vation reported is probably related to the presence of an "ACTH-like" molecule. A similar observation occurred when sera from individuals with Sheehan's or para-neoplastic syndromes were evaluated. We are currently pursuing two lines of investigations, isolating and characterizing the Sheehan's syndrome plasma and studying plasma lipoproteins. The data at this time are far from conclusive.

Among the known interferences to our system, heparin is the single most serious problem. Only trace amounts of heparin will adversely affect the antibody binding sites, yielding a lower binding percent and simulating higher ACTH values. If we assume the eight questionable specimens were drawn at relatively the same time of day, and treated in the same manner as the previous 124, and that the subject's status was unremarkable, there remain two possible conclusions: the values were in fact accurate, though remarkable, or that there remains an as-yet-unidentified plasma factor.

To examine the first possibility, one might attempt a linearity dilution study on the suspect specimen, with use of low ACTH plasma as a diluent. If the second conclusion is preferred, one might objectively evaluate ACTH values in proper context with the cortisol information and reject it as spurious data. The reagents offered in the CIS ACT kit are the finest available; considering its vast methodological improvement and increased diagnostic flexibility with smaller plasma requirements, we believe the benefits far outweigh the few percent requiring objective [sic] analysis.

John D. Sakelaris
CIS Radiopharmaceuticals
Bedford, MA 01730

Lowered High-Density-Lipoprotein Cholesterol in Viral Illness

To the Editor:

We have been performing high-density lipoprotein (HDL) determinations for the last 18 months by the magnesium-phosphotungstate precipitation method (1) with subsequent determination of cholesterol in the supernate. We have continually correlated our methodology with Lipid Research Clinic Laboratory values by an on-going program of assay of our pool, first by the Center for Disease Control in Atlanta and more recently by the LRC Laboratory in Seattle. During the past several months we have observed that there were several patients who had very low HDL values, which were unexpected by the attending physician in light of the known cardiac history and coronary risk assessment.

We investigated groups of patients with low values and found 15 with HDL-cholesterol (HDL-C) values of 200 mg/L or less (Table 1). Review of the hospital chart and personal communication with the attending physicians of all of these patients revealed that 11 of the 15 had either acute viral disease at the time the sample was drawn or had adequate history of recent viral illness within the previous two to three weeks. One patient, M.H., a 16-year-old white woman, had severe viral myocarditis documented at autopsy. The HDL-C value for her was 110 mg/L with a corresponding total cholesterol of 620 mg/L. A second patient, N.A., a 45-year-old woman, had severe viral hepatitis, was positive for hepatitis B antigen, and had an HDL-C of 190 mg/L with corresponding total cholesterol of 1.60 g/L. None of the remaining patients had viral cultures or viral serological studies performed. Patient E.D. with viral pneumonia had an HDL-C value of 20 mg/L on one occasion; two days later the value was 70 mg/L. This extremely low value was confirmed by two other laboratories. Review of other groups of patients showed that one of 11 patients with HDL-C values between 210 and 250 mg/L had a history of definite viral illness. Forty-nine patients with HDL-C values between 250 and 300 mg/L included only three patients with diagnostic viral symptomatology.

These observations suggest strongly that there is a decrease in HDL-C values in many patients with acute viral disease and in some patients with a history of recent viral illness. It appears that patients with diagnostic symptomatology of severe viral illness have substantially subnormal HDL-C in a high percentage of cases and, indeed, for values below 200 mg/L the vast majority of patients have viral disorders. This same group of patients often, but not always, have lower than average total cholesterol values. Although triglyceride values are included in the Table, they did not appear to help in the clinical interpretation. Likewise, ratios of total cholesterol to HDL-C or percentage of HDL-C present did not appear to be useful in distinguishing this subgroup of patients.

The clinical usefulness of the lipid tests appears to be diminished by calculating any sort of ratio or percentage in any of the patients having lipid profiles and, on an epidemiologic basis, is about the same as making a ratio of systolic blood pressure and number of cigarettes smoked.

It also appears that the 200 mg/L cutoff point of HDL-C is a possible useful index value, because only four patients with values below 300 and above 200 mg/L for HDL-C had diagnostic symptomatology of viral disease.

The case history of one of us (E.E.B.) may shed some light on the matter. His HDL-C usually is in the range of 500-595 mg/L, depending on exercise and diet. Ten days after a viral illness (sore throat, low-grade temperature, upset stomach, and aching muscles), his HDL-C value was 420 mg/L, returning to former "normal" values again in one month.

Certainly some patients with higher values may have had viral disorders; however, the symptoms were not severe enough to allow the physician to make a written diagnosis. These observations need to be substantiated by prospective studies, and, if confirmed, have implications in the interpretation of HDL-C values in patients with recent viral illnesses. A possible explanation is disruption of the

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>HDL-C Total</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.H.</td>
<td>Viral myocarditis</td>
<td>120</td>
<td>620</td>
</tr>
<tr>
<td>N.A.</td>
<td>Viral hepatitis HBsAg pos.</td>
<td>190</td>
<td>1670</td>
</tr>
<tr>
<td>E.D.</td>
<td>Viral pneumonia</td>
<td>20</td>
<td>2610</td>
</tr>
<tr>
<td>H.S.</td>
<td>Viral illness</td>
<td>200</td>
<td>1970</td>
</tr>
<tr>
<td>R.H.</td>
<td>Viral hepatitis</td>
<td>190</td>
<td>2330</td>
</tr>
<tr>
<td>E.H.</td>
<td>Viral flu</td>
<td>140</td>
<td>2040</td>
</tr>
<tr>
<td>F.G.</td>
<td>Upper resp. illness (viral)</td>
<td>100</td>
<td>1290</td>
</tr>
<tr>
<td>D.L.</td>
<td>Viral pneumonia; herpes simplex of eye</td>
<td>190</td>
<td>1610</td>
</tr>
<tr>
<td>K.P.</td>
<td>Viral pneumonia</td>
<td>160</td>
<td>1510</td>
</tr>
<tr>
<td>J.B.</td>
<td>Viral illness</td>
<td>200</td>
<td>1360</td>
</tr>
<tr>
<td>E.B.</td>
<td>Viral pneumonia</td>
<td>200</td>
<td>630</td>
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<tr>
<td>R.C.</td>
<td>Melanoma re-excision</td>
<td>140</td>
<td>2450</td>
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<tr>
<td>W.C.</td>
<td>Acute myocardial infarct</td>
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<td>2480</td>
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<tr>
<td>G.B.</td>
<td>Hypertensive cardiovascular disease</td>
<td>190</td>
<td>2420</td>
</tr>
<tr>
<td>D.T.</td>
<td>Atherosclerotic coronary heart disease</td>
<td>190</td>
<td>3210</td>
</tr>
</tbody>
</table>
usual lipid metabolism in the liver and (or) small bowel secondary to the severity of the viral infection and may explain why some patients are affected more than others.

Reference

E. Eugene Baille 
C. William Orr 
Anderson Memorial Hospital 
Anderson, SC 29621

Phadebas Amylase Test Kits

To the Editor:
The observation by Hafkenscheid (1) that Phadebas Amylase Test kits with bovine serum albumin (BSA) gave lower results than those without BSA is, as he infers, evidently caused by differences between the standard curves supplied by the manufacturer.

We found rather better agreement for plasma assays between the old- and new-formulation tablets (2). However, we routinely check the calibration curve for each lot of tablets against the stated values of Phadebas Reference Serum and Phadebas ACR (high amylase) serum. If there is a small discrepancy between our calibration line thus derived and that supplied by Pharmacia, we use our own line when it has been checked and we are satisfied that it is correct for our conditions. We have previously discussed this point (3).

In our comparison of the old and new tablets (2), we made a slight alteration to the calibration line for the old tablets, but found it to be unnecessary for those with BSA. This had the effect of slightly lowering the results with the old tablets. It would be interesting to know whether Hafkenscheid has any assay results for the Phadebas control sera by the two methods.

In our opinion, it would be wrong to introduce a new reference range for the tablets with BSA on the basis of the evidence now available. The discrepancy could just as easily have resulted from a faulty calibration line for the old batch of tablets.

References


C. H. Foot 
K. Wiener 
North Manchester Gen'l Hosp. 
Crumpsall, Manchester, M8 6RB, 
U.K.

Dr. Hafkenscheid responds:

To the Editor:
Wiener and Foot observed better agreement between the amylase activity determined with the old method (tablets without BSA) and the new method (tablets with BSA), although the results of the two studies are not impressive (1, 2) (y = 0.97x + 10.91 and y = 0.93x – 14.4, respectively; where y represents results with new tablets and x with old tablets).

I did not check the calibration curves supplied by the manufacturer as did Wiener and Foot. The main point is that, once corrected for the calibration curves, exactly the same results can be obtained with the old and new method.

When control sera were used I obtained the same results. The enzymic activity in the absence of BSA is higher than in the presence of it, but the absorbances at 620 nm are the same, so there is no difference between results for normal human sera and control sera.

I agree (2) with Wiener and Foot that it will not be necessary to introduce a new normal range for amylase activity determined with the new method.

References

J. C. M. Hafkenscheid 
Laboratory for Clinical Chemistry 
Department of Internal Medicine 
St. Radboud Hospital 
University of Nijmegen 
Nijmegen, The Netherlands

Correlation Coefficients as a Verification of Linearity

To the Editor:
We noted the recent Letter by Gindler [Clin. Chem. 25, 357 (1979)] with interest. We agree that the assumption of linear relationship in regressing data must be verified. However, a simple and straightforward method is offered by calculating the correlation coefficient. This is conveniently included in most inexpensive programmable calculators to which the author refers, and correlation coefficients are routinely cited in published papers.

If the absolute value of the correlation coefficient deviates significantly from 1.00, a more thorough exploration of the causes is indicated. It may well be that the curve fitting proposed by Gindler is appropriate in some instances, but this, too, must be tested by calculating the corresponding correlation coefficient. Thus, while we fully agree that an automatic application of linear regression is wrong, we also suggest that if the relationship is not linear, more sophisticated investigation is needed than the automatic assumption [that there is] yet another relationship.

Lee B. Eppstein 
Gabor B. Levy 
Photovolt Corp. 
1115 Broadway 
New York, NY 10010

Dr. Gindler responds:

To the Editor:
The suggestion of Eppstein and Levy with regard to the simplicity and straightforwardness of the correlation coefficient is, unintentionally to be sure, deceptive, because the shortcomings of that function were pointed out in reference (1) of my Letter (2). It has long been known that the scatter of data produced by chance alone will cause correlation coefficient (r) values that are considerably less than 1.00, even when the equation y = mx (y = dependent variable, x = independent variable, m = constant) holds and there are several values of x and y, such acceptable values having been tabulated (3).

On the other hand, the equation and technique which I suggested allows for such scatter due to chance and not only indicates whether or not the system is linear but also gives an inkling of what the actual relationship may be. This situation is unlike that of the correlation coefficient technique suggested by Eppstein and Levy, where a value of r that is less than 1.000 is unanswered the important question of whether it is due to chance or true nonlinearity, even where considerable scatter of data may exist. My associates and I have been gathering data, from the literature as well as from our own studies, which indicate that the suggested equation (2) empirically fits many practical systems, and this work has been submitted for presentation at the 31st national meeting of the AACC later this year. This verifies my statement that this equation describes at least part of an existing curvilinear relationship. At no