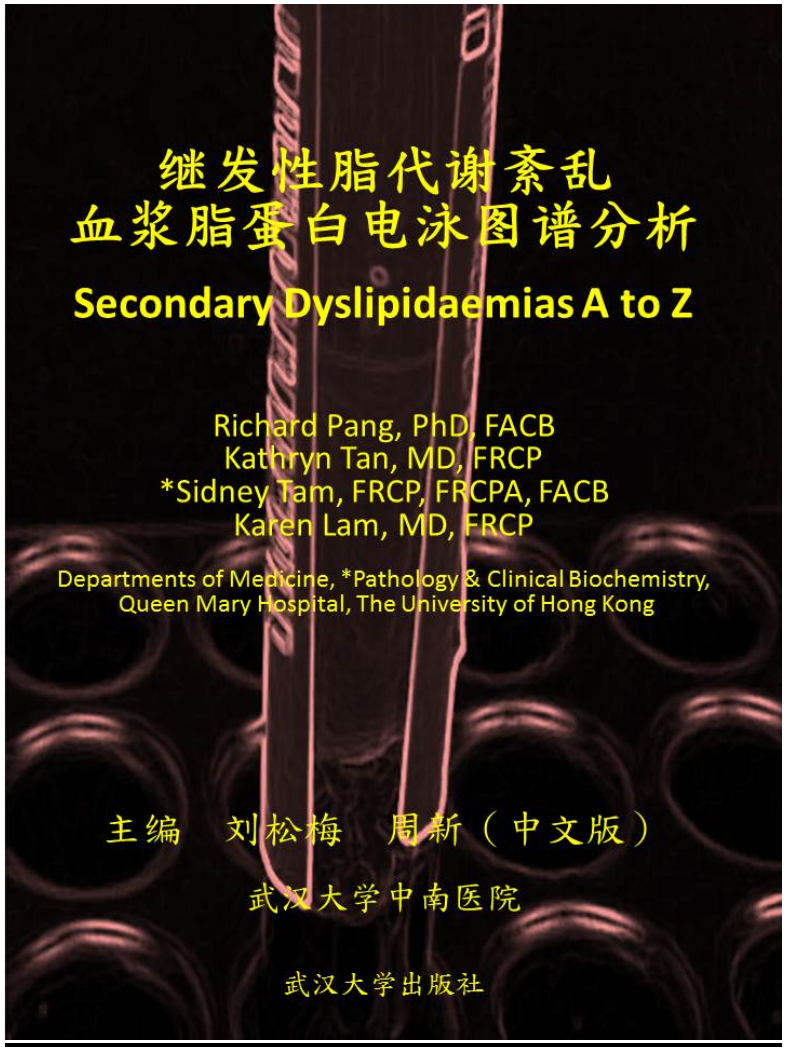


继发性脂代谢紊乱
血浆脂蛋白电泳图谱分析

Secondary Dyslipidaemias A to Z

Richard Pang, PhD, FACB

Kathryn Tan, MD, FRCP

***Sidney Tam, FRCP, FRCPA, FACB**

Karen Lam, MD, FRCP

Departments of Medicine, *Pathology & Clinical Biochemistry,
Queen Mary Hospital, The University of Hong Kong

主编　刘松梅　周新（中文版）

参编　徐凤霞　齐佳会　孙　力
　　黎四维　鲁双艳　沈　璠
　　余雪琛　朱铭安　刘兴晖

序　言

脂蛋白电泳检测是对临床高脂血症病人分型的一种简便有效的诊断方法，通过电泳图谱分析可初步判断疾病的严重程度，再有针对性地作进一步的诊治。

高脂血症是临床常见疾病，发病率很高，涉及到临床各科病人。因为高脂血症首先损伤的是动脉血管壁内皮细胞，最终导致动脉粥样硬化，从大动脉血管到小动脉血管，无一幸免。重视高脂血症早期诊断和治疗监测，是有关动脉粥样硬化性疾病防治的重大举措。

彭永祥（Richard Pang）博士是我国著名的临床生化学家，在临床检验诊断专业领域学术造诣很深，是武汉大学医学部特聘教授，他是本书英文主编。彭永祥教授在临床检验工作中，收集临床各种类型的高脂血症病人脂蛋白电泳图谱，经系统分析并整理成文，以英文和中文两种语言形式出版，供临床各科临床医师和检验医师参考。参与英文编写的教授还有香港大学玛丽医院的 Kathryn Tan、Sidney Tam 和 Karen Lam。

该书首先简介脂蛋白代谢概况，其中着重介绍美国 NCEP ATPⅢ指南中有关脂蛋白的临床诊断意义。全书按继发性脂蛋白代谢紊乱疾病的英文名称 A 到 Z 的顺序，逐一阐述其血浆脂蛋白电泳图谱特征，结合临床生化检验相关参数，进行分析和讨论，对临床高脂血症的防治具有一定指导意义。

该书的出版得到海伦娜公司和贝克曼公司的大力支持，在此表示感谢。

由于编译者水平所限，书中错误难免，恳请读者不吝赐正。

周新

缘　起

原香港大学玛丽医院临床生化科学主任彭永祥博士，曾任中华医学会检验分会血脂专家委员会副主任委员。现受聘为武汉大学医学部兼职教授，于 2010 年 8 月应邀在湖北省宜昌市举行的第十届全国脂蛋白学术会议和第五届全国血脂分析与临床学术会议，以继发性脂代谢紊乱(Secondary Dyslipidaemias A to Z)为题在大会发言。与会者对彭博士引用的临床病例血脂电泳图谱非常感兴趣。鉴于此类参考读物不多，希望彭博士能将具体的临床典型病例进行系统整理，汇编成册出版，以供参考。

继发性脂代谢紊乱首先表现为血浆脂质和脂蛋白水平异常,其影响因素有多种,较为常见的因素是原发性遗传缺陷。即便是患者有明确的遗传因素，也应考虑影响血脂水平的继发性因素。准确、全面的脂质谱检测越来越重要，因为它既可以评估病人心血管疾病风险，还可以指导血脂恢复治疗的起始用药和疗效监测，从而降低脂代谢紊乱的风险。

本书以 26 个临床典型病例血脂电泳图谱的形式，用两种语言分析和讨论继发性脂代谢紊乱。可供从事临床医二学和检验医学的临床、教学、科研人员参考，有助于对血脂检查结果的分析，提高对继发性脂代谢紊乱的临床疾病及相关诱发因素的认识，指导临床治疗方案决策，避免错误用药和无效用药。

刘松梅

FOREWORD

While the relationship between abnormal lipid profile and cardiovascular disease is widely recognized, emphasis is usually placed on genetic factors which regulate the levels of lipoproteins.

This book draws our attention to the wide range of diseases which may produce abnormal patterns of lipoproteins, i.e. secondary dyslipidaemias, using a wide range of clinical conditions as examples. This will help us interpret the laboratory results which may at first sight appear to be very puzzling.

I think this book is a very useful companion for medical students and young doctors engaged in clinical practice.

I wish to congratulate Dr. Pang and his colleagues for their painstaking effort to collect these case studies and to make the entire book user friendly.

Rosie Young Tse Tse
Emeritus Professor
Department of Medicine
The University of Hong Kong

ABBREVIATIONS 缩略词

英文缩写	英文全称	中文全称
Apo A1	apolipoprotein A1	载脂蛋白 A1
Apo A5	apolipoprotein A5	载脂蛋白 A5
Apo B	apolipoprotein B	载脂蛋白 B
Apo C2	apolipoprotein C2	载脂蛋白 C2
Apo E	apolipoprotein E	载脂蛋白 E
ARH	autosomal recessive hypercholesterolemia	常染色体隐形遗传性高胆固醇血症
CETP	cholesterol ester transfer protein	胆固醇酯转移蛋白
CHD	coronary heart disease	冠心病
FCHL	familial combined hyperlipidaemia	家族性混合型高脂血症
FDB	familial defective apolipoprotein B	家族性载脂蛋白B缺陷
FH	familial hypercholesterolemia	家族性高胆固醇血症
FHA	familial hypoalpha-lipoproteinaemia	家族性低高密度脂蛋白血症
FFA	free fatty acid	游离脂肪酸

HDL	high-density lipoprotein	高密度脂蛋白
HDL-C	high-density lipoprotein-cholesterol	高密度脂蛋白-胆固醇

缩略词（续）

英文缩写	英文全称	中文全称
HL	hepatic lipase	肝酯酶
IDL	intermediate-density lipoprotein	中间密度脂蛋白
LCAT	lecithin:cholesterol acyltransferase	卵磷脂胆固醇酰基转移酶
LDL	low-density lipoprotein	低密度脂蛋白
LDL-C	low-density lipoprotein-cholesterol	低密度脂蛋白-胆固醇
LDLR	LDL receptor	低密度脂蛋白受体
LDLRAP1	LDLR adaptor protein 1	低密度脂蛋白受体衔接蛋白1
LPL	lipoprotein lipase	脂蛋白脂肪酶
Lp(a)	lipoprotein(a)	脂蛋白(a)

PCSK9	proprotein convert-ase subtilisin-like kexin type 9	抗人枯草溶菌素转化酶9
TC	total cholesterol	总胆固醇
TG	triglycerides	甘油三酯
VLDL	very low-density lipoprotein	极低密度脂蛋白
INT	interference	干扰
N/A	not available	缺失
LFT	liver function test	肝功能检测
RFT	renal function test	肾功能检测

ACKNOWLEDGEMENTS

The Authors and the Editors would like to thank the staff members in the Queen Mary Hospital (QMH), The University of Hong Kong (HKU) particularly Wu King Wah, Kitty Chong, Felicia Ling and Gladys Chu for their expert technical assistance, and our professional colleagues in the Zhongnan Hospital affiliated to Wuhan University for the contribution to this work.

NOTICE

CONTENTS

目　录

Introduction

绪　论

Dyslipidaemias are disorders of lipoprotein metabolism, including lipoprotein overproduction or deficiency. The importance of treating dyslipidaemias based on cardiovascular risk factors is highlighted by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines. The first step in evaluation is to exclude secondary causes of dyslipidaemia.

脂代谢紊乱也可称为脂蛋白代谢紊乱，包括脂蛋白过多或缺陷。血浆脂蛋白代谢紊乱是心血管疾病的危险因素，美国国家胆固醇教育计划（NCEP）ATP-Ⅲ指南强调脂代谢紊乱的诊治非常重要。评估脂代谢紊乱首先必须排除继发性因素。

Dyslipidaemia is more often secondary to other causes than a primary genetic predisposition. Even in patients with known genetic abnormalities, it is important to consider secondary factors that may affect lipid levels. These include obesity; lifestyle influences such as diet, exercise, smoking, and the use of alcohol; endocrine disorders such as diabetes mellitus and hypothyroidism; and liver and renal diseases or other disorders affecting lipoprotein metabolism. Another important cause for secondary dyslipidaemia is the use of pharmacological agents.

脂代谢紊乱的继发性因素较原发性遗传缺陷更为常见。即使患者有明确的遗传因素，也应考虑影响血脂水平的继发因素：肥胖、生活方式（如饮食、锻炼、吸烟及饮酒）、内分泌紊乱性疾病（如糖尿病及甲状腺功能减

低）、肝肾疾病，以及其它影响脂蛋白代谢的疾病。此外，服用某些药物也是继发性脂代谢紊乱的另一重要诱因。

Accurate and comprehensive lipid profile testing are increasingly critical because it is used both to stratify a patient's risk for cardiovascular disease and to guide the initiation and monitoring of lipid-modifying therapy to reduce that risk, using the NCEP ATP III guidelines. However there are limitations in the routine lipid profile testing. The routine lipid profile/panel, which measures total cholesterol, HDL-C, and triglycerides and calculates LDL-C, has been shown to have an unexpectedly low predictive value for coronary heart disease (CHD). Part of the problem for this low predictive value is the inaccuracies inherent in the Friedewald formula used to calculate LDL-C, with the error rate (underestimation) increasing as triglycerides increased. This underestimation has resulted in more than one quarter of patients being misclassified to the wrong CHD risk category. Treatment goals practically rely on LDL-C values for high-risk patients, the Friedewald equation is too inaccurate for clinical use.

准确、全面的血脂检测越来越重视，因为血脂水平既可以评估病人心血管疾病风险，还可以指导血脂治疗的起始用药和疗效监测，从而降低风险。血脂监测和治疗应遵循 NCEP ATP-III 指南。然而，常规血脂检查存在一些不足，如 TC、HDL-C、TG 和由公式计算的 LDL-C 水平对冠心病（CHD）的风险预测价值不高。预测价值不高的部分原因是 Friedewald 公式计算结果的不准确性。当 TG 水平升高时，使用 Friedewald 公式计算 LDL-C，错误的可能性增加。这已经导致超过 1/4 病人的冠心病风险分类错误。LDL-C 水平是高风险病人的血脂治疗靶标，临床上使用

Friedewald 公式计算的结果很不准确。

Cholesterol is a well-defined molecule, providing a basis for a definitive method for its accurate measurement. On the contrary, lipoproteins are complex, heterogeneous, and polydisperse particles with overlapping properties that have not been fully characterized. VLDL, LDL, HDL and other lipoprotein particles vary in size and density.

胆固醇很容易准确检测。相比之下，脂蛋白复杂、多样、还有一些颗粒的性质尚不明确，而且 VLDL, LDL, HDL 及其他的脂蛋白颗粒的大小和密度也不尽相同。

Considering the complexity of the lipoprotein particles, although it is possible to separate out the different sizes of lipoprotein particles by density (through ultracentrifugation) or size and electrical charge (through electrophoresis) but it may not be possible to unambiguously define the fractions of interest and to develop definitive methods for their measurements. This raises problems of global standardization for the analytical methods.

如果不考虑脂蛋白的复杂成分，通过密度（超速离心）、大小或者电荷（电泳）可将这些不同大小的脂蛋白颗粒分开，然而却不能准确检测某一亚组分，也难以建立准确的检测方法。这已成为脂蛋白分析方法国际标准化的难题。

Total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) can be measured in both fasting and non fasting states. Triglycerides (TG) should be measured after 10-12 hours of fasting. Low-density lipoprotein cholesterol (LDL-C) is calculated using the Friedewald equation:

LDL-C (mmol/L) = TC – [HDL-C] – [TG/2.2]

If TG > 4.5 mmol/L (and/or non-fasting), this formula is not valid.

血浆总胆固醇（TC）和高密度脂蛋白胆固醇（HDL-C）在空腹和非空腹状态下都可以检测。甘油三酯（TG）只能在餐后 10～12 小时检测。LDL-C 浓度的计算可用 Friedewald 公式：LDL-C (mmol/L) = TC – [HDL-C] – [TG/2.2]。但是，当 TG > 4.5 mmol/L（空腹或者非空腹）时，公式就不再适用。

More recent data suggest that when TG > 2.3 mmol/L, LDL-C calculation using the above formula may not be accurate. Triglyceride-rich remnant lipoproteins (small VLDL and IDL) are also significantly elevated. In this situation, LDL –C measurement alone does not reflect the entire atherogenic lipoprotein fraction.

最新数据显示，当 TG > 2.3 mmol/L 时，由上述公式计算的 LDL-C 结果不准确，富含 TG 的脂蛋白残粒（小 VLDL 和 IDL）会明显升高。这种情况下，仅仅检测 LDL-C 不能反映导致动脉粥样硬化的全部脂蛋白含量。

Measurement of Non-HDL-C is more representative of all atherogenic lipoproteins. This can be calculated by the following formula:

Non-HDL-C (mmol/L) = TC – [HDL-C]

Non HDL-C levels can be calculated from a non-fasting serum.

非 HDL-C 的脂蛋白检测能更好地反映导致动脉粥样硬化的脂蛋白含量。计算公式为：Non-HDL-C (mmol/L) = TC – [HDL-C]。非 HDL-C 水平检测可以采用非空腹血浆。

An important clinical consideration is that when two LDL-C

values (calculated vs direct measurement) are available but different; particularly when the value is borderline, requiring a decision to treat or not to treat, such a difference would be of concern. Discrepancies between the results of calculated LDL-C and the results of the direct homogeneous LDL-C assays are primarily caused by elevated triglycerides and, to a lesser extent, by associated insulin resistance, liver or kidney diseases, and genetic defects in lipid and lipoprotein metabolism.

当通过公式计算和直接检测的 LDL-C 值不同时，应重视两者之间的差异，尤其是当结果处于临界值时，临床上须慎重考虑是否需要治疗。通过计算和直接测定 LDL-C 所得到的结果不一致，主要受高 TG 的影响，同时也受胰岛素抵抗、肝肾功能疾病、脂类及脂蛋白代谢遗传缺陷等因素的影响。

Dyslipidaemias were traditionally classified by patterns of elevation in lipids and lipoproteins (Fredrickson classification of hyperlipoproteinaemia) to six characteristic patterns (phenotypes) based on changes in the individual lipid moieties. It is worth noting that HDL is NOT considered in this classification system. It is NOT a diagnostic classification and does NOT distinguish between primary and secondary dyslipidaemias nor accurately predict risk of future coronary heart disease events. A more practical system categorizes dyslipidaemias as primary or secondary and characterizes them by increases in cholesterol only (hypercholesterolaemia), increases in TG only (hypertriglyceridaemia), or increases in both cholesterol and TG (mixed or combined hyperlipidaemias). This system does not take into account specific lipoprotein abnormalities (eg, low HDL or high LDL) that may contribute to disease despite normal cholesterol and TG levels.

血浆脂蛋白的传统分类（Fredrickson 高脂血症分类方法）是根据不同的脂质和脂蛋白升高来进行的。人体内的脂质成分改变有六种典型的模式（表型）。值得注意的是该分类标准未考虑 HDL-C,不属于诊断分类标准，既不能区分原发性和继发性脂代谢紊乱，也不能准确预测心血管疾病风险。按原发性或继发性对脂代谢紊乱进行系统分类会更实用，如仅胆固醇水平升高（高胆固醇血症）、或 TG 水平升高（高 TG 血症），或胆固醇和 TG 同时升高（混合的或复合的高脂血症）。这个分类体系未考虑特殊的脂蛋白异常（如低 HDL 或高 LDL），因为, 血胆固醇和 TG 水平尽管处于正常水平，仍可能会因特殊脂蛋白的异常而导致动脉粥样硬化等一些疾病的发生。

Lipoproteins are a spectrum of particles of different sizes and densities (Table 1). They are assembled primarily in the liver. The only exception is that chylomicrons (CM) are assembled in the intestinal wall and transported to the general circulation via lymphatics, and their secretion is regulated mainly by the flow of fatty acids and their intra-hepatic disposition. The entire process of chylomicron metabolism is relatively rapid and the presence of chylomicrons in the serum after an overnight fast is considered an indicator of defective triglyceride-rich lipoprotein (TRL) metabolism. Besides their structural proteins, lipoproteins transport proteins with functions other than lipoprotein metabolism, conferring special properties to the apolipoproteins (Table 2). Systematic reviews of lipoproteins and apolipoproteins are dealt with in more detail elsewhere.

Table 1. Lipoprotein Classes

Lipoprotein	Density (g/mL)	Major Lipid Component	Major Apolipoproteins
Chylomicrons	<0.95	Dietary Triglycerides and Cholesterol Esters	A1, A2, A4, B48, C1, C2, C3, E
Chylomicron Remnants	<1.006	Dietary Cholesterol Esters	B48, E
VLDL	<1.006	Endogenous Triglycerides	B100, C1, C2, C3, E
IDL	1.006-1.019	Endogenous Cholesterol Esters	B100, E
LDL	1.019-1.063	Endogenous Cholesterol Esters	B100
HDL2	1.063-1.125	Cholesterol Esters and Phospholipids	A1, A2, C1, C2, C3, E
HDL3	1.125-1.210	Phospholipids	A1, A2, C1, C2, C3, E

血浆脂蛋白由一系列大小和密度不同的颗粒组成(表 1)，主要在肝脏中合成。只有乳糜微粒 (CM) 在肠壁合成，通过淋巴管进入血液循环，其分泌主要受脂肪酸

含量以及肝内降解速度调节。CM 代谢过程较快，经过夜空腹，血清中还存在 CM 被认为是富含 TG 的脂蛋白(TRL)代谢缺陷的标志。此外，不同的载脂蛋白具有不同的特性（表 2）。除了其结构蛋白，载脂蛋白具有转运功能，并参与脂蛋白代谢。鉴于脂蛋白和载脂蛋白的结构及代谢有大量医学文献可供参考，本书不再赘述。

表 1　脂蛋白分类

脂蛋白	密度 (g/mL)	主要脂质成分	主要载脂蛋白
CM	<0.95	食入 TG 和胆固醇酯	A1, A2, A4, B48, C1, C2, C3, E
CM 残粒	<1.006	食入胆固醇酯	B48, E
VLDL	<1.006	内源性 TG	B100, C1, C2, C3, E
IDL	1.006-1.019	内源性胆固醇酯	B100, E
LDL	1.019-1.063	内源性胆固醇酯	B100
HDL2	1.063-1.125	胆固醇酯和磷脂	A1, A2, C1, C2, C3, E
HDL3	1.125-1.210	磷脂	A1, A2, C1, C2, C3, E

Table 2. Apolipoproteins

Apolipoprotein	Molecular Weight (kDa)	Amino acids	Lipoprotein	Function	Main Genetic Abnormalities
Apo A1	28.1	243	HDL	Main structural apolipoprotein of HDL	ApoA1-C3-A4 polymorphism. ApoA1 Milano
Apo A2	18.4	77	HDL	Structural apo-lipoprotein of HDL	Unknown
Apo A4	46	376	HDL, Chylomicrons	Antioxidant Anti-inflammatory Activator LCAT Regulator food intake	Apo A1-C3-A4 polymorphism
Apo A5	39	366	HDL, VLDL	Regulator of triglyceride	Gene polymorphism associated with

Apolipoprotein	Molecular Weight (kDa)	Amino acids	Lipoprotein	Function	Main Genetic Abnormalities
				metabolism	triglyceride level
Apo B100	?	4563	LDL, VLDL	Main structural apolipoprotein of LDL & VLDL	ApoB 3500 single point mutation
Apo B48	?	2152	Chylomicrons	Main structural apolipoprotein of chylomicrons	Unknown
Apo C1	6.6	57	VLDL, HDL	Activator LCAT Inhibitor CETP	Gene polymorphism associated with cholelithiasis, Alzheimer's disease
Apo C2	8.8	79	VLDL, HDL	Main Activator LPL	ApoC2 deficiency is associated with chylomicronaemia
Apo C3	8.8	79	VLDL, HDL	Main inhibitor to	Gene polymorphism

Apolipoprotein	Molecular Weight (kDa)	Amino acids	Lipoprotein	Function	Main Genetic Abnormalities
				VLDL catabolism	associated with hypertriglyceridaemia
Apo E	34.2	299	VLDL, HDL	Regulator of removal of atherogenic protein remnants	E2 isomorph and point mutations result in type III dyslipoproteinaemia. E4 isomorph is associated with atherosclerosis and Alzheimer's disease
Apo (a)	<300->800	?	LDL	?	?

表 2　载脂蛋白

载脂蛋白	分子量 (kDa)	氨基酸	脂蛋白	功能	主要遗传缺陷
Apo A1	28.1	243	HDL	HDL 主要结构载脂蛋白	ApoA1-C3-A4 多态性. Apo A1 Milano
Apo A2	18.4	77	HDL	HDL 结构载脂蛋白	不详
Apo A4	46	376	HDL, CM	抗氧化 抗炎 LCAT 催化剂 食物摄取调节	ApoA1-C3-A4 多态性
Apo A5	39	366	HDL, VLDL	TG 代谢调节因子	与 TG 水平相关的基因多态性
Apo B100	?	4563	LDL, VLDL	LDL 与 VLDL 的主要结构载脂蛋白	ApoB 3500 个点突变
Apo	?	2152	CM	CM 的主要结构载脂	不详

表 2　载脂蛋白					
载脂蛋白	分子量 (kDa)	氨基酸	脂蛋白	功能	主要遗传缺陷
B48				蛋白	
Apo C1	6.6	57	VLDL, HDL	LCAT 催化剂 CETP 抑制剂	与胆石病，阿尔茨海默氏病有关的基因多态性
Apo C2	8.8	79	VLDL, HDL	LPL 的主要催化剂	ApoC2 缺陷与乳糜微粒血症有关
Apo C3	8.8	79	VLDL, HDL	VLDL 分解代谢的主要抑制剂	与高 TG 血症相关的基因多态性
Apo E	34.2	299	VLDL, HDL	去除致动脉粥样硬化蛋白质的调节因子	E2 型和点突变可以导致 III 型血脂紊乱，E4 型与动脉粥样硬化及阿尔茨海默氏病有关
Apo(a)	<300->800	?	LDL	?	?

The most commonly employed procedures for the separation of lipoproteins are ultracentrifugation and electrophoresis. The method of ultracentrifugation is based on the separation of lipoproteins according to hydrated densities and floatation rates. The procedure is most accurate and provides separation of uncontaminated lipoprotein fractions. However, it is time consuming and requires 24-72 hours for the separation of all lipoprotein fractions. Lipoprotein agarose gel electrophoresis is frequently performed to help measure the relative cholesterol (and triglyceride) content of each lipoprotein class based on its mobility in an electrical field. The procedure is much simpler and less time consuming and provides substantial information necessary for phenotyping hyperlipoproteinaemias. However, the method is based on lipid staining and densitometric quantitation of lipoproteins, which fails to provide information about absolute cholesterol and triglyceride content of individual lipoprotein classes.

最常用的血浆脂蛋白分离方法为超速离心和电泳。超速离心法分离脂蛋白是根据不同组分的水合密度和浮选率不同。该方法最为准确，并且可以分离出不含杂质的脂蛋白成分，但是非常耗时，完成所有脂蛋白的分离需要 24-72 小时。血浆脂蛋白琼脂糖凝胶电泳常用于检测脂蛋白的种类和含量，以分析心血管疾病的潜在风险。这种脂蛋白电泳的方法比较简单、时间较短，能够提供大量的高脂蛋白血症表型的必要信息。然而，该方法是基于脂质染色和脂蛋白密度定量，不能提供体内不同脂蛋白中的胆固醇和 TG 的绝对含量的相关信息。

In addition to the standard lipid profile testing, plasma lipoproteins can be analyzed using agarose gel

electrophoresis in routine practice (Figure 1). It is particularly useful for identifying **β**-VLDL (e.g. in Type III hyperlipoproteinaemia) and the analysis of lipoprotein classes when plasma triglycerides are high (>4.5 mmol/L). This has been mentioned before that when two LDL-C values (calculated vs direct measurement) are available but different; particularly when the value is borderline, requiring a decision to treat or not to treat, such a difference would be of concern.

除了标准脂蛋白电泳谱检测之外，血浆脂蛋白也可采用琼脂糖凝胶电泳方法分析（图 1）。在 **β**-VLDL（如Ⅲ型高脂血症）和 TG 较高(>4.5 mmol/L)的情况下，分析脂蛋白类型时特别有意义。如前所述，当临床上遇到通过公式计算和直接检测的 LDL-C 水平有差异，尤其是处于临界值，在决策是否需要治疗的时候，应考虑到这一差异。

Fig.1 Lipoprotein Electrophoresis
图 1. 脂蛋白电泳

Dyslipidaemias have been traditionally classified in accordance with the abnormal lipoprotein pattern using the Fredrickson Classification of the Phenotypes of

Dyslipidaemias (Figure 2 and Table 3). In many patients dyslipidaemia is caused by some underlying "non-lipid" disease rather than a primary disorder of lipid and lipoprotein metabolism. Secondary causes contribute to most cases of dyslipidaemia in adults.

传统脂代谢紊乱的血浆脂蛋白分型常采用 Fredrickson 血脂异常表型分类方法（图 2 和表 3）。很多病人的血脂紊乱是由于潜在的“非血脂因素”疾病引起，而非原发性脂质和脂蛋白代谢紊乱所致。多数成年人血脂紊乱属继发性。

Fredrickson (WHO) 高脂血症表型

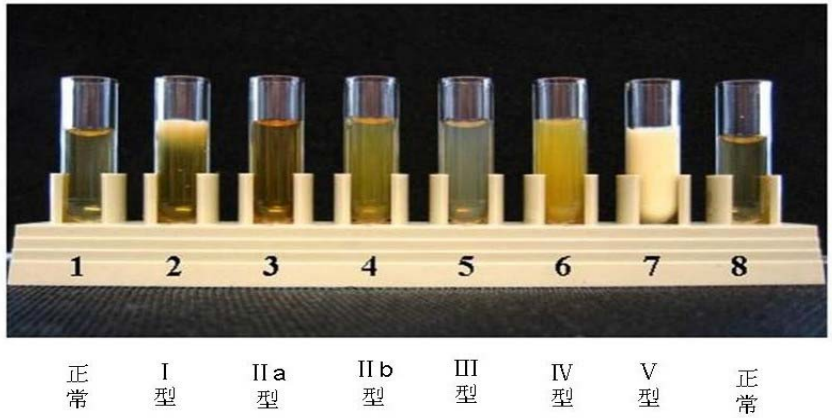


Fig. 2 Fredrickson Classification of the Phenotypes of Dyslipidaemias

图 2 Fredrickson (WHO) 高脂血症表型

Note that the Fredrickson classification is simply a biochemical phenotypic classification, and was devised before the importance of HDL as a prognostic indicator was recognized. The Fredrickson classification system is NOT

etiologic, does NOT distinguish between primary and secondary hyperlipidaemias, and does NOT include HDL.

Fredrickson 分型是一种简单的生化分型，在 HDL 可以作为风险预测指标之前就已采用。需要强调的是：Fredrickson 分型体系不是病因学的分型方法，也不是用来区分原发性和继发性血脂紊乱的标准，而且也不包括 HDL。

Table 3 Lipoprotein Pattern (Fredrickson Phenotypes)

Phenotype	Elevated Lipoprotein(s)	Elevated Lipids
I	Chylomicrons	TG
IIa	LDL	Cholesterol
IIb	LDL and VLDL	TG and cholesterol
III	VLDL and chylomicron remnants	TG and cholesterol
IV	VLDL	TG
V	Chylomicrons and VLDL	TG and cholesterol

表 3 脂蛋白分型—Fredrickson 表型

表型	升高的脂蛋白	升高的脂质
I	CM	TG
IIa	LDL	胆固醇
IIb	LDL, VLDL	TG 胆固醇
III	VLDL CM 残粒	TG 胆固醇
IV	VLDL	TG
V	CM 与 VLDL	TG 胆固醇

Secondary causes of dyslipidaemia may occur in association with diabetes mellitus, alcoholism, obesity, chronic renal insufficiency and/or failure, hypothyroidism, primary biliary cirrhosis and other cholestatic liver diseases. Certain therapeutic agents and or by concomitant therapy of various clinical disorders had adverse effects on lipid and lipoprotein metabolism that might interfere with the management, i.e drug-induced lipid and lipoprotein abnormalities, such as thiazides, β-blockers, antipsychotics, highly active antiretroviral agents, estrogen and progestins, and glucocorticoids. Many of these are discussed in more

detail elsewhere.

继发性脂代谢紊乱的因素有糖尿病、酗酒、肥胖、慢性肾功能不全和/或肾衰竭、甲状腺功能减退、原发性胆汁型肝硬化或者其他原因引起的胆汁淤积性肝病。此外，很多医学文献报道，药物治疗对脂质和脂蛋白的代谢也产生影响，从而干扰检测结果，如噻嗪类、β-阻断剂、抗精神病药物、高活性抗逆转录病毒药物、雌激素和孕激素、糖皮质激素等。

There are numerous pitfalls and inaccuracies in the routine lipid profile testing. Tests for secondary causes of dyslipidaemia should include measurements of fasting glucose, liver enzymes, creatinine, thyroid stimulating hormone (TSH), and urinary proteins (microalbumin) are also recommended in most patients with newly diagnosed dyslipidaemia, and when a component of the lipid profile has inexplicably changed for the worse.

常规脂质检测存在很多的不足和不确定性。继发性脂代谢紊乱的检查还应加测：空腹血糖、肝脏酶谱、肌酐、促甲状腺激素（TSH）和尿蛋白（微量白蛋白）。推荐新诊断的血脂紊乱病人、脂质检测中某一成分发生不明原因改变的病人进行脂蛋白电泳分析。

While LDL-C is the primary lipid marker for assessing the risk of cardiovascular disease, the NCEP ATP III guidelines state that emerging risk factors should be taken into consideration as optional modifiers of therapy. These include lipoprotein(a) [Lp(a)], LDL pattern density (small, dense Pattern B or large, buoyant Pattern A), HDL subtypes (HDL2 and HDL3), VLDL, and intermediate density lipoprotein (IDL). Our current knowledge and technology have advanced and so the question becomes whether our

general practices (clinical and laboratory) now should also change.

LDL-C 是评价心血管疾病风险的首要指标，但是 NCEP ATP III 指南指出，血脂治疗还应该考虑到新的风险指标：包括脂蛋白（a）[Lp(a)]、LDL 颗粒（小而密的 B 型，大而疏的 A 型）、HDL 亚类（HDL2 和 HDL3）、VLDL，以及中间密度脂蛋白（IDL）。随着科学技术的发展，目前我们所面临的问题是：在实际临床和实验室工作中是否也应做出相应的改变。

This casebook consists of case-oriented and problem-based teaching materials. It is not our purpose to provide an exhaustive account for all aspects of secondary dyslipidaemia. There are 26 illustrative cases A to Z of commonly encountered secondary dyslipidaemia, including a highlight of the clinical history.

本书是一本以临床病例为导向和问题为基础的参考资料，其目的不是对继发性脂代谢紊乱等因素进行全面的分类，而是以 26 个临床典型病例血浆脂蛋白电泳图谱形式，按照疾病的英文名称首字母 A 到 Z 顺序，系统整理临床病史、分析和讨论继发性脂代谢紊乱,将有助于读者查阅和索引。

Units of Expression

Total Cholesterol (mmol/L)
Triglycerides (mmol/L)
HDL-C (mmol/L)
LDL-C (mmol/L)
Apo A1 (g/L)
Apo B (g/L)

所用单位

总胆固醇, TC (mmol/L)
甘油三酯, TG (mmol/L)
高密度脂蛋白胆固醇, HDL-C (mmol/L)
低密度脂蛋白胆固醇, LDL-C (mmol/L)
载脂蛋白 A1，Apo A1 (g/L)
载脂蛋白 B，Apo B (g/L)

References

参考文献

Overview of Lipid Metabolism in the Merck Manual: http://www.merckmanuals.com/professional/endocrine_and_metabolic_disorders/lipid_disorders/overview_of_lipid_metabolism.html

Harper's Illustrated Biochemistry. 28th Edition (2009) web version by Robert K. Murray, David A Bender, Kathleen M. Botham, Peter J. Kennelly, Victor W. Rodwell, P. Anthony Weil [Chapters 25 & 26]. http://www.accessmedicine.com/content.aspx?aid=5227427

Endocrinology of Aging: [Chapter 4] Management of Dyslipidemia in the Elderly: http://www.endotext.org/aging/aging4/agingframe4.htm

(徐凤霞译)

CASE A　ALCOHOL ABUSE

酗酒

History

- 58/M, heavy drinker, was referred because of incidental finding of marked hypertriglyceridaemia
- No previous history of pancreatitis or family history of lipid disorders
- Physical examination was unremarkable.

案例 A

病史

- 58 岁，男性，重度酗酒者，偶然发现严重高甘油三酯（TG）血症。
- 无胰腺炎既往史，无脂代谢紊乱家族史。
- 体格检查无异常。

Lipid Profile

	At Presentation	**Half-year after lipid lowering therapy**
Total Cholesterol	12.0	6.3
Triglycerides	46.3	22.6
HDL-C	INT	1.45
LDL-C calc	N/A	N/A

LDL-C direct	INT	0.1
Non HDL-C	N/A	4.8
Appearance	Lipaemic	Lipaemic
Apo A1	N/A	0.96
Apo B	N/A	0.65

血脂结果

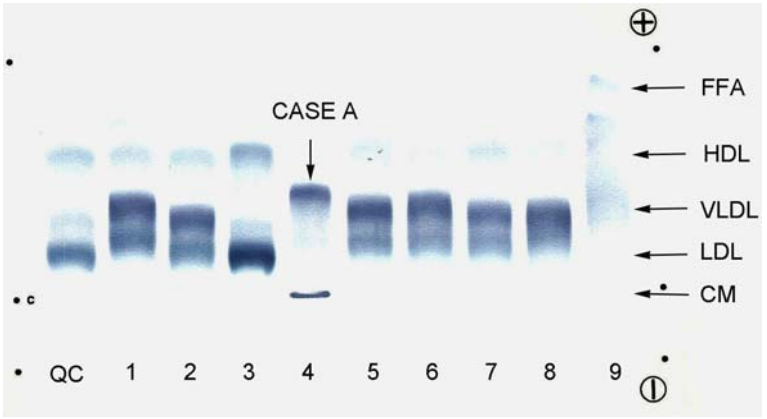
	本次就诊	降脂治疗半年后
总胆固醇, TC	12.0	6.3
甘油三酯, TG	46.3	22.6
高密度脂蛋白胆固醇, HDL-C	—	1.45
低密度脂蛋白胆固醇, LDL-C(计算）	—	—
低密度脂蛋白胆固醇,LDL-C(测量)	—	0.1
非 HDL-C	—	4.8
外观	脂血	脂血
载脂蛋白 A1, Apo A1	—	0.96
载脂蛋白 B, Apo B	—	0.65

Lipoprotein Electrophoresis

Marked chylomicronaemia syndrome of type I hyperlipoproteinaemia.

脂蛋白电泳

脂蛋白电泳图谱（图 3）第 4 号标本显示：明显的 I 型高脂蛋白血症乳糜微粒（CM）血症。



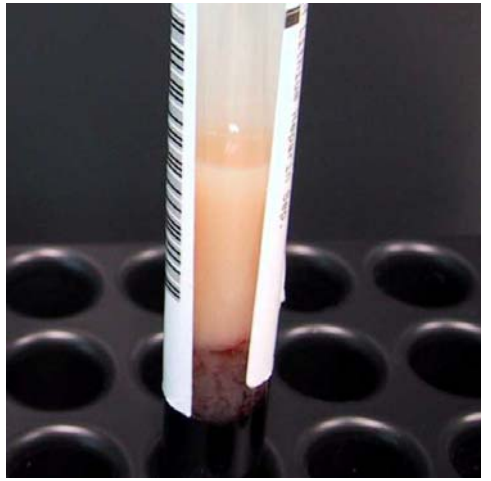


Fig. 3 Alcohol Abuse — Chylomicronaemia

图 3 酗酒—乳糜微粒血症

Interpretation

The most common lipid/lipoprotein abnormality associated with the use of ethanol is hypertriglyceridaemia. Causes

may be due to an increased synthesis of VLDL and a decreased removal by lipoprotein lipase after alcohol ingestion. Ethanol also increases HDL-C in a dose dependent fashion. It is one of the few exceptions that there is an inverse relation between triglyceride and HDL-C levels.

解释

高 TG 血症是与酒精使用有关的最常见脂质/脂蛋白异常。酒精代谢可导致 VLDL 的合成增加、脂蛋白脂肪酶水解降低。酒精还可使 HDL-C 水平呈剂量依赖性升高，较为罕见，通常 TG 与 HDL-C 水平呈反比。??????

Comment

Excessive alcohol intake and high-carbohydrate diets (>60% of caloric intake) are frequent causes of hypertriglyceridaemia. Hypermetabolic state of the liver occurs in response to alcohol metabolism, causing hypoxia and free radical–induced lipid peroxidative damage. Other nonspecific serum changes in acute and chronic alcoholics include elevations in uric acid, lactate, and reductions in glucose and magnesium.

评论

过量的酒精摄入和高碳水化合物饮食（>60%的热量摄取）是高 TG 血症的常见原因。酒精代谢还可使肝脏代谢亢进，引起组织缺氧、自由基诱导的脂质过氧化损伤。此外，急性和慢性酒精中毒患者的非特异性的血清变化，

包括血尿酸、乳酸水平升高，血葡萄糖和镁含量降低。

References

参考文献

O'Keefe JH, Bybee KA, Lavie CJ. Alcohol and Cardiovascular Health: The Razor-Sharp Double-Edged Sword. J Am Coll Cardiol 2007; 50: 1009-1014 Published online August 23, 2007.

Fortson MR, Freedman SN, Webster PD. Clinical assessment of hyperlipidemic pancreatitis. Am J Gastroenterol 1995; 90: 2134-2139.

Margolis S, Dobs AS. Nutritional management of plasma lipid disorders. J Am Coll Nutr 1989; 8[Suppl]: 33S-45S.

(孙力译)

CASE B　BILE DUCT STRICTURE

胆管狭窄

History

- 50/M was admitted because of cholangitis and found to have hypercholesterolaemia.
- History of chronic hepatitis B with liver failure and living donor transplantation performed 5 years ago. Complicated by development of liver abscess and stricture at the hepatoenteric anastomosis post-transplantation.
- Non-drinker. On tacrolimus, prednisolone and lamivudine.
- Lipid profile 2 months post liver transplantation was normal.

案例 B

病史

- 50 岁，男性，因胆管炎入院就诊，发现高胆固醇血症。
- 有慢性乙肝伴肝功能损伤病史，于 5 年前行活体器官移植，移植后并发肝脓肿、肝小肠区缝合处狭窄。
- 不饮酒，正在服用他克莫司，泼尼松龙和拉米夫定。
- 肝移植 2 月后血脂结果正常。

Lipid Profile

Total Cholesterol	9.6
Triglycerides	1.8
HDL-C	0.26
LDL-C calc	8.5
LDL-C direct	2.0
Non HDL-C	9.4
Appearance	Turbid
Apo A1	0.60
Apo B	0.93

血脂结果

总胆固醇, TC	9.6
甘油三酯, TG	1.8
高密度脂蛋白胆固醇, HDL-C	0.26
低密度脂蛋白胆固醇, LDL-C(计算）	8.5
低密度脂蛋白胆固醇, LDL-C(测量)	2.0
非 HDL-C	9.4
外观	浑浊
载脂蛋白 A1, Apo A1	0.60
载脂蛋白 B, Apo B	0.93

Lipoprotein Electrophoresis

Dysbetalipoproteinaemia was evident by electrophoresis and the discordant LDL-C (calculated vs direct measurement) as well as the disproportionately low Apo B results, likely to be LP-X (which lacks Apo B) and/or co-existent with LP-Y, a triglyceride-rich LDL commonly seen in post-live transplant hyperlipidaemia. The faint alpha (HDL) band is consistent with the relatively low Apo A1 level in the

plasma. No chylomicrons.

脂蛋白电泳

脂蛋白电泳图谱（图 4）第 9 号标本显示：明显的 β 脂蛋白异常血症???。直接检测的 LDL-C 水平与计算结果不一致，以及不成比例的低 ApoB 水平，可能为脂蛋白 X（缺乏 Apo B）和/或与脂蛋白 Y 共存，常见于肝脏移植后高脂血症，是一种富含 TG 的 LDL。微弱的 α （HDL）条带与较低的血浆 Apo A1 水平一致。无乳糜微粒。

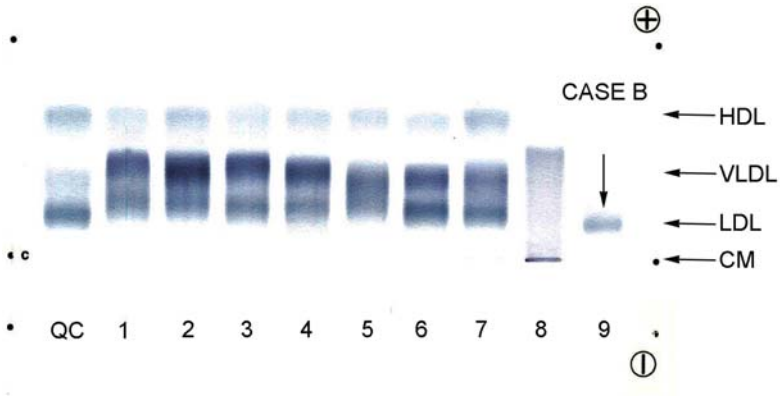


Fig. 4 Bile Duct Stricture — Dysbetalipoproteinaemia

图 4　　胆管狭窄—β 脂蛋白异常血症

Interpretation

Frank jaundice and elevated bilirubin are clinical indicators of biliary obstruction. Total cholesterol and LDL-C levels may be elevated in patients with chronic cholestatic

disorders. Depending on the underlying cause, stricture of the bile duct can be either benign or cancerous in nature, and the clinical manifestations of obstructive jaundice may develop rapidly or slowly.

解释

黄疸和胆红素水平升高是胆道阻塞的临床指征。慢性胆汁淤积的病人总胆固醇和 LDL-C 水平升高。胆道狭窄可以是良性的也可以是恶性的。阻塞性黄疸的临床表现进展的快慢取决于发病原因。

Comment

Cholestasis is characterized by hypercholesterolaemia and the presence of an abnormal lipoprotein, lipoprotein X (LP-X) in plasma. Experimental studies in mice indicate that the formation of LP-X and the hypercholesterolaemia associated with obstructive cholestasis is correlated with an increase in hepatic cholesterol synthesis. The mechanisms responsible for this cholestatic dyslipoproteinaemia are not fully understood but are independent of plasma HDL levels, LCAT activity, VLDL synthesis, and ATP-binding cassette A1 (ABCA1) and scavenger receptor class B type I (SR-BI) expression.

评论

胆汁淤积的特点是高胆固醇血症和血浆中出现异常脂蛋白（脂蛋白 X，LP-X）。在鼠模型上的研究发现，与胆道阻塞相关的高胆固醇血症及脂蛋白 X 的产生，与肝脏胆

固醇合成加强有关。这种胆汁淤积的血脂表型的发生机制尚未完全明确，但与血浆 HDL 水平、卵磷脂胆固醇酯酰转移酶（LCAT）活性、极低密度脂蛋白（VLDL）合成以及 ATP 结合盒 A1（ABCA1）和 B 类 I 型清道夫受体（SR-BI）的表达无关。

References

参考文献

Schwartz DA, Petersen BT, Poterucha JJ: Endoscopic therapy of anastomotic bile duct strictures occurring after liver transplantation. Gastrointest Endosc 2000; 51: 169-174.

Fickert P, Moustafa T, Trauner M. Primary sclerosing cholangitis – The arteriosclerosis of the bile duct? Lipids in Health and Disease 2007, 6:3. Available online: www.lipidworld.com/content/6/1/3

Bravo I, Amigo L, Cohen DE, Nervi F, Rigotti A, Francone O, Zanlungo S. Role of plasma and liver cholesterol and lipoprotein metabolism determinants in LpX formation in the mouse. Biochim Biophys Acta 2007; 1770: 979-988.

Oude Elferink, RPJ, Ottenhoff R, Jan van Marle, Frijters CMG, Smith AJ, Groen AK. Class III P-Glycoproteins Mediate the Formation of Lipoprotein X in the Mouse. J. Clin. Invest 1998; 102: 1749-1757.

(孙力译)

CASE C　CHRONIC RENAL FAILURE

慢性肾衰竭

History

- 80/M with chronic renal failure was started on continuous ambulatory peritoneal dialysis
- History of type 2 diabetes previously on oral hypoglycaemic agents
- Found to have hypertriglyceridaemia

案例 C

病史

- 80 岁，男性，慢性肾衰竭始发于持续性不卧床腹膜透析。
- 2 型糖尿病（T2DM）既往史，口服降糖药物。
- 高甘油三酯（TG）血症。

Lipid Profile

Total Cholesterol	4.6
Triglycerides	5.2
HDL-C	0.75
LDL-C calc	N/A
LDL-C direct	1.7
Non HDL-C	3.9
Appearance	Slightly Turbid
Apo A1	1.10

Apo B 0.83

血脂结果

总胆固醇, TC	4.6
甘油三酯, TG	5.2
高密度脂蛋白胆固醇, HDL-C	0.75
低密度脂蛋白胆固醇, LDL-C(计算）	—
低密度脂蛋白胆固醇, LDL-C(测量)	1.7
非 HDL-C	3.9
外观	轻度混浊
载脂蛋白 A1, Apo A1	1.10
载脂蛋白 B, Apo B	0.83

Lipoprotein Electrophoresis

Increased VLDL and a reduced HDL consistent with CRF on CAPD treatment.

脂蛋白电泳

脂蛋白电泳图谱（图 5）第 2 号标本可发现，VLDL 水平升高和 HDL 水平降低，与慢性肾衰竭的持续性不卧床腹膜透析治疗结果一致。

图 5 慢性肾衰竭—VLDL 水平升高、HDL 水平降低

Fig.5 Chronic Renal Failure—Increased VLDL and a reduced HDL

Interpretation

Significant dyslipidaemia often exist in patients who have chronic renal failure. Alterations of lipoprotein concentrations may result from an imbalance between lipoprotein synthesis and degradation. Lipolytic enzyme activity is known to be reduced in patients with renal failure, particularly lipoprotein lipase (LPL), hepatic triglyceride lipase (HTGL), and lecithin-cholesterol acyltransferase (LCAT). The reduced activity usually occurs at a glomerular filtration rate of 50 mL/min. The underlying mechanisms for reduced LPL activity are unclear, but may include functional insulin deficiency or resistance (possibly mediated via increased levels of parathyroid hormone and/or vitamin D deficiency), and the presence of a nondialyzable inhibitor of LPL in the plasma of uraemic patients.

解释

慢性肾衰竭的病人常表现出明显的脂代谢紊乱，脂蛋白浓度的变化通常由于脂蛋白的合成和降解失衡而导致。肾功衰病人的脂肪分解酶活性降低，尤其是脂蛋白脂肪酶（LPL)、肝酯酶（HTGL）以及卵磷脂胆固醇酯酰转移酶（LCAT)；当肾小球过滤率为 50 ml/min 时，可检测到酶活性降低。LPL 活性降低的基本机制尚不清楚，可能包括：功能性的胰岛素缺乏或胰岛素抵抗（与维生素 D 缺乏和/或甲状旁腺激素水平升高有关)，尿毒症患者血浆中存在不可透析的 LPL 活性抑制物。

Comment

Reduced LPL activity results in delayed hydrolysis of ApoB-containing lipoproteins. There is an increase of intact or partially metabolized, triglyceride-rich, ApoB-containing lipoproteins with a disproportionate elevation of ApoC3. Plasma lipid and lipoprotein levels are affected by individual variations in lipoprotein production rates, LPL and HTGL activities, and the composition of lipoproteins. The end result is a decrease in levels of nonartherogenic ApoA-containing high-density lipoproteins, and an increase in levels of proatherogenic ApoC3 enriched ApoB-containing lipoproteins (VLDL, IDL and LDL)..

评论

LPL 活性降低可导致含 ApoB 的脂蛋白水解减慢。完整的或部分代谢的、富含甘油三酯的、含 ApoB 的脂蛋白合成增多，与 ApoC3 的升高不成比例。脂蛋白的合成速

率、LPL 和 HTGL 活性、以及脂蛋白组分的个体差异影响血浆脂质和脂蛋白水平。最终结果是含 ApoA 的高密度脂蛋白水平下降，高密度脂蛋白具有抗动脉粥样硬化作用；而促动脉粥样硬化的 ApoC3 水平升高，ApoC3 富含 ApoB 脂蛋白(VLDL, IDL 及 LDL)。

References

参考文献

Attman P, Samuelsson O, and Alaupovic P. Lipoprotein metabolism and renal failure. Am J Kidney Dis 1993; 21:573–592.

Lindholm B and Norbeck HE. Serum lipids and lipoproteins during continuous ambulatory peritoneal dialysis. Acta Med Scand 1986; 220:143–151.

Rader DJ, Rosas S. Management of selected lipid abnormalities. Hypertriglyceridemia, low HDL cholesterol, lipoprotein(a), in thyroid and renal diseases, and post-transplantation. Med Clin North Am. Jan 2000; 84(1): 43-61.

（孙力译）

CASE D DIABETES MELLITUS (TYPE 2)

2 型糖尿病

History

- 60/M, non-smoker, presented with mild symptoms of polyuria and polydipsia and found to have type 2 diabetes mellitus.
- Currently on diet and metformin.
- Urine sugar and albumin both negative.

案例 D

病史

- 60 岁，男性，不吸烟，因轻微多尿、烦渴症状诊断为 2 型糖尿病（T2DM）。
- 控制饮食、服用二甲双胍。
- 尿糖和尿蛋白均为阴性。

Lipid Profile

Total Cholesterol	5.5
Triglycerides	6.4
HDL-C	1.21
LDL-C calc	N/A
LDL-C direct	1.7
Non HDL-C	4.3
Appearance	Slightly Turbid

Apo A1	1.29
Apo B	0.87

血脂结果

总胆固醇, TC	5.5
甘油三酯, TG	6.4
高密度脂蛋白胆固醇, HDL-C	1.21
低密度脂蛋白胆固醇, LDL-C(计算）	N/A
低密度脂蛋白胆固醇, LDL-C(测量)	1.7
非 HDL-C	4.3
外观	轻微浑浊
载脂蛋白 A1, Apo A1	1.29
载脂蛋白 B, Apo B	0.87

Lipoprotein Electrophoresis

Dysbetalipoproteinaemia (broad beta band) was evident. Suggest collecting sample for apoE genotyping. Any other secondary causes ?

脂蛋白电泳

脂蛋白电泳图谱（图 6）第 7 号标本可见：明显的 β 脂蛋白血症（宽 β 带）。建议收集样本进行 ApoE 基因分型，分析是否存在其它的继发性诱因。

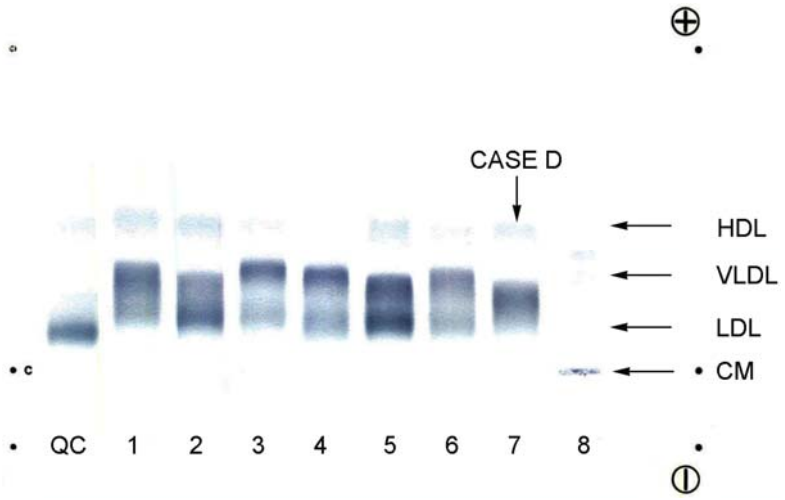


Fig. 6　T2DM — Dysbetalipoproteinaemia

图 6　2 型糖尿病—β 脂蛋白血症

Interpretation

Lipid abnormalities are common in diabetes mellitus, particularly type 2 DM. Patients who have type 2 diabetes classically have elevated levels of VLDL (both VLDL1 and VLDL2) and its remnants (IDL, appeared as board beta band on electrophoresis) with an increase in the plasma triglycerides. This is often but not always accompanied by a reduced HDL-C. The total cholesterol and LDL-C concentrations are usually normal.

解释

血脂异常在糖尿病中很常见，尤其是 T2DM。T2DM 患者有典型的血浆 VLDL（包括 VLDL-1 和 VLDL-2）、

VLDL 残粒（IDL，在电泳中表现为宽 β 带）和 TG 水平升高。且常伴有 HDL-C 水平下降，而 TC 和 LDL-C 水平正常。

Comment

Abnormal lipoprotein concentrations can result from changes in the production, conversion, or catabolism of lipoprotein particles. However, it should also be remembered that normal levels of plasma lipids and lipoproteins do not necessarily indicate that lipoprotein production or clearance is normal. Dynamic alterations in lipoprotein interconversion and in lipoprotein composition may occur in relation to the degree of insulin resistance and glycaemic control, even in the absence of evident dyslipidaemia. It has been reported that the degradation rates of VLDL and IDL are regulated by different pathways. Activity of lipoprotein lipase appears to be modulated by insulin resistance activity but hepatic lipase could be independent of insulin action and essentially modulated by changes of IDL composition.

评论

脂蛋白颗粒在生成、转换或代谢过程中的变化，可引起脂蛋白水平异常。然而，血脂和脂蛋白水平正常，并不意味着脂蛋白的合成和清除正常。即使血脂异常不明显，脂蛋白之间的相互转化及其组分也可能发生动态变化，这种动态变化与胰岛素抵抗程度和血糖控制有关。据报道，VLDL 和 IDL 降解速率的调控途径不同。脂蛋白脂肪酶活性与胰岛素抵抗有关，但肝酯酶活性不受胰岛素

调控，而是受 IDL 组分变化的调控。

References

参考文献

Ouguerram K, Magot T, Zäir Y, Marchini JS, Charbonnel B, Laouenan H, Krempf M. Effect of atorvastatin on apolipoprotein B100 containing lipoprotein metabolism in type-2 diabetes. JPET 2003; 306: 332-337.

Goldberg IJ. Diabetic dyslipidemia: causes and consequences. J Clin Endocrin Metab 2001; 86**:** 965-971.

Abrahamson MJ. Diabetes mellitus (DM) in adults. Best Practice of Medicine. December 2003. Online version: http://www.micromedex.com/products/updates/diseasedexgen_updates/diabetes.pdf

(沈璠译)

CASE E　END-STAGE RENAL FAILURE

肾功能衰竭终末期

History

- 45/F
- End stage renal failure on continuous ambulatory peritoneal dialysis
- Admitted because of exit site infection
- On cefazolin and rifampicin

案例 E

病史

- 45 岁，女性
- 采用连续不卧床腹膜透析的肾功能衰竭终末期患者
- 由于出口部位感染收治入院
- 使用头孢唑啉和利福平治疗

Lipid Profile

Total Cholesterol	11.1
Triglycerides	6.7
HDL-C	0.99
LDL-C calc	N/A
LDL-C direct	7.4
Non HDL-C	10.1
Appearance	Slightly Turbid

ApoA1	0.88
ApoB	1.75

血脂结果

总胆固醇, TC	11.1
甘油三酯, TG	6.7
高密度脂蛋白胆固醇, HDL-C	0.99
低密度脂蛋白胆固醇, LDL-C(计算）	—
低密度脂蛋白胆固醇, LDL-C(测量)	7.4
非 HDL-C	10.1
外观	轻微混浊
载脂蛋白 A1, Apo A1	0.88
载脂蛋白 B, Apo B	1.75

Lipoprotein Electrophoresis

Markedly elevated ApoB-containing lipoproteins, mainly LDL consistent with nephrotic syndrome of ESRF.

脂蛋白电泳

脂蛋白电泳结果（图 7）第 2 号标符合肾功能衰竭终末期（ESRF）的肾病综合症：含 ApoB 的脂蛋白水平显著升高，以 LDL 为主,宽β…。

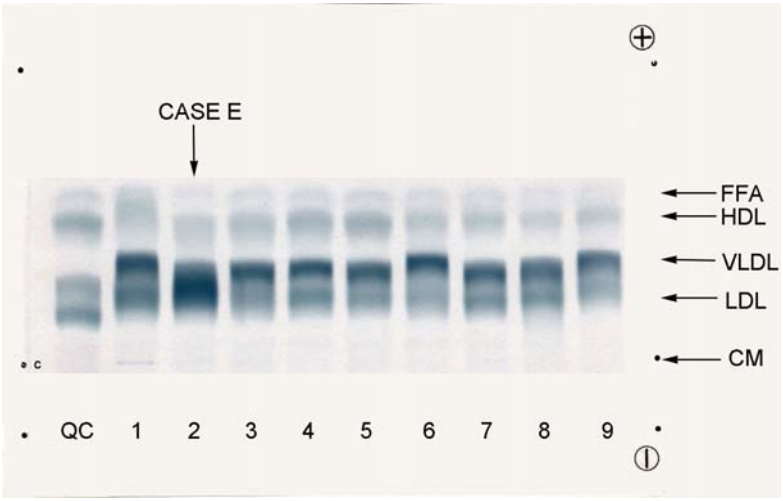


Fig. 7 ESRF—Markedly elevated ApoB-containing lipoproteins.

图 7 肾功能衰竭终末期—含 ApoB 的脂蛋白显著升高

Interpretation

Lipid disorders are common in end-stage renal failure (ESRF) as a consequence of both systemic metabolic derangements and the uremic milieu itself. Hypertriglyceridaemia is the most commonly observed lipid abnormality. The dyslipidaemia of ESRF is also characterized by an abnormal apolipoprotein profile with decreased concentrations of apoA-containing lipoproteins in HDL and increased concentrations of triglyceride-rich apoB-containing lipoproteins in VLDL, IDL, and LDL..

解释

脂代谢紊乱在ESRF中很常见，主要由全身代谢紊乱和尿毒症共同导致。血脂异常以高TG最为常见。ESRF血脂异常的特点是：载脂蛋白异常，HDL中含ApoA的脂蛋白浓度降低，VLDL、IDL和LDL中富含TG的ApoB脂蛋白浓度升高。

Comment

Disturbances of lipoprotein metabolism are common in the early stage of renal insufficiency and become more pronounced with progressive loss of renal functions particularly in continuous ambulatory peritoneal dialysis (CAPD). Peritoneal dialysis induced hypertriglyceridaemia may be caused by exposure to high glucose concentrations of the peritoneal solutions and due also to the loss of proteins via the peritoneum. Lipoprotein abnormalities may worsen with time on CAPD treatment since glucose may act as a substrate for lipoprotein synthesis. Abnormal VLDL remnant metabolism persists during long-term dialysis therapy because of the possibility that glucose loading may worsen insulin sensitivity. Reduced activity of the enzymes, lipoprotein lipase and hepatic lipase, as well as increased levels of ApoC3 in VLDL, which are critical in the reduced clearance of these lipoproteins

评论

脂蛋白代谢紊乱在肾功能不全早期很常见，并随着肾脏功能进行性的丧失而逐渐加重，这种情况在连续不卧床腹膜透析（CAPD）中更明显。腹膜液中高浓度的糖和腹膜透析中蛋白质的丢失可引起高TG血症。糖是脂蛋白合

成的底物，脂蛋白的异常可随着CAPD时间的延长而加剧。由于糖负荷可降低胰岛素敏感性，长期透析治疗的患者VLDL残粒代谢异常。脂蛋白脂肪酶和肝酯酶活性降低，以及VLDL中ApoC3水平的升高，均可引起这些脂蛋白清除减慢。

References

参考文献

Kagan A, Bar-Khayim Y, Schafer Z, Fainaru M. Kinetics of peritoneal protein loss during CAPD: II. Lipoprotein leakage and its impact on plasma lipid levels. Kidney Int 1990; 37: 980-90.

Wheeler DC: Abnormalities of lipoprotein metabolism in CAPD patients. Kidney Int 1996; 50: S41-6.

Kobayashi S, Maejima S , Ikeda T, Nagase M. Impact of dialysis therapy on insulin resistance in end-stage renal disease: comparison of haemodialysis and continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant 2000; 15: 65-70.

(黎四维译)

CASE F　FISH-OIL SUPPLEMENT

鱼油添加剂

History

- 44/F
- Obese with mixed hyperlipidaemia
- On fenofibrate and maxepa
- Plasma free fatty acids > 3.0 mmol/L

案例 F

病史

- 44 岁，女性
- 肥胖伴混合性高脂血症
- 服用非诺贝特胶囊和脉适宝
- 血浆 FFA> 3.0 mmol/L

Lipid Profile

Total Cholesterol	10.4
Triglycerides	16.1
HDL-C	1.11
LDL-C calc	N/A
LDL-C direct	4.4
Non HDL-C	9.3
Appearance	Turbid

ApoA1	1.28
ApoB	2..11

血脂结果

总胆固醇, TC	10.4
甘油三酯, TG	16.1
高密度脂蛋白胆固醇, HDL-C	1.11
低密度脂蛋白胆固醇, LDL-C(计算）	N/A
低密度脂蛋白胆固醇, LDL-C(测量)	4.4
非 HDL-C	9.3
外观	混浊
载脂蛋白 A1, Apo A1	1.28
载脂蛋白 B, Apo B	2.11

Lipoprotein Electrophoresis

An electronegative subfraction of pre-beta lipoproteins was noted. Chylomicrons also present. Fish-oil supplements may interfere with the electrophoretic mobility of all lipoproteins.

脂蛋白电泳

脂蛋白电泳图谱（图 8）第 5 号标本结果可见：带负电荷的前-β 脂蛋白及乳糜微粒。鱼油添加剂可能对所有脂蛋白电泳移动速率有影响。

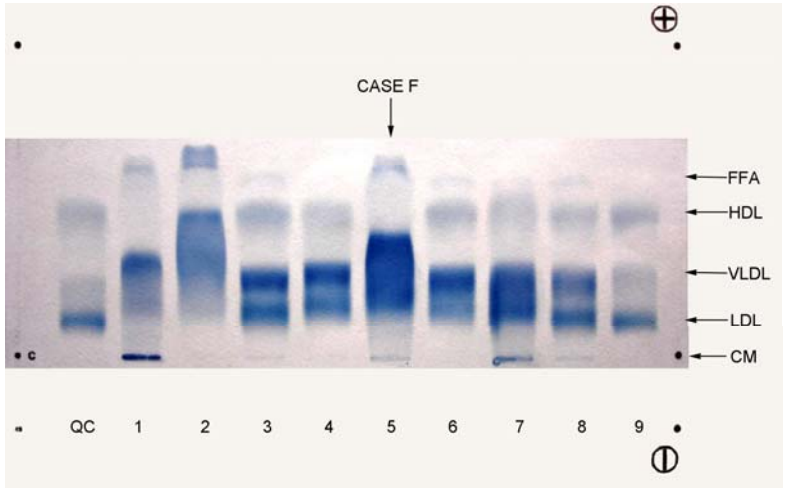


Fig. 8　鱼油添加剂—前-β脂蛋白及乳糜微粒

图 8　Fish-oil Supplement—pre-beta lipoproteins and CM

Interpretation

The n-3 fatty acids (omega-3 fatty acids) have been shown to have beneficial effects on atherosclerosis in patients with dyslipoproteinaemia. The two major bioactive omega-3 fatty acids, eicosapentanoic and docosahexanoic acids, are derived primarily from dietary sources, and are enriched in cold-water fish. However, a practical limitation of lipoprotein electrophoresis techniques is that the mobilities of all lipoprotein classes are markedly altered when the concentration of FFA in serum is >2 mmol/L. Under such conditions, severe distortions of the lipoprotein electrophoresis pattern may occur, and the result would become misleading.

解释

ω-3脂肪酸对脂蛋白代谢紊乱的动脉粥样硬化病人具有保护作用。人体具有生物活性的两种主要ω-3脂肪酸是二十碳五烯酸和二十二碳六烯酸，主要来源于食物，淡水鱼中含量尤为丰富。然而，由于脂蛋白电泳技术的限制，当血清富含FFA >2 mmol/L时，各种脂蛋白的迁移速率发生改变。这种情况下，脂蛋白电泳图谱可能发生很大的变化，所得的结果也可能有误。

Comment

The other common treatment-related cause of high FFA concentrations is the administration of heparin to prevent or treat patients with thromboemboblism. Heparin releases lipoprotein lipase in vivo from the capillary endothelium of adipose tissue, heart, skeletal muscle, and lung. It greatly enhances the rate at which triglycerides from chylomicrons and VLDL are hydrolyzed in the blood and leads to an increase of FFA and monoglycerides. Elevated plasma FFA may also be found in severe forms of primary hypertriglyceridaemia, insulin-treated diabetes mellitus, obesity, nephrotic syndrome, or hyperthyroidism. In the presence of high concentrations of FFA, lipid analysis by lipoprotein electrophoresis with subsequent cholesterol staining is inaccurate.

评论

高FFA血症还可因治疗而致，如病人使用肝素预防或治疗血栓。在体内，肝素可促使脂肪组织、心脏、骨骼肌

和肺部的毛细血管内皮细胞释放LPL，加速血液中CM和VLDL水解，生成TG，从而使血清FFA和单酸甘油酯水平升高。血浆FFA浓度升高还可见于：原发性高TG血症、使用胰岛素治疗的糖尿病、肥胖、肾病综合征和甲状腺功能亢进。采用脂蛋白电泳及胆固醇染色的方法分析高FFA血浆结果不准确。

Notes

Omega-3 fatty acids offer a host of therapeutic benefits for dyslipidaemias by mediating cell membrane function and structure, and the synthesis of lipid mediators. Since cell membrane fatty acids play a crucial role in signal transduction, it is believed that the dramatic lipid-altering effects of omega-3 fatty acids are mediated via the mechanism of modifying gene expression of such lipid mediators. Subjects should maintain their usual diet and stop the supplement for at least one week prior to the determination of their lipid profile.

注意事项

ω-3脂肪酸通过介导细胞膜功能和结构、脂质合成的调节而发挥对血脂异常的治疗作用。细胞膜脂肪酸在信号转导过程中起着重要作用，ω-3脂肪酸通过调控脂类调节基因的表达发挥改变脂质的效应。受试者应该保持正常饮食，至少在检测血脂前一周停止食用鱼油添加剂。

References

参考文献

Laurell S. The effect of free fatty acids on the migration rates of lipoproteins in paper electrophoresis. Scand J Clin Invest 1955; 7: 28-31.

Shafir E. Partition of unesterified fatty acids in normal and nephrotic syndrome serum and its effect on serum electrophoretic pattern. J Clin Invest 1958; 37:1775-82.

Nauck M, Marz W, Wieland H. Adding albumin normalizes electrophoretic mobility of lipoproteins in sera with high concentrations of free fatty acids. Clin Chem 1996; 42: 1283-1285.

（鲁双艳译）

CASE G GLYCOGEN STORAGE DISEASE (TYPE IA)

Ia 型糖原贮积病

History

- 15/M, admitted for investigation of liver mass
- Known case of GSD type Ia confirmed by mutation analysis
- No recent symptomatic hypoglycemia, poor compliance with allopurinol
- Ultrasound scan showed progressive hepatomegaly, fatty liver and 2 liver lesions.
- Investigations: AFP < 2 ng/ml and CEA 0.4 ng/ml, L/RFT normal, fasting glucose 5.9 mmol/L, lactate 3.0 mmol/L, blood gas - no acidosis, urate 402 umol/L.

案例 G

病史

- 15 岁，男性，因肝内包块入院检查
- 经突变分析确认患有 Ia 型糖原贮积症
- 近期无症状性低血糖，服用别嘌呤醇药物依从性差
- 超声提示进行性肝肿大、脂肪肝和肝损伤。
- 检查： 甲胎蛋白(AFP) < 2 ng/mL, 癌胚抗原(CEA) 0.4 ng/mL, 肝肾功能正常，空腹血糖 5.9 mmol/L，乳酸 3.0 mmol/L, 血气分析：无酸中毒，尿酸 402

μ mol/L。

Lipid Profile

Total Cholesterol	5.3
Triglycerides	7.2
HDL-C	0.92
LDL-C calc	N/A
LDL-C direct	2.4
Non HDL-C	4.3
Appearance	Slightly Turbid
ApoA1	1.19
ApoB	1.21

血脂结果

总胆固醇, TC	5.3
甘油三酯, TG	7.2
高密度脂蛋白胆固醇, HDL-C	
低密度脂蛋白胆固醇, LDL-C(计算）	N/A
低密度脂蛋白胆固醇, LDL-C(测量)	2.4
非 HDL-C	4.3
外观	轻微浑浊
载脂蛋白 A1, Apo A1	1.19
载脂蛋白 B, Apo B	1.21

Lipoprotein Electrophoresis

Increased VLDL and a reduced HDL consistent with dyslipidaemia of GSD type Ia phenotype.

脂蛋白电泳

脂蛋白电泳图谱（图 9）第 9 号标本的结果符合 Ia 型糖原贮积症表型：VLDL 升高，HDL 下降。

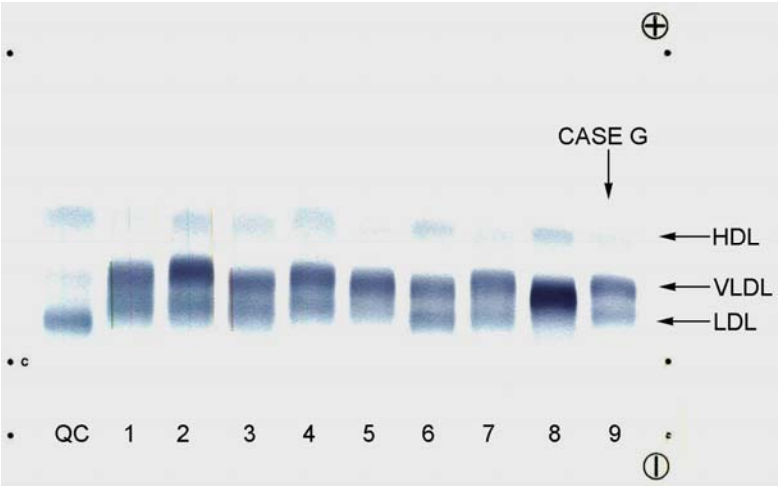


Fig. 9　GSD Type Ia—Increased VLDL and a reduced HDL

图 9　Ia 型糖原贮积症—VLDL 升高，HDL 下降

Interpretation

Type Ia is the most common form of glycogen storage disease (GSD) in children, characterized by a defect in glucose-6-phosphatase activity. The clinical picture of GSD I is very complex, characterized by hypoglycaemia, lactic acidosis, hypertriglyceridaemia, moderate increase in transaminase levels and hyperuricaemia. The clinical findings of massive hepatomegaly, enlarged kidneys and

growth failure, and the association of rapid onset of postprandial hypoglycemia, elevated lactic acid levels and marked hypertriglyceridaemia were sufficient to establish the diagnosis of GSD Ia. The degree of hypertriglyceridaemia would depend on the degree of hypoglycaemia before feeding.

解释

儿童糖原贮积症（GSD）最常见类型为 Ia 型，其特点是葡萄糖-6-磷酸酶活性缺陷。I型GSD的临床表现复杂：肝肾肿大、发育迟缓，生化检查：低血糖，乳酸酸中毒，高TG血症，转氨酶中度升高，高尿酸血症。根据临床表现：肝肿大、发育迟缓、餐后很快发生低血糖、乳酸水平升高、明显的高TG血症，即可诊断为Ia型GSD。高TG血症的程度取决于进食前的低血糖程度。

Comment

Epinephrine is secreted in response to severe hypoglycemia. This activates lipoprotein lipase and the release of FFAs, where they are transported to the liver for the synthesis of triglycerides and are exported as VLDL, which is the cause of hypertriglyceridaemia in these patients. It has been reported that sera from patients with GSD Ia are able to more efficiently promote scavenger receptor class B type I–mediated cellular cholesterol efflux.

评论

严重的低血糖刺激机体分泌肾上腺素，肾上腺素激活脂

蛋白脂肪酶，释放FFAs。脂肪酸被运输到肝脏，作为合成TG的原料，并以VLDL形式输出，是这类病人出现高TG血症的原因。据报道Ia型GSD患者血浆能更有效地促进B类清道夫Ⅰ介导的细胞内胆固醇外流。

References

参考文献

Chou JY, Matern D, Mansfield BC, Chen YT. Type I glycogen storage diseases: disorders of the glucose-6-phosphatase complex. Curr Mol Med 2002; 2:121-143.

Nguyen AD, Pan CJ, Weinstein DA, Chou JY. Increased scavenger receptor class B type I-mediated cellular cholesterol efflux and antioxidant capacity in the sera of glycogen storage disease type Ia patients. Mol Genet Metab 2006; 89: 233-238.

Ubels FL, Rake JP, Slaets JP, Smit JP, Smit AJ. Is glycogen storage disease type Ia associated with atherosclerosis? Eur J Pediatr 2002; 161: s62-s64.

Bandsma RH, Rake JP, Visser G, et al. Increased lipogenesis and resistance of lipoproteins to oxidative modification in two patients with glycogen storage disease type 1a. J Pediatr 2002; 140: 256-260.

Greene HL, Swift LL, Knapp HR. Hyperlipidemia and fatty acid composition in patients treated for type IA glycogen storage disease. J Pediatr 1991; 119: 398-403.

(鲁双艳译)

CASE H　HYPOPITUITARISM

垂体功能减退症

History

- 26/F, obese
- Craniopharyngioma diagnosed during childhood
- Presented as delayed puberty and primary amenorrhoea
- Underwent surgery and radiotherapy 10 years ago
- Panhypopituitarism with decreased growth hormone, cortisol and gonadotropins, prolactin normal, FT4 borderline low.
- On hormone replacement and gemfibrozil
- No family history of hyperlipidaemia.

案例 H

病史

- 26 岁，女性，肥胖
- 儿童时期诊断为颅咽管瘤。
- 青春期发育迟缓、原发性闭经
- 十年前有手术和放疗史。
- 垂体功能减退伴有生长激素、皮质醇、促性腺激素降低，泌乳素正常，FT4 水平处于参考值下限。
- 激素替代治疗和吉非贝齐降脂治疗。
- 无高血脂家族史。

Lipid Profile

Total Cholesterol	7.8
Triglycerides	8.9
HDL-C	1.00
LDL-C calc	N/A
LDL-C direct	3.2
Non HDL-C	6.8
Appearance	Slightly Turbid
ApoA1	1.42
ApoB	1.43
ApoE Genotype	E4/3

血脂结果

总胆固醇, TC	7.8
甘油三酯, TG	8.9
高密度脂蛋白胆固醇, HDL-C	1.00
低密度脂蛋白胆固醇, LDL-C(计算）	—
低密度脂蛋白胆固醇, LDL-C(测量)	3.2
非 HDL-C	6.8
外观	轻微混浊
载脂蛋白 A1, Apo A1	1.42
载脂蛋白 B, Apo B	1.43
载脂蛋白 E 基因型	E4/3

Lipoprotein Electrophoresis

Markerly elevated Apo B-containing lipoproteins (LDL and VLDL). No evidence of broad beta band. Patients with panhypopituitarism usually have adverse lipid profiles, and

hypothalamic obesity is a major complication of craniopharyngioma treatment – For clinical correlation.

脂蛋白电泳

脂蛋白电泳图谱（图 10）第 6 号标本可见：含 Apo B 的脂蛋白（LDL 和 VLDL）明显升高，未见宽 β 带。基于临床相关性，垂体功能减退患者通常伴有异常脂质谱，下丘脑性肥胖是颅咽管瘤治疗的主要并发症。

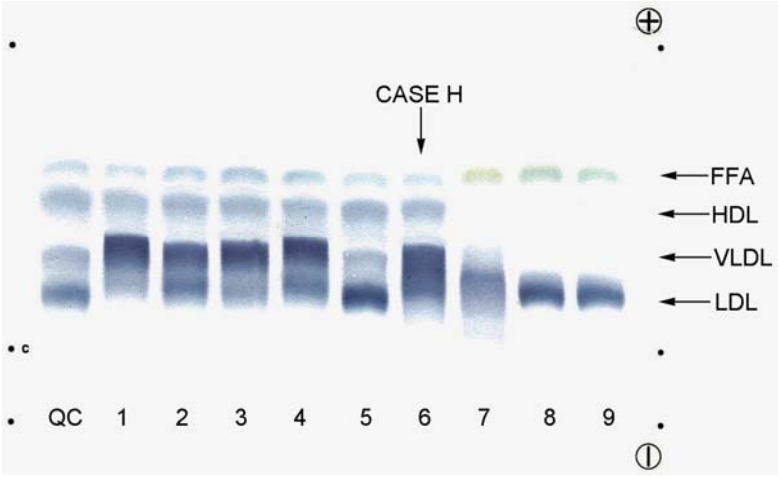


Fig. 10　Hypopituitarism—Markerly elevated LDL and VLDL

图 10　垂体功能减退 — LDL 和 VLDL 明显升高

Interpretation

The dyslipidaemia associated with hypopituitarism is often characterized by an increase in total cholesterol and LDL-C.

It is mainly attributed to growth hormone (GH) deficiency. The underlying mechanisms are not fully elucidated. Studies on the pathogenesis of hypertriglyceridaemia in patients with pituitary insufficiency have found that their plasma lipoprotein lipase and hepatic triglyceride lipase activities were subnormal, and the dyslipidaemia subsided after corticosteroid and thyroid hormone replacement therapy. The other possible mechanism is an increased hepatic secretion of VLDL- ApoB.

解释

与垂体功能低下相关的血脂异常表现为 TC 和 LDL-C 升高。主要归因于生长激素（GH）缺乏，其基本的机制尚未完全阐明。对垂体功能减退伴高 TG 血症发病机制的研究发现，血浆脂蛋白脂肪酶和肝酯酶活性低于正常，采用皮质类固醇和甲状腺激素替代治疗可改善脂代谢紊乱。另一种可能的机制是肝脏分泌的 VLDL-Apo B 增加。

Comment

Chronic pituitary insufficiency may also cause symptoms of hypogonadism, hypothyroidism, and hypoadrenalism, and GH deficiency. Higher plasma TG concentrations and TG enrichment of VLDL may result from an increase in production, reduced catabolism of VLDL triglyceride, or both. VLDL triglyceride is partly removed via CETP. It has been reported that a decrease in CETP activity with GH replacement in hypopituitary subjects.

评论

慢性垂体功能不全可引起性腺功能减退、甲状腺功能减退和肾上腺功能减退的症状，生长激素缺乏以及脂代谢紊乱。血浆 TG 和富含 TG 的 VLDL 浓度升高是由于它们的合成增加和/或分解降低。富含 TG 的 VLDL 分解降低可导致 TG 升高。富含 TG 的 VLDL 部分通过 CETP 清除。有研究报道，垂体功能减退患者采用生长激素替代治疗，CETP 活性降低。

Notes

Replacement of the deficient hormones has become mandatory in patients with hypopituitarism because the disorder usually affects the synthesis and release of other hormones. GH may play an important role in HDL metabolism, as demonstrated by GH-induced reversal of the low HDL levels observed in hypopituitarism. However, the hypertriglyceridaemia associated with hypopituitarism has rarely been ameliorated by GH replacement. Inappropriate and nonphysiological replacement with hydrocortisone, thyroxine, and sex hormones have shown to be associated with lipid abnormalities..

注意

垂体功能低下患者由于一种或多种垂体激素分泌减少，可出现多种不同的体征和临床症状。这种紊乱通常会影响到其他激素的合成和释放，针对缺乏激素进行替代治疗是必须的。生长激素（GH）可使垂体功能低下患者低

HDL 水平发生逆转，说明生长激素在 HDL 代谢中发挥重要作用。然而，与垂体功能低下相关的高 TG 血症很少能通过 GH 的替代治疗得以改善。不当的和非生理的氢化可的松、甲状腺素、性激素替代治疗与血脂紊乱有关。

References

参考文献

Ishibashi S, Murase T, Yamada N, Tanaka K, Takaku F, Sato K. Hyperlipidaemia in patients with hypopituitarism. Acta Endocrinol 1985; 110: 456-460.

Chrisoulidou, A., E. Kousta, S. Venkatesan, R. Gray, P. A. Bannister, J. J. Gallagher, and D. G. Johnston. Very-low-density lipoprotein apolipoprotein B100 kinetics in adult hypopituitarism. Metabolism 1999; 48:1057-1062.

Kearney T, de Gallegos C N, Chrisoulidou A, Gray R, Bannister P, Venkatesan S,. Johnston DG. Hypopituitarsim is associated with triglyceride enrichment of very low-density lipoprotein. J Clin Endocrinol Metab 2001; 86: 3900-3906.

Christ ER, Cummings MH, Stolinski M, Jackson N, Lumb PJ, Wierzbicki AS, Sonksen PH, Russell-Jones DL, Umpleby AM. Low-density lipoprotein apolipoprotein B100 turnover in hypopituitary patients with GH deficiency: a stable isotope study. Eur J Endocrinol 2006; 154: 459–466.

(沈璠译)

CASE I IgA NEPHROPATHY

IgA 肾病

History

- 48/F
- Presented with gross ankle edema
- Found to have heavy proteinuria
- Diagnosed IgA nephropathy by renal biopsy
- On metorpolol, nifidipine and ramipril

案例 I

病史

- 48 岁，女性
- 出现肉眼可见的踝部浮肿
- 发现有严重蛋白尿
- 通过肾穿刺活检诊断为 IgA 肾病
- 使用美托舍酯，尼菲霉素和雷米普利治疗

Lipid Profile

Total Cholesterol	6.6
Triglycerides	10.1
HDL-C	0.56
LDL-C calc	N/A
LDL-C direct	2.7
Non HDL-C	6.1

Appearance	Turbid
ApoA1	1.10
ApoB	1.18

血脂结果

总胆固醇, TC	6.6
甘油三酯, TG	10.1
高密度脂蛋白胆固醇, HDL-C	0.56
低密度脂蛋白胆固醇, LDL-C(计算）	N/A
低密度脂蛋白胆固醇, LDL-C(测量)	2.7
非 HDL-C	6.1
外观	混浊
载脂蛋白 A1, Apo A1	1.10
载脂蛋白 B, Apo B	1.18

Lipoprotein Electrophoresis

Increased VLDL. Chylomicrons also present consistent with IgA nephropathy and hypertension.

脂蛋白电泳

脂蛋白电泳图谱（图 11）第 4 号标本结果符合 IgA 肾病和高血压： VLDL 升高、出现 CM 条带。

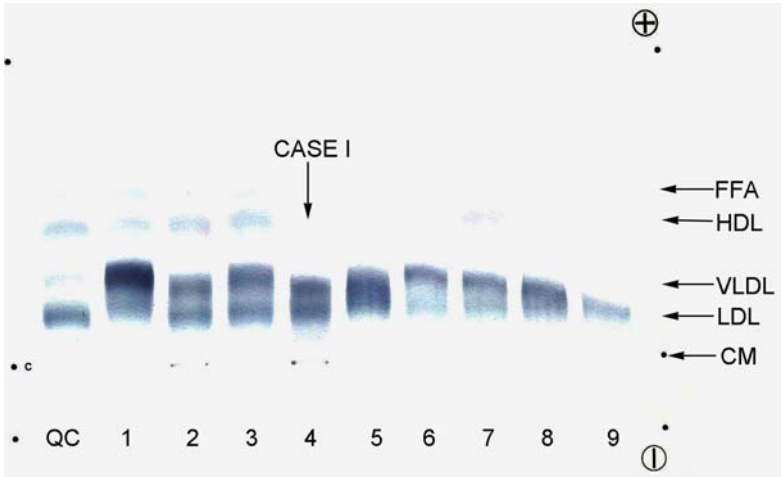


Fig. 11 IgA Nephropathy —Increased VLDL, CM

图 11 IgA 肾病 — VLDL 升高，出现 CM 条带

Interpretation

Immunoglobulin A (IgA) nephropathy is the most common form of glomerulonephritis. Primary IgA nephropathy is characterized by deposition of the IgA antibody in the glomerulus. The progression of renal failure in patients with IgA nephropathy is associated with glomerular and tubulo-interstitial inflammation and injury. Dyslipidaemia is very common in chronic renal insufficiency patients, and in patients who have heavy proteinuria. Hypertriglyceridaemia is common and hypercholesterolaemia is almost universal in those who have significant proteinuria.

解释

免疫球蛋白 A（IGA）肾病是肾小球肾炎中最常见的一种。原发性 IgA 肾病的特点是肾小球有 IgA 抗体沉积。IgA 肾病患者的肾功衰进展与肾小球肾炎、间质性炎症及损伤相关。血脂异常在慢性肾功能不全和严重蛋白尿的患者中十分常见。高 TG 血症和高胆固醇血症在严重蛋白尿的患者中也很普遍。

Comment

Increased loss of glomerular protein in the urine leads to hypoalbuminaemia**,** and a compensatory overproduction of lipoproteins by the liver results in hyperlipidaemia. The concentration of plasma apolipoproteins in patients with IgA nephropathy generally reflects abnormalities of lipoprotein metabolism. There are elevated levels of ApoB and E, which are associated with VLDL and LDL. However, the levels of the major apolipoproteins associated with HDL, ApoA1 and A2, are usually normal or even reduced. The elevation in triglyceride levels is due partly to an alteration in the composition of circulating TG (which become enriched with ApoC3) and, reductions in the activity of lipoprotein lipase and hepatic triglyceride lipase may contribute to the decrease in TG removal..

评论

蛋白质随尿液不断丢失导致低白蛋白血症，肝脏代偿性加强脂蛋白分泌可引起高脂血症。IgA 肾病患者血浆载脂蛋白的浓度反映了体内载脂蛋白代谢的变化。ApoB 和 ApoE 水平的升高与 VLDL、LDL 相关。另一方面，与 HDL 相关的主要载脂蛋白，如 ApoA1 和 A2 的水平通常

正常或下降。循环 TG 的组份改变（变为富含 ApoC3）、脂蛋白脂肪酶和肝酯酶的活性降低，都使得 TG 的清除率降低。

References

参考文献

Syrjanen J, Mustonen J, Pasternack A: Hypertriglyceridaemia and hyperuricaemia are risk factors for progression of IgA nephropathy. Nephrol Dial Transplant 2000; 15: 34–42.

Donadio JV Jr, Larson TS, Bergstralh EJ, Grande JP. A randomized trial of high-dose compared with low-dose omega-3 fatty acids in severe IgA nephropathy. J Am Soc Nephrol 2001;12: 791-799.

Strippoli GF, Manno C, Schena FP. An "evidence-based" survey of therapeutic options for IgA nephropathy: assessment and criticism. Am J Kidney Dis 2003; 41: 1129–39.

Tang S, Lai KN. IgA nephropathy: Thirty years on, Medical Progress 1999; 26: 8-14.

Kilgore LL, Patterson BW, Parenti DM, Fisher WR. Immune complex hyperlipidemia induced by an apolipoprotein-reactive immunoglobulin A paraprotein from a patient with multiple myeloma: characterization of this immunoglobulin. J Clin Invest 1985; 76: 225-232.

(黎四维　余雪琛译)

CASE J JEJUNAL ATRESIA

空肠闭锁

History

- 2/M
- History of suspected alagille syndrome, biliary atresia/jejunal atresia
- Failed kasai operation
- Admitted for nausea and vomiting
- Chronic/intermittent diarrhoea with fever

案例 J

病史

- 2 岁，男性
- 曾怀疑 Alagille 综合征，胆道闭锁/空肠闭锁
- 卡萨伊手术失败
- 因恶心和呕吐入院
- 慢性/间歇性腹泻和发烧

Lipid Profile

Total Cholesterol	11.7
Triglycerides	2.2
HDL-C	0.25
LDL-C calc	10.4
LDL-C direct	2.8

Non HDL-C	11.4
Appearance	Clear
ApoA1	0.29
ApoB	1.43

血脂结果

总胆固醇, TC	11.7
甘油三酯, TG	2.2
高密度脂蛋白胆固醇, HDL-C	0.25
低密度脂蛋白胆固醇, LDL-C(计算）	10.4
低密度脂蛋白胆固醇, LDL-C(测量)	2.8
非 HDL-C	11.4
外观	清亮
载脂蛋白 A1, Apo A1	0.29
载脂蛋白 B, Apo B	1.43

Lipoprotein Electrophoresis

Abnormal beta-lipoprotein which migrates to the cathode was noted, likely to be lipoprotein X that cannot be detected by direct LDL-C assay. Albumin bound (delta) bilirubin was also evident in the free fatty acid region near the anode.

脂蛋白电泳

脂蛋白电泳图谱（图 12）第 1 号标本显示：迁移至负极的异常 β-脂蛋白，可能是脂蛋白 X(LpX)，这种脂蛋白不能采用直接检测 LDL-C 的方法测定；在阳极附近的游离脂肪酸部位出现明显的白蛋白结合（δ）胆红素。

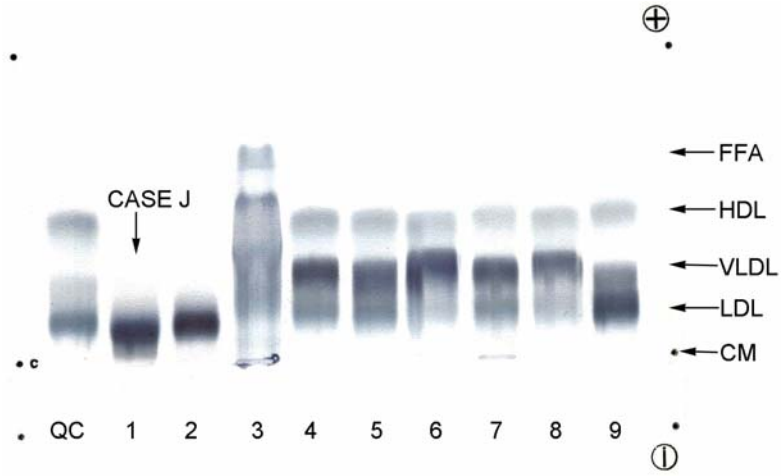


Fig.12　Jejunal Atresia —Abnormal beta-lipoprotein, LpX

图 12　空肠闭锁 —异常 β-脂蛋白，可能是 LpX

Interpretation

Total parenteral nutrition (TPN) associated cholestatic jaundice in premature infants should be acknowledged as one of the major differential diagnoses of biliary atresia. Hypercholesterolaemia and hypertriglyceridaemia are commonly present. The increase in serum cholesterol levels is largely due to an increased level of lLpX, an abnormal lipoprotein that is rich in free cholesterol and phospholipids, with particle size within the LDL density region. The mechanisms responsible for this cholestatic plasma lipid phenotype are not fully understood. It could result from either regurgitation of biliary lipids into plasma or from the accumulation of phospholipid and free cholesterol in serum because of reduced LCAT activity.

解释

早产儿完全肠外营养（TPN）过程中出现的胆汁淤积性黄疸应作为胆道闭锁的主要鉴别诊断之一。患者常发生高胆固醇血症和高TG血症。血清胆固醇水平升高主要是由于LpX水平的增加。LpX是一种异常的脂蛋白颗粒，存在于富含游离胆固醇和磷脂的LDL密度层。胆汁淤积的血脂表型机制尚不十分明确，可能由于脂质从胆道返流至血浆，或是因为LCAT活性降低导致血清磷脂和游离胆固醇堆积。

Comment

Jejunal atresia is a rare birth defect where developmental abnormalities result in the small intestine being completely absent or blocked. Patients with Alagille syndrome and total TPN-related cholestasis can resemble all the features of biliary atresia. The need for prolonged TPN in the infant with short bowel syndrome may result in cholestasis that can be lethal. It is important to identify the infants with jaundice who have direct (conjugated) hyperbilirubinemia. High delta bilirubin (greater than 50% of total bilirubin) in newborns was associated with intra- and extra-hepatic cholestasis.

评论

空肠闭锁是一种罕见的先天缺陷，其结果是小肠在发育过程中先天畸形，完全缺失或阻塞。Alagille 综合征、完全 TPN 有关的胆汁淤积症与胆道闭锁具有相似的肝组织学检查结果。长期 TPN 的短肠综合征婴儿可能出现致命

性的胆汁淤积。确诊黄疸婴儿有高直接（结合）胆红素血症非常关键。新生儿高 δ-胆红素（高于总胆红素 50%）与肝内、肝外胆汁淤积有关。

References

参考文献

Fete CLR, Cuendet A, Berclaz J. An unusual association of small bowel atresia and biliary atresia: A case report. J Pediatr Surg 1983; 18:136-137.

Witt J, Ober M. Lp-X in newborns: incidence of positive tests without cholestasis. J Clin Chem Clin Biochem 1976; 14: 197-202.

Han SJ, Han A, Choi SH, Oh J, Hwang EH. Biliary atresia associated with meconium peritonitis caused by perforation of small bowel atresia. J Pediatr Surg 2001; 36: 1390-1393.

Kilani, RA, Hmiel P, Garver MK, Srinathan SK, Wickline KM, Langer JC. Familial jejunal atresia with renal dysplasia. J Pediat Surg 1996; 31:1427-1429.

Martin LW, Zerella JT. Jejunoileal atresia: a proposed classification. J Pediat Surg 1976; 11: 399-403.

De Lorimier AA, Fonkalsrud EW, Hays DM. Congenital atresia and stenosis of the jejunum and ileum. Surgery 1969; 65:819-827.

(黎四维译)

CASE K　KETOACIDOSIS

酮症酸中毒

History

- 44/M
- Known case of type 2 diabetes mellitus, hypertension and gout.
- Noted high blood glucose with ketonuira on admission
- Poor glycaemic control, HbA1c=17.9%, glucose=31.7 mmol/L
- Blood ketone=2.9 mmol/L
- pH=7.34, bicarbonate=15 mmol/L, BE=-9

病例 K

病史

- 44 岁，男性；
- 患有 2 型糖尿病（T2DM）、高血压和痛风；
- 入院时血糖高、尿酮体阳性；
- 血糖控制不良，糖化血红蛋白（HbA1c）17.9%，血糖 31.7 mmol/L；
- 血酮 2.9 mmol/L；
- 血液 pH7.34，碳酸氢盐 15 mmol/L，碱剩余（BE）-9。

Lipid Profile

Total Cholesterol	5.8
Triglycerides	9.7
HDL-C	0.68
LDL-C calc	N/A
LDL-C direct	2.0
Non HDL-C	5.1
Appearance	Turbid
ApoA1	0.90
ApoB	1.30

血脂结果

总胆固醇, TC	5.8
甘油三酯, TG	9.7
高密度脂蛋白胆固醇, HDL-C	0.68
低密度脂蛋白胆固醇, LDL-C(计算）	N/A
低密度脂蛋白胆固醇, LDL-C(测量)	2.0
非 HDL-C	5.1
外观	混浊
载脂蛋白 A1, Apo A1	0.90
载脂蛋白 B, Apo B	1.30

Lipoprotein Electrophoresis

Increased VLDL and a reduced HDL. Chylomicron remnants also present.

脂蛋白电泳

脂蛋白电泳图谱（图 13）第 6 号标本显示： VLDL 增高，

HDL 降低，有 CM 条带。

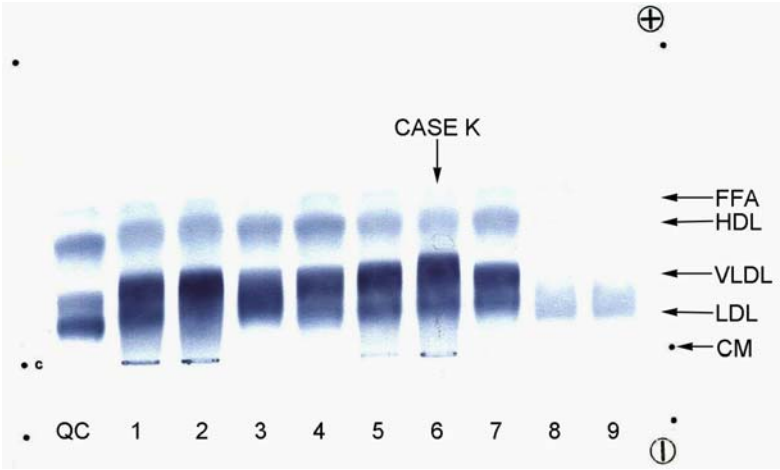


Fig. 13 Ketoacidosis —Increased VLDL and a reduced HDL. Chylomicron remnants also present

图 13 酮症酸中毒—VLDL 增高，HDL 降低，CM 条带

Interpretation

Ketoacidosis and hyperosmolar hyperglycaemia are the most serious acute metabolic complications of diabetes. In diabetes, elevated triglycerides can represent an accumulation of atherogenic lipoproteins (chylomicron remnants, VLDL remnants and IDL particles). This is frequently associated with an increase in potentially atherogenic triglyceride-rich, small-dense LDL particles and triglyceride enriched HDL.

解释

酮症酸中毒和高渗性高血糖是糖尿病最严重的急性代谢并发症。糖尿病患者 TG 升高反映致动脉粥样硬化的 CM 残粒、VLDL 残粒和 IDL 颗粒堆积。这通常与潜在致动脉粥样硬化的富含 TG、小而密的 LDL 颗粒，富含 TG 的 HDL 增加有关。

Comment

Moderate hypertriglyceridaemia in hypoinsulinaemia was common. Patients with type 1 diabetes may develop diabetic ketoacidosis (DKA) due to an absolute insulin deficiency. Insulin deficiency appears to be a requirement for the development of DKA in type 2 diabetes. In DKA, the low insulin levels combined with increased levels of stress hormones (catecholamines, cortisol and growth hormone) will activate hormone-sensitive lipase, which will cause the body to metabolize triglycerides instead of glucose for energy and release of free fatty acids. Thus, serum levels of glycerol and FFAs rise because of the unrestrained lipolysis..

评论

低胰岛素血症常伴有中度高TG血症。1型糖尿病患者由于胰岛素绝对不足，可发生糖尿病酮症酸中毒（DKA）。胰岛素不足似乎是T2DM患者发生DKA的一个必要条件。酮症酸中毒时，低水平胰岛素伴儿茶酚胺、皮质醇和生长激素增高可以激活激素敏感性脂肪酶，促使机体通过利用TG而非葡萄糖来获取能量。因此，由于脂肪不断分解导致血清甘油和FFAs水平升高。

Notes

Regular insulin by continuous IV infusion is the preferred treatment for patients with DKA. Omega-3 fatty acids may be useful in the treatment of marked hypertriglyceridaemia, but with a tendency to aggravate hyperglycaemia. Nicotinic acid is effective in lowering triglycerides and increasing HDL-C. It also lowers LDL-C level, but side effects, including worsening of glycaemic control, limit its usefulness in diabetes.

注意事项

定期持续静脉注射胰岛素是糖尿病酮症酸中毒的首选治疗。ω- 3脂肪酸可能有助于严重高TG血症的治疗，但是有加重高血糖的趋势。烟酸可降低TG、升高HDL-C，还可降低LDL-C水平。但烟酸存在一些副作用，包括进行性血糖控制不良，限制了其在糖尿病中的应用。

References

参考文献

Foster DW, McGarry JD. The metabolic derangements and treatment of diabetic ketoacidosis. N Engl J Med 1983; 309:159-69.

Goldberg RB, Machado R: Atypical ketoacidosis in type 2 diabetes. Hosp Pract 1998;33:105-108.

Westphal SA: The occurrence of diabetic ketoacidosis in non-insulin-dependent diabetes and newly diagnosed

diabetic adults. Am J Med 1996; 101:19-24.

Leung GM, Lam KSL. Diabetic complications and their implications on health care in Asia. HKMJ 2000; 6: 61-68.

（沈璠译）

CASE L　LIVER CIRRHOSIS

肝硬化

History

- 53/M
- Ex-chronic drinker
- Cholecystectomy for gallstone 5 years ago
- USG: liver cirrhosis with splenomegaly
- Admitted for malaise and vomiting undigested food
- Found worsening LFT and RFT

案例 L

病史

- 53 岁，男性
- 曾经长期饮酒
- 5 年前因胆结石行胆囊切除术
- 超声检查：肝硬化、脾大
- 因不适、呕吐未消化食物入院
- 肝功能和肾功能进行性恶化

Lipid Profile

Total Cholesterol	1.8
Triglycerides	1.3
HDL-C	0.26
LDL-C calc	0.9

LDL-C direct	N/A
Non HDL-C	1.5
Appearance	Clear
apoA1	<0.25
apoB	0.59

血脂结果

总胆固醇, TC	1.8
甘油三酯, TG	1.3
高密度脂蛋白胆固醇, HDL-C	0.26
低密度脂蛋白胆固醇, LDL-C(计算）	0.9
低密度脂蛋白胆固醇, LDL-C(测量)	—
非 HDL-C	1.5
外观	清亮
载脂蛋白 A1, Apo A1	<0.25
载脂蛋白 B, Apo B	0.59

Lipoprotein Electrophoresis

A reduced HDL consistent with dyslipidaemia of liver cirrhosis.

脂蛋白电泳

脂蛋白电泳图谱（图 14）第 7 号标本结果符合肝硬化血脂代谢紊乱：低 HDL。

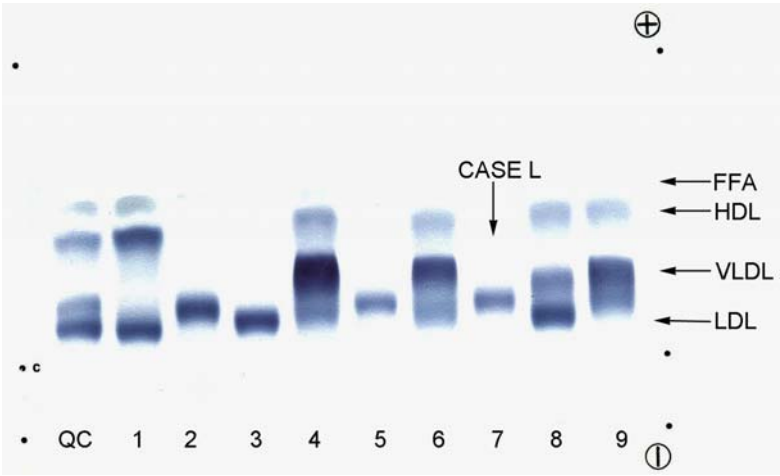


Fig. 14　Liver Cirrhosis —A reduced HDL
图 14　肝硬化 — HDL 降低

Interpretation

The liver has a very central role in the production and regulation of cholesterol homeostasis. HDL and VLDL are synthesized by the liver. Declining lipoprotein cholesterol may reflect deteriorating liver function.

解释

肝脏在合成和调节体内胆固醇的平衡中发挥重要作用。HDL 和 VLDL 都由肝脏合成。脂蛋白胆固醇的减少可以反映肝功能恶化状态。

Comment

The pathogenesis of the low HDL levels associated with cirrhosis is reported to be multifactorial. In cirrhosis, there is a progressive decrease in the synthesis and secretion of ApoA1, which is the major apolipoprotein of HDL. Cirrhosis of the liver is irreversible but treatment of the underlying causes may slow or stop the progression. Such treatment depends upon the underlying etiology, and treatment must also be directed at the complications. Liver transplantation is highly effective for the treatment of end-stage cirrhosis.

评论

低 HDL 与肝硬化相关的发病机理是多因素的。肝硬化时，HDL 的主要载脂蛋白 ApoA1 的合成和分泌减少，并随肝功能的恶化呈进行性下降。虽然肝硬化是不可逆的，但是针对肝病起因治疗可以延缓甚至阻止肝硬化的进程。临床治疗应根据基本病因学，同时必须直接针对并发症。对于晚期肝硬化患者，肝移植是很有效的治疗方法。

References

参考文献

Menon KV, Kamath PS. Managing the complications of cirrhosis. Mayo Clinic Proceedings 2000; 75: 501–509.

Iredale JP. Cirrhosis: new research provides a basis for rational and targeted treatments.BMJ 2003; 327: 143-147.

(余雪琛译)

CASE M　MYELOMA KIDNEY

骨髓瘤肾病

History

- 46/F, social worker
- Renal biopsy: Stage III IgD multiple myeloma
- PET-CT: multiple lytic lesion
- Ig pattern: immuniparesis, IgA/IgG decreased, IgD3578 mg/L
- High beta2-microglobulin level
- Heavy proteinuria, urine free light chain (Lambda) positve
- On chemotherapy

案例 M

病史

- 46 岁，女性，社会工作者
- 肾活检：IgD 型多发性骨髓瘤三期
- PET- CT：多发性溶解性病损
- 免疫球蛋白：免疫麻痹，IgA / IgG 比值降低，IgD 3578 mg/L
- β2-微球蛋白水平升高
- 严重蛋白尿，尿液游离轻链（λ）阳性
- 正在化疗

Lipid Profile

Total Cholesterol	7.6
Triglycerides	3.4
HDL-C	0.46
LDL-C calc	5.6
LDL-C direct	5.6
Non HDL-C	7.1
Appearance	Clear
ApoA1	0.53
ApoB	1.82

血脂结果

总胆固醇, TC	7.6
甘油三酯, TG	3.4
高密度脂蛋白胆固醇, HDL-C	0.46
低密度脂蛋白胆固醇, LDL-C(计算）	5.6
低密度脂蛋白胆固醇, LDL-C(测量)	5.6
非 HDL-C	7.1
外观	清澈
载脂蛋白 A1, Apo A1	0.53
载脂蛋白 B, Apo B	1.82

Lipoprotein Electrophoresis

Increased apo B-containing lipoproteins, mainly LDL suggestive of type IIb hyperlipoproteinaemia of nephrotic syndrome of myeloma.

脂蛋白电泳

脂蛋白电泳图谱（图 15）第 3 号标本显示：含 ApoB 的脂蛋白水平升高，主要是 LDL，提示骨髓瘤引起肾病综合征继发 IIb 型高脂蛋白血症。

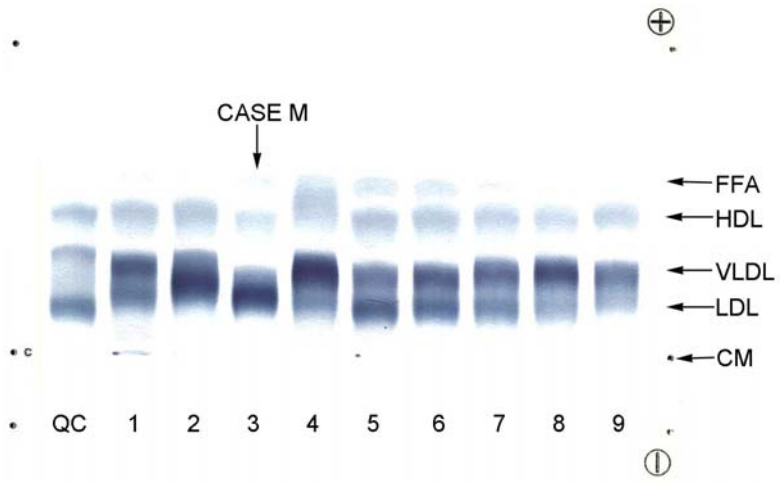


Fig.15 Myeloma Kidney —Type IIb hyperlipoproteinaemia

图 15　骨髓瘤肾病—IIb 型高脂蛋白血症

Interpretation

Immunoglobulin D (IgD) multiple myeloma (MM) is a rare plasma cell disorder with fewer than 2% of all MM cases. Renal impairment in patients with MM may be secondary to dehydration, hypercalcaemia, myeloma of the kidney, or light-chain and heavy-chain deposition in the kidneys, leading to both tubular injury and intratubular cast formation and obstruction. MM induced nephrotic syndrome may cause secondary hypercholesterolaemia and or hypertriglyceridaemia. The Apo B-containing

lipoproteins are usually elevated.

解释

免疫球蛋白 D（IgD）型多发性骨髓瘤（MM）是一种罕见的浆细胞异常，在多发性骨髓瘤中所占比例低于 2%。多发性骨髓瘤肾损害继发于：脱水、高钙血症、肾脏骨髓瘤、轻链和重链沉积导致肾小管损伤和肾小管内管型形成，阻塞而引起。多发性骨髓瘤诱发的肾病综合征可能引起继发性高胆固醇血症和/或高 TG 血症，含 ApoB 的脂蛋白水平通常升高。

Comment

Oral or intravenous chemotherapy is employed to destroy or control myeloma cells. Radiation may also be used. MM associated dyslipidaemia has been treated with melphalan and prednisolone to reduce the immunoglobins, which produced a concomitant reduction in TC and TG levels.

评论

口服或静脉化疗是杀伤或控制骨髓瘤细胞的标准治疗方案，放疗也可以。与多发性骨髓瘤相关的高脂血症，可采用美法仑和泼尼松龙治疗，降低免疫球蛋白，同时也可降低 TC 和 TG 水平。

References

参考文献

Fukadome K, Kato J, Ohashi T, Yamammoto Y, Eto T. Hyperlipidemia associated with multiple myeloma. Intern Med 1996; 35: 337-340.

Duvic C, Sarret D, De Revel T, Herody M, Didelot F, Labaye J, Nedelec G. IgD myeloma manifesting as acute renal insufficiency. Rev Med Interne 2000; 21: 799-803.

Goldschmidt H, Lannert H, Bommer J, Ho AD. Multiple myeloma and renal failure. Nephrol Dial Transplant 2000; 15: 301-4.

Winearls CG. Acute myeloma kidney. Kidney Int 1995; 48: 1347-1361.

（黎四维译）

CASE N　NEPHROTIC SYNDROME

肾病综合症

History

- 34/M presented with intermittent right loin pain for 5 months and heavy proteinuria. He was found to have nephrotic syndrome and renal biopsy showed focal segmental glomerulosclerosis with chronic tubulointerstitial changes.
- Past history of primary hypothyroidism on thyroxine replacement.
- No improvement in proteinuria after 3 months of prednisolone at reasonable dose.

案例 N

病史

- 34 岁，男性，间歇性腰部右侧疼痛 5 个月，严重蛋白尿。患有肾病综合症，肾活检显示有局灶性节段性肾小球硬化和慢性肾小管间质性变化。
- 曾用甲状腺素替代治疗原发性甲状腺功能减退。
- 适当剂量泼尼松龙治疗蛋白尿 3 个月，无改善。

Lipid Profile

Total Cholesterol　　11.9

Triglycerides	6.0
HDL-C	1.62
LDL-C calc	N/A
LDL-C direct	8.5
Non HDL-C	10.3
Appearance	Slightly Turbid
ApoA1	1.45
ApoB	2.70

血脂结果

总胆固醇, TC	11.9
甘油三酯, TG	6.0
高密度脂蛋白胆固醇, HDL-C	1.62
低密度脂蛋白胆固醇, LDL-C(计算）	N/A
低密度脂蛋白胆固醇, LDL-C(测量)	8.5
非 HDL-C	10.3
外观	轻微混浊
载脂蛋白 A1, Apo A1	1.45
载脂蛋白 B, Apo B	2.70

Lipoprotein Electrophoresis

Markedly elevated apoB - containing lipoproteins (LDL and VLDL) consistent with nephrotic syndrome. No chylomicrons.

脂蛋白电泳

脂蛋白电泳结果（图 16）第 5 号标本符合肾病综合症：

含 ApoB 的脂蛋白（LDL 和 VLDL）显著升高，无乳糜微粒。

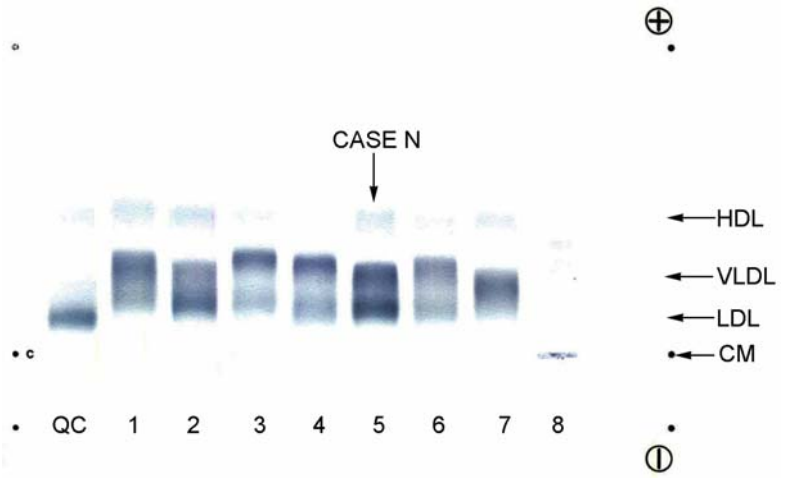


Fig. 16 Nephrotic Syndrome — Markedly elevated apoB - containing lipoproteins (LDL and VLDL)

图 16　肾病综合征—LDL,VLDL 显著升高，无乳糜微粒

Interpretation

Nephrotic syndrome (NS) is a variety of conditions that damage the glomeruli of the kidney. Patients with NS also have mixed hyperlipidaemia (hypercholesterolaemia and hypertriglyceridaemia), which appear to be related to the proteinuria. Albumin, and other key enzymes involved in cholesterol metabolism, are lost through the glomeruli. Changes in lipid and lipoprotein metabolism occur subsequently, the LDL-C is increased often accompanied by a decrease in HDL-C.

解释

肾病综合征（NS）通常是由一组损害肾小球的疾病所致。NS 患者发生混合性高脂血症（高胆固醇血症和高甘油三酯血症）与蛋白尿相关。白蛋白和胆固醇代谢关键酶可通过肾小球丢失，引起脂质和脂蛋白代谢发生改变，导致 LDL-C 升高，并常伴有 HDL-C 降低。

Comment

The dyslipidaemia in patients with NS is not necessarily related to the cause of the damaged glomeruli and may be associated with all lipoprotein phenotypes, except type 1. The dyslipidaemia is a result of increased synthesis of Apo B-containing lipoproteins, with increased conversion of Apo B remnants to LDL. The elevated triglyceride level also may reflect hyperinsulinaemia, caused by acquired insulin resistance, and increased rates of VLDL secretion.

评论

NS 患者血脂异常与肾小球损害的病因没有必然的联系，可能会出现各种脂蛋白电泳图谱表型（1 型除外）。血脂异常是由于含 ApoB 的脂蛋白合成增加，由 ApoB 残粒转变的 LDL 也相应增加。TG 水平升高归因于获得性胰岛素抵抗引起的高胰岛素血症和 VLDL 分泌增加。

Notes

NS can be treated with corticosteroids, immunosuppressive drugs, and in some cases, cytotoxic

agents depending on the underlying cause of the disease. If kidney failure occurs, the patient will need dialysis or a kidney transplant. In addition to addressing the underlying cause, treatment of NS focuses on reducing high cholesterol, blood pressure, and proteinuria. Hypercholesterolaemia typically reverses when the disease resolves, so most patients are initially treated with a lipid lowering drug

注意事项

根据疾病的致病原因不同，NS 可以采用皮质类固醇、免疫抑制药物，在某些情况下可用细胞毒性药物进行治疗。如果出现肾功能衰竭，病人则需要透析或肾移植。除了寻找潜在的致病原因，肾病综合征的治疗重点在于降低高胆固醇、控制高血压和蛋白尿。当疾病好转时，高胆固醇血症通常会缓解。因此大多数患者最初就采用降脂药物治疗。

References

参考文献

Eddy AA, Symons JM. Nephrotic syndrome in childhood. Lancet 2003; 362: 629–639.

Madaio MP, Harrington JT. The diagnosis of glomerular diseases: Acute glomerulonephritis and the nephrotic syndrome. Archives of Internal Medicine 2001;161: 25-34.

Hodson EM, Willis NS, Craig JC. Corticosteroid therapy for nephrotic syndrome in children. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD001533.

DOI: 10.1002/14651858.CD001533.pub4.

Orth, SR, Ritz, E. The nephrotic syndrome [Review]. N Engl J Med 1998; 338: 1202-1211.

Grundy SM; Vega GL. Rationale and management of hyperlipidemia of the nephrotic syndrome. Am J Med 1989; 87(5N):3N-11N.

（黎四维译）

CASE O　OBESITY

肥胖

History

- M/14, obese since the age of 8, presented with symptoms of polyuria and polydipsia for 5 months.
- No family history of obesity. Mother has type 2 diabetes mellitus.
- Weight 126.7 kg, height 177.6 cm.
- Morbid obesity, BMI 40.2 kg/m2
- Investigation confirmed diabetes mellitus

病例 O

病史

- 男性，14 岁，8 岁起肥胖，出现多尿、烦渴症状 5 个月；
- 无肥胖家族史，母亲患有 2 型糖尿病（T2DM）；
- 体重 126.7kg，身高 177.6cm；
- 病态肥胖，体重指数（BMI）为 40.2 kg/m^2 ；
- 确诊为糖尿病。

Lipid Profile

Total Cholesterol	4.7
Triglycerides	5.9
HDL-C	0.65

LDL-C calc	N/A
LDL-C direct	2.3
Non HDL-C	4.1
Appearance	Slightly Turbid
ApoA1	0.97
ApoB	1.02

血脂结果

总胆固醇, TC	4.7
甘油三酯, TG	5.9
高密度脂蛋白胆固醇, HDL-C	0.65
低密度脂蛋白胆固醇, LDL-C(计算）	—
低密度脂蛋白胆固醇, LDL-C(测量)	2.3
非 HDL-C	4.1
外观	轻度混浊
载脂蛋白 A1, Apo A1	0.97
载脂蛋白 B, Apo B	1.02

Lipoprotein Electrophoresis

Increased VLDL and a reduced HDL consistent with insulin resistance of diabetes and obesity.

脂蛋白电泳

脂蛋白电泳结果（图 17）第 8 号标本符合糖尿病胰岛素抵抗及肥胖胰岛素抵抗：VLDL 增高、HDL 降低。

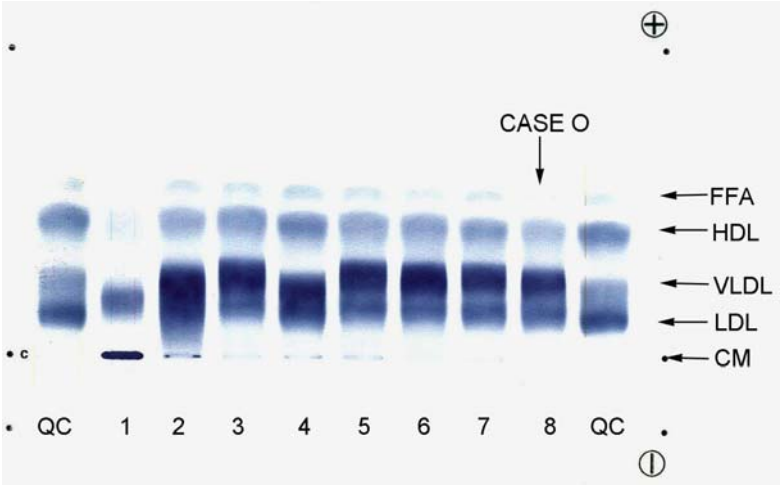


Fig. 17　Obesity —Increased VLDL and a reduced HDL

图 17　肥胖 —VLDL 增高、HDL 降低

Interpretation

Obesity can lead to adverse lipid metabolism that may result in abnormalities of lipoproteins VLDL, LDL and HDL. It has been reported that development of obesity is frequently associated with acquired insulin resistance and or hyperinsulinaemia, especially central obesity. The predominant effect is an overproduction of VLDL particles and an increased secretory rate of Apo B-containing lipoproteins..

解释

肥胖可引起脂代谢不良，致使 VLDL、LDL 和 HDL 异常。胰岛素抵抗和/或高胰岛素血症常常与肥胖相关，尤其是

中心性肥胖。最主要的影响是，与胰岛素抵抗和/或高胰岛素血症相关的 VLDL 颗粒生成过多，胰岛素抵抗可进一步促进含 ApoB 脂蛋白的分泌。

Comment

Overproduction of VLDL can result in hypertriglyceridaemia, which is the most common lipid abnormality associated with obesity. The conversion of VLDL to VLDL remnants and LDL is augmented by an increase in LPL activity and enhanced lipolysis of VLDL-triglyceride. Obesity also frequently associated with a reduced HDL-C and a low Apo A1 level as well..

评论

VLDL 生成过多所致的高 TG 血症，是肥胖者最常见的血脂异常。脂蛋白脂肪酶（LPL）活性增强和 VLDL-甘油三酯分解加速均可促进 VLDL 转化为 VLDL 残粒和 LDL。肥胖是与 HDL-C 和 Apo A1 水平低相关的诸多因素之一。

Notes

In general, patients who have abdominal obesity have greater hypertriglyceridaemia and lower HDL-C levels than those who have peripheral obesity with regard to the degree of insulin resistance. In treating patients with obesity, weight loss would be expected to improve or reverse not only the hypertriglyceridaemia but also the low HDL-C levels. They should also be monitored for development of

the metabolic syndrome..

注意事项

通常，腹部肥胖患者较类似的伴有一定程度胰岛素抵抗的非中心性肥胖患者，有更严重的高 TG 血症和低 HDL-C 水平。减肥可改善或逆转高 TG 血症和低 HDL-C 水平。在治疗病人高 TG 血症的同时应该监测代谢综合征的发展。

References

参考文献

Artz E, Haqq A, Freemark M. Hormonal and metabolic consequences of childhood obesity. Endocrinology and Metabolism Clinics of North America. 2005; 34: 643-658.

Weiss R, Dziura J, Burgert TS, et al. Obesity and the metabolic syndrome in children and adolescents. N Engl J Med 2004; 350: 2362-74.

Dunican KC, Desilets AR, Montalbano JK. Pharmacotherapeutic options for overweight adolescents. Ann Pharmacother 2007; 41: 1445-55.

(沈璠译)

CASE P PARAPROTEINAEMIA

病变蛋白血症

History

- Two illustrative cases are reported below: one falsely low and the other dubiously high HDL-C results. The spurious results seemed to be related to the nature (IgG or IgM) as well as the concentration of the paraproteins.

案例 P

病史

- 以两个案例说明：案例一出现低 HDL-C 的假象，案例二则出现虚高的 HDL-C。这些结果的偏差与病变蛋白的种类（IgG 或 IgM）和浓度有关。

Lipid Profile

	Monoclonal IgG	**Monoclonal IgM**
Total Cholesterol	3.3	2.7
Triglycerides	0.70	0.6
HDL-C	4.27	0.20
LDL-C calc	N/A	2.2
LDL-C direct	1.9	1.8

Non HDL-C	INT	2.1
Appearance	Clear	Clear
ApoA1	1.02	0.73

血脂结果

	单克隆	
	IgG	IgM
总胆固醇, TC	3.3	2.7
甘油三酯, TG	0.7	0.6
高密度脂蛋白胆固醇, HDL-C	4.27	0.2
低密度脂蛋白胆固醇, LDL-C(计算）	—	2.2
低密度脂蛋白胆固醇, LDL-C(测量)	1.9	1.8
非 HDL-C	—	2.1
外观	清亮	清亮
载脂蛋白 A1, Apo A1	1.02	0.73

Lipoprotein Electrophoresis

Lipoprotein electrophoresis of two atypical specimens with monoclonal IgG (lane 2) and IgM (lane 6) paraproteinaemia.

脂蛋白电泳

两份不典型病变蛋白血症的脂蛋白电泳（图 18）第 2、6 号标本结果：泳道 2，单克隆 IgG；泳道 6，单克隆 IgM。

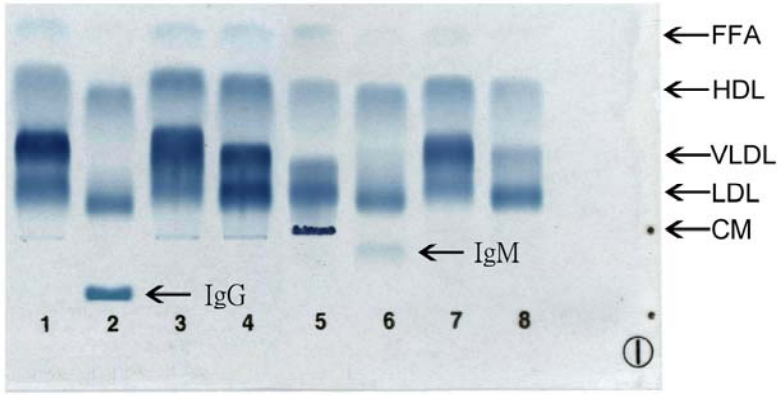


Fig. 18　Paraproteinaemia — IgG and IgM

图 18　病变蛋白血症 —IgG 和 IgM

Interpretation

The first case was a 56-year-old woman with multiple myeloma and a monoclonal paraprotein of IgG/Kappa. The serum IgG concentration was grossly elevated (120 g/L). Initial lipid profile showed a dubious HDL-C of 4.27 mmol/L flagged with an error code LIMTH, prompting to dilution. Subsequent results obtained from the reduced volume mode according to the manufacturer's instructions and by a manual dilution protocol 1:1 with normal saline (9 g/L NaCl) were 0.92 and 0.20 mmol/L, respectively. The result given by the conventional precipitation method (Polyethylene glycol, PEG 8000, Sigma) was 0.80 mmol/L suggesting interference of the paraprotein with the direct HDL-C assay. On agarose gel electrophoresis, an abnormal band was detected at a position cathodic to all the lipoprotein fractions and chylomicrons (lane 2).

案例一：56 岁，女性，多发性骨髓瘤伴有单克隆 IgG/κ。血清 IgG 浓度显著升高（120 g/L）。最初的血脂分析结果 HDL-C 浓度为 4.27 mmol/L，出现 LIMTH 错误信息，提示应将标本稀释后再检测。依照说明书，将标本与生理盐水（9 g/L NaCl）按体积比 1:1 稀释，所测结果分别为 0.92、0.20 mmol/L。常规沉淀法（聚乙二醇，PEG 8000, Sigma）所测结果为 0.80 mmol/L，提示直接检测 HDL-C 受到病变蛋白干扰。琼脂糖凝胶电泳，在所有脂蛋白和乳糜微粒的负极位置出现一条异常条带（泳道 2）。

The second case was a 75-year-old man with foreign body giant cells in the left cheek lump. Agarose gel lipoprotein electrophoresis revealed a normal pattern. But the intensity of the alpha-band was inconsistent with the low HDL level of 0.20 mmol/L in the plasma. An abnormal band was, however, detected at a position close to chylomicrons. The extraneous band was subsequently identified to be a monoclonal IgM/Lambda by immunofixation (lane 6). The serum IgM concentration was 38.2 g/L. The HDL-C result obtained by the PEG precipitation method was 0.60 mmol/L. Employing the Friedewald formula, the estimated HDL-C results in atypical specimens of case 1 and case 2 were 1.08 and 0.63 mmol/L, respectively.

案例二：75 岁，男性，左脸颊肿块中有异物巨细胞。琼脂糖凝胶脂蛋白电泳结果正常，但是 α 带的强度与血浆低 HDL 水平(0.20 mmol/L)不符。在靠近乳糜微粒条带处出现异常条带, 经免疫固定法鉴定为单克隆 IgM/λ（泳道 6）。血清 IgM 浓度为 38.2 g/L。聚乙二醇沉淀法所测的的 HDL-C 浓度为 0.60 mmol/L。根据 Friedewald 公式计算，案例 1 和案例 2 非典型样本的 HDL-C 结果分别是

1.08 和 0.63 mmol/L。

Comment

Since the introduction of the homogeneous HDL-C assays, there have been continuing reports, mostly anecdotal though, of discrepant HDL-C values in atypical specimens generated by the direct measurements and the conventional precipitation methods that might confound treatment decisions. The presence of paraproteins may cause dubious HDL-C results in some plasma specimens due to paraproteins reacting nonspecifically with the PEG-modified enzymes and alpha-cyclodextrin sulfate reagents at different time points during the absorbance measurements. Reports of significant discrepancies deserve further studies. It has been recommeded that an internal laboratory protocol in which any specimen with an undetectable or dubious HDL-C result should automatically undergoes evaluation for a monoclonal gammopathy. Newer HDL-C reagent formulation that could reduce interference from samples with abnormal proteins should be used.

评论

自同质性 HDL-C 测定法问世，陆续有报道：采用直接测量法及常规沉淀法检测非典型样本，多数情况下所得的 HDL-C 结果不一致，干扰治疗方案的制定。在吸光度检测过程中，病变蛋白可以与聚乙二醇修饰的酶类、α -硫酸环糊精试剂发生非特异性反应，导致一些病变蛋白的血浆样本出现可疑的 HDL-C 结果。明显不一致的结果需要进一步分析，推荐那些未检出 HDL-C 或 HDL-C 值可

疑的样本，按照实验操作规程进行单克隆免疫球蛋白病的评估。应采用更新的 HDL-C 检测试剂，减少样品中异常蛋白的干扰。

References

参考文献

Kadri N, Douville P, Lachance P. Monoclonal paraprotein may interfere with the Roche direct HDL-C plus assay. Clin Chem 2002; 48: 964.

Bakker AJ, Zijlstra A, Leemhuis MP. False negative results in the Roche assay for HDL-cholesterol. Ann Clin Biochem 2003; 40: 572–575.

Pang RWC, TamSCF. Novel use of the Friedewald formula to tackle anomalous HDL-C results in two cases of paraproteinaemia Clin Biochem 2004; 37: 238-240.

Hoefner DM. New HDL-cholesterol reagent formulation reduces interference from samples with abnormal proteins. Clin Chim Acta 2006; 374: 142-146.

（余雪琛译）

CASE Q　QUETIAPINE-INDUCED

喹硫平诱导的代谢障碍

History

- Atypical antipsychotics have been associated with significant elevation of serum triglycerides that may be an additional obesity/insulin resistance-related mechanism contributing to the development of type 2 diabetes. The largest increases in triglycerides appear to occur with clozapine, olanzapine and quetiapine. Patients were characterised by the 'atherogenic' metabolic triad comprising hyperinsulinaemia, increased ApoB concentration, and small, dense LDL. Quetiapine is not sufficiently investigated with respect to metabolic side-effects.
- 22/M,
- Known case of Schizophrenia
- History of opioid overdose
- Given artane, fluoxetine and risperidone

案例 Q

病史

- 血浆 TG 显著升高与非典型抗精神病药物有关，可能与肥胖、胰岛素抵抗机制协同作用促进 2 型糖尿病（T2DM）的发展。使用氯氮平、奥氮平和喹硫平 TG 升高最为明显。患者都表现出致动脉粥样化三联征：高胰岛素血症、 ApoB 水平升高、小而密 LDL

增加。目前关于喹硫平在代谢方面副作用的研究还不是很充分。
- 22 岁，男性
- 精神分裂症患者
- 服用过量类吗啡物质
- 给予苯海索，氟西汀和利培酮治疗

Lipid Profile

Total Cholesterol	6.2
Triglycerides	12.3
HDL-C	0.67
LDL-C calc	N/A
LDL-C direct	1.4
Non HDL-C	5.5
Appearance	Lipaemic
ApoA1	0.96
ApoB	1.05

血脂结果

总胆固醇, TC	6.2
甘油三酯, TG	12.3
高密度脂蛋白胆固醇, HDL-C	0.67
低密度脂蛋白胆固醇, LDL-C(计算）	—
低密度脂蛋白胆固醇, LDL-C(测量)	1.4
非 HDL-C	5.5
外观	黄体脂蛋白
载脂蛋白 A1, Apo A1	0.96

载脂蛋白 B, Apo B	1.05

Lipoprotein Electrophoresis

Marked chylomicronaemia syndrome. Certain atypical antipsychotics had adverse effects on lipoprotein metabolism. Full lipid profile should be performed three monthly or during routine health monitoring. This frequency may be decreased depending on the results obtained and the agent used.

脂蛋白电泳 ?????

脂蛋白电泳图谱（图 19）第 3 号标本显示为明显 CM 血症。某些非典型的抗精神病药对脂蛋白代谢具有副作用。应每三个月作一次全面的血脂检查，或在常规健康体检时检查血脂。检查频率可视检查结果及使用药物而适当减少。

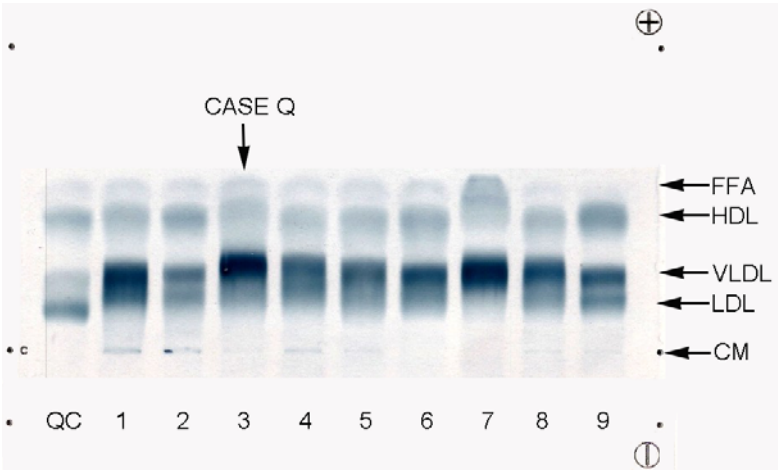


Fig.19 Quetiapine-induced —Marked chylomicronaemia syndrome.

图 19 喹硫平诱导的代谢障碍 — 明显的乳糜微粒血症

Interpretation

Quetiapine is an atypical antipsychotics used to treat schizophrenia and acute manic episodes of bipolar disorder. Some but not all atypical antipsychotics have substantial side effects upon many systems leading to metabolic complications, including obesity, hyperglycemia, insulin resistance; type 2 diabetes, diabetic ketoacidosis, and dyslipidemia. Quetiapine administration has been associated with increases from baseline in plasma cholesterol and triglycerides.

解释

喹硫平是一种非典型抗精神病药，用于治疗精神分裂症

和双相性精神障碍偶发性狂躁症。并非所有的非典型抗精神病药都引起代谢综合征，如肥胖、高血糖、胰岛素抵抗、2 型糖尿病、糖尿病酮症酸中毒和血脂紊乱。喹硫平治疗与血浆胆固醇和 TG 基线水平升高有关。

Comment

Atypical antipsychotics have been associated with hypertriglyceridaemia. Increased insulin resistance in patients after treatment with olanzapine, risperidone or quetiapine has been reported. The hypertriglyceridaemia is modest in patients receiving quetiapine and minimal in those who are on risperidone. However, there has been considerable debate about whether it is the cause or effect of insulin resistance. Baseline and periodic posttreatment monitoring for metabolic complications on all the atypical agents was recommended. Routine monitoring of glucose and lipid profile during treatment with novel antipsychotics should be advocated.

评论

非典型抗精神病药物与高TG血症有关。使用奥氮平、利培酮或喹硫平治疗，胰岛素抵抗增强。喹硫平治疗的患者TG水平中度升高，利培酮治疗的患者TG水平升高幅度最小。但是，关于生活/行为方式或者药物引起胰岛素抵抗是否为疾病的根本原因仍存在争论。推荐所有非典型抗精神病药物使用者监测基线和治疗后的代谢性并发症。建议使用新的抗精神病药的患者在治疗期间进行常规的血糖和血脂水平监测。

References

参考文献

Bobes J, Rejas J, Garcia-Garcia M, et al. Weight gain in patients with schizophrenia treated with risperidone, olanzapine, quetiapine or haloperidol: results of the EIRE study. Schizophr Res. 2003;62:77-88.

Wirshing DA, Boyd JA, Meng LR, Ballon JS, Marder SR, Wirshing WC. The effects of novel antipsychotics on glucose and lipid levels. J Clin Psychiatry 2002; 63: 856-865.

Atmaca M, Kuloglu M, Tezcan E, Ustundag B. Serum leptin and triglyceride levels in patients on treatment with atypical antipsychotics. J Clin Psychiatry 2003; 64: 598-604.

Carnahan RM, Reanteso AA, Teegarden BA, Pogue T. Severe hyperlipidemia associated with olanzapine and quetiapine use. Am J Psychiatry. 2007; 164: 1614-1615.

Casey DE. Dyslipidemia and Atypical Antipsychotic Drugs. J Clin Psychiatry 2004; 65[suppl 18]: 27–35.

(余雪琛译)

CASE R　RHEUMATOID ARTHRITIS

类风湿性关节炎

History

- 77/F, presented with symptoms of rheumatoid arthritis and found to have type 2 diabetes mellitus.
- Currently on OHA, prednisolone, MTx (Methotrexate) and folate.
- Joint pain under fair control with normal CRP.

案例 R

病史

- 77 岁，女性；有类风湿性关节炎症状，T2DM。
- 现正口服降糖药，泼尼松龙，甲氨蝶呤和叶酸。
- 关节疼痛得到很好的控制，C 反应蛋白(CRP)正常

Lipid Profile

Total Cholesterol	5.3
Triglycerides	2.5
HDL-C	0.83
LDL-C calc	3.3
LDL-C direct	N/A
Non HDL-C	4.5
Appearance	Clear

血脂结果

总胆固醇, TC	5.3
甘油三酯, TG	2.5
高密度脂蛋白胆固醇, HDL-C	0.83
低密度脂蛋白胆固醇, LDL-C(计算）	3.3
低密度脂蛋白胆固醇, LDL-C(测量)	—
非 HDL-C	4.5
外观	清亮

Lipoprotein Electrophoresis

Increased VLDL and a reduced HDL consistent with dyslipidaemia of acute phase response to rheumatoid arthritis

脂蛋白电泳

脂蛋白电泳图谱（图 20）第 7 号标本为关节炎急性时相反应的脂代谢紊乱表现： VLDL 升高、HDL 降低。

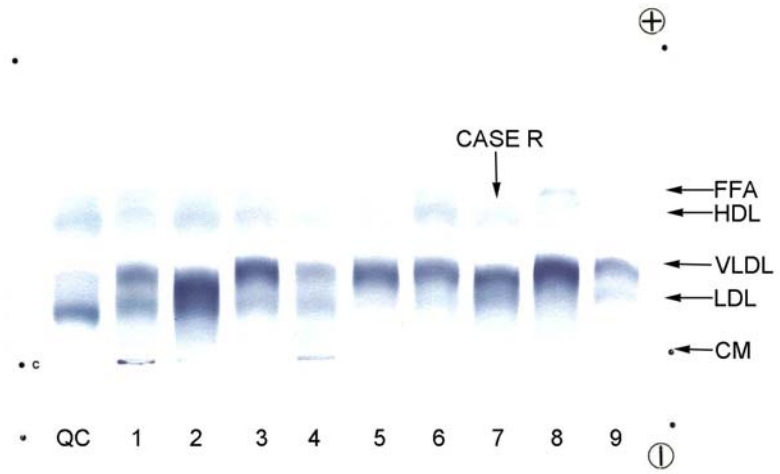


Fig.20 Rheumatoid Arthritis —Increased VLDL and a reduced HDL

图 20 类风湿性关节炎 —VLDL 升高、HDL 降低

Interpretation

Patients with rheumatoid arthritis (RA) have a high prevalence of insulin resistance and dyslipidaemia. This high prevalence could be due to acute phase response to inflammatory arthritis per se. The cause for the dyslipidaemia is not fully understood. The lipid profile of patients with active or untreated RA is primarily characterized by a decrease in serum levels of HDL-C whereas contrasting findings have been reported on TC and LDL-C

解释

类风湿性关节炎（RA）的病人常会伴有胰岛素抵抗和血脂紊乱。虽然关节炎的炎症急性时相反应可以解释这一现象，但却无法完全解释血脂紊乱。未接受治疗和活动期的 RA 病人的主要特点是血清 HDL-C 水平降低、TC 和 LDL-C 水平反而升高。

Comment

The acute phase response in patients suffering from RA and other inflammatory arthritides is associated with low HDL-C, as well as insulin resistance. The cholesterol ester transfer protein (CETP) plays a central role in HDL metabolism. CETP exchanges cholesterol esters with triglycerides between HDL and apo B-containing lipoproteins and thus significantly contributes to the reverse cholesterol transport pathway. It has been reported that patients with RA exhibited significantly higher CETP activity leading to a reduction in HDL-C levels and an atherogenic lipoprotein profile.

评论

类风湿性关节炎（RA）和其他关节炎患者的急性时相反应与HDL-C水平低及胰岛素抵抗相关。CETP在HDL代谢、循环HDL-C水平调节过程起重要作用。CETP参与HDL和含apoB脂蛋白之间的TG与胆固醇酯交换，从而促进胆固醇的逆向转运。研究发现，类风湿性关节炎病人的CETP活性明显升高。CETP活性升高导致HDL-C水平降低，并呈现致动脉粥样硬化的脂质谱。

Notes

The use of disease modifying antirheumatic drugs (DMARDs), methotrexate (MTX) or systemic steroids in controlling the RA disease activity may reduce articular damage. Patients receiving MTX have profound effects on inflammation profile. But MTX also had adverse effects on lipid and lipoprotein metabolism. The use of corticosteroids is associated with dyslipidaemia and hypertension and is potentially atherogenic.

注意事项

使用抗风湿药物(DMARD)，甲氨蝶呤(MTX)或全身性类固醇药物缓解和控制类风湿性关节炎可减少关节损伤。甲氨蝶呤治疗的患者可以有效地控制炎症，但是该药对脂质和脂蛋白代谢有副作用。使用皮质类固醇可引起血脂代谢紊乱和高血压，并具有潜在的致动脉粥样硬化危险。

References

参考文献

Dessein PH, Joffe BI, Stanwix A, Botha AS, Moomal Z. The acute phase response does not fully predict the presence of insulin resistance and dyslipidemia in inflammatory arthritis. J Rheumatol 2002, 24:462-466.

Svenson KL, Lithell H, Hallgren R, Vessby B. Serum lipoprotein in active rheumatoid arthritis and other chronic inflammatory arthritides. Arch Intern Med 1987; 147:1917-1920.

Georgiadis AN, Papavasiliou EC, Lourida ES, Alamanos Y, Kostara C, Tselepis AD, Drosos AA. Atherogenic lipid profile is a feature characteristic of patients with early rheumatoid arthritis: effect of early treatment - a prospective, controlled study. Arthritis Res Ther 2006; 8: R82. This article is online at:
http://arthritis-research.com/content/8/3/R82

Munro R, Morrison E, McDonald AG, Hunter JA, Madhok R, Capell HA. Effect of disease modifying agents on the lipid profiles of patients with rheumatoid arthritis. Ann Rheum Dis 1997, 56:374-377.

(余雪琛译)

CASE S SEPTIC SHOCK

脓毒性休克

History

- 56/F
- ESRD on CAPD, DM
- Lipid profile results unremarkable at last visit
- Septic shock at admission

案例 S

病史

- 56 岁，女性
- 终末期肾衰竭，采用持续性不卧床腹膜透析治疗，糖尿病
- 最近一次复查时血脂结果无明显异常
- 入院时脓毒性休克

Lipid Profile

	Last visit	This admission
Total Cholesterol	5.1	5.7
Triglycerides	1.7	10.7
HDL-C	1.39	<0.10
LDL-C calc	2.9	N/A

LDL-C direct	N/A	<0.1
Non HDL-C	3.7	N/A
Appearance	Clear	Turbid
ApoA1	N/A	<0.25
ApoB	N/A	0.80

血脂结果

	最近一次结果	本次就诊
总胆固醇, TC	5.1	5.7
甘油三酯, TG	1.7	10.7
高密度脂蛋白胆固醇, HDL-C	1.39	<0.10
低密度脂蛋白胆固醇, LDL-C(计算）	2.9	—
低密度脂蛋白胆固醇, LDL-C(测量)	—	<0.1
非 HDL-C	3.7	N/A
外观	清晰	浑浊
载脂蛋白 A1, Apo A1	—	<0.25
载脂蛋白 B, Apo B	—	0.80

Lipoprotein Electrophoresis

Marked chylomicronaemia syndrome. The faint alpha-band is consistent with the low plasma HDL-C and ApoA1 levels.

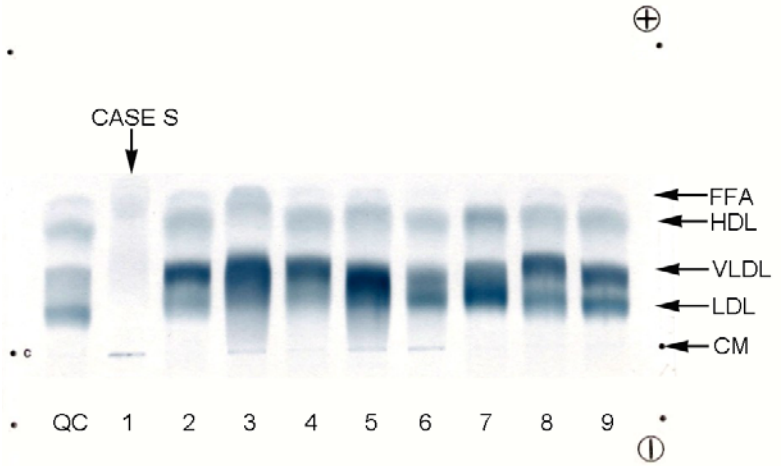


Fig. 21 Septic shock—Marked chylomicronaemia syndrome

图 21　脓毒性休克—乳糜微粒血症

脂蛋白电泳

脂蛋白电泳图谱（图 21）第 1 号标本可见：明显的高 CM 血症。微弱的 α 条带与血浆中低浓度的 HDL-C 和 ApoA1 结果一致。

Interpretation

Sepsis has been defined as the systemic inflammatory response to infection. Patients with bacterial infections and viral infections who exacerbated their inflammatory state have increased plasma triglyceride levels. Multiple cytokines increase plasma triglyceride levels suggesting that hypertriglyceridaemia is a very sensitive response of the host to infection. Plasma triglyceride levels increase from

overproduction of VLDL in adipose tissue, increased hepatic fatty acid synthesis, and suppression of fatty acid oxidation. With more severe infection, VLDL clearance decreases secondary to decreased lipoprotein lipase and Apo E in VLDL. Significantly lower plasma levels of HDL-C and Apo A1 are associated with septic shock. HDL binds and neutralizes the bioactivity of the potent bacterial lipids, lipopolysaccharide (LPS) and lipoteichoic acid that stimulate host innate immune responses. HDL is generally thought to be anti-inflammatory in health and disease..

解释

脓毒血症是指感染引起的全身性炎症反应。细菌感染和病毒感染的病人血浆 TG 浓度升高。多种细胞因子可使血浆 TG 水平升高，表明高 TG 血症是宿主对感染的一种非常敏感的生理性反应。VLDL 分泌增多所致的血浆 TG 水平升高是由于脂肪组织脂解、肝脏脂肪酸合成增加和脂肪酸氧化受抑。随着感染进一步加重，VLDL 清除率下降继发于脂蛋白脂酶和 VLDL 中的 Apo E 减少。炎性休克病人血浆中 HDL-C 和 Apo A1 浓度明显降低。HDL 能够结合及中和有生物活性的细菌脂质(脂多糖 LPS 和磷壁酸脂)，刺激宿主的天然免疫反应。HDL 在健康人和感染性疾病患者体内均有抗炎作用。

Comment

Not much is currently known about lipoproteins and its role in septic shock. Many studies have suggested that lipoproteins play key roles in promoting innate immunity against invading microorganisms. The beneficial effects of

lipoproteins in sepsis may be related to their capability to neutralize LPS and lipoteichoic acid, which are bacterial toxins. Of all lipoproteins, HDL has the highest binding capacity for LPS and lipoteichoic acid. Decreased plasma levels of HDL-C and Apo A1 may indicate a poor prognosis. Although the exact mechanism has not been fully elucidated, one hypothesis proposes that HDL is decreased because of massive release of endotoxin and subsequent increased consumption of HDL. Another possibility is that high concentrations of proinflammatory cytokines suppress lipoprotein production during sepsis.

评论

目前，对于脂蛋白及其在脓毒性休克中的作用尚不清楚。最近，很多研究涉及脂蛋白与 LPS 天然免疫——宿主防御微生物入侵的第一道防线。脓毒血症时，脂蛋白的作用与其中和细菌毒素（LPS 和磷壁酸脂）的能力有关。血浆 HDL 和 ApoA1 水平的降低可能指示不良预后。虽然确切的机制尚未完全阐明，一种假说提出，由于大量内毒素的释放和 HDL 的相继消耗导致了 HDL 的减少。另一种可能是在脓毒血症时，高浓度的促炎症反应细胞因子可抑制脂蛋白的合成。

References

参考文献

Navab M, Anantharamaiah G.M, Fogelman AM. The role of high-density lipoprotein in inflammation. Trends Cardiovasc Med 2005; 15: 158-161.

Chien, JY, Jerng JS,. Yu CJ, Yang PC. Low serum level of high-density lipoprotein cholesterol is a poor prognostic factor for severe sepsis. Crit Care Med 2005; 33: 1688-1693.

Alvarez C, Ramos A. Lipids, lipoproteins, and apoproteins in serum during infection. Clin Chem 1986; 32: 142-145.

Wu A, Hinds CJ, Thiemermann C. High-density lipoproteins in sepsis and septic shock: metabolism, actions, and therapeutic applications. Shock 2004; 21: 210-221.

Barter PJ, Nicholls S, Rye KA, Anantharamaiah GM, Navab M, Fogelman AM. Antiinflammatory properties of HDL. Circ Res 2004; 95: 764-772.

Movva R, Rader DJ. Laboratory Assessment of HDL Heterogeneity and Function. Clin Chem 2008; 54: 788-800.

Cohen J. The immunopathogenesis of sepsis. Nature 2002; 420**:** 885-891.

(孙力译)

CASE T　TOXIC ACUTE TUBULAR NECROSIS

中毒性急性肾小管坏死

History

- 49/M
- Old TB, BPH
- fever for few days
- malaise, runny nose
- taken herbs and voltaren with subjective decreased urine output
- referred for acute renal failure

案例 T

病史

- 49 岁，男性
- 陈旧性结核，良性前列腺增生
- 发烧数日
- 全身乏力，流鼻涕
- 服用中草药和扶他林片，自觉尿排出量减少
- 诊断为急性肾功能衰竭

Lipid Profile

Total Cholesterol	7.0
Triglycerides	5.0
HDL-C	0.19
LDL-C calc	N/A

LDL-C direct	1.1
Non HDL-C	6.9
Appearance	Turbid
ApoA1	0.25
ApoB	0.95
Lp(a)	<20

血脂结果

总胆固醇, TC	7.0
甘油三酯, TG	5.0
高密度脂蛋白胆固醇, HDL-C	0.19
低密度脂蛋白胆固醇, LDL-C(计算）	—
低密度脂蛋白胆固醇, LDL-C(测量)	1.1
非 HDL-C	6.9
外观	浑浊
载脂蛋白 A1, Apo A1	0.25
载脂蛋白 B, Apo B	0.95
脂蛋白(a), Lp(a)	<20

Lipoprotein Electrophoresis

Lipoprotein agarose gel electrophoresis showed that the beta-lipoprotein fraction was more negatively charged and moved relatively faster toward the anode than the control subjects. The faint (nearly absent) alpha-fraction was in agreement with the low HDL-C and Apo A1 levels. No evidence of paraprotein interference with the direct HDL/LDL assays. The presence of LPX is unlikely (in view of the normal Apo B). LDL particles are heterogeneous with regard to their chemical and physical properties. The patient

had toxic nephropathy and ATN with recent nonsteroidal anti-inflammatory drug (NSAID) and herbal use. The lipoprotein metabolism is specifically altered by the effects of drugs. Re-testing after abstinence from herbs and NSAIDs that may affect the oxidation status is recommended because altered electromobilities may represent a crude index for chemical changes in LDL.

脂蛋白电泳

脂蛋白琼脂糖凝胶电泳结果（图 22）第 8、9 号标本显示：与对照相比，患者 β-脂蛋白带有更多负电荷，向阳极迁移较快。微弱的（几乎没有）α 带与低 HDL-C 和 ApoA1 水平一致。无

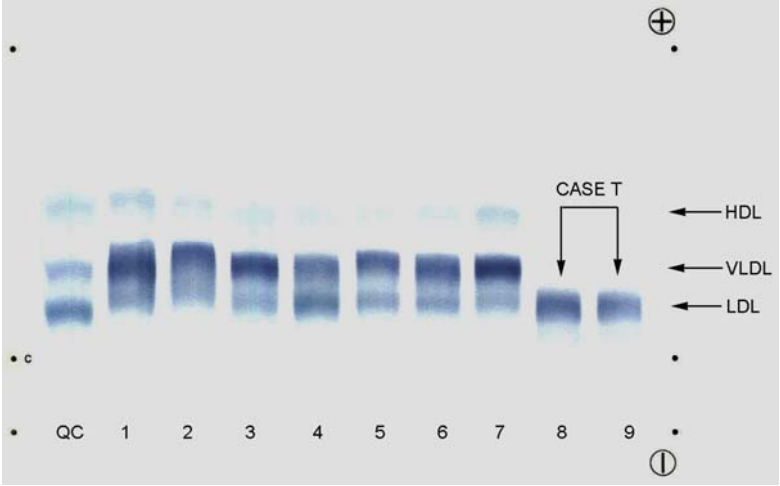


Fig.22　Toxic ATN —beta-lipoprotein fraction

图 22　中毒性急性肾小管坏死 —β-脂蛋白

证据表明病变蛋白干扰 HDL/LDL 的直接检测分析。ApoB 结果正常，说明不存在 LpX。LDL 颗粒因其化学和物理性质而存在异质性。患者近期使用了类固醇消炎药(NSAID)和中草药，有中毒性肾病和急性肾小管坏死。药物作用明显影响脂蛋白的代谢。建议在停用影响氧化代谢的类固醇消炎药和中草药后重新检测，因为电泳迁移率的改变只是 LDL 化学改变的粗略指标。

解释

中毒性急性肾小管坏死（ATN）可由药物（如抗生素、细胞增殖抑制剂）、有毒中草药以及化学品的毒性所致。急性肾功能衰竭（ARF）也可以由内毒素引起，如游离血红蛋白或肌红蛋白，患者血脂异常的主要原因是脂肪分解异常。研究发现，高 TG 血症患者的 LDL、或体外通过交换 VLDL 中的胆固醇酯合成的 LDL 均富含 TG。琼脂糖凝胶电泳迁移率取决于 LDL 表面电荷的密度，影响 LDL 表面电荷的生化试剂仍有待研究。血浆高浓度 LP（a），可导致 LDL 的电荷差异。但是，该患者 Lp(a) 的水平低于 20 mg/L，不可能因 Lp(a) 导致 LDL 电荷改变。

Comment

Toxic lymphokines of interstitial inflammation might be implicated by high or prolonged dosing of NSAIDs. Elevated fasting triglyceride levels increase the triglyceride content of LDL in a process mediated by the action of plasma lipid-transfer proteins. The patient had toxic nephropathy and ATN with recent NSAID and herbal use. Patients with ATN may be more likely to develop insulin

resistance due to loss of renal function. Impaired hepatic lipase (HL) activity may result in an enrichment of LDL and HDL particles with triglycerides and depleted in CE. The accumulation of such large, buoyant, triglyceride-rich LDL-like particles may in turn produce changes in the physical properties of the lipoprotein surface and core, and thus the mobility on electrophoresis. Avoid nephrotoxic agents (NSAIDs/toxic herbs), as they may delay recovery of the tubular function.

评论

淋巴毒性慢性间质性肾炎可能与大剂量或长期使用非类固醇性抗炎药物有关。空腹TG水平升高使得LDL中TG含量增加，其过程由血浆脂质转移蛋白介导。患者近期使用了类固醇消炎药和中草药，并有中毒性肾病和急性肾小管坏死。由于肾脏代谢功能丧失，急性肾小管坏死的患者更容易发展为胰岛素抵抗。肝酯酶活性受损导致富含TG、缺失胆固醇酯的LDL和HDL颗粒增加。这些大而轻、富含TG的LDL样颗粒的积累，导致脂蛋白的表面和核心的物理性质发生改变，从而影响电泳迁移率的变化。应尽量避免使用肾毒性药物（非类固醇性抗炎药、有毒中草药），因为这些药物会延缓肾小管功能的恢复。

References

参考文献

Sevanian A, Bittolo-Bon G, Cazzolato G, Hodis H, Hwang J, Zamburlini A, Maiorino M, Ursini F. Electronegative LDL is a lipid hydroperoxide-enriched circulating lipoprotein. J Lipid Res 1997; 38: 419–428.

La Belle M, Blanche PJ, Krauss RM. Charge properties of low density lipoprotein subclasses. J Lipid Res 1997; 38: 690-700.

Sherman MB, Orlova EV, Decker G.L, Chiu W, Pownall HJ. Structure of triglyceride-rich human low-density lipoproteins according to cryoelectron microscopy. Biochemistry 2003; 42: 14988–14993.

Gill N, Nally Jr JV, Fatica RA. Renal failure secondary to acute tubular necrosis: epidemiology, diagnosis, and management. Chest 2005; 128: 2847-2863.

Epstein M. Non-steroidal anti-inflammatory drugs and the continuum of renal dysfunction. J Hypertens Suppl 2002; 20: S17-S23.

Wojcikowski K, Johnson DW, Gobe G. Medicinal herbal extracts - renal friend or foe? Part one: the toxicities of medicinal herbs. Nephrology (Carlton) 2004; 9:313-318.

Clive DM, Stoff JS. Renal syndromes associated with nonsteroidal antiinflammatory drugs. N Engl J Med 1984; 310: 563–572.

Henrich WL. Nephrotoxicity of several newer agents. Kidney Int 2005; 67 (Suppl): S107–S109.

Rossert J. Drug-induced acute interstitial nephritis. Kidney Int 2001; 60: 804–817.

Kwan TH, Tong MKH, Leung KT, Lai CK, Poon WT, Chan YW, Lo WH, Au TC. Acute renal failure associated with prolonged intake of slimming pills containing anthraquinones. Hong Kong Med J 2006; 12: 394-397.

Isnard Bagnis C, Deray G, Baumelou A, Le Quintrec M, Vanherweghem JL. Herbs and the kidney. Am J Kidney Dis 2004; 44: 1-11.

(黎四维译)

CASE U UNCONTROLLED TYPE 2 DIABETES

控制不良的 2 型糖尿病

History

- 48/M, travel agent.
- Chronic smoker.
- History of type 2 DM >20 years with triopathy
- Ischemic cardiomyopathy, poorly controlled DM
- HbA1c 17.8%, glucose 32.3 mmol/L.
- RFT was normal except mild hyponatraemia (possibly pseudohyponatraemia caused by hypertriglyceridaemia and the hyperglycaemia per se)
- Declined ICD after seeing family doctor.
- FU Medical with drugs.

病例 U

病史

- 48 岁，男性，旅行社工作；
- 长期吸烟；
- 患 2 型糖尿病（T2DM）20 余年，伴随视网膜病变、神经病变和肾脏病变；
- 缺血性心肌病，糖尿病控制不佳；
- 糖化血红蛋白（HbA1c） 17.8%，血糖 32.3 mmol/L;
- 肾功能检查除轻度低钠血症外均正常（可能是高甘油三酯（TG）血症和高糖血症引起的假性低钠血

症）；

- 家庭医生检查后病人不接受植入式心律转复除颤器；
- 转内科复诊及药物治疗。

Lipid Profile

Total Cholesterol	7.5
Triglycerides	6.7
HDL-C	0.92
LDL-C calc	N/A
LDL-C direct	4.3
Non HDL-C	6.6
Appearance	Slightly Turbid
ApoA1	1.26
ApoB	1.63

血脂结果

总胆固醇, TC	7.5
甘油三酯, TG	6.7
高密度脂蛋白胆固醇, HDL-C	0.92
低密度脂蛋白胆固醇, LDL-C(计算）	N/A
低密度脂蛋白胆固醇, LDL-C(测量)	4.3
非 HDL-C	6.6
外观	微混浊
载脂蛋白 A1, Apo A1	1.26
载脂蛋白 B, Apo B	1.63

Lipoprotein Electrophoresis

Markedly elevated apo B-containing lipoproteins (LDL and VLDL). Diabetes should be monitored optimally to reverse the dyslipidaemia.

脂蛋白电泳

脂蛋白电泳图谱（图 23）第 1 号标本显示：含 apo B 脂蛋白（LDL 和 VLDL）明显升高。糖尿病患者应监测血脂水平，以理想控制脂代谢紊乱。

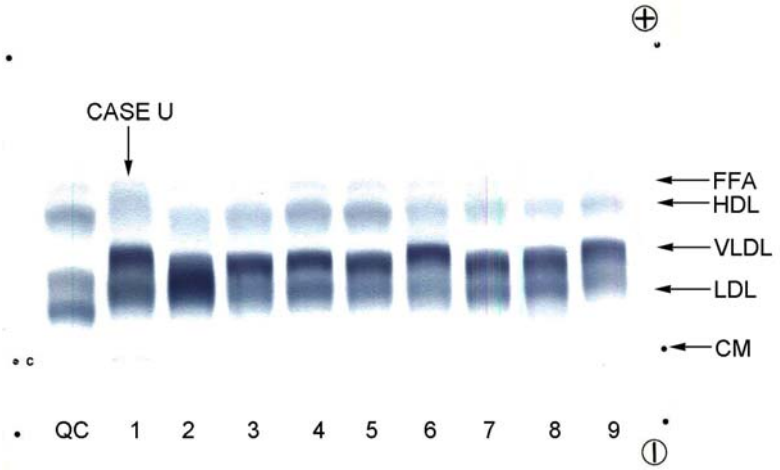


Fig. 23 Uncontrolled T2DM —Markedly elevated LDL and VLDL

图 23 控制不良的 2 型糖尿病—LDL 和 VLDL 明显升高

Interpretation

Dyslipidaemia is associated with poor glycaemic control, most notably for increased triglyceride and decreased

HDL-C levels. Even if concentration of LDL-C is not significantly increased, however, type 2 diabetic patients typically have a preponderance of smaller, denser LDL particles, which are potentially atherogenic. The underlying abnormality responsible for all these changes is insulin resistance.

解释

血糖控制不佳的糖尿病患者脂代谢紊乱常表现为 TG 水平升高和 HDL-C 水平降低，LDL-C 水平升高或许不明显。然而，T2DM 以小而密 LDL 升高为主，即使 LDL-C 水平升高不明显，也会增加动脉粥样硬化发生的风险。胰岛素抵抗是这些代谢异常的根本原因。

Comment

Poor glycemic control refers to persistently elevated blood glucose and HbA1c levels over months and years before severe complications occur. Insulin deficiency reduces lipoprotein lipase (LPL) activity and results in defective removal of triglyceride-rich lipoproteins. Low cholesteryl ester transfer protein (CETP) is observed in type 2 diabetics while its activity tends to be higher in patients with type 1 diabetes. CETP mediates the exchange of cholesteryl esters in HDL particles for triglycerides in VLDL particles. It plays a critical role in reverse cholesterol transport pathway. However, CETP produces VLDL particles that are enriched with cholesteryl-ester and decreases HDL-C levels. Reduced HDL-C levels may also be due to increased catabolism, resulting from increased hepatic triglyceride lipase action of HDL particles with higher triglyceride content.

评论

血糖控制不佳是指血糖和 HbA1c 水平持续慢性升高，数月或数年后即可发生严重并发症。胰岛素缺陷使脂蛋白脂肪酶（LPL）活性降低，导致富含 TG 脂蛋白的清除障碍。T2DM 患者的胆固醇酯转移蛋白（CETP）水平低，但活性较 1 型糖尿病高。CETP 介导 HDL 颗粒中胆固醇酯与 VLDL 颗粒中 TG 的交换，在胆固醇的逆向运输中起有重要作用。然而，通过 CETP 生成的 VLDL 颗粒富含胆固醇酯，并最终导致 HDL-C 水平降低。HDL-C 水平低归因于肝酯酶对 TG 含量较高的 HDL 颗粒的代谢作用加强。

Notes

Levels of HbA1c offer a good indication of the lipid profile of patients with type 2 diabetes. The combination of statin and fibrate results in improvement in all aspects of diabetic dyslipidaemia. Improved glycaemic control can be very effective to reduce TG levels; however, complete reversal of dyslipidaemia is usually unachievable.

注意事项

HbA1c 水平可很好地反应 T2DM 的血脂情况。他汀和贝特类药物联合使用可以全面改善糖尿病血脂紊乱，非常有效地降低 TG 水平。然而，通过改善高血糖的控制来完全逆转血脂紊乱通常难以实现。

References

参考文献

Goldberg IJ: Diabetic dyslipidemia: causes and consequences. J Clin Endocrinol Metab 2001; 86: 965-971.

Perez A, Caixas A, Carreras G, Mauricio D, Pou JM, Serrat J, Gomez-Gerique J, de Leiva A. Lipoprotein compositional abnormalities in type I diabetes: effect of improved glycaemic control. Diabetes Res Clin Pract 1997; 36: 83-90.

American Diabetes Association: Standards of medical care in diabetes: 2011. Diabetes Care 2011; 34 (Suppl.1): S11–S61.

Idzior-Walus B, Mattock MB, Solnica B, Stevens L, Fuller JH. Factors associated with plasma lipids and lipoproteins in type 1 diabetes mellitus: the EURODIAB IDDM Complications Study. Diabet Med 2001; 18: 786-796.

Krentz AJ: Lipoprotein abnormalities and their consequences for patients with type 2 diabetes. Diabetes Obes Metab 2003; 5 (Suppl.1): S19-S27.

(沈璠译)

CASE V VIRAL HEPATITIS

病毒性肝炎

History

- 55/M
- HBV positve
- History of HCC with cadaveric liver transplant in China 4 years ago
- Lipid profile results unremarkable at last visit
- Recurrent hepatitis B and deranged liver function at admission
- USG: Parenchymal change in transplant liver

案例 V

病史

- 55 岁，男性
- HBV 阳性
- 4 年前因肝细胞癌在中国接受尸体肝脏移植
- 最后一次血脂检查结果无明显异常
- 因乙型肝炎复发、肝功能紊乱就诊
- 超声检查：移植肝脏内实质性病变

Lipid Profile

	Last visit	**This visit**

Total Cholesterol	4.9	2.4
Triglycerides	1.2	1.5
HDL-C	0.98	0.13
LDL-C calc	3.3	1.5
LDL-C direct	N/A	N/A
Non HDL-C	3.9	2.2
Appearance	Clear	Clear
ApoA1	N/A	0.25
ApoB	N/A	0.83

血脂结果

	最近一次结果	本次就诊
总胆固醇, TC	4.9	2.4
甘油三酯, TG	1.2	1.5
高密度脂蛋白胆固醇, HDL-C	0.98	0.13
低密度脂蛋白胆固醇, LDL-C(计算）	3.3	1.5
低密度脂蛋白胆固醇, LDL-C(测量)	—	—
非 HDL-C	3.9	2.2
外观	清亮	清亮
载脂蛋白 A1, Apo A1	—	0.25
载脂蛋白 B, Apo B	—	0.83

Lipoprotein Electrophoresis

A reduced HDL-C consistent with hepatic dysfunction of recurrent HBV infection

脂蛋白电泳

脂蛋白电泳图谱（图 24）第 3 号标本为复发性乙肝病毒（HBV）感染表现： HDL-C 水平下降。

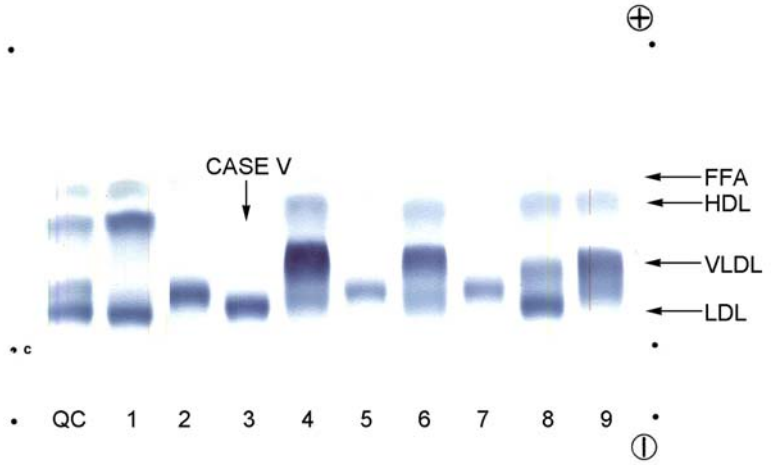


Fig. 24 Viral Hepatitis — Reduced HDL-C

图 24 病毒性肝炎 —HDL-C 水平下降

Interpretation

Viral hepatitis is often associated with a reduced plasma HDL-C since the liver is the major site of HDL synthesis. Hepatic injury also leads to impaired synthesis or excretion of two key enzymes: 1) Lecithin cholesterol acyltransferase (LCAT), which is responsible for all lipoprotein cholesteryl esterification; and 2) Hepatic triglyceride lipase, located in hepatic endothelial cells, plays a unique role in the conversion of IDL to LDL, as well as in the regulation of HDL. Hepatic dysfunction differs from most other causes of secondary dyslipidaemia in that the alterations in lipoproteins are not only present in abnormal amounts but is

also associated with abnormal composition, appearance and electrophoretic mobility.

解释

病毒性肝炎与 HDL-C 的减少有关，因为肝脏是 HDL 合成的主要场所。肝损伤导致两个关键酶的合成或排泄受损：第一，负责脂蛋白胆固醇酯化反应的卵磷脂胆固醇酰基转移酶(LACT)；第二，位于肝脏内皮细胞，在 IDL 转换为 LDL 以及 HDL 的调节过程中起着独特作用的甘油三酯脂酶。肝功能障碍导致血浆脂质、脂蛋白发生改变并不同于其他原因所致的继发性血脂紊乱，不仅表现在数量的异常而且也经常表现为成份、外观和电泳迁移率的改变。

Comment

Patients suffering from viral hepatitis often present features of liver inflammation and deranged LFT. It is well established that chronic inflammation causes a reduction of LDL-C, and, to some extent, HDL-C. Depending on the kind of viral infection involved (HBV or HCV), endogenous cytokines have been related to changes in plasma lipid and lipoprotein composition

评论

病毒性肝炎感染者经常表现为肝炎和肝功能受损。已经证实慢性炎症可以引起 LDL-C 下降，甚至在某种程度上导致 HDL-C 降低。内源性细胞因子与血脂及脂蛋白成分

的变化有关，并取决于感染病毒种类（HBV 或 HCV）。

Notes

Liver plays a key role in the metabolism of plasma lipids, lipoproteins and apolipoproteins. It has been suggested that the lipid profile results in patients suffering from viral hepatitis may reflect the hepatic cellular impairment status. Decreased plasma levels of cholesterol and apoA1 may indicate a poor prognosis.

注意事项

肝脏在血脂、脂蛋白和载脂蛋白的代谢中至关重要。病毒性肝炎感染者的血脂结果可以反映肝细胞的损伤情况。血浆胆固醇与 apoA1 水平降低可能是预后不良的征兆。

References

参考文献

Colombo E, Mauri A, Scapaticci R, Bosoni AM, Bertella M, Nutta G. Clinical significance of HDL-cholesterol variations in viral hepatitis. Arch Sci Med (Torino) 1982; 139**:**187-191.

Su TC, Lee YT, Cheng TJ, Chien HP, Wang JD. Chronic hepatitis B virus infection and dyslipidemia. J Formos Med Assoc 2004; 103: 286-291.

Siagris D, Christofidou M, Theocharis GJ, Papadimitriou C, Lekkou A, Thomopoulos K, Starakis I, Tsamandas AC, Labropoulou-Karatza C. Serum lipid pattern in chronic hepatitis C: histological and virological correlations. J Viral Hepat 2006; 13: 56-61.

Andre P, Perlemuter G, Budkowska A, Brechot C, Lotteau V. Hepatitis C virus particles and lipoprotein metabolism. Semin Liver Dis 2005; 25: 93-104.

(鲁双艳译)

CASE W　WILSON'S DISEASE

威尔逊病

History

- 47/F
- Work in nursing home (cleaner)
- Nondrinker, Nonsmoker
- Admitted for Child's C liver cirrhosis complicated by gastric varices, heptic encephalopathy and and ascites with associated splenomegaly and acute hepatic decompensation.
- HBsAg negative
- HBsAb positive; HCV negative; AFP normal
- Ceruloplasmin ↓; urine copper ↑; started pencillamine 250 mg daily
- Diagnosed Wilson's disease with Kayser-Fleischer (KF) ring and Child's C cirrhosis pending liver transplantation

病例 W

病史

- 47 岁，女性；
- 家政工作（清洁工）；
- 不饮酒，不抽烟；
- 患有丙型肝炎肝硬化，肝硬变按 Child 等级分类为 C 级。因脾肿大和急性肝功失代偿并发胃底静脉曲张、

肝性脑病变和腹水而入院；

- 乙肝表面抗原（HBsAg）阴性
- 乙肝表面抗体（HBsAb）阳性; 丙肝病毒（HCV） 阴性；甲胎蛋白（AFP）水平正常
- 血浆铜蓝蛋白↓；尿铜↑；开始使用青霉胺每日剂量为 250 毫克；
- 诊断：威尔森氏症伴凯瑟-弗莱舍（KF）环、Child C 级肝硬化待肝移植

Lipid Profile

Total Cholesterol	2.0
Triglycerides	0.9
HDL-C	0.44
LDL-C calc	1.2
LDL-C direct	N/A
Non HDL-C	1.6
Appearance	Clear
ApoA1	<0.25
ApoB	<0.35

血脂结果

总胆固醇, TC	2.0
甘油三酯, TG	0.9
高密度脂蛋白胆固醇, HDL-C	0.44
低密度脂蛋白胆固醇, LDL-C(计算）	1.2
低密度脂蛋白胆固醇, LDL-C(测量)	N/A
非 HDL-C	1.6
外观	清亮

载脂蛋白 A1, Apo A1	<0.25
载脂蛋白 B, Apo B	<0.35

Lipoprotein Electrophoresis

A reduced HDL consistent with the faint alpha-lipoprotein fraction in patients with cirrhosis.

脂蛋白电泳

脂蛋白电泳结果（图 25）第 5 号标本为肝硬化患者表现，HDL 水平降低及微量 α-脂蛋白。

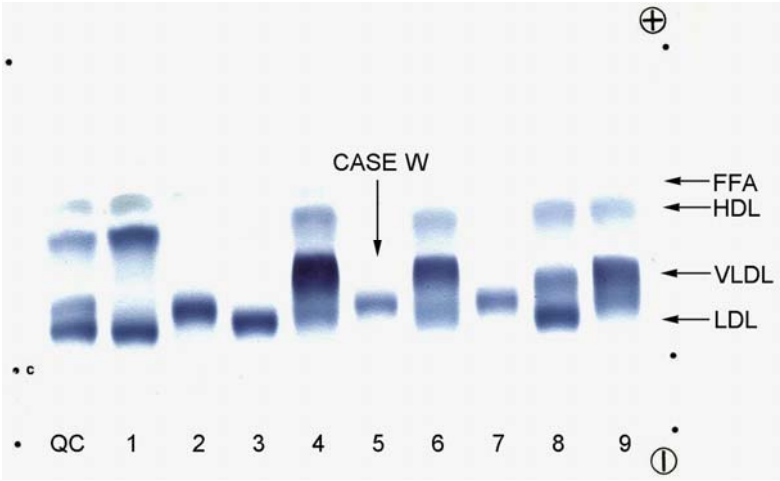


Fig. 25　Wilson’s Disease — Reduced HDL

图 25　威尔逊病 — HDL 水平降低

Interpretation

Wilson's disease is a rare cause of liver cirrhosis. Cirrhosis usually develops after years of liver inflammation. Hepatic injury slows the processing of nutrients, hormones, drugs, and toxins by the liver. It is well known that liver plays a key role in serum lipoprotein synthesis and metabolism, and that chronic inflammation causes hypocholesterolaemia. Many patients with Wilson's disease who are cirrhotic have a reduction of LDL; and, to some extent, HDL, although it is usually mild.

解释

威尔森氏症是肝硬化的一种罕见起因。肝硬化通常发生在肝炎之后的几年内。肝组织受损使得营养物质、激素、药物和毒素在肝脏中的代谢减缓。众所周知，肝脏在血清脂蛋白合成和代谢中非常关键，慢性炎症往往引起低胆固醇血症。很多威尔森氏症患者都伴有肝硬化，脂代谢受损而导致 LDL 降低，在某种程度上 HDL 也降低，尽管是轻度的。

Comment

Cirrhotics are both hypolipidaemic and hypermetabolic. The hypolipidaemic state may be due to the fact that cirrhosis is a diffuse parenchymal disease causing poor hepatic synthesis of lipids and lipoproteins. Increased energy needs may produce a hypermetabolic response by increased utilization of lipid stores. The liver plays a crucial role in production and degradation of lipoproteins. Declining lipoprotein cholesterol may reflect deteriorating liver function. It has been reported that all plasma lipids (TC, VLDL, LDL, HDL and TG) were significantly lower in

cirrhotics. Their adipose tissues and lipid metabolism are insensitivity to insulin.

评论

肝硬化患者处于一种低脂血症和高代谢状态。低脂血症可能是由于肝硬化这种弥漫性实质病变引起肝脏脂质和脂蛋白合成不足所致。能量需求增加，产生高代谢反应，导致存储脂质利用增加。肝脏在脂蛋白的生成和降解过程中起着关键作用。脂蛋白胆固醇降低可反映肝功能恶化。据报道，肝硬化患者血脂（TC, VLDL, LDL和TG）显著降低。此外，肝硬化患者的脂肪组织和脂质代谢对胰岛素不敏感。

References

参考文献

Ala A, Walker AP, Ashkan K, Dooley JS, Schilsky ML. Wilson's disease. Lancet 2007; 369: 397-408.

Miller JP: Dyslipoproteinaemia of liver disease**.** Baillieres Clin Endocrinol Metab 1990; 4: 807-832.

Kaye GL, Kruszynska YT, Harry DS, Heslop K, Johnston DG, McIntyre N. Lipid metabolism and insulin resistance in cirrhosis. J Hepatol 1994; 20: 782-791.

(沈璠译)

CASE X　LIPOPROTEIN-X (LP-X)

脂蛋白 X

History

- 2/F
- History of biliary atresia
- Post-Kassai operation with no improvement of liver function, persistent cholestasis
- Work up for Aligalle syndrome
- Total bilirubin 187 umol/L, Delta bilirubin 76 umol/L

案例 X

病史

- 2 岁，女性
- 胆道闭锁
- 卡萨伊手术后没有改善肝功能，持久性胆汁淤积
- 视为 Aligalle 综合征
- 总胆红素= 187 umol / L，δ 胆红素= 76 umol / L

Lipid Profile

Total Cholesterol	21.2
Triglycerides	2.9
HDL-C	1.34
LDL-C calc	18.5

LDL-C direct	3.8
Non HDL-C	19.8
Appearance	Clear
ApoA1	0.56
ApoB	1.39

血脂结果

总胆固醇, TC	21.2
甘油三酯, TG	2.9
高密度脂蛋白胆固醇, HDL-C	1.34
低密度脂蛋白胆固醇, LDL-C(计算）	18.5
低密度脂蛋白胆固醇, LDL-C(测量)	3.8
非 HDL-C	19.8
外观	清亮
载脂蛋白 A1, Apo A1	0.56
载脂蛋白 B, Apo B	1.39

Lipoprotein Electrophoresis

Abnormal beta-lipoprotein which migrates to the cathode was noted, likely to be lipoprotein X (LP-X) that cannot be detected by direct LDL-C assay and corresponds to the discordant LDL-C (direct vs calculation), and a disproportionately (relatively) low apo B results. Albumin bound (delta) bilirubin was also evident in the free fatty acid region near the anode.

脂蛋白电泳

脂蛋白电泳图谱（图 26）第 4 号标本可见：迁移至负极的异常 ß 脂蛋白，可能是脂蛋白 X (LP-X)，它不能通过直接测定 LDL-C 的方法检测，可引起直接测定的 LDL-C 与计算的 LDL-C 结果不一致，与低 apoB 的结果也不成比例；阳极附近游离脂肪酸区域白蛋白结合胆红素也很明显。

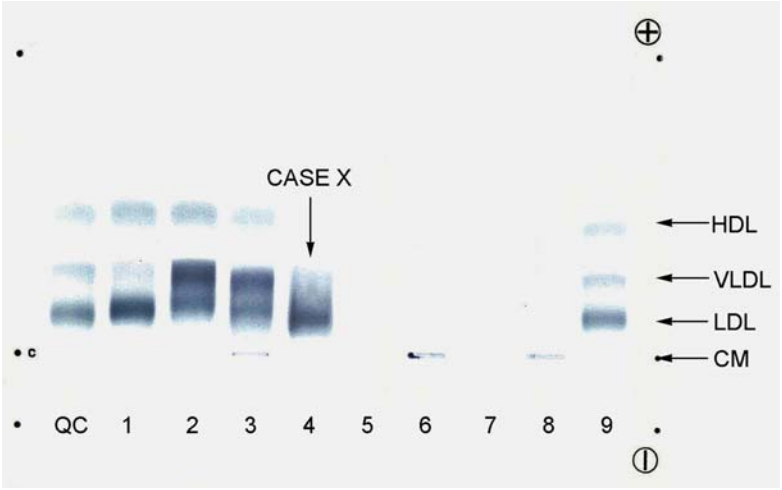


Fig. 26　Lipoprotein-X

图 26　脂蛋白 X

Interpretation

In patients with cholestatic liver disease, the increase in plasma cholesterol levels is largely due to an increased level of lipoprotein-X (LP-X), an abnormal lipoprotein particle within the LDL density region that is rich in free cholesterol and phospholipids (PL). Since both LP-X and bile vesicles are composed of PL and free cholesterol, LP-X particles are formed when biliary vesicles regurgitated from liver into

plasma or from the accumulation of PL and free cholesterol because of reduced lecithin:cholesterol acyltransferase (LCAT) activity in the plasma. Upon agarose gel electrophoresis, plasma LP-X migrates toward the anode more slowly than all normal lipoproteins.

解释

胆汁淤积性肝脏疾病患者，血浆胆固醇的增高（图27）主要由脂蛋白X（LP-X）水平的增加所致。LP-X 是一种异常的脂蛋白颗粒、存在于LDL部分，富含游离胆固醇和磷脂。磷脂和游离胆固醇是LP-X 和胆汁小囊泡的组分，由于血浆卵磷脂胆固醇酰基转移酶（LCAT）的活性降低，从肝脏逆流到血浆的胆汁小囊泡、淤积的磷脂和游离胆固醇形成了LP-X。琼脂糖电泳时血浆LP-X 向阳极迁移的速度慢于其它所有的正常脂蛋白。

Fig. 27　Plasma of a patient with cholestatic liver disease

图 27　胆汁淤积性肝脏疾病患者的血浆

Comment

Using small angle X-ray scattering, it has been shown that LP-X is a 40-100 nm bilamellar particle with an aqueous lumen, predominantly composed of PL and free cholesterol in equimolar amounts and containing only 3% of triglycerides and 2% of cholesteryl ester. Gradient ultracentrifugation revealed that LP-X is isolated in the LDL fraction and contains apo C and albumin but lacking apo B100. LP-X inhibits the oxidation of normal LDL particles and prevents oxidized LDL from disrupting survival mechanisms in vascular endothelial cells. It has been shown to have antiatherogenic properties. The cholesterol content of LP-X is predominantly unesterified cholesterol raising the possibility that LP-X could remove cholesterol from tissue similar to the unesterified cholesterol uptake by HDL in the reverse cholesterol transport pathway. LP-X also impedes chylomicron remnant hepatic uptake in isolated hepatocytes..

评论

小角度X 线散射分析发现脂蛋白X为40-100 nm的水腔双层小囊泡。主要由等摩尔的脂蛋白和游离胆固醇组成，仅含3%的TG和2％的胆固醇酯。梯度超速离心显示LP-X独立存在于LDL部分，含有apoC 和白蛋白但缺乏apo B100。已经证实LP-X能够抑制正常LDL颗粒氧化、阻止氧化LDL分解残存在血管内皮细胞，具有抗动脉粥样硬化的功能。LP-X中的胆固醇主要是非酯化胆固醇，增加

了LP-X类似HDL摄取非酯化胆固醇清除组织中的胆固醇的可能性。LP-X也抑制肝细胞摄取乳糜微粒残粒。

References

参考文献

Nishiwaki M, Ikewaki K, Bader G, Nazih H, Hannuksela M, Remaley AT, Shamburek RD, Brewer HB Jr. Human lecithin:cholesterol acyltransferase deficiency: in vivo kinetics of low-density lipoprotein and lipoprotein-X. Arterioscler Thromb Vasc Biol 2006; 26: 1370-1375.

Simon JB, Poon RW. Lipoprotein-X levels in extrahepatic versus intrahepatic cholestasis. Gastroenterology 1978; 75: 177-80.

Narayanan S. Lipoprotein-X. CRC Crit Rev Clin Lab Sci 1979; 11: 31–51.

Bos ES, van der Doelen AA, Denissen AE, Goverde BC, Magnani HN, Kostner GM.A novel assay for the quantitative determination of lipoprotein-X (LP-X) in serum. Clin Chim Acta 1983; 127: 383-90.

Laggner, P., O. Glatter, K. Muller, O. Kratky, G. Kostner, and A. Holasek.The lipid bilayer structure of the abnormal human plasma lipoprotein X. An X-ray small-angle-scattering study. Eur J Biochem 1977; 77: 165-171.

Chang PY, Lu SC, Su TC, et al. Lipoprotein-X reduces LDL atherogenicity in primary biliary cirrhosis by preventing LDL oxidation. J Lipid Res 2004; 45: 2116–22.

Manzato E, Fellin R, Baggio G, Walch S , Neubeck W, Seidel D. Formation of lipoprotein-X. Its relationship to bile compounds. J Clin Invest 1976; 57: 1248–60.

Sörös P, Böttcher J, Maschek H, Selberg O, Müller MJ. Lipoprotein-X in patients with cirrhosis: its relationship to cholestasis and hypercholesterolemia. Hepatology. 1998; 28: 1199-1205.

Seidel D, Büff HU, Fauser U, Bleyl U. On the metabolism of lipoprotein-X (LP-X). Clin Chim Acta 1976; 66: 195-207.

Seidel D, Alaupovic P, Furman RH, McConathy J. A lipoprotein characterizing obstructive jaundice. II. Isolation and partial characterization of the protein moieties of low density lipoproteins. J Clin Invest 1970; 49: 2396-2407.

Hauser H, Kostner G, Muller M, Skrabal P. The structure and morphology of the abnormal serum lipoprotein-X. Biochim Biophys Acta 1977; 489: 247-261.

(鲁双艳译)

CASE Y　LIPOPROTEIN-Y (LP-Y)

脂蛋白 Y

History

- 47/F
- History of adult polycystic liver disease with cadveric liver transplantation
- Found persistent deranged LFT on follow up
- Complicated by HBV infection and CBD stricture

案例 Y

病史

- 47 岁，女性
- 因成人多囊肝病接受过尸体肝移植
- 随防发现持续肝功能紊乱
- 合并乙肝病毒感染和胆总管狭窄

Lipid Profile

Total Cholesterol	8.5
Triglycerides	3.7
HDL-C	0.17
LDL-C calc	6.6
LDL-C direct	0.3
Non HDL-C	8.3
Appearance	Clear

ApoA1	<0.25
ApoB	2.01

血脂结果

总胆固醇, TC	8.5
甘油三酯, TG	3.7
高密度脂蛋白胆固醇, HDL-C	0.17
低密度脂蛋白胆固醇, LDL-C(计算）	6.6
低密度脂蛋白胆固醇, LDL-C(测量)	0.3
非 HDL-C	8.3
外观	清亮
载脂蛋白 A1, Apo A1	<0.25
载脂蛋白 B, Apo B	2.01

Lipoprotein Electrophoresis

Discordant LDL-C results between calculation and direct measurement. The presence of modified LDL particles, and the coexistence of LP-X and LP-Y is common in patients with progressive cholestasis or biliary atresia.
Note different electrophoretic mobility compared with sample which contains LP-X.

脂蛋白电泳

脂蛋白电泳结果（图 28）第 2 号标本发现：LDL-C 的计算值与直接测量值不一致。进行性胆汁淤积或胆道闭锁患者体内存在修饰的 LDL 颗粒，脂蛋白 X 和脂蛋白 Y 的共存也很常见。需要注意的是：电泳迁移率不同于含

有脂蛋白 X 的样本。

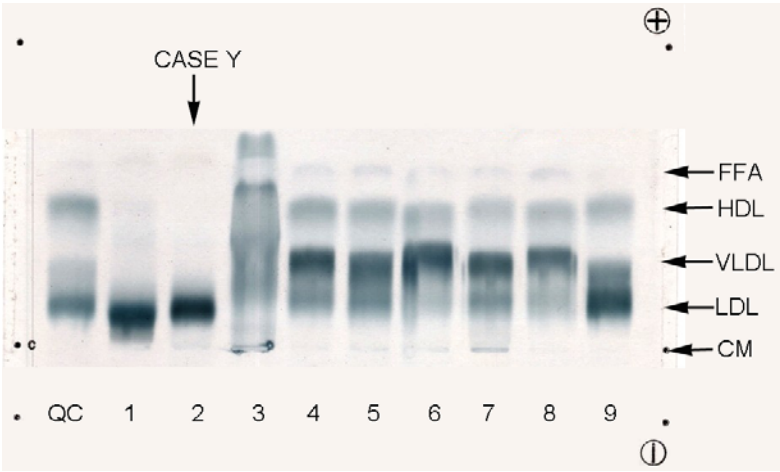


Fig. 28　Lipoprotein-Y

图 28　脂蛋白 Y

Interpretation

Abnormal lipoproteins such as LP-X and LP-Y are frequently observed in patients with cholestatic liver disease and are reported to influence homogeneous LDL-C assays. As previously mentioned, LP-X is a cholesterol rich lipoprotein that migrates toward the cathodic side of LDL on electrophoresis. The presence of LP-X is associated with jaundice and progressive cholestasis. LP-Y resembles LP-X in mobility and pathology, but is triglyceride-rich. In post liver transplantation it is not uncommon for the patient to go through a cholestatic phase. The electrophoretic pattern of lipoproteins was generally characterized by the presence of LP-X, and may also contain a larger LDL particle (LP-Y),

which is depleted in cholesteryl esters and rich in triglycerides, and a decrease in alpha band intensity as well. The LDL, however, is heterogeneous as reflected in the discordant LDL-C and apo B results

解释

胆汁淤积性肝病患者往往存在异常脂蛋白，如脂蛋白 X (LP-X)和脂蛋白 Y (LP-Y)，影响 LDL-C 的匀相检测。如前所述，LP-X 是一种富含胆固醇的脂蛋白，电泳时出现在 LDL 的负极侧。LP-X 的出现与黄疸和早期胆汁淤积有关。LP-Y 的迁移率和病理性质类似于 LP-X，但含有更多的 TG。接受肝移植的病人通常会经历胆汁淤积期。脂蛋白电泳图谱的一般特点是：α 带强度降低，可能含有大量富含 TG 的 LDL 颗粒（LP-Y），以及外观更正常的颗粒，这种颗粒缺少胆固醇酯、富含 TG。而 LDL 的异质性表现在 LDL-C 与 apoB 的结果不一致。

Comment

The interpretation of lipoprotein patterns in patients with cholestatic liver disease has been tricky because the dyslipidaemia can be extreme with marked elevations of free cholesterol and phospholipids. Pre-beta and alpha bands can be absent on electrophoresis. When patients with cholestasis are hypertriglyceridaemic the excess triglyceride is to be found predominantly in the LDL fractions rather than in VLDL. Lipoproteins of the density range 1.019-1.063 g/cm^3 occurring in the plasma of patients with obstructive jaundice, and the LDL, however, is heterogeneous. Subfractionation of this density class by

combined sodium phosphotungstate precipitation, ultracentrifugation, and column chromatography on hydroxyapatite and agarose gel yielded essentially three fractions: (1) LP-X, an abnormal LDL which lacks apo B, with a vesicular structure that appears in rouleaux formation under the electron microscope. (2) a triglyceride-rich lipoprotein for which is depleted in cholesteryl esters, called LP-Y and (3) apparently normal buoyant apo B-containing LDL particles. Marked differences between these fractions with respect to electron-microscopic appearance, hydrated densities, chemical composition and immunochemical characteristics were observed, and the relative distribution of these fractions varied from patient to patient. The protein moiety of LP-X consisted primarily of apo C and albumin. LP-Y showed, in addition to apo C, the presence of apo B. The apparently normal apo B-containing lipoprotein fraction had higher triglyceride and free cholesterol contents than that of normal individuals and an unusually high content of apo C. It is important to consider the coexistence of LP-Y with LP-X in screening patients for cholestasis

评论

肝脏疾病不同于其他大多数继发性血脂异常，胆汁淤积性肝病患者的血脂电泳图谱的解读非常棘手，患者常有严重的高脂血症伴游离胆固醇和磷脂极度升高。电泳未见前 β 带和 α 带，当胆汁淤积患者发生高 TG 血症时，过多的 TG 主要存在于 LDL 内，而不是 VLDL 中。梗阻性黄疸患者血浆脂蛋白的密度范围在 1.019-1.063 g/cm^3。但是 LDL 存在异质性。这类密度的亚组分经联合磷钨酸钠沉淀、超速离心、柱状亲和层析及琼脂糖凝胶电泳可分为三部分：（1）LP-X，一种异常的 LDL，缺乏 apoB。

在电子显微镜下观察具有多孔结构并排列成钱串形状；（2）富含 TG 的脂蛋白，缺乏胆固醇酯，称为 LP-Y；（3）比较正常的含有 apoB 的颗粒。这些颗粒的电子显微镜下形态、水合密度、化学成分和免疫化学特点均有明显差异，而且相对分布也因病人而异。LP-X 的蛋白部分主要为 apoC 和白蛋白。LP-Y 除了含有 apoC 外，还有 apoB。正常外观的含 apoB 脂蛋白颗粒的 TG 和游离胆固醇含量高于正常对照，apoC 含量通常也高。筛查胆汁淤积患者时，应考虑 LP-Y 的共存性。

References

参考文献

Kostner GM, Laggner P, Prexl HJ, Holasek A. Investigation of the abnormal low-density lipoproteins occurring in patients with obstructive jaundice. Biochem J 1976; 157: 401-407.

Watanabe M. Lipoprotein abnormalities in cholestasis. I. Electrophoretic and ultracentrifugal analyses. Acta Med Okayama 1979; 33: 269-285.

Miller JP. Dyslipoproteinaemia of liver disease. Baillieres Clin Endocrinol Metab 1990; 4: 807–32.

Iwasaki Y, Matsuyama H, Nakashima N. Improved specificity of a new homogeneous assay for LDL-cholesterol in serum with abnormal lipoproteins. Clin Chem 2006; 52: 886-888.

(黎四维译)

CASE Z　ZIEVE'S SYNDROME

Zieve's 综合征

History

- 58/M, drinker.
- Elevated plasma TG, abdominal pain.
- Deranged LFT and jaundice.
- Haemolytic anaemia was noted.

案例 Z

病史

- 58 岁，男性，酗酒。
- 高甘油三酯（TG）血症，腹痛。
- 肝功能不全和黄疸。
- 溶血性贫血。

Lipid Profile

Total Cholesterol	4.2
Triglycerides	5.4
HDL-C	<0.10
LDL-C calc	N/A
LDL-C direct	0.1
Non HDL-C	4.1
Appearance	Slightly turbid

ApoA1	0.29
ApoB	0.68

血脂结果

总胆固醇, TC	4.2
甘油三酯, TG	5.4
高密度脂蛋白胆固醇, HDL-C	<0.10
低密度脂蛋白胆固醇, LDL-C(计算）	—
低密度脂蛋白胆固醇, LDL-C(测量)	0.1
非 HDL-C	4.1
外观	轻度浑浊
载脂蛋白 A1, Apo A1	0.29
载脂蛋白 B, Apo B	0.68

Lipoprotein Electrophoresis

Increased VLDL and a reduced HDL consistent with dyslipidaemia of hepatic dysfunction

脂蛋白电泳

脂蛋白电泳结果（图 29）第 1 号标本显示： VLDL 升高、HDL 降低，为肝功能不良的脂代谢紊乱表现。

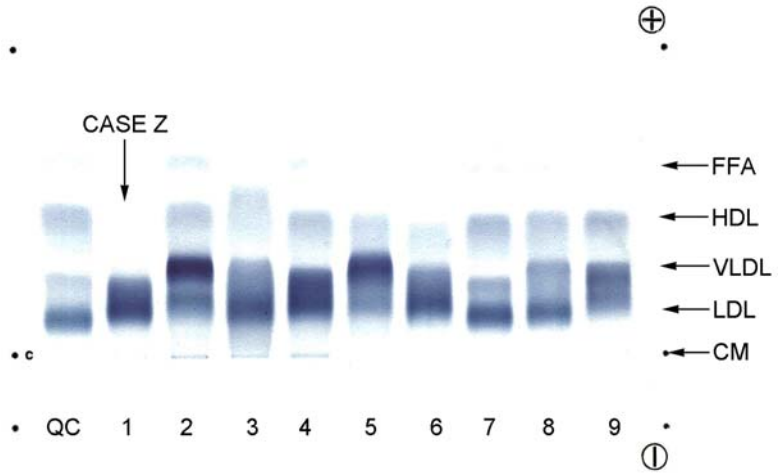


Fig. 29　Zieve's syndrome —Increased VLDL and a reduced HDL

图 29　Zieve's 综合征 — VLDL 升高, HDL 降低

Interpretation

Zieve's syndrome consists of jaundice, hepatic dysfunction, hypertriglyceridaemia and transient haemolytic anaemia associated with alcohol abuse. It is a rare form of alcoholic haemolysis exhibits some of the symptoms of acquired pyruvate kinase (PK) deficiency anaemia. The oxidative form of PK is unstable. It has been suggested that acetaldehyde, a metabolite of ethanol, may account for oxidation of PK in the erythrocytes. The finding of hypertriglyceridemia in patients with congenital PK deficiency supports that acquired PK deficiency contributes to the clinical features of Zieve’s syndrome.

解释

Zieve's 综合征表现有黄疸、肝功能不全、高TG血症和短暂性的溶血性贫血，这些症状与酒精滥用有关。Zieve's综合征是一种罕见的酒精中毒性溶血，有获得性丙酮酸激酶(PK)缺陷的部分症状。Zieve’s 综合征患者的红细胞PK以氧化形式存在、稳定性低。在这种情况下，乙醇的代谢产物乙醛可能导致PK被氧化。先天性丙酮酸激酶缺陷患者的高TG血症揭示Zieve’s 综合征的临床表现归因于获得性酮酸激酶缺陷。

Comment

Mild or transient hemolysis and acanthocytes are observed in individuals with Zieve’s syndrome. Alcohol intoxication can alter plasma lipid composition and the membrane integrity of red blood cells. It has been reported that secondary vitamin E–deficient red cells due to chronic alcoholism have increased oxidant sensitivity and tend to hemolyze more easily. Specifically, the lipoproteins ApoB–48 and ApoB-100 are deficient because of the abnormal assembly or defective secretion, leading to absent cellular secretion from hepatocytes or intestinal epithelial cells. Formation of normal chylomicrons is inhibited and prevents intestinal absorption of lipids, resulting in severe fat malabsorption.

评论

Zieve’s 综合征患者体内可出现轻度或短暂性溶血和棘红

细胞。酒精中毒可以改变血浆脂质成分和红细胞膜的完整性。除此之外，继发性维生素 E 缺乏红细胞对氧化剂更为敏感，更易发生溶血。尤其是由于异常合成或分泌不足引起的 ApoB-48 和 ApoB-100 缺陷，导致肝细胞或肠上皮细胞分泌功能障碍。正常乳糜微粒的形成受抑、肠道脂质吸收受阻，从而导致严重的脂肪吸收不良。

References

参考文献

Zieve L. Jaundice, hyperlipidaemia, and haemolytic anaemia: a heretofore unrecognised syndrome associated with alcoholic fatty liver and cirrhosis. Ann Intern Med 1958; 4: 471-96.

Kunz F, Stummvoll W. The significance of plasma phospholipids in Zieve's syndrome. Blut 1970; 1: 210-26.

Goebel KM, Goebel FD, Schubotz R, Schneider J. Red cell metabolic and membrane features in hemolytic anemia of alcoholic liver disease (Zieve’s syndrome). Br J Hematol 1977; 35: 573-585.

Morse EE, Jilani F, Brassel J. Acquired pyruvate kinase deficiency. Ann Clin Lab Sci 1977; 7: 399-404.

Druml W, Grimm G, Laggner AN, Schneeweiss B, Lenz K. Hyperlipidemia in acute hemolysis. Klin Wochenschr 1991; 69: 426-492.

Lewis G, Wise MP, Poynton C, Godkin A. A case of persistent anemia and alcohol abuse. Nature Clinical Practice Gastroenterology & Hepatology 2007; 4: 521-526.

Rao A, Hulbert M, Wilson DB. Severe hypertriglyceridemia in an infant with red cell pyruvate kinase deficiency. Indian Pediatrics 2007;44:303-305.

(余雪琛译)

声　明

医学是一门不断发展的学科。为确保本书出版时的信息正确性，作者和编者尽最大努力与相关专业人员进行沟通核对。然而，由于我们的学术水平所限，书中的缺陷、错误在所难免，希望广大读者悉心批评、指正。对于本书的使用和信任不承担任何法律责任。本书所包含的信息不形成任何形式的医疗建议。

致　谢

作者和编者向香港大学玛丽医院和武汉大学中南医院致以诚挚的谢意，感谢他们的参与及贡献，特别是在撰写过程中提供的支持。