Interferenza da varianti emoglobiniche nella misura dell'HbA_{1c}

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9 Maggio 2009 - Desenzano del Garda

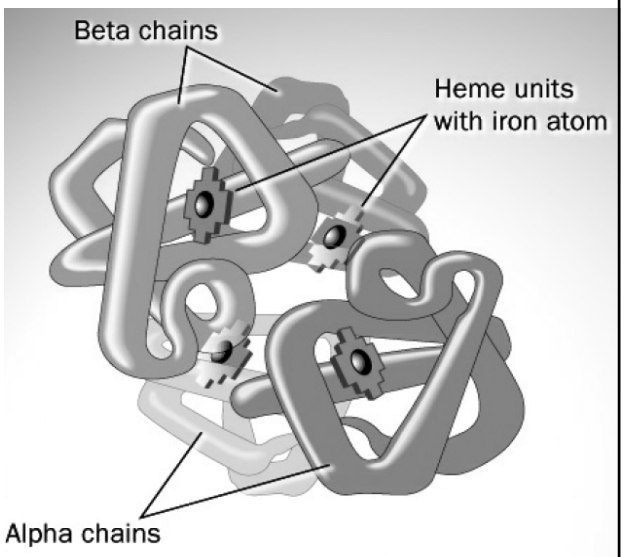
E m o g l o b i n a (Hb)

- *Proteina del sangue contenuta negli eritrociti*
- *Concentrazione di Hb nel sangue*
  - *13-18 g/dL nell'uomo*
  - *12-16 g/dL nella donna*
- *Quantità di eritrociti:*
  - *4.6-6.2M /μL nell'uomo*
  - *4.2-5.4M /μL nella donna*

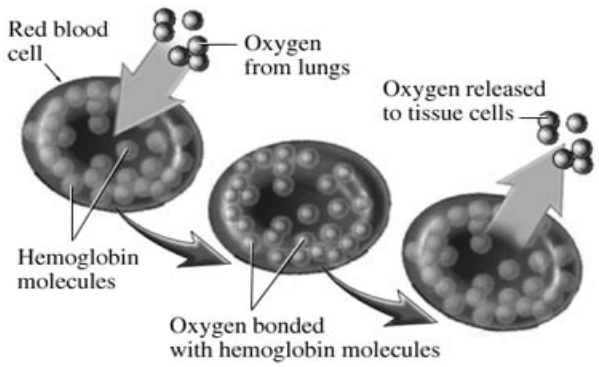
Struttura dell'emoglobina (HbA)

E' un etero-tetramero composto da:
2 subunità Alfa
2 subunità Beta
GLOBINE $\alpha_2\beta_2$

Ogni subunità è coniugata ad un gruppo eme, un composto in cui è presente un atomo di ferro, il quale lega l'ossigeno e la CO2



F u n z i o n i



Hb: Varianti fisiologiche

Emoglobine embrionali
geni Alfa, Zeta, Epsilon e Gamma presenti
Gower 1 ($\zeta_2\varepsilon_2$)
Gower 2 ($\alpha_2\varepsilon_2$)
Portland ($\zeta_2\gamma_2$)

Emoglobina fetale (Hb F)
geni Alfa e Gamma presenti
HbF ($\alpha_2\gamma_2$)

Emoglobine adulte (HbA)
geni Alfa, Beta e Delta presenti
HbA ($\alpha_2\beta_2$, > 95%)
HbA_2 ($\alpha_2\delta_2$, < 3%)

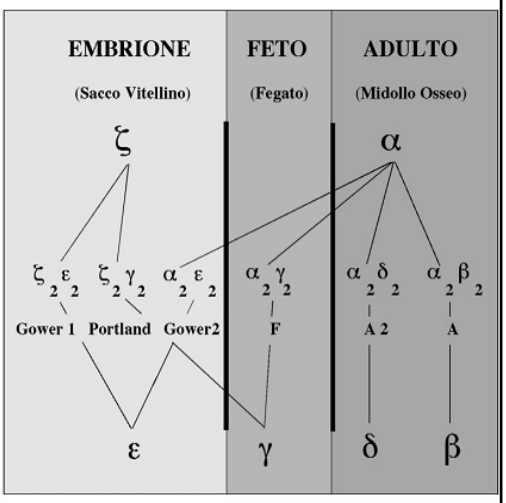


Fig.2. Composizione delle emoglobine (Gower 1, Gower 2, Portland, F, A, A2) prodotte nell'uomo dall'embrione, dal feto e dall'adulto. Tra parentesi sono indicati i siti di eritropoiesi.

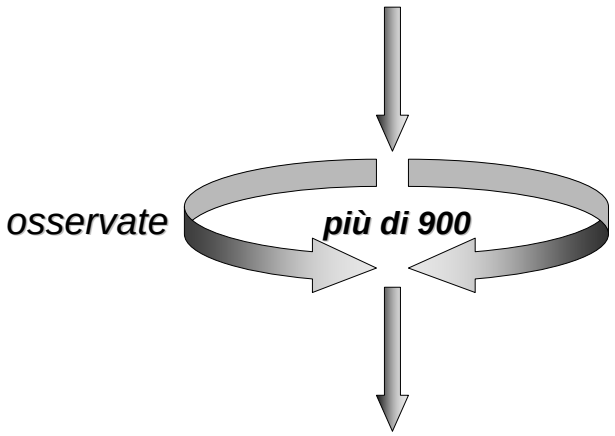
Emoglobinopatie

Patologie determinate da disordini ereditari dell'emoglobina

Talassemie

Emoglobine varianti
(HbS, HbC, HbE, Hb Lepore…)

Varianti Emoglobiniche



in continuo aumento

Normal beta chain

ATG GTG CAC CTG ACT CCT GAG GAG AAG TCT GCC GTT ACT GCC CTG TGG GGC AAG GTG AAC GTG GAT GAA GTT GGT GGT GAG GCC CTG GGC
Val His Leu Thr Pro Glu Glu Lys Ser Ala Val Thr Ala Leu Trp Gly Lys Val Asn Val Asp Glu Val Gly Gly Glu Ala Leu Gly

HbS Sickle cell (missense)

ATG GTG CAC CTG ACT CCT GTG GAG AAG TCT GCC GTT ACT GCC CTG TGG GGC AAG GTG AAC GTG GAT GAA GTT GGT GGT GAG GCC CTG GGC
Val His Leu Thr Pro Val Glu Lys Ser Ala Val Thr Ala Leu Trp Gly Lys Val Asn Val Asp Glu Val Gly Gly Glu Ala Leu Gly

HbC (missense)

ATG GTG CAC CTG ACT CCT AAG GAG AAG TCT GCC GTT ACT GCC CTG TGG GGC AAG GTG AAC GTG GAT GAA GTT GGT GGT GAG GCC CTG GGC
Val His Leu Thr Pro Lys Glu Lys Ser Ala Val Thr Ala Leu Trp Gly Lys Val Asn Val Asp Glu Val Gly Gly Glu Ala Leu Gly

HbThalassemia (nonsense)

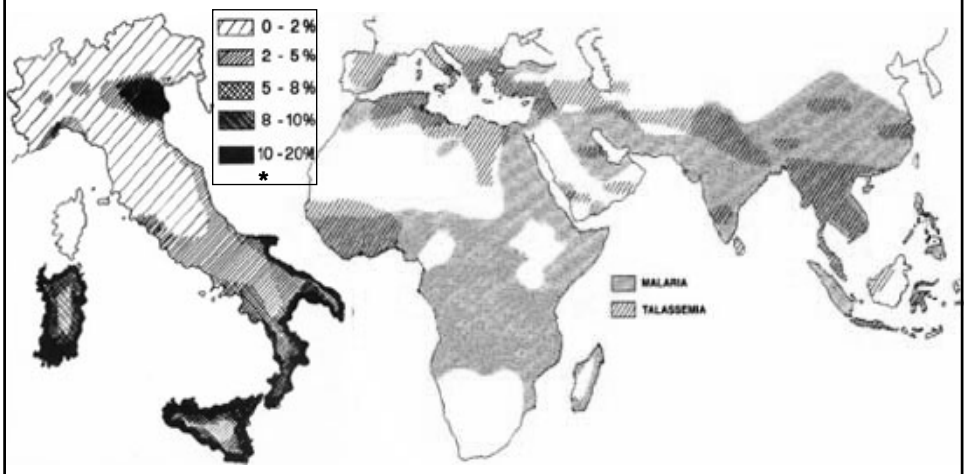
ATG GTG CAC CTG ACT CCT GAG GAG AAG TCT GCC GTT ACT GCC CTG TGG GGC TAG GTG AAC GTG GAT GAA GTT GGT GGT GAG GCC CTG GGC
Val His Leu Thr Pro Glu Glu Lys Ser Ala Val Thr Ala Leu Trp Gly Stop

HbThalassemia (frameshift) -AA

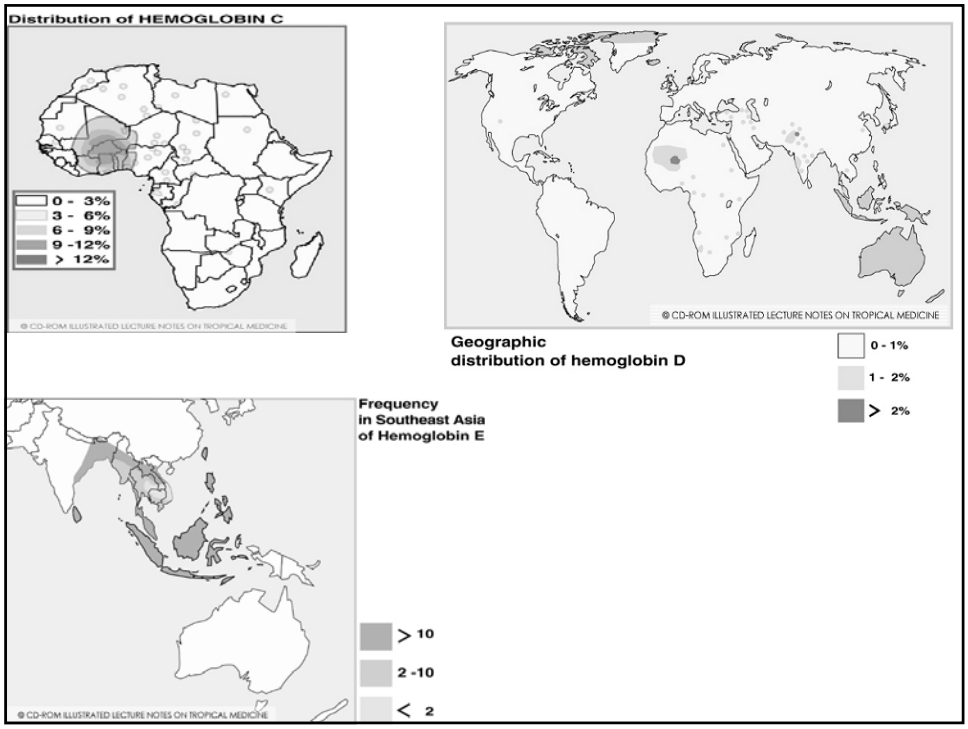
ATG GTG CAC CTG ACT CCT GAG GAG GTC TGC GGT TAC TGC CCT GTG GGG CAA GGT GAA GGT GGA TGA AGT TGG TGG TGA GGC CCT GGG C
Val His Leu Thr Pro Glu Glu Val Cys Arg Tyr Cys Pro Val Gly Gln Gly Glu Arg Ala Stop

Le maggiori varianti emoglobiniche

Hb S	*Bacino Mediterraneo* *Africa (regioni orientali 40%)* *Arabia* *India*
Hb C	*Africa (regioni occidentali 20%)*
Hb D	*India Nord-Ovest*
Hb E	*Sud-Est Asiatico (15-30%)*



* percentuali Microcitemie in Italia non aggiornate (flusso immigratorio)



Esistono variazioni post-traduzionali determinate da

legami con altri composti chimici presenti

nel globulo rosso dovuti processi di

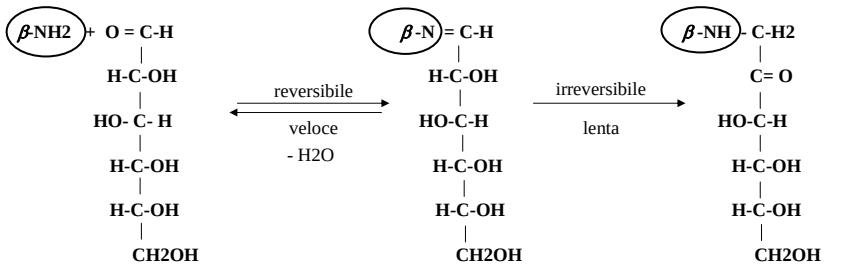
C a r b a m i l a z i o n e

A c e t i l a z i o n e

G l i c a z i o n e

Reazione di glicazione non enzimatica

gruppo aldeidico del glucosio + il gruppo amminico N-terminale delle catene β dell' Hb



Schiff Base (Aldimine)

Amadori Product (Ketoamine)

HbA_{1c} Labile emivita 8 min

HbA_{1c} Stabile emivita 5 gg

Emoglobine: cenni storici

Soggetto normale adulto

HbA ($\alpha_2\beta_2$) circa 95% ***HbA2 ($\alpha_2\delta_2$) fra 2 e 3.5%*** ***HbF ($\alpha_2\gamma_2$) meno del 2%***

1955 Elettroforesi su amido	***Resina a scambio cationico eluizione da colonnine di IRC-50***	***Anno '68 circa***	***Anni '80 Bunn et al.***
Frazioni emoglobiniche "minori" Modifiche post-traduzionali	***A_{1a} A_{1b} A_{1c} A_{1d} A_{1e}***	***A_{1c} aumenta in soggetti affetti da diabete mellito***	***circa 60% del glucosio lega le valine N-terminali delle catene β dell'HbA_{1c}***

Sistemi di misura dell' HbA_{1c}

Differenza di carica elettrica

- *separazione tra HbA_{1c} e HbA* { *HPLC*, *minicolonnine*, *isoelettrofocalizzazione*, *elettroforesi* }

Immunochimici

- *dosaggio senza separazione dall' emoglobina non-glicata*
- *non interferenze biochimiche dovute a varianti emoglobiniche*
- *possibili interferenze biologiche dovute al rapido turnover dell'emoglobina (vita media degli eritrociti)*

Cromatografia di affinità

- *valuta la presenza di glucosio legato covalentemente all'emoglobina*

C r o m a t o g r a f i a

Tecnica di separazione basata sulle proprietà chimico-fisiche dei composti

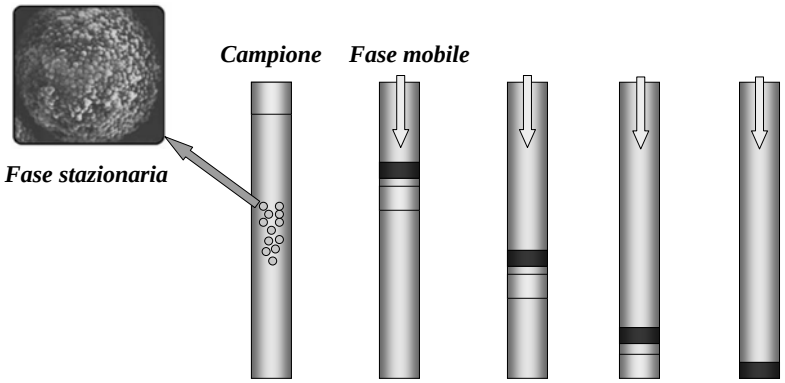
Elevata pressione ⟶ *maggiore velocità di flusso dell' eluente*

Fase Stazionaria	*- Silice microporosa (diametro 3-10 um)* *- Allumina* *- Resina a scambio ionico immiscibile posta in una colonna (vetro, acciaio, titanio) o su una superficie solida*
Fase Mobile	*- Gas* *- Liquido o fluido supercritico* *-Tamponi a diverso pH e forza ionica*

High Performance Liquid Chromatography

High Performance Liquid Chromatography (HPLC) can help identify the types and quantities of haemoglobin made by an individual

HPLC also allows you to detect structurally abnormal haemoglobins



Traguardi analitici per l'HbA$_{1c}$

Precisione, Accuratezza, Variabilità Biologica

CV_b = circa 1 %

CV_w = 3,9 – 7,9 % = circa 5 % → **ET_a = 6,2 %**

CV_a = 2,5 %

ET_a	errore totale ammissibile
CV_a	coefficiente di variazione analitico (limite di imprecisione)
CV_b	coefficiente di variazione intra-individuale
CV_w	coefficiente di variazione inter-individuale

Ricos et al. [Scand J Clin Lab Invest 1999]

2007 GH2-A (fresh pooled samples)

* = NGSP certified at the time of the survey

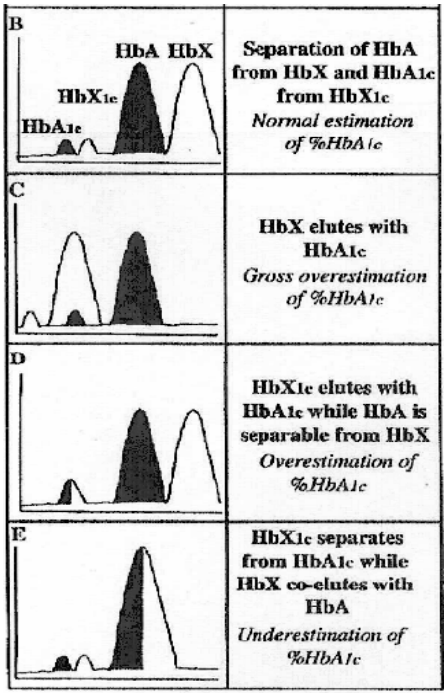
		GH2-01		GH2-02		GH2-03	
NGSP Reference Value[1]		5.4		11.6		7.6	
	no. labs	Median	%CV	Median	%CV	Median	%CV
Methods reporting HbA1c (or equivalent)							
* Abbott Architect	47	5.0	5.0	11.2	3.9	7.4	4.1
* Bayer Advia	33	5.5	4.2	11.3	4.9	7.7	5.2
* Bayer DCA 2000	227	5.2	2.9	11.5	4.8	7.4	2.7
* Beckman Synchron System	385	5.3	4.6	11.7	5.4	7.3	4.6
* Bio-Rad D-10	169	5.5	2.7	12.6	2.3	8.1	2.5
* Bio-Rad Diastat	11	5.2	3.5	11.8	4.4	7.3	3.7
* Bio-Rad Variant A1c	17	5.2	2.6	11.5	2.2	7.5	3.7
* Bio-Rad Variant II A1c	253	5.4	3.4	12.3	2.5	7.9	2.6
* Bio-Rad Variant II Turbo A1c	95	5.4	2.7	12.0	2.6	7.8	2.3
* Dade Behring Dimension	593	5.8	3.1	11.3	3.5	7.6	2.8
* Metrika A1cNOW	23	5.3	6.1	11.7	6.3	7.4	7.7
* Olympus AU system	30	5.6	6.2	12.2	6.1	8.2	5.5
* Pointe Scientific	5	5.0	-	11.0	-	7.5	-
* Primus HPLC (affinity)	36	5.3	2.7	11.7	2.5	7.6	2.3
* Roche cobas c501	6	5.8	-	11.4	-	7.5	-
* Roche Cobas Integra	239	5.5	3.4	11.8	3.7	7.7	3.6
* Roche Cobas Integra Gen.2	72	5.5	3.3	11.7	2.8	7.5	2.3
* Roche/Hitachi (Tina Quant II)	63	5.5	5.2	11.8	4.2	7.5	3.5
* Tosoh A1c 2.2 Plus	186	5.4	3.5	12.4	2.7	8.0	2.9
* Tosoh G7 Auto HPLC	261	5.4	2.4	12.3	1.8	7.9	2.0
* Vitros 5,1 FS Chem Syst	66	5.7	3.6	12.3	4.4	7.7	4.0
[5]Methods reporting Total GHB							
Bio-Rad Variant	10	5.4	6.5	14.1	4.2	8.8	3.9
Primus	15	6.2	4.3	17.1	2.3	10.0	2.9

CV inter-laboratorio <3%

College of American Pathologists (CAP) Survey Data:
(updated 5/07)

Principali interferenti nella misura della HbA_{1c}

• *Emoglobinopatie*	*Interferenza analitica o biologica*
• *Frazione labile*	*Falsi positivi. No per metodi cromatografici ed immunochimici*
• *Insufficienza renale*	*Hb carbamilata*
• *Invecchiamento del campione*	*Interferenza positiva*
• *Ipertrigliceridemia*	*Interferenza positiva per metodi immunoturbidimetrici*
• *Variabilità stagionale*	*Discreto effetto ciclico*
• *Processi emolitici*	*falsi negativi (diminuzione vita media eritrocitaria)*
• *Aumento WBC*	*Interferenze positive*



HPLC

- *Separa le Hb sulla base delle differenze di carica*
- *Uno spettrofotometro misura la concentrazione di Hb in ogni frazione*
- *Eluizione con tamponi che aumentano la forza ionica*
- *Risultati inesatti di HbA1c si verificano quando HbX, o HbX1c non possono essere separati da HbA0 o da HbA1c*

Clinical Chemistry 54:8
000–000 (2008)

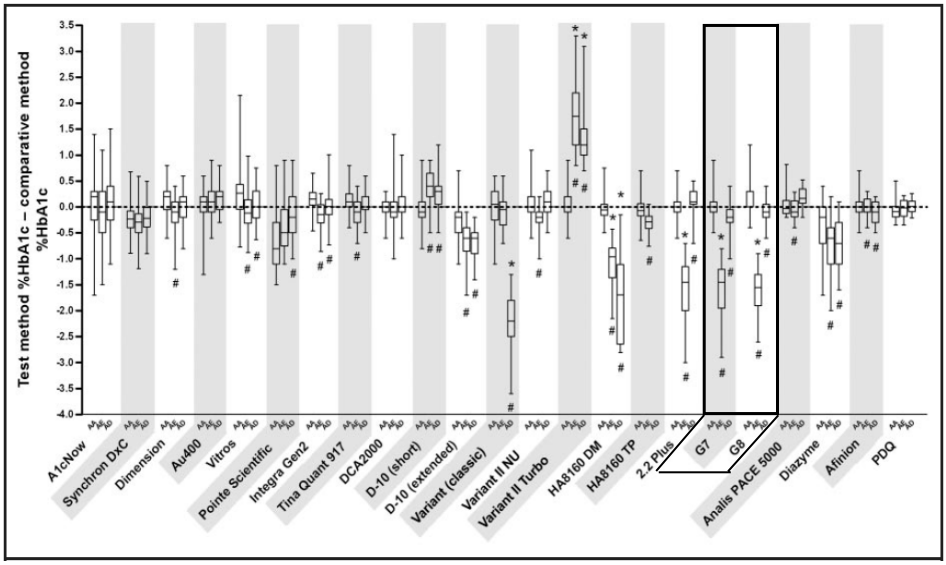
Effects of Hemoglobin (Hb) E and HbD Traits on Measurements of Glycated Hb (HbA_{1c}) by 23 Methods

Randie R. Little,[1*] Curt L. Rohlfing,[1] Steve Hanson,[1] Shawn Connolly,[1] Trefor Higgins,[2] Cas W. Weykamp,[3] Mario D'Costa,[4] Veronica Luzzi,[5] William E. Owen,[6] and William L. Roberts[7]

Effects of Hemoglobin C and S Traits on Glycohemoglobin Measurements by Eleven Methods, *William L. Roberts,[1*] Sekineh Safar-Pour,[2] Barun K. De,[3] Curt L. Rohlfing,[4] Cas W. Weykamp,[5] and Randie R. Little[4]* ([1] Department of Pathology, ARUP Institute for Clinical & Experimental Pathology, University of Utah, Salt Lake City, UT; [2] ARUP Laboratories, Salt Lake City, UT; [3] Department of Pathology, University of Arizona, Tucson, AZ; [4] Departments of Pathology & Anatomical Sciences and Child Health, University of Missouri-Columbia School of Medicine, Columbia, MO; [5] Queen Beatrix Hospital, Winterswijk, The Netherlands; * address correspondence to this author at: ARUP

Clinical Chemistry 51, No. 4, 2005

Effects of Hemoglobin HbE and HbD Traits
on Measurements of Glycated Hb (HbA_{1c}) by 23 Methods



Clinical Chemistry **54:8 (2008)**

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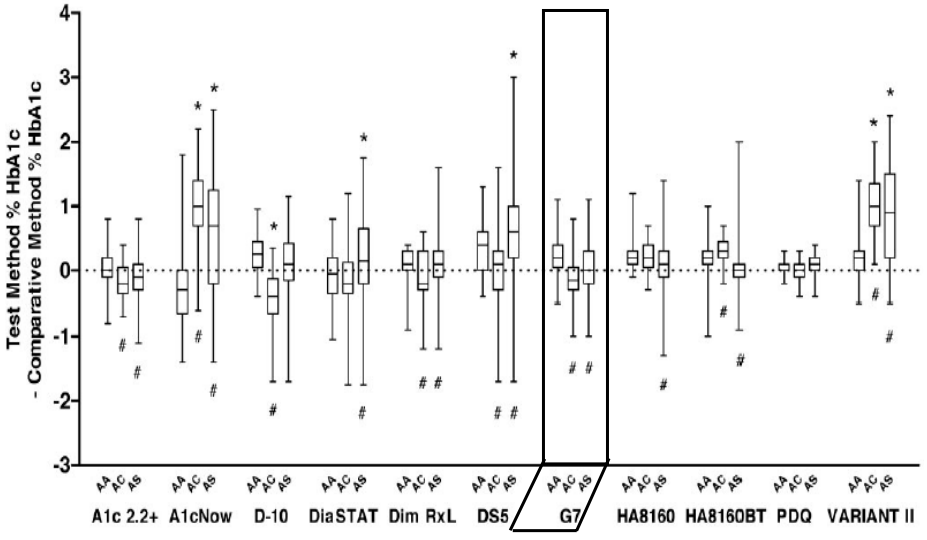


Clinical Chemistry **51, No. 4, 2005**

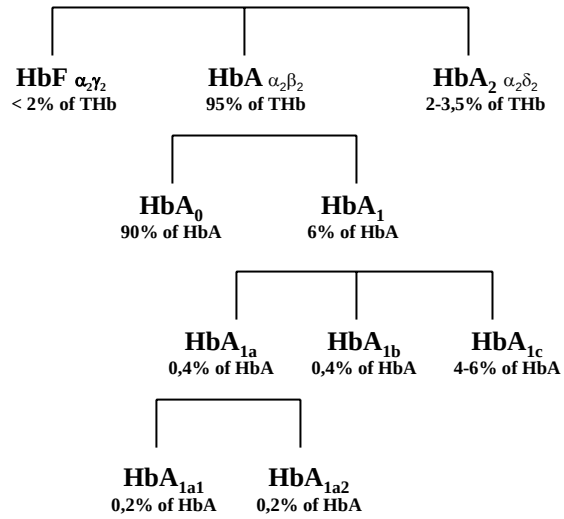
Calculation of HbA_{1c}

What is Hemoglobin?

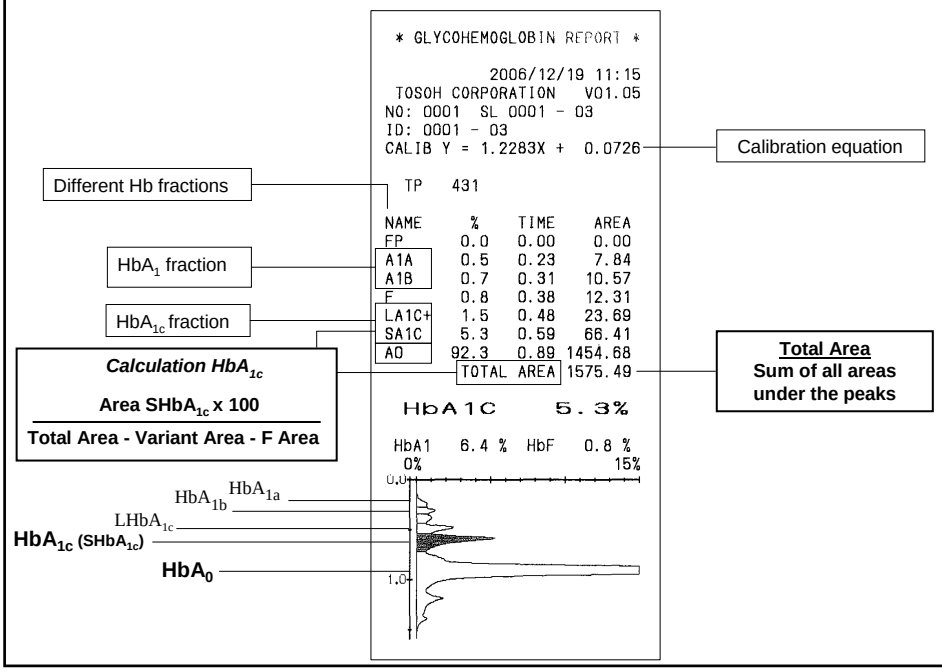
What is HbA_{1c}?

How is HbA_{1c} calculated?

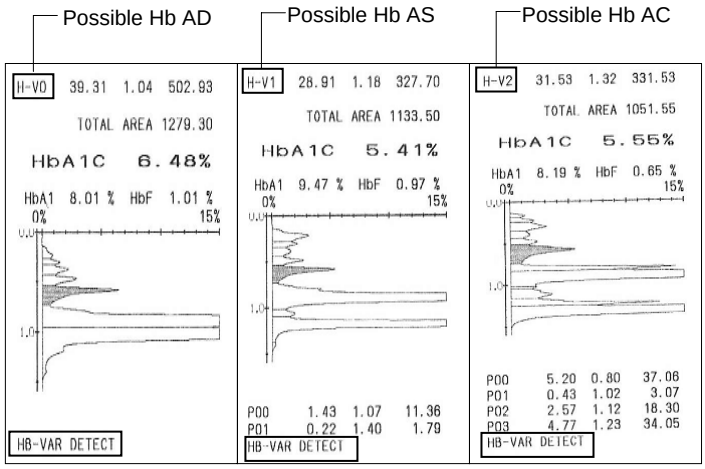
Total Haemoglobin (THb)



C r o m a t o g r a m m a



When variants are eluting in the H-V0, H-V1 and/or H-V2 window, they will be automatically excluded from the calculation to ensure a correct value



Why on Total Area and not on area of HbA_0 ?

Ratio should be calculated using the <u>total amount of</u> HbA $\alpha_2\beta_2$ and not only HbA_0

HbA_0 is only one fraction of the HbA

```
 * GLYCOHEMOGLOBIN REPORT *

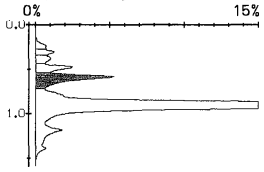
            2006/12/19 11:15
 TOSOH CORPORATION    V01.05
NO: 0001  SL 0001 - 03
ID: 0001 - 03
CALIB Y = 1.2283X +  0.0726

  TP   431

NAME      %     TIME     AREA
FP      0.0     0.00     0.00
A1A     0.5     0.23     7.84
A1B     0.7     0.31    10.57
F       0.8     0.38    12.31
LA1C+   1.5     0.48    23.69
SA1C    5.3     0.59    66.41
A0     92.3     0.89  1454.68
       TOTAL AREA  1575.49

HbA1C      5.3%

HbA1   6.4 %  HbF   0.8 %
 0%                    15%
```



```
 TOSOH CORPORATION    V03.00
NO: 0001  SL 0001 - 01
ID: 0001 - 01
CALIB Y = 1.1034X +  0.5726

  TP   566

NAME      %     TIME     AREA
FP      0.00    0.00     0.00
A1A     0.76    0.24     5.77
A1B     0.77    0.31     5.88
F       1.01    0.38    12.97
LA1C+   2.15    0.47    16.43
SA1C    6.48    0.59    40.87
A0     90.97    0.89   694.46

H-V0   39.31    1.04   502.93

       TOTAL AREA 1279.30

HbA1C    6.48%

HbA1  8.01 %  HbF  1.01 %
 0%                    15%
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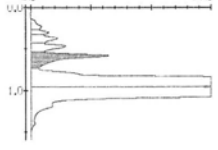

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HB-VAR DETECT
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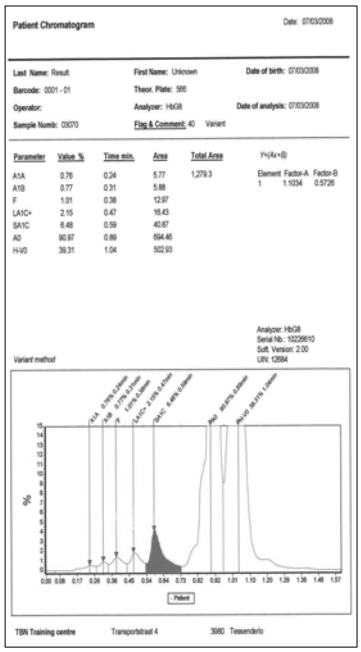
Possible HbAD patient

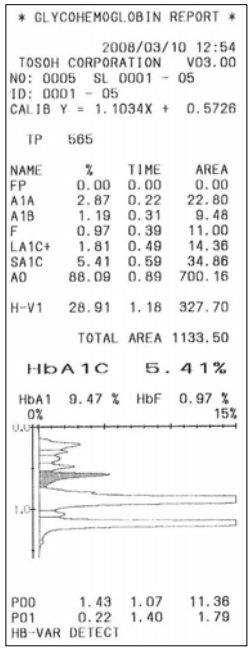
H-V0 present of 39.31%

HbA_{1c} higher than normal

Normal range can not be used

Result can be reported
Remark: Possible HbAD





```
* GLYCOHEMOGLOBIN REPORT *
            2008/03/10 12:54
 TOSOH CORPORATION    V03.00
NO: 0005  SL 0001 - 05
ID: 0001 - 05
CALIB Y = 1.1034X +  0.5726

  TP   565

NAME      %    TIME    AREA
FP     0.00   0.00    0.00
A1A    2.87   0.22   22.80
A1B    1.19   0.31    9.48
F      0.97   0.39   11.00
LA1C+  1.81   0.49   14.36
SA1C   5.41   0.59   34.86
A0    88.09   0.89  700.16

H-V1  28.91   1.18  327.70

          TOTAL AREA 1133.50

     HbA1C    5.41%

HbA1  9.47 %  HbF  0.97 %
 0%                    15%
P00     1.43   1.07   11.36
P01     0.22   1.40    1.79
HB-VAR DETECT
```

Possible HbAS patient

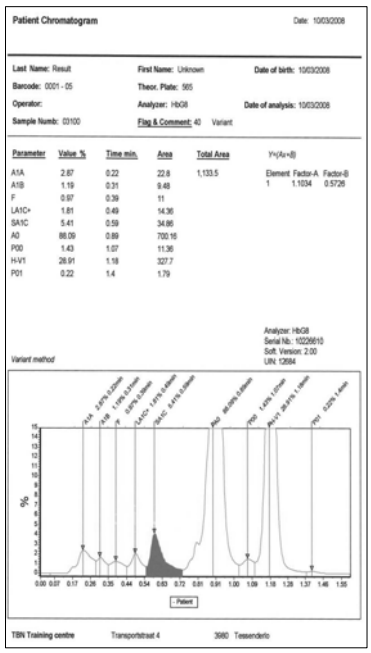
H-V1 present of 28.91%

HbA_{1c} is normal

P00 is glycated HbS

P01 is not significant

Result can be reported
Remark: Possible HbAS



Patient Chromatogram

Date: 10/03/2008

Last Name: Result — First Name: Unknown — Date of birth: 10/03/2008
Barcode: 0001 - 05 — Theor. Plate: 565
Operator: — Analyzer: HbG8 — Date of analysis: 10/03/2008
Sample Numb: 03100 — Flag & Comment: 40 Variant

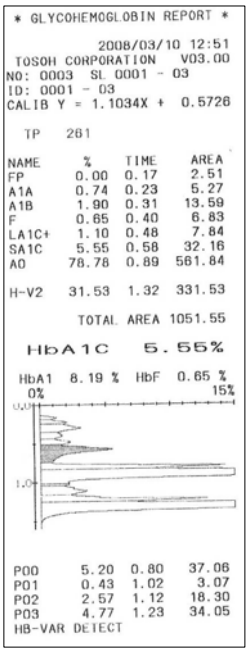
Parameter	Value %	Time min.	Area	Total Area
A1A	2.87	0.22	22.8	1,133.5
A1B	1.19	0.31	9.48	
F	0.97	0.39	11	
LA1C+	1.81	0.49	14.36	
SA1C	5.41	0.59	34.86	
A0	88.09	0.89	700.16	
P00	1.43	1.07	11.36	
H-V1	28.91	1.18	327.7	
P01	0.22	1.4	1.79	

Y=(Ax+B) — Element Factor-A Factor-B: 1 1.1034 0.5726

Analyzer: HbG8
Serial Nb.: 10226610
Soft. Version: 2.00
URN: 12684

Variant method

TBN Training centre — Transportstraat 4 — 3980 Tessenderlo



```
* GLYCOHEMOGLOBIN REPORT *
            2008/03/10 12:51
 TOSOH CORPORATION    V03.00
NO: 0003  SL 0001 - 03
ID: 0001 - 03
CALIB Y = 1.1034X +  0.5726

  TP   261

NAME      %    TIME    AREA
FP     0.00   0.17    2.51
A1A    0.74   0.23    5.27
A1B    1.90   0.31   13.59
F      0.65   0.40    6.83
LA1C+  1.10   0.48    7.84
SA1C   5.55   0.58   32.16
A0    78.78   0.89  561.84

H-V2  31.53   1.32  331.53

          TOTAL AREA 1051.55

     HbA1C    5.55%

HbA1  8.19 %  HbF  0.65 %
 0%                    15%
P00     5.20   0.80   37.06
P01     0.43   1.02    3.07
P02     2.57   1.12   18.30
P03     4.77   1.23   34.05
HB-VAR DETECT
```

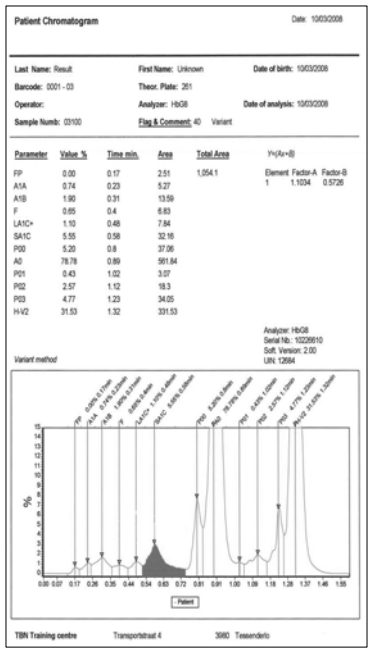
Possible HbAC patient

H-V2 present

HbA_{1c} is normal

A lot of P0 peaks → aged sample

Result can not be reported due to aging
Remark: Possible HbAC



Patient Chromatogram

Date: 10/03/2008

Last Name: Result — First Name: Unknown — Date of birth: 10/03/2008
Barcode: 0001 - 03 — Theor. Plate: 261
Operator: — Analyzer: HbG8 — Date of analysis: 10/03/2008
Sample Numb: 03100 — Flag & Comment: 40 Variant

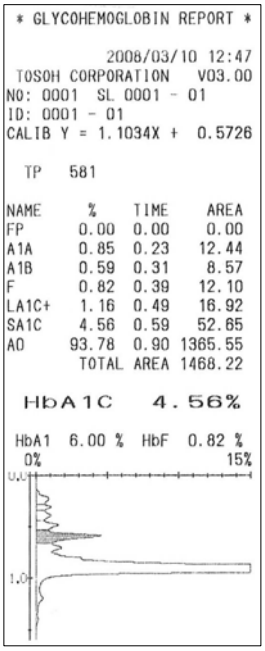
Parameter	Value %	Time min.	Area	Total Area
FP	0.00	0.17	2.51	1,054.1
A1A	0.74	0.23	5.27	
A1B	1.90	0.31	13.59	
F	0.65	0.4	6.83	
LA1C+	1.10	0.48	7.84	
SA1C	5.55	0.58	32.16	
P00	5.20	0.8	37.06	
A0	78.78	0.89	561.84	
P01	0.43	1.02	3.07	
P02	2.57	1.12	18.3	
P03	4.77	1.23	34.05	
H-V2	31.53	1.32	331.53	

Y=(Ax+B) — Element Factor-A Factor-B: 1 1.1034 0.5726

Analyzer: HbG8
Serial Nb.: 10226610
Soft. Version: 2.00
URN: 12684

Variant method

TBN Training centre — Transportstraat 4 — 3980 Tessenderlo



```
* GLYCOHEMOGLOBIN REPORT *

          2008/03/10 12:47
 TOSOH CORPORATION    V03.00
NO: 0001  SL 0001 - 01
ID: 0001 - 01
CALIB Y = 1.1034X +  0.5726

  TP   581

NAME      %    TIME     AREA
FP     0.00   0.00     0.00
A1A    0.85   0.23    12.44
A1B    0.59   0.31     8.57
F      0.82   0.39    12.10
LA1C+  1.16   0.49    16.92
SA1C   4.56   0.59    52.65
A0    93.78   0.90  1365.55
        TOTAL AREA  1468.22

      HbA1C    4.56%

HbA1  6.00 %  HbF  0.82 %
 0%                    15%
```

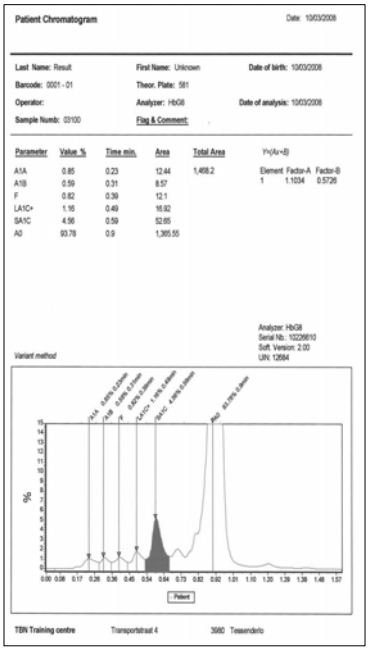

Possible HbAE patient

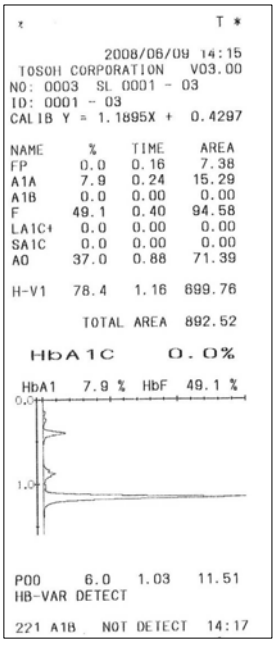
HbA_{1c} is normal

E variant under A0

Small shoulder between SA1c and A0 → glycated E

Result can not be reported
Remark: Possible HbAE





```
*                          T *

          2008/06/09 14:15
 TOSOH CORPORATION    V03.00
NO: 0003  SL 0001 - 03
ID: 0001 - 03
CALIB Y = 1.1895X +  0.4297

NAME      %    TIME     AREA
FP     0.0   0.16     7.38
A1A    7.9   0.24    15.29
A1B    0.0   0.00     0.00
F     49.1   0.40    94.58
LA1C+  0.0   0.00     0.00
SA1C   0.0   0.00     0.00
A0    37.0   0.88    71.39

H-V1  78.4   1.16   699.76

        TOTAL AREA  892.52

      HbA1C     0.0%

HbA1  7.9 %  HbF  49.1 %
```



```
P00     6.0   1.03    11.51
HB-VAR DETECT

221 A1B   NOT DETECT  14:17
```

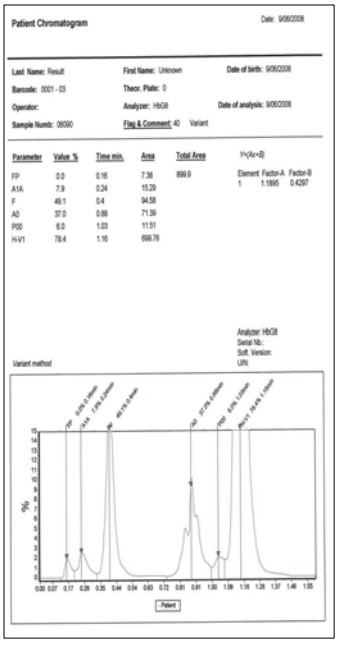
Possible HbSS patient

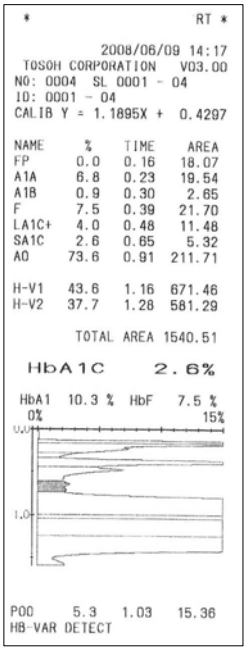
H-V1 peak of 78.4%

HbA_{1c} of 0.0%

No HbA present because HbSS

No HbA_{1c} present
Remark: Possible HbSS





```
*                              RT *
                    2008/06/09 14:17
 TOSOH CORPORATION          V03.00
NO: 0004  SL 0001 - 04
ID: 0001 - 04
CALIB Y = 1.1895X +  0.4297

NAME      %     TIME     AREA
FP       0.0    0.16    18.07
A1A      6.8    0.23    19.54
A1B      0.9    0.30     2.65
F        7.5    0.39    21.70
LA1C+    4.0    0.48    11.48
SA1C     2.6    0.65     5.32
A0      73.6    0.91   211.71

H-V1    43.6    1.16   671.46
H-V2    37.7    1.28   581.29

          TOTAL AREA 1540.51

      HbA1C      2.6%

HbA1  10.3 %  HbF   7.5 %
 0%                    15%
```



```
P00      5.3    1.03    15.36
HB-VAR DETECT
```

Possible HbSC patient

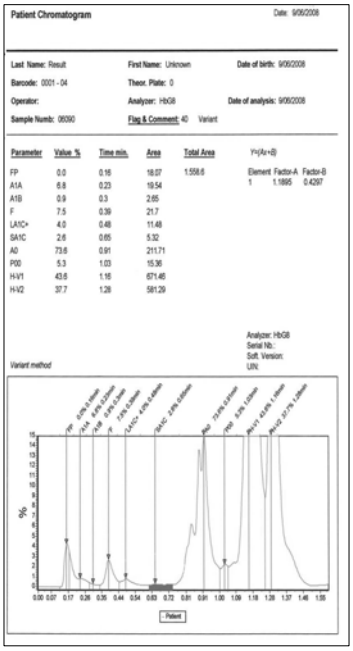
H-V1 peak of 43.6% → HbS

H-V2 peak of 37.7% → HbC

HbA_{1c} is lower than normal

2.6% is not HbA1c → no HbA present because HbSC

HbA_{1c} result can not be reported
Remark: Possible HbSC



Patient Chromatogram

Date: 9/09/2008

Last Name: Result First Name: Unknown Date of birth: 9/09/2008

Barcode: 0001 - 04 Theor. Plate: 0

Operator: Analyzer: HbG8 Date of analysis: 9/09/2008

Sample Numb: 09390 Flag & Comment: 40 Variant

Parameter	Value %	Time min.	Area	Total Area
FP	0.0	0.16	18.07	1.558.6
A1A	6.8	0.23	19.54	
A1B	0.9	0.3	2.65	
F	7.5	0.39	21.7	
LA1C+	4.0	0.48	11.48	
SA1C	2.6	0.65	5.32	
A0	73.6	0.91	211.71	
P00	5.3	1.03	15.36	
H-V1	43.6	1.16	671.46	
H-V2	37.7	1.28	581.29	

Y=(Ax+B)

Element	Factor-A	Factor-B
1	1.1895	0.4297

Analyzer: HbG8
Serial Nb.:
Soft. Version:
LRN:

Variant method

AZIENDA OSPEDALIERA OSPEDALI RIUNITI DI BERGAMO

Confronto fra due metodi HPLC nella rilevazione dell'HbA_{1c} in campioni con e senza varianti emoglobiniche

Freddi C.*, Amboni P.* , Nani C.* , Maestroni C.*, Calufetti I.*, DeMarinis R.°, Ottomano C.*

**** Dipartimento di Medicina di Laboratorio, Laboratorio Analisi Chimico Cliniche, A.O. Ospedali Riuniti di Bergamo, Italy***

° Tosoh Bioscience, S.r.l.,Torino, Italy

biochimica clinica, 2008, vol. 32, n. 5

Numero campioni processati : 287

- ✓ *Campioni rilevanti picchi anomali con richiesta dosaggio HbA_{1c}*
- ✓ *Campioni con probabili varianti con richiesta dosaggio Hb Patologiche*
- ✓ *Dati emocromo*
- ✓ *Sangue intero (K_3EDTA / Litio Eparina)*
- ✓ *Processati in tempo reale*
- ✓ *Conservati a 2-8 ℃ se analizzati entro 7 giorni*
- ✓ *Congelati e scongelati se analizzati oltre tale limite di tempo*

Tosoh H723G7BetaThal Mode
Tosoh HLC-723G7HbA1c Variant Mode

```
* GLYCOHEMOGLOBIN REPORT *

 TOSOH CORPORATION    V01.15
NO:
ID:
CALIB Y = 1.1091X +  0.8654

  TP   636

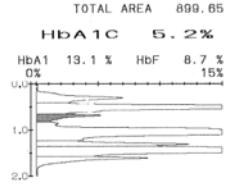
NAME      %     TIME     AREA
FP      0.0     0.00     0.00
A1A     7.9     0.31    14.23
A1B     0.0     0.00     0.00
F       8.7     0.52    77.97
LA1C+   0.0     0.00     0.00
SA1C    5.2     0.70     7.76
A0     71.7     1.08   128.79

H-V1   71.4     1.44   641.96

          TOTAL AREA    899.65

        HbA1C    5.2%

HbA1  13.1 %   HbF   8.7 %
 0%                    15%
```



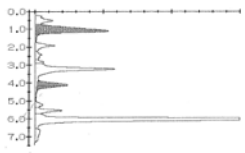
```
P00      8.6     1.32    15.50
P01      7.5     1.82    13.44
HB-VAR DETECT
```

```
** THALASSEMIA    REPORT **
   OSP.RIUNITI <BG>
 TOSOH CORPORATION    V01.15
NO:
ID:
CALIB F   Y = 0.9978X
      A2  Y = 1.8156X

  TP  2074

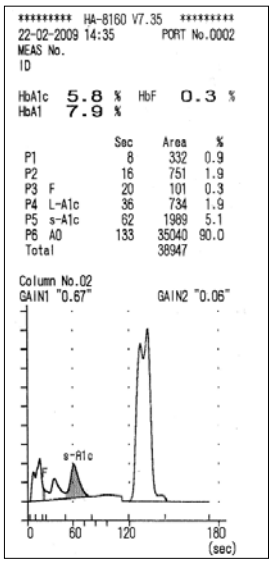
NAME      %     TIME     AREA
F       8.4     1.11   161.15
A0      8.2     3.22   156.08
A2      4.8     4.12    56.07
D+      0.0     0.00     0.00
S+     72.4     8.03  1378.66
C+      0.0     0.00     0.00
        TOTAL AREA    1904.11

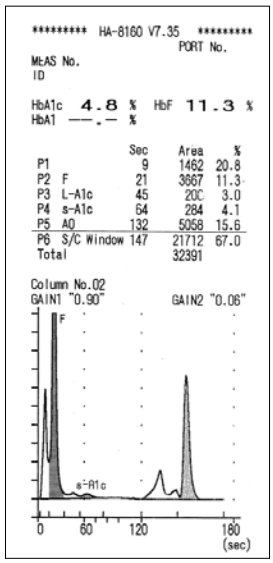
     F :    8.4%
     A2:    4.8%
```



```
P00      1.8     0.52    34.14
P01      1.5     1.91    27.75
P02      0.7     2.41    13.82
P03      0.5     2.85     8.35
P04      0.7     5.23    12.64
P05      1.8     6.55    34.21
P06      1.1     8.67    20.24
```

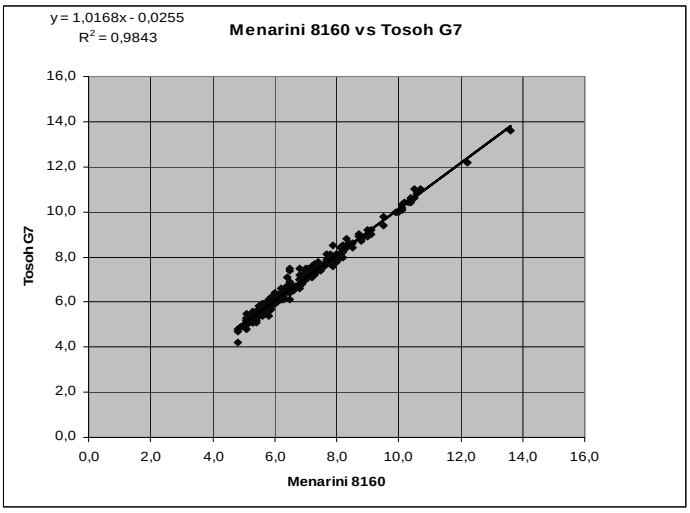
Menarini Adams A1c HA-8160





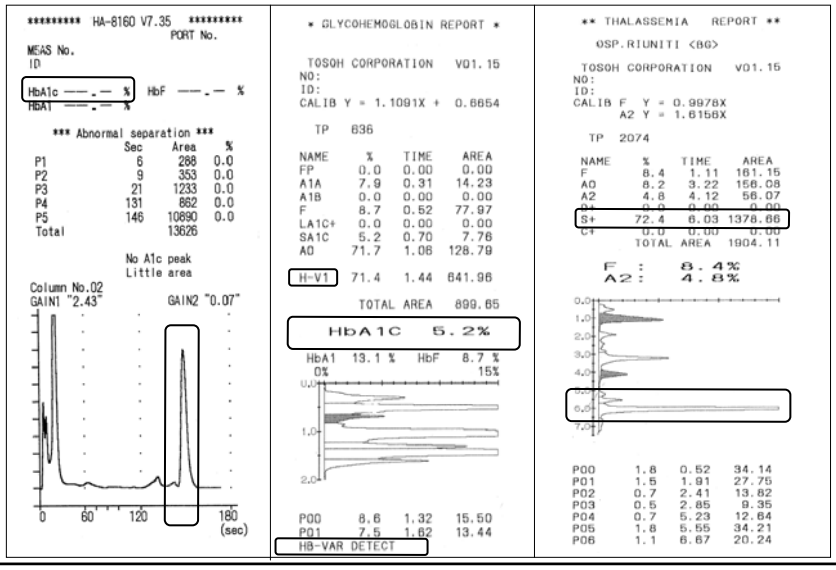
Menarini Adams A1c HA-8160
Tosoh HLC-723G7HbA1c Variant Mode

I due sistemi, su <u>campioni normali</u> (269), presentano una buona correlazione (R^2 = 0.9843)



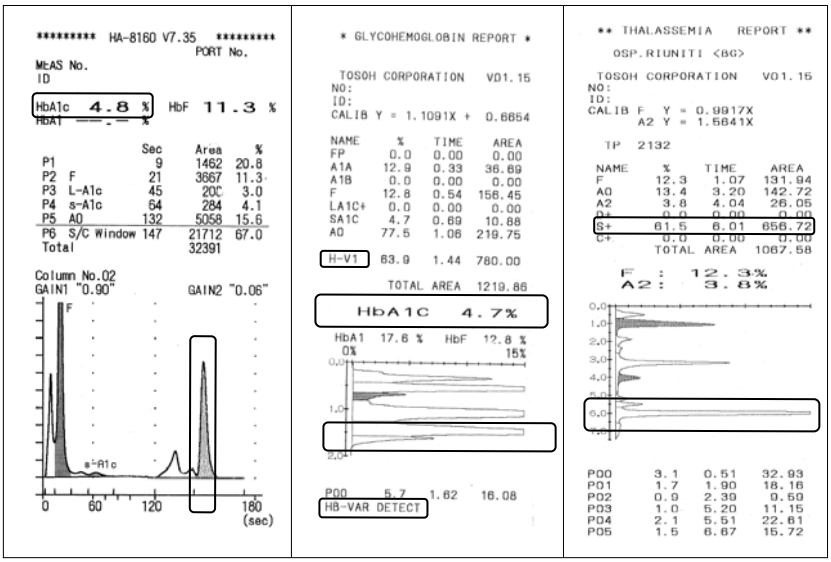
HbS Variante omozigote

i n e s a t t e z z a a n a l i t i c a
(assenza o verosimile sottostima)



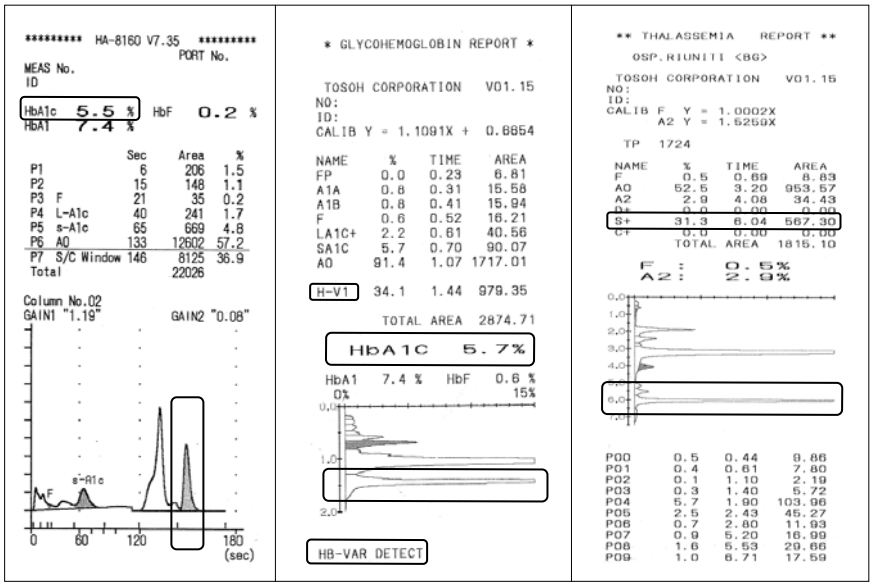
HbS Variante omozigote

i n e s a t t e z z a a n a l i t i c a
(assenza o verosimile sottostima)



HbS Variante eterozigote

S o v r a p p o n i b i l i



********* HA-8160 V7.35 *********
PORT No.
MEAS No.
ID

HbA1c 5.5 % HbF 0.2 %
HbA1 7.4 %

	Sec	Area	%
P1	6	206	1.5
P2	15	148	1.1
P3 F	21	35	0.2
P4 L-A1c	40	241	1.7
P5 s-A1c	65	669	4.8
P6 A0	133	12602	57.2
P7 S/C Window	146	8125	36.9
Total		22026	

Column No.02
GAIN1 "1.19" GAIN2 "0.08"

* GLYCOHEMOGLOBIN REPORT *

TOSOH CORPORATION V01.15
NO:
ID:
CALIB Y = 1.1091X + 0.8654

NAME	%	TIME	AREA
FP	0.0	0.23	6.81
A1A	0.8	0.31	15.58
A1B	0.8	0.41	15.94
F	0.6	0.52	16.21
LA1C+	2.2	0.61	40.56
SA1C	5.7	0.70	90.07
A0	91.4	1.07	1717.01
H-V1	34.1	1.44	979.35

TOTAL AREA 2874.71

HbA1C 5.7%

HbA1 7.4 % HbF 0.6 %
0% 15%

HB-VAR DETECT

** THALASSEMIA REPORT **
OSP.RIUNITI <BG>

TOSOH CORPORATION V01.15
NO:
ID:
CALIB F Y = 1.0002X
A2 Y = 1.5260X

TP 1724

NAME	%	TIME	AREA
F	0.5	0.69	8.83
A0	52.5	3.20	953.57
A2	2.9	4.08	34.43
D+	0.0	0.00	0.00
S+	31.3	6.04	567.30
C+	0.0	0.00	0.00

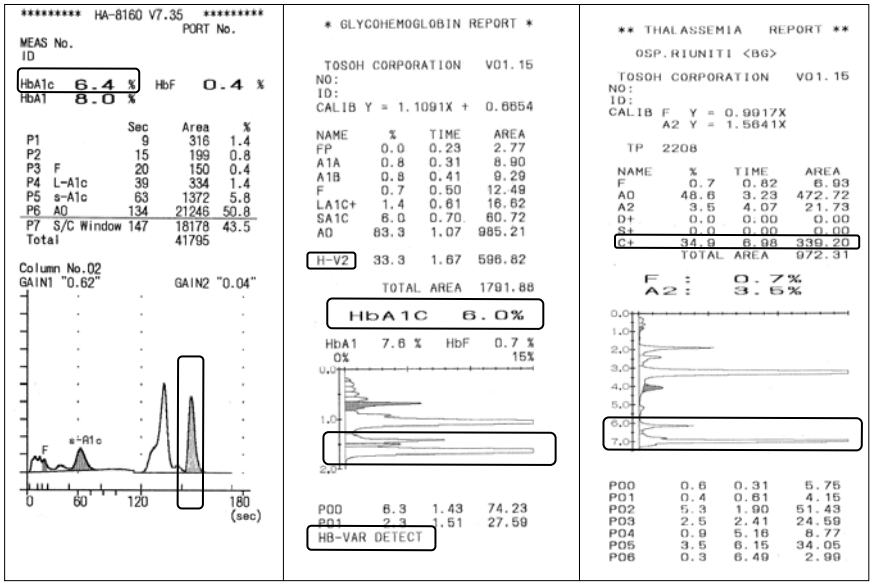
TOTAL AREA 1815.10

F : 0.5%
A2 : 2.9%

P00	0.5	0.44	9.86
P01	0.4	0.61	7.80
P02	0.1	1.10	2.19
P03	0.3	1.40	5.72
P04	5.7	1.90	103.96
P05	2.5	2.43	45.27
P06	0.7	2.80	11.93
P07	0.9	5.20	16.99
P08	1.6	5.53	29.66
P09	1.0	6.71	17.59

HbC Variante eterozigote

S o v r a p p o n i b i l i



********* HA-8160 V7.35 *********
PORT No.
MEAS No.
ID

HbA1c 6.4 % HbF 0.4 %
HbA1 8.0 %

	Sec	Area	%
P1	9	316	1.4
P2	15	199	0.8
P3 F	20	150	0.4
P4 L-A1c	39	334	1.4
P5 s-A1c	63	1372	5.8
P6 A0	134	21246	50.8
P7 S/C Window	147	18178	43.5
Total		41795	

Column No.02
GAIN1 "0.62" GAIN2 "0.04"

* GLYCOHEMOGLOBIN REPORT *

TOSOH CORPORATION V01.15
NO:
ID:
CALIB Y = 1.1091X + 0.8654

NAME	%	TIME	AREA
FP	0.0	0.23	2.77
A1A	0.8	0.31	8.90
A1B	0.8	0.41	9.29
F	0.7	0.50	12.48
LA1C+	1.4	0.61	16.62
SA1C	6.0	0.70	60.72
A0	83.3	1.07	985.21
H-V2	33.3	1.67	596.82

TOTAL AREA 1791.88

HbA1C 6.0%

HbA1 7.6 % HbF 0.7 %
0% 15%

P00	6.3	1.43	74.23
P01	2.3	1.51	27.59

HB-VAR DETECT

** THALASSEMIA REPORT **
OSP.RIUNITI <BG>

TOSOH CORPORATION V01.15
NO:
ID:
CALIB F Y = 0.9917X
A2 Y = 1.5641X

TP 2208

NAME	%	TIME	AREA
F	0.7	0.82	6.93
A0	48.8	3.23	472.72
A2	3.5	4.07	21.73
D+	0.0	0.00	0.00
S+	0.0	0.00	0.00
C+	34.9	6.98	339.20

TOTAL AREA 972.31

F : 0.7%
A2 : 3.5%

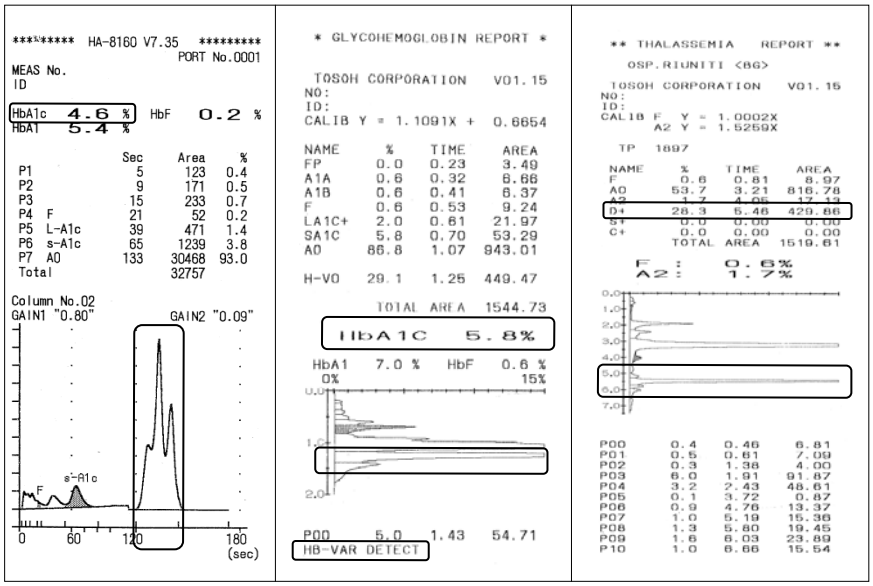
P00	0.6	0.31	5.75
P01	0.4	0.61	4.15
P02	5.3	1.90	51.43
P03	2.5	2.41	24.59
P04	0.9	5.18	8.77
P05	3.5	6.15	34.05
P06	0.3	6.49	2.99

HbD Variante eterozigote

Sensibile sottostima

Menarini Adams
A1c HA-8160

Tosoh
HLC-723G7HbA1c Variant Mode



G r a z i e