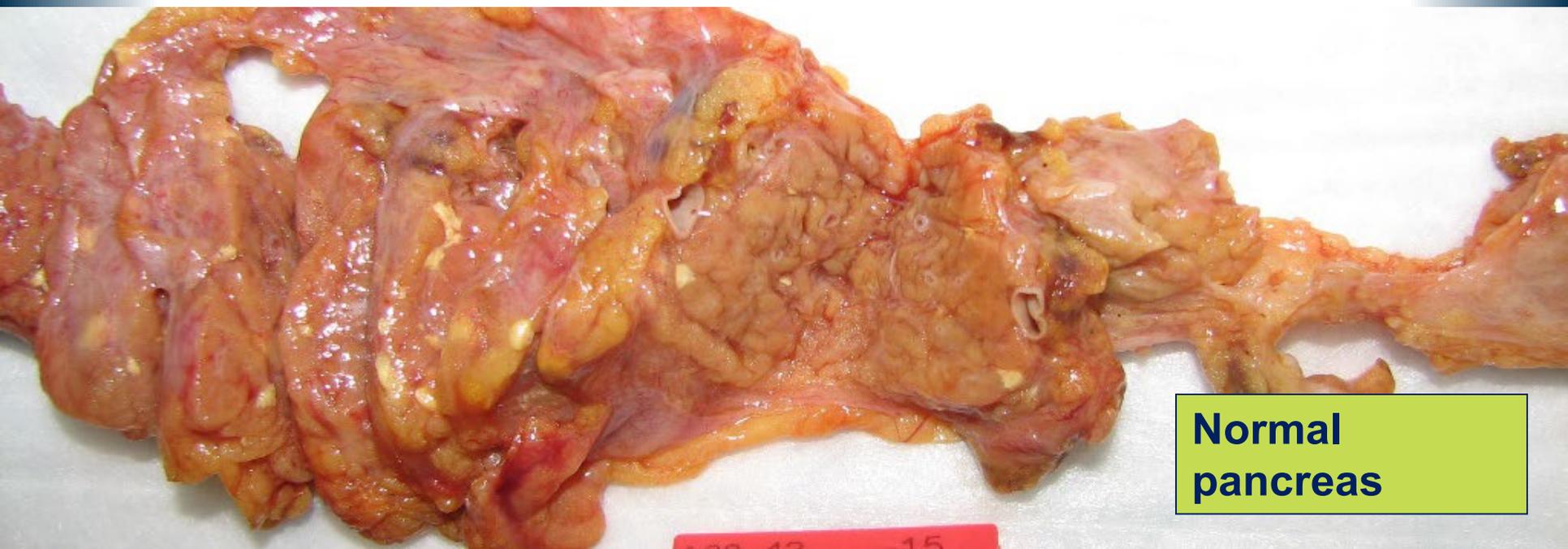
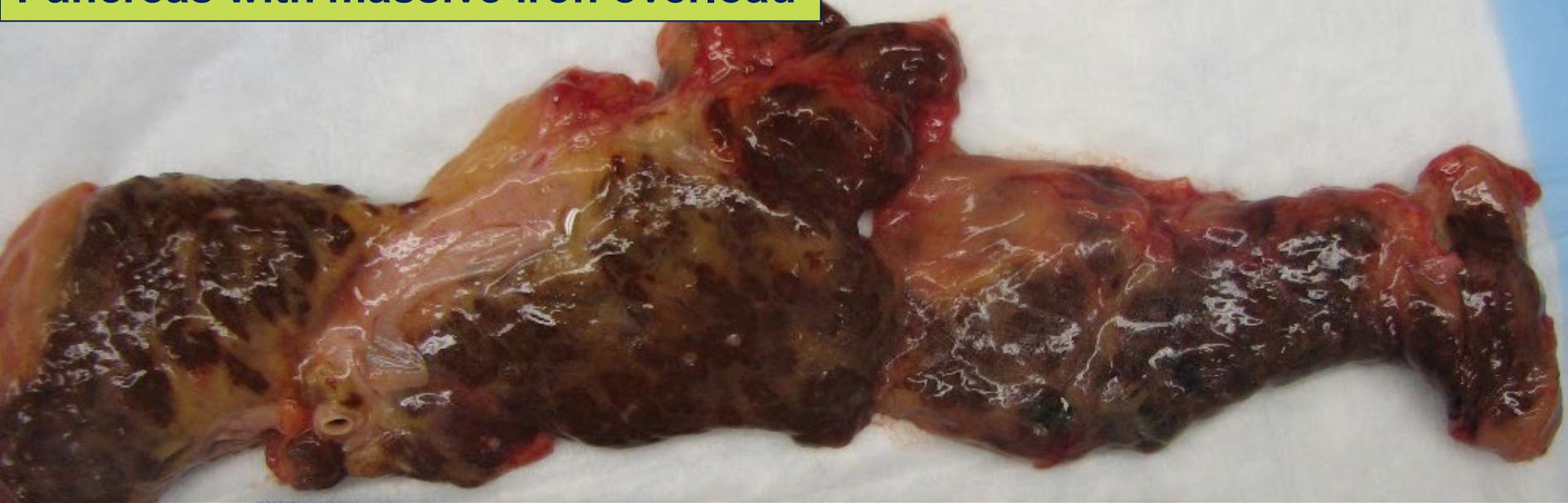


Hypertrophic cardiomyopathy

Iron stain of heart



Pancreas with massive iron overload



Normal pancreas