which is attributable to a relatively small tubular secretion of creatinine (24, 25). The Cockcroft–Gault and abbreviated MDRD algorithms for calculating GFR correlated closely with $^{51}$Cr-EDTA clearance when calculated with the creatinine results from the HPLC, enzymatic, and rate-blanked compensated Jaffe methods. However, the results obtained with the same algorithms were lower than the $^{51}$Cr-EDTA clearance when based on uncompensated Jaffe test results. The abbreviated MDRD and Cockcroft–Gault equations correlated well.

The median GFRs obtained with the Schwartz equation varied by 39%, depending on the creatinine method used. In children, the use of the enzymatic method produced the highest estimated GFR and the uncompensated Jaffe the lowest.

In children, practical problems in timed urine collection have contributed largely to the widespread use of calculated CrCl values based on serum or plasma creatinine concentration and body length. In contrast to the results for adults, the results obtained with Schwartz CrCl values in children and infants are significantly higher (in our series up to twofold higher in 4 of 23 cases) than inulin clearances when the compensated Jaffe or enzymatic creatinine method is used. If the uncompensated Jaffe test is used, the negative analytical effect of the protein error on CrCl is countered by the positive physiologic effect of the relatively more important tubular secretion of creatinine. Because serum creatinine values are lower in children, especially between ages 1 and 3 years, relative differences between compensated and uncompensated creatinine methods are very important.

Care should be taken when using estimated GFRs based on CrCl algorithms for drug administration, in particular for drugs such as cis-platinum and aminoglycoside antibiotics. In the example of the cytostatic drug cis-platinum, it is recommended to administer one-half the dose when CrCl decreases to <60 mL/min.

In conclusion, because collection of timed urine is cumbersome and susceptible to errors, calculated GFRs (Cockcroft–Gault and MDRD algorithms in adults and Schwartz algorithm in children) are often used. However, care should be taken in the choice of the serum creatinine method when applying these formulas.

We wish to thank Dr. G. Klein, Prof. W. Hoelzel, and Dr. Engel (Roche) for kindly providing the diagnostic reagent sets for this study.

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Multiple Lipoprotein Abnormalities Associated with Insulin Resistance in Healthy Volunteers Are Identified by the Vertical Auto Profile-II Methodology, James W. Chu,1 Fahim Abbasi,1 Krishnaji R. Kulkarni,2 Cynthia Lamendola,1 Tracey L. McLaughlin,1 Janet N. Scalisi,2 and Gerald M. Reaven1,* (1 Stanford University School of Medicine, Department of Medicine, Stanford, CA 43050; 2 Atherotech, Birmingham, AL 35221; * address correspondence to this author at: Falk Cardiovascular Research Center, Stanford University Medical Center, Stanford, CA 43050; fax 650-725-1599, e-mail greaven@cvmed.stanford.edu)

The lipoprotein abnormalities first associated with insulin resistance (IR) and compensatory hyperinsulinemia were high plasma triglyceride (TG) and low HDL-cholesterol
proatherogenic lipoprotein abnormalities. It is now known that the characteristic IR-associated dyslipidemia also includes a shift to smaller, denser LDL particles (pattern B), enhanced postprandial lipemia, and decreased concentration of the more buoyant HDL particle, HDL₂ (3–5). Recently, the IR-associated lipoprotein abnormalities that increase risk of coronary heart disease (CHD) have continued to expand. In addition to high plasma TG and low HDL-C concentrations (6, 7), at least three classes of TG-rich lipoproteins are both atherogenic and associated with increased CHD risk, including intermediate density lipoprotein (IDL; a TG-rich remnant product derived from VLDL metabolism) (8, 9), VLDL₃ (the dense VLDL subclass) (10, 11), and TG-rich chylomicron remnants (8, 12, 13).

Despite awareness of the myriad IR-associated proatherogenic lipoprotein abnormalities (1–5, 14–17), we are unaware of previous publications in which both IR and all relevant lipoproteins were quantified in the same cohort of individuals. This is likely partly attributable to the unavailability of analytical methods to measure multiple lipoprotein CHD risk factors in a clinically useful manner. However, the validated vertical auto profile-II (VAP-II) methodology (18) provides a means to comprehensively identify the IR-associated dyslipidemic profile, and we have used VAP-II to compare lipoprotein characteristics of nondiabetic individuals stratified into IR and insulin-sensitive (IS) groups.

The Stanford University Human Subjects Committee approved this study, and healthy volunteers from the San Francisco Bay Area gave informed consent. Participants underwent medical interview, anthropometric measurements, and a physical examination. Exclusion criteria included fasting plasma glucose >7.0 mmol/L (126 mg/dL), total bilirubin >34 μmol/L (2.0 mg/dL), serum albumin <30 g/L or creatinine >175 μmol/L (2.0 mg/dL), weight change >3.0 kg in 3 months, and active substance abuse. Results of a complete blood count, chemical screening battery, and electrocardiogram were normal in all participants.

Each participant underwent the insulin-suppression test, as introduced previously and validated by our group (19). Bilateral antecubital intravenous catheters were used for (a) 180-min infusion of octreotide acetate (0.27 μg·m⁻²·min⁻¹), insulin (32 mIU·m⁻²·min⁻¹), and glucose (267 mg·m⁻²·min⁻¹); and (b) collection of timed blood samples every 30 min initially, and then every 10 min from 150 to 180 min of the infusion. These last four time points were used to determine the steady-state plasma glucose (SSPG) and insulin (SSPI) concentrations. Because SSPI concentrations are similar among individuals, the SSPG concentration directly measures the ability of insulin to mediate disposal of an infused glucose load; higher SSPG values indicate increasing IR.

SSPG concentrations >10.8 mmol/L (195 mg/dL) were defined as IR, and SSPG <5.3 mmol/L (95 mg/dL) was defined as IS. These cut-points represent the SSPG values differentiating the upper and lower 30% of a population of >400 nondiabetic individuals that we tested previously (20). Using these criteria, we selected two groups: 23 IS and 21 IR individuals, none taking drugs known to affect blood pressure, glucose, or lipid metabolism. On a separate occasion, plasma glucose concentrations were determined before and 120 min after an oral 75-g glucose challenge.

Plasma samples obtained after an overnight fast were stored frozen at −70°C until lipoprotein analysis by the VAP-II method (18). VAP-II is a comprehensive lipoprotein profile testing method that directly measures cholesterol concentration in HDL₂, HDL₃, IDL, LDL, VLDL, and lipoprotein(a) [Lp(a)] in a single test. VAP-II has been extensively validated with the Lipid Research Clinics β-quantification method performed at Northwest Lipid Research Laboratories at the University of Washington, Seattle, WA (18, 21). It should be emphasized that this method provides a specific measure of narrow-density LDL-C (ND-LDL-C), in contrast to the commonly measured LDL-C defined by the National Cholesterol Education Program, which includes both Lp(a) and IDL-C.

In VAP-II, the ND-LDL-C subclass pattern is further evaluated by determining the LDL peak maximum time, i.e., the relative position of the LDL peak in the density gradient on a relative scale of 0–200 s, with 0 s corresponding to the beginning of the HDL (the most dense lipoprotein) peak and 200 s corresponding to the VLDL (the least dense lipoprotein) peak maximum. Therefore, a patient with predominantly small, dense LDL has a lower LDL peak maximum time compared with the LDL peak maximum time of a patient with predominantly large, buoyant LDL. Thus, LDL pattern A (predominantly large and buoyant LDL subclass) is defined by a LDL maximum time >118 s, LDL pattern B by a LDL maximum time ≤115 s, and intermediate pattern (A/B) by LDL maximum time >115 and ≤118 s. Because the density and size of LDL are inversely related, we have compared VAP-II LDL peak maximum time (a function of density) with LDL size obtained by a commonly used 2–16% nondenaturing polyacrylamide gradient gel electrophoresis method performed at Pacific Biometrics Inc. (a CDC lipid-standardized laboratory), with a correlation coefficient of 0.832, and with the Nuclear Magnetic Resonance method performed at Liposcience Inc. (Raleigh, NC), with a correlation coefficient of 0.91 (unpublished data). VAP-II is based on use of a density gradient formed with 40-fold-diluted (40 μL of original serum) and density-adjusted (1.21 kg/L) serum and 1.006 kg/L density saline in a centrifuge tube. The gradient is subjected to a single vertical spin density-gradient ultracentrifugation at 416 000×g for 36 min, using the Beckman Optima-XL 100K ultracentrifuge. The separated lipoprotein classes and subclasses are then continuously drained from the bottom of the centrifuge tube into the VAP-II continuous flow analyzer, where they react sequentially with a cholesterol-specific enzymatic reagent, producing a concentration-dependent lipoprotein absorbance profile monitored by a spectrophotometer. The digital output of the spectrophotometer is also acquired by a computer and is further deconvoluted with use of in-house-developed software to
provide cholesterol concentrations of individual lipoprotein classes and subclasses. The VAP is provided by Atherotech, Inc., a CDC-National Heart, Lung, and Blood Institute-standardized lipid laboratory.

Data are expressed as the mean (SE). The Student t-test and the \( \chi^2 \) test were used to make comparisons between experimental groups. All statistical evaluations were performed with the SYSTAT 10.0 software package for Windows. Statistical significance was assigned at \( P < 0.05 \).

The two experimental groups (IR and IS) were comparable in age [45 (2) vs 46 (3) years], gender distribution (11 males and 10 females vs 11 males and 12 females), and body mass index [28.5 (0.5) vs 28.6 (0.8) kg/m\(^2\)]; all \( P > 0.60 \). By selection, SSPG concentrations were higher in the IR group [13.1 (0.3) vs 4.0 (0.1) mmol/L; \( P < 0.01 \)]. Fasting and 120-min post-glucose load concentrations of glucose were also higher in the IR group [5.6 (0.1) vs 5.2 (0.1) and 7.2 (0.4) vs 4.9 (0.3) mmol/L; both \( P < 0.01 \)].

The VAP lipoprotein analysis is given in Table 1. The IR group had lower concentrations of both HDL subclasses, HDL\(_1\) (\( P < 0.001 \)) and HDL\(_2\) (\( P < 0.001 \)). Moreover, total TG concentrations were higher in the IR individuals (\( P < 0.01 \), as were concentrations of all measured TG-rich lipoprotein classes, including IDL (\( P = 0.02 \)); large, buoyant TG-rich VLDL\(_1 + 2\) (\( P < 0.01 \)); and the small, dense cholesterol-rich VLDL\(_{3a} + 3b\) (\( P < 0.001 \)). Although LDL-C appeared to be higher in the IR individuals (3.44 vs 3.24 mmol/L; \( P = 0.39 \)), this effect was partially attributable to the effects of a significantly higher IDL (0.49 vs 0.39 mmol/L; \( P = 0.02 \)) in the setting of almost identical Lp(a) concentrations (0.19 vs 0.18 mmol/L; \( P = 0.85 \)). Consequently, the directly measured ND-LDL-C concentrations were similar in the two groups (2.77 vs 2.67 mmol/L; \( P = 0.62 \)). However, despite the similar concentrations of ND-LDL-C, the IR group had, on average, a small, denser LDL particle as indicated by a lower LDL maximum time (\( P < 0.001 \)), accompanied by a significantly higher proportion (\( P < 0.001 \)) of IR individuals identified with LDL pattern B (17 of 21) compared with IS individuals (4 of 23).

The results of this study demonstrate that IR individuals have increased concentrations of TG and various TG-rich lipoprotein cholesterol, decreased concentrations of both HDL subclasses, and a pattern of small, dense LDL. All of these lipoprotein patterns predispose to an increased risk of CHD (6–12). Although these findings have previously been reported separately to associate with the metabolic syndrome, they are not all routinely measured in assessing the impact of IR on lipoprotein metabolism. The importance of IR and its consequences have recently been emphasized by the report of the Adult Treatment Panel III outlining diagnostic criteria for identifying IR/hyperinsulinemic individuals with the metabolic syndrome (22). Because ~25% of the US population appears to have the metabolic syndrome as defined by the suggested criteria (23), it is of obvious importance to understand the relationship between the various components of IR and CHD. Although abnormal lipoprotein metabolism in the metabolic syndrome clearly contributes to CHD risk, the precise roles played by any particular member of the IR-associated atherogenic profile remain unclear (Table 1). The ability to quantify all such lipoprotein variables would help to further elucidate these complex relationships.

In conclusion, our results demonstrate that multiple abnormalities in lipoprotein metabolism constitute the atherogenic lipoprotein profile present in nondiabetic IR individuals. The VAP-II method provides a relatively simple approach to identifying all such components in an

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### Table 1. Lipoprotein concentrations in 44 healthy nondiabetic volunteers as measured by the VAP-II methodology.\(^a\)

<table>
<thead>
<tr>
<th>Lipoprotein measurement</th>
<th>SSPG (&lt;5.3) mmol/L ((n = 23))</th>
<th>SSPG (\geq5.8) mmol/L ((n = 21))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAP-II direct measurements of cholesterol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>4.82 (0.16)</td>
<td>5.18 (0.21)</td>
<td>0.21</td>
</tr>
<tr>
<td>HDL-C</td>
<td>1.24 (0.08)</td>
<td>0.85 (0.05)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>VLDL(_1 + 2)-C</td>
<td>0.16 (0.02)</td>
<td>0.48 (0.10)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>HDL-C subfractions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL(_2)-C</td>
<td>0.26 (0.03)</td>
<td>0.16 (0.00)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HDL(_3)-C</td>
<td>0.98 (0.05)</td>
<td>0.73 (0.03)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TG-rich lipoproteins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>1.08 (0.12)</td>
<td>2.54 (0.40)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>VLDL(_{3a} + 3b)-C</td>
<td>0.21 (0.03)</td>
<td>0.36 (0.03)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IDL-C</td>
<td>0.39 (0.03)</td>
<td>0.49 (0.05)</td>
<td>0.02</td>
</tr>
<tr>
<td>Lp(a)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lp(a)-C</td>
<td>0.18 (0.02)</td>
<td>0.19 (0.04)</td>
<td>0.85</td>
</tr>
<tr>
<td>LDL-C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ND-LDL-C</td>
<td>3.24 (0.16)</td>
<td>3.44 (0.21)</td>
<td>0.39</td>
</tr>
<tr>
<td>LDL maximum time, s</td>
<td>118 (1)</td>
<td>111 (1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LDL pattern</td>
<td>13 A; 6 intermediate ((A/B); 4 B)</td>
<td>3 A; 1 intermediate ((A/B); 17 B)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

\(^a\) All values are the mean (SE) in mmol/L unless otherwise noted.
individual. The application of VAP-II may be useful not only in elucidating the roles played by specific lipoprotein abnormalities in contributing to CHD, but also in yielding valuable insight into the specific benefits of therapeutic regimens to decrease CHD risk.

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Utilization, Reliability, and Clinical Impact of Point-of-Care Testing during Critical Care Transport: Six Years of Experience, Amy C. Gruszecki,1 Glen Horton,2 John Lam,3 Diane Kahler,4 Debbie Smith,4 Julie Vines,4 Lee Lancaster,4 Thomas M. Daly,1 C. Andrew Robinson,1 and Robert W. Hardy* 1Department of Pathology, 3 Departments of Medicine, Pathology, and Surgery and the Gene Therapy Center, and 4 Department of Critical Care Transport, University of Alabama at Birmingham, Birmingham, AL 35233; 2 Department of Laboratory Medicine, National Institutes of Health, Bethesda, MD 20892; * address correspondence to this author at: Department of Pathology and Laboratory Medicine, University of Alabama at Birmingham, WP230, 619 South 19th St, Birmingham, AL 35233; fax 205-975-4468, e-mail rhardy@path.uab.edu)

The use of point-of-care testing (POCT) has been reported in the setting of critical care transport (1–6), although the overall benefits have not been evaluated in depth. In addition, problems with testing reliability may be uncovered only after an extended period of field use. This report describes the use of POCT by our critical care transport program over 6 years.

All critical care transports made from January 1996 to December 2001 were reviewed. Transport vehicles were ambulances or twin-engine jets. The transport teams consisted of a physician on transport or with radio contact, a respiratory therapist, and a registered nurse. All transports were equipped with i-STAT® portable analyzers (i-STAT® Corporation) and disposable cartridges for testing. The analyzer and cartridges were stored in an insulated bag for temperature control during the trip. The analytical performance verification protocol (electronic controls) recommended in the i-STAT System Manual was followed before each patient test. Liquid controls were run monthly. Proficiency testing was completed in accordance with the requirements of the College of American Pathologists.

The manufacturer’s test cartridges were the G3, 6+, 6G7+, and glucose. Tests included pH, Pco2, Po2, calculated bicarbonate, total CO2, base excess, oxygen saturation, sodium, potassium, chloride, urea, glucose, hematocrit, and calculated hemoglobin and glucose. Each cartridge requires 65 µL of whole blood for testing. The blood was drawn and analyzed by physician order. From 1997 through 2001, the team filled out an evaluation form for quality review after cases where POCT was performed.

Patient test results and charts for each POCT episode were reviewed retrospectively to identify changes in