




# NUTRITIONAL

## IRON DEFICIENCY ANEMIA

### (缺铁性贫血)

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# Case study

- Boy , 9 months
- Pale for 9 months, cough 3days
- Preterm twins, birth weight 2.7kg: Breast feeding until now

date	WBC	N	L	RBC	Hb	MCV	MCH	MCH C	PLT	Ret
4.24	24.28	0.75	0.25	4.05	56	61.5	13.8	225	779	
4.25	26	0.53	0.42	3.95	55	61	13	227	735	0.022
4.26	16	0.24	0.71	4.31	68	63	15	27	624	0.022

 Hypochromic microcytic anemia ?

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# Case study

- Hypochromic microcytic anemia
- HbF1.40, HbA2 1.80%, 血红蛋白电泳 (-), SI 6.15(11-30)umol/L, TIBC 85 (50-70)umol/L, TS 7.2%.
- 4.25 CR: 双肺纹理增多、紊乱、模糊、中内带见片絮影, 双肺充气过度, 心影胸腺部分重叠。肺炎。

What kind of Anemia is this?

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# Classification- Etiology

造血减少所致贫血

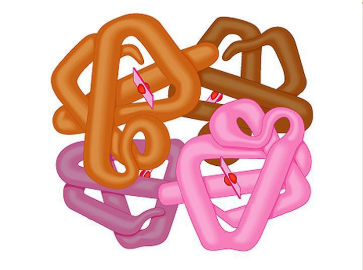
Reduced capacity to produce red blood cells--deficiency syndrome

溶血性贫血: Hemolysis

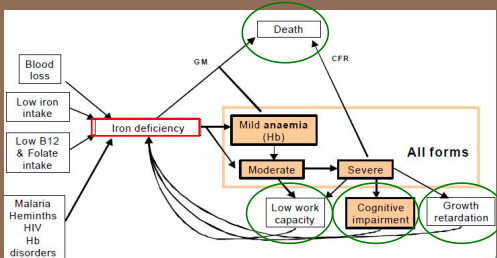
失血性贫血: Blood Loss

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# Iron and Hemoglobin



# The impact of IDA



```

graph TD
    ID[Iron deficiency] --> MA[Mild anaemia Hb]
    ID --> M[Moderate]
    ID --> S[Severe]
    S --> LWC[Low work capacity]
    S --> CI[Cognitive impairment]
    S --> GR[Growth retardation]
    MA --> LWC
    MA --> CI
    MA --> GR
    M --> LWC
    M --> CI
    M --> GR
    ID --> D[Death]
    MA --> D
    M --> D
    S --> D
    ID --> LWC
    ID --> CI
    ID --> GR
    ID --> L[Low iron intake]
    ID --> B[Blood loss]
    ID --> F[Low B12 & Folate intake]
    ID --> M1[Malaria Hemiphs HIV Hb disorders]
    
```

## CONTENTS

- INDUCTION
- IRON METABOLISM
- ✿ ETIOLOGY /PATHOGENESIS
- ✿ MANIFESTATIONS
- ✿ LABORATORY FINDINGS
- ✿ DIAGNOSIS & DIFFERENTIAL
- ✿ PREVENTION & TREATMENT



## INTRODUCTION

- **Definition of the iron deficiency anemia (IDA)**
  - 由于体内铁缺乏最终导致储存铁减少血红蛋白合成减少所致的贫血
  - N-IDA: The anemia caused by insufficient dietary iron uptake, in which the iron storage and hemoglobin synthesis decreased.

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## INTRODUCTION

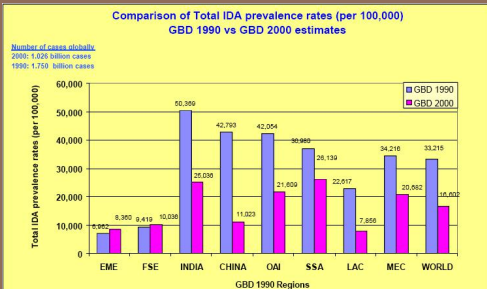
- **Clinical characteristics (临床特征)**
  - 贫血: ↓hemoglobin concentration, microcytic hypochromic anemia,
  - 铁生化: ↓ serum ferritin (SF), ↓ serum iron (SI), ↓transferrin saturation (TS)
  - 治疗反应: good response to iron therapy.
  - 年龄: 6mo to 3 yrs.
- **Incidence**

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## INTRODUCTION

- **The prevalence:**
  - In China (2004). an investigation from 9118 children in 15 provinces and 26 cities revealed that the prevalence
    - is 30.1% vs 16.8% for the children with 7 ~12mos
    - and 15.5% vs 4.4% for the children with 13 ~36mos
  - In the US
    - It is about 9% of 1-2 yr-olds are iron deficient; 3% have anemia.
    - Of adolescent girls, 9% are iron deficient and 2% have anemia.

## INTRODUCTION



## IRON METABOLISM

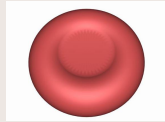
- **CONTENTS**
  - New born 75mg/kg
  - Children 35-70mg/kg
  - Adults
    - M 50mg/kg
    - F 35mg/kg
- **COMPARTMENT**
  - Hemoglobin 64%
  - Storage iron 30%
    - Ferritin-SF
    - hemosiderin
  - Myoglobin 3%
  - Enzyme iron 0.4%
  - Serum iron 0.4%

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## IRON METABOLISM

### • Iron sources

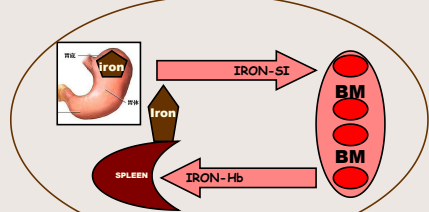
- Hemoglobin iron
- Dietary iron



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## IRON METABOLISM

- Iron sources: Hemoglobin iron + Dietary iron



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## IRON METABOLISM

### • Dietary iron

- High in iron
  - Red meat/ liver kidney/ oily fish
- Average iron
  - Beans / fortified cereals/ dark green vegetables/ dried fruit/ nuts and seeds
- Poor in iron
  - Milk (1.5 vs 0.5mg/L)

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## IRON METABOLISM

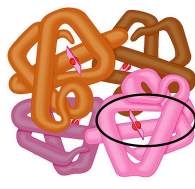
### • Iron absorption

<b>general absorption</b>	<b>1-20%</b>
- Meat/ fish/ chicken	10-25%
- Cereals/vegetables	1%
- Breast/cow's milk	50%/10%

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Fe

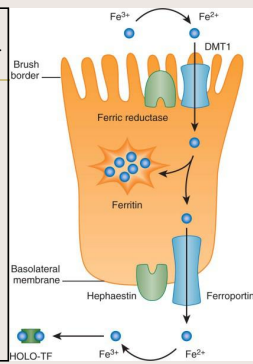


## Iron absorption and transportation

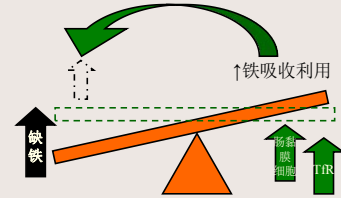


(图1)

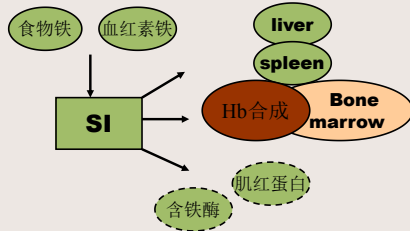
FIGURE 12-2 Duodenal iron transfer. Iron is taken up by enterocytes lining the duodenal villi. These absorptive cells start out as undifferentiated precursors in the intestinal crypts. Crypt cells appear to be programmed for an iron absorption "set-point" that is determined in response to iron needs. As the cells differentiate, they migrate up the villi and begin to express iron transporter proteins. According to current models, nonheme iron uptake occurs in mature enterocytes through the enzymatic reduction of iron, transmembrane import into the cell by DMT1, transmembrane export from the cell by ferroportin, and enzymatic oxidation by hephaestin before loading onto apotransferrin to produce diferric transferrin (HOLO-TF).  
*Nat Rev Genet. 2000;1:208-217.*



## 铁吸收的调节 REGULATION



## • Iron stores and utilizing



## IRON METABOLISM



### • Requirement and excretion

	<u>demand</u>	<u>excretion</u>
adults	1mg/d	1mg/d
4mo-3yr	1mg//kg	(15ug/kg/d)
premature	2mg/kg	

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## IRON METABOLISM



### • Summary and key points

- Iron compartment or function
  - Hb
  - Stores (SF - hemosiderin)
  - Myoglobin
  - Enzyme
  - Serum iron
- Iron sources
- Iron absorption and transportation
  - SF /SI /TIBC
- Iron daily requirement and excretion

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## ETIOLOGY & PATHOGENESIS

- **ETIOLOGY** 病因
  - Poor iron stores
  - Poor dietary intake of iron\*
  - Overdevelop
  - Chronic bleeding
  - Absorption problems

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## ETIOLOGY & PATHOGENESIS

- **Poor iron stores**
  - Premature birth
  - Multiple birth /Low weight birth
  - Cord blood
  - Mother iron reserve
- Poor dietary intake of iron\*
- overdevelop
- Blood loss and iron depletion

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## ETIOLOGY & PATHOGENESIS

- Poor iron stores
- **Poor dietary intake of iron\***
  - Milk and cereals
  - Factors influencing absorption
- Overdevelop
- Blood loss and iron depletion

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## ETIOLOGY & PATHOGENESIS

- Poor iron stores
- Poor dietary intake of iron\*
- **Overdevelop**
  - 3-5mo/ 1yr
  - Premature birth
  - Puberty
- Chronic bleeding

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## ETIOLOGY & PATHOGENESIS

- Poor iron stores
- Poor dietary intake of iron\*
- overdevelop
- **Chronic bleeding**
  - Cow's milk
  - Hookworm infection
  - Menstruating
  - Others:
    - idiopathic pulmonary hemosiderosis (肺含铁...)
    - ulcer, gastritis (溃疡、胃炎)
    - hemangioma, meckel diverticulum.



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## ETIOLOGY & PATHOGENESIS

- Poor iron stores
- overdevelop
- Poor dietary intake of iron\*
- Chronic bleeding
- **Absorption problems**
  - Diarrhea / Infection

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## ETIOLOGY & PATHOGENESIS

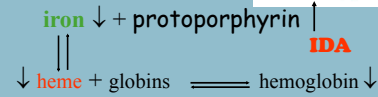
**QA:** Girl, 11 months, pale for one month, development is good, no black stool, no disease history, breast-fed only. Birth weight 3kg, now 10kg. Mother is in health. Diagnosis is IDA. The possible reason?

- A. poor iron store 先天储铁不足
- B. poor iron intake 铁摄入量不足
- C. overdevelopment 生长发育过快
- D. problem with iron absorption
- E. iron loss 铁丢失过多

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## ETIOLOGY & PATHOGENESIS

### • Pathogenesis



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## ETIOLOGY & PATHOGENESIS

- ID. Iron deficiency (铁减少期)
  - decreased iron store-SF
- IDE. Iron deficiency erythropoiesis (红细胞生成铁减少期)
  - decreased iron store-SF
  - Increase FEP
- IDA. Iron deficiency anemia (缺铁性贫血期)
  - decreased iron store-SF
  - Increased FEP
  - SI, TIBC, TS
  - Hypochromic/microcytic anemia

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## ETIOLOGY & PATHOGENESIS

### • Pathogenesis

- Hypochromic / microcytic anemia
  - ID. Iron deficiency
  - IDE. Iron deficiency erythropoiesis
  - IDA. Iron deficiency anemia
- Enzymes
- Immune function
- Skin/mucosal

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## CLINICAL MANIFESTATIONS

### • Features 特点

- Age: 6mo~3yrs
- The onset of the IDA
- The degree of anemia

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## CLINICAL MANIFESTATIONS

- Pallor 苍白
- Extramedullary hematopoiesis 髓外造血
  - The slight splenomegaly is found in 10-15% of the cases

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## CLINICAL MANIFESTATIONS

### • Moderate / Severe condition

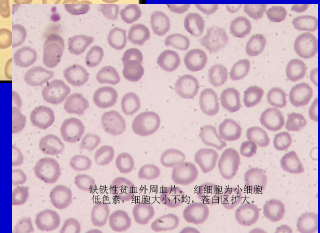
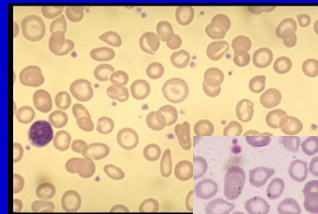
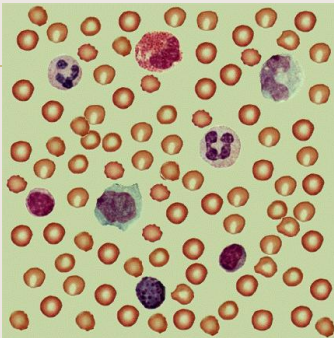
- Digestive system
  - 食欲减低、恶心呕吐、腹泻、舌炎、胃炎
- Cardiac function
  - tachycardia, cardiac dilatation and systolic murmurs are often present
- Neurology/ intellectual
  - 神萎或烦躁、头晕、耳鸣、注意力不集中、反应迟钝、学习能力和智力
- Immune function

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## LABORATORY FINDINGS

- Hemoglobin :
  - below the acceptable level for age
- Red cell indices:
  - $\downarrow$  MCV  $< 80$ fl,  $\downarrow$  MCH  $< 26$ ug,  $\downarrow$  MCHC  $< 0.31$ , high RDW
- Blood smear:
  - Hypochromics and microcytic with anisocytosis and poikilocytosis

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铁缺乏性贫血血片内，红细胞为小细胞低色素，细胞大小不均，宽分布大。

## LABORATORY FINDINGS

- Reticulocyte count:
  - is usually normal but in severe IDA associated with bleeding, a reticulocyte count of 3-4% may occur
- Platelet count
  - It varies from thrombocytopenia to thrombocytosis. Thrombocytopenia is more common in severe IDA; thrombocytosis is present when there is associated bleeding from the gut.
- Free erythrocyte protoporphyrin
  - FEPElevation occurs as soon as the body stores of iron are depleted, before microcytic anemia develops. An elevated FEPE level is therefore an indication for iron therapy even when anemia and microcytosis have not yet developed.

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## LABORATORY FINDINGS

- Serum ferritin
  - It reflects the level of body iron stores; it is quantitative, reproducible, specific and sensitive. A concentration of less than 12ng/ml is considered diagnosis of iron deficiency.
- Serum iron and iron saturation percentage
  - $\downarrow$  SI:  $< 9-10.7 \mu\text{mol/L}$  ( $12.8-31.3 \mu\text{mol/L}$ )  
or  $< 50-60 \mu\text{g/dl}$  ( $75-175 \mu\text{g/dl}$ )
  - $\uparrow$  TIBC:  $> 62.7 \mu\text{mol/L}$  ( $> 350 \mu\text{g/dl}$ )
  - $\downarrow$  TS:  $< 15\%$  ( $30-50\%$ )



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## LABORATORY FINDINGS

- Serum transferrin receptor levels (STfR)
  - Its sensitive and correlates with Hb and other Lab parameters of iron status.
  - It is increased in instances of hyperplasia of erythroid precursors such as IDA and thalassemia
  - It is unaffected by infection and inflammation
- Bone marrow: Erythroid hyperplasia ;Stainable iron↓



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	Normal	ID	IDE	IDA
Marrow iron	+ ~ ++	↓	↓	0
SF (ug %)	100±60	↓	↓↓	<10-20
FEP			↑	↑
SI				↓
TIBC				↑
TS				↓
Hb				↓
MCV				↓
MCH				↓↓

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## DIAGNOSIS & DIFFERENTIAL

### • Diagnosis

- Impression
  - 6月-24月/36月
  - 生产史、喂养史
  - 小细胞低色素性贫血
- Diagnosis: biochemical change
  - SF减低; FEP升高;
  - SI减低, TIBC升高, TS降低
- Proven by therapy



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Table 3-8 Diagnostic Tests for Iron-deficiency Anemia

1. Blood smear <ul style="list-style-type: none"> <li>a) Hypochromic microcytic red cells, confirmed by RBC indices:                     <ul style="list-style-type: none"> <li>i. MCV less than normal range of age</li> <li>ii. MCH less than 27.0pg</li> <li>iii. MCHC less than 30%</li> </ul> </li> <li>b) RDW greater than 14.5%</li> </ul>
2. Free erythrocyte protoporphyrin: elevated
3. Serum ferritin: decreased
4. Serum iron and iron binding capacity <ul style="list-style-type: none"> <li>a) Decreased serum iron</li> <li>b) Increased iron binding capacity</li> <li>c) Decreased iron saturation(16% or less)</li> </ul>
5. Serum transferrin receptor level: elevated
6. Bone marrow <ul style="list-style-type: none"> <li>a) Delayed cytoplasmic maturation</li> <li>b) Decreased or absent stainable iron</li> </ul>
7. Therapeutic responses to oral iron <ul style="list-style-type: none"> <li>a) Reticulocytosis with peak 5-10 days after institution of therapy</li> <li>b) Following peak reticulocytosis Hb level rises on average by 0.25-0.4g/dl/dy or hematocrit rises 1%/day</li> </ul>

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## DIAGNOSIS & DIFFERENTIAL

### • Differential

- 地中海贫血 alassemia
- Chronic & inflammatory diseases
- 肺含铁血黄素沉着症 Pulmonary hemosiderosis
- 铁粒幼细胞贫血 Siderblastic anemia

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## DIAGNOSIS & DIFFERENTIAL

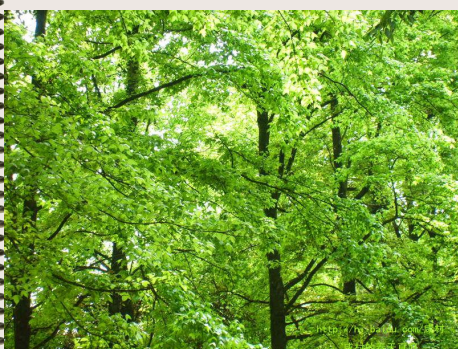
### • Differential — Thalassemia

- 是血红蛋白珠蛋白肽链合成障碍引起的一组遗传性溶血性贫血。
- 地区性明显, 有家族史;
- 轻型临床上难以区别, 重型常有特殊面容, 肝脾肿大明显;
- 外周血涂片可见靶形红细胞和有核红细胞
- 血红蛋白检查显示胎儿血红蛋白水平异常增高或血红蛋白电泳出现异常成分区带;
- 血清铁增高, 骨髓铁粒幼细胞增多



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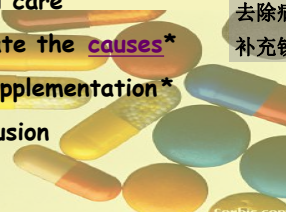
## PREVENTION&TREATMENT



原则

去除病因  
补充铁剂

- General care
- Eradicate the **causes**\*
- Iron **supplementation**\*
- Transfusion



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## 预防和治疗 (Treatment)

### • Q A

- 哪些因素或病因是可以预防的?
- 哪些因素或病因是可以去除的?

## 预防(Prevention)

### • Nutritional Counseling 喂养指导

- Maintain breastfeeding for at least 6mo
- Use an iron -fortified infant formula until 1 year age
- Use iron -fortified cereal from 6mo-1year
- Facilitators of iron absorption such as VC-rich foods, meat, fish and poultry should be included in the diet and inhibitors of iron absorption such tea, phosphate and phytates common in vegetarian diets should be eliminated

## 预防(Prevention)

### • Preterm 早产儿

- who is fed human milk should receive a supplement of elemental iron at 2 mg / kg per day, by 1 mo -12mo
- Who is fed a standard formula will receive approximately 2 mg/kg per day of iron



## 预防(Prevention)

### • Term, Breastfed Infants

- Therefore, at 4 months of age, breastfed infants should be supplemented with 1 mg/kg per day of oral iron until appropriate iron-containing complementary foods are introduced in the diet

### • Term, formula-fed infants

- the iron needs for the first 12 months of life can be met by a standard infant formula and the introduction of iron-containing complementary foods after 4 to 6 months of age, including iron-fortified cereals.
- Whole milk should not be used before 12 completed months of age.



## TREATMENT

- **Iron supplementation** (补铁)
  - Elemental iron: 4-6mg/kg/d
  - Oral iron medication
    - Types-ferrous form
    - Administration
      - Between meals
      - Vitamin C
      - Course: 6-8weeks after Hb normalization

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**Table: Ferrous salts and the iron contents**

Ferrous Salts	4mg/kg/d
Ferrous sulfate (20%) (硫酸亚铁)	20mg/kg/d
ferrous fumarate (30%) (富马酸亚铁)	13mg/kg/d
Ferrous gluconate (11%) (葡萄糖酸亚铁)	40mg/kg/d

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## TREATMENT

- **Iron supplementation** (补铁)
  - Parenteral iron (胃肠外注射铁)
    - Indication: intolerant to oral iron or absorption problem
    - types:

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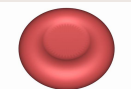
## IRON THERAPY RESPONSE (from Nelson)

time	response
12-24 hr	Replacement of iron enzymes, subjective improvement
36-48 hr	Initial marrow response: erythroid hyperplasia
48-72 hr	Reticulocytes peaking 5-7d
4-30 days	Hemoglobin level ↑
1-3 mo	Replenish of stores

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## TREATMENT

- **Transfusion** (输血)
  - Indications
    - Severe anemia
    - Infection
    - Pre-operation
  - Component: red blood cells
  - Volume: Hb <30g/L, 3-5ml/kg  
Hb 30-60g/L, 5-10ml/kg
  - Attentions



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Review these contents after class, try to make the summary on:

1. The etiology of IDA and personal history
2. Laboratory findings according to the stages
3. Diagnosis and Differentials: esp with thalassemia
4. Important treatment: oral iron related
5. MA diagnosis
6. Case study



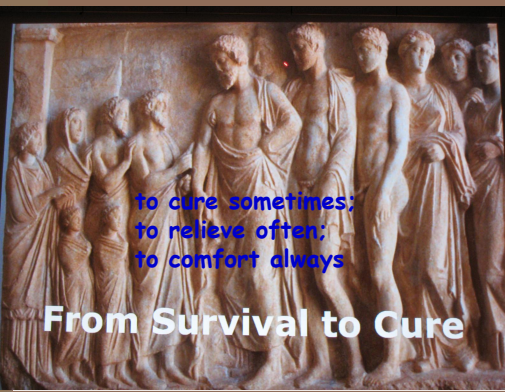
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## CASE STUDY

- 男孩，9月，发现面色苍黄9+月，发热咳嗽气促3+天就诊。
- 体温38.8度，咽充血，R52次/分，肺音清，HR132次/分，有力，律齐；肝脾未触及
- 血常规
  - WBC  $24.28 \times 10^9/L$ , N0.75, L0.25,
  - RBC  $4.05 \times 10^{12}/L$ , Hb56g/L, MCV61.5fl, MCH13.8g/L, MCHC225g/L,
  - PLT  $779 \times 10^9/L$
  - 外周血红细胞大小不均，苍白区扩大。

## CASE STUDY

- Q1: 进一步询问病史?
- A1:
  - 生产史: 第3胎, 第4产, 孕32+4周, 双胎自然分娩, 双胎之小, 出生体重2.70kg;
  - 喂养史: 单纯母乳喂养, 6月加稀饭, 偶尔鸡蛋、肉食
  - 反复感冒
- Q2: 进一步检验?
- A2:
  - 血清铁: 6.15  $\mu\text{mol/L}$ ; 铁结合力85  $\mu\text{mol/L}$ ; 转铁蛋白饱和度: 7.2%
  - CR: 肺炎
- Q3A3: 诊断: 缺铁性贫血



## IRON METABOLISM



### • Factors influencing Iron absorption

- Positive factors
  - Ascorbic acid/ gastric acid/amino acid
- Negative factors
  - Phosphate/phytate/
  - Tea / coffee



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## IRON METABOLISM



### • 概念 (Concepts) :

- 血清铁 (serum iron, SI)
- 血清总铁结合力
- (total iron binding capacity, TIBC)
- 转铁蛋白饱和度
- (transferrin saturation, TS)
- $= SI / TIBC$



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