Familial Study on "Sinking pre-beta", the Lp(a) Lipoprotein, and its Relationship with Serum Lipids, Apolipoprotein A-I and B and Clinical Atherosclerosis

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Summary: A total of 42 family members, 21 females and 21 males, distributed in 3 generations were studied; 32 were blood related while 10 were controls (not blood related).

The familial propositus, a young male subject 36 years old, who had suffered from juvenile acute myocardial infarction, exhibited upon lipoprotein agarose gel electrophoresis two distinct pre-beta bands. The slow pre-beta component turned out to be a "sinking pre-beta", the Lp(a) lipoprotein. The familial distribution of the character "sinking pre-beta lipoprotein", as it appeared on agarose gel electrophoresis of whole serum, and the segregation analysis data confirm an autosomal dominant transmission.

No sex differences were observed in the prevalence of the sinking pre-beta lipoprotein. Serum mean levels of total cholesterol, triglycerides, apolipoprotein A-I and B and of the very low density total cholesterol/triglycerides ratio did not discriminate between (+) and (−) "sinking pre-beta lipoprotein". In all the family members the Lp(a) antigen was measured by rocket immunoelectrophoresis.

Comparing the Lp(a) values with the behaviour of the "sinking pre-beta lipoprotein" in agarose gel electrophoresis, we demonstrated that the ability to visualize a slow moving pre-beta component, identified as the "sinking pre-beta lipoprotein", is correlated with serum Lp(a) levels above 0.3 g/l.

An inverse relationship between apolipoprotein A-I and Lp(a) values was observed (r = 0.36; p < 0.05). In spite of relatively low apolipoprotein A-I levels and high Lp(a) values, no clinical patterns of atherosclerotic diseases were found in the family members. The reasons for this discrepancy are discussed.

Familien-Studie über „sinking prae-beta", das Lp(a)-Lipoprotein und seine Beziehungen zu Serumlipiden, Apolipoprotein A-1 und B sowie klinisch manifester Arteriosklerose

Zusammenfassung: Aus drei Generationen wurden insgesamt 42 Familienangehörige, 21 männlich und 21 weiblich, untersucht; davon waren 32 blutsverwandt, während 10 nicht-blutsverwandte als Kontrollen dienten.

Der vorgestellte Fall, ein 36jähriger Mann, der an jugendlichem akuten Myokardinfarkt erkrankte, zeigte in der Lipoprotein-Agarosegelelektrophorese zwei deutlich unterschiedene prae-β-Banden. Die langsame prae-β-Komponente erweist sich als ein „sinking prae-β", das Lp(a)-Lipoprotein.

Die familiäre Verteilung des Charakteristikums „sinking prae-β"-Lipoprotein, nachgewiesen durch Agargelelektrophorese des Gesamt-Serums, und die Daten der Aufspaltungsanalyse bestätigen eine autosomal dominante Vererbung.

In der Prävalenz des „sinking prae-β"-Lipoproteins wurden keine Geschlechtsunterschiede bemerkt. Die Konzentrationen von Gesamt-Cholesterin, Triglyceriden, Apolipoprotein A-I und B im Serum sowie das Verhältnis Gesamt-Cholesterin/Triglyceride in den VLDL ließen nicht zwischen „sinking prae-β"-positiv oder -negativ unterscheiden. Bei allen Familienangehörigen wurde das Lp(a)-Antigen durch *Laurell* („rocket")-Immunelektrophorese gemessen. Durch Vergleich der Lp(a)-Werte mit dem Verhalten des „sinking prea-β"-Lipoproteins in der Agargelelektrophorese zeigten wir, daß das Sichtbarmachen einer langsam wandernden prae-β-Komponente, identifiziert als das „sinking prae-β", an Lp(a)-Konzentrationen > 0,3 g/l Serum gebunden ist.

Eine umgekehrte Beziehung zwischen Apolipoprotein A-I- und Lp(a)-Werten wurde beobachtet ($r = 0,36$; $p \leqslant 0,05$). Trotz relativ geringer Apolipoprotein A-I- und hoher Lp(a)-Werte wurde keine klinisch manifeste Arteriosklerose bei den Familienangehörigen gefunden. Die Ursachen für diese Diskrepanz werden diskutiert.

Introduction

The general interest concerning the Lp(a) lipoprotein, also called "sinking pre-beta", is mainly due to its possible relationship with the development of premature atherosclerosis (1–6). Although the reported prevalence of the "sinking pre-beta", as recorded by agarose gel electrophoresis, is quite variable (2, 4, 5, 7), detectable amounts of the Lp(a) lipoprotein, as determined by immunological methods, are present almost in all subjects. The aim of our study was to analyse the correlation between serum Lp(a) levels, as measured by rocket immunoelectrophoresis, and the electrophoretic appearance of the "sinking pre-beta". Moreover, we have evaluated in a large family the familial aggregation of the "sinking pre-beta" (Lp(a) lipoprotein) and its relationship with serum lipids, A-I and B apolipoproteins and finally the prevalence of clinical atherosclerosis.

Materials and Methods

The propositus of our family study is a male subject 36 years old, admitted to our clinic for an acute myocardial infarction. The diagnosis of myocardial infarction was made on the usual clinical, enzymatic and electrocardiographic criteria. Some clinical and chemical data concerning the propositus are refferred in table 1. Besides the propositus, 41 family members were included in the study: 10 controls (not blood related) and 31 blood relatives belonging to 3 generations (tab. 2). Rest and exercise electrocardiograms were performed on all the blood relatives; the Minnesota Code was used for the interpretation of the electrocardiographic tracings. Blood pressure was taken in supine position by means of a *Riva-Rocci* instrument. Diastolic blood pressure was recorded at the disappearance of the *Korotkow* tones (V phase).

Agarose gel electrophoresis was performed according to a modification (8) of the technique of *Noble* (9). Serum total cholesterol and triglycerides were measured on Autoanalyzer Technicon II according to standard enzymatic methods. The intermediate density lipoprotein fraction (d = 1.006 to 1.019 kg/l) was obtained by ultracentrifugation according to *Havel* et al. (10). In order to confirm the true "sinking" nature of the slow moving pre-beta band, agarose gel electrophoresis was performed with serum as well as with the d = 1.019 kg/l bottom fraction and the d < 1.006 kg/l

Tab. 1. Clinical and chemical data concerning the propositus (B. B.).

Age (a)	Sex	Blood pressure (mmHg)	Smoking cigarettes (number)	Blood glucose (g/l)	Total cholesterol (TC) (g/l)	Triglycerides (TG) (g/l)	VLDL TC/TG ratio	Lp(a) (g/l)	Apolipoprotein A-I (g/l)	B (g/l)
36	♂	150/95	20	0.95	3.05	1.84	0.27	0.77	1.09	1.57

fraction (very low density lipoproteins) for all family members. Sinking pre-beta positive refers to the appearance of the slow moving pre-beta band upon agarose gel electrophoresis of whole serum. Sinking pre-beta negative refers to the absence of the slow moving pre-beta band upon agarose gel electrophoresis in the whole serum and in d = 1.019 kg/l bottom fraction. Serum concentrations of Lp(a) lipoprotein, apolipoprotein A-I and B were measured by rocket immunoelectrophoresis by the *Laurell* technique as reported previously (6, 11, 12).

Tab. 2. Presentation of the family members.

Subjects	Number	Sex δ	$\female$	Age (a) $\bar{x} \pm SD$
Blood relatives	14 (I, II)	9	5	53.2 ± 13.6
	18 (III)	9	9	15.1 ± 4.2
Controls (not blood related)	10	3	7	48.2 ± 14.9
All	42	21	21	35.7 ± 21.1

I, II = Ist and IInd generation
III = IIIrd generation

Results

In the propositus (B. B. age 36) the slow moving pre-beta component observed in the serum sank at density 1.019 kg/l (fig. 1). In the family kindred the prevalence of the double pre-beta lipoproteinaemia was 28%.

Figure 2 shows the family distribution of the character "sinking pre-beta" positive. The appearance of the character sinking pre-beta among the family members is consistent with an autosomal dominant

transmission, as confirmed by segregation analysis: no "sinking pre-beta" positive children are observed when this character is absent in both of the parents.

No sex differences were observed in the prevalence of the ."sinking pre-beta". The family history was negative for ischaemic heart diseases such as angina pectoris and myocardial infarction or cerebrovascular accidents. The exclusion of coronary heart disease was based on the clinical electrocardiographic and exercise test criteria. As for the other major risk factors, hypertension (blood pressure > 160/90 mmHg) was present in 3 family members (nos. 2, 3, 4), clinical diabetes in one (no. 5), cigarette smoking
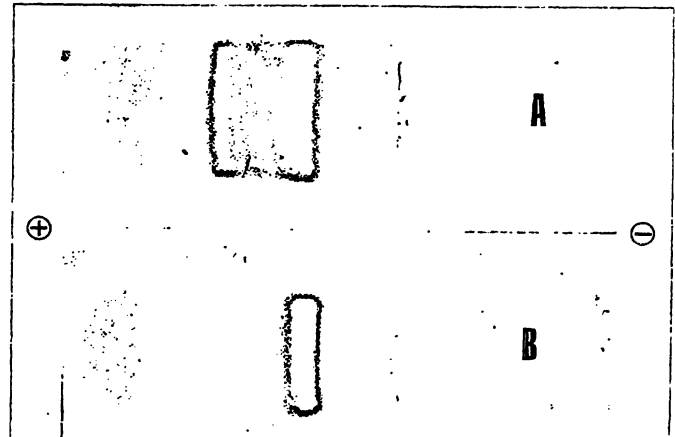

Fig. 1. (B. B. age 36): Agarose gel electrophoresis of whole serum (A) and of the 1.019 kg/l bottom fraction (B). In A two pre-beta components are clearly shown. In B the "sinking pre-β" band is represented.
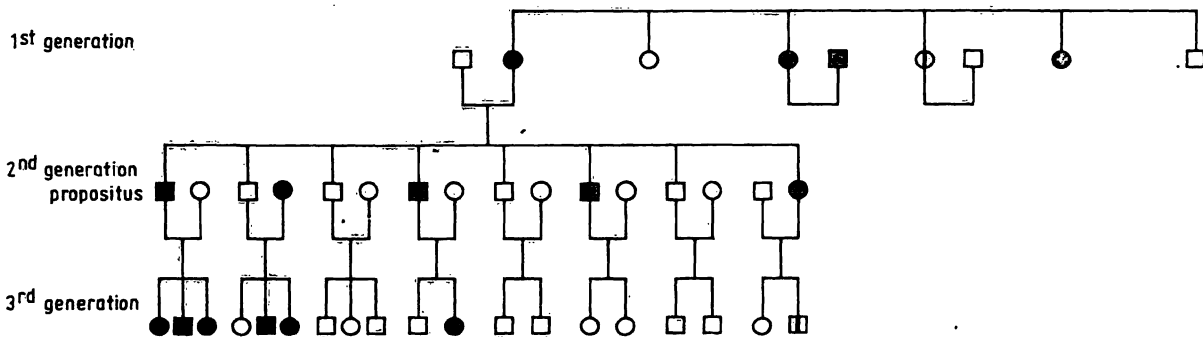

Fig. 2. Family tree subdivided into 3 generations. The mean age and the number of subjects belonging to 3 generations are as follows: 1st generation n 8, age 68.4 ± 8.0; 2nd generation n 16, age 42.5 ± 6.1; 3rd generation n 18, age 15.2 ± 4.2.
□ δ
○ $\female$
□ ⊙ not studied
● ■ "sinking pre-beta" on agarose gel electrophoresis of whole serum (Lp(a) > 0.3 g/l)

(> 15/day) in one (no. 4), moderate hypercholeste-rolaemia in two (nos. 2 and 7); in no. 2 hypercholes-terolaemia was associated with high Lp(a) values; all these subjects belonged to the 1st generation (tab. 5). In fact, except for the propositus none of these relevant risk factors were present in the younger generations (IInd and IIIrd).

The "sinking pre-beta" negative subjects exhibited the lowest Lp(a) values, while the highest were ob-served in the "sinking pre-beta" positive: interme-diate values of Lp(a) were recorded in the subjects showing the "sinking pre-beta" phenomenon only in the density d = 1.019 kg/l bottom fraction (tab. 3). The distribution of the Lp(a) values clearly shows that no significant overlapping is observed according to the presence or absence of the "sinking pre-beta" phenomenon (tab. 3 and fig. 3); a Lp(a) value of 0.3 g/l represents the lowest level for the electropho-retic appearance of the "sinking pre-beta".

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Tab. 3. Mean Lp(a) ± standard deviation (SD) in "sinking pre-beta" positive and negative individuals.

"Sinking pre-beta"	Lp(a) (g/l) x̄ ± SD	Range (g/l)
Positive in serum (n 16)	0.70 ± 0.20*	0.36 – 1.21
Negative in d = 1.019 kg/l bottom (n 6)	0.32 ± 0.11	0.19 – 0.47
Negative (n 20)	0.12 ± 0.08	0.02 – 0.30

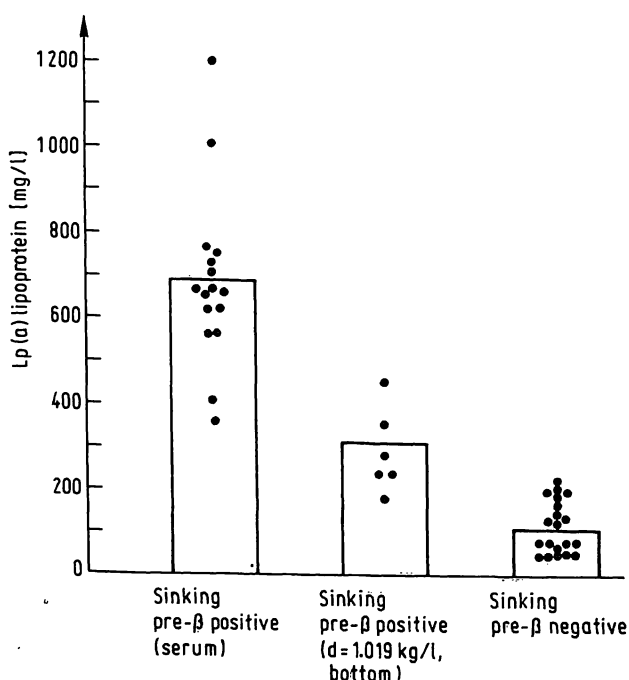* Significantly different from each other (p < 0.01).

Fig. 3. Lp(a) values in "sinking pre-beta" positive and "sinking pre-beta" negative individuals.

Serum levels of total cholesterol, very low density lipoprotein (VLDL) total cholesterol/triglycerides ratio and apolipoprotein A-I and B did not signifi-cantly differ between "sinking pre-beta" positive and "sinking pre-beta" negative subjects, while mean serum triglycerides were significantly higher in the former group (tab. 4).

Tab. 4. Comparison of mean ± SD serum total cholesterol, tri-glycerides, their very low density lipoprotein ratio; apoli-poprotein A–I, B, and age between "sinking pre-beta" positive and negative individuals.

	"Sinking pre-beta"		
	positive (n = 16)	negative (n = 20)	p
Age (a)	40.1 ± 22.6	32.9 ± 21.0	n. s.
Total cholesterol (g/l)	2.16 ± 0.48	2.10 ± 0.50	n. s.
Triglycerides (g/l)	1.03 ± 0.65	0.63 ± 0.32	p < 0.05
VLDL TC/TG	0.25 ± 0.12	0.29 ± 0.01	n. s.
Apolipoprotein A–I (g/l)	1.07 ± 0.22	1.22 ± 0.22	n. s.
Apolipoprotein B (g/l)	0.86 ± 0.34	0.73 ± 0.34	n. s.
Apo B/Apo A–I	0.86 ± 0.48	0.61 ± 0.32	n. s.

A significant correlation was found between serum total cholesterol and Lp(a) values in "sinking pre-beta" positive subjects (n 16; r = 0.50 p < 0.05), but not in the "sinking pre-beta" negative ones (n 20; r = 0.10 p n. s.).

Apolipoprotein A-I was inversely correlated with Lp(a) (n 42; r = 0.36 p < 0.05). This correlation was consistently higher (n 32; r = 0.60 p < 0.01) when the oldest subjects, belonging to the 1st generation were excluded. After this exclusion, mean apolipo-protein A-1 levels were significantly lower in the "sinking pre-beta" positives as compared to the "sinking pre-beta" negatives (apoprotein A-I: 1.08 ± 0.11 g/l against 1.22 ± 0.22 g/l; p < 0.05).

No significant correlation was found for the follow-ing parameters: Lp(a) vs triglycerides (r = 0.09), tri-glycerides vs apolipoprotein A-I (r = 0.20). Lp(a) did not correlate with apolipoprotein B in the total collective of subjects (r = 0.14), or in the "sinking pre-beta" positive subjects alone (r = 0.30).

Discussion

In previous papers it was stressed that the presence of an atypical slow moving pre-beta component up-on lipoprotein agarose gel electrophoresis of serum

does not invariably refer to the presence of Lp(a), being often related to a very low density lipoprotein population, the so called "Double floating pre-beta very low density lipoprotein" or "Late pre-beta" (13—14).

Comparing the Lp(a) values with the behaviour of the "sinking pre-beta" in agarose gel electrophoresis, we demonstrated that the ability to visualize a slow moving pre-beta component, identified as the "sinking pre-beta", is correlated with serum Lp(a) levels above 0.3 g/l.

The familial transmission of the "sinking pre-beta" ascertained previously through an autosomal dominant trait (1, 4, 15) is confirmed in the present study.

Concerning the relationship between Lp(a) and serum lipids (total cholesterol and triglycerides), no significant difference between "sinking pre-beta" positive and negative subjects was found, thus confirming previous data (4, 5). However a significant correlation was found between serum total cholesterol and Lp(a) in "sinking pre-beta" positive, but not in "sinking pre-beta" negative subjects.

This correlation was higher when the oldest subjects, belonging to the 1st generation were excluded. The exclusion of the oldest subjects is pertinent if we consider that serum Lp(a) concentrations are age related (16). The positive correlation observed between serum total cholesterol and Lp(a) lipoprotein in "sinking pre-beta" positive subjects suggests that Lp(a) lipoprotein gives a consistent contribution to total serum cholesterol only when its serum levels are abnormally high, resulting in the electrophoretic appearance of the "sinking pre-beta" band. The inverse relationship observed between apolipoprotein A-I and Lp(a) is interesting in the light of several studies (1—6, 17—19), which report an increased prevalence of atherosclerotic complications in subjects having abnormally high levels of serum Lp(a) (and/or "sinking pre-beta" positive), and of studies showing lower levels of apolipoprotein A-I or high

density lipoproteins-cholesterol in patients affected by atherosclerosis as compared to normal subjects (11, 20—23). Since Lp(a) is thought to be an independent positive risk factor for atherosclerosis (6) and apolipoprotein A-I a negative one (11, 24), the inverse correlation observed in our study needs further investigation.

As for the clinical pattern of atherosclerosis in this family, it is surprising that, in spite of relatively low apolipoprotein A-I and high Lp(a) levels, no other significant cases of atherosclerotic diseases were found, except for the propositus.

This discrepancy may be partly explained as follows
1) the majority of our familial members are young (second and third generation); it will therefore be interesting to follow-up these young "sinking pre-beta" positive subjects in order to evaluate the incidence of new clinical atherosclerotic events;

2) the absence of significant cardiovascular events in the oldest family members (1st generation), despite the presence of the "sinking pre-beta" in five and relatively low levels of apolipoprotein A-I in four subjects, might be due to the low levels of apolipoprotein B which characterizes all the subjects, except for no. 7; other risk factors such as hypertension, smoking cigarettes, diabetes and dyslipidaemia are scarce (tab. 5).

This finding confirms our view (11) that apolipoprotein B is the most effective parameter in discriminating between atherosclerotic subjects and controls. In other words, low levels of apolipoprotein A-I and of Lp(a), may be irrelevant if the levels of apolipoprotein B are lower than normal.

Finally the occurrence in the propositus of a juvenile myocardial infarction was justified by the presence of other risk factors such as moderate hypertension, cigarette smoking and relatively high serum apolipoprotein B levels.

Tab. 5. Clinical and chemical data concerning the oldest subjects.

No.	Name	Age (a)	Sex	Blood pressure (mmHg)	Smoking (cigarettes)	Blood glucose (g/l)	Total cholesterol (g/l)	Triglycerides (TG) (g/l)	VLDL TC/TG ratio	Lp(a) (g/l)	Apolipoprotein A-I (g/l)	Apolipoprotein B (g/l)
1	B. T.	79	♂	140/80	−	0.97	1.84	0.51	0.29	0.02	0.99	0.59
2	B. C.	73	♀	190/120	−	1.02	3.02	1.78	0.23	0.77	1.00	1.06
3	B. A.	67	♀	170/80	−	0.97	2.48	0.84	0.25	1.21	1.50	1.08
4	B. G.	62	♂	160/100	10−15	1.14	2.24	0.90	0.22	0.73	1.46	1.00
5	B. V.	65	♀	150/85	−	2.24	2.70	0.81	0.20	1.01	1.44	0.82
6	M. P.	72	♂	150/80	−	0.93	2.21	0.71	0.17	0.68	0.71	1.33
7	B. M.	54	♀	150/85	−	1.04	3.35	1.13	0.25	0.11	1.29	1.60
8	C. B.	75	♂	150/80	−	1.01	1.76	0.60	0.16	0.15	0.79	0.98

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Der Test auf den Sie gewartet haben – Nur von BIO-RAD

Hämoglobin A_{1c}-Säulentest

- **Spezifisch** **Isolierung der klinisch signifikanten HbA_{1c}-Unterfraktion**
- **Genau** **Eliminierung der labilen Schiff'schen Base**
- **Einfach** **3 Kalibratoren zur Temperaturkorrektur**
- **Schnell** **Einfache Testausführung**

Hämoglobin A_{1c} (HbA_{1c}) – die spezifische Unterfraktion

Hämoglobin A_{1c} ist schon lange als die Glykohämoglobin-Unterfraktion anerkannt, welche die größte klinische Bedeutung in der Erkennung und Überwachung des Diabetes mellitus besitzt.[1] Jedoch sind die gegenwärtigen Methoden zur Abtrennung des HbA_{1c} von HbA_{1a} und HbA_{1b} sehr zeitaufwendig und teuer.

Abb. 1 Hämoglobin A_{1c}-Normalwert-Verteilung.[2]
Es wurden 220 nicht-diabetische Frauen und Männer untersucht. Der Mittelwert der HbA_{1c}-Werte lag bei 4,77%, mit einem Bereich von 2,9% – 7,1% und einer Standardabweichung von 0,67%. Der 95% Vertrauensbereich beträgt 3,43% – 6,11%.

Daher wurde die Bestimmung des Gesamt-HbA_1 in der Diabetes-Diagnostik akzeptiert, trotz der Tatsache, daß die HbA_{1a} und HbA_{1b}-Unterfraktionen zu falsch erhöhten Werten beitragen können.[3]

Dazu kommt, daß sich bei der Reaktion von Hämoglobin mit Glukose zunächst eine labile Schiff'sche Base bildet, welche zusammen mit HbA_{1c} eluiert wird und die Wahrscheinlichkeit ungenauer Werte erhöht.[4]

Der im Blut von nicht-diabetischen Alkoholikern vorkommende Acetaldehyd, die Carbamylierung von Hämoglobin bei urämischen Patienten, sowie ein hoher Lipidgehalt im Blut stillender Frauen, erhöhen ebenfalls die Wahrscheinlichkeit ungenauer Gesamt-HbA_1-Werte.[5,6,7]
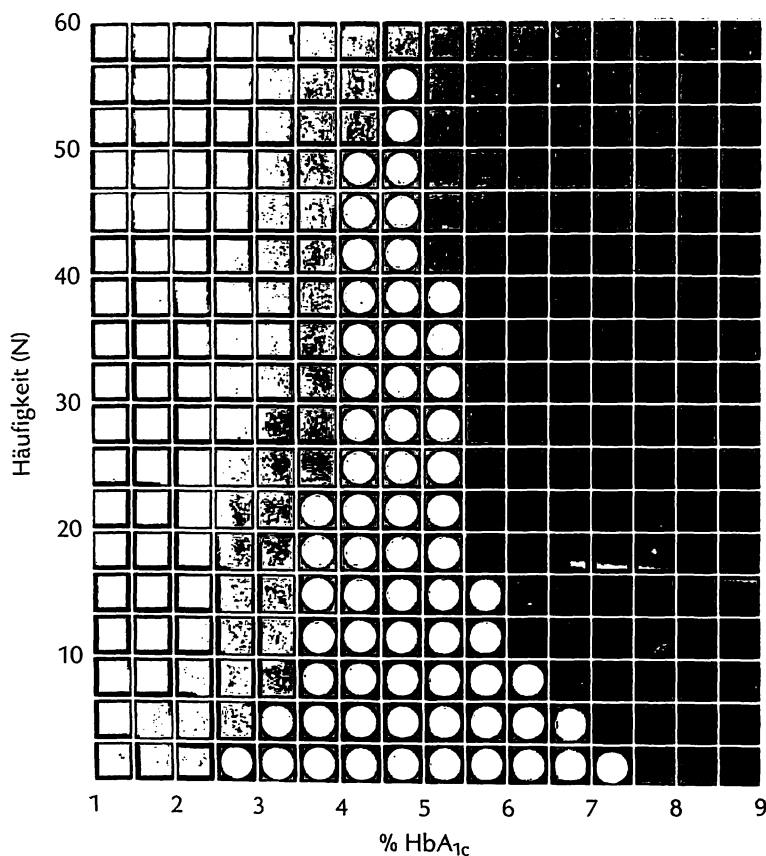
Der BIO-RAD Hämoglobin A_{1c}-Säulentest

Der BIO-RAD Hämoglobin A_{1c}-Säulentest ermöglicht die Bestimmung der spezifischen HbA_{1c}-Fraktion (Abb. 2). Mehr noch, ohne Dialyse oder spezielle Inkubation wird bei diesem HbA_{1c}-Test die labile Schiff'sche Base – oder pre-HbA_{1c} – eliminiert, welche die HbA_1-Werte fälschlicherweise um 3% oder mehr erhöhen kann. Lipämische Proben stören den Test nicht (Abb. 3, 4, 5).
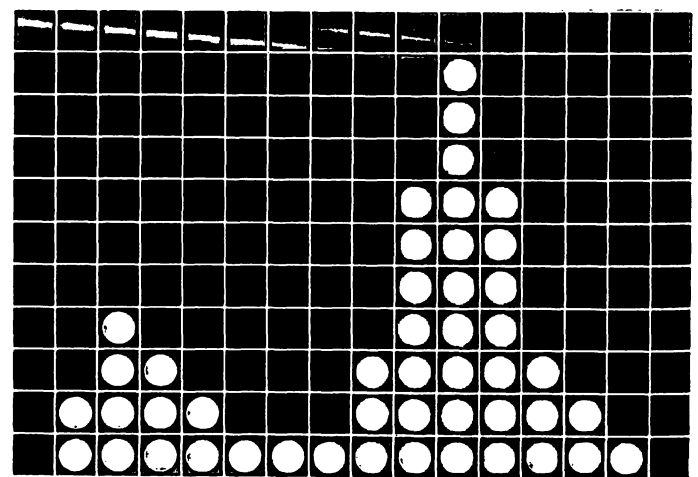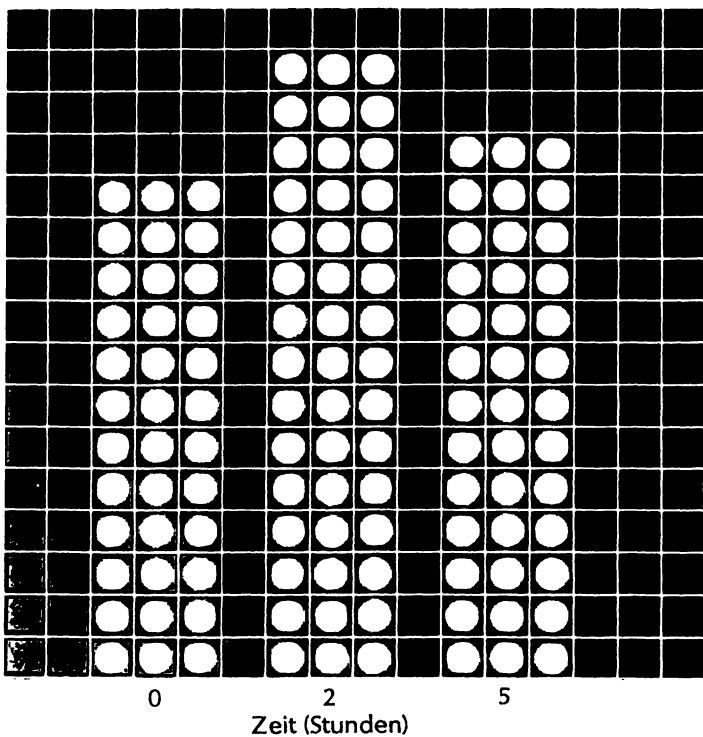

Abb. 2 Hämoglobin-Elutionsprofil eines Diabetikers. Testausführung bei 24° C.

- HbA_{1a1b}
- HbA_{1c}

0   2   5

Zeit (Stunden)

○ Schiff'sche Base, gemessen vor, 2 Stunden und 5 Stunden nach einem Standard-Frühstück.

○ Stabiles Hämoglobin A_{1c}

3 Eliminierung der labilen Schiff'schen Base.
nisse einer Studie an Diabetikern. Der Anteil der labilen schen Base ändert sich mit den akuten Blutzucker-inkungen kurz vor der Probennahme. Die Eliminierung der n Schiff'schen Base ist erforderlich, um die Langzeitwirkung Monate) einer strengen Kohlenhydrat-Kontrolle richtig erzugeben.[8]

Spezifität und Richtigkeit
Schnell und einfach

1. Um die roten Blutzellen zu hämolysieren, wird Vollblut mit Hämolysereagenz gemischt. Die Eliminierung der labilen Schiff'schen Base wird beim Hämolyseschritt bereits durch die Bindung der Glukose an Borat eingeleitet.

2. Die Probenhämolysate werden auf die Säulen gegeben und anschließend durch Zugabe des ersten Elutions/ Entwicklungs-Reagenz HbA_{1a} + HbA_{1b} von HbA_{1c} getrennt. Gleichzeitig wird noch vorhandene Schiff'sche Base quantitativ eliminiert.

3. Mit dem zweiten Elutions/Entwicklungs-Reagenz wird das HbA_{1c} eluiert. Die quantitative Bestimmung erfolgt am Spektralphotometer bei 415 nm (Filterphotometer 405 mm).

Drei Kalibratoren mit unterschiedlichem Gehalt an HbA_{1c} sichern jederzeit genaue Werte.

Eine weitere BIO-RAD Exklusivität. In jedem Hämoglobin A_{1c}-Kit sind Kalibratoren mit unterschiedlichem Gehalt an HbA_{1c} inbegriffen, womit Temperaturunterschiede von 20°C – 28°C korrigiert werden.
Durch Auftragen der gemessenen Kalibratorwerte gegen die 24°C-Sollwerte ergibt sich eine Standardkurve, aus der die korrigierten 24°C-Probenwerte abgelesen werden.

Wird der Test bei 24°C ausgeführt, können die Kalibratoren als Kontrollen verwendet werden, um Richtigkeit und Präzision des Tests zu ermitteln.

tientenprobe	·· HbA₁ (Methode A)	% HbA₁ᵥ (Methode B)
i0 mg/dl	11,41	5,15
)0 mg/dl	12,19	5,19
)00 mg/dl	12,99	5,08
ontrolle	10,83	5,23

4 Effizienz der Eliminierung der Schiff'schen Base beim RAD Hämoglobin A_{1c}-Test.
Patientenprobe wurde angereichert mit Glukose (linke Spalte), nterschiedliche Konzentrationen zu erzielen; mitgeführt wurde falls eine Kontrolle, welcher keine Glucose zugesetzt wurde. Bildung der labilen Schiff'schen Base wurden die Proben sowohl einem kommerziellen Gesamt-HbA₁-Test ohne Eliminierung der en Schiff'schen Base (A), als auch mit dem BIO-RAD-HbA₁ᴄ-Test (B) ysiert.

A₁ᴄ-Test (Bio-Rad) Hämoglobin A₁ᴄ)	HbA₁-Test (kommerziell) (% Hämoglobin A₁)
cht gewasch. Probe A 9,11	Nicht gewasch. Probe B 23,29
waschene Probe A 9,80	Gewaschene Probe B 13,61

.5 Interferenz durch erhöhte Lipidkonzentrationen.
se Tabelle zeigt die Fähigkeit des BIO-RAD Hämoglobin A₁ᴄ-Tests, Vergleich zu einer kommerziellen Methode zur Bestimmung des amt-HbA₁, sogar die größtmögliche Störung durch erhöhte dkonzentrationen zu eliminieren.

·	Mittelwert % HbA₁ᴄ	% HbA₁ᴄ auf 24°C korrigierter Wert
Test-Temp. 20°C		
Stoffwechselgesunder	4,10	5,50
Diabetiker	7,87	9,50
Test-Temp. 28°C		
Stoffwechselgesunder	6,29	5,40
Diabetiker	10,09	8,99

Abb. 6 Richtigkeit der Hämoglobin A_{1c}-Temperaturkorrektur
Der bei der optimalen Testtemperatur von 24°C ermittelte Prozentsatz an HbA_{1c} in der nicht-diabetischen Patientenprobe war 5,6% und beim Diabetiker 9,43%.

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Hämoglobin A$_{1c}$-Säulentest

Testkomponenten für 100 Bestimmungen (Best.Nr. 191–9001)

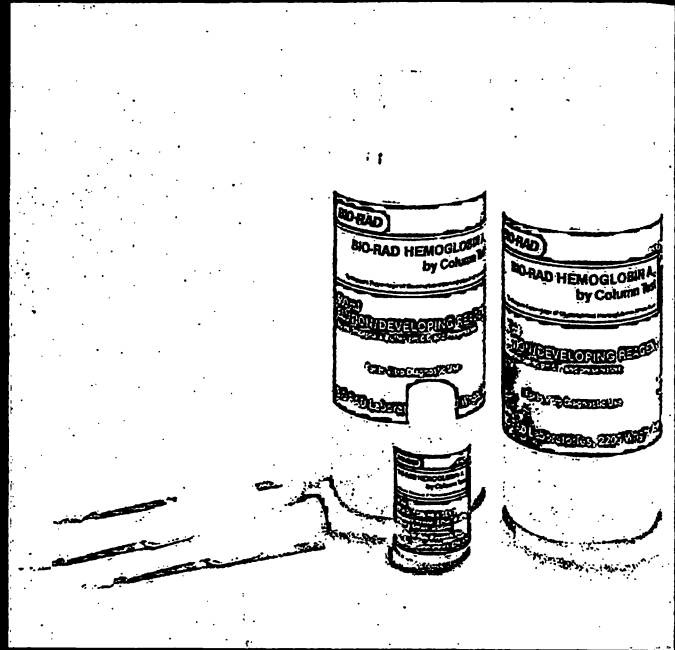|	
Hämolyse-Reagenz	Ein Fläschchen mit 60 ml Polyoxyethylen-äther/Boratpuffer (0,33% V/V).
Elutions/Entwicklungs-Reagenz	**Elutionspuffer I.** Eine Flasche mit 500 ml Elutions/Entwicklungs-Reagenz (Borat/Phosphatpuffer pH 6,7 und Konservierungsmittel). **Elutionspuffer II.** Drei Flaschen mit je 750 ml Elutions/Entwicklungs-Reagenz (Phosphatpuffer pH 6,7 und Konservierungsmittel).
Harzsäulen	100 Stück Kationenaustauscher-Chromatographiesäulen.
HbA$_{1c}$-Kalibratoren Level I, II, III	3 Fläschchen mit lyophilisiertem Human-Vollbluthämolysat und Konservierungsmitteln.
Teflon-beschichtete Kappen	3 Teflon-beschichtete Kappen.