[심포지움]

고지혈증 환자의 임상 운동생리학적 기전

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Hyperlipidemia = Dyslipoproteinemia

The Criteria for Hyperlipidemia(mg%)

Type	Normal	Caution	Hyperlipidemia
TC	< 200	200 – 239	> 240
LDL – C	< 130	130 – 159	> 160
HDL – C	> 45	36 – 45	< 35
TG	< 200	200 - 249	> 250

National Cholesterol Education Progrom, NCEP(USA), 2003

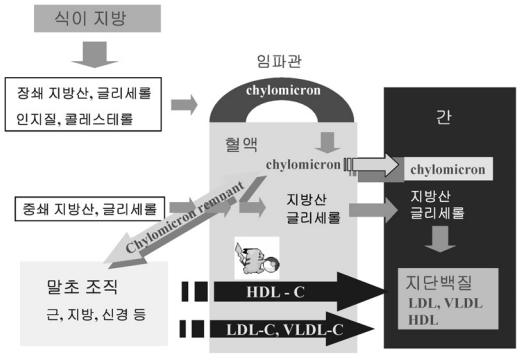
ATP III Classification of Blood Lipid

LDL – Cholesterol	
optimal	100 mg% 이하

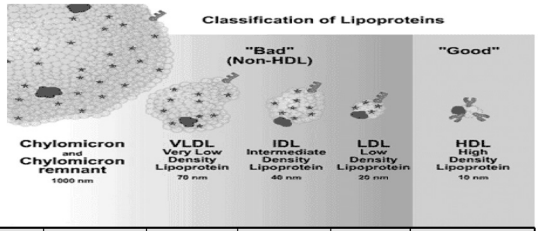
Etiology of Hyperlipidemia

1. A family history
   - ① LDL receptor 구조나 기능의 유전적 결함
   - ② 간의 지질대사 결함
   - ③ apo-단백의 결핍이나 결함
2. A Dietary Factor
   - Dietary Saturated Fat, Trans Fat, Cholesterol, Carbohydrate 섭취량 증가. Smoking, Alcohol 등
3. Obesity, Aging : LDH receptor activity 감소(?)
4. Cirtain Conditions, including
   - Diabetes, Low Thyroid, Kidney Problems, Liver Disease, Cushing's Syndrome, Cease of Estrogen(estrogen –stimulated L DL 합성감소)
   - Excess Progesterone etc.

Outline of Lipoprotein Pathway

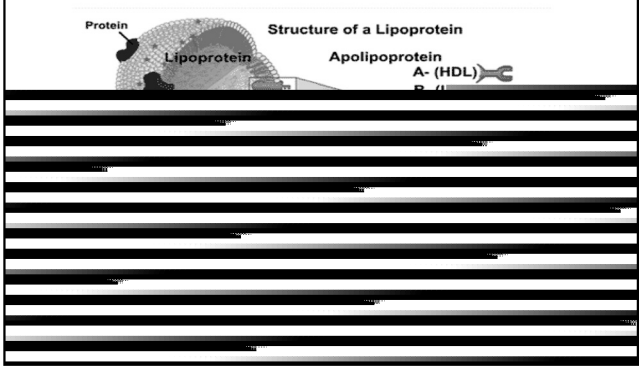


Classification of Lipoproteins

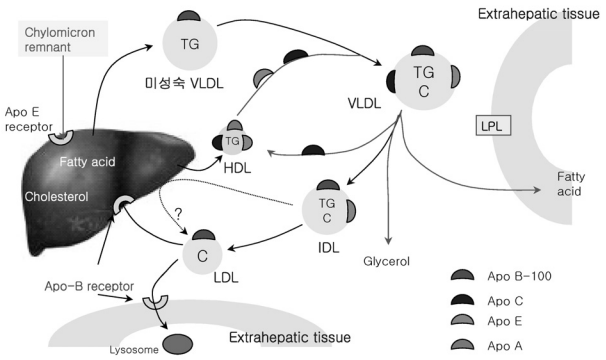


Apo-지단백	A-1, A-2, A-4, B-48	B-48, C, E	B-100, E	B-100	A-1, A-2
Subfra-ction	Chylomicron remnant			Large LDL Small LDL (LDL - III)	HDL_1, HDL_2 HDL_3

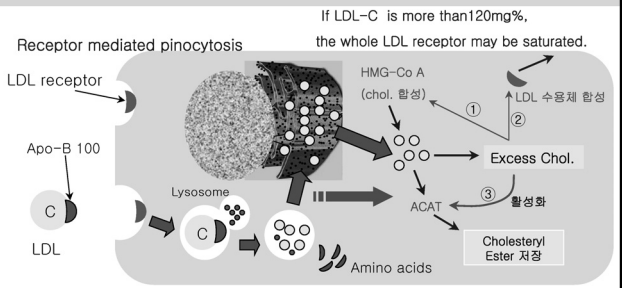
Structure of Lipoprotein



VLDL Pathway



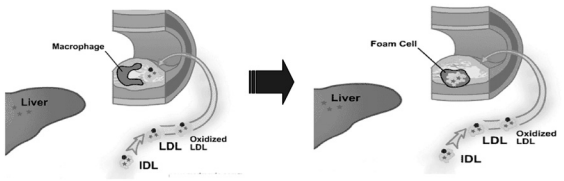
Control of LDL Metabolism



If two much cholesterol is uptaked through the LDL receptor

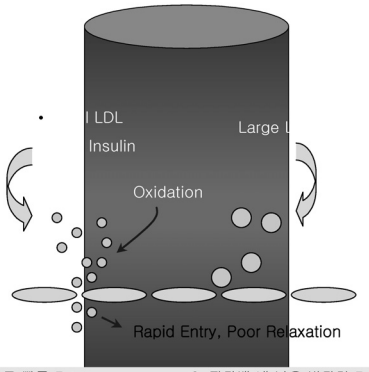
- HMG-Co A reductase ↓: Acetyl – Co A → mevalonic acid 율속효소
- LDL reductase ↓ : LDL 수용체 합성 억제
- ACAT(acyl-CoA cholesterol acyltransferase) 활성화 : Free cholesterol → Cholesterol esters로 전환 저장

The Process of Atherosclerosis



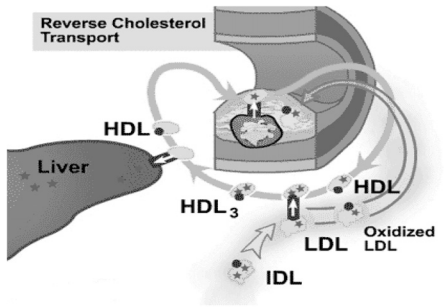
1. 식후 TG상승과 baseline 회복 지연 : LDL core cholesterol esters 촉진 →
   LDL become more dense and smaller → more atherogenic
2. LDL apo-receptor가 동맥 intima 내 proteoglycan과 결합
3. Oxidized LDL입자 축적부위 – 상피세포 투과도증가 → 더 많은 LDL축적
4. Macrophage가 동맥 평활근의 병변부에서 지질을 삼키고 Foam Cell로 전환
5. 병적 상태에서 scavenger receptor가 지속적으로 산화된 LDL의 세포 내 유입촉진
6. 주로 "lipid-laden foam cell"로 된 fatty streak → atherosclerotic plaque 형성 (석회화)

Small, dense LDL

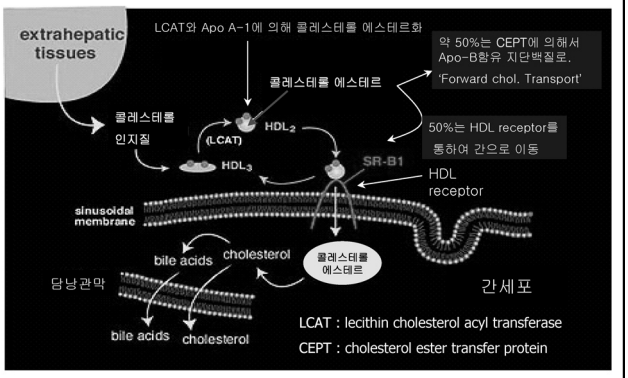


1. 동맥벽으로 빠른 Entry
2. 지단백 내 낮은 비타민 E
3. 산화적 손상에 취약
4. 혈중 고 Insulin
5. 식후 fat 수준이 이 패턴에서 double
6. 혈관의 poor relaxation

HDL Pathway(Reverse Cholesterol Transport)



HDL Pathway(Reverse Cholesterol Transport)



The Changes following Chronic Exercise

- Toshitaka et al.(1991) : age 30-70 yrs. Both sex runners vs sedentary Runners Group campared to Sedentary Group
  - ① higher Apo A-1, Apo E and higher HDL mainly due to HDL_2
  - ② lower VLDL and LDL-C/HDL-C ratio
  - ③ lower Apo B-48 ratio in VLDL
  - ④ higher Apo A-1 + Apo A-2 / Apo B ratio (Anti-atherogenic Index)
- Sato, Y. et al.(1992) : Hyperlipoproteinemia patient, 10,000 steps walking/day
  - ① TG, VLDL-TG, VLDL-C의 유의한 감소
  - ② IDL, Apo E의 유의한 감소
- Williams et al.(1990) : Regular Exercise habit
  Large LDL subfraction ↑, Small, dense LDL subfraction ↓

The Changes following Chronic Exercise

- Hellsten G. et al(1989) : 스웨덴 8일간 Cross country ski (age :18-46, male)
  Lipoprotein(a) : 166mg/dl → 129mg/dl 로 유의한 감소
- Despres JP(1994) : Chronic Ex. HDL and HDL_2 를 증가시킴
- Berg A(1994) : Endurance Trained Male
  Higher LDL_1(Large LDL), Lower LDL_3(Small and dense LDL)
- Williams et al.(1990) : Weight Loss through Diet + Exercise
  Significant Decrease of LDL_3
- Tom RT & Tom L(1996) : Review
  Chronic Exercise → LPL, LCAT, TG lipase(HSL) ↑, LDL receptor의 up-regulation, Hepatic lipase는 일반적으로 감소

The Changes following Chronic Exercise

- Seip RL et al.(1993) : 운동훈련에 의해 Lipoprotein(a)는 반응이 잘 나타나지 않음, CETP는 감소 또는 증가로 일정치 않음
- Kraus RM et al.(1979) : 지구성운동 Hepatic Lipase(HDL_2→HDL_3)의 감소
  LCAT, LPL의 증가, Hepatic Lipase감소에 의해 Atherogenic Lipoprotein 감소
- Hurley BF(1989) : 저항훈련 효과
  Body Builder는 Power lifter보다 바람직한 Lipid Profile을 보임
- Toshitaka T et al.(1991) : Trained Male,
  주당 달린거리 ∝ HDL level(dose – response 관계)
  HDL은 주당 50-60km까지 달린 거리에 비례하여 증가