
Vall d'Hebron
Hospital
Dr. Joan Lima
Dr. Jose Loureiro
¿Qué puede haber detrás de una dislipemia grave?
SEMI
SOCIEDAD ESPAÑOLA DE MEDICINA INTERNA
Grupo de Riesgo Vascular

Caso clínico

- Varón 41 años remitido a CCEE por dislipemia
- Dislipemia 4 años antes.
- Fumador 20 cig/día
- HTA (enalapril)
- Psoriasis
- Peso 82 kg, Talla 173 cm. IMC 27.4 kg/m^2
- Perímetro abdominal 102 cm
- AF: madre y padre con DLP pero sin ECV conocida. Dos hijos no estudiados.

Institut Català de la Salut

Laboratori Clínic Bon Pastor
C/ Mollerussa s/n. Tf: 93 345.65.58 - Fax: 93 345.66.97

CIP	Centre	Remitent
[redacted]	[redacted]	[redacted]

Nom del Pacient	D.Naixement	Sexe	Data Petició	Nº Petició
[redacted]	09/12/1971	Masculí	02/11/2012	[redacted]

Bioquímica General

Validat per : Joaquin Ruiz Altarejos

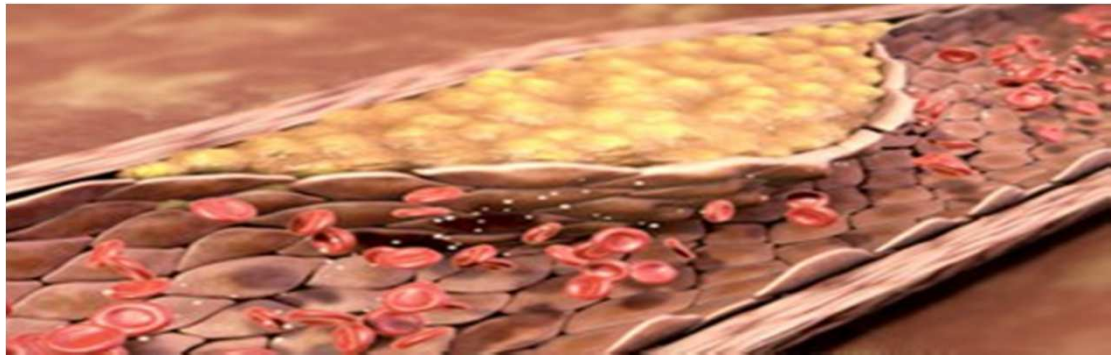
Determinació	Resultat	Unitats	Valors de referència	!
Srm-Glucosa; c.subst.	**94**	mg/dL	70 - 110	
Srm-Urat; c.subst.	**6,0**	mg/dL	3,8 - 7,7	
Srm-Creatinini; c.subst.	**0,68**	mg/dL	0,65 - 1,25	
Càlcul Filtrat Glomerular (Fórmula MDRD-IDMS)	**> 60**	mL/min	> 60	
Srm-Colesterol; c.subst. Valor recomanat < 200 mg/dl	**664** Resultat repetit i comprovat.	mg/dL	142 - 240	*
Srm-Colesterol d'HDL; c.subst. Valor recomanat >45 mg/dl	**79**	mg/dL	> 35	
Srm-Colesterol d'LDL (càlcul Friedewald) Valor recomanat < 160 mg/dl	**535**	mg/dL	< 160	*
Srm-Triglicèrid; c.subst. Valor recomanat < 200 mg/dl	**249**	mg/dL	44 - 200	*
Srm-Bilirubina; c.subst.	**0,17**	mg/dL	0,20 - 1,30	*
Srm-Alanina- aminotransferasa; c.cat	**13**	U/L	< 41	
Srm-Gamma-glutamiltransferasa; c.cat.	**41**	U/L	7 - 50	
Srm-Fosfatasa alcalina; c.cat.	**85**	U/L	40 - 129	
Srm-Ió sodi; c.subst.	**139**	mmol/L	135 - 147	

Cifras que fueron confirmadas a las dos semanas, con función tiroidea añadida.

Determinació	Resultat	Unitats	Valors de referència
Srm-Tirotropina(TSH); c.subst.arb.	**7,8191**	mU/L	0,4000 - 4,0000
Comentari TSH	**Atenció: Nous valors discriminants**		
Srm-Tiroxina lliure(FT4); c.subst.	**10,50**	pmol/L	9,09 - 19,00

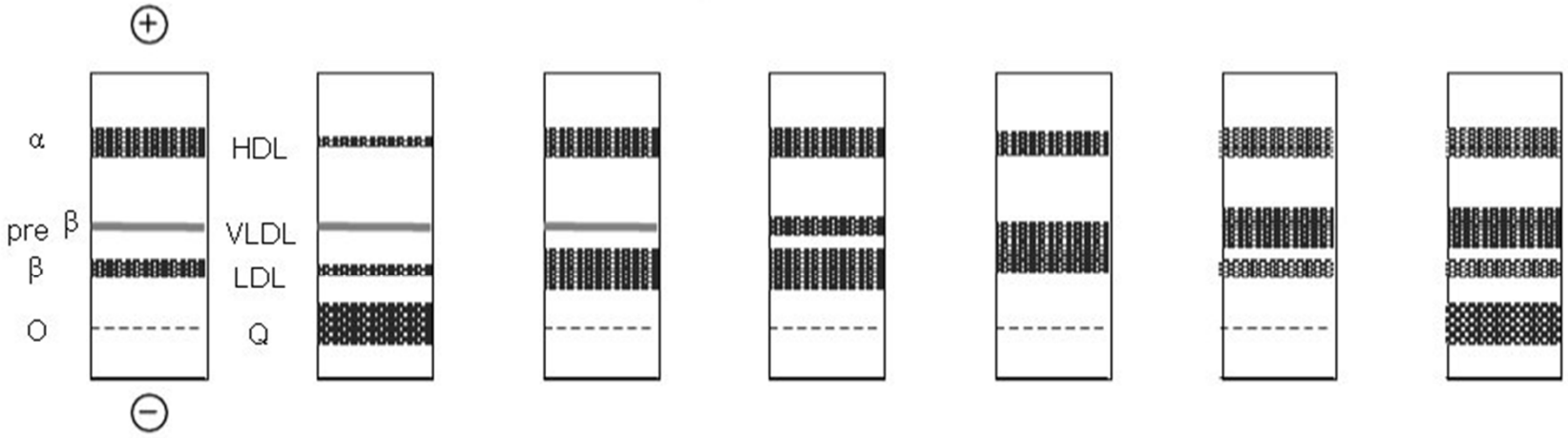
Clasificación de las dislipemias

CT / *TG*	< 200	> 200
< 200	Normal	Hipertrigliceridemia
> 200	Hipercolesterolemia	Hiperlipemia mixta

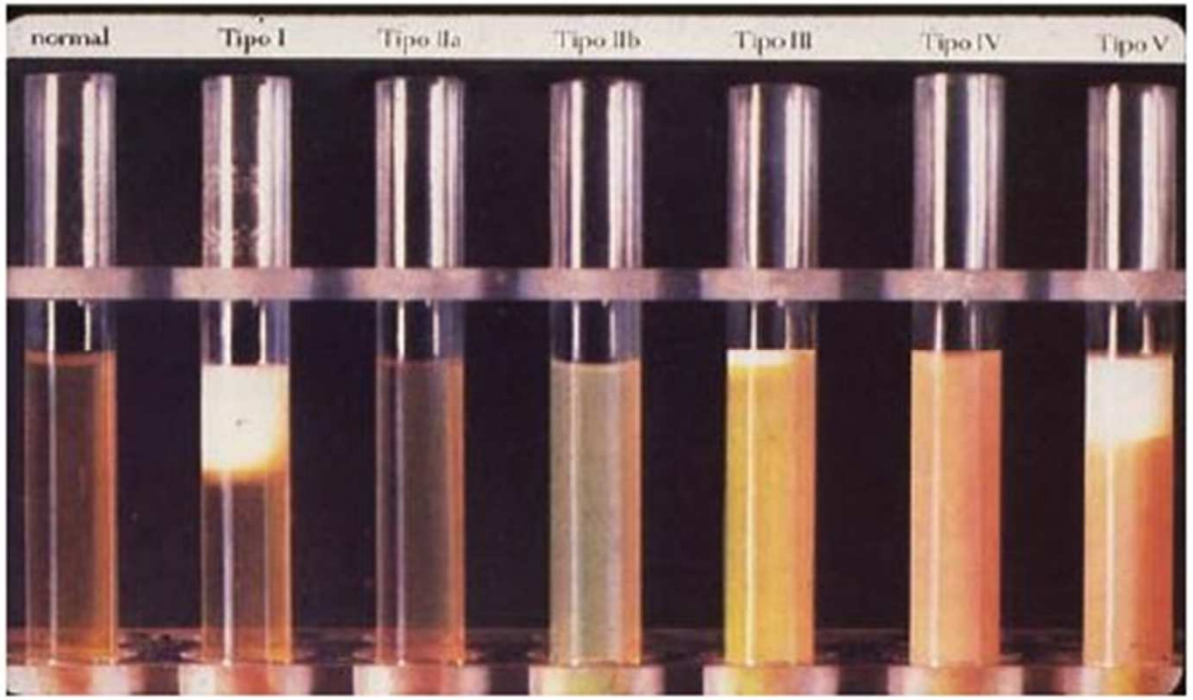


Clasificación fenotípica

Fenotipo	Lipoproteínas	Lípidos	Aspecto suero
I	Qm	TG	Anillo cremoso
IIa	LDL	Col	Transparente
IIb	LDL y VLDL	Col y TG	Opalescente
III	IDL	TG y Col	Opalescente
IV	VLDL	TG	Opalescente
V	Qm y VLDL	TG y Col	Opalescente con anillo cremoso

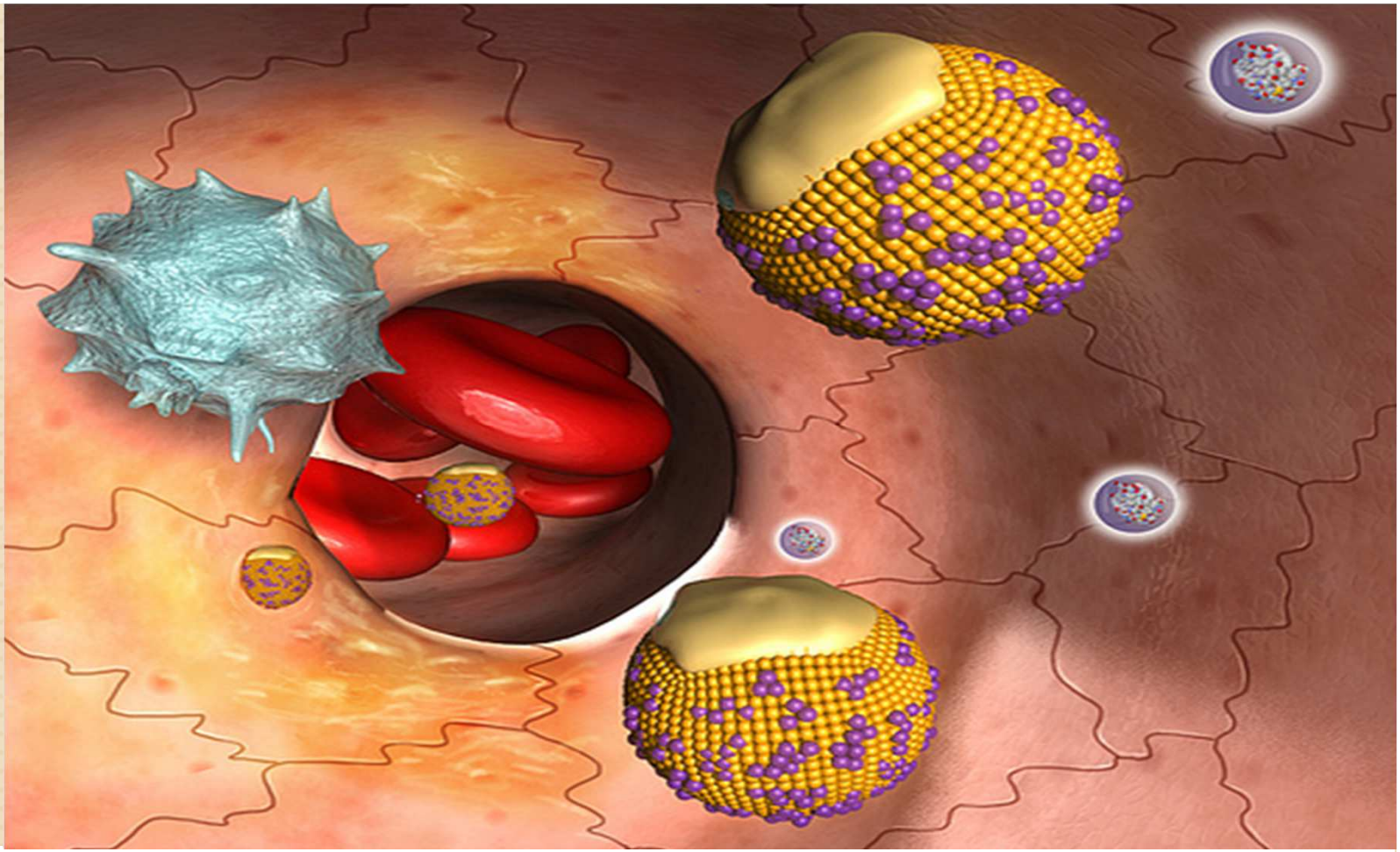


NORMAL Tipo I Tipo IIa Tipo IIb Tipo III Tipo IV Tipo V



¿....y esto qué?

- Es un error analítico?
- Es una dislipemia esporádica?
- Se trata de una dislipemia primaria ?
- Es un síndrome metabólico?
- Hay que buscar otras causas secundarias?



Dislipemias primarias

¿Cuándo sospechar una primaria?

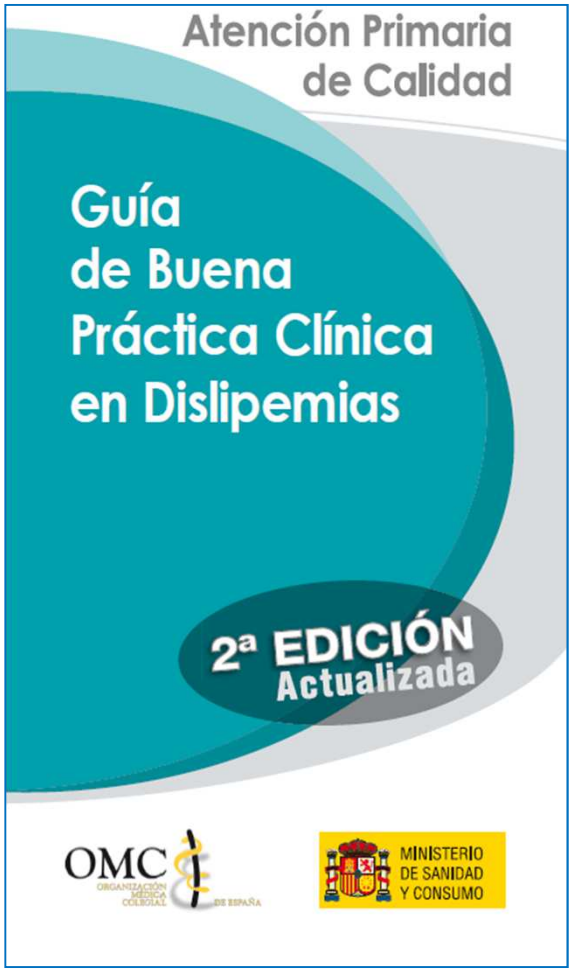
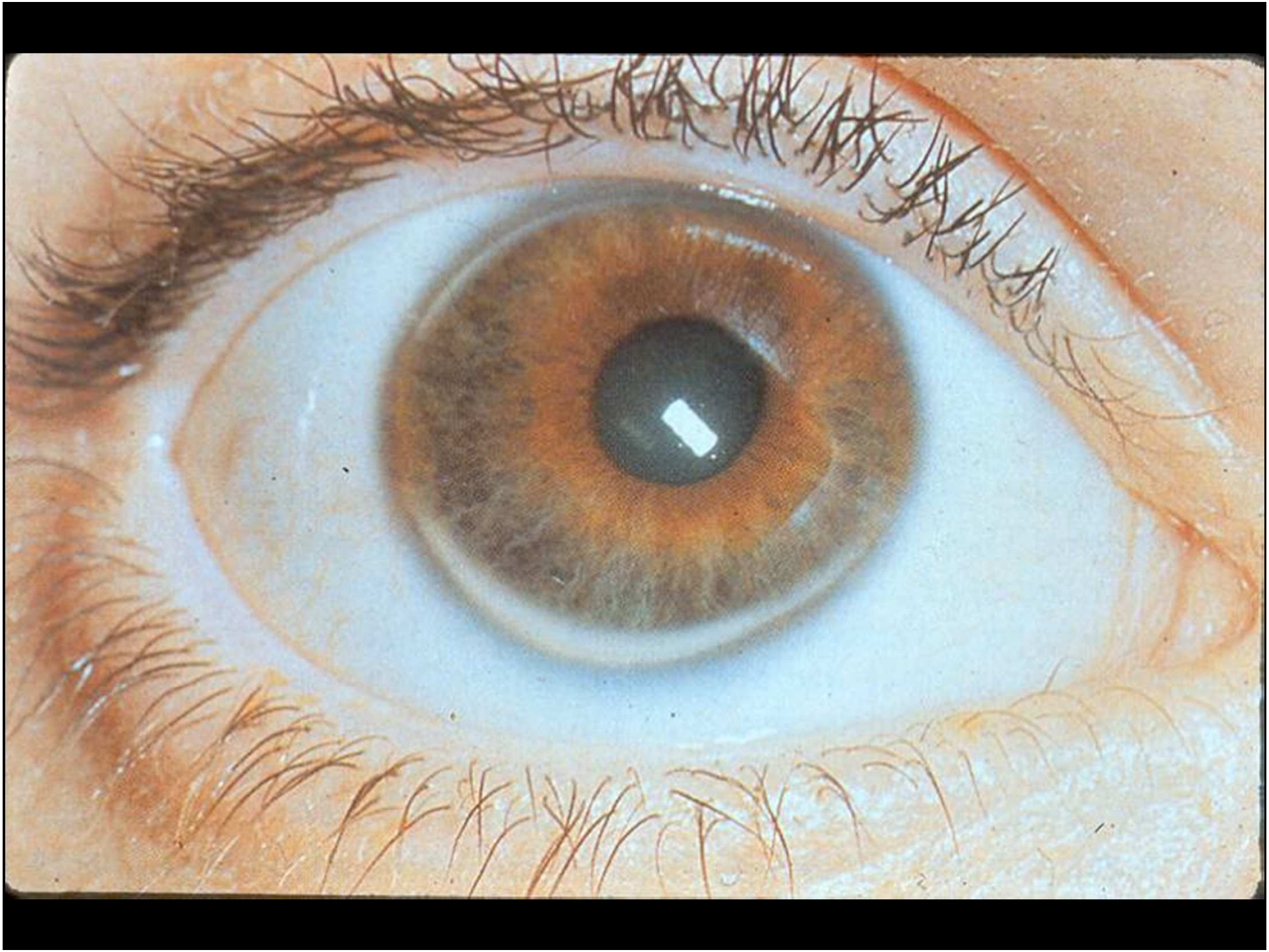
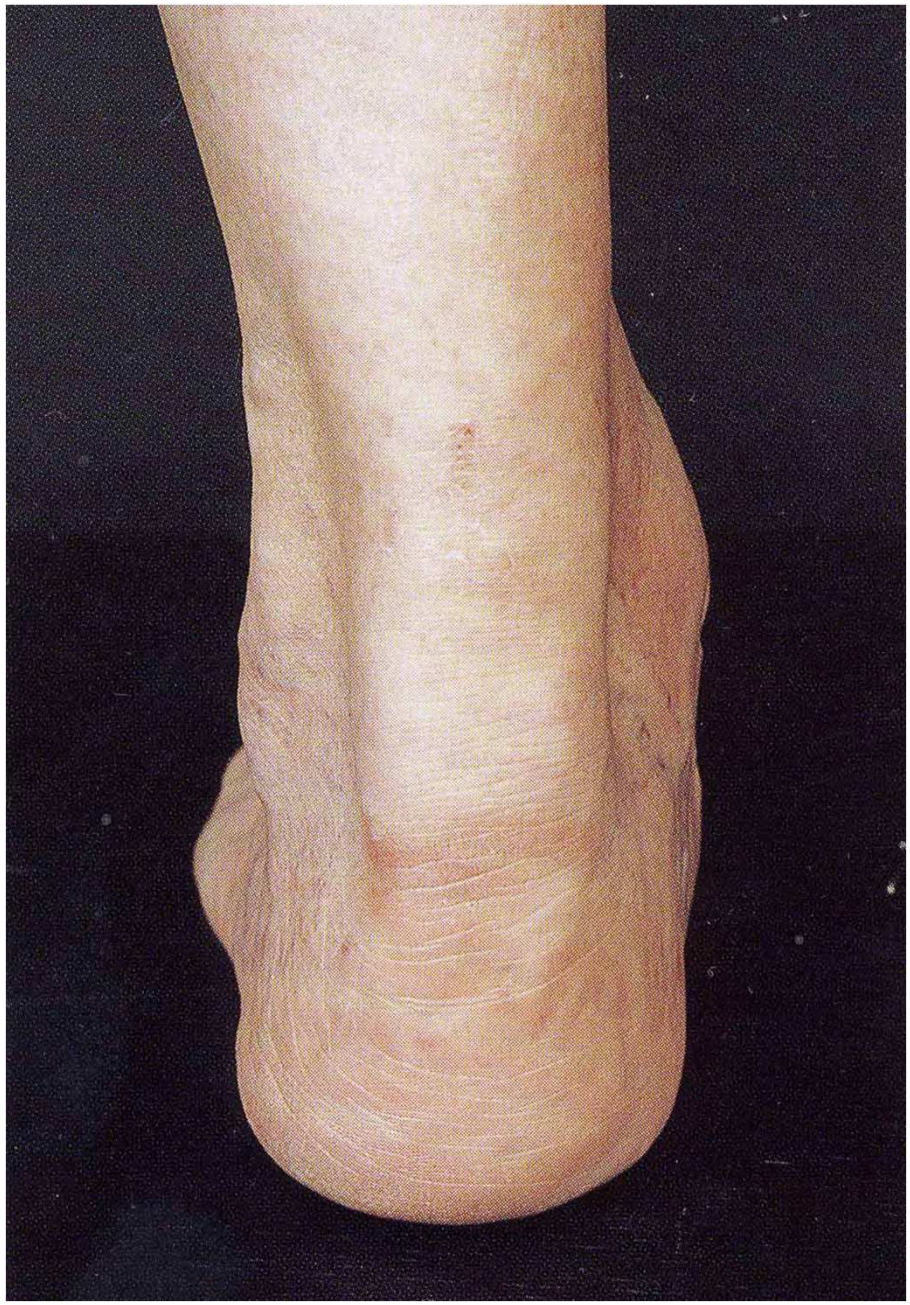
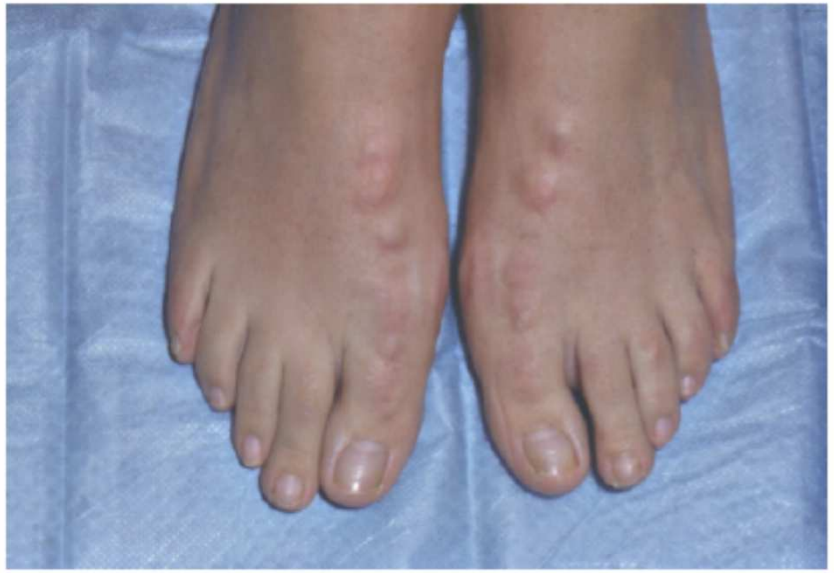


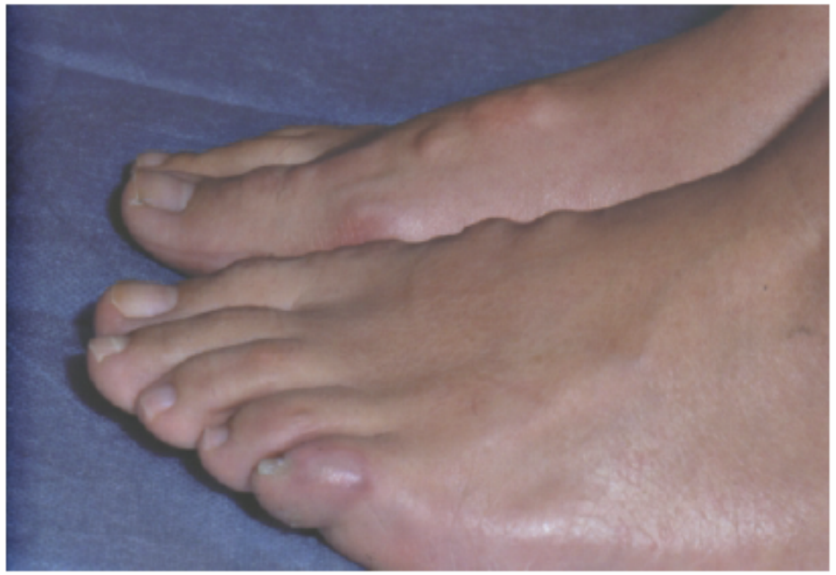
Tabla 6. Criterios de sospecha de una dislipemia primaria
• Hipercolesterolemia severa (colesterol total > 300 mg/dl).
• Triglicéridos > 400 mg/dl (descartar antes causa secundaria).
• Elevación conjunta del colesterol y de los triglicéridos.
• Antecedentes familiares de primer grado de cardiopatía isquémica precoz*.
• Antecedentes familiares de dislipemias.
• Arco corneal de aparición antes de los 45 años.
• Xantomas tendinosos o tuberoeruptivos.

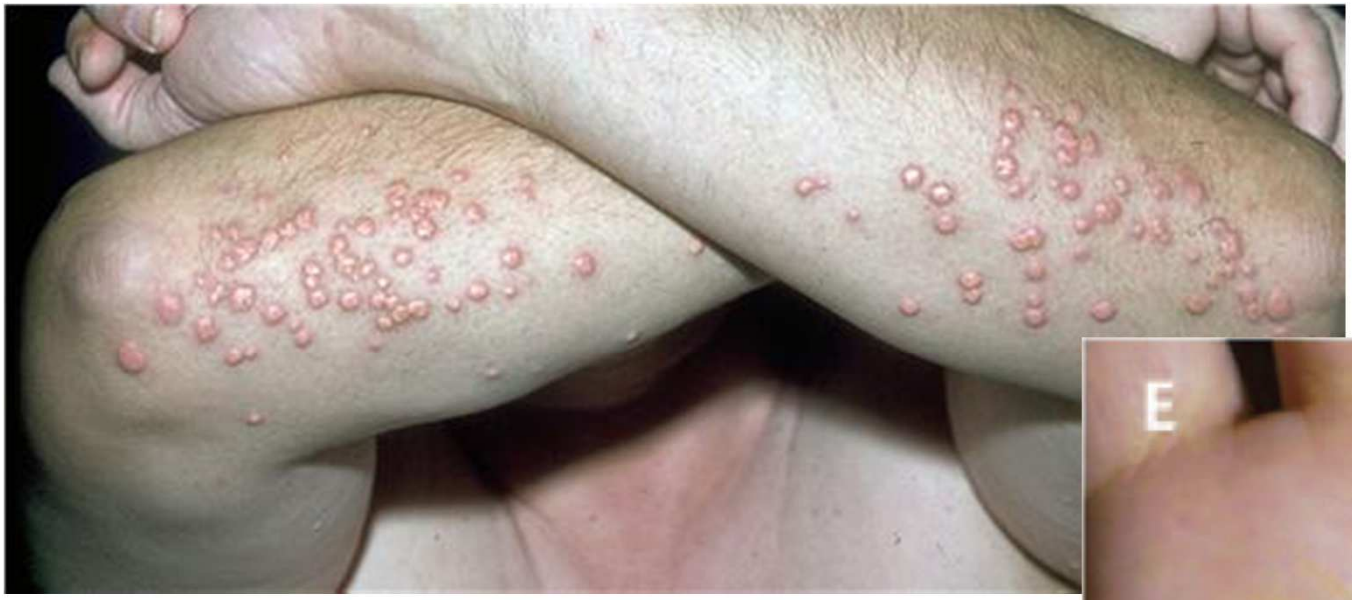
* Antes de los de los 65 años en mujeres y antes de los 55 años en varones.









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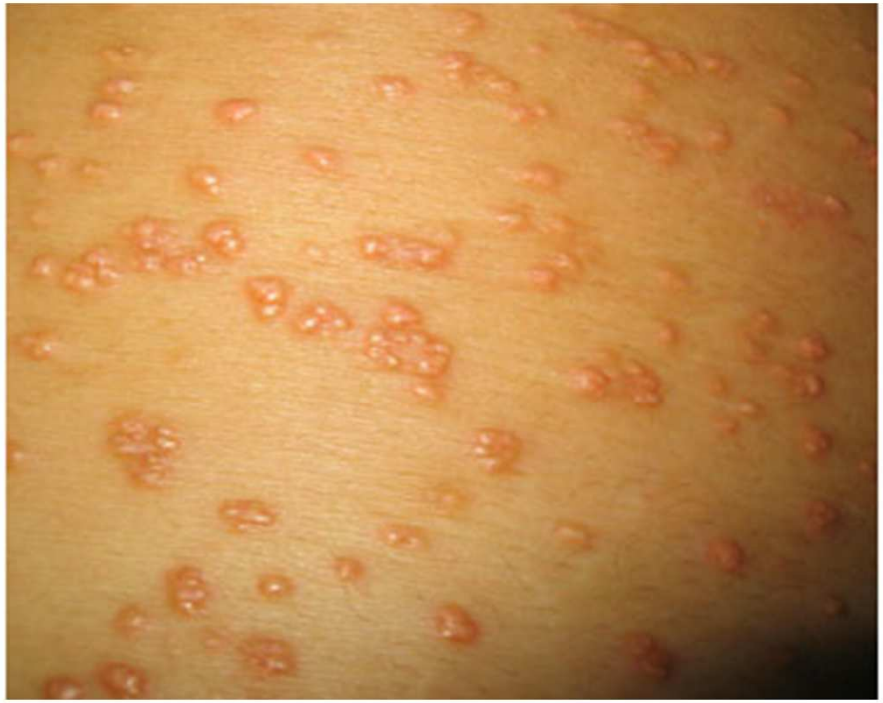
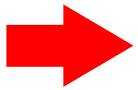
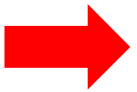


Hiperlipoproteinemias primarias

Entidad	Prevalencia
Hipercolesterolemias primarias	
Hipercolesterolemia familiar	1/500
Apoproteína B100 defectuosa familiar	1/500
Hipercolesterolemia autosómica recesiva	Muy rara
Hipercolesterolemia poligénica	1/50
Hiperalfalipoproteinemia familiar	Muy rara
Hipertrigliceridemias primarias	
Déficits de lipoproteinlipasa y apo-C_{II}	1/1.000.000
Hipertrigliceridemia familiar	1/100
Hiperlipidemias mixtas primarias	
Disbetalipoproteinemia familiar	1/10.000
Hiperlipemia familiar combinada	1/100





Hipercolesterolemias primarias

	Hipercolesterolemia familiar	Hiperlipemia familiar combinada	Hipercolesterolemia poligénica
Prevalencia	0.2%	1-2%	3-4%
Herencia	Monogénica AD	Poligénica	Poligénica
Patogenia	Defecto del receptor LDL	↑ síntesis hepática apo-B y VLDL	↑ síntesis LDL ↓ aclaramiento
Edad inicio	Nacimiento	> 20 años	> 20 años
Colesterol	300-500 mg/dL	260-350 mg/dL	280-320 mg/dL
Lipoproteínas	↑ LDL	↑ LDL y/o VLDL, ↓ HDL	↑ LDL
Xantomas	Frecuentes	Poco frecuentes	Ausentes
C. isquémica	30-55 años	45-55 años	60 años
AF 1er grado	50%	50%	10-20%
HTA, obesidad, DM	No	Si	Si

Hipercolesterolemia familiar

TABLA 1. Criterios diagnósticos de hipercolesterolemia familiar heterocigota (programa internacional de la OMS, Med-Ped)

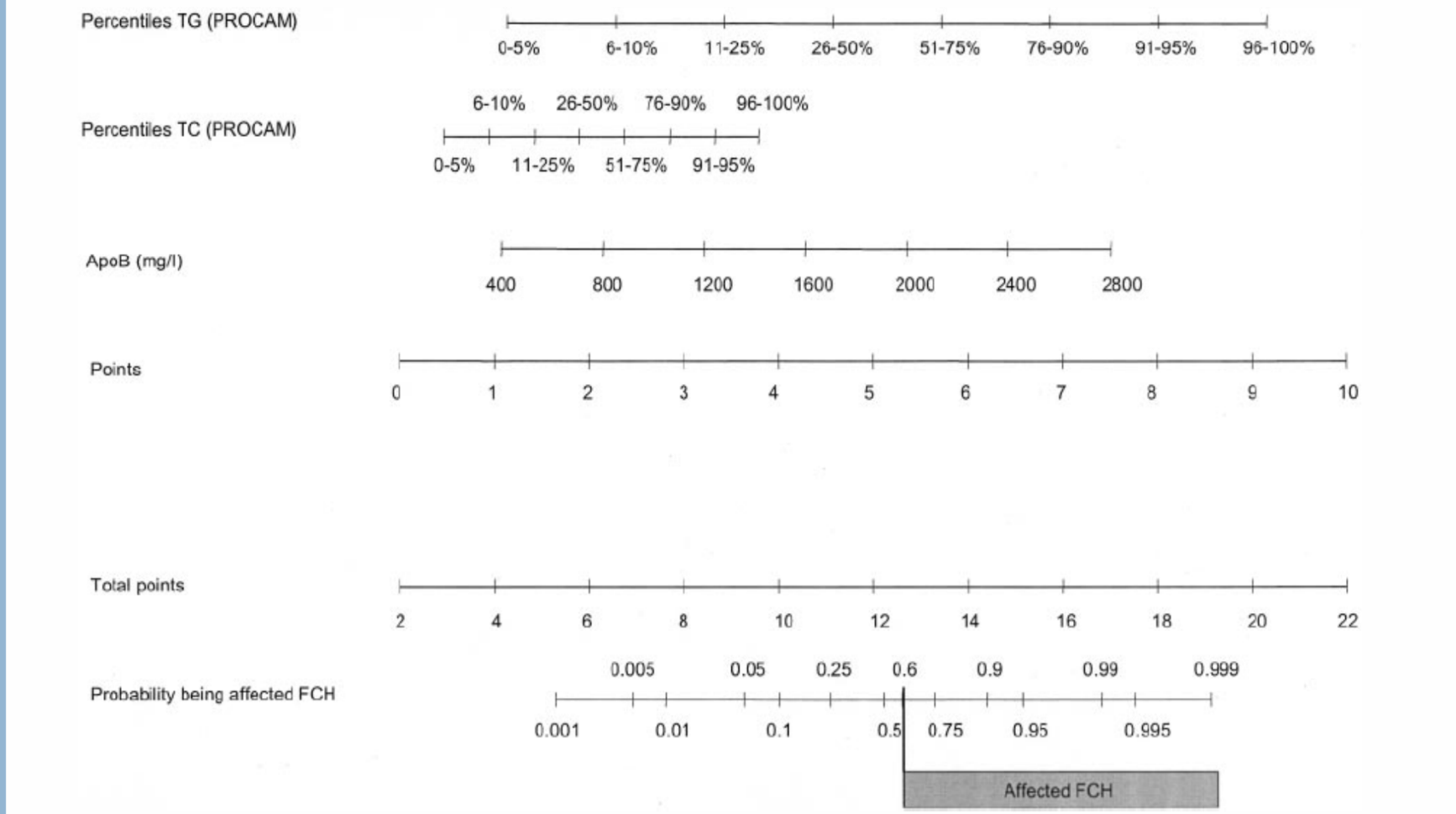
	Puntuación en caso afirmativo
Historia familiar	
I. Familiar de primer grado con enfermedad coronaria y/o vascular precoz	1
II. Familiar de primer grado con cLDL ≥ 210 mg/dl	1
III. Familiar de primer grado con xantomas y/o arco corneal	2
IV. Niño (hijo o hermano) menor de 18 años con cLDL ≥ 150 mg/dl	2
Historia personal	
I. Antecedentes de enfermedad coronaria precoz	2
II. Antecedentes de enfermedad vascular periférica o cerebral precoz (< 55 años en varones y < 60 años en mujeres)	1
Examen físico	
I. Xantomas tendinosos	6
II. Arco corneal antes de los 45 años	4
Analítica en ayunas, con triglicéridos < 200 mg/dl	
I. cLDL ≥ 330 mg/dl	8
II. cLDL, 250-329 mg/dl	5
III. cLDL, 190-249 mg/dl	3
IV. cLDL, 155-189 mg/dl	1
Análisis genético del rLDL	8

PUNTUACIÓN

- ≥ 8 puntos: certeza
- 6-7 puntos: probable
- 3-5 puntos: posible

Nomogram to Diagnose Familial Combined Hyperlipidemia on the Basis of Results of a 5-Year Follow-Up Study

Mario J. Veerkamp, MD; Jacqueline de Graaf, MD, PhD; Jan C.M. Hendriks, PhD;
Pierre N.M. Demacker, PhD; Anton F.H. Stalenhoef, MD, PhD (*Circulation*. 2004;109:2980-2985.)



Circulation. 2004;109:2980-2985.

¿...y qué hacemos?

- Repetir la analítica en 2 meses?
- Calcular el riesgo cardiovascular?
- Medidas de estilo de vida?
- Iniciar tratamiento con simvastatina 40 mg?
- Iniciar tratamiento con atorvastatina 80 mg?

Stone NJ, et al.
2013 ACC/AHA Blood Cholesterol Guideline

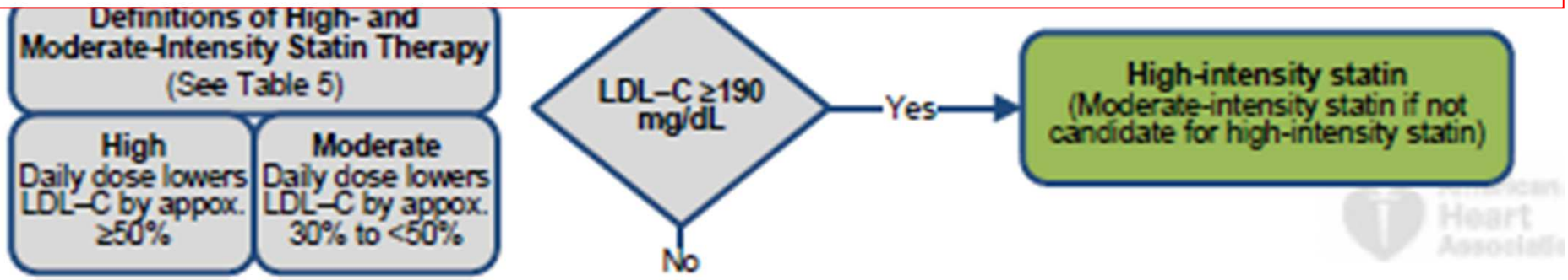
Figure 2. Major recommendations for statin therapy for ASCVD prevention

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Neil J. Stone, Jennifer Robinson, Alice H. Lichtenstein, C. Noel Bairey Merz, Conrad B. Blum, Robert H. Eckel, Anne C. Goldberg, David Gordon, Daniel Levy, Donald M. Lloyd-Jones, Patrick McBride, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Karol Watson and Peter W.F. Wilson



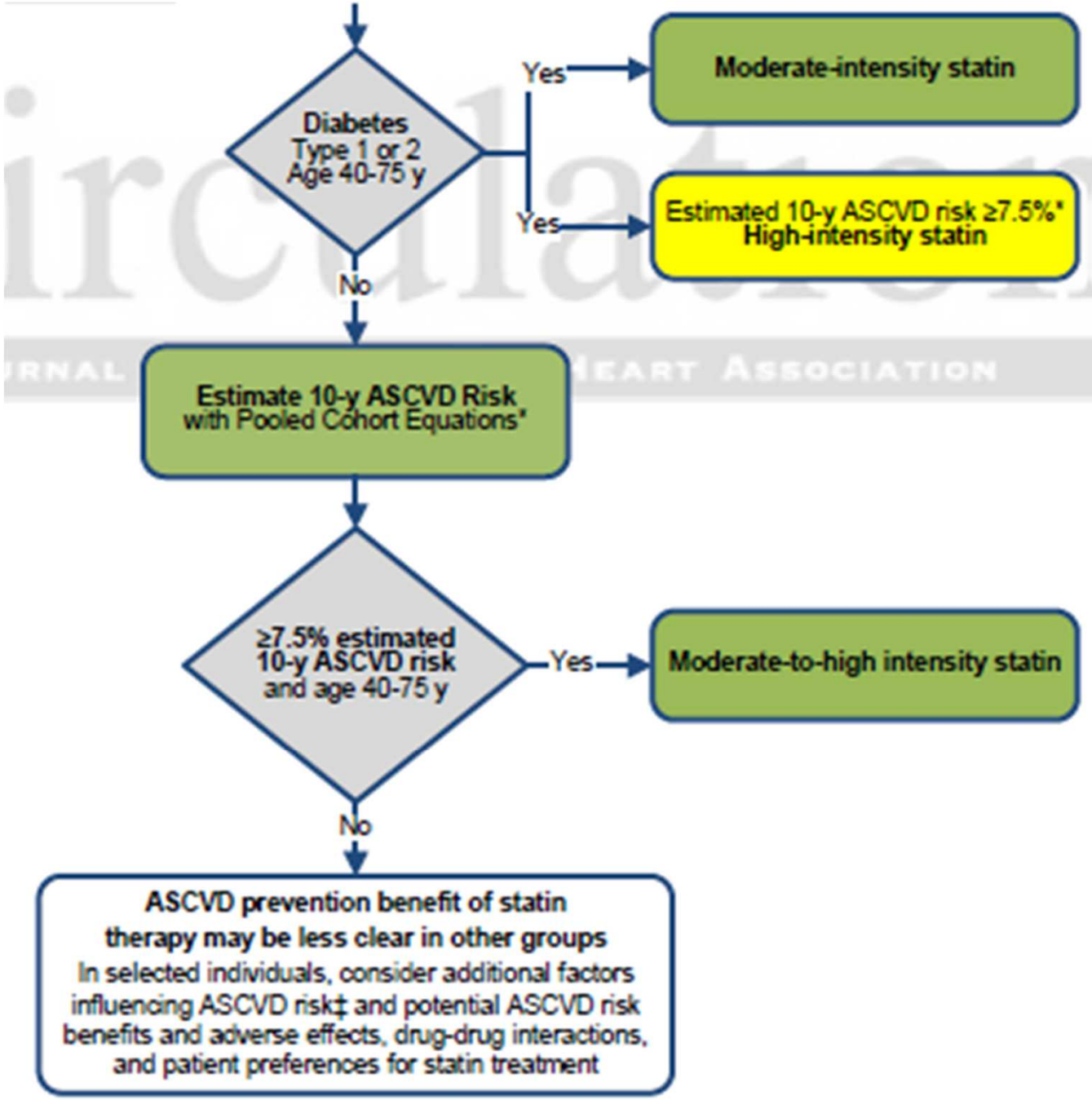

Diabetes
Type 1 or 2
Age 40-75 y
Yes
Moderate-intensity statin
Yes
Estimated 10-y ASCVD risk ≥7.5%*
High-intensity statin
No
Estimate 10-y ASCVD Risk
with Pooled Cohort Equations*
≥7.5% estimated
10-y ASCVD risk
and age 40-75 y
Yes
Moderate-to-high intensity statin
No
ASCVD prevention benefit of statin
therapy may be less clear in other groups
In selected individuals, consider additional factors
influencing ASCVD risk‡ and potential ASCVD risk
benefits and adverse effects, drug-drug interactions,
and patient preferences for statin treatment

Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20 *(40)* mg**	**Atorvastatin 10 *(20)* mg** **Rosuvastatin (5) 10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40 *(80)* mg** **Lovastatin 40 mg** ***Fluvastatin XL 80 mg*** **Fluvastatin 40 mg bid** ***Pitavastatin 2–4 mg***	***Simvastatin 10 mg*** **Pravastatin 10–20 mg** **Lovastatin 20 mg** ***Fluvastatin 20–40 mg*** ***Pitavastatin 1 mg***

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Primary Prevention in Individuals ≥21 Years of Age With LDL–C ≥190 mg/dL				
1. Individuals with LDL–C ≥190 mg/dL or triglycerides ≥500 mg/dL should be evaluated for secondary causes of hyperlipidemia (Table 6).	B (Moderate)	75	I‡	B (44,45)
2 Adults ≥21 years of age with primary LDL–C ≥190 mg/dL should be treated with statin therapy (10-year ASCVD risk estimation is not required): • Use high-intensity statin therapy unless contraindicated. • For individuals unable to tolerate high-intensity statin therapy, use the maximum tolerated statin	B (Moderate)	6, 19, 28, 33-35, 37, 38	I§	B

Nuestro paciente…

- EF normal salvo sobrepeso y lesiones de psoriasis

- Se inicia rosuvastatina 40 mg/día
- En abril 2013
  - CT 365 mg/dL (LDL 260 mg/dL, HDL 80 mg/dL)
  - TG 121 mg/dL

Causas de respuesta terapéutica insuficiente

- **Mala adherencia terapéutica**
- Dosis de estatinas insuficiente
- Concentración de Lipoproteína(a) elevada
- Causa subyacente oculta

Lipoproteína (a)

Genome-wide association study of genetic determinants of LDL-c response to atorvastatin therapy: importance of Lp(a)[S]

Harshal A. Deshmukh,[1,*] Helen M. Colhoun,[1,2,*] Toby Johnson,[†] Paul M. McKeigue,[§] D. John Betteridge,[**] Paul N. Durrington,[††] John H. Fuller,[**] Shona Livingstone,[*] Valentine Charlton-Menys,[††] Andrew Neil,[§§] Neil Poulter,[***] Peter Sever,[***] Denis C. Shields,[†††] Alice V. Stanton,[§§§] Aurobindo Chatterjee,[****] Craig Hyde,[****] Roberto A. Calle,[****] David A. DeMicco,[****] Stella Trompet,[††††] Iris Postmus,[§§§§] Ian Ford,[*****] J. Wouter Jukema,[††††,†††††] Mark Caulfield,[3,†] and Graham A. Hitman,[3,†] on behalf of the CARDS, ASCOT, and PROSPER investigators

University of Dundee,[*] Dundee, United Kingdom; Barts and The London School of Medicine and Dentistry,[†] Queen Mary University of London, London, United Kingdom; University of Edinburgh,[§] Edinburgh, United Kingdom; University College London,[**] London, United Kingdom; University of Manchester,[††] Manchester, United Kingdom; University of Oxford,[§§] Oxford, United Kingdom; International Centre for Circulatory Health,[***] Imperial College London, United Kingdom; Complex and Adaptive Systems Laboratory,[†††] University College Dublin, Dublin, Ireland; Royal College of Surgeons in Ireland,[§§§] Dublin, Ireland; Pfizer Ltd.,[****] New York, NY; Department of Cardiology[††††] and Department of Geriatrics and Gerontology,[§§§§] Leiden University Medical Center, Leiden, The Netherlands; Robertson Centre for Biostatistics,[*****] University of Glasgow, Glasgow, United Kingdom; and Interuniversity Cardiology Institute of the Netherlands,[†††††] Utrecht, The Netherlands

J Lipid Res. 2012 May;53(5):1000-11

Lipoproteína (a)

Abstract We carried out a genome-wide association study (GWAS) of LDL-c response to statin using data from participants in the Collaborative Atorvastatin Diabetes Study (CARDS; n = 1,156), the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT; n = 895), and the observational phase of ASCOT (n = 651), all of whom were prescribed atorvastatin 10 mg. Following genome-wide imputation, we combined data from the three studies in a meta-analysis. We found associations of LDL-c response to atorvastatin that reached genome-wide significance at rs10455872 ($P = 6.13 \times 10^{-9}$) within the *LPA* gene and at two single nucleotide polymorphisms (SNP) within the *APOE* region (rs445925; $P = 2.22 \times 10^{-16}$ and rs4420638; $P = 1.01 \times 10^{-11}$) that are proxies for the ε2 and ε4 variants, respectively, in APOE. The novel association with the *LPA* SNP was replicated in the PROspective Study of Pravastatin in the Elderly at Risk (PROSPER) trial ($P = 0.009$). Using CARDS data, we further showed that atorvastatin therapy did not alter lipoprotein(a) [Lp(a)] and that Lp(a) levels accounted for all of the associations of SNPs in the LPA gene and the apparent LDL-c response levels. However, statin therapy had a similar effect in reducing cardiovascular disease (CVD) in patients in the top quartile for serum Lp(a) levels (HR = 0.60) compared with those in the lower three quartiles (HR = 0.66; $P = 0.8$ for interaction). The data emphasize that high Lp(a) levels affect the measurement of LDL-c and the clinical estimation of LDL-c response. Therefore, an apparently lower LDL-c response to statin therapy may indicate a need for measurement of Lp(a). However, statin therapy seems beneficial even in those with high Lp(a).—Deshmukh, H. A., H. M. Colhoun, T. Johnson, P. M. McKeigue, D. J. Betteridge, P. N.

The CARDS trial was cofunded by Pfizer Ltd., Diabetes UK, and National Health Service R&D. Genotyping was funded by Pfizer Ltd. The Anglo-Scandinavian

¿...y qué hacemos ahora?

- Que confiese que toma la estatina de forma irregular...
- Determinar la Lp(a)
- Asociar ezetimiba
- Buscar una causa secundaria

Dislipemias secundarias

Descartar causar secundarias...

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Table 4. Recommendations for Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults—Statin Treatment
(High-, moderate-, and low-statin intensities are defined in Table 5)

Recommendations	NHLBI Grade	NHLBI Evidence Statements	ACC/AHA COR	ACC/AHA LOE
Primary Prevention in Individuals ≥21 Years of Age With LDL–C ≥190 mg/dL				
1. Individuals with LDL–C ≥190 mg/dL or triglycerides ≥500 mg/dL should be evaluated for secondary causes of hyperlipidemia (Table 6).	B (Moderate)	75	I‡	B (44,45)

	↑ LDL	↑ TG
Dieta	Grasas saturadas o trans Obesidad Anorexia	**Alcohol** Obesidad Dieta muy alta en grasas Carbohidratos refinados
Fármacos	**Diuréticos** **Glucocorticoides** Amiodarona Ciclosporina Azatioprina	**Estrógenos orales** **Tamoxifeno y raloxifeno** **Glucocorticoides** Betabloqueantes Tiazidas Secuestradores de ácidos biliares Inhibidores de proteasa Retinoides (isotretinoína) Sirolimus
Enfermedades	**Hipotiroidismo** **Síndrome de Cushing** **Síndrome nefrótico** Hepatopatía obstructiva Porfiria aguda	**Hipotiroidismo** **Síndrome nefrótico** **Enfermedad renal crónica** **SOP** LES Lipodistrofias

Tabla 2. Evaluación clínica del paciente con dislipemia

Historia clínica:

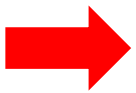
1. Anamnesis:
   - Antecedentes familiares de dislipemia y de enfermedad cardiovascular prematura.
   - Antecedentes personales:
     - Presencia de enfermedad cardiovascular o pancreatitis.
     - Presencia de otros factores de riesgo mayores.
     - Características de la dislipemia:
       - Grado de intensidad.
       - Edad de diagnóstico.
       - Respuesta al tratamiento.
     - Hábitos dietéticos.
     - Actividad física.
     - Consumo de tabaco y alcohol.
2. Exploración física:
   - Presión arterial, frecuencia cardiaca, peso, talla, índice de masa corporal, perímetro de cintura abdominal, auscultación cardiaca y soplos vasculares, exploración de pulsos, búsqueda de xantomas y arco corneal, bocio.

Pruebas complementarios recomendadas en la valoración inicial

- Hemograma
- Bioquímica
  - Perfil lípido (CT, HDL, LDL, TG)
  - Glu, Crea, Úrico, transaminasas, GGT
  - TSH si:
    - Sospecha clínica de hipotiroidismo
    - Sospecha clínica de disbetalipoproteinemia
    - Diabetes mellitus
    - Colesterol > 300 mg/dL
    - Hipercolesterolemia de aparición en >50 años
    - Mala respuesta al tratamiento
- Sistemático de orina (con microalbuminuria en diabéticos)
- ECG
- Índice tobillo/brazo ± ecografía carotídea

B I O Q U Í M I C A

SUBSTRATS				
Sm-Glucosa		94	mg/dL	78 - 114
Sm-Urea	*	19	mg/dL	21 - 52
Sm-Creatinini		0.75	mg/dL	0.67 - 1.17
Sm-Urat		7.4	mg/dL	2.5 - 7.5
Sm-Bilirubina total	*	0.28	mg/dL	0.29 - 1.02
Sm-Bilirubina esterificada		0.13	mg/dL	0.10 - 0.57
IONS				
Sm-Sodi		139.3	mmol/L	136.5 - 145.1
Sm-Potassi		4.70	mmol/L	3.72 - 4.84
Sm-Clorur		106	mmol/L	98 - 107
Sm-Fosfat inorgànic		2.7	mg/dL	2.5 - 4.5
Sm-Calci	*	8.5	mg/dL	8.8 - 10.2
ENZIMS				
Sm-Aspartat aminotransferasa		18	UI/L	12 - 40
Sm-Alanin aminotransferasa		16	UI/L	8 - 44
Sm-Fosfatasa alcalina		65	UI/L	35 - 110
Sm-Gamma-glutamil transferasa		45	UI/L	9 - 55
Sm-Creatina cinasa		146	UI/L	55 - 195
LIPIDS i LIPOPROTEÏNES				
Sm-Colesterol	*	365	mg/dL	132 - 220
Sm-Colesterol HDL		80.8	mg/dL	> 40.0
Sm-Colesterol LDL	*	260.00	mg/dL	< 130.00
Sm-Triglicèrid		121	mg/dL	43 - 200
PROTEÏNES				
Sm-Proteïna	*	5.05	g/dL	6.67 - 8.13
Sm-Albúmina	*	2.38	g/dL	3.40 - 4.80



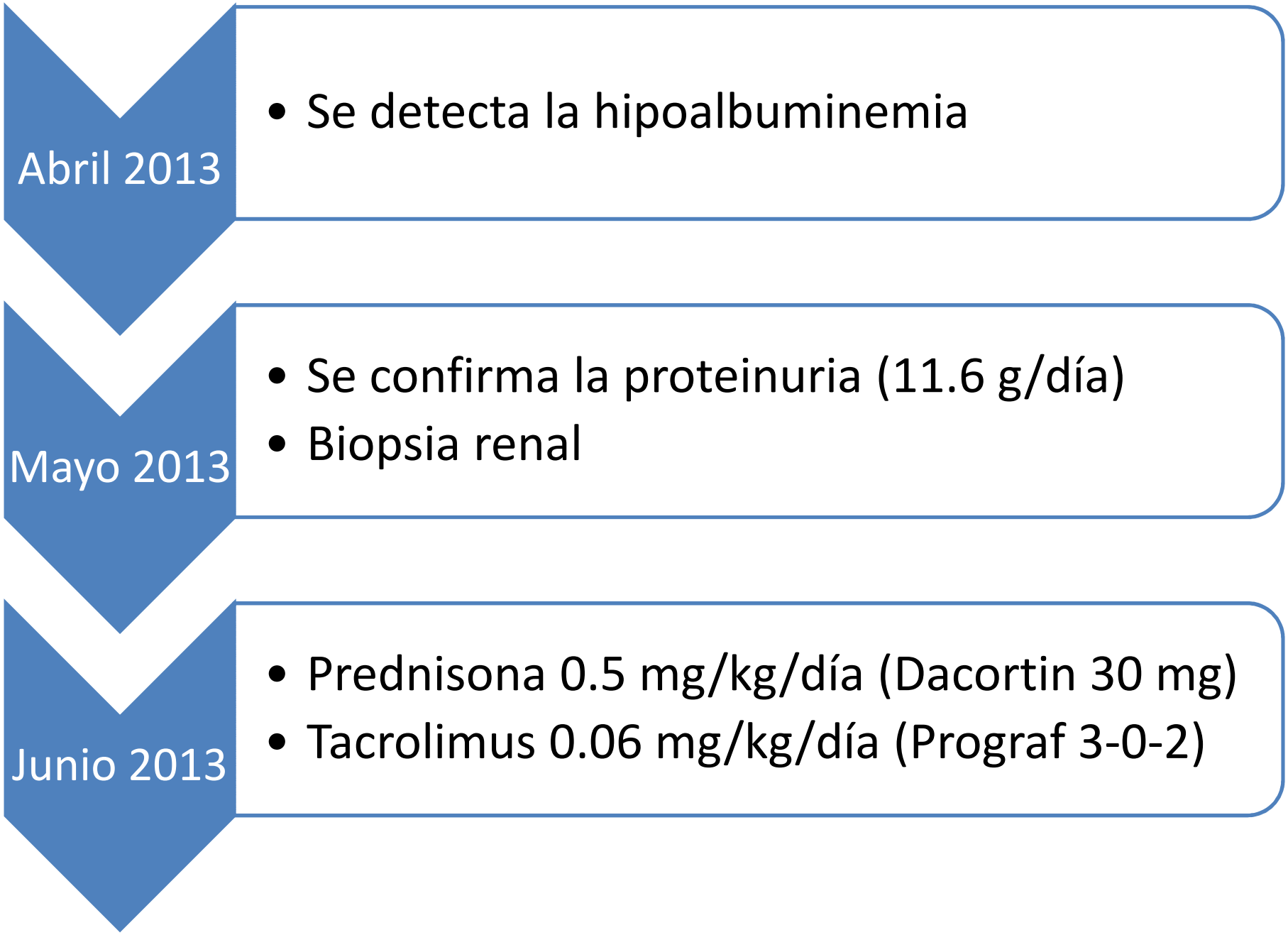
Completando el estudio…

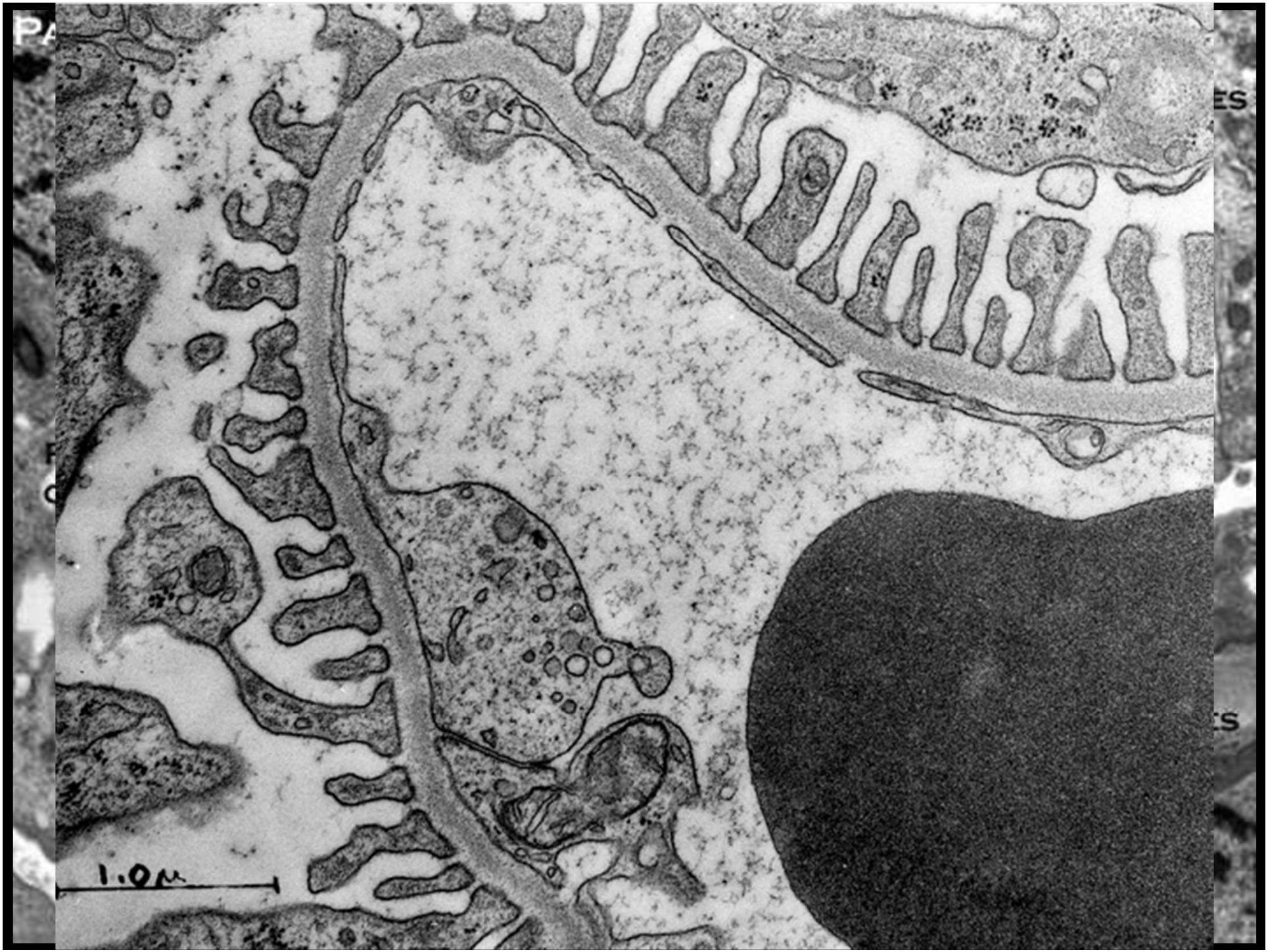
A N A L I S I D'O R I N A

Estudi Elements Formes Orina			
Leucòcits	0	cel/µL	< 20
Hematies	4	cel/µL	< 15
Cèl.lules de l'epiteli escamós	0	cel/µL	
Cilindres hialins	0	cil/µL	
Bacteris	102	bact/µL	< 250

Volum orina 24h		1500	mL
PROTEÏNES			
Uri-Proteïna	*	**775.9**	mg/dL
Uri-Proteïna (dia)		11638.5	mg/24h

Lipoproteïna a	**156**	**mg/dL**


Abril 2013
• Se detecta la hipoalbuminemia
Mayo 2013
• Se confirma la proteinuria (11.6 g/día)
• Biopsia renal
Junio 2013
• Prednisona 0.5 mg/kg/día (Dacortin 30 mg)
• Tacrolimus 0.06 mg/kg/día (Prograf 3-0-2)


1.0μ

Última analítica (abril 2014)

A N A L I S I D'O R I N A

SUBSTRATS			
Volum orina 24h		1450	mL
Uri-Creatinini		135.0	mg/dL
Uri-Creatinini (dia)	*	**1957.5**	mg/24h
Uri-Aclariment de creatinina	*	**140.1**	ml/min
PROTEÏNES			
Uri-Proteïna		5.0	mg/dL
Uri-Proteïna (dia)		72.5	mg/24h
Filtrat glomerular (estimació CKD-EPI)		96	mL/min/ 1.73 m2

Última analítica (abril 2014)

LIPIDS i LIPOPROTEÏNES			
Srm-Colesterol		161	mg/dL
Srm-Colesterol HDL		65.8	mg/dL
Srm-Colesterol LDL	*	**71.40**	mg/dL
Srm-Triglicèrid		119	mg/dL
Lipoproteïna a		**34**	**mg/dL**

Dislipemia y síndrome nefrótico

Una relación íntima y compleja

Síndrome nefrótico

- DEFINICIÓN: proteinuria > 3.5 g/1.73m^2/24h

- Hipoalbuminemia
- Hipercolesterolemia
- Microhematuria
- Hipertensión arterial
- Edemas, ascitis, derrame pleural
- Astenia

Causas primarias de SN

- GN cambios mínimos
  - → causa más frecuente en niños
- GN membranosa
- GN focal y segmentaria

- GN IgA
- GN membranoproliferativa

Causas secundarias de SN

- Diabetes mellitus
- LES
- Hepatitis B o C
- AINE
- Amiloidosis
- Mieloma múltiple
- HIV
- Hipertensión arterial

Complicaciones del SN

- Infecciones
- Tromboembolismo venoso: TVP, TEP, TVR
- Dislipemia → riesgo cardiovascular ?
- Shock hipovolémico
- Insuficiencia renal
- Hipotiroidismo
- Hipocalcemia

Riesgo cardiovascular en el SN

Kidney International, Vol. 44 (1993), pp. 638–642

The increased risk of coronary heart disease associated with nephrotic syndrome

JUAN D. ORDOÑEZ, ROBERT A. HIATT, ELLEN J. KILLEBREW, and BRUCE H. FIREMAN

Department of Medicine and the Division of Research, Kaiser Permanente Medical Care Program, Oakland, California, USA

Riesgo cardiovascular en el SN

	NS subjects		Control subjects		Relative risk		95% Confidence interval
	No.	Rate/ 1000 py	No.	Rate/ 1000 py	Unadjusted	Adjusted[a]	
MI	11	14.9	4	2.6	5.8	5.5	1.6–18.3
MI + AP + CI	14	19.2	8	5.4	3.2	2.7	1.1–7.0
MI + AP + CI + ECG	18	25.2	13	8.9	3.1	2.3	1.0–5.2
Deaths (all)	58	52.2	10	6.5	7.7	7.2	3.6–14.2
Deaths (CHD)	7	6.3	3	1.9	3.1	2.8	0.7–11.3

Kidney International, Vol. 44 (1993), pp. 638–642

Common lipid abnormalities in patients with renal disease

	LDL and cholesterol	Triglycerides	HDL
Nephrotic syndrome	↑↑	↑	N
CKD without nephrotic syndrome	N↓	↑	↓
Hemodialysis	N↓	↑	↓
Peritoneal dialysis	↑	↑↑	↓

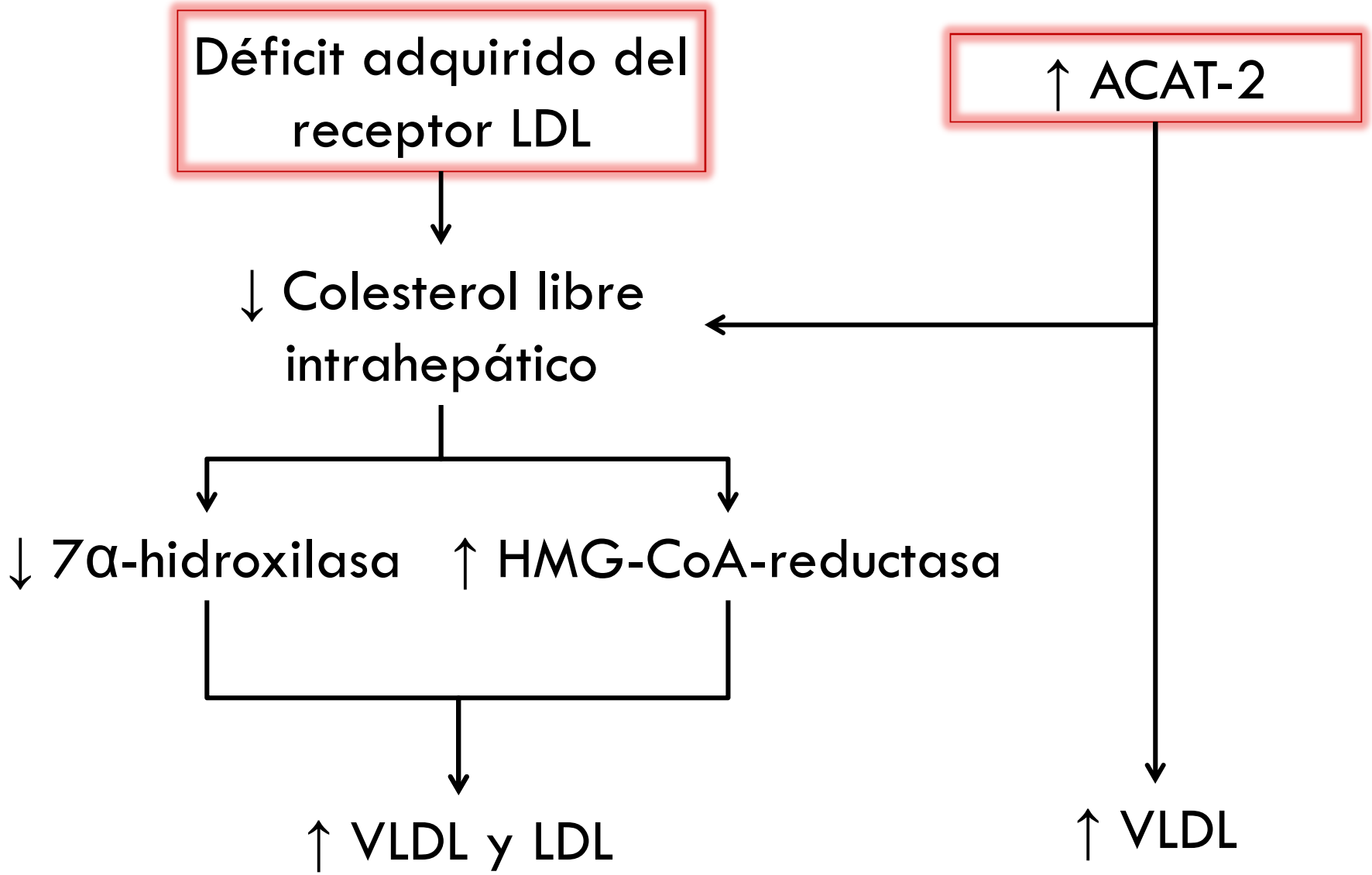
Abbreviations: CKD, chronic kidney disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

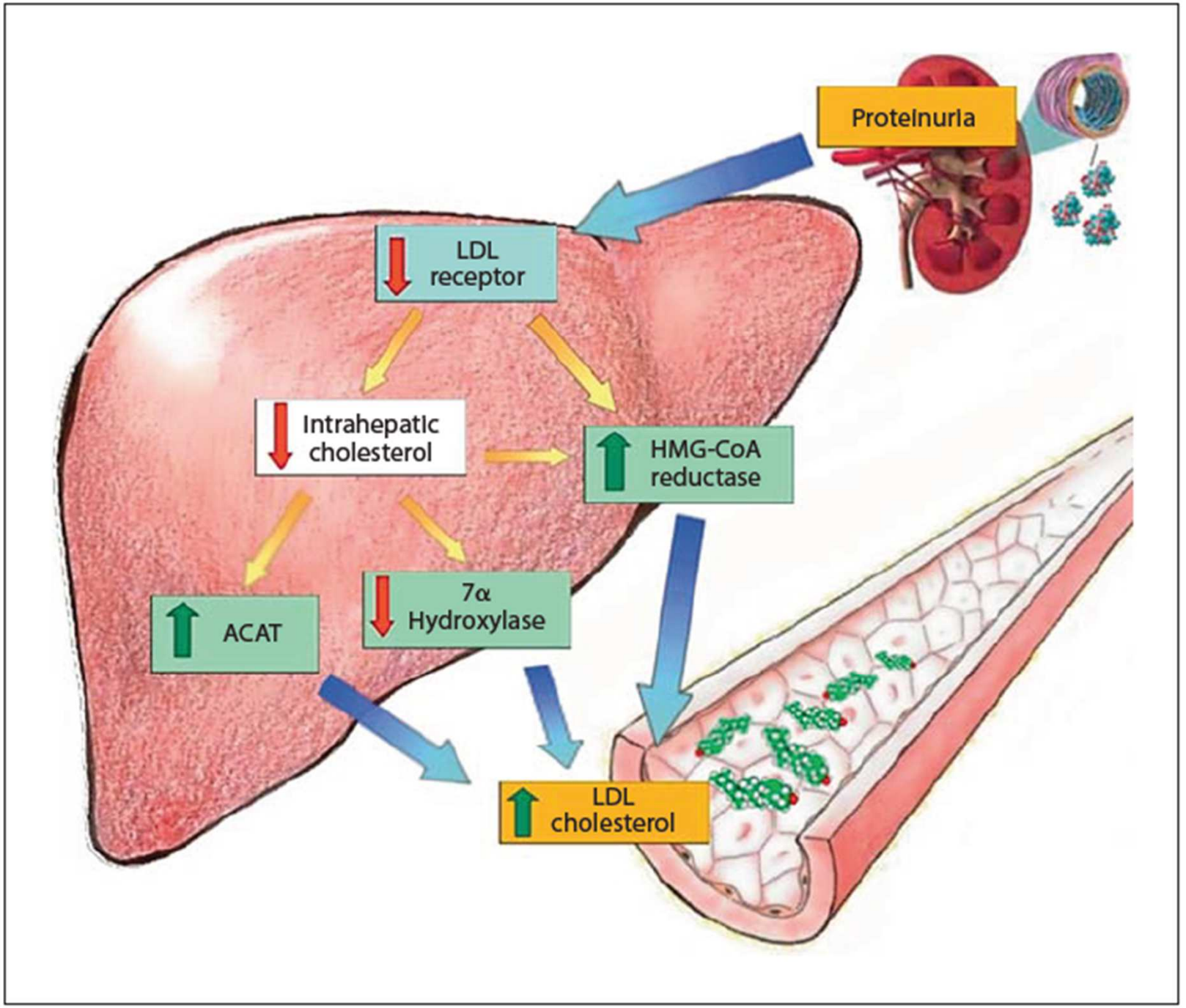
Kidney International (2013) **84,** 451–456

Cambios lipídicos en el SN

- ↑ Colesterol total y LDL
- Predominio de LDL pequeñas y densas
- HDL ↓ ó normal , pero ratio LDL/HDL ↑ ↑
- ↑ Triglicéridos
- ↑ Lipoproteína a

- Perfil lipídido altamente aterogénico!!


Déficit adquirido del receptor LDL
↑ ACAT-2
↓ Colesterol libre intrahepático
↓ 7α-hidroxilasa
↑ HMG-CoA-reductasa
↑ VLDL y LDL
↑ VLDL


Proteinuria
LDL receptor
Intrahepatic cholesterol
HMG-CoA reductase
ACAT
7α Hydroxylase
LDL cholesterol

Mecanismos de la hipercolesterolemia

Nephrol Dial Transplant (2014) 29: 538–543
doi: 10.1093/ndt/gft439
Advance Access publication 28 October 2013

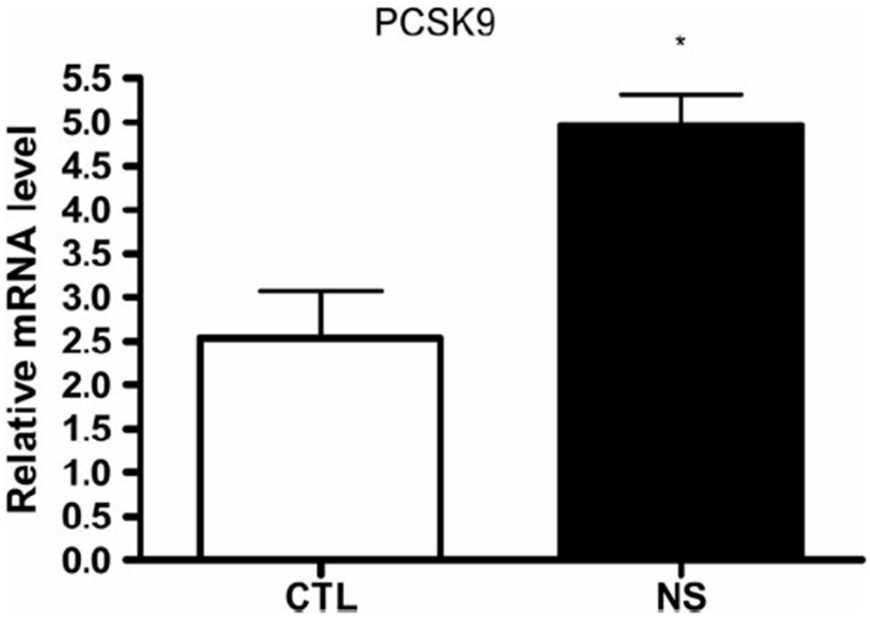
ORIGINAL ARTICLE

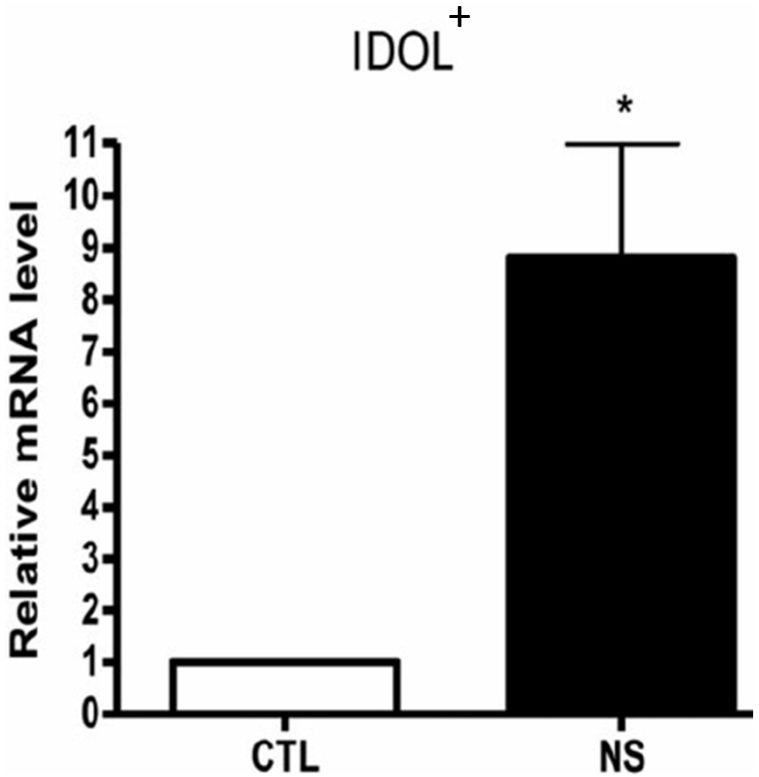
Role of PCSK9 and IDOL in the pathogenesis of acquired LDL receptor deficiency and hypercholesterolemia in nephrotic syndrome

Shuman Liu and Nosratola D. Vaziri

Division of Nephrology and Hypertension, Department of Medicine, University of California, Irvine, CA, USA

Role of PCSK9 and IDOL in the pathogenesis of acquired LDL receptor deficiency and hypercholesterolemia in nephrotic syndrome

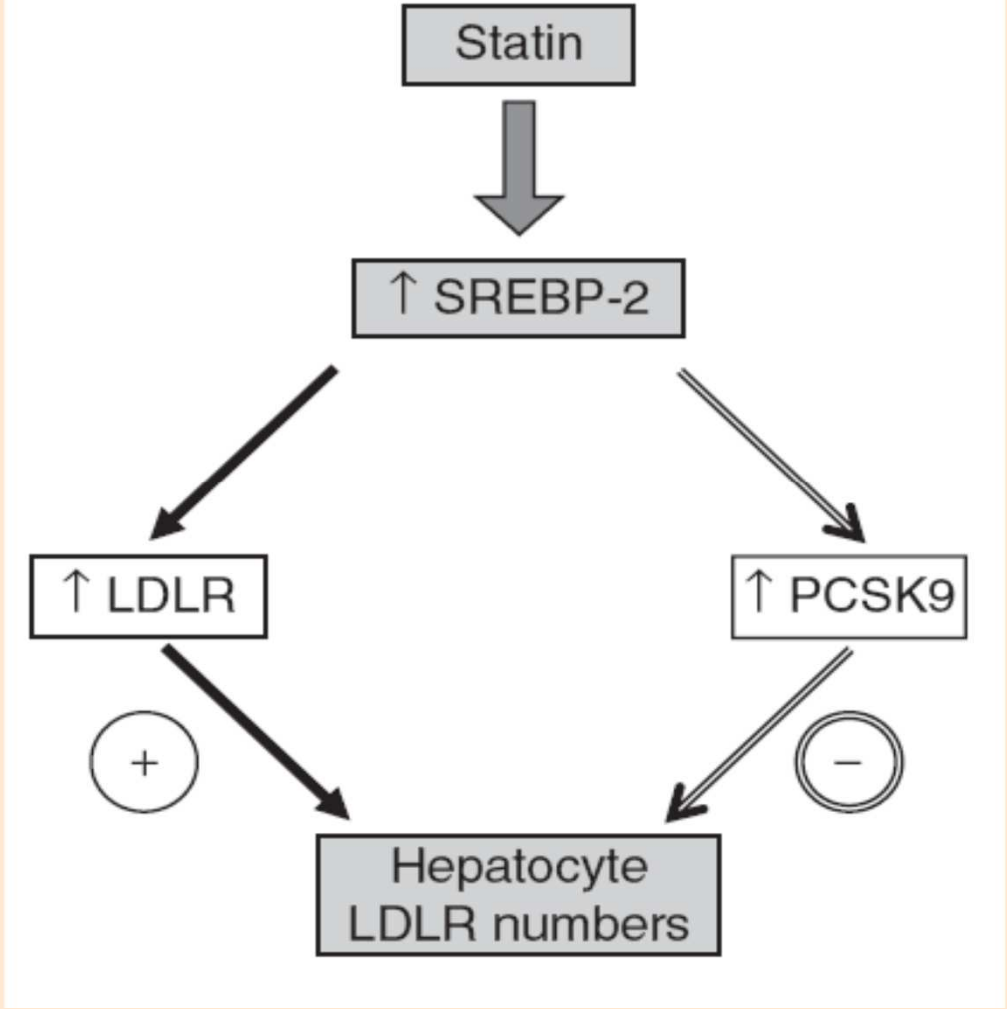




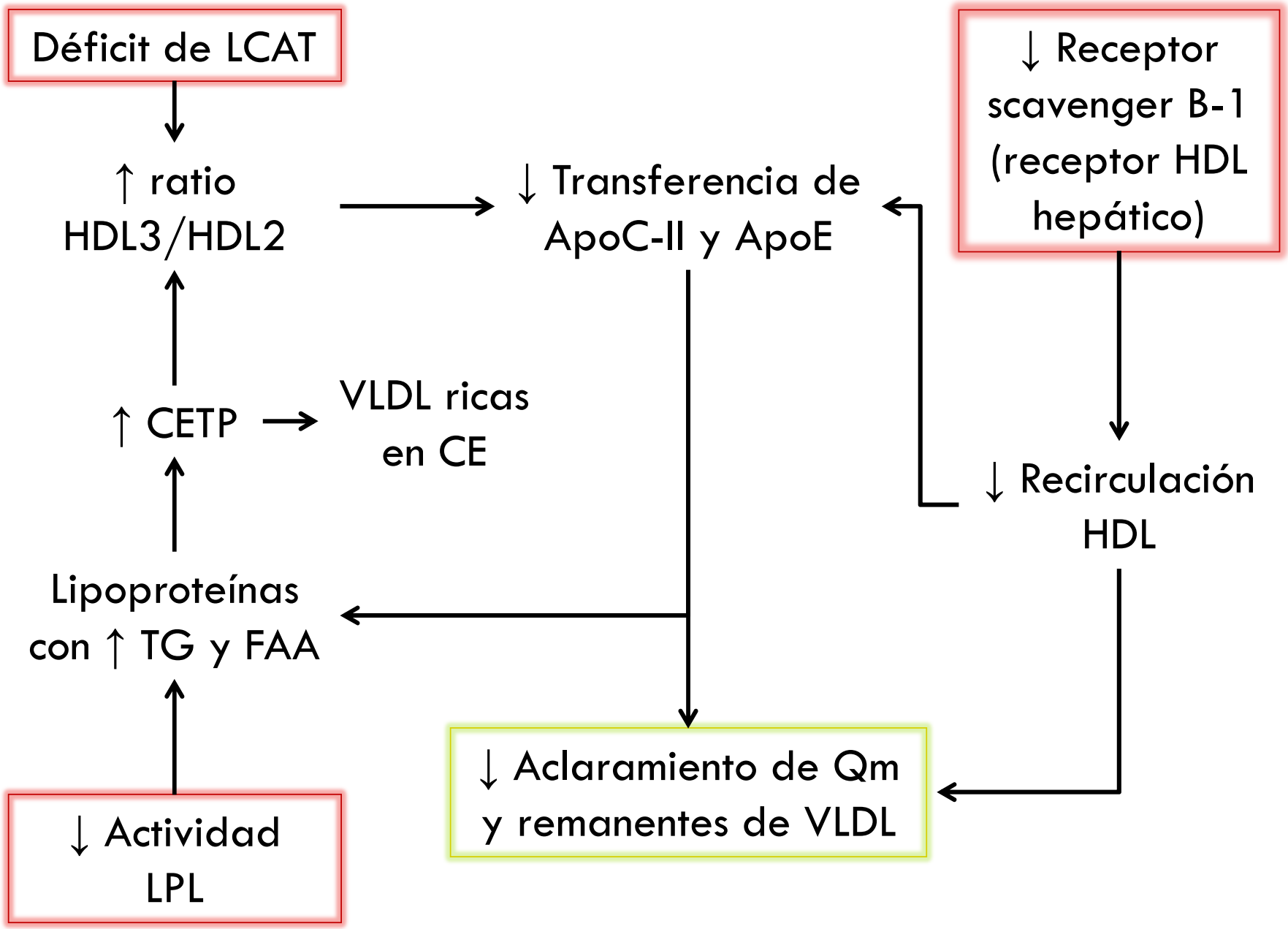
+ IDOL: Inducible degrader of the LDL receptor

Nephrol Dial Transplant (2014) 29: 538–543

Paradoxical effect of statin treatment on LDL-r protein expression



Am J Cardiovasc Drugs 2011; 11 (3): 145-152


Déficit de LCAT
↑ ratio HDL3/HDL2
↓ Transferencia de ApoC-II y ApoE
↓ Receptor scavenger B-1 (receptor HDL hepático)
↑ CETP
VLDL ricas en CE
↓ Recirculación HDL
Lipoproteínas con ↑ TG y FAA
↓ Aclaramiento de Qm y remanentes de VLDL
↓ Actividad LPL

Mecanismos de la hipertrigliceridemia

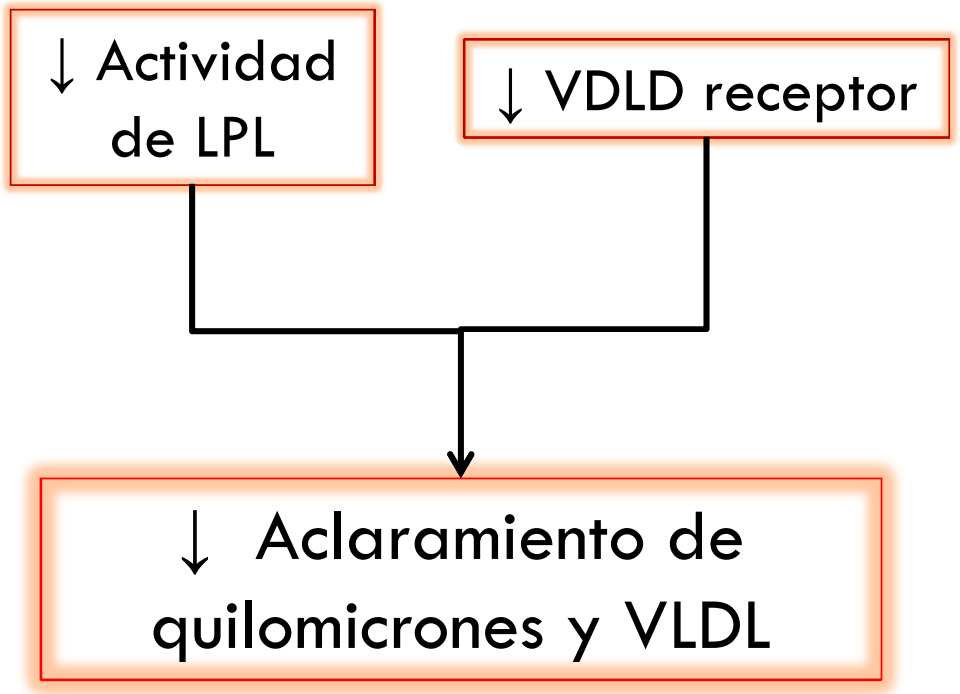
↓ P oncótica

↓

↑ Producción hepática de apolipoproteína B, ácidos grasos y TG

↓

↑ VLDL y LDL



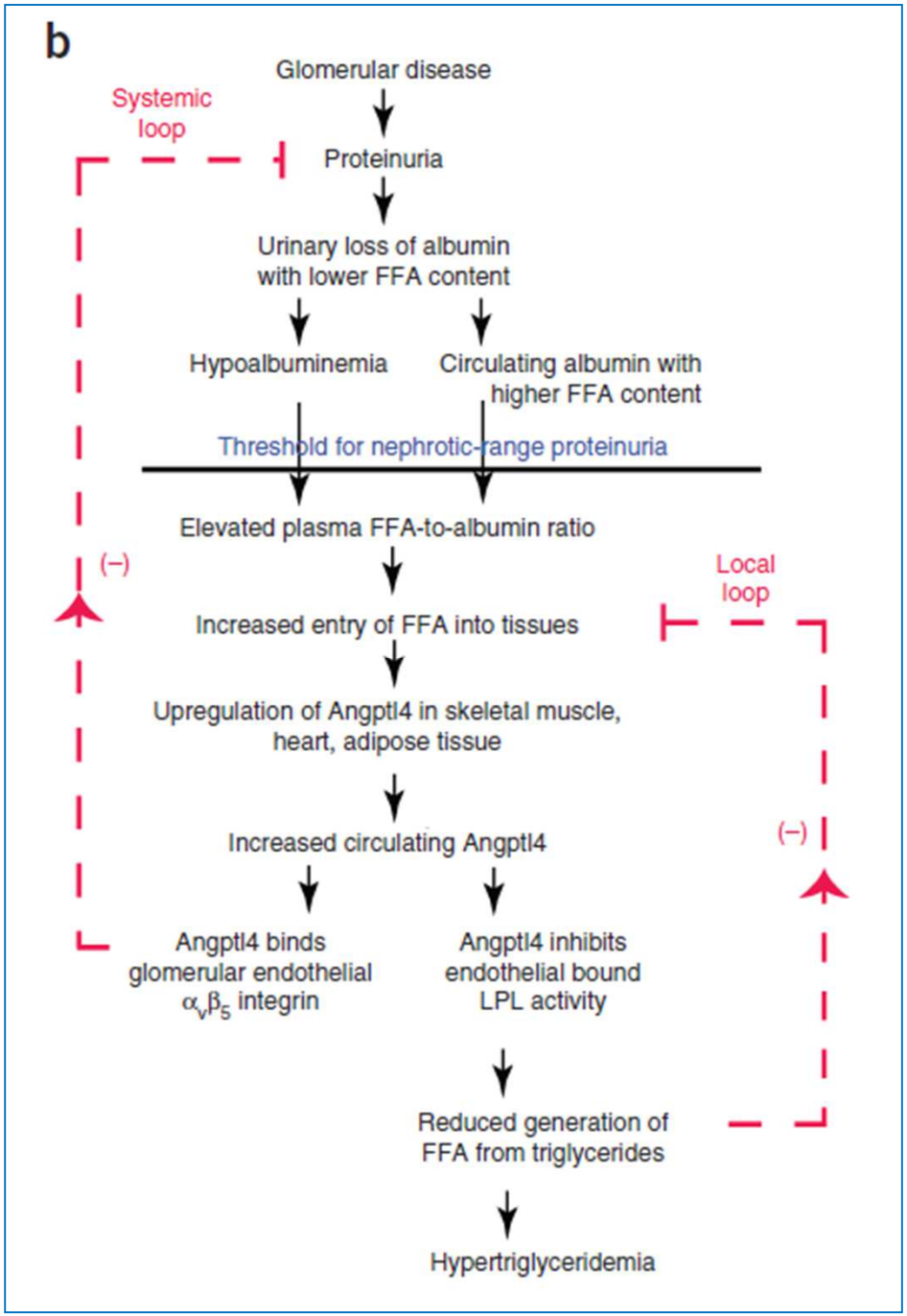
Mecanismos de la hipertrigliceridemia

nature medicine

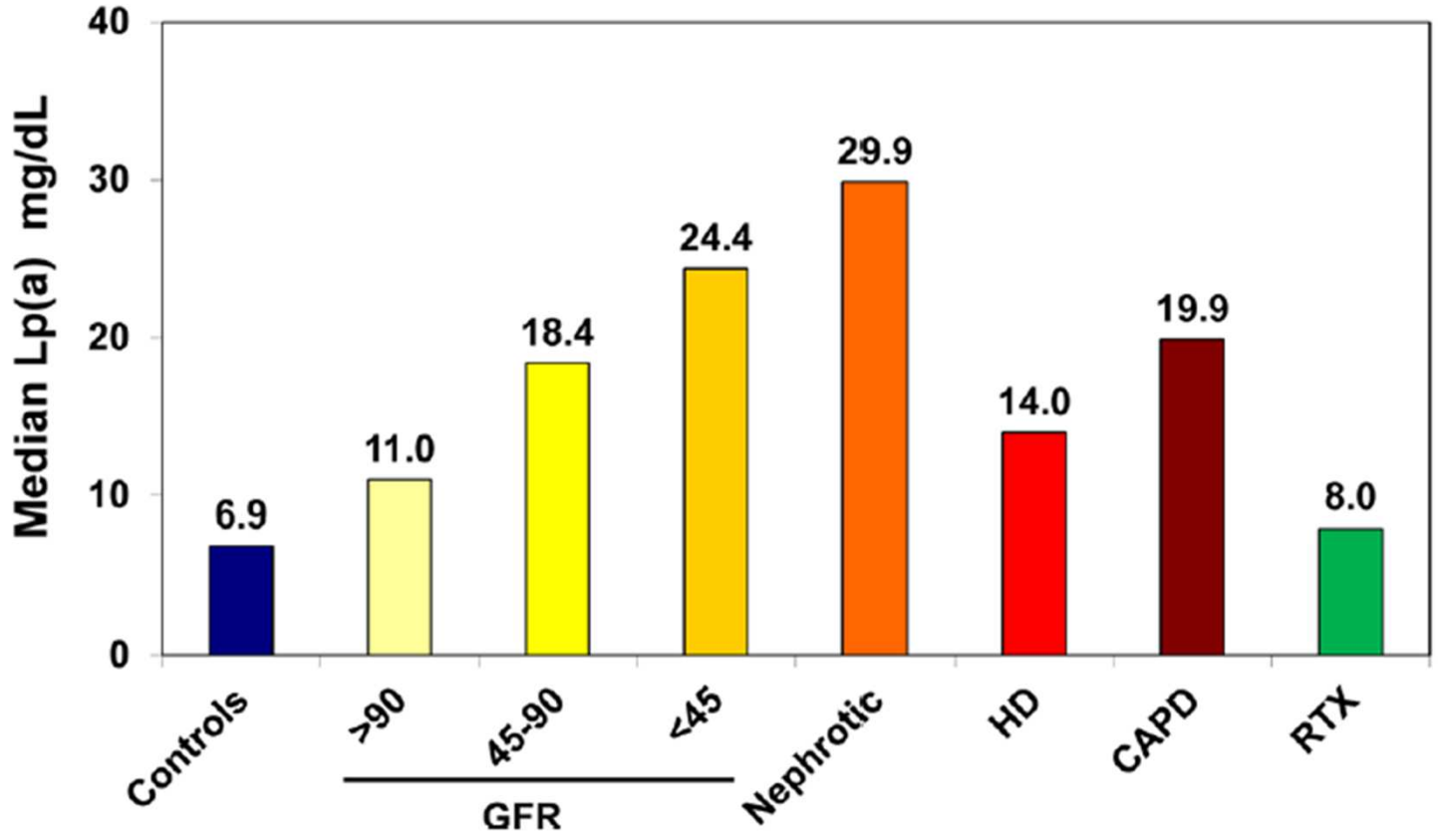
Circulating angiopoietin-like 4 links proteinuria with hypertriglyceridemia in nephrotic syndrome

Lionel C Clement[1,6], Camille Macé[1,6], Carmen Avila-Casado[2,3], Jaap A Joles[4], Sander Kersten[5] & Sumant S Chugh[1]

NATURE MEDICINE VOLUME 20 | NUMBER 1 | JANUARY 2014

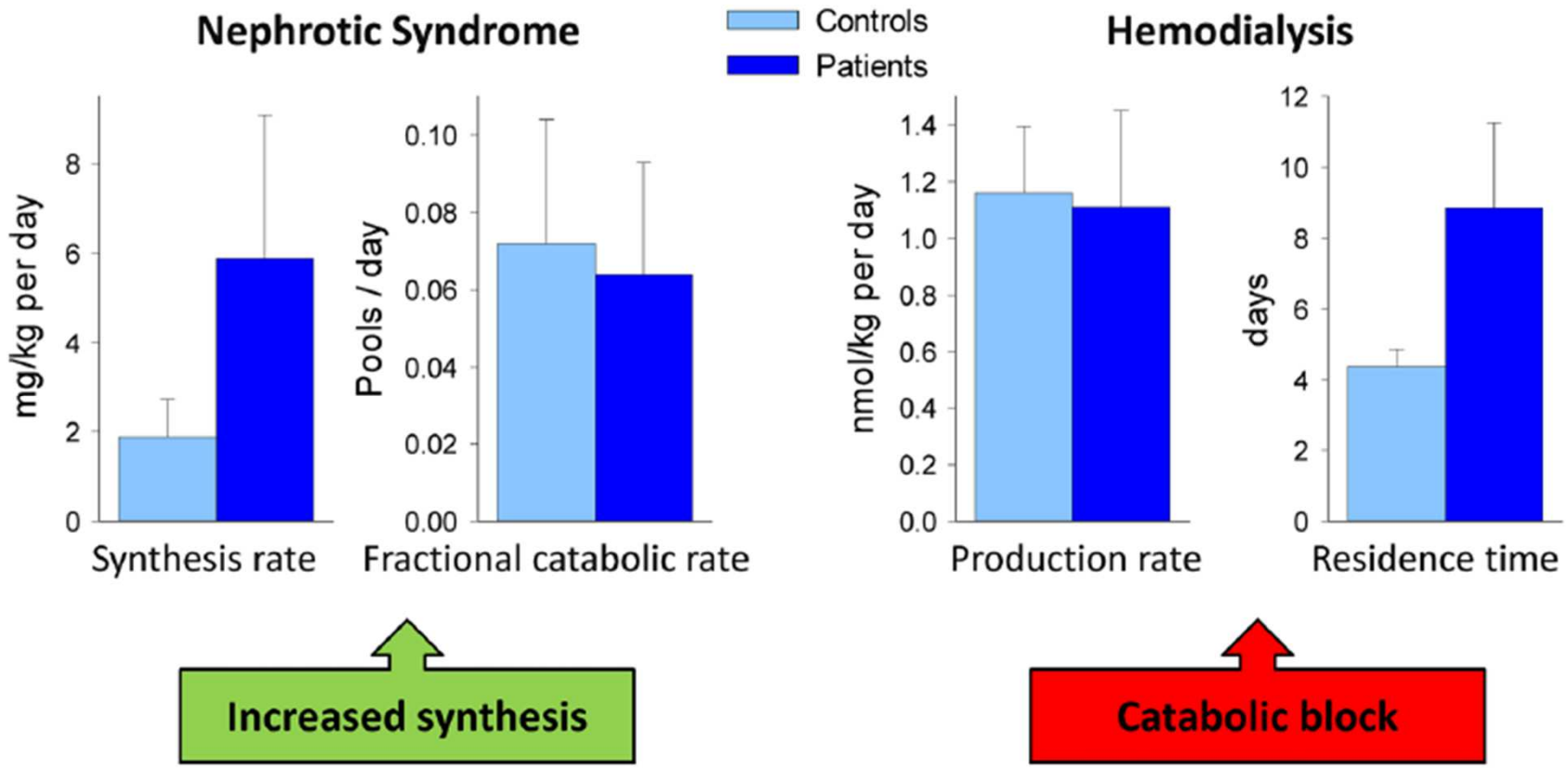

b
Glomerular disease
Systemic loop
Proteinuria
Urinary loss of albumin with lower FFA content
Hypoalbuminemia
Circulating albumin with higher FFA content
Threshold for nephrotic-range proteinuria
Elevated plasma FFA-to-albumin ratio
(–)
Local loop
Increased entry of FFA into tissues
Upregulation of Angptl4 in skeletal muscle, heart, adipose tissue
Increased circulating Angptl4
(–)
Angptl4 binds glomerular endothelial $\alpha_v\beta_5$ integrin
Angptl4 inhibits endothelial bound LPL activity
Reduced generation of FFA from triglycerides
Hypertriglyceridemia

Alteración de la lp(a) en la enfermedad renal



Clin Exp Nephrol (2014) 18:234–237

Fisiopatología de la elevación de la lp(a) en la enfermedad renal



Clin Exp Nephrol (2014) 18:234–237

Resumen de la fisiopatología de la dislipemia en el SN

- Déficit de receptor LDL
  - ↓ aclaramiento de LDL → ↑ LDL
- Déficit de LCAT, ↑ CETP, déficit de SRB-1 (HDLr)
  - Composición anormal, maduración defectuosa y disminución del aclaramiento de HDL
- ↑ ACAT-2
- ↑ HMG-CoA reductasa, ↓ colesterol 7α-hidroxilasa
  - Hipercolesterolemia
- ↑ síntesis y ↓ catabolismo hepático de (apo) B-100 y lipoproteína (a)
- ↓ LPL, VLDL receptor y lipasa hepática
- ↑ DGAT, acetil-CoA carboxilasa y sintetasa de ácidos grasos
  - ↑ Biosíntesis hepática de triglicéridos y ácidos grasos

Tratamiento de la dislipemia en el SN

Lipid-lowering agents for nephrotic syndrome (Review)

Kong X, Yuan H, Fan J, Li Z, Wu T, Jiang L

THE COCHRANE COLLABORATION®

Citation: Kong X, Yuan H, Fan J, Li Z, Wu T, Jiang L. Lipid-lowering agents for nephrotic syndrome. *Cochrane Database of Systematic Reviews* 2013, Issue 12. Art. No.: CD005425. DOI: 10.1002/14651858.CD005425.pub2.

Tratamiento de la dislipemia en el SN

- 5 RCT (203 pacientes)
  - 4 RCT estatina vs placebo
  - 1 RCT fibrato vs placebo
- Ningún estudio con objetivos de mortalidad o eventos cardiovasculares

- No queda claro el beneficio en términos de mortalidad cardiovascular.

Take-home message

European Heart Journal (2013) **34**, 3478–3490
doi:10.1093/eurheartj/eht273

CURRENT OPINION

Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease

Consensus Statement of the European Atherosclerosis Society

Releer las guías

Diagnosis

Diagnosis of FH relies on five criteria: family history, clinical history of premature CHD, physical examination for xanthomas and corneal arcus, very high LDL cholesterol on repeated measurements, and/or a causative mutation detected by molecular genetics[22] (Table 1). Secondary causes of hyperlipidaemia must be excluded by determining that liver enzymes, renal function, and thyroid hormones are normal and that there is no hyperglycaemia or albuminuria.

La dislipemia en el síndrome nefrótico

Pocas respuestas para muchas preguntas

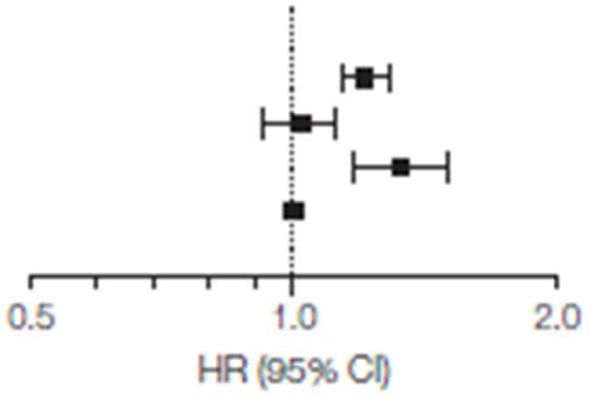
Tabla 5. Características de las principales dislipemias primarias		
	Hipercolesterolemia familiar	**Apo B-100 defectuosa familiar**
Frecuencia	0,2% heterocigotos $1/10^6$ homocigotos	1/1.000
Edad de inicio	Nacimiento	Nacimiento
Tipo de herencia	Dominante monogénica	Dominante
Patogenia	Defecto del receptor LDL	Mutación gen Apo B
Colesterol (mg/dl)	Homocigoto > 600 Heterocigoto > 300	250 – 400
Lipoproteína	Aumento de LDL	Aumento de LDL
Xantomas	Tendinosos, arco corneal	Tendinosos, arco corneal
Edad inicio de CI	30-50 años Homocigotos < 20 años	> 40 años
Dislipemia en familiares de primer grado	50%	50%
Asociación a HTA, obesidad, diabetes o gota	No	No

Hiperlipemia familiar combinada	Hipercolesterolemia poligénica	Disbetalipo-proteinemia
0,5-1%	3-5%	1/10.000
< 20 años	> 20 años	Variable
Dominante	Poligénica	Variable
Desconocida	Desconocida	Apo E2
260-350 y/o TG > 200-400	280-320	Dislipemia mixta TG hasta 300-600
Aumento de LDL y/o VLDL y descenso HDL	Aumento de LDL	Aumento de IDL
Poco frecuentes	No	80%, palmares y tuberoeruptivos
> 40 años	> 60 años	> 40 años Arteriopatía periférica
50%	10%	Raramente
Sí	No	Sí

Lipoproteína (a)

Figure 3. Risk of Major Cardiovascular Events by LDL and non-HDL Cholesterol Categories

Target Level		No. of Major Cardiovascular Events	Total No. of Participants	HR (95% CI)
LDL-C	Non–HDL-C			
≥100 mg/dL	≥130 mg/dL	1877	10419	1.21 (1.13-1.29)
≥100 mg/dL	<130 mg/dL	467	2873	1.02 (0.92-1.12)
<100 mg/dL	≥130 mg/dL	283	1435	1.32 (1.17-1.50)
<100 mg/dL	<130 mg/dL	2760	23426	1.00 [Reference]



Data markers indicate hazard ratios (HRs) and 95% CIs for risk of major cardiovascular events. Results are shown for 4 categories of statin-treated patients based on whether or not they reached the low-density lipoprotein cholesterol (LDL-C) target of 100 mg/dL and the non–high-density lipoprotein cholesterol (non–HDL-C) target of 130 mg/dL. HRs were adjusted for sex, age, smoking, diabetes, systolic blood pressure, and trial.

Mecanismos de la hipercolesterolemia

↓ P oncótica

↓

↑ Producción hepática de apolipoproteína B

↓

↑ VLDL y LDL

Disminución del catabolismo de VLDL y LDL

↑ Producción hepática de apolipoproteína (a) ⟶ ↑ Lp(a)