Table 1. Concentrations of THC metabolite and EFV metabolites in patient urines tested for THC metabolites by immunoassay reagents from multiple vendors.

Patient	nor-THCOOH,[a] μg/L	EFV,[b] mg/L	EFV-8-OH,[b] mg/L	EFT-8-G,[b] mg/L	Immunoassay result[c]					
					BioSite	Dade-Behring	OraSure	Immunalysis	Abbott	Cedia-Dau
1	1.4	<0.1	3.8	39.6	THC+	Neg	Neg	THC+	Neg	THC+
2	<0.1	0.1	23.7	11.2	THC+	Neg	Neg	THC+	Neg	THC+
3	<0.1	<0.1	94.8	0.9	Neg	Neg	Neg	THC+	Neg	Neg
4	0.7	<0.1	4.4	3.6	Neg	Neg	Neg	THC+	Neg	THC+
5	3.4	0.1	27.0	1.8	Neg	Neg	Neg	THC+	Neg	THC+
6	0.4	<0.1	20.4	2.6	Neg	Neg	Neg	THC+	Neg	THC+
7	<0.1	<0.1	65.5	14.0	THC+	Neg	Neg	THC+	Neg	THC+
8	<0.1	<0.1	13.0	16.6	THC+	Neg	Neg	THC+	Neg	THC+

[a] nor-THCOOH, 11-nor-Δ^9-tetrahydrocannabinol-9-carboxylic acid, as measured by GC-MS.

[b] Concentrations of EFV, EFV-8-OH, and EFV-8-G were determined by HPLC with ultraviolet detection, and peak purity and identify were confirmed by nanospray MS/MS.

[c] THC+, positive test result indicating THC metabolite concentration greater than the stated cutoff value (50 μg/L); Neg, negative test result indicating THC metabolite concentration below the stated cutoff value.

munalysis Corporation [Cannabinoids (THCA/CTHC) Direct ELISA Kit] were subject to interference attributable to urinary EFV-8-G. Reagents from these 3 vendors produced test results indicating the presence of THC metabolite above the immunoassay cutoff value of 50 μg/L, although GC-MS analysis gave a measured THC metabolite concentration <5 μg/L in all samples. False-positive findings from the above immunoassays were reversed by acid hydrolysis of urine before re-testing, with a single exception (patient 1). Nanospray MS/MS of acid-treated urine verified the conversion of EFV-8-G into EFV-8-OH in all cross-reacting samples except for the single sample that remained cross-reactive; this sample exhibited incomplete hydrolysis (20% hydrolysis). There were no occurrences of false-positive findings in immunoassays performed with reagents from Dade-Behring Incorporated (Syva® DAT), OraSure Technologies (Cannabinoids Intercept MicroPlate EIA), and Abbott Laboratories (Ax-SYM Cannabinoids Reagents).

Despite the existence of extensive anecdotal literature concerning interference by EFV in urinary THC immunoassays, these data are the first characterization of the nature and extent of this interference with commonly used "Drugs of Abuse" screening reagents. These findings demonstrate that some, but not all, immunoassay reagents used for the detection of THC metabolite are susceptible to cross-reaction errors resulting from the presence of EFV (metabolite) in human urine.

We sincerely appreciate the clinical support provided by the University of California, San Diego, HIV Neurobehavioral Research Center. Microgenics Corporation (Fremont, CA), BioSite Incorporated (San Diego, CA), Immunalysis Corporation (Pomona, CA), and OraSure Technologies (Bethlehem, PA) graciously provided complimentary assays or reagents. These studies were funded in part by the Center for Medicinal Cannabis Research, University of California, San Diego.

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DOI: 10.1373/clinchem.2006.067058

Metabolic Syndrome: Older than Usually Assumed, But Still Too Young to Die

To the Editor:

In a recent issue of the Journal, Dr. Gerald Reaven informed us of the death of the metabolic syndrome *(1)*.

Dr. Reaven played an important role in the development of this concept, which consolidates several cardiovascular risk factors into a single entity called "syndrome X". In 1988 he highlighted the clinical importance of the syndrome, identifying insulin resistance as the central pathophysiologic feature *(2)*. In 2001, the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) renamed the cluster of cardiovascular risk factors and metabolic disorders "metabolic syndrome" *(3)*. Their report *(3)* and the 1988 article by Reaven *(2)* are considered the birth certificates of the metabolic syndrome; we might therefore be celebrating its 18th or 5th birthday. However, it was 80 years ago that Kylin *(4)* described a clustering of hypertension, hyperglycemia, and gout, and approximately 40 years ago, Vague *(5)* reported that upper body obesity is often associated with certain metabolic abnormalities. The term metabolic syndrome was already introduced into the scientific literature in 1975 by Hermann Haller, former head of the Department of Medicine, Medical Academy Dresden, Germany. He concluded that the combination of hypertension, obesity, dyslipidemia, and disturbed glucose metabolism with a consecutive increase of cardiovascular disease risk occurs more often than might be expected by chance *(6)*. Haller also recognized that hyperuricemia and hepatic steatosis were associated with the syndrome, not as risk factors, but as a consequence. He proposed that obesity is the common causative factor. An article from the same group published 6 years later *(7)* again provided a definition of the term metabolic syndrome identical to current concepts. Although this latter article is listed in PubMed, both of these publications appear to be completely neglected in today's scientific literature. In conclusion, the concept and term of the metabolic syndrome has already reached the age of 30 years, which is more mature than usually assumed but possibly still too young to die.

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DOI: 10.1373/clinchem.2006.067801

The Metabolic Syndrome: What's in a Name?
Reply to: Meisinger et al. Metabolic Syndrome: Older than Usually Assumed, But Still Too Young to Die

To the Editor:

To respond to the letter by Meisinger et al., it is necessary to make a distinction between metabolic syndrome as a diagnostic category and metabolic syndrome as a pathophysiologic entity designating a cluster of related metabolic abnormalities; a differentiation that Meisinger and colleagues either did not discern or thought not important enough to make. The metabolic syndrome as a diagnostic entity, with specific components and cut points, was introduced by the WHO in 1998 *(1)*; therefore, it is less than 10 years old. My suggestion that there was no reason for it to live any longer *(2)*, a point of view that stimulated the letter by Meisinger and colleagues, may be considered excessively cruel, but it was echoed in the recent joint report from the American Diabetes Association and the European Association for the Study of Diabetes *(3)*.

Turning now to the pathophysiologic entity designated as the metabolic syndrome, it is always a bit chancy to open discussions of who said what first. There is an undertone in the letter by Meisinger et al. that the concepts outlined in my Banting Lecture in 1988 preempted the valuable contributions of Kylin *(4)*, Vague *(5)*, and Haller's research group *(6, 7)*. I believe that what distinguishes my efforts from theirs was the presentation of evidence from a series of studies carried out over the previous 25 years that insulin resistance at the level of the muscle and adipose tissue (a concept that was certainly foreign to Kylin and Vague and not offered by Haller and colleagues) was the common abnormality that increased the likelihood of an individual developing not only type 2 diabetes but also cardiovascular disease (CVD) *(8)*. At that time I suggested that the combination of insulin resistance and compensatory hyperinsulinemia that predicted the development of type 2 diabetes also increased the chances that an individual would develop a cluster of related abnormalities that increased CVD risk. I do believe that there is a difference between offering a testable hypothesis as to why certain CVD risk factors cluster together to increase CVD risk and simply noting that certain abnormities seem to co-