



# Living with Thalassaemia

## Thalassaemia Treatment

Prof. Yesim AYDINOK  
Ege University Hospital  
Department of Paediatric Haematology  
Director of Hospital Blood Bank  
Izmir - Turkey

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# Treatment strategies in Thalassaemia

## Key elements of treatment

- Transfusion
- Iron chelation

## Supportive treatments

- Splenectomy
- Monitoring and managing organ disturbances
- Prevention and treatment of infections

## Cure

- Stem cell transplantation

# Treatment strategies in Thalassaemia

## Key elements of treatment

- Transfusion
- **Iron chelation**

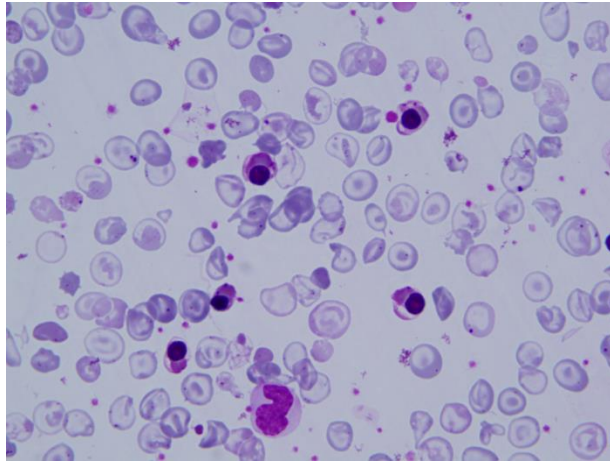
## Supportive treatments

- Splenectomy
- Monitoring and managing complications
  - cardiac, liver, endocrine
- Prevention and treatment of infections

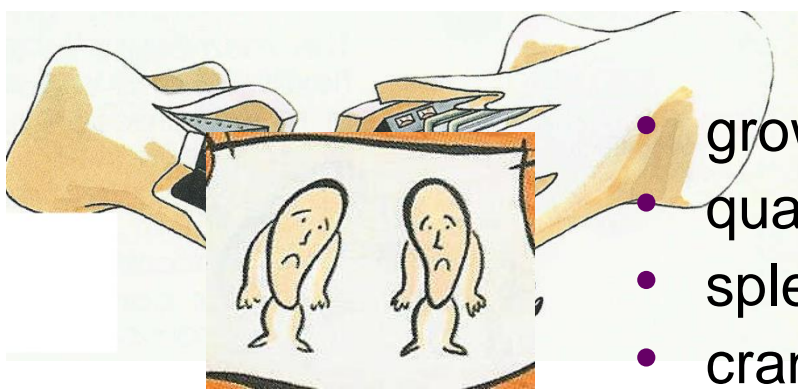
## Cure

- Stem cell transplantation

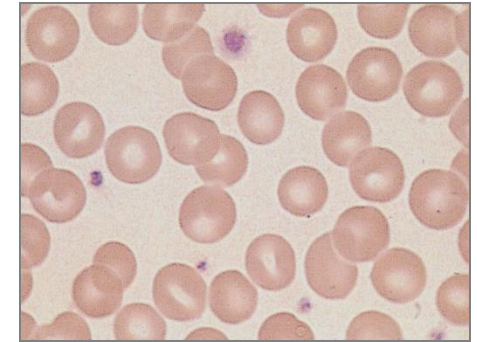
# Why do thalassaemia patients need transfusion?



Red cells of thalassaemia patients



Normal red cells



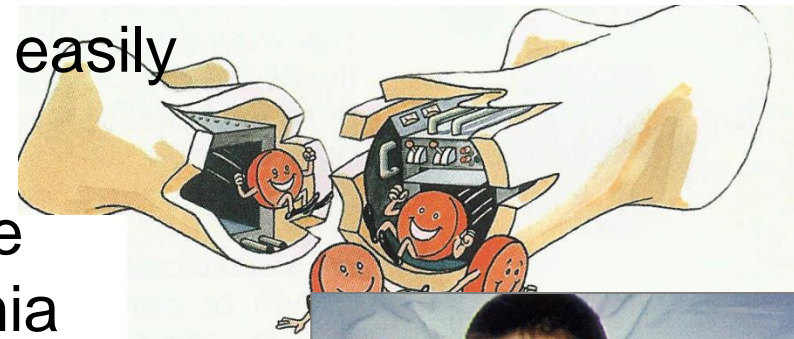
Abnormal red cells are produced and breakdown easily



severe anaemia

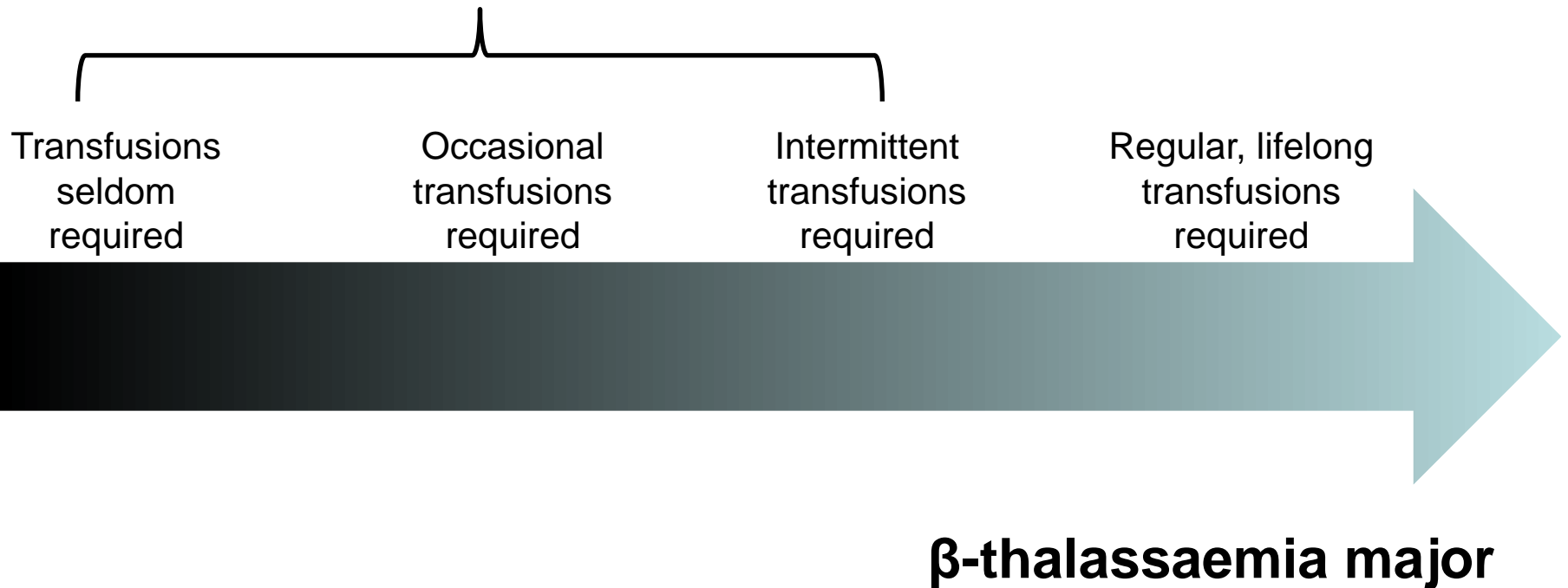


- growth is impaired
- quality of life is diminished
- spleen size increases progressively
- cranial and a facial distortion



# Spectrum of transfusion requirement in thalassaemia

## $\beta$ -Thalassaemia intermedia



# Sources of iron accumulation in thalassaemias

## Thalassaemia intermedia



Increased absorption of iron  
(primary source of iron)  
4 mg/day



Episodic transfusion  
(secondary source of iron)

- surgeries
- pregnancy
- infections
- etc.

## Thalassaemia major



Regular blood transfusions  
(primary source of iron)

- 1 unit blood contains 200 mg iron
- Transfusions by 2-4 units/month
- Annual intake; 5000-10000 mg



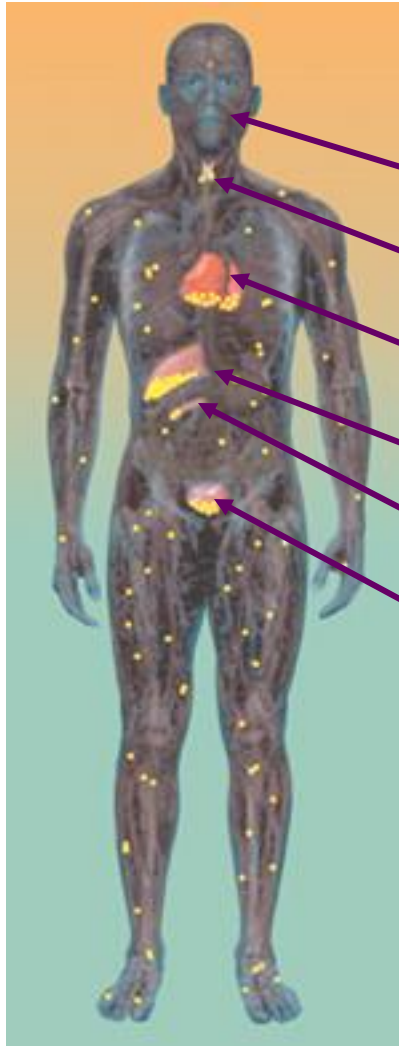
Increased absorption of iron  
(secondary source of iron)

**The body has no mechanism for excreting excess iron**

*Under normal conditions, iron absorption and loss are balanced at ~1mg/day*

# Organ systems susceptible to iron overload

## Clinical sequel of iron overload



- |           |   |                            |
|-----------|---|----------------------------|
| Pituitary | → | impaired growth & puberty  |
| Thyroid   | → | hypothyroidism             |
| Heart     | → | cardiac failure            |
| Liver     | → | hepatic failure            |
| Pancreas  | → | diabetes mellitus          |
| Gonads    | → | diminishes sexual function |

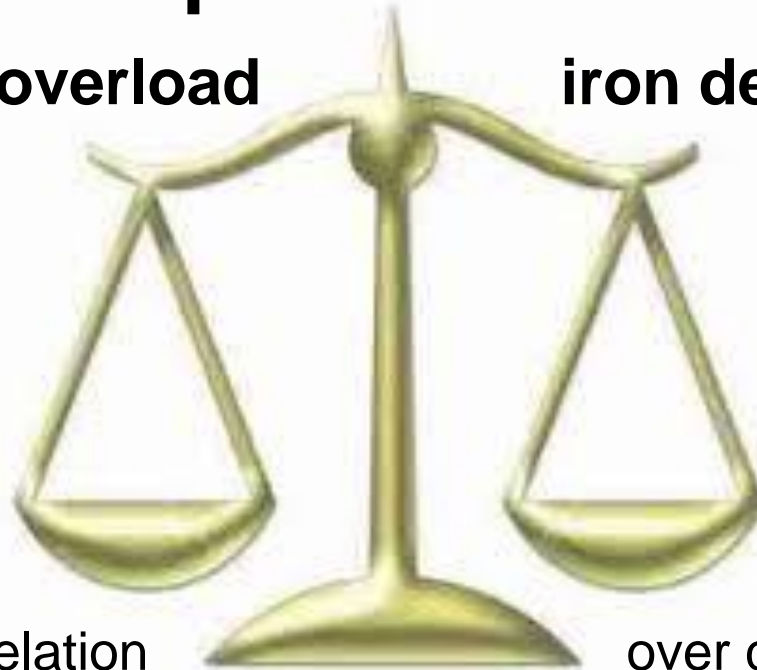
**Untreated iron overload results in damage to the liver, hormon secreting glands and most importantly to the heart**

# The assessment and monitoring of iron burden

## Optimal balance

iron overload

iron depletion



inadequate iron chelation  
can not prevent iron overload  
and is resulted with organ damage

over chelation may lead to  
depletion of iron that is needed  
for normal tissue metabolism



# Assessment of body iron stores

## Serum ferritin

- Representative of storage iron
- Easy to measure from 1 spoon blood
- monthly or bi-monthly monitoring is recommended

## Measurement of organ iron stores by MRI machine

- liver iron concentration;
  - yearly monitoring whenever available
- cardiac iron;
  - yearly monitoring after 10 years old



# Management of iron clearance therapy in thalassemia major

Iron clearance therapy is started when;

- patients have received 10-20 times blood transfusions
- serum ferritin reaches to 1000  $\mu\text{g/L}$
- liver iron exceeds 3.2 mg iron
- and maintained;

Serum Ferritin ( $\mu\text{g/L}$ )	Liver iron (mg Fe/ g dw)	Cardiac iron (ms)	Body iron burden
<100	0.6–1.2	>20	Normal
<b>500-1000</b>	<b>3.2–7.0</b>	<b>&gt;20</b>	<b>Optimal</b>
1000-2500	> 7.0–15	10-20	Moderate
>2500	> 15	<10	Severe

# Evolution of iron chelation therapy

Standard management of iron overload

1980

® Desferal



applicable by pump and syringe to under the skin by a needle during 10 hours at least 5 days a week

1999

® Ferriprox

pill and syrup forms are available, swallow 3 times a day



2005

® Exjade

water soluble tablet form, swallow once daily



Desferrithiocin

2010

1960

1970

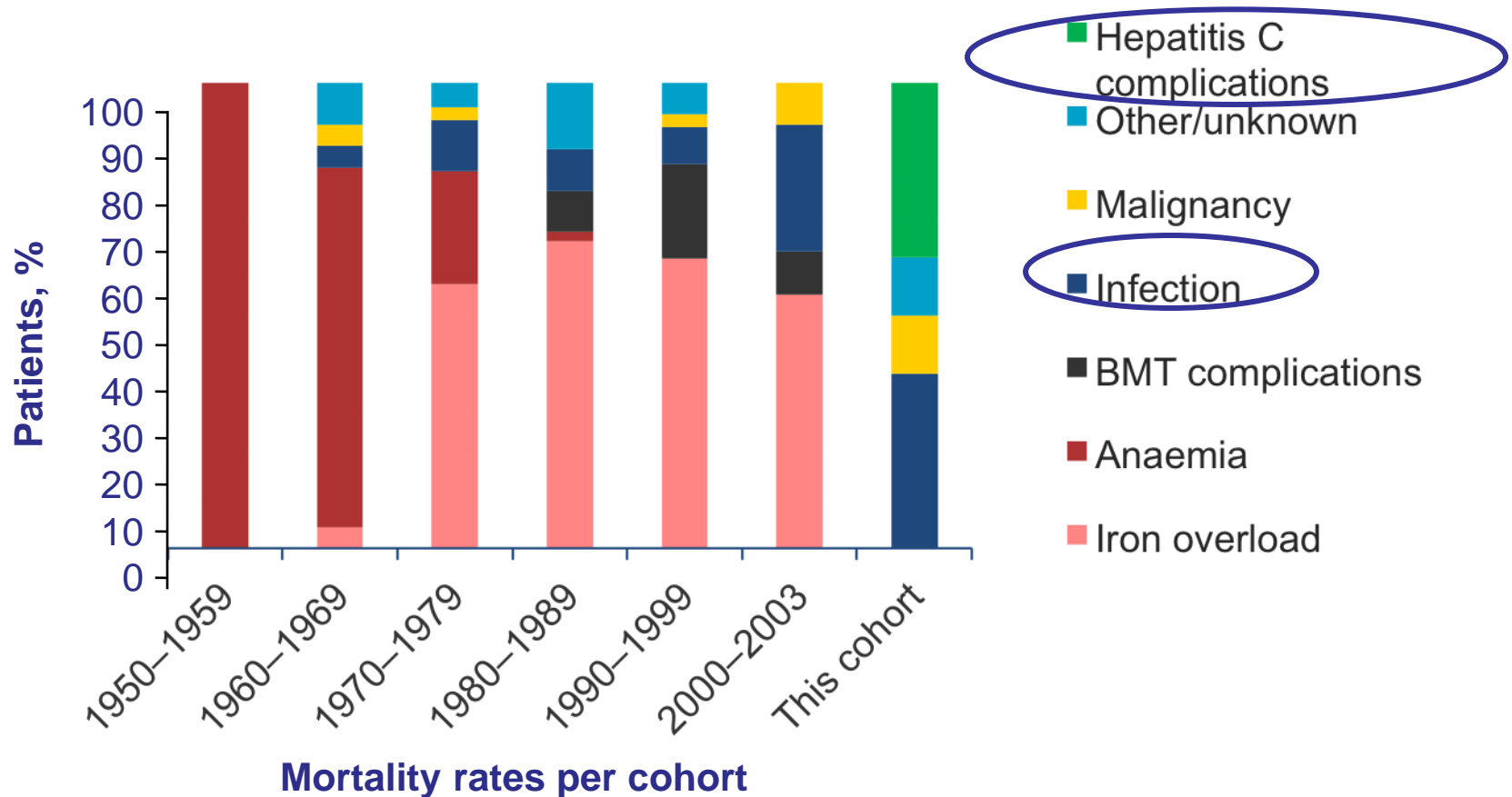
1980

# Comparison of iron chelators

Property	® Desferal	® Ferriprox	® Exjade
Usual dose	20–60 mg/kg/day	75–100 mg/kg/day	10–40 mg/kg/day
2-6 years-old	first-line	limited experience	second line*
>6 years old	first-line	second line	first-line
Side effects	local reactions, eye & ear toxicity bone abnormalities Yersinia infections	prone to infection (1%) abdominal discomfort nausea, vomiting (30%) joint pain(4-40%) liver (7%) zinc deficiency	abdominal discomfort nausea, vomiting (15%) transient rash (12%) liver (8%) kidney toxicity (6%)
Advantages	long term experience	<b>best for cardiac iron</b>	once daily dosing <b>effective in removal of liver and heart iron</b>
Disadvantages	<b>compliance</b>	<b>less effective in liver weekly blood count</b>	cost

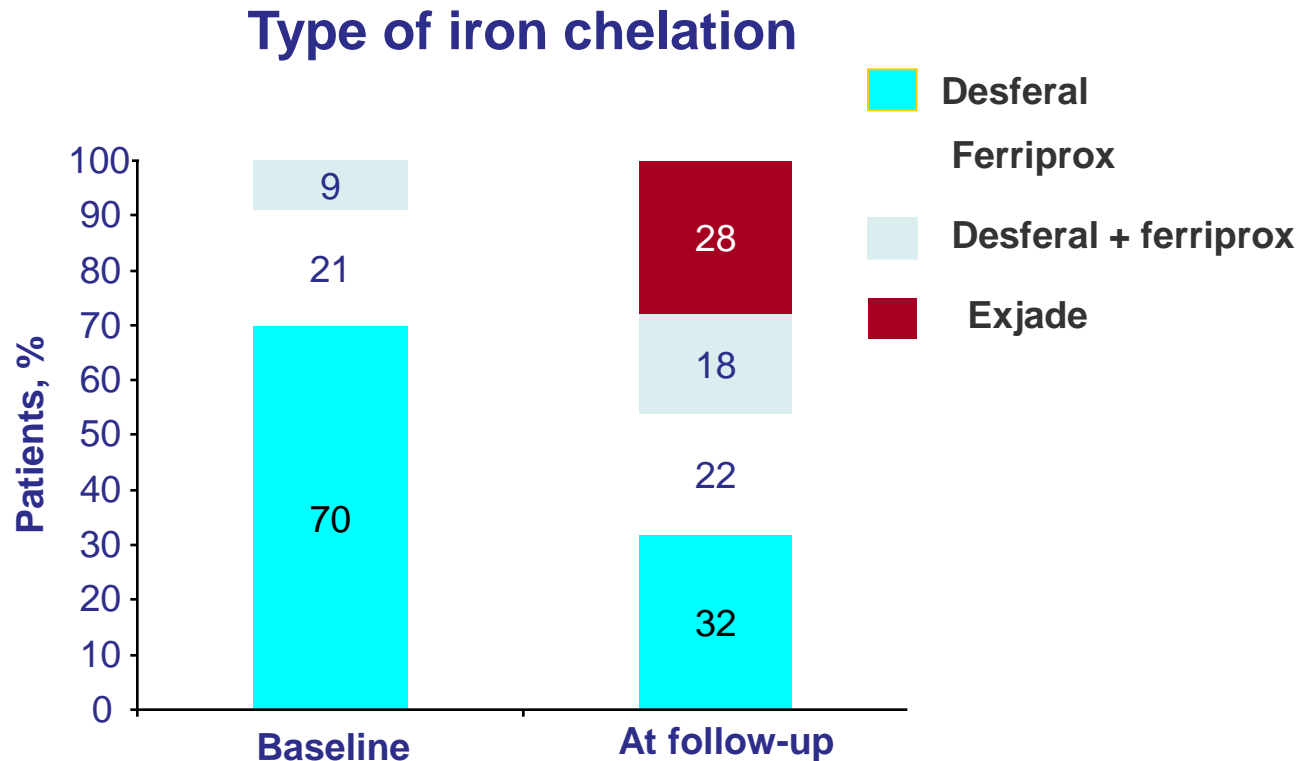
\* *First line in US and rest of the world*

# Cardiac iron overload-related mortality is no longer a leading cause of death



Use of modern iron chelation therapy and regular CMR monitoring has dramatically reduced the cardiac iron overload-related mortality in the Red Cell Disorders Unit

# In 2 UK centers, about 50% of patients with $\beta$ -thalassaemia currently receive oral iron chelators (Ferriprox and Exjade)



# Current chelation practice of patients with $\beta$ -thalassaemia in Ege University Thalassaemia Center

