Micral-Test Sensitivity

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We feel a need to comment on the interpretation of results in a recent publication by Tiu et al. (1). There is an apparent error in Table 2. The last line in this table should read 50–2-0–0 instead of 33–3-2–1 as indicated. Nonetheless, Tiu et al. conclude that the Micral-Test was more specific yet less sensitive than the Microbumintest. This conclusion is based on a small true-positive population of $n = 12$. The question that really needs to be addressed is this: Was this a large enough true-positive population to draw such conclusions? We think not.

For example, if we assume the true sensitivity of Micral-Test to be ≥90% (2,3), then how likely is it that one would observe a sensitivity of ≤75% in repeated sampling as was observed in this study? With only 12 samples, a test with a true sensitivity of 90% will yield results equal to or worse than this study 11–12% of the time. And this assumes that the test was performed perfectly according to the manufacturer's packaging instructions. In other words, if 100 sites were to do the same identical experiment as performed in this study, obtaining only 12 positive samples and testing as indicated, one would expect that 11 or 12 of these sites would show results equal to or worse than this study.

Increasing the positive sample size from $n = 12$ to $n = 24$ dramatically lowers the chances of this scenario from 11–12 to 2–3%. If a sample size of $n = 60$ were attained, then this would drop to <0.1%. Therefore, one has to conclude that a sample size of $n = 12$ is not enough to give a clear indication of the true sensitivity, with high confidence, of either product. Furthermore, we do not recommend freezing and preserving the urine samples before testing, which was apparently part of the study design. This is indicated in the Micral-Test package insert.

Fresh urine samples were used for both the Micral-Test and Microbumintest, as recommended in the package inserts of these tests. Samples were frozen and stored for the quantitative tests only after they were tested with these two tests.

We agree that the number of positive samples in our 75 samples was small. The same limitation in drawing conclusions on sensitivity applies to the Microbumintest also. It would be helpful to verify our conclusion in studies with larger positive sample sizes.

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RIA, RADIOIMMUNOASSAY.

References

1. Tiu SC, Lee SS, Cheng MW: Comparison of six commercial techniques in the measurement of microalbuminuria in diabetic patients. *Diabetes Care* 16:616–20, 1993
2. Marshall SM, Shearing PA, Alberti KGMM: Micral-Test strips evaluated for screening for albuminuria. *Clin Chem* 38:588, 1992
3. Boehringer Mannheim Corporation: Micral-Test package insert, data on file

Response to Chmielewski and Miller

We would like to thank Steven A. Chmielewski and Earl E. Miller for pointing out the error in Table 2 of our study (1) and for their comments. The correct table appears here.

References

1. Tiu SC, Lee SS, Cheng MW: Comparison of six commercial techniques in the mea-

Table 2—*Micral-Test and Microbumintest testing of 75 urine samples, as compared with RIA*

	Concentrations by RIA (mg/L)					
	0–10	10–20	20–30	30–50	50–80	80–130
Micral-Test (mg/L)						
100						
50			1		1	2
20	6	2	4	1		
10	15	4				
0	33	3	2	1		
Microbumintest (intensity of color change)						
++					1	2
+	4	7	7	2		
−	50	2				

Numbers indicate patients showing the particular result. From Tiu et al. (1).

surement of microalbuminuria in diabetic patients. *Diabetes Care* 16:616–20, 1993

Hyperinsulinemia in type II diabetic patients with microalbuminuria

Microalbuminuria predicts reduced survival in type II diabetes and is associated with both cardiovascular disease and cardiovascular death (1,2). So far, no risk markers have been clearly identified as a potential explanation for the increased cardiovascular morbidity and mortality among type II diabetic patients with microalbuminuria (3). In the general population, hyperinsulinemia has emerged as an independent predictor of coronary heart disease (4). Because many variables (such as body weight, age, duration of disease, sex) may be important confounders of any putative relation between hyperinsulinemia and microalbuminuria, we have compared fasting and postglucagon C-peptide levels of 43 type II diabetic patients with microalbuminuria (albumin excretion rate >20 μg/min, range 25–278 μg/min) to those of 43 normoalbuminuric (albumin excretion rate <20 μg/min) type II diabetic patients attending our outpatient clinic individually matched for age (54 ± 1.4 vs. 54 ± 1.4 yr; mean ± SD), sex (30 M/13 F in each group), BMI (30 ± 1.3 vs. 30.1 ± 1.3 kg/m^2), known duration of diabetes (7.82 ± 0.92 vs. 7.79 ± 0.90 yr), and treatment (10 patients were treated by dietary advice, 29 were taking oral antidiabetic therapy, and 4 were on injected insulin in each group). Serum creatinine concentration was in the normal range (<120 μM) in all patients. No significant differences were found between the two groups in total serum cholesterol, sBP, dBP, prevalence of smoking, FBG, and GHb. Only basal and postglucagon C-peptide and triglyceride plasma levels were significantly higher in patients with microalbuminuria (Table 1).

Table 1—*Clinical and selected biochemical data in microalbuminuric and normoalbuminuric type II diabetic patients*

	Type II diabetic patients	
	Microalbuminuric	Normoalbuminuric
n	43	43
sBP (mmHg)	150 ± 3	148 ± 3
dBP (mmHg)	87 ± 3	87 ± 2
Total cholesterol (mM)	5.88 ± 0.28	5.92 ± 0.24
Triglycerides (mM)	3.04 ± 0.42*	1.98 ± 0.53
Blood glucose (mM)	12.2 ± 0.7	12.1 ± 0.7
GHb (%)	8.8 ± 0.4	8.8 ± 0.3
Basal C-peptide (ng/ml)	2.9 ± 2.2*	2.0 ± 1.3
C-peptide after glucagon (ng/ml)	4.5 ± 3.1†	3.3 ± 1.8
Prevalence of smoking (%)	25	26

Data are means ± SD.
*$P < 0.005$.
†$P < 0.01$.

Microalbuminuria was also associated with a significantly increased prevalence of coronary heart disease (37.2 vs. 18.6%; $P < 0.05$). We conclude that conventional risk factors cannot explain the increased cardiovascular morbidity of microalbuminuric patients. The higher C-peptide concentrations, along with elevated plasma triglyceride plasma levels in patients with microalbuminuria, would suggest peripheral hyperinsulinemia, possibly because of a greater insulin resistance. In view of these data, the possibility must be considered that hyperinsulinemia and/or insulin resistance would be the underlying factor for the association between microalbuminuria and cardiovascular disease.

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TYPE II DIABETES, NON-INSULIN-DEPENDENT DIABETES MELLITUS; BMI, BODY MASS INDEX; sBP, SYSTOLIC BLOOD PRESSURE; dBP, DIASTOLIC BLOOD PRESSURE; FBG, FASTING BLOOD GLUCOSE.

References

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2. Mogensen CE: Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. *N Engl J Med* 310:356–60, 1984
3. Allawi J, Jarrett RJ: Microalbuminuria and cardiovascular risk factors in type II diabetes mellitus. *Diabetic Med* 7:115–18, 1990
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