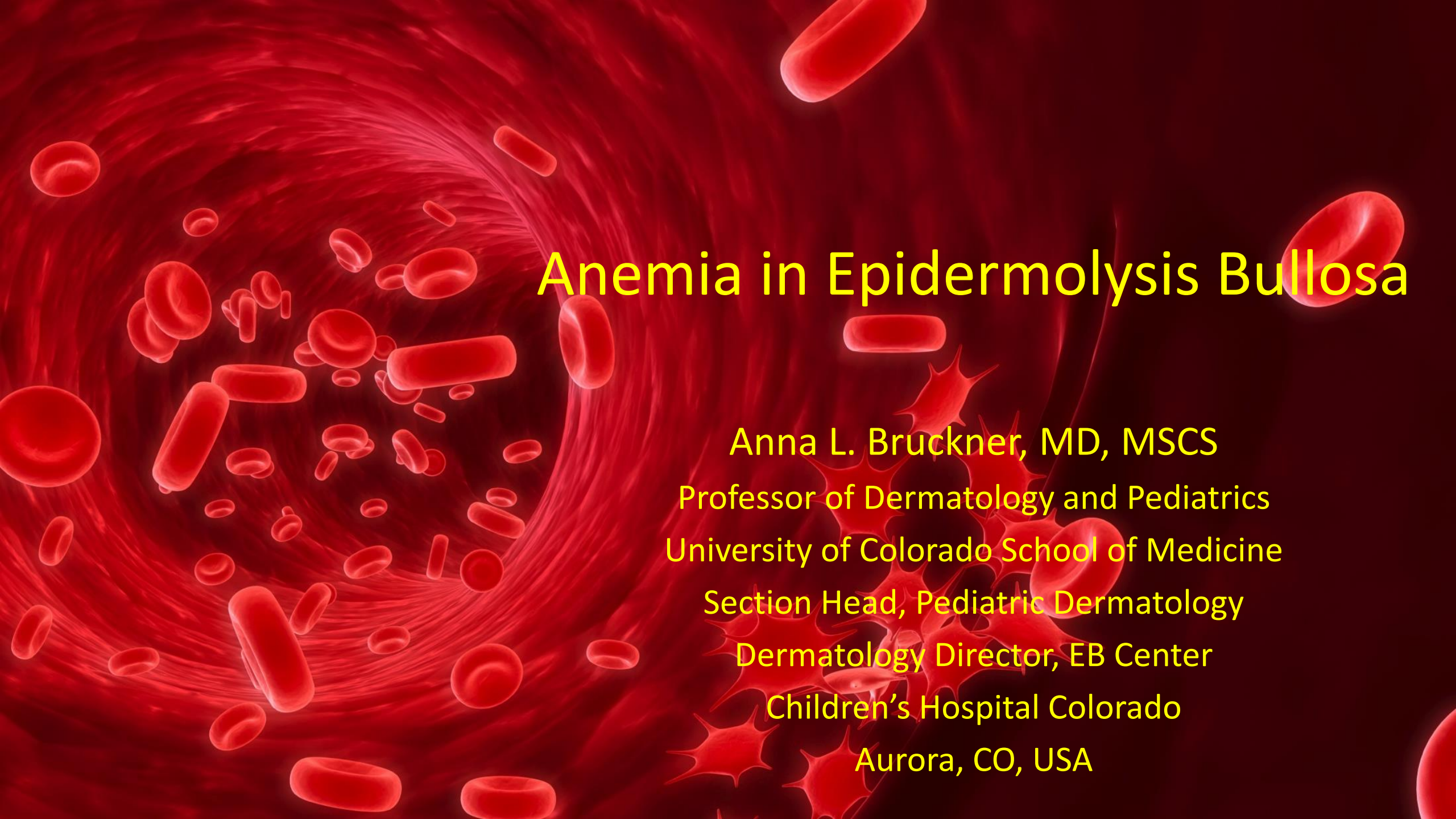


Anemia in Epidermolysis Bullosa

Anna L. Bruckner, MD, MSCS
Professor of Dermatology and Pediatrics
University of Colorado School of Medicine
Section Head, Pediatric Dermatology
Dermatology Director, EB Center
Children's Hospital Colorado
Aurora, CO, USA

Disclosures

- EB-related:
  - Amicus/Scioderm (contracted and investigator-initiated research, advisor/consultant)
  - Amryt Pharma/Chiesi (contracted research, advisor, speaker)
  - Castle Creek/Fibrocell (contracted research, advisor/consultant)
  - Krystal Bio (consultant)
  - Phoenix Tissue Repair (contracted research)
  - Phoenicis Therapeutics (formerly ProQR/Wings) (contracted research)
  - Twi Biotechnology (consultant)

Objectives

- Understand the epidemiology and pathogenesis of anemia in EB
- Review current guidelines on the diagnosis and management of anemia in EB

Anemia in EB

- Anemia
  - A condition in which the body does not have enough healthy red blood cells
  - Typically defined as below normal level of hemoglobin
- Symptoms
  - Fatigue, lack of energy, poor endurance, loss of appetite
  - Poor wound healing in EB

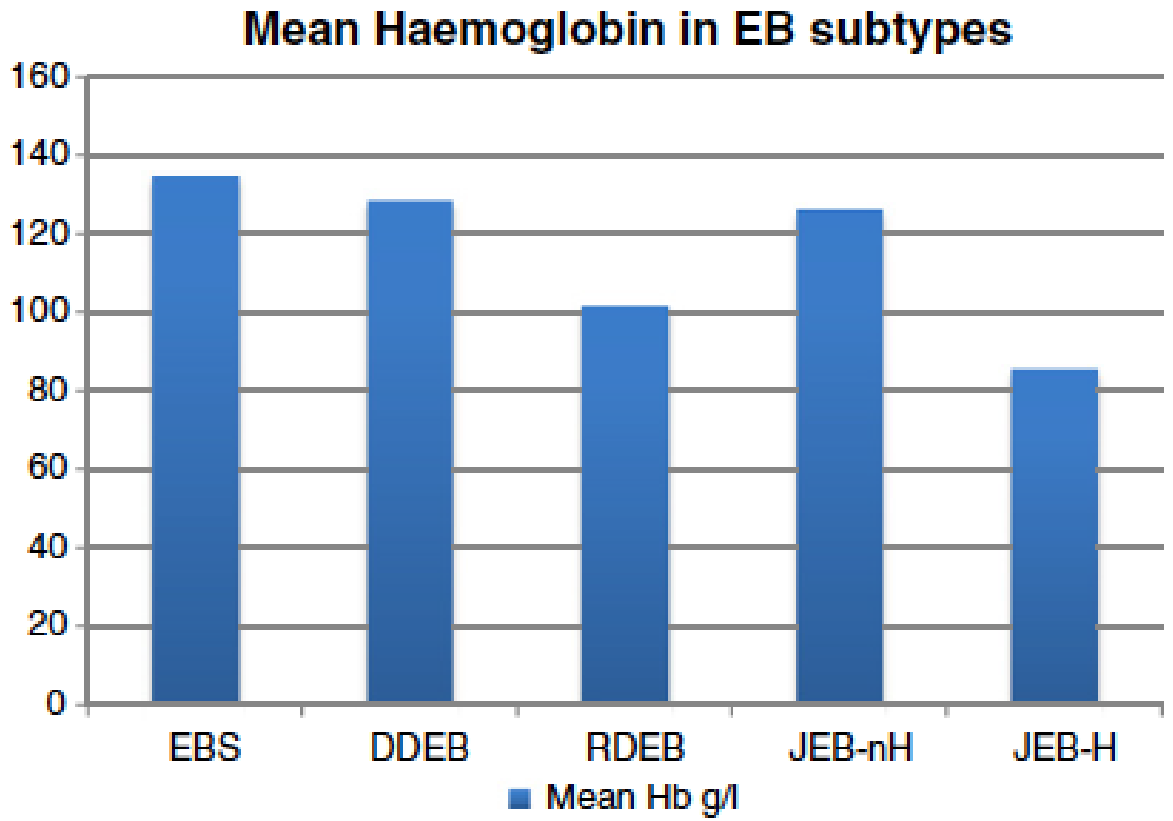
How common is anemia in EB?

- Frequency of anemia:

	EBS	JEB	DEB-u	DDEB	RDEB
USA[1]	5.8%	37.8%	7.4%	10%	49.1%
Australia[2]	11.3%	37.5%		25.6%	68%
Germany[3]		75%			91%

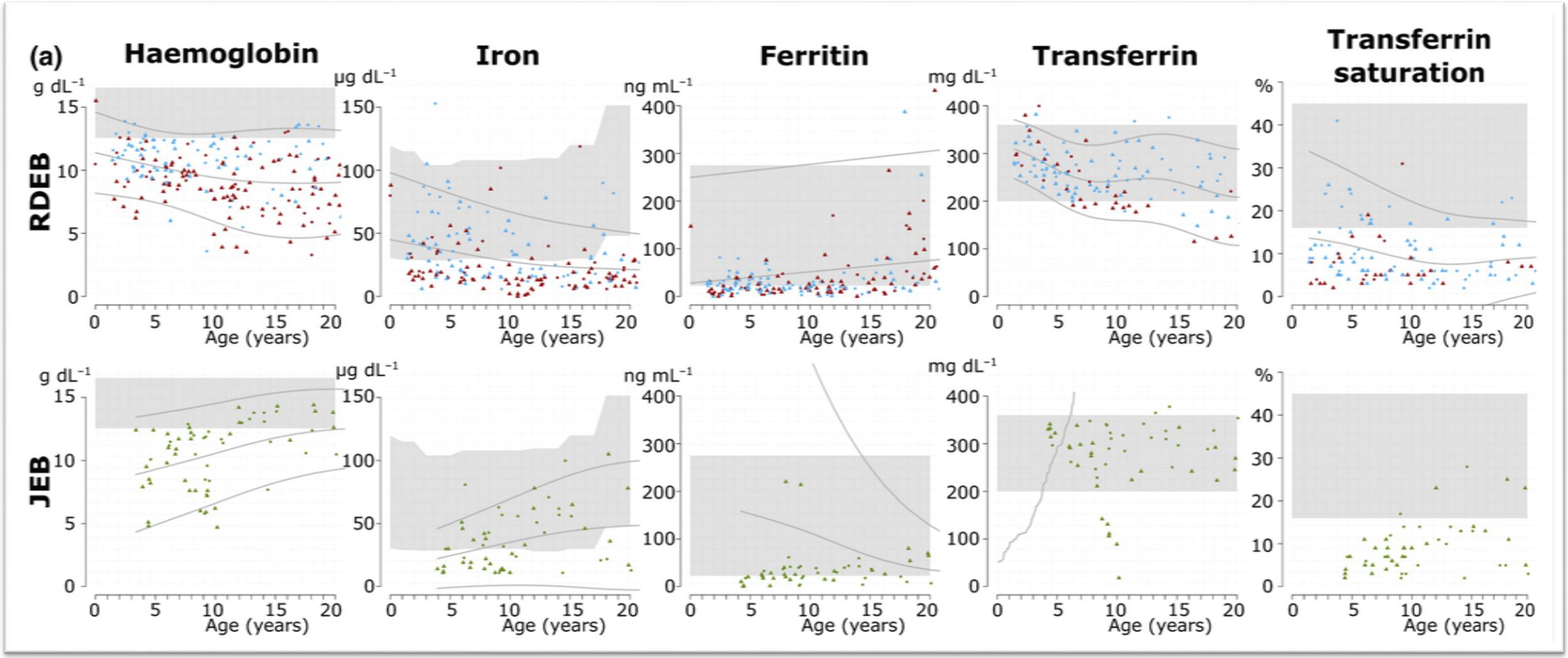
1) National EB Registry (over 2,600 patients seen from 1986-1995). Fine J-D et al. Epidermolysis Bullosa, 1999.
2) Australian EB Registry (169 patients reported; JEB includes JEB-I only). Hwang et al. Int J Women's Dermatol, 2015.
3) Freiburg referral center (200 patients, ages 0-25). Reimer et al. Br J Dermatol, 2020.

Range of hemoglobin values in EB



Australian EB Registry (169 patients).
Hwang et al. Int J Women's Dermatol, 2015.

Hemoglobin and iron studies in RDEB and JEB

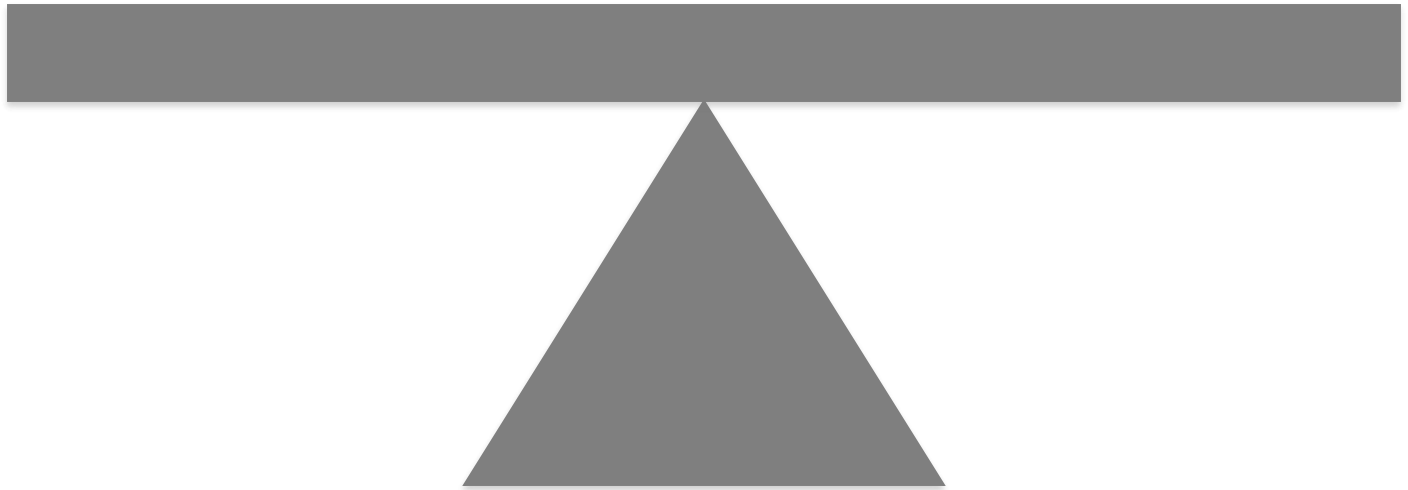


Freiburg referral center (200 patients, ages 0-25). Reimer et al. Br J Dermatol, 2020.

Pathophysiology: normal iron “steady state”

Iron intake:
-Food
-Dietary supplements

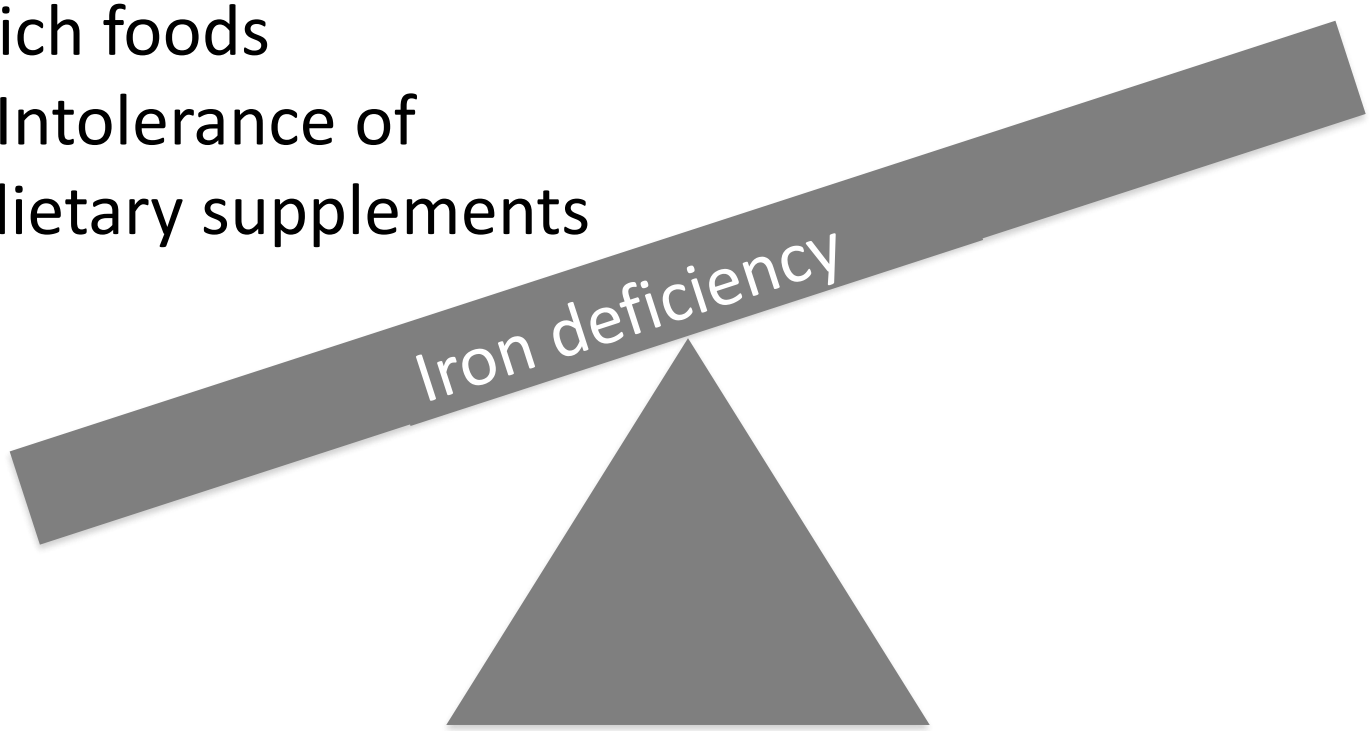
Iron loss:
-Skin
-GI



Anemia in EB is multifactorial

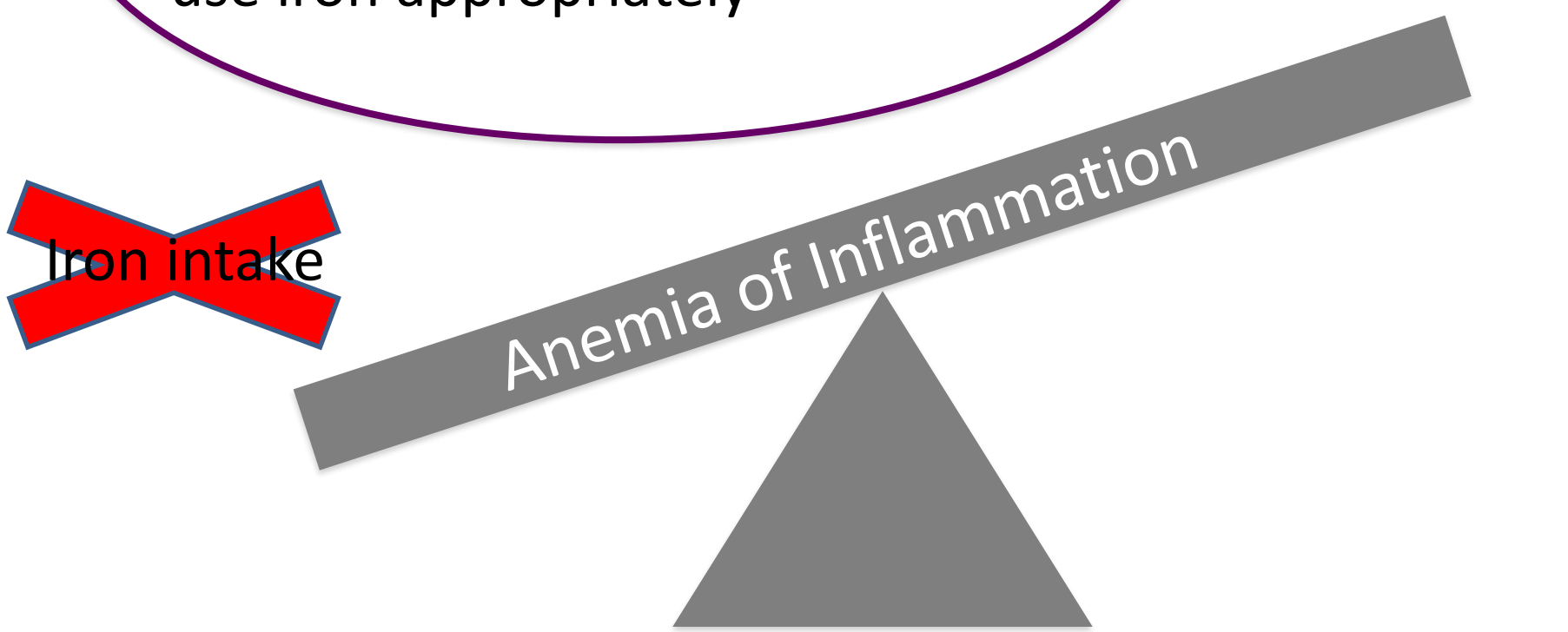
Iron intake:
-Difficulty eating iron rich foods
-Intolerance of dietary supplements

Iron loss:
-Bleeding from skin and GI tract

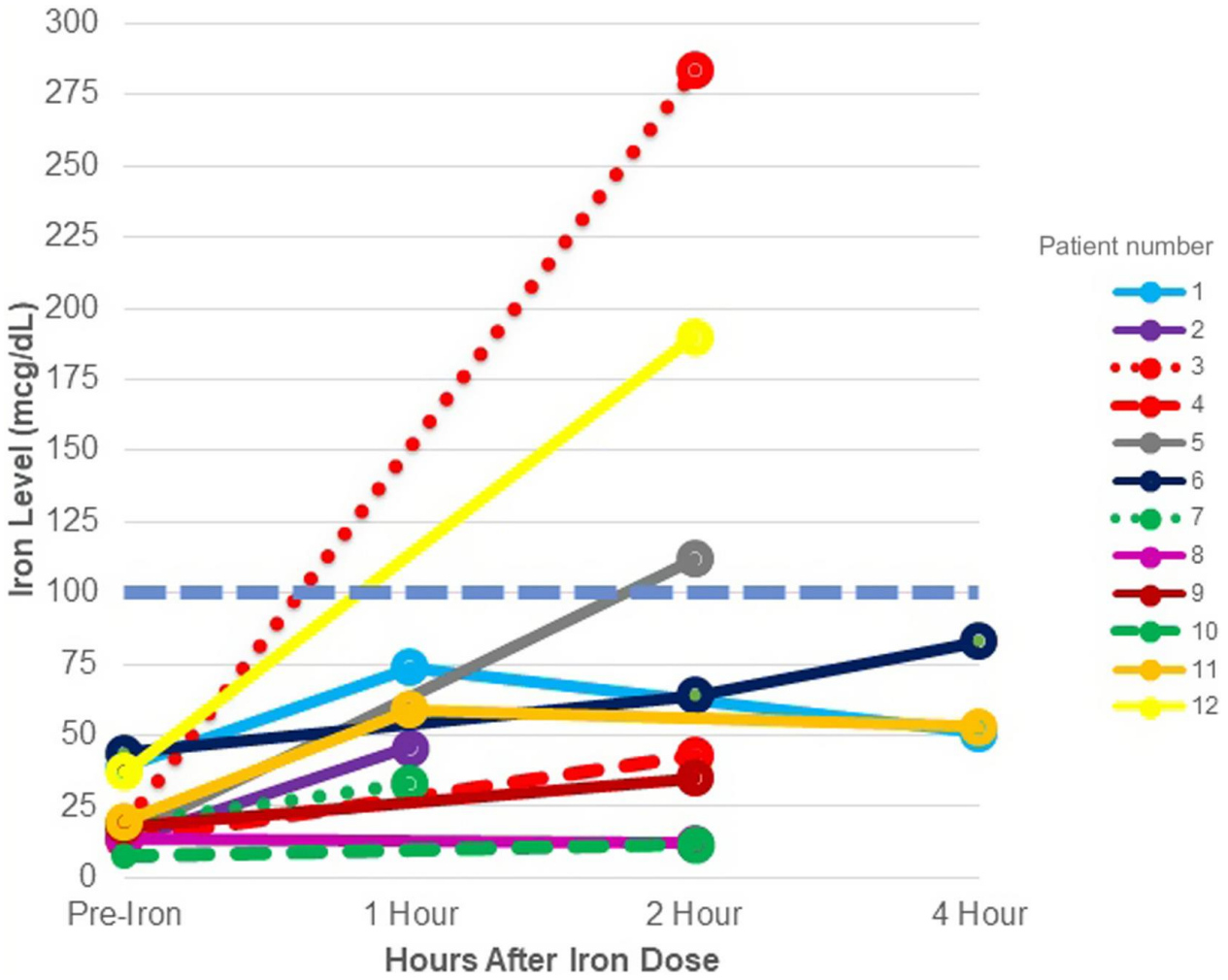


Anemia in EB is multifactorial

Inflammation interferes with iron absorption and the body's ability to use iron appropriately



Poor iron absorption in EB



Augsburger BD et al. Pediatric Dermatology, 2020.

Liy-Wong *et al.*
Orphanet Journal of Rare Diseases (2023) 18:38
https://doi.org/10.1186/s13023-022-02448-w

Orphanet Journal of
Rare Diseases

REVIEW Open Access

Consensus guidelines for diagnosis and management of anemia in epidermolysis bullosa

Carmen Liy-Wong[1*], Cristina Tarango[2], Elena Pope[3], Thomas Coates[4], Anna L. Bruckner[5], James A. Feinstein[5], Agnes Schwieger-Briel[6], Lynne D. Hubbard[7], Clapham Jane[8], Mauricio Torres-Pradilla[9], Matija Zmazek[10^] and Irene Lara-Corrales[3]

Abstract

Background Anemia is a common complication of severe forms of epidermolysis bullosa (EB). To date, there are no guidelines outlining best clinical practices to manage anemia in the EB population. The objective of this manuscript is to present the first consensus guidelines for the diagnosis and management of anemia in EB.

Results Due to the lack of high-quality evidence, a consensus methodology was followed. An initial survey exploring patient preferences, concerns and symptoms related to anemia was sent to EB patients and their family members. A second survey was distributed to EB experts and focused on screening, diagnosis, monitoring and management of anemia in the different types of EB. Information from these surveys was collated and used by the panel to generate 26 consensus statements. Consensus statements were sent to healthcare providers that care for EB patients through EB-Clinet. Statements that received more than 70% approval (completely agree/agree) were adopted.

Conclusions The end result was a series of 6 recommendations which include 20 statements that will help guide management of anemia in EB patients. In patients with moderate to severe forms of EB, the minimum desirable level of Hb is 100 g/L. Treatment should be individualized. Dietary measures should be offered as part of management of anemia in all EB patients, oral iron supplementation should be used for mild anemia; while iron infusion is reserved for moderate to severe anemia, if Hb levels of > 80–100 g/L (8–10 g/dL) and symptomatic; and transfusion should be administered if Hb is < 80 g/L (8 g/dL) in adults and < 60 g/L (6 g/dL) in children.

Keywords Epidermolysis bullosa, Anemia, Recessive dystrophic epidermolysis bullosa, Iron deficiency, Chronic anemia of inflammation

Evaluating for anemia

- History and physical examination
- Laboratory testing to confirm diagnosis and assign severity
  - Complete blood count
  - Iron studies: ferritin, serum iron, total iron-binding capacity (TIBC), transferrin saturation, soluble transferrin receptor
  - Reticulocyte count
  - C-Reactive Protein

Anemia is diagnosed when hemoglobin is below normal

World Health Organization (WHO) definitions of anemia

Population	Anemia			
	Non-anemia	Mild[a]	Moderate	Severe
Children 6–59 months of age	110 or higher	100–109	70–99	Lower than 70
Children 5–11 years of age	115 or higher	110–114	80–109	Lower than 80
Children 12–14 years of age	120 or higher	110–119	80–109	Lower than 80
Non-pregnant women (15 years of age and above)	120 or higher	110–119	80–109	lower than 80
Pregnant women	110 or higher	100–109	70–99	Lower than 70
Men (15 years of age and above)	130 or higher	110–129	80–109	Lower than 80

Initiation and frequency of laboratory testing depends on EB severity

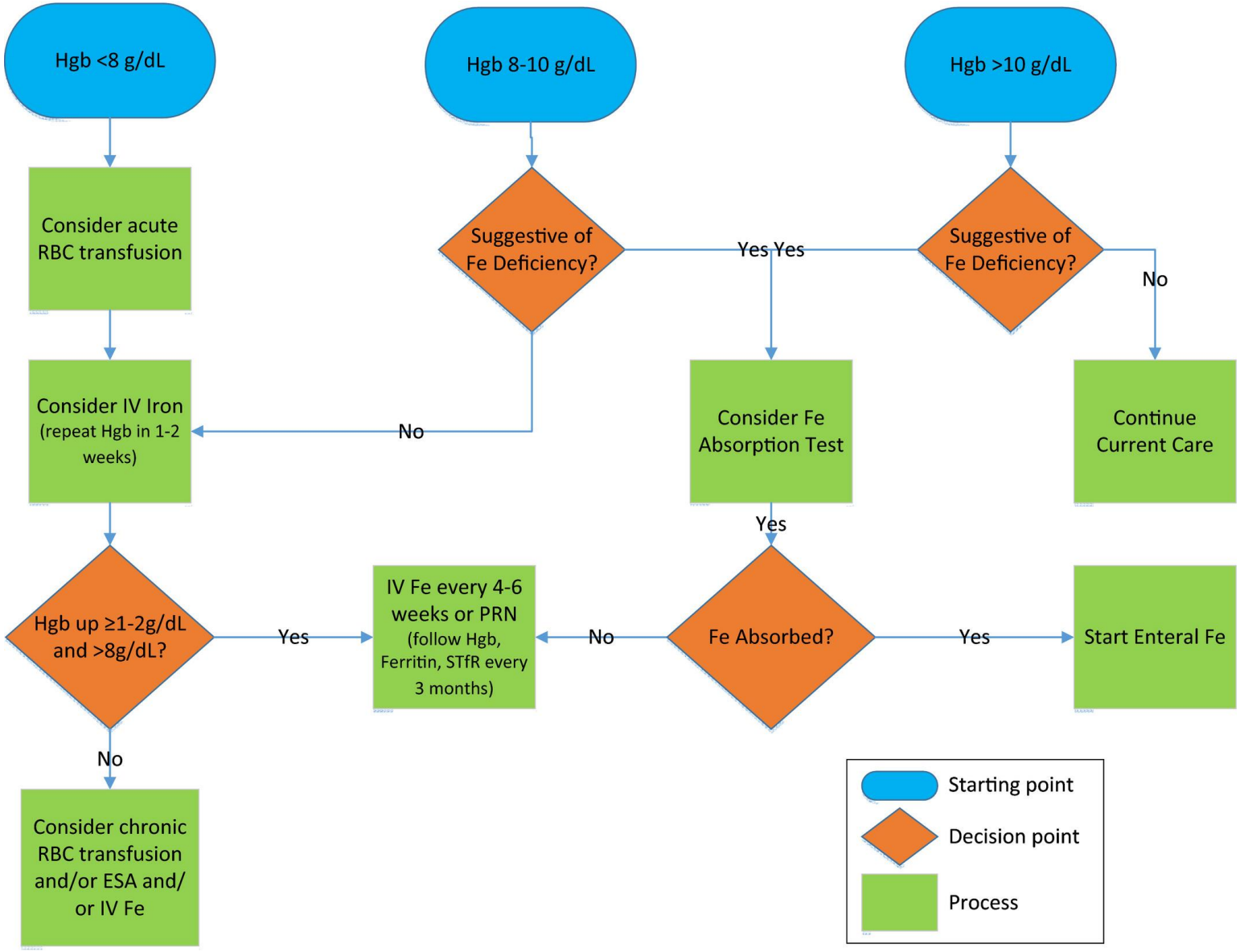
- For severe or generalized forms of EB:
  - Initial tests at time of diagnosis
  - Recheck every 6 months
  - Check when symptomatic
- For moderate forms of EB:
  - Start screening at 1 year of age
- For EB simplex
  - Based on symptoms

Managing anemia in severe EB

- Treat the whole patient
- Prevention
  - Include iron rich foods in diet
    - See recommendations in Consensus Guidelines
  - Consider daily multivitamin with iron
  - Optimize wound healing and other care

RDEB management algorithm

Simpson B et al. Pediatric Dermatology, 2018



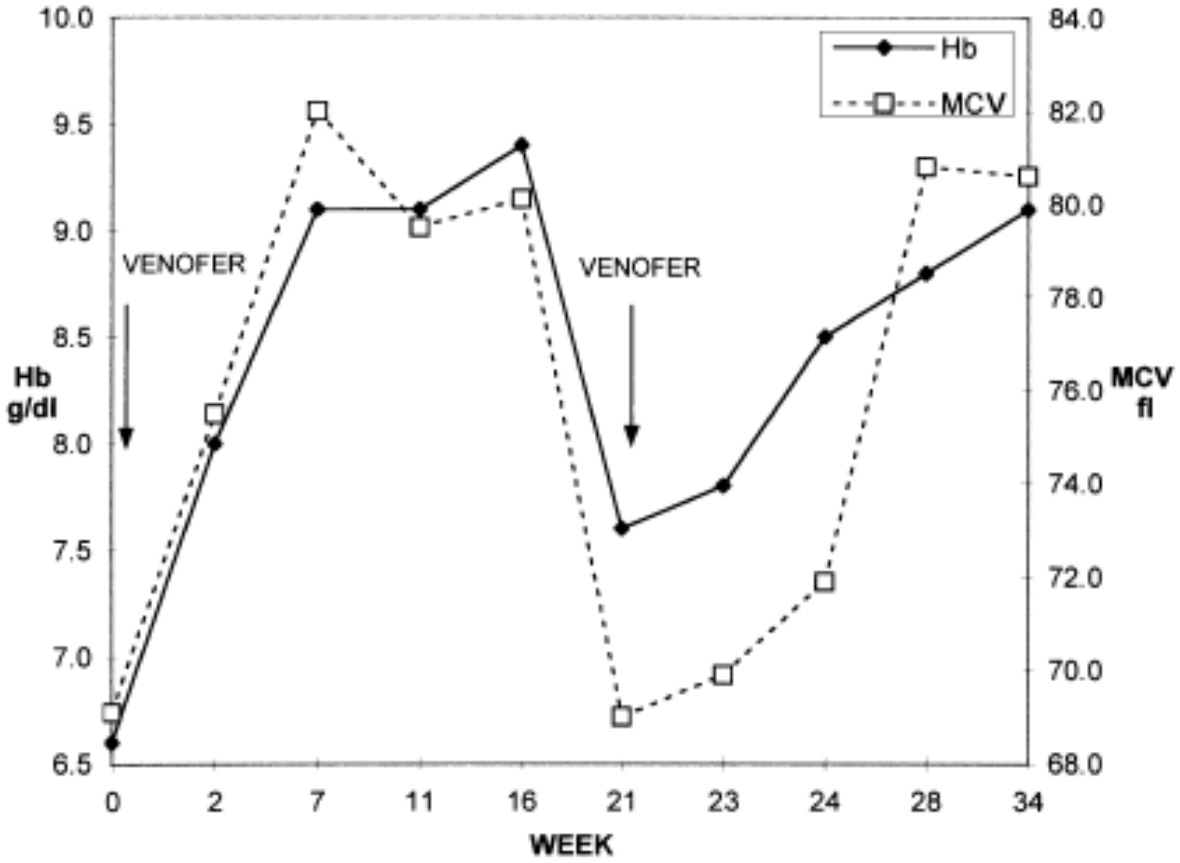
Oral iron for mild anemia

- Many forms available
  - Use what is available locally
  - See recommendations in Consensus Guidelines
- Every other day dosing
- Needs to be tried for at least 4 weeks
- Disadvantages:
  - Some forms taste terrible
  - Constipation
  - Poor absorption

Intravenous iron

- Bypasses poor absorption in the GI tract
- May help reduce need for transfusions
- Disadvantages:
  - IV access, several infusions needed over time
  - Allergic reactions (less common with newer forms of iron)

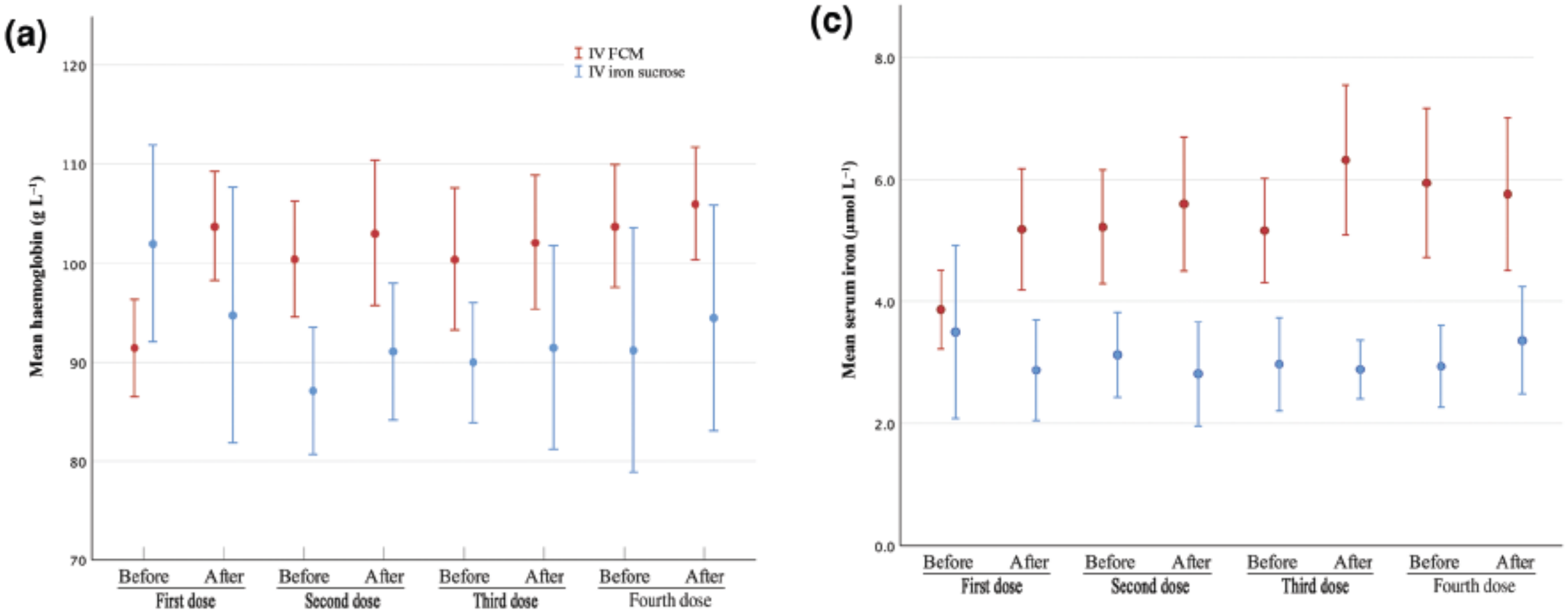
Intravenous iron in severe RDEB



- While the combination of IV iron and erythropoietin has shown benefit in small case series, the incremental benefit (if any) of erythropoietin is not clear

Atherton DJ, et al. Br J Dermatol 1999;140:773.

Ferric carboxymaltose has advantages over iron sucrose (in adults with EB)



Alheggi A et al. Br J Dermatol 2023;188:306-7.

Red blood cell transfusion

- Rapidly restores hemoglobin
  - Treatment of severe anemia (hemoglobin <7-8 g/dl)
  - Preparation for surgery, procedures
- Disadvantages:
  - IV access
  - Transfusion reactions
  - Risk of acquired infection
  - Iron overload and subsequent complications?

Assess (and reassess) outcomes

- Successful management of anemia includes
  - Improvement of symptoms
  - Improvement of laboratory parameters

Anemia: summary and conclusions

- Anemia is common in JEB and RDEB and compromises health and quality of life
- Both iron deficiency and inflammation play a role
- Oral iron has both utility and limitations
- IV iron is effective for moderate to severe anemia in EB
- Transfusions are indicated for severe anemia or when rapid improvement is needed

Acknowledgements

- Mentors
- Collaborators
- Funders
- Advocates
- Patients with EB and their families