Infektion und Dyslipoproteinämie

Mechanismus und Bedeutung für die Atherosklerose

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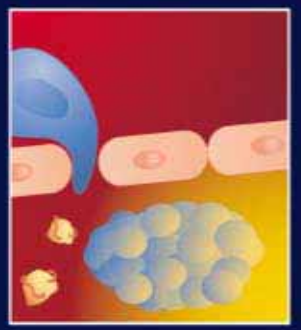
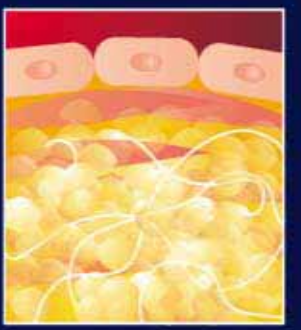
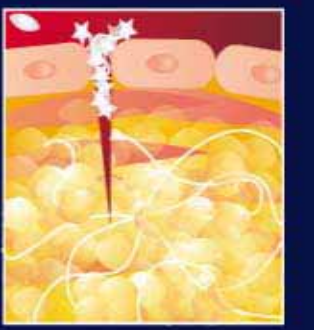
- **Lipide , Lipoproteine, Inflammation und Atherosklerose**
- **Dyslipoproteinämie bei Infektion**
- **HIV und Lipide**
- **Behandlung der Dyslipoproteinämie bei HIV-Patienten**

Inflammation is Involved in the Different Stages of Atherosclerosis

Stade I	Stade II	Stade III	Stade IV	Stade V	Stade VI
					
Isolated foam cells	Fatty streak	Extra-cell lipid accumulation	Lipid core	Fibrosis around the lipid core	Complicated atheroma: rupture, hemorragy and thrombosis

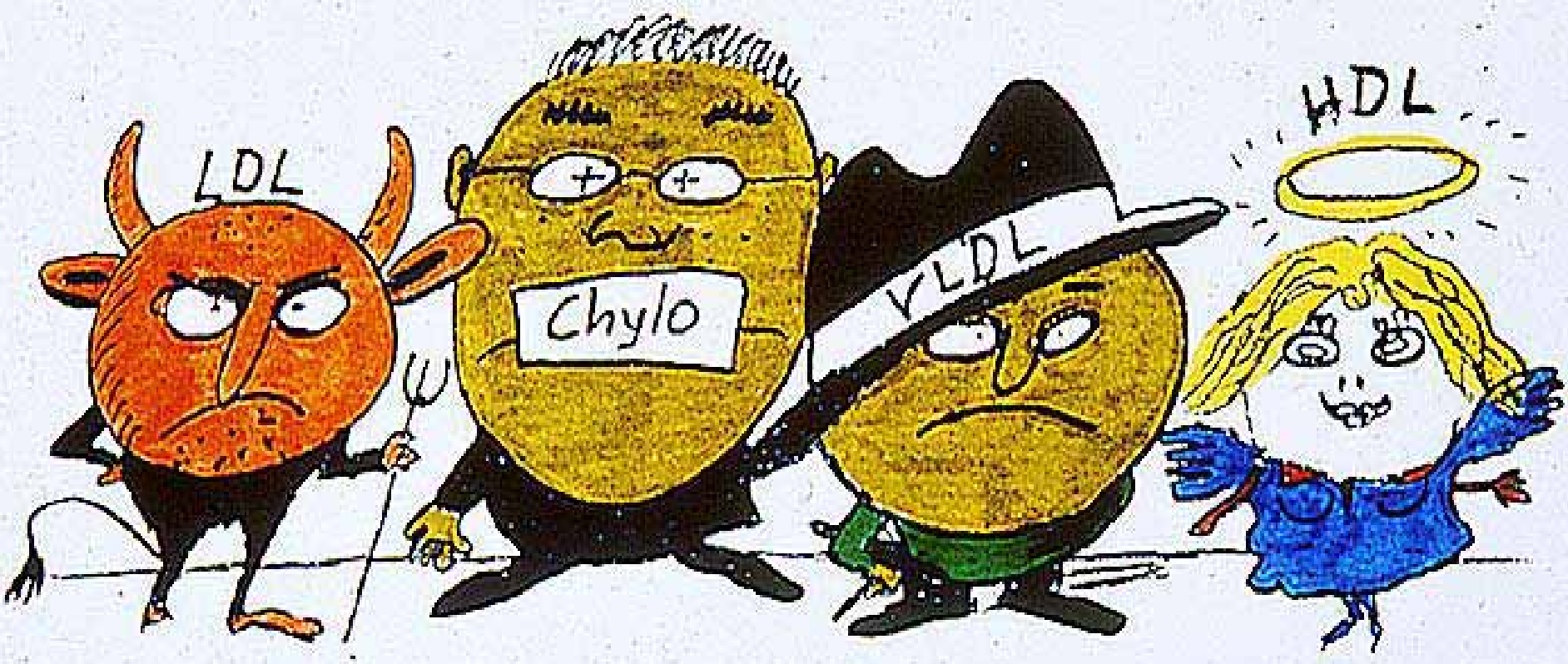
The earliest atherosclerotic lesion is almost purely an inflammatory lesion consisting of monocyte-derived, lipid-laden macrophages and T lymphocytes

During atheroma progression and growth, activated macrophages secrete a multitude of mediators including metalloproteinases which weaken the fibrous cap

Kategorien von Risikofaktoren (ATP III)

- **Hauptsächliche, unabhängige Risikofaktoren**
  - Alter, Familiengeschichte, Rauchen, Blutdruck
  - Gesamt-, LDL-, HDL-Cholesterin
  - Diabetes mellitus
- **Prädisponierende Risikofaktoren**
  Übergewicht, körperliche Inaktivität, atherogene Ernährung
- **Neue ("emerging") Risikofaktoren**
  - CRP
  - Homocystein
  - thrombotische Faktoren
  - Lp(a)
  - small dense LDL

ATHEROGENICITY OF LIPOPROTEINS

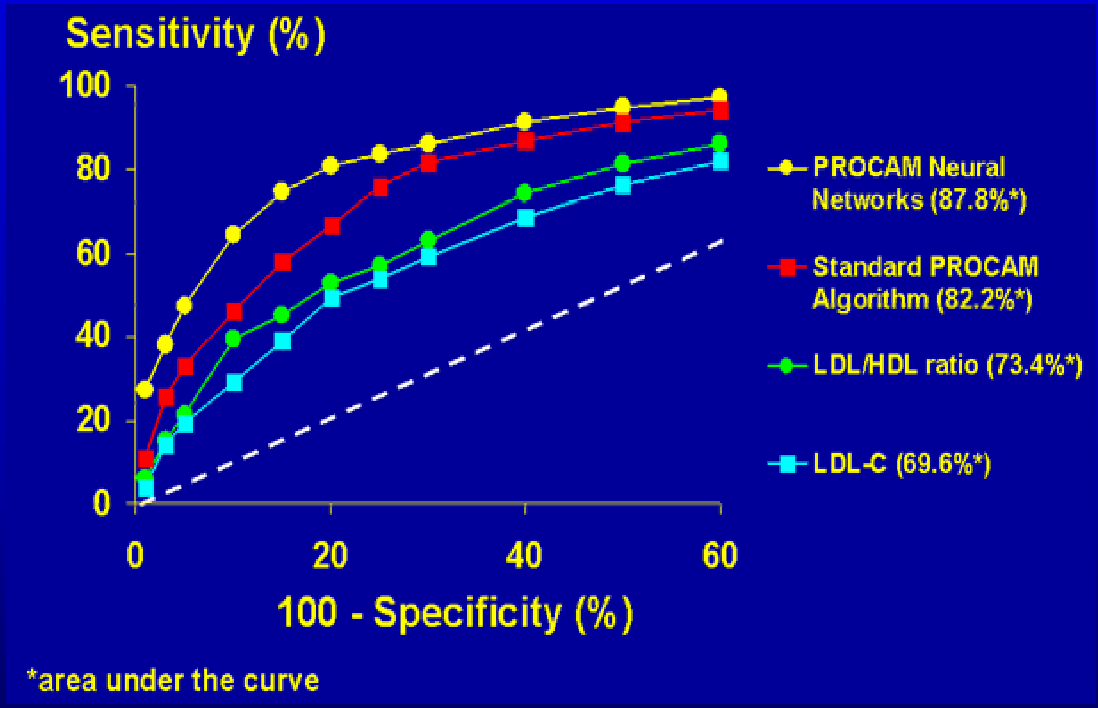


very atherogenic

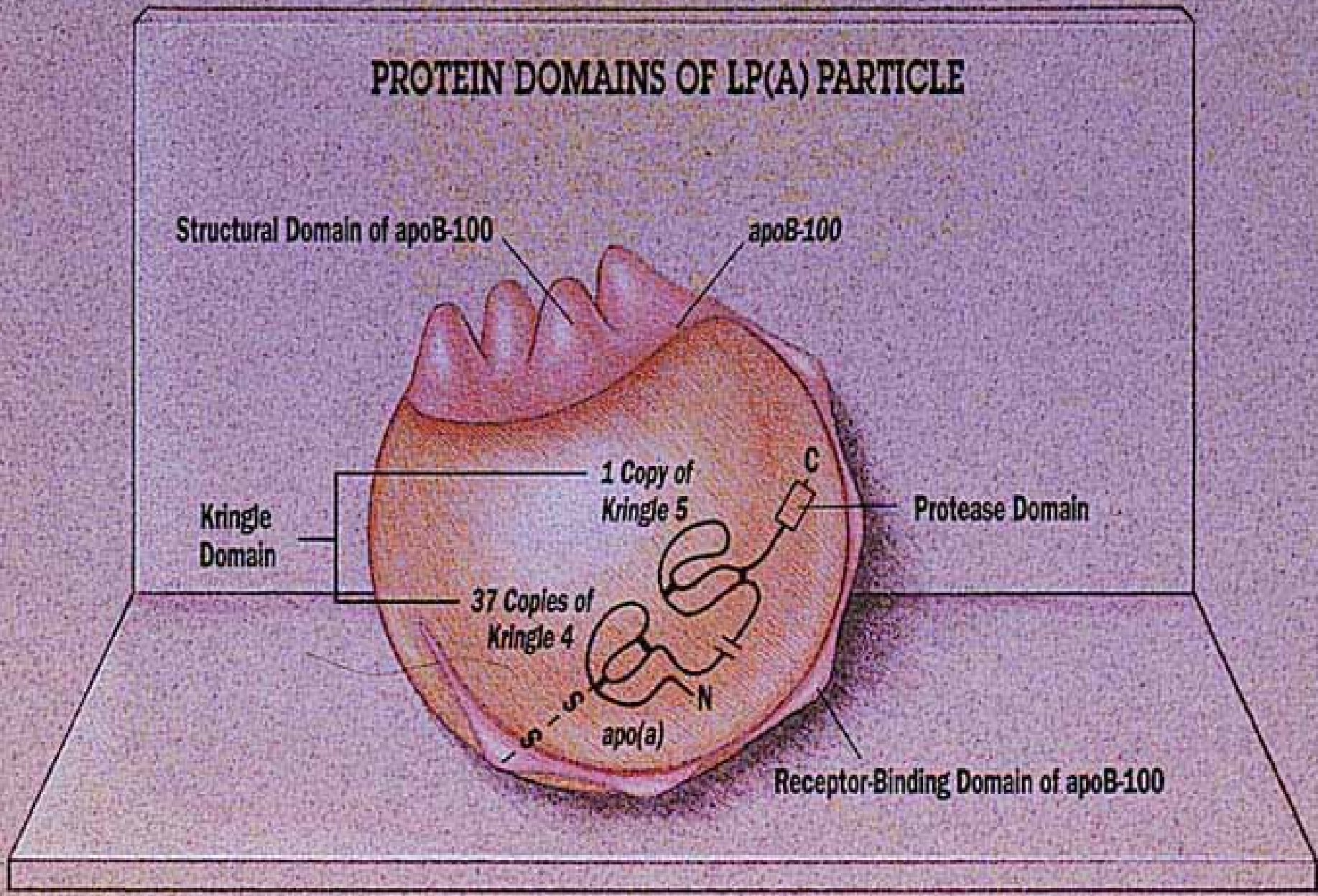
potentially atherogenic

anti - atherogenic

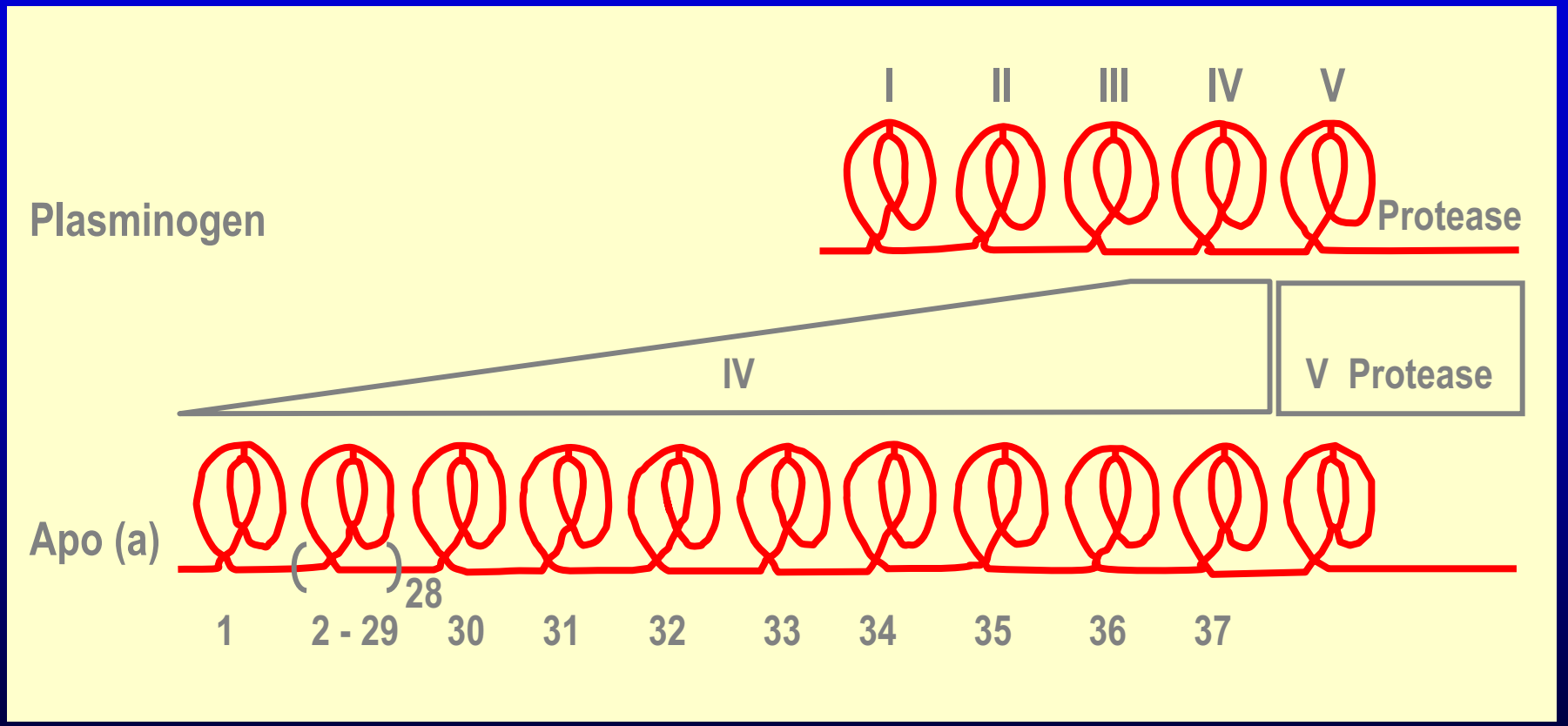
Scientific background for global risk assessment



- In predicting the occurrence of myocardial infarctions, risk algorithms are superior to individual risk factors.
- The better an algorithm is able to detect a risk patient, the more effective resources can be applied.

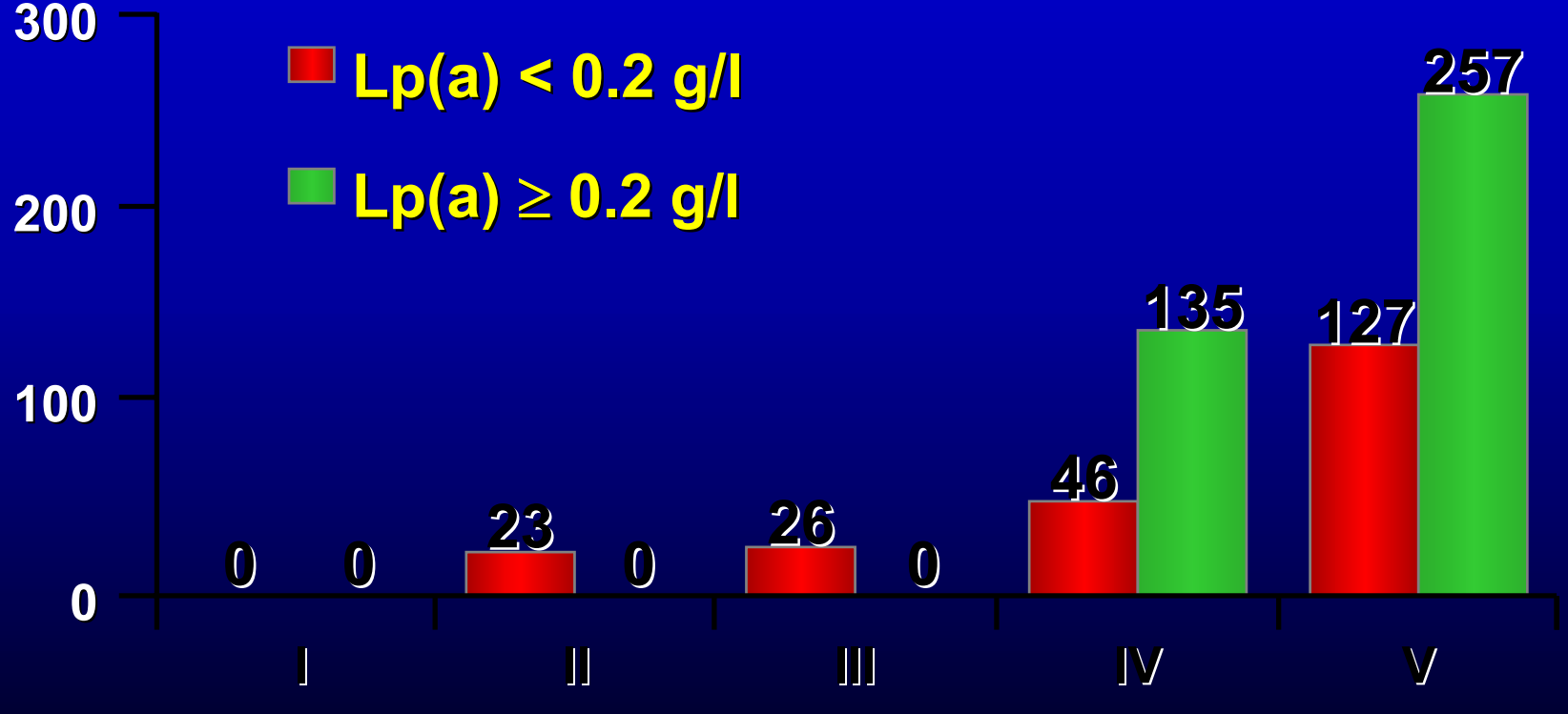

PROTEIN DOMAINS OF LP(A) PARTICLE
Structural Domain of apoB-100
apoB-100
1 Copy of
Kringle 5
C
Protease Domain
Kringle
Domain
37 Copies of
Kringle 4
N
S
S
apo(a)
Receptor-Binding Domain of apoB-100

Strukturelle Verwandtschaft von Lp(a) und Plasminogen



Incidence of Coronary Events
(per 1'000 in 10 years)

Data from PROCAM



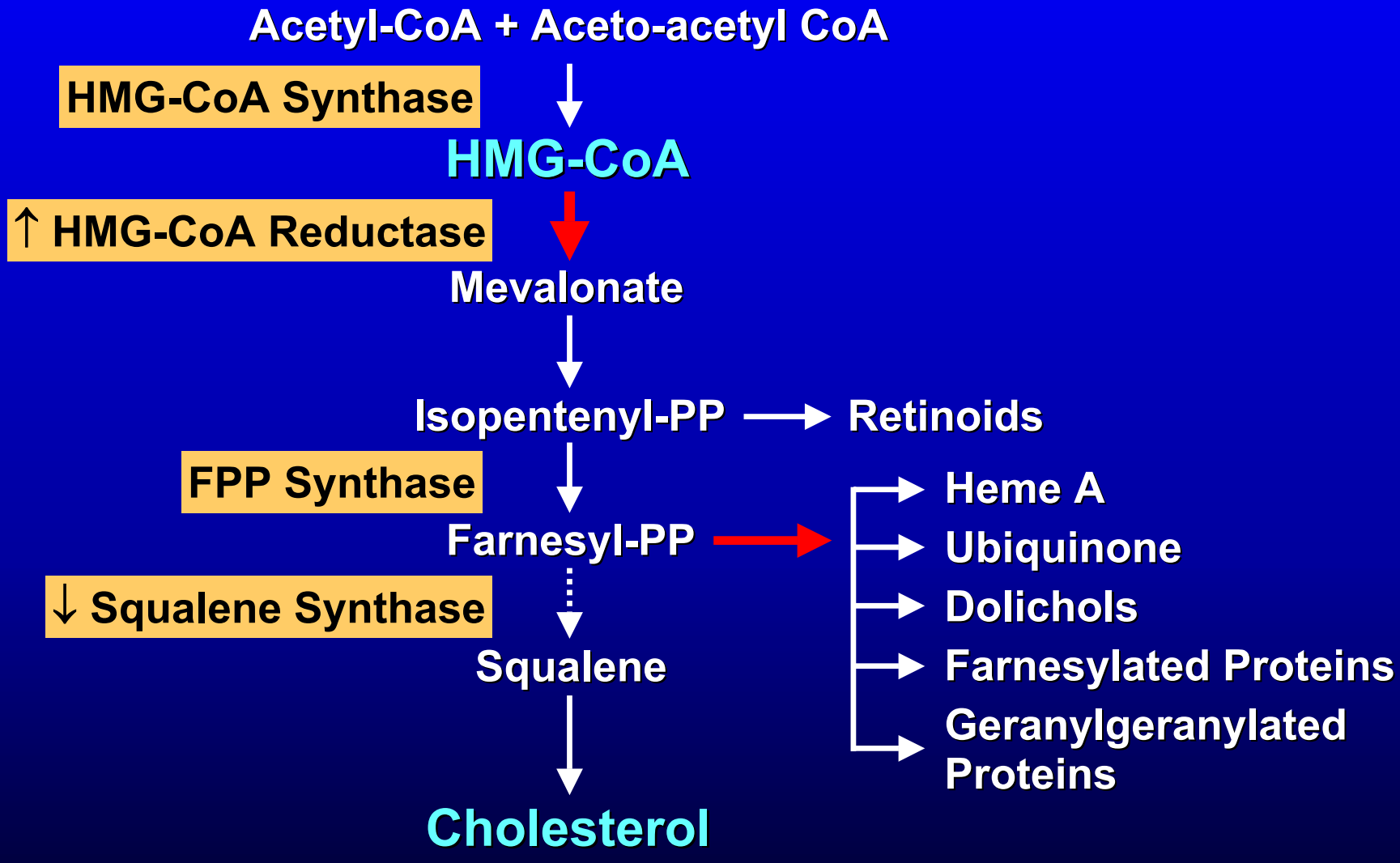
Von Eckardstein: JACC, 2001

- Lipide , Lipoproteine und Atherosklerose
- Dyslipoproteinämie bei Infektion
- HIV und Lipide
- Behandlung der Dyslipoproteinämie bei HIV-Patienten

Cholesterinmetabolismus

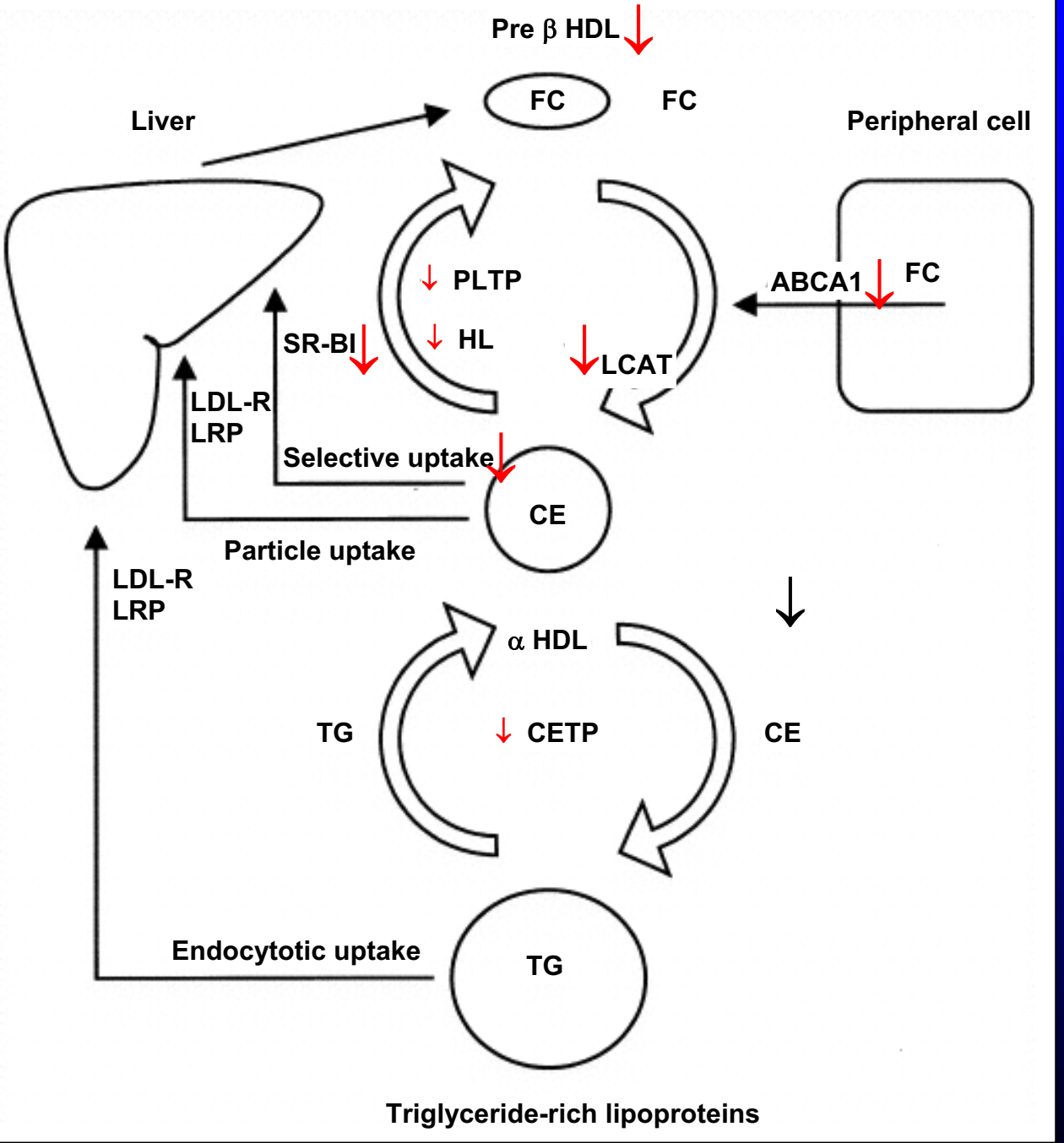
1) Hepatische Cholesterinsynthese ↓
2) LDL-Abbau ↓, small dense LDL
3) Verminderter hepatischer Chol. Katab. und -Sekretion
4) Lipoprotein (a)
5) HDL-Metabolismus und verminderter „reverse cholesterol transport“

Cholesterol Metabolism during the APR



Infektion/Inflammation sind mit einer Zunahme der HMG-CoA Reduktase assoziiert.
Allerdings ist die Expression der übrigen Enzyme mit Mevalonatmetabolismus vermindert.

→ Mässige Zunahme der hepatischen Cholesterinsynthese und andere Mevalonatmetaboliten werden Non-Sterol-Wegen zugeführt.



Reverse Cholesterol Transport Process is Decreased during Infection and Inflammation

Périard et al: Circulation 1999; 100: 700-705

Triglyceridmetabolismus

1) Erhöhte VLDL-Produktion

- Zunahme der Neusynthese von freien Fettsäuren und Triglyceriden (durch direkte Effekte vo. Cytokinen)

- Vermehrte Lipolyse durch das Fettgewebe

- Verminderte hepatische Fettsäure-oxidation und Ketogenese

2) Verminderter VLDL-Abbau

Potential Proatherogenic Changes and Effects of Lipoprotein during Infection and Inflammation

Changes	Effects
VLDL	
• Increased VLDL levels	Provides lipid substrates for macrophage uptake
• Decreased LPL and HL	Decreases clearance of triglyceride-rich lipoproteins
• Decreased tissue apo E expression	Decreases lipoprotein clearance
LDL	
• Increased small dense LDL	Increases susceptibility to oxidation; increases LDL penetration through endothelium; increases interaction with arterial wall proteoglycans and LDL retention in arterial wall
• Increased sphingo-lipid content	Facilitates LDL aggregation and uptake into macrophages
• Increased ceruloplasmin	Increases LDL oxidation
HDL	
• Decreased HDL and apo A-I	Impairs apolipoprotein-mediated cholesterol removal from cells
• Decreased LCAT	Impairs cholesterol removal from cells by diffusion mechanism
• Decreased CETP	Impairs cholesterol transfer to triglyceride-rich lipoproteins
• Decreased HL	Reduces pre-β HDL generation
• Decreased PLTP	Reduces pre-β HDL generation; decreases HDL phospholipid content and impairs cholesterol removal by increasing cholesterol flux from HDL into cells

Colagreco: J of Ass Nurses in AIDS Care 2004; 15: 30-41

Reported Changes of Lipids during Infection

Study	Species	Infecting agent	TC	TG	HDL-C	α-LP	β-LP	preβ-LP
1	Hu	Gram +	↓					
2	Hu	Gram + and –	↓					
3	Hu	Gram –	↓				↑	
4	Ra	Gram +						
5	Hu	Gram +	↓	N				
		Gram –	N	↑				↑
		Viral hepatitis	↑	↑			↑	↑
6	Ra	Gram +	↑	↑		↓	↑	↓
7	Mo	Gram +	↓	↑		↓		↑
		Gram –	↓	↑		↑	↓	↑
8	Hu	Virus	↓	↑↓	N		↓	N–↑
9	Ra	Gram +						
10	Hu	Gram –	↓	↑		0	↑	↓
11	Ha	Virus		↑				↑
12	Mo	Gram +	N	N				
		Gram –	N	↑				
13	Hu	Virus		↑				↑
14	Hu	Viral hepatitis		↑		0		0
15	Hu	P. vivax				0		0
16	Hu	Virus	↓–N	↑	↓			
17	Hu	P. vivax				↓	↑	↑
18	Hu	Cytomegalovirus	↓	↑	↓			
19	Hu	Gram + and –	↓	↑	↓			

Clin Chem 32, 1986

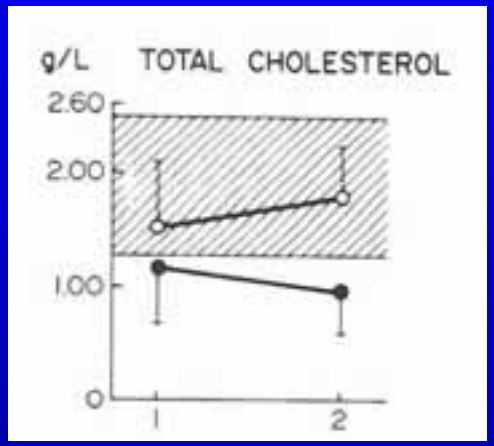
Concentrations of Lipids in Serum of the Reference Normal Population, Patients with Sepsis, and Patients with Similar Pathologies but without Infections (Controls)

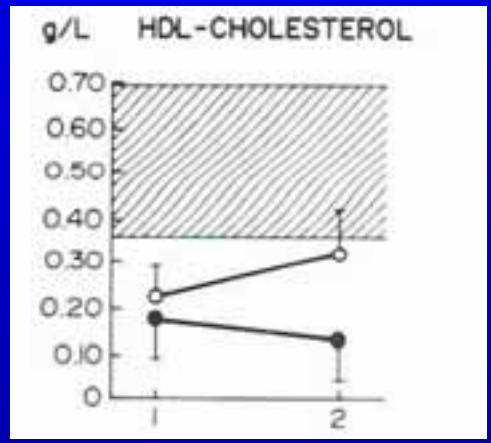
	TC mmol/l	HDL-C mmol/l	TG mmol/l	Albumin	Apo-A g/L	Apo-B
Reference normal population						
n	310	352	122	92	141	137
mean	4.9	1.3	1.2	45.6	2.12	0.75
SD	0.7	0.2	0.4	1.8	0.41	0.23
Control						
n	286	286	286	72		
mean	4.4[a]	1.2[a]	1.4[a]	38.6[a]		
SD	1.0	0.3	0.7	5.3		
Septic patients						
n	54	54	54	54	44	26
mean	3.4[b]	0.6[b]	2.4[b]	26.3[b]	0.98[a]	0.52[a]
SD	1.2	0.4	1.3	7.6	0.57	0.24

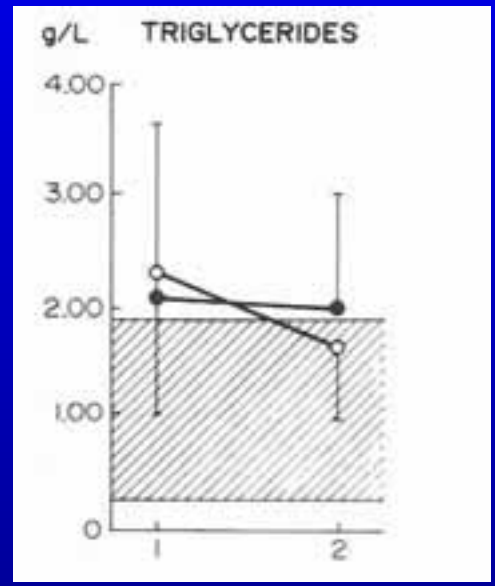
Significantly ($p < 0.05$) different from [a]the reference normal population or [b]the controls.

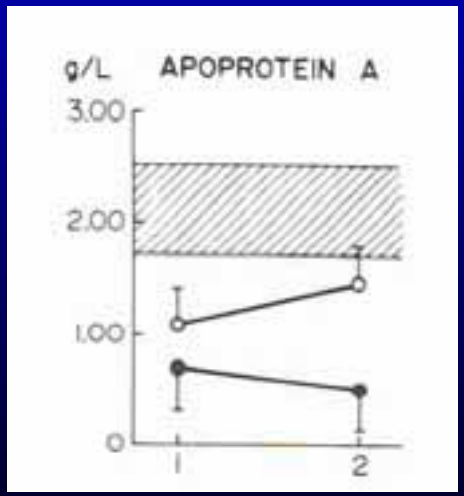
Clin Chem 32, 1986

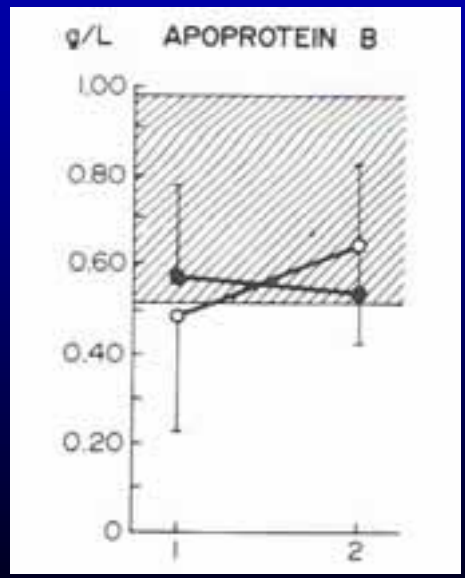
Mean Values for Serum Lipids, Apoproteins, and Albumin in Patients who died (•) or recovered (o)

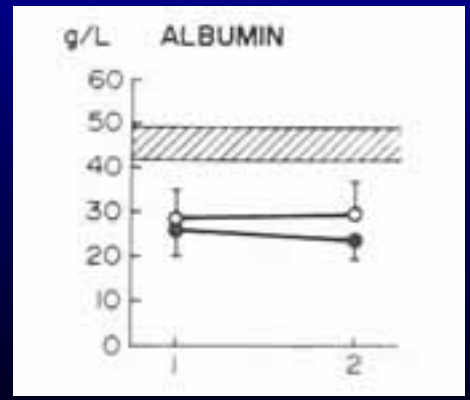












Bars **indicate mean and SD.** ***Shaded areas*** **indicate normal range.**

Günstige Effekte der infektionsbedingten Lipoproteinveränderungen

A) Lipoproteine binden u. neutralisieren bakterielles Endotoxin

B) Lipoproteine binden und neutralisieren DNA und RNA Viren

C) Lipoproteine schützen vor gewissen Infekt. mit Parasiten (z.B.Trypanosome lytic factor TLF1 und TLF2 in HDL)

- Lipide , Lipoproteine und Atherosklerose
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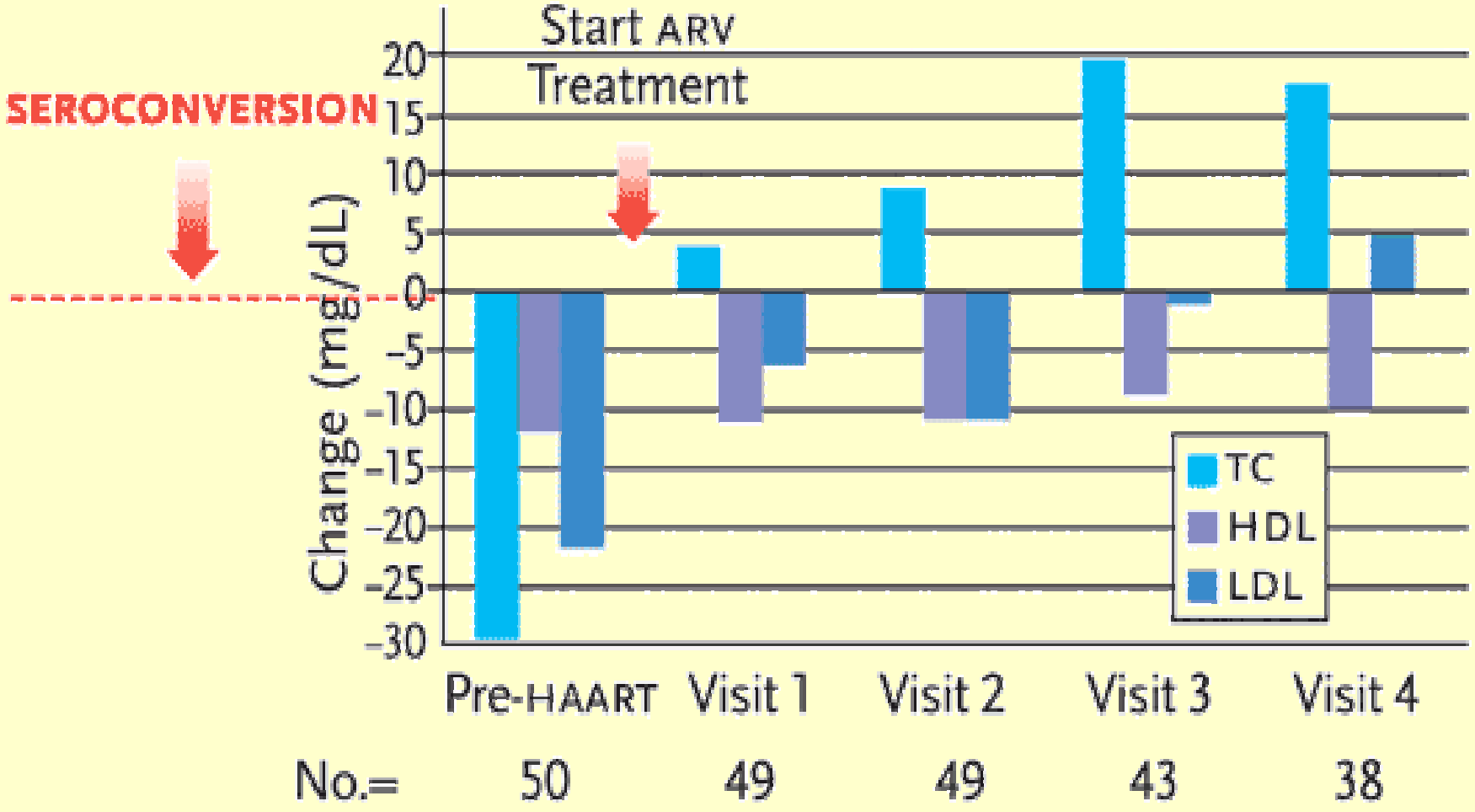
Change in Lipids Relative to Pre-Seroconversion Values (MACS)

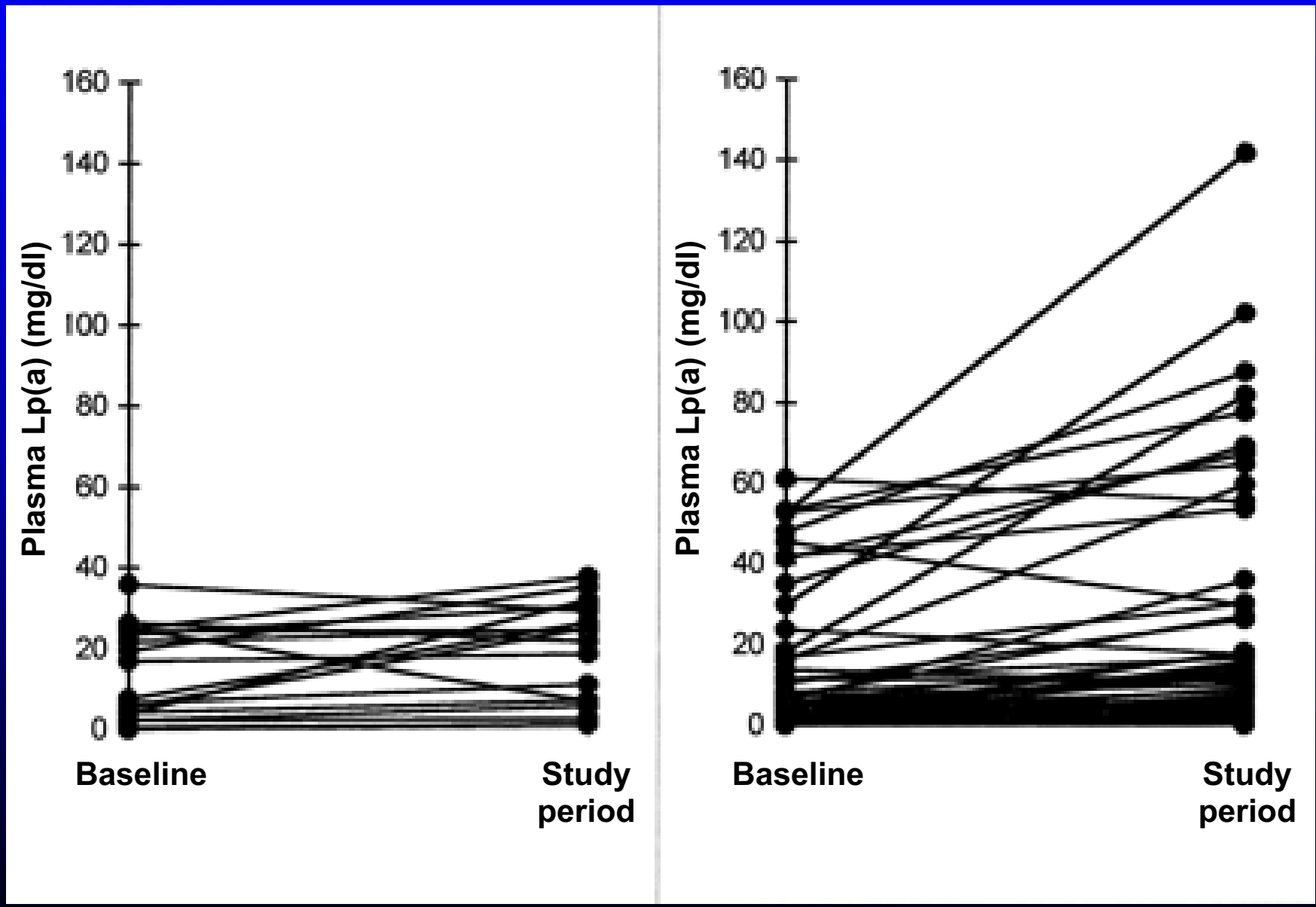


Mean Change in Blood Lipids for 50 Seroconverters Initiating HAART

	Lipid Measurements mg/dL	TC	HDL-C	LDL-C
	Preseroconversion (n = 50)	201 (179 to 222)	51 (46 to 57)	122 (102 to 143)
Mean Change from Preseroconversion Values (95% Confidence Interval)	Last visit before HAART (n = 50)	-30 (-52 to -9)	-12 (-19 to -6)	-22 (-45 to 1)
	First visit after HAART (n = 49)	4 (-17 to 25)	-11 (-16 to -6)	-6 (-29 to 17)
	Second visit after HAART (n = 49)	9 (-16 to 34)	-11 (-16 to -6)	-1 (-24 to 22)
	Third visit after HAART (n = 43)	20 (-1 to 41)	-9 (-16 to -2)	-1 (-25 to 22)
	Fourth visit after HAART (n = 38)	18 (-7 to 42)	-10 (-16 to -3)	5 (-20 to 30)

Riddler et al: *JAMA* 2003; 289: 2978-2982

Lp(a) in PI-naive (left) and PI-treated (right) HIV-infected Patients



Périard et al: Circulation 1999; 100: 700-705

Lipid and Lipoprotein Parameters in HIV Patients

	Group 1 (PI) n=22	Group 2 (no PI) n=15	P
Lipids, mmol/L			
Total cholesterol	5.68 ± 1.82	4.43 ± 1.31	0.007
Triglycerides	4.42 ± 5.20	1.98 ± 1.31	0.009
HDL-C	1.07 ± 0.36	1.09 ± 0.28	0.429
Non-HDL-C	4.65 ± 1.85	3.34 ± 1.33	0.017
Lipoproteins, mmol/L			
Chylomicrons	0.04 ± 0.06	0.01 ± 0.03	0.070
Total VLDL	2.92 ± 2.19	1.55 ± 1.14	0.022
Large VLDL	1.67 ± 1.54	0.66 ± 0.80	0.012
Intermediate VLDL	1.00 ± 0.83	0.68 ± 0.57	0.124
Small VLDL	0.24 ± 0.21	0.21 ± 0.08	0.320
Total LDL	3.44 ± 1.41	3.05 ± 1.33	0.213
IDL	0.19 ± 0.21	0.07 ± 0.10	0.023
Large LDL	0.61 ± 1.03	0.43 ± 0.60	0.300
Intermediate LDL	0.39 ± 0.75	0.93 ± 0.84	0.061
Small LDL	2.25 ± 1.96	1.62 ± 1.63	0.145
Total HDL	0.99 ± 0.26	1.01 ± 0.28	0.390
Large HDL	0.59 ± 0.37	0.71 ± 0.35	0.193
Small HDL	0.39 ± 0.18	0.31 ± 0.19	0.090
Mean lipoprotein diameters, nm			
VLDL	59.9 ± 12.8	54.0 ± 11.8	0.083
LDL	19.9 ± 1.10	20.0 ± 0.80	0.311
HDL	8.7 ± 0.4	8.7 ± 0.4	0.500
LDL particles, nmol/L	1765 ± 869	1511 ± 766	0.189

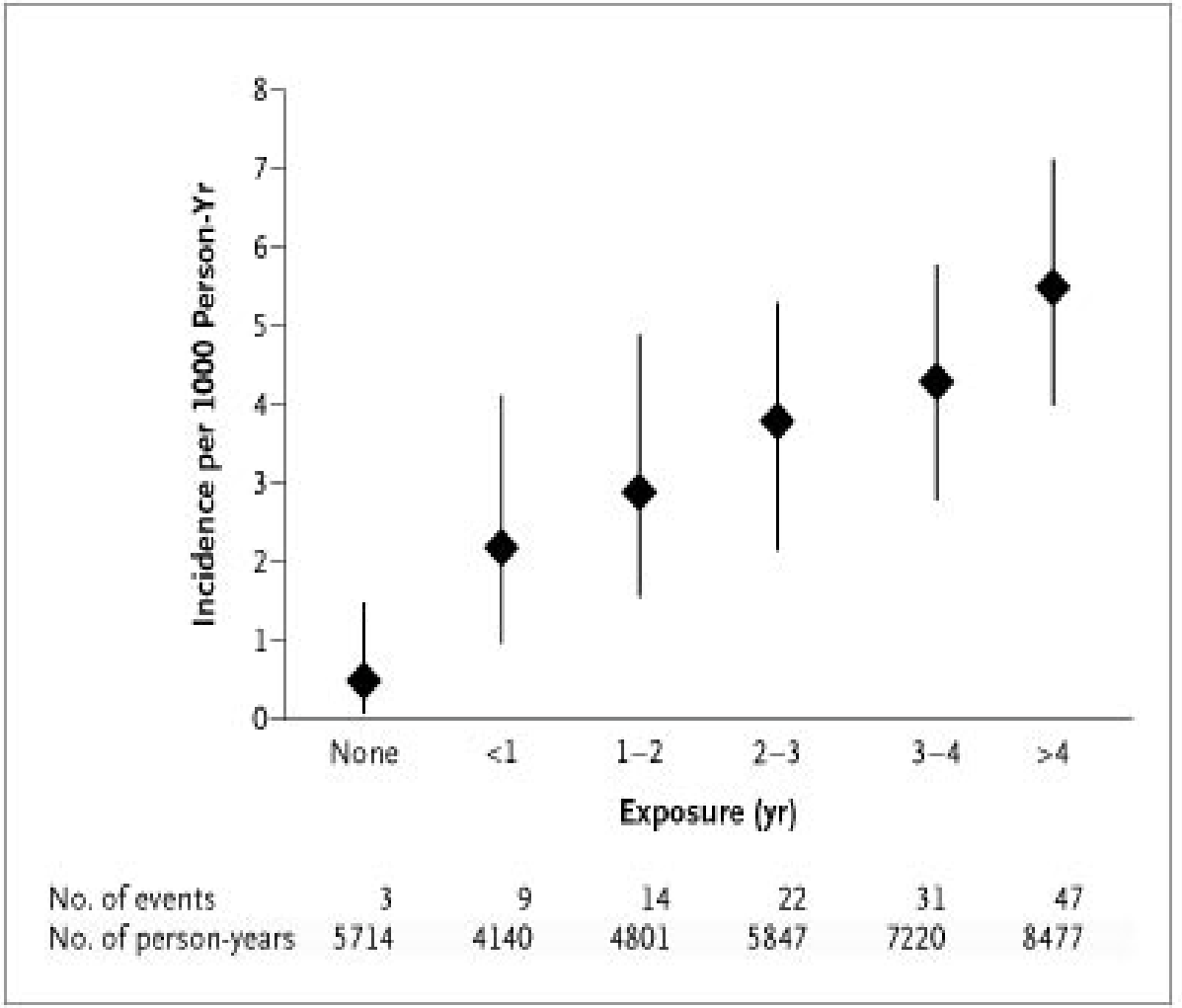
Stein et al: Circulation 2001; 17: 257-262

BA Ultrasound Parameters

	Group 1	Group 2	P
Resting BA diameter, mm	4.1 ± 0.5	3.8 ± 1.0	0.128
Resting BA blood flow, ml/min	56.1 ± 33.8	52.2 ± 45.3	0.789
Hyperemic flow, % rest	731.7 ± 331.6	636.7 ± 321.5	0.961
FMD, %	2.6 ± 4,6	8.1 ± 6.7	0.005
Nitroglycerin flow, % baseline	141.5 ± 98.1	107.5 ± 85.6	0.675
NTGMD, %	18.5 ± 6.8	20.1 ± 4.8	0.302

Stein et al: Circulation 2001; 17: 257-262

Incidence of Myocardial Infarction According to the Duration of Exposure to Combination Antiretroviral Therapy



The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group, N Engl J Med 2003;349:199

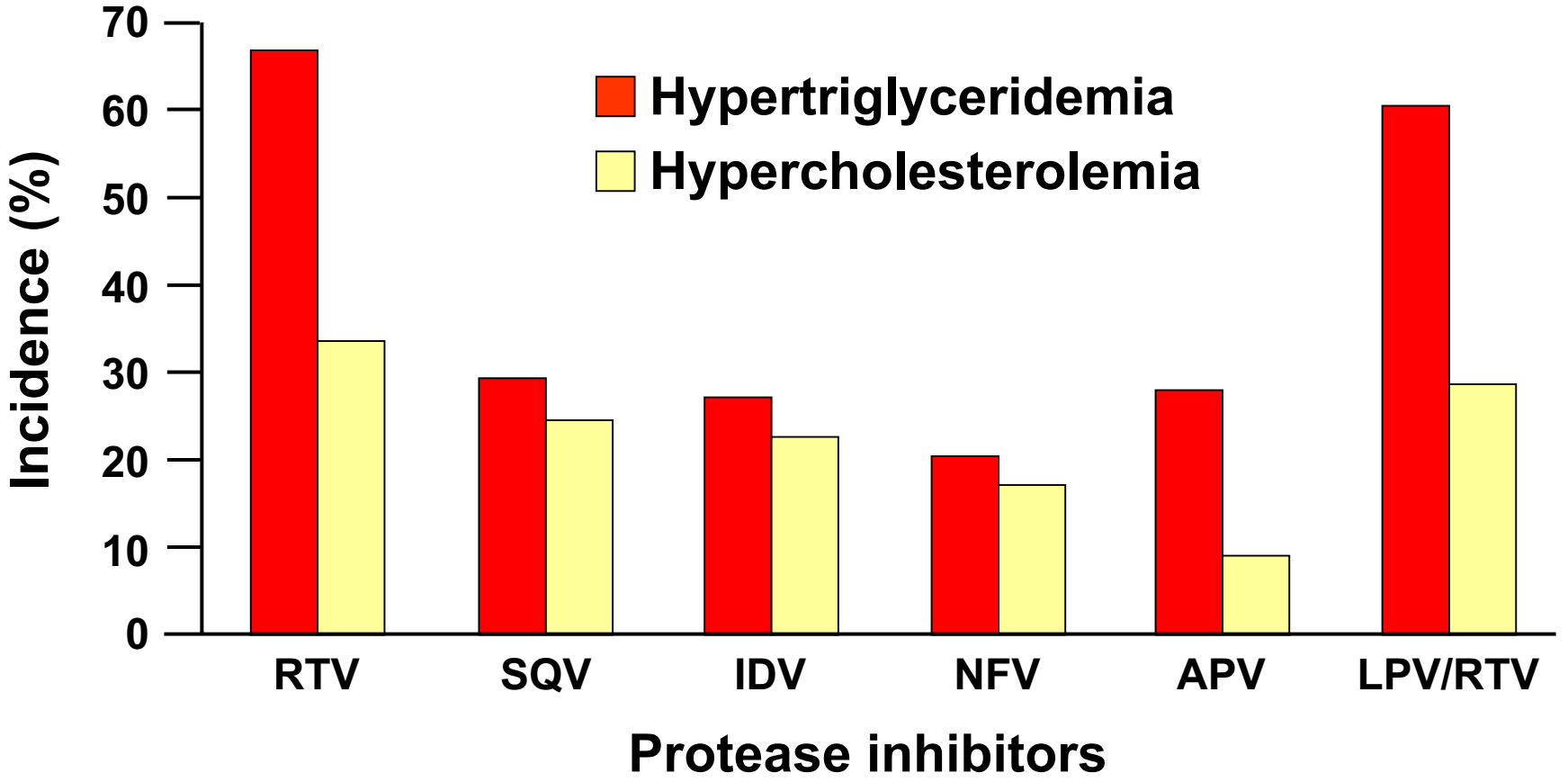
Plasma Levels of Lipids

	Change			
	Ritonavir[1]	Indinavir	Nelfinavir[2]	PI-Naive
Total cholesterol, mmol/l	2.0 ± 0.3[3]	0.8 ± 0.2[4]	1.2 ± 0.2[5]	0.1 ± 0.2
HDL-cholesterol, mmol/l	0.0 ± 0.0	0.1 ± 0.1	0.1 ± 0.1	–0.2 ± 0.1
LDL-cholesterol, mmol/l	1.4 ± 0.3[3]	0.8 ± 0.2	1.0 ± 0.2[4]	0.3 ± 0.2
Triglycerides, mmol/l	1.83 ± 0.46[5]	–0.14 ± 0.19	0.12 ± 0.59	–0.1 ± 0.1
Apo B, g/l	0.47 ± 0.06[3]	0.26 ± 0.08	0.26 ± 0.08	0.11 ± 0.04
Lp(a), mg/dl	1.4	2.7	0.6	1.8

[1]Group includes 37 subjects receiving ritonavir + saquinavir and 9 subjects receiving ritonavir alone
[2]Group includes 11 subjects receiving nelfinavir + saquinavir and 10 subjects receiving nelfinavir alone
[3]P≤0.001 vs change in PI-naive group
[4] P≤0.05 vs change in PI-naive group
[5] P≤0.01 vs change in PI-naive group

Périard et al: Circulation 1999; 100: 700-705

Incidence of Abnormalities of Serum Lipid Levels at the End of 1 Year Follow-up in 212 HIV-infected treated Patients who received different PI



Calza et al: JAC 2004; 53: 10-14

Conclusion

Use of HIV PIs is associated with atherogenic lipoprotein changes and endothelial dysfunction. Because these metabolic and vascular changes predispose to atherosclerosis, monitoring and treatment of dyslipidemia in patients taking these medications is warranted.

Circulation 2001; 104: 257-262

Association of Combination Antiretroviral Therapy and Other Cardiovascular Risk Factors with the Rate of Myocardial Infarction (23'468 Patients)

Variable	Univariable Model Relative Rate (95% CI)	P Value	Multivariable Model Relative Rate (95% CI)	P Value
Exposure to combination antiretroviral therapy (per additional yr)	1.22 (1.09-1.38)	<0.001	1.26 (1.12-1.41)	<0.001
Age (per additional 5 yr)	1.44 (1.34-1.55)	<0.001	1.38 (1.26-1.50)	<0.001
Male sex	3.07 (1.69-5.57)	<0.001	1.99 (1.04-3.79)	0.04
Body-mass index		0.7		0.77
<18	0.60 (0.15-2.44)		0.54 (0.13-2.23)	
18-26	1.00		1.00	
26-30	1.20 (0.72-2.01)		1.00 (0.60-1.69)	
>30	1.21 (0.53-2.78)		1.28 (0.55-2.98)	
Unknown	0.88 (0.54-1.44)		0.80 (0.45-1.41)	
Mode of HIV-1 transmission		0.32		0.28
Homosexual	1.00		1.00	
Heterosexual	0.69 (0.44-1.08)		1.13 (0.69-1.88)	
Intravenous drug use	0.76 (0.47-1.23)		1.49 (0.88-2.55)	
Other	0.32 (0.04-2.31)		0.30 (0.04-2.19)	
Unknown	0.98 (0.50-1.90)		1.40 (0.68-2.86)	

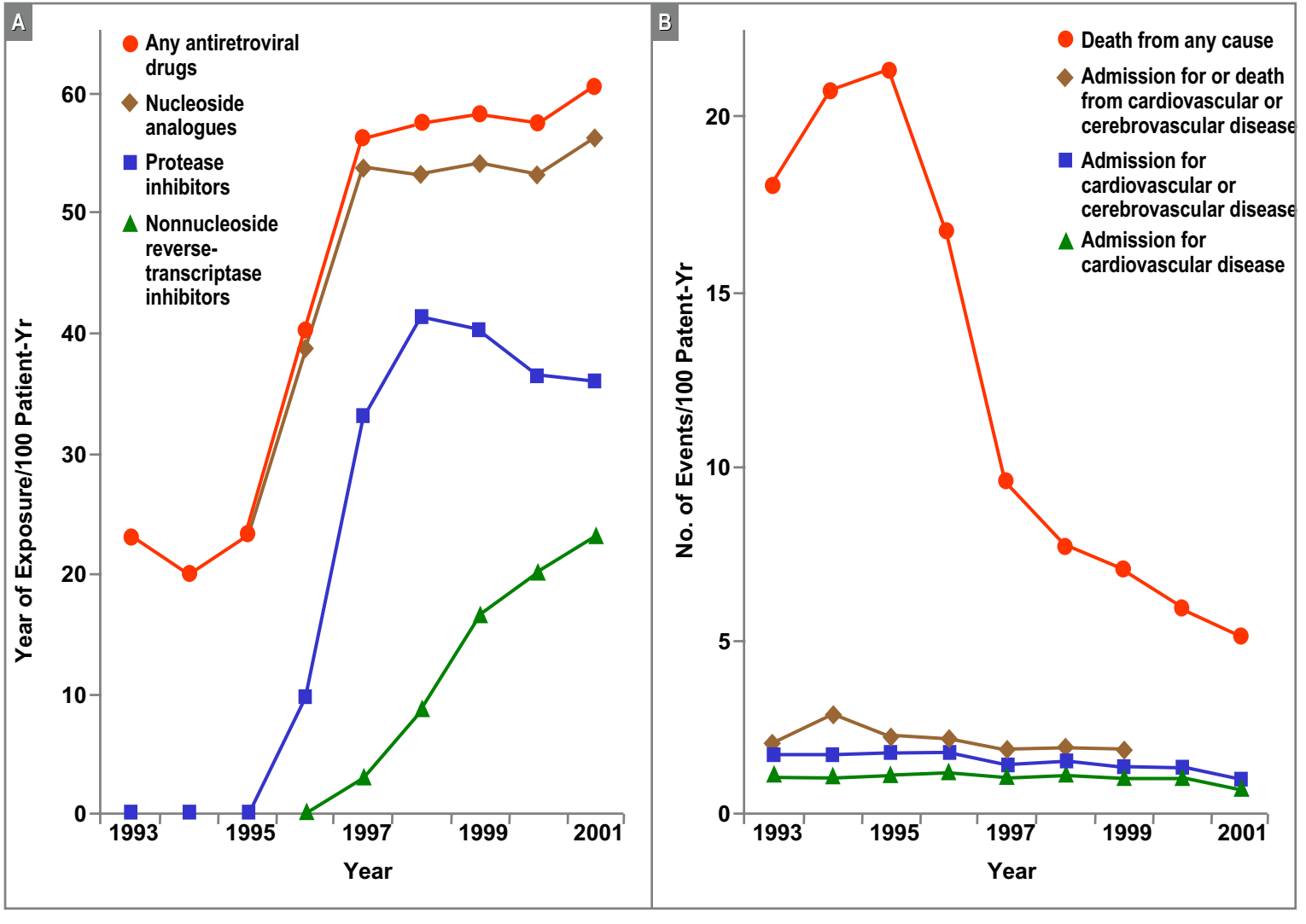
The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group, *N Engl J Med* 2003; 349: 1993-2003

Association of Combination Antiretroviral Therapy and Other Cardiovascular Risk Factors with the Rate of Myocardial Infarction (23'468 Patients) cont.

Variable	Univariable Model Relative Rate (95% CI)	P Value	Multivariable Model Relative Rate (95% CI)	P Value
Race		0.002		0.60
White	1.00		1.00	
Black	0.52 (0.03-1.34)		0.82 (0.36-1.90)	
Other	0.19 (0.03-1.34)		0.32 (0.04-2.38)	
Unknown	0.55 (0.38-0.81)		0.91 (0.46-1.81)	
Family history of CHD		0.44		0.78
No	1.00		1.00	
Yes	1.50 (0.83-2.72)		1.18 (0.64-2.17)	
Unknown	1.07 (0.74-1.55		1.18 (0.66-2.13)	
Smoking status		0.007		0.007
Current or former	2.08 (1.28-3.39)		2.17 (1.30-3.62)	
Never	1.00		1.00	
Unknown	1.73 (0.95-3.18)		1.39 (0.57-3.38)	
Previous cardiovascular disease		<0.001		<0.001
No	1.00		1.00	
Yes	13.77 (8.62-21.99)		5.84 (3.51-9.72)	

The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group, *N Engl J Med* 2003; 349: 1993-2003

Changing Rates of Use of Antiretroviral Drugs (Panel A) and Vascular Events and Death (Panel B)



Bozzette, S. A. et al. N Engl J Med 2003;348:702-710

- Lipide , Lipoproteine und Atherosklerose
- Dyslipoproteinämie bei Infektion
- HIV und Lipide
- Behandlung der Dyslipoproteinämie bei HIV-Patienten

Lipid-lowering Response in Dyslipidemic HAART-treated HIV-infected Patients

Drug regimens	No. of patients[a]	% Change mean (median)		
		Triglycerides mg/dl	Total cholesterol mg/dl	HDL-cholesterol mg/dl
First line LLD regimen[b] (median follow-up 44 weeks)	103	-26 (-32) p<0.002	-19 (-17) p<0.003	+9 (+5) p=NS
Second line LLD regimen[c] (median follow-up 25 weeks)	33	-44 (-40)	-25 (-26 p<0.02	+0.5 (+0.4)
Third line LLD regimen[d] (median follow-up 20 weeks)	15	-25 (-30)	-9 (-10) p = NS	+7 (+5)
Pooled lipid lowering effect stratified by drug class:				
Fibrates	77	-11 (-40)[e]	-9 (-7)[e]	+24 (+1)
Fibrates + statins[f]	20	-32 (-42)[g]	-23 (-22)[e]	+5 (+5)
Statins[f]	38	-1 (-21)	-11 (-14)[g]	+2 (0)

[a] More than one drug and drug class were used for a single patient

[b] First line LLD regimen: 71% treated with fibrates, 28% with statins and 1% with fibrates + statins; median follow-up of 44 weeks

[c] Second line LLD regimen: 15% treated with fibrates, 39% with statins and 45% with fibrates + statins; median follow-up of 30 weeks

[d] Third line LLD regimen: 13% treated with fibrates, 40% with statins and 47% with fibrates + statins; median follow-up of 20 weeks.

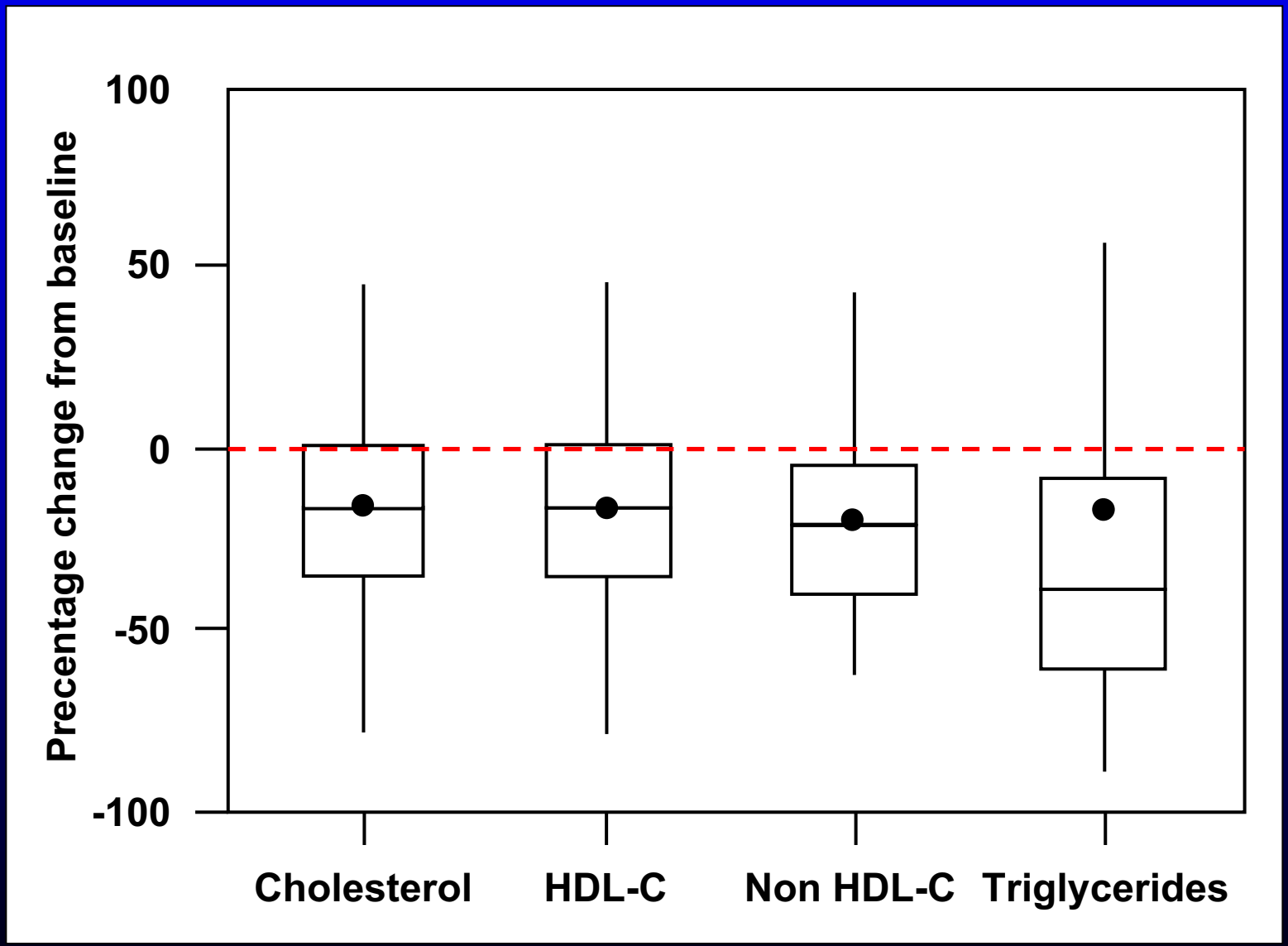
[e] = p<0.001

[f] Statins used were: atorvastatin 49%, pravastatin 20%, simvastatin 19%, lovastatin 12%

[g] = p<0.05

Visnegarwala et al: J of Infection 2004; 49: 283-290

Overall Response to Lipid-lowering Drugs among Dyslipidemic HAART-treated HIV-infected Patients (N=103)



Visnegarwala et al: J of Infection 2004; 49: 283-290

Antiretrovirals and Lipid-Lowering Therapy

- PIs and NNRTIs are metabolized by or affect the function of various CYP isoforms
- The primary route of metabolism for most statins is via oxidation using CYP3A4
- Inhibitors of CYP3A4 (eg PIs) can increase the concentration of certain statins
- Drug-drug interactions with statins and NNTIs are possible, but data are not available
- Certain PIs may have little (Indinavir, Sequinavir), if any (Atazanavir) effect on possible plasma lipid concentrations

Current Strategies for Management of Dyslipidemia in the Setting of HIV Therapy

	Nursing Intervention
General considerations	• Monitor patient fasting lipid profiles • Counsel patient on nonpharmacologic and pharmacologic lipid-lowering interventions • Monitor medication adherence and adherence to follow-up (laboratories and scheduled appointments) • Monitor for expected outcome (e.g. improved lipid levels) • Educate patient about disease process and health promotion
Use of statins	• Monitor prescribed medications for PI-statin drug-drug interactions • Recommend use of pravastatin (or atorvastatin) when total and LDL cholesterol levels are increased • Review signs and symptoms of common and adverse drug reactions (e.g. signs and symptoms of Myopathy)
Replace statins with fibrates	• Recommend that fibrates replace statins when the primary lipid abnormality is hypertriglyceridemia • Recommend that fibrates be considered as therapy for mixed dyslipidemia • Review medication administration regimen (review drug-food interactions) • Review signs and symptoms of common and adverse drug reactions
Use non-PI-based strategies	• Monitor antiretroviral drug history and resistance profiles • Recommend possible use of non-PI-based regimens in presence of hypercholesterolemia
Substitute new PIs such as atazanavir that have no effect on lipid metabolism	• Recommend consideration of atazanavir in presence of hypercholesterolemia and/or hypertriglyceridemia

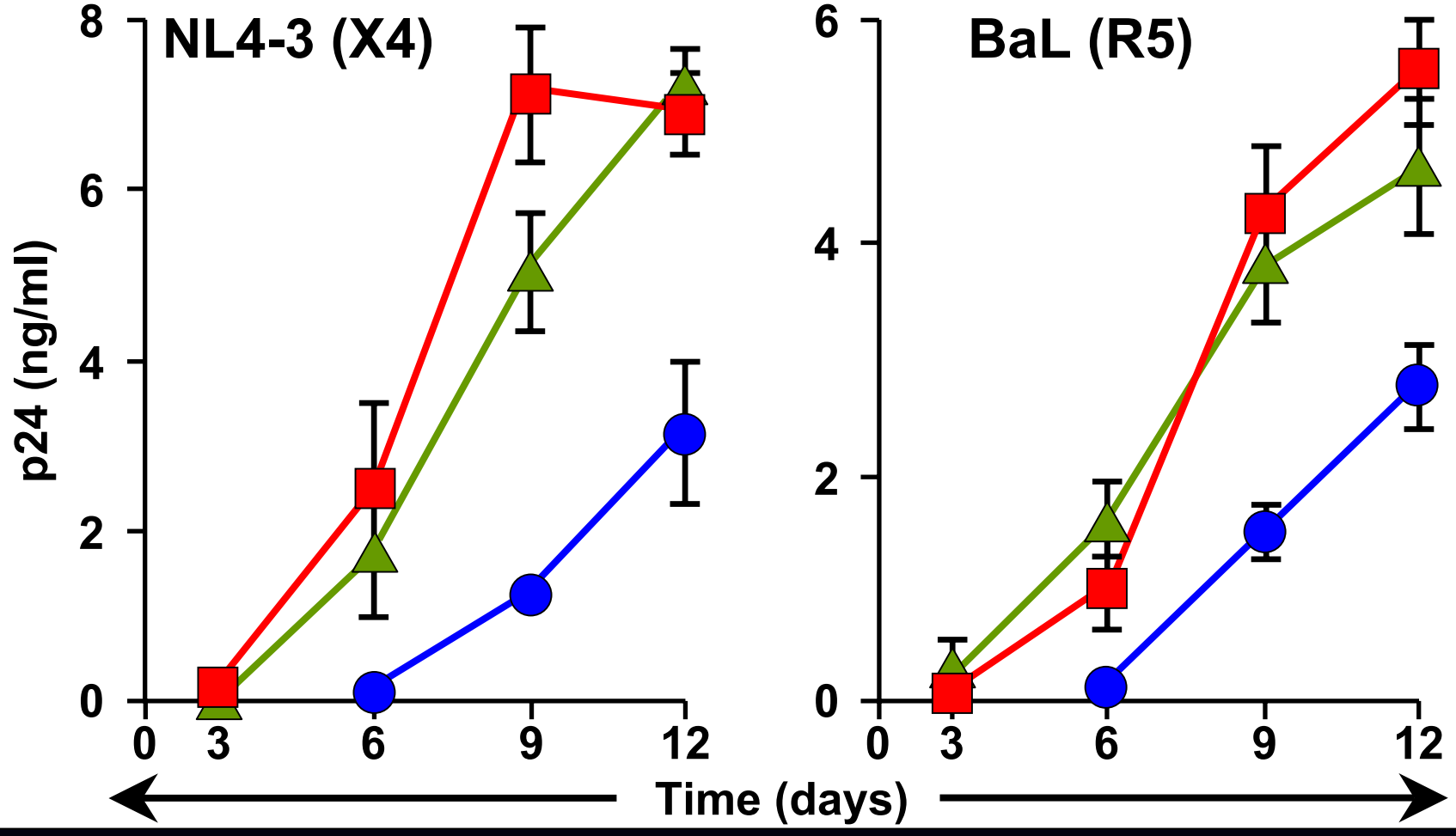
Modif.afterColagreco: J of Ass Nurses in AIDS Care 2004; 15: 30-41

Choice of Initial Drug Therapy for Dyslipidemia in Patients with HIV on Antiretroviral Therapy

Lipid Abnormality	Therapy	
	First Choice	Alternative(s)
Elevated LDL-C with TG 1.7 – 4.5 mmol/L	Statin	Fibrate or Niacin
Triglyceride > 4.5 mmol/L	Fibrate	Niacin or Fish oils

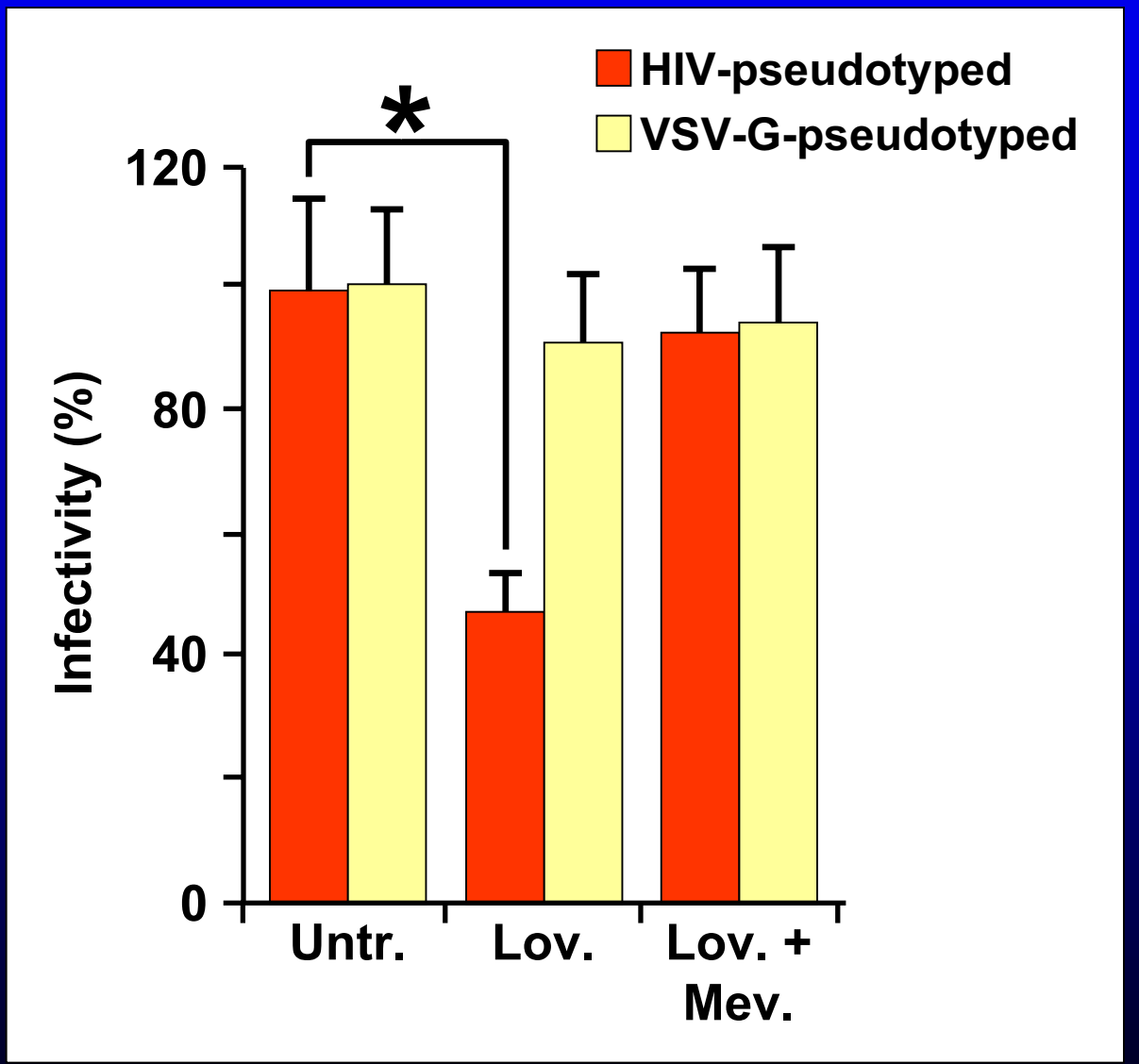
Statins Inhibit in vitro and in vivo HIV-1 Infection of Human PBMCs

Infection of untreated (■), Lov- (●), or Love plus Mev-treated (▲) PHA activated human PBMCs by X4 or R5 HIV-1 viral strains.
Data are mean ± SD of triplicate points (n=3).



del Real et al: J Exp Med 2004; 4: 541-547

Statins Inhibit HIV-1-Entry and Exit

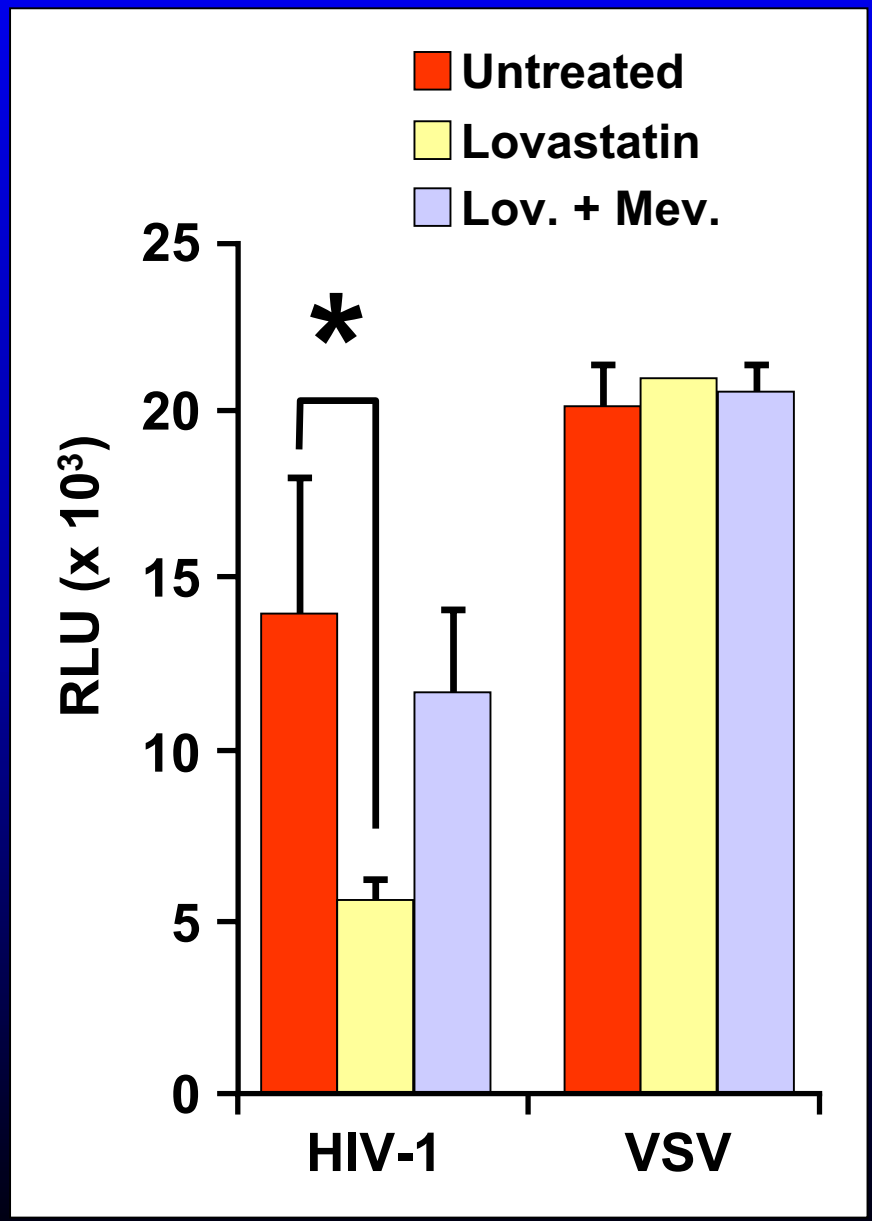


Single-round infections were performed in untreated, Lov-, and Lov plus Mev-treated MT2-CCR5 cells using a replication-defective NL4-3 virus bearing the luciferase reporter pseudotyped with HIV-1_{Ada} or VSV-G envelopes.

Cell infection was normalized using untreated cells as 100%.

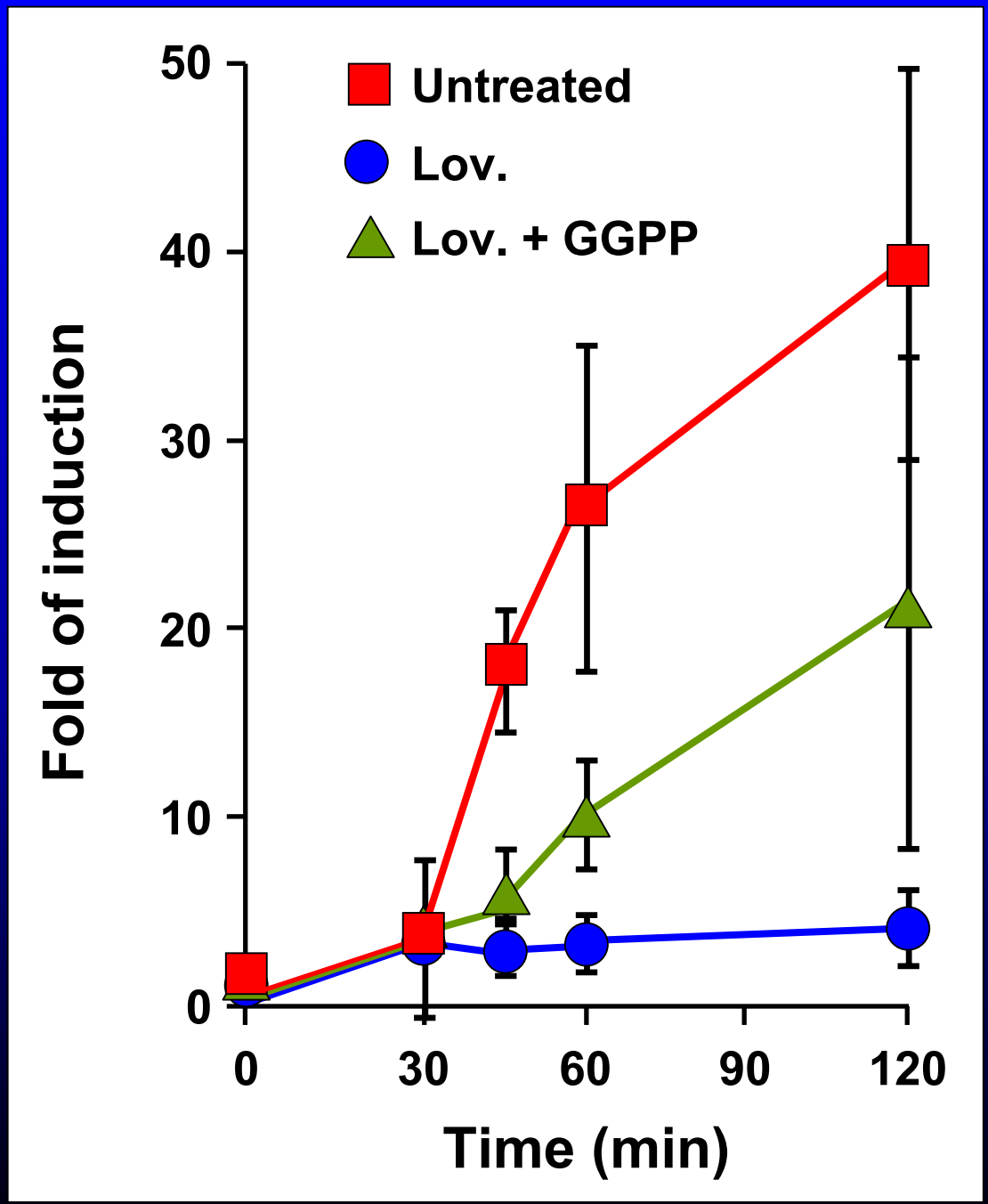
del Real et al: J Exp Med 2004; 4: 541-547

Statins Inhibit HIV-1-Entry and Exit



Virus production was measured by titration of viral stocks produced in untreated Lov-, and Lov plus Mev-treated HEK-293T cells transfected with replication-defective NL4-3 virus. Relative luciferase units were calculated after normalization with luciferase activity from extracts of stock-producing cells.

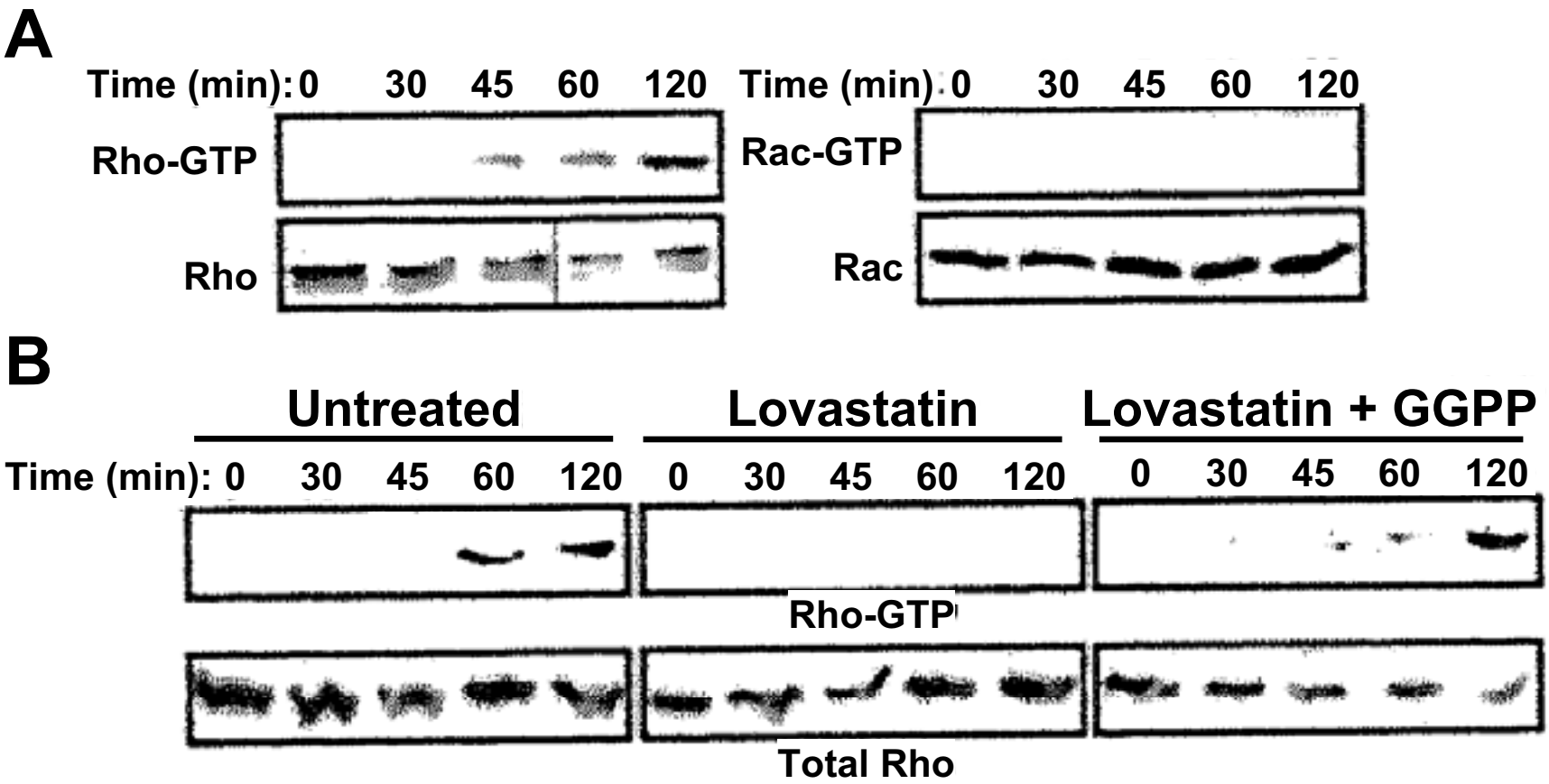
del Real et al: J Exp Med 2004; 4: 541-547



Statins Inhibit HIV-1 Infection by Down-regulating Rho Activation

del Real et al: J Exp Med 2004; 4: 541-547

Statins Inhibit HIV-1 Infection by Down-regulating Rho Activation



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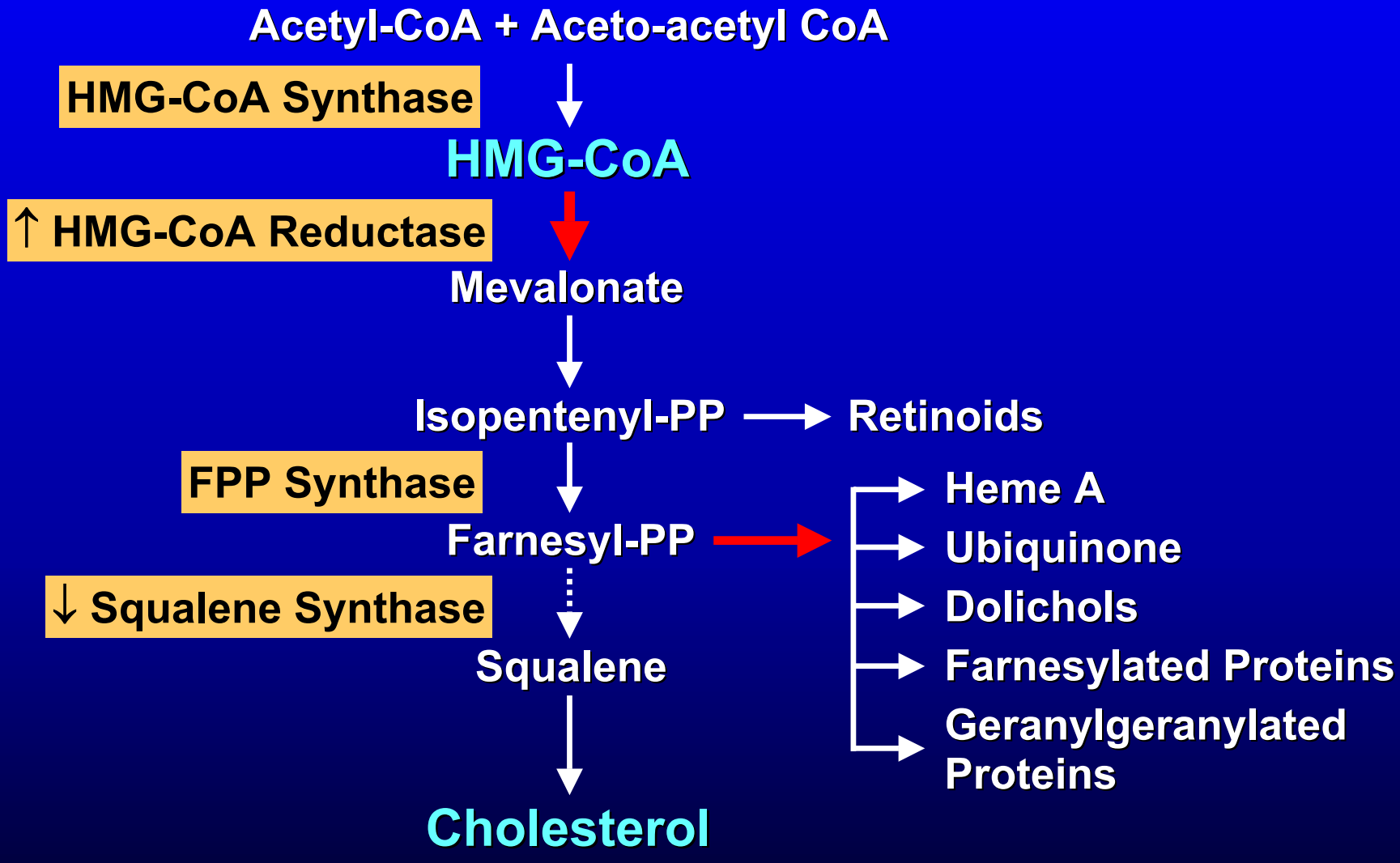
Cholesterol Metabolism during the APR



Infektion/Inflammation sind mit einer Zunahme der HMG-CoA Reduktase assoziiert.
Allerdings ist die Expression der übrigen Enzyme mit Mevalonatmetabolismus vermindert.

→ Mässige Zunahme der hepatischen Cholesterinsynthese und andere Mevalonatmetaboliten werden Non-Sterol-Wegen zugeführt.

Zusammenfassung

Infektionen gehen mit Veränderungen der Serumlipide und Serumlipoproteine einher.

1) Erhöhte VLDL-Synthese und verminderter VLDL-Abbau → erhöhte Triglyceride
2) Infektionen/Inflammationen erniedrigen sowohl LDL als auch HDL → erniedrigter „cholesterol reverse transport“ und vermehrte Cholesterinabgabe an Immunzellen.
3) Die Oxidation von LDL und VLDL nimmt zu, HDL wird ein pro-iflammatorisches Molekül
4) Unter Therapie mit Proteaseinhibitoren werden diese Veränderungen bei HIV-Patienten noch verstärkt. Diese Medikamente gehen mit einer veränderten Fettverteilung und Insulinresistenz einher → vorzeitige Atherosklerose und Pankreatitis

5) Der Einsatz von PIs sollte wenn möglich vermieden werden, bzw sollten PIs, die keinen Einfluss auf den Lipoproteinstoffwechsel haben, eingesetzt werden (Atazanavir), insbeso bei Hyperchol./Hypertriglyc.

6) Zur Behandlung der PI-induzierten Dyslipoproteinämie werden als erste Wahl Statine eingesetzt (bei vorwiegender Cholesterinerhöhung), bzw Fibrate (bei vorwiegender Triglyceriderhöhung).

Bei der Statinbehandlung sollte potentiellen Interaktionen mit anderen Medikamenten (Abbau über CYP450) Aufmerksamkeit geschenkt werden.