

USE OF HYDROXYUREA (HYDROXYCARBAMIDE) IN THALASSEMIA

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Hydroxyurea (Hydroxycarbamide) , a potent ribonucleotide reductase inhibitor.

An important cytostatic; easy to use; tolerable, with few side (rapidly reversible) effects. Not expensive.

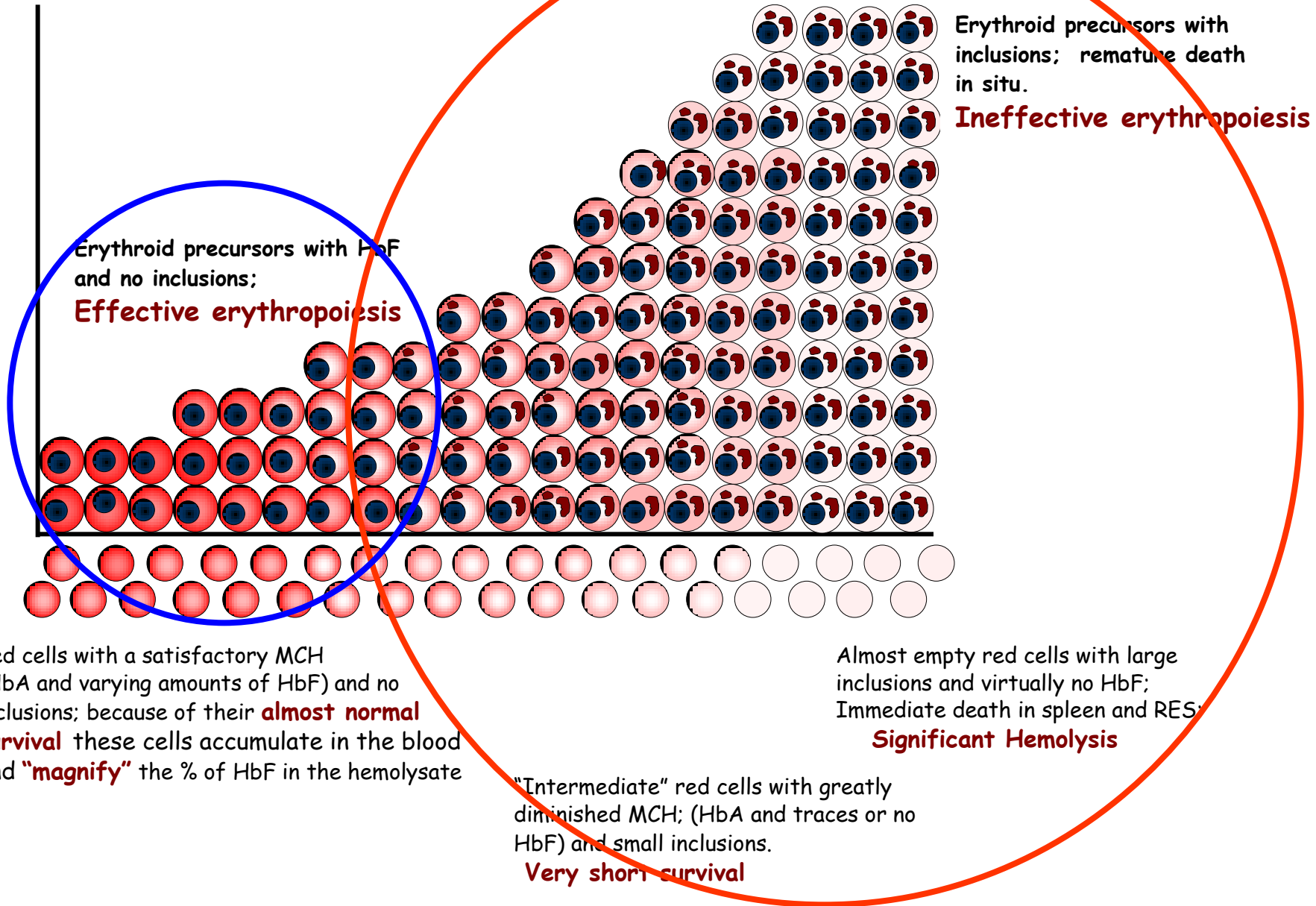
Main indications : Rx of Chronic Myeloproliferative Diseases;
Chronic Myelogenous Leukemia;
Polycythemia Vera;
Essential Thrombocythemia

Also **extremely valuable in Sickle Cell Disease** achieving
Prevention of vaso-occlusive crises .
Increasing the interval between transfusions
Preventing Acute Chest Syndrome
and finally, Increasing Life Expectancy

Two mechanisms of action :

Increasing HbF
Decreasing adhesion / flow retardation of leucocytes,
platelets, reticulocytes and endothelial cells

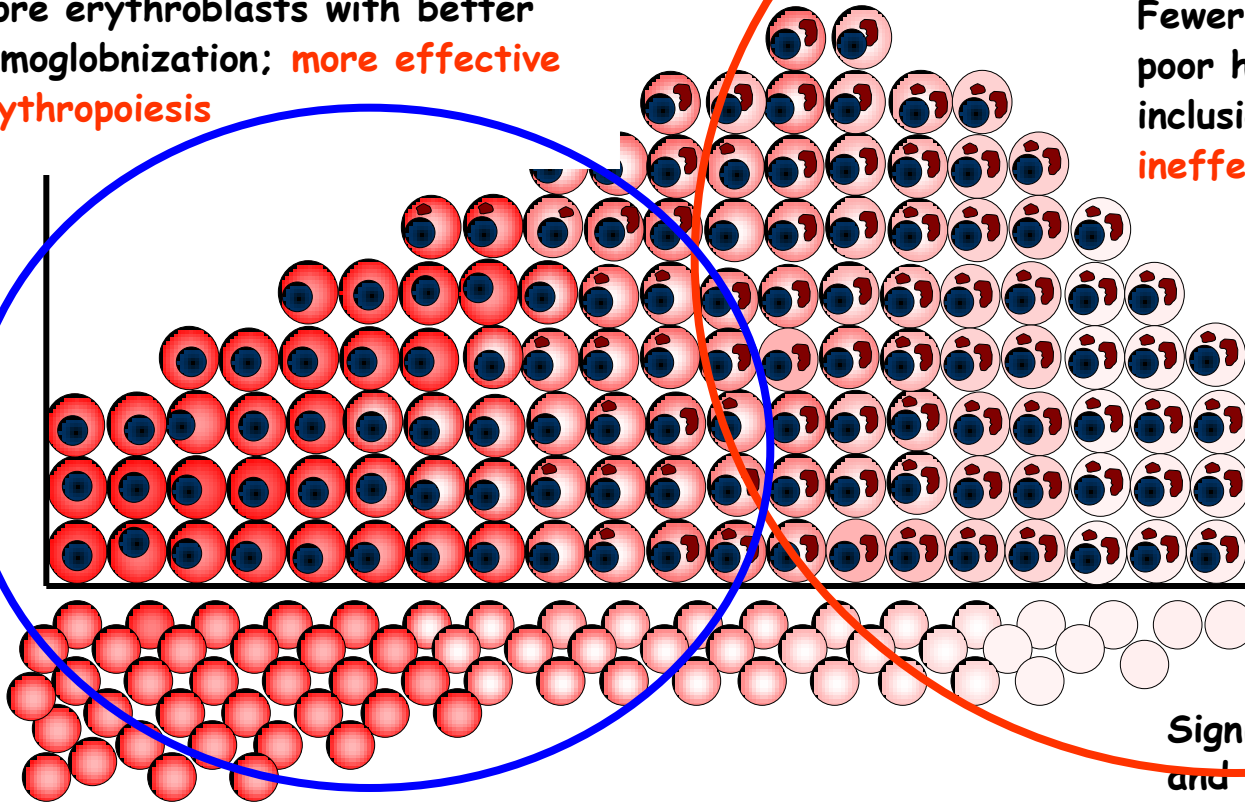
Thalassemic Erythropoiesis



Increased production of HbF containing red cells by enhancing γ -enhancing γ -chain synthesis or by promoting the proliferation of early erythroid progenitors maintaining the program of γ -chain synthesis

More erythroblasts with better hemoglobinization; **more effective erythropoiesis**

Fewer erythroblasts with poor hemoglobinization and inclusion bodies. **Less ineffective erythropoiesis**

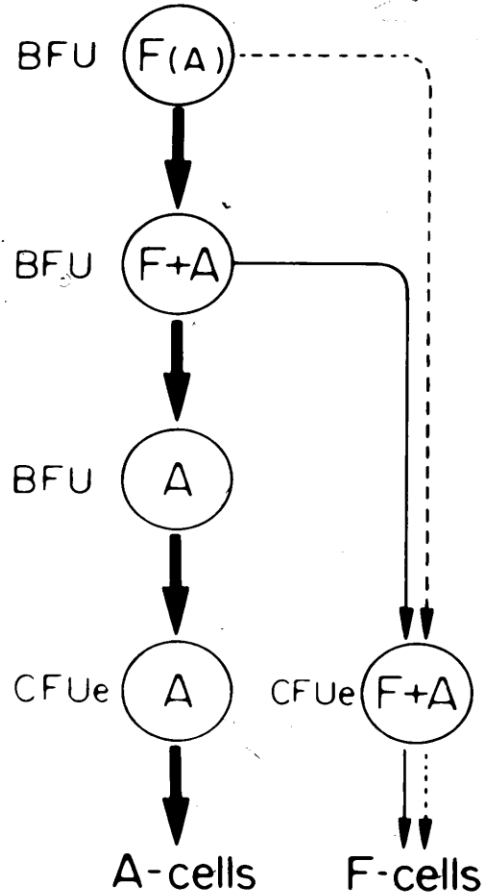


Well hemoglobinized red cells without α -chain inclusions. **Almost normal survival. Less hemolysis.** Also, factitious increase of HbF in the hemolysate.

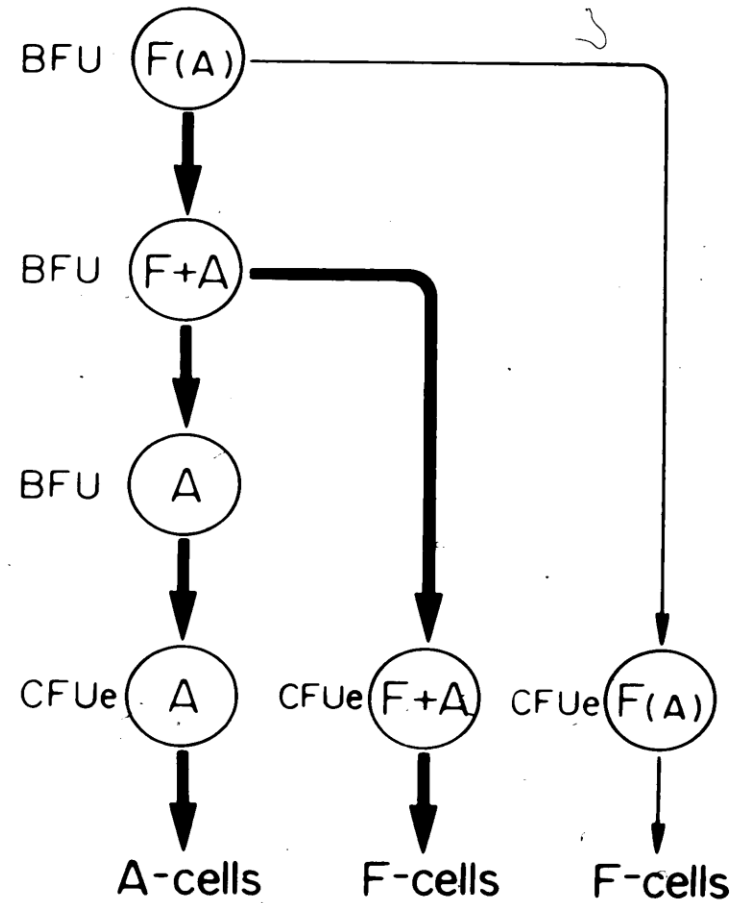
Significantly fewer "empty" and fragmented inclusion carrying red cells; **Decreased peripheral hemolysis**

Normal vs Stressed Erythropoiesis; in the latter, a number of erythroid precursors maintaining the program for γ -chain synthesis are "recruited"

a. Normal Adult



b. Acute Erythropoietic Stress



EARLY STUDIES

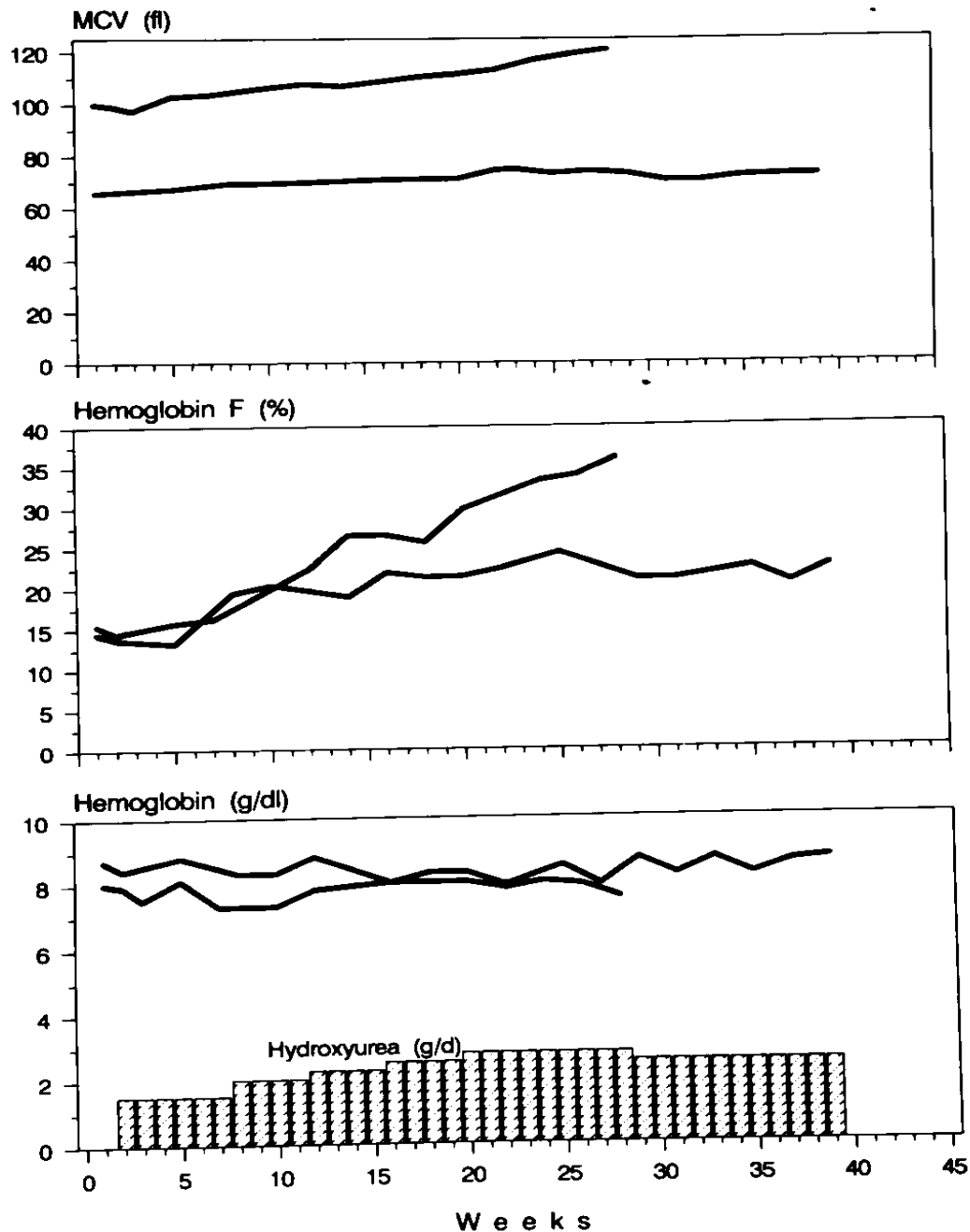
Hajjar and Pearson.
J.Pediatrics, 1994

Fucharoen et al, (HbE/ β -thal)
Blood 1996

Styles, Lewis, Foote, Cuda,
Vichinsky (HbE/ β -thal)
NYAcadSci, 1998

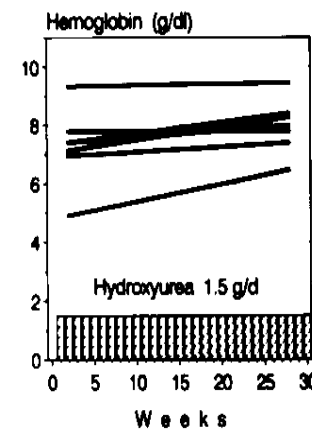
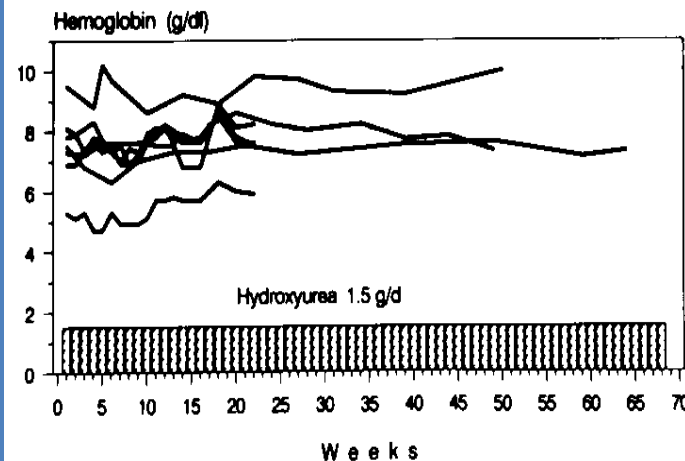
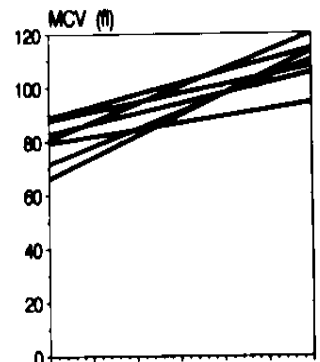
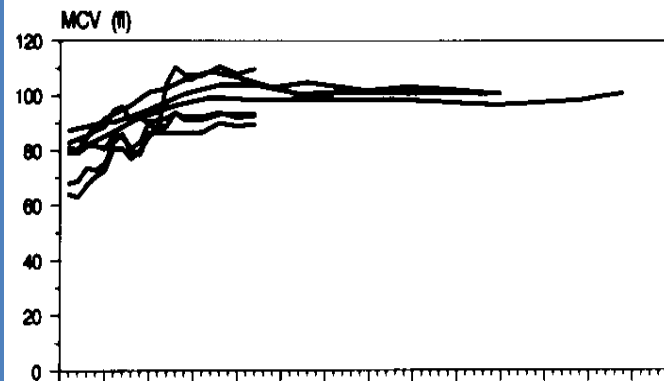
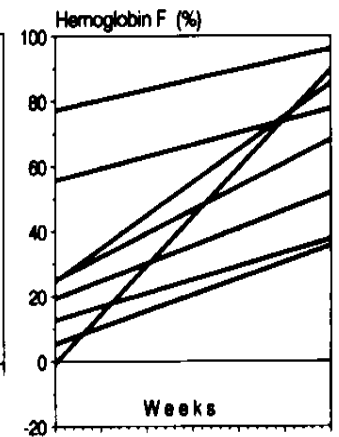
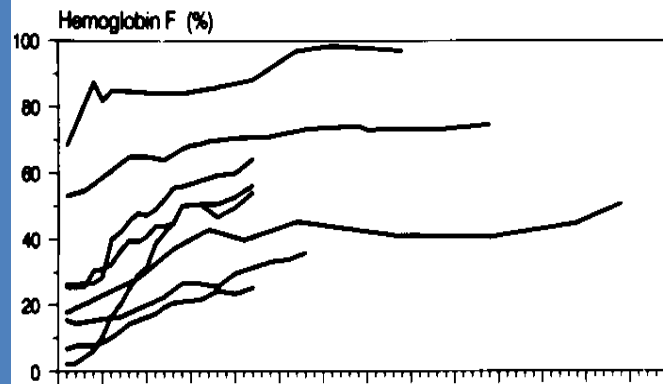
Saxon, Wayne, Olivieri,
NYAcadSci, 1998

Loukopoulos et al,
NYAcadSci, 1998



Response to a standard dose of hydroxyurea of the initial group of patients

- Increase of HbF
- Increase of MCV
- No significant changes of Hb levels



Long-term hydroxyurea therapy in beta-thalassaemia patients

Brazil

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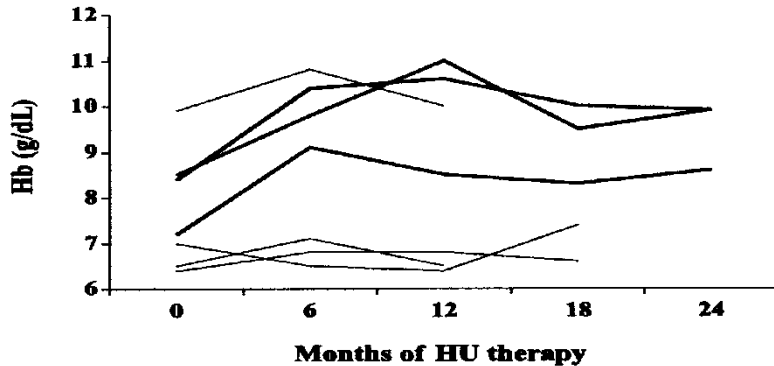


Fig. 1. Changes in total haemoglobin obtained from seven beta-thalassaemia intermedia patients before and every 6 months during hydroxyurea treatment. Thick lines indicate responding patients.

Eur.J.Haematol., 70:151-155, 2003
7 pts. with thalassaemia intermedia;
10-20 mg/kg-d HU over 6 months.
4 responders with increase of HbF/total Hb

Table 2. Haematological changes in seven beta-thalassaemia intermedia patients obtained before and after 6 months of hydroxyurea therapy

Case	Hb (g/dL)		Ret ($\times 10^9/L$)		MCV (fl)		MCH (pg)		HbF (%)	
	Baseline	HU	Baseline	HU	Baseline	HU	Baseline	HU	Baseline	HU
5	9.9	10.8	1680.0	220.0	71	74	23.2	27.3	97.2	98.0
6	8.5	9.8	294.0	72.0	68	77	21.4	28.6	20.9	48.0
7	8.4	10.4	1000.0	90.0	78	83	24.9	28.8	98.4	98.4
8	7.2	9.1	519.0	44.0	66	79	20.5	26.7	23.3	30.0
9	6.4	6.8	90.0	80.0	73	72	23.9	24.8	23.0	55.0
10	6.5	7.1	NA	NA	75	71	24.9	23.7	NA	NA
11	7.0	6.5	210.0	97.0	61	82	21.3	27	6.7	14.0

Hb, haemoglobin; Ret, reticulocyte; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; HbF, foetal haemoglobin; HU, hydroxyurea; NA, not available.

37 pts with TI, age 4-50 y; 10 mg /d HU increasing to MTD (20 mg/kg-d) over 12 months (4-36). 26 pts responded (46% major" response). $a^{3.7}$ deletion favours response; **No correlation with *XmnI* polymorphism;**

Ashish Dixit · T. C. Chatterjee · Pravas Mishra · Dharma R. Choudhry · M. Mahapatra · S. Tyagi · Madhulika Kabra · Renu Saxena · V. P. Choudhry

Hydroxyurea in thalassemia intermedia—a promising therapy . INDIA

Table 3 Comparative data of major responders ($n=17$). *NRBCs/100 WBC* nucleated red blood cells per 100 WBCs, *Ret* reticulocytes, *MCV* mean cell volume, *MCHb* mean cell hemoglobin, *MCHC* mean cell hemoglobin concentration, *RDW* red cell distribution width and standard deviation (SD)

Mean	Hb (g/l)	NRBCs/100 WBC	Ret (%)	MCV (fl)	MCHb (pg)	MCHC (g/l)	RDW (SD)	F cells (%)	HbF (%)
Pre-therapy	65±9 (45–85)	14.6±27.7 (1–105)	3.1±2.3 (1–9.1)	71.7±1.7 (58.9–90.8)	22.1±2.8 (18.5–28.6)	311±17 (284–335)	59.5±9.4 (46.6–80.6)	72.4±18.4 (45–92)	67.0±25.7 (13.6–96)
Post-therapy	91±10 (80–119)	4.2±8.5 (0–36)	2.3±1.4 (1–6)	74.0±9.2 (57.5–88.7)	23.7±3.9 (17.0–31.0)	321±18 (290–352)	60.9±9.4 (42.6–82.5)	81.7±18.2 (55–99)	76.0±22.2 (25.6–94.6)
<i>p</i> value	<0.001	<0.05	<0.05	<0.05	<0.01	<0.05	>0.05	<0.01	<0.01

Table 5 Comparative data of nonresponders ($n=11$). *NRBCs/100 WBC* nucleated red blood cells per 100 WBCs, *Ret* reticulocytes, *MCV* mean cell volume, *MCHb* mean cell hemoglobin, *MCHC* mean cell hemoglobin concentration, *RDW* red cell distribution width and standard deviation (SD)

Mean	Hb (g/l)	NRBCs/100 WBC	Ret (%)	MCV (fl)	MCHb (pg)	MCHC (g/l)	RDW (SD)	F cells (%)	HbF (%)
Pre-therapy	65±15 (40–92)	7.2±10.1 (0–30)	2.8±1.4 (1.0–5.0)	68.8±2.5 (63.3–72.6)	21.5±2.0 (18.9–25.8)	314±23 (270–365)	54.3±12.4 (30.6–70.8)	36.2±40.8 (2–90)	40.9±41.1 (0.3–89.6)
Post-therapy	70±14 (47–100)	5.1±6.6 (0–23)	2.7±1.3 (1.0–5.0)	71.2±4.2 (65.0–79.4)	21.8±2.4 (19.0–26.0)	311±17 (268–328)	53.7±10.7 (33.3–67.9)	36.2±40.8 (2–90)	41.9±39.3 (0.5–88.5)
<i>p</i> value	<0.05 ^a	>0.05	>0.05	<0.05 ^a	>0.05	>0.05	>0.05	>0.05	>0.05

^aOnly in transfusion independent patients

Hematologic and Clinical Responses of Thalassemia Intermedia Patients to Hydroxyurea During 6 Years of Therapy in Iran

Mehran Karimi, MD, Hadi Darzi, MD, and Majid Yavarian, PhD

Karimi et al

J Pediatr Hematol Oncol • Volume 27, Number 7, July 2005

TABLE 1. Hematologic Profiles and Electrophoretic Indices After HU Therapy in Transfusion-Dependent Thalassemia Intermedia Patients

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Hb (g/dL)*	9.42 ± 1.28	9.46 ± 1.31	9.48 ± 1.25	9.43 ± 1.42	9.44 ± 1.26	9.4 ± 1.3
MCV (fl)	76.28 ± 9.03	77.39 ± 8.96	77.43 ± 8.44	77.14 ± 8.61	77.40 ± 8.50	77.35 ± 8.4
MCH (pg)	23.83 ± 2.66	24.09 ± 2.38	24.14 ± 2.29	24.14 ± 2.11	24.50 ± 2.40	24.4 ± 2.35
WBC	10,800 ± 1,350	10,000 ± 2,250	10,000 ± 1,000	9,100 ± 1,700	9,050 ± 1,900	9,150 ± 1,800
Platelets (×10 ³)	450 ± 210	474 ± 227	493 ± 237	481 ± 239	479 ± 225	483 ± 230
Normal red blood cells/100 WBC	170 ± 264	180 ± 267	166 ± 249	167 ± 260	169 ± 250	172 ± 260
HbF (g/dL)	7.86 ± 2.11	8.61 ± 1.89	8.74 ± 1.96	8.72 ± 1.9	8.75 ± 1.96	8.7 ± 1.91
HbA ₁ (g/dL)	1.21 ± 1.44	0.65 ± 1.18	0.61 ± 1.21	0.54 ± 1.12	0.59 ± 1.15	0.6 ± 1.2

Data are given as mean ± SD.

*HbA₂ (g/dL) is not included in this table.

Thalassemia intermedia : pts who maintain Hb levels 6-7 g/dl until ca. age 6 but are eventually put on transfusion therapy in order to avoid facial deformities.

163 pts totally : 106 transfusion dependent, 43 receiving Tx occasionally, 14 not transfused. HU dose 8-12 mg/kg-d adjusted to response **over up to 6 years**.

Results : 83/106 Tx dependent pts and 16/43 pts on occasional Tx did not require any further transfusions. Hb levels (as well as HbF and MCV) increased significantly. Pts stated feeling well. No other changes. No major side effects. **Authors advise trial with HU whenever this form of thalassemia is established.**



[haematologica]
2004;89:1172-1178

MAJID YAVARIAN
MEHRAN KARIMI
EGBERT BAKKER
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PIERO C. GIORDANO

Response to hydroxyurea treatment in Iranian transfusion-dependent β -thalassemia patients

133 pts with transfusion dependent thalassemia; severe; transfusion dependent since infancy; varying molecular defects, mostly β^0 -thalassemia; Gender : 67 M-67 F; Age 8-31 y. 69 pts splenectomized. Median HU dose : 10-15 mg/kg; median duration of therapy : 42 mo (24-60 mo).

Results : 3 categories.

Good responders (61%). No further transfusions !

Moderate responders (23%); Hb maintained at 7.5-9.5 g/dl; occasional Tx.

No responders (16%).

Table 4. Frequencies of the β -gene framework among 266 alleles in the patients grouped according to response to HU treatment.

Clinical responses	I N (%)	II N (%)	III N (%)	Asian N (%)
Good response	56 (34.5)	83 (51.4)	15 (9.2)	8 (4.9)
Moderate response	31 (50.0)	21 (33.9)	4 (6.5)	6 (9.7)
No response	23 (54.8)	8 (19.0)	4 (9.5)	7 (16.7)

Table 3. Frequency of the XmnI polymorphism in correlation to the three response categories to HU treatment.

Patients	n	C/C (%)	C/T (%)	T/T (%)
Good response	81	19.1	42.5	38.4
Moderate response	31	65.5	31.0	3.5
No response	21	61.9	33.3	4.8

Hydroxyurea can eliminate transfusion requirements in children with severe β -thalassemia **Algeria**

Mohamed Bradai, Mohand Tayeb Abad, Serge Pissard, Fatima Lamraoui, Laurent Skopinski, and Mariane de Montalembert

7 children with transfusion dependent thalassemia; mean HU dose : ca. 18.5 mg/kg-d.
 Median follow-up : 19 mo (13-21 mo). All good responders (Hb from 6.5 to 10.5 g/dl);
 discontinued transfusions. Good clinical and hematological safety. Spleen size reduced (6 to 3 cm)

Table 1. Main clinical and biologic characteristics of patient population

Patient	Age, y/sex	Genotype	Xmn polymorphism	Initial Hb, g/dL	Phenotype	Age at 1st transfusion, mo	EC/y	Splenectomy
1	12/M	Codon 6(-A)/codon 39(C>T)	+/-	6.7	Intermediate	30	5	Total
2	12/F	Codon 6(-A)/IVS1-nt110G>A	+/-	6.4	Intermediate	48	3	No
3	16/M	Homozygous IVS1-nt110G>A	-/-	4.9	Major	9	15	Partial
4	12/F	Homozygous codon 6(-A)	+/+	4.2	Major	13	15	No
5	8/F	Homozygous IVS1-nt110G>A	-/-	5.9	Major	15	18	No
6	4/M	Homozygous codon 6(-A)	+/+	3.9	Major	13	9	No
7	6/M	Codon 6(-A)/codon 39(C>T)	+/-	3.6	Major	16	13	Total

EC indicates erythrocyte concentrate-packed red blood cells.

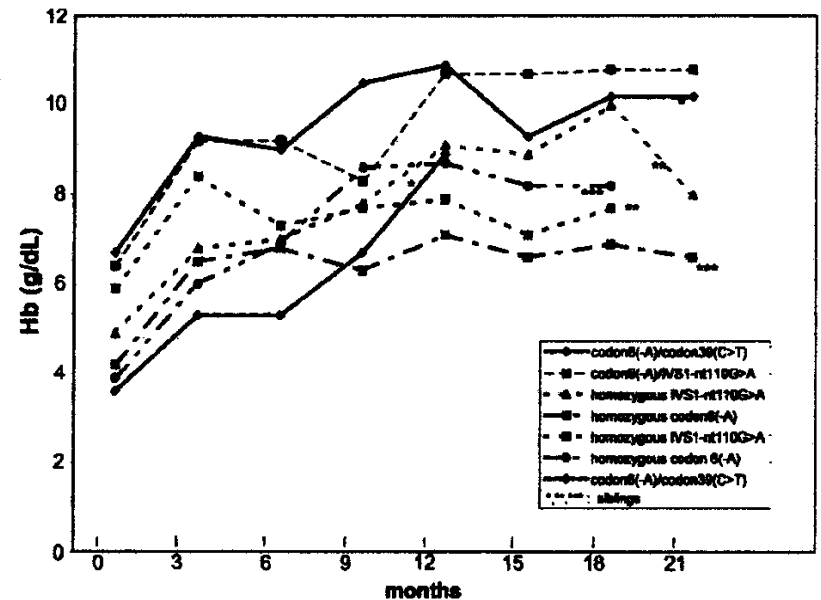


Figure 1. Hb levels under HU. Changes in hemoglobin (Hb) levels with hydroxyurea treatment in 7 transfusion-dependent β -thalassemic children.

Use of hydroxycarbamide in thalassemia **major**; a meta-analysis

GOOD RESPONDERS DISCONTINUING TRANSFUSIONS

Authors	Responders vs total	AGE years	Follow-up (months)	Dose mg/kg-d	Transfusion frequency	Total Hb increment (g/dl)
Thalassemia major (β-th/β-th)						
Bradai et al 2003	7/7	9-48 months	13-21	18.3±3.5	To keep pts alive Pre-Tx 4.2 g/dl	Pre-Rx 4.5±0.9 Post-Rx 7.9±0.8
De Paula 2003	1 / 4	16-22	6-96	10-20	Regularly	+4.1
Yavarian et al 2004	81/133	8-31 y	24-60	10-15	to keep Hb>6.0 g/dl	At the end of the study : 10.3
Karimi et al 2005	106/120	4-35 y	up to 6 y	8-12 to toxicity	to keep Hb>7.0 g/dl	At the end of the study : 9.5
Bradai et al 2007	20/45		12	17.4±2.4* to toxicity	To keep pts alive Pre-Tx 4.2 g/dl	+1.5 Tx needs ↓ by 70%
Koren et al 2008	9/11	9-34 y	6-60 46±25	10.9±3.0	ml of blood/year 137±49	48 mo after HU initiation 8.2±0.7

Use of hydroxycarbamide in thalassemia **intermedia**

defined as a thalassemic condition with good growth, relatively high Hb, no major facial deformities, and no need for transfusions; most instances include also pts with rare Tx's (ca 2/y). **A GOOD RESPONSE defined as DISCONTINUATION of transfusions or a significant INCREASE of total hemoglobin.**

Authors	Responders vs total	AGE years	Follow-up (months)	HU Dose (mg/kg-d)	Increment of Total Hb (g/dl)	Increment of Hemoglobin F
Loukopoulos et al 1998	7/7	Adults	48 +	20-25	Pre-Rx 7.5 ± 1.3 At 6 mo 7.7 ± 1.2	32.9 ± 27.1 59.2 ± 22.3
Da Paula et al 2003	3/7	16-68	12-69	20	Pre-Rx 7.7 ± 1.3 At 6 mo 8.7 ± 1.8	44.9 ± 41.4 57.2 ± 34.8
Karimi et al 2005	16/43	4-35	up to 6 y	8-12	Pre-Rx 8.7 ± 1.0 At 12 mo 9.6 ± 1.2	No information
Koren et al 2008	9/11 0-8 Tx/y	9-34	4	10-20	Pre-Rx 6.7 ± ... At 12 mo 6.9 ± ... No Tx anymore	
Ali Ehsani et al 2009	16/16	10.7	6	20 mg/d x 4 d/w	Hb increment (g/dl) 1.6 ± 0.98	HbF increase (g/dl) 1.7±0.96

Use of hydroxycarbamide in HbE/ β -thalassemia

Authors	Responders vs total	AGE years	Follow-up (mo)	HU (mg/kg-d)	Increment of Total Hb (g/dl)	Increment of Hemoglobin F
Fucharoen et al 1996	12/13	18-55		10 to 20	Minimal in 10%	42 \pm 11 to 56 \pm 8 in all patients
Singer et al 2005	16/42		24	up to 20	1.3 \pm 0.4	29 \pm 11 to 37 \pm 9 in all patients
Italia et al 2010	4/11 (Tx dependent)	8-34	20	15-20	<p>Responders (4) Baseline 5.8 \pm 2.1 2-4 mo 7.7 \pm 1.1</p> <p>Partial Responders (4) Baseline 6.3 \pm 1.6 2-4 mo 6.3 \pm 1.1</p>	<p>Ceased Tx</p> <p>Less Transfusions</p>

PREDICTION OF RESPONSE

in vivo. The Xmn I polymorphism, -158 nt 5' to the $\zeta\gamma$ gene

Bradai et al.
2003

7 Transfusion dependent infants received HU over several months.
All responded and ceased being transfused
2/7 were Xmn I (+/+), and 3/7 (+/-); 2/7 were (-/-)

Yavarian

133 patients with Tx dependent thalassemia (age 8-31) received HU over long periods of time; the goal was to keep Hb > 6.0 g/dl. 81 of them responded well, ceased requiring Tx's and maintained Hb levels as high as 10.3 g/dl. 82 % were Xmn I (+/+) and 40% (+/-)

Koren et al
2005

11 Tx dependent patients (30-71 blood Units/2 y) treated with HU (10 mg/kg-d) over > 2 years. 9/11 responded and ceased being transfused
5/9 were Xmn I (+/+), 2 were (+/-) and 2 were (-/-);
2/11 patients failed to respond. Both were Xmn I (-/-).

Dixit et al

37 Thalassemia intermedia patients requiring only ca. 4 blood units/year. 17/37 responded well, ceased Tx's; total Hb increased by > 2.0 g/dl
Response did not show any correlation with the Xmn I polymorphism.

Ali Taher

7 patients with TI treated with HU over 17 mo. 2/7 responded with an increase of total Hb of 2 and 3 g/dl. None was Xmn I positive.

Conclusion :

Co-inheritance of the Xmn I G to C polymorphism may favor the prompt increase of HbF in response to HU ; no definitive proof

Use of hydroxycarbamide in thalassemia

PREDICTION OF RESPONSE

The α deletion

Panigrahi et al. 2005

20 patients with thalassemia Intermedia (albeit transfused) received 10-20 mg/kg-d HU over 12 months.

12 showed a good response with a significant elevation of total Hb and HbF; 4/20 ceased being transfused.

4/12 carried an $\alpha(3.7)$ gene.

3 / 4 were also Xmn I positive

none of the 8 non-responders carried the α -gene deletion

Conclusion : α gene deletions and the Xmn I (+) polymorphism favour response; a "synergy"

Use of hydroxycarbamide in thalassemia

PREDICTION OF RESPONSE *in vitro*

Watanapokasin et al. 2005

THAILAND

13 patients treated with HU over 2 years; evaluation of response.
Erythroid cultures from these persons supplemented with HU showed an increase of γ -mRNA along with an increase of the HbF in most cases.

INDIA

A similar report from India is in keeping with these findings. **Unpublished**

Use of hydroxycarbamide in thalassemia

A contradictory report :

Zeng et al, 1995

2 Chinese patients with β^+ thalassemia treated with low doses of HU over 10 months showed

- a significant increase of Hb (4.1 to 6. and 6.5 to 9.7)
- a significant INCREASE of HbA (with the respective decrease of HbF) expressed as an increase of the β/α ratio on globin biosynthesis; (from 0.301 to 0.581 and from 0.348 to 0.487)

COMBINATIONS OF HYDROXYUREA WITH OTHER AGENTS. I

Karimi et al, 2009 120 pts with thalassemia intermedia (no Tx's)
having already received HU over the past 6 months .

Carnitine added as a γ -chain synthesis inducer; as an antioxidant

Magnesium added as a membrane stabilizer; also as an anti-oxidant

Added drug GROUPS		Age (years; rounded)	Hemoglobin baseline (g/dl)	Hemoglobin at 6 months (g/dl)	Hb F (%)
A	HU only	17±6	28.3±3.5	28.7±3.4	88
B	L-carnitine	20±4	27.3±3.1	30.6±2.9	92
C	Magnesium	18±7	26.2±2.9	29.1±3.2	84
D	Carnitine and Magnesium	21±7	27.6±3.8	30.1±3.3	86

MCV increased ($p < 0.01$) in group B only

MCH increased ($p < 0.01$) in groups A, B and C, but not D implying a better hemoglobinization of RBC through additional HbF.

However, not expected in A; expected in B and C; unclear in D

No other data regarding Xmn I status and molecular types

COMBINATIONS OF HYDROXYUREA WITH OTHER AGENTS. II

Hoppe et al 1999

5 patients with TI (3 with HbE/ β -th) given HU until maximum tolerated dose and then adding Sodium Phenylbutyrate (10 g/m² d)

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5
Baseline Hb (g/dl)	8.1	7.1	7.1	6.5	5.6
HU only	11.5	7.7	8.8	7.8	9.6
HU plus PB	11.3	7.8	nd	nd	nd

- **Carnitine** added as a γ -chain synthesis inducer; as an antioxidant
- Magnesium** added as a membrane stabilizer; also as an anti-oxidant

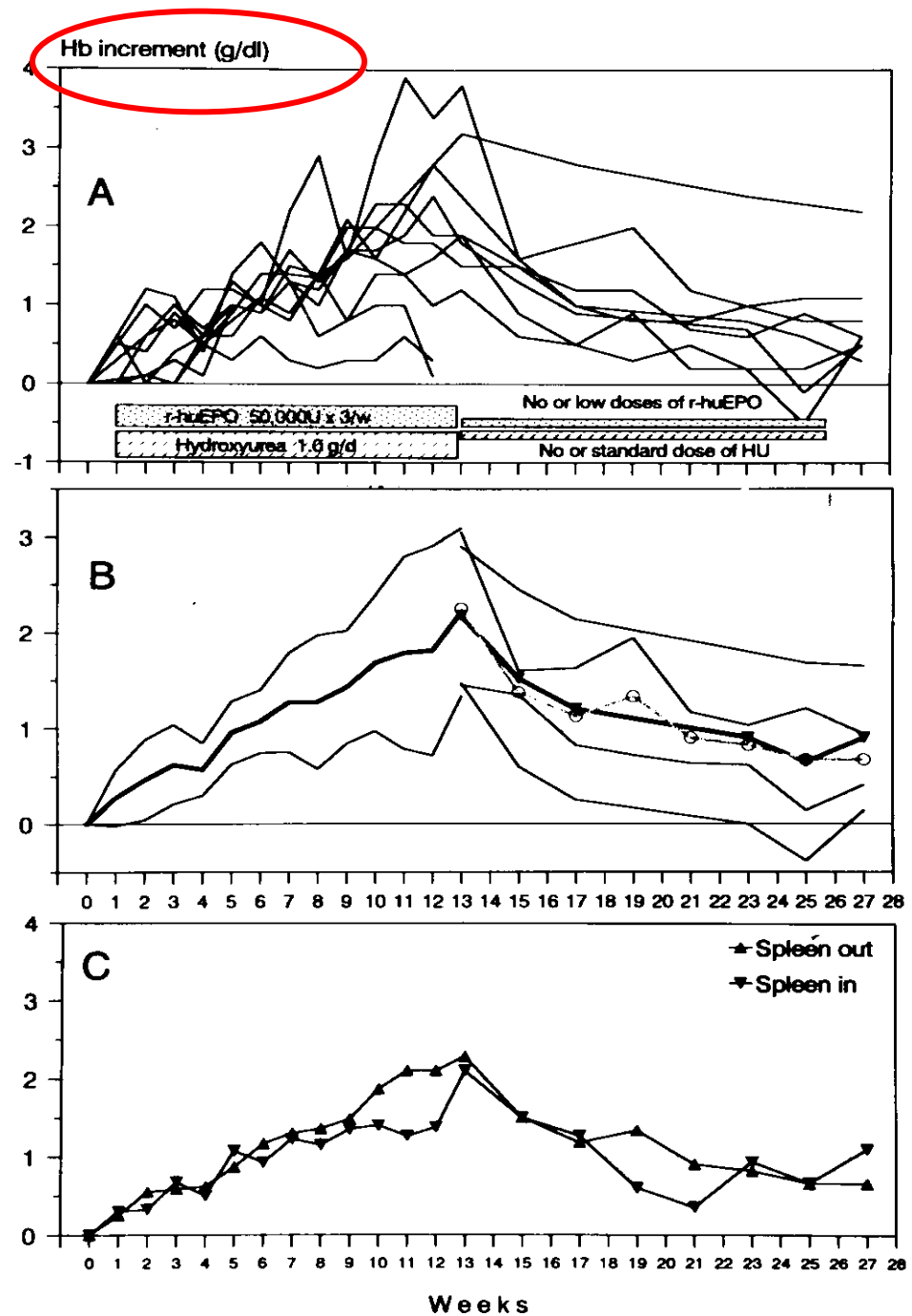
HYDROXYUREA WITH ERYTHROPOIETIN

Initial observation: Rodgers et al,
N Engl J Med, 328:73-80, 1993

Then, Loukopoulos et al,
NY Acad Sci, 120-128, 1998

- A: All 10 patients with thalassemia intermedia
- B: Responders only
- C: Effect of splenectomy

Recently, one additional patient
Kohli-Kumar et al, J Ped Hematol/
Oncol, 24:777-778, 2002



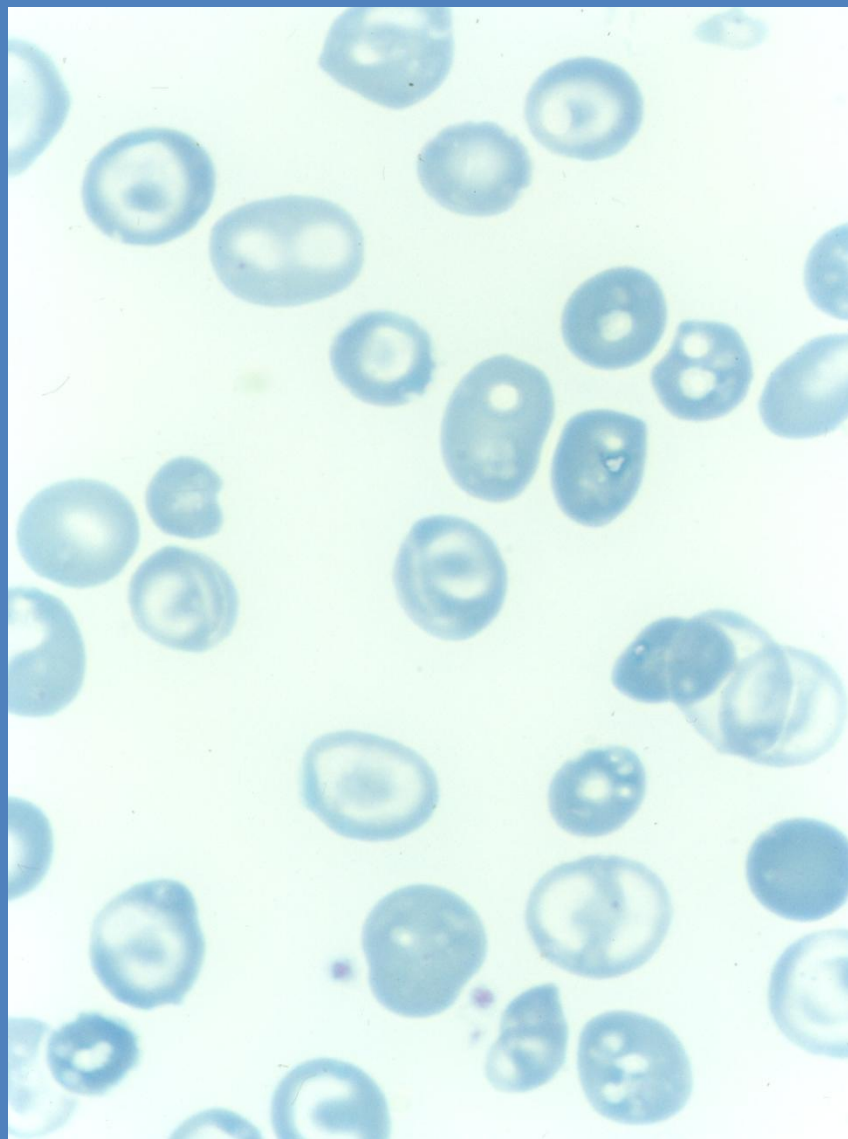
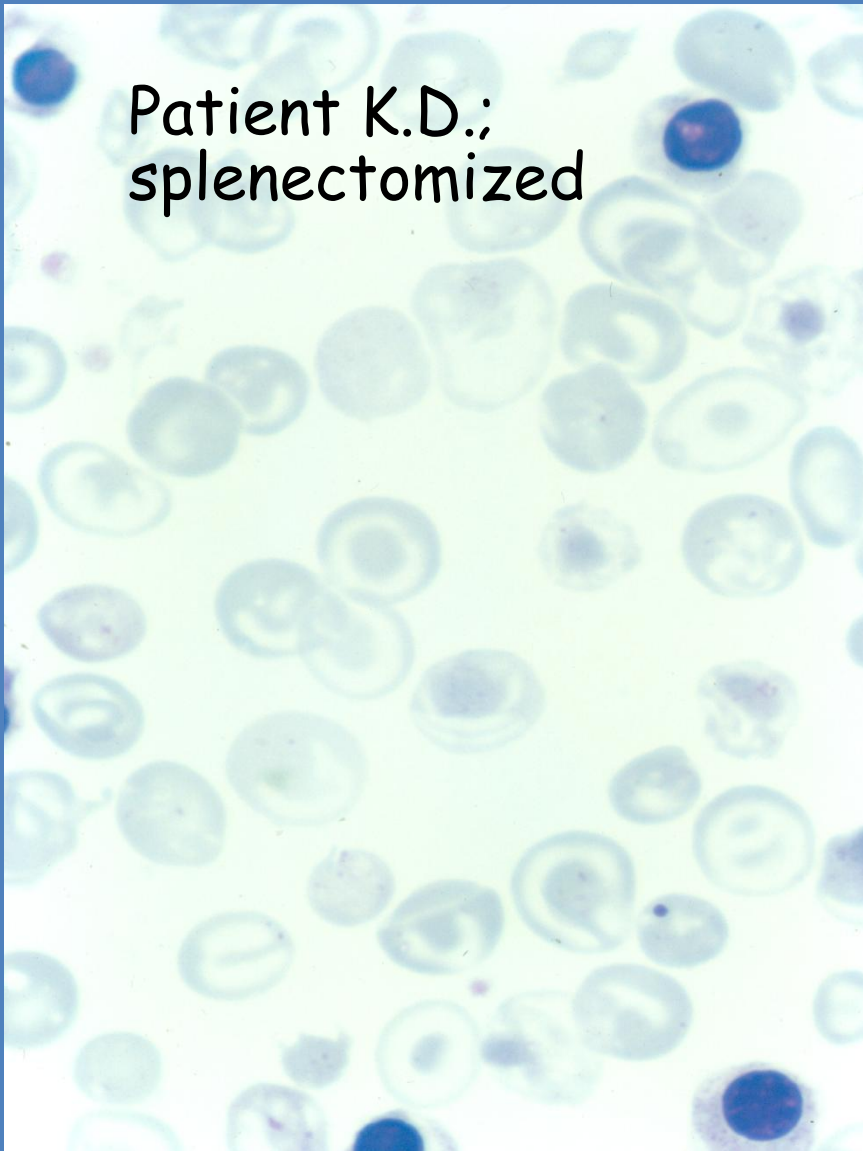
Use of hydroxycarbamide in thalassemia

INTERESTING FEATURES

Improvement of hemoglobinization; rarely evaluated.

Implies addition of HbF in cells; difficult to assess in β^0/β^0 thalassemia, where the whole MCH is HbF

Patient K.D.;
splenectomized



Prior treatment with hydroxyurea After

Long-term hydroxyurea therapy in beta-thalassaemia patients

Brazil

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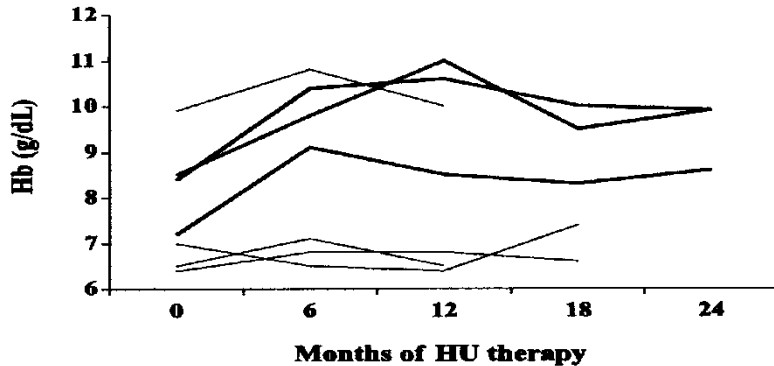


Fig. 1. Changes in total haemoglobin obtained from seven beta-thalassaemia intermedia patients before and every 6 months during hydroxyurea treatment. Thick lines indicate responding patients.

Eur. J. Haematol., 70:151-155, 2003

7 pts. with thalassaemia intermedia;

10-20 mg/kg-d HU over 6 months.

4 responders with increase of HbF/total Hb

Table 2. Haematological changes in seven beta-thalassaemia intermedia patients obtained before and after 6 months of hydroxyurea therapy

Case	Hb (g/dL)		Ret ($\times 10^9/L$)		MCV (fl)		MCH (pg)		HbF (%)	
	Baseline	HU	Baseline	HU	Baseline	HU	Baseline	HU	Baseline	HU
5	9.9	10.8	1680.0	220.0	71	74	23.2	27.3	97.2	98.0
6	8.5	9.8	294.0	72.0	68	77	21.4	28.6	20.9	48.0
7	8.4	10.4	1000.0	90.0	78	83	24.9	28.8	98.4	98.4
8	7.2	9.1	519.0	44.0	66	79	20.5	26.7	23.3	30.0
9	6.4	6.8	90.0	80.0	73	72	23.9	24.8	23.0	55.0
10	6.5	7.1	NA	NA	75	71	24.9	23.7	NA	NA
11	7.0	6.5	210.0	97.0	61	82	21.3	27	6.7	14.0

Hb, haemoglobin; Ret, reticulocyte; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; HbF, foetal haemoglobin; HU, hydroxyurea; NA, not available.

Use of hydroxycarbamide in thalassemia

INTERESTING FEATURES

“Feeling better” !

May reflect

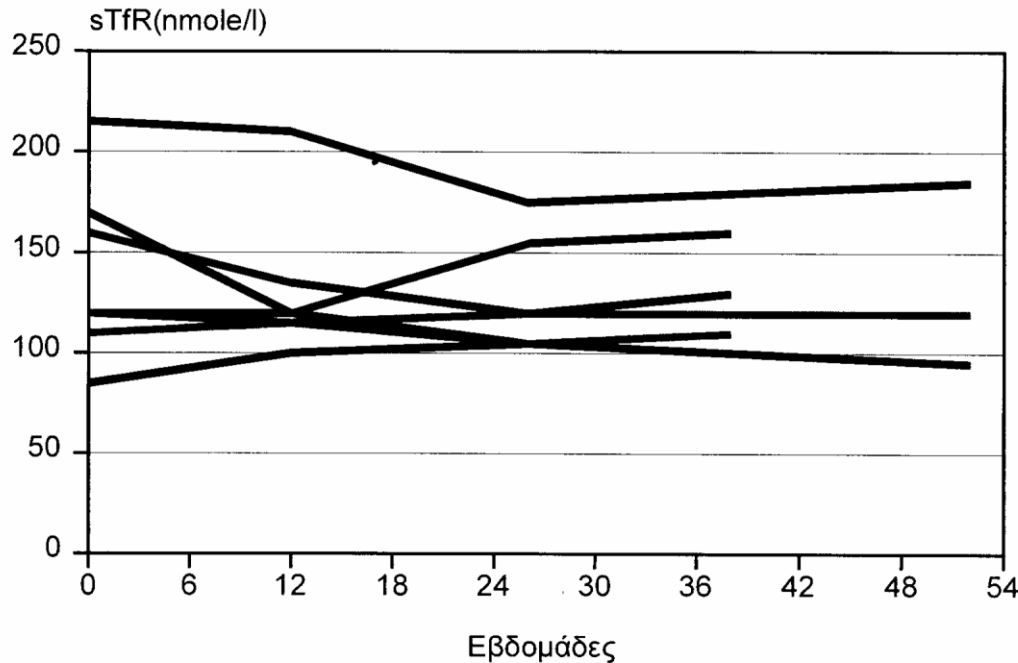
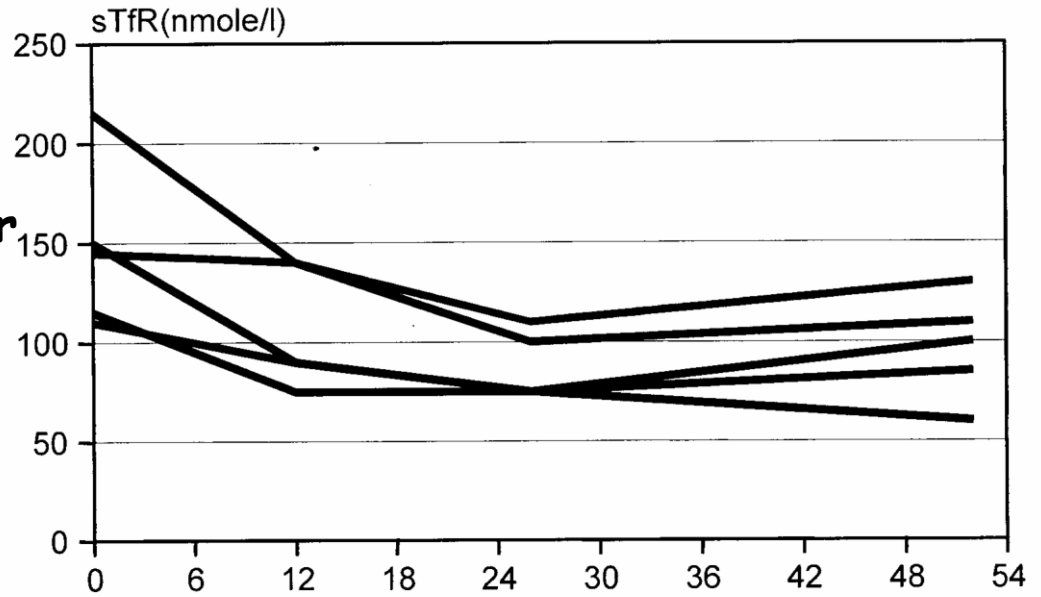
Elimination of transfusions (psychologic)

Decreased energy consumption as a result
of elimination of non-effective erythropoiesis

Mentioned in several reports; within a few days;
not quantified objectively

Tsiarta et al; a Thesis

6 TI patients treated with HU (20 mg/kg-d) over 1 year



Tsiarta et al; a Thesis

6 TI patients treated with HU (5 mg/kg-d) over 1 year;
No response in terms of Total Hb and HbF increase

Use of hydroxycarbamide in thalassemia

THE QUESTION OF A LOWER DOSAGE

Wang M et al; 2002

Confirmed in erythroid cell cultures where low concentrations of HU resulted in an increase of the number of colonies and total Hb along with a dose dependent upregulation of the GATA 2 mRNA

Use of hydroxycarbamide in thalassemia

CONCLUSIONS

Hydroxycarbamide MAY have be useful in thalassemia, both intermedia and transfusion dependent, most probably acting by reducing ineffective erythropoiesis and increasing HbF.

Further studies are required; precise , common protocol; foillow-up of all necessary parameters; parallel molecular studies and in vitro experiments wherever possible.

Use of hydroxycarbamide in thalassemia

CONCLUSIONS

Hydroxycarbamide *MAY* have be useful in thalassemia, both intermedia and transfusion dependent, most probably acting by reducing ineffective erythropoiesis and increasing HbF.

Further studies are required; precise , common protocol; follow-up of all necessary parameters; parallel molecular studies and in vitro experiments wherever possible.

MERCI DE VOTRE ATTENTION !