



# A Simple, Reliable Blood Test Helps Detect Chronic Alcohol Abuse

Regina Reppin, PhD, University Clinic in Magdeburg, Germany, and Jos P. M. Wielders, PhD, Meander Medical Center in Amersfoort, Netherlands, are helping physicians diagnose chronic alcohol abuse using a specific blood test and analysis systems that deliver reliable, fast results.

By Matthias Manych

The first thing that suffers from chronic alcohol abuse is the abuser's own health. But the consequences can also be devastating to families, often destroying social relationships. The harmful health effects of excessive alcohol consumption have become a constant strain on society. In the United States, there are nearly 14 million alcoholics or people who abuse alcohol. In 1998, the financial losses due to alcohol-related illnesses, premature deaths, and crimes were estimated at 185 million U.S. dollars.<sup>1</sup> According to information provided by the World Health Organization (WHO), the situation is even more severe in Europe, where the

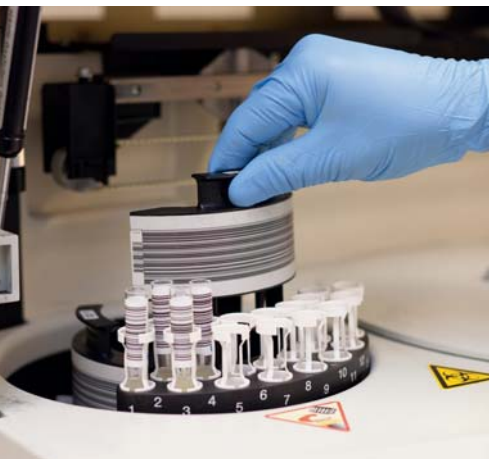
incidence of illness and premature death resulting from alcohol problems is the highest in the world.<sup>2</sup>

Regina Reppin works at the Institute for Clinical Chemistry and Pathobiochemistry at the University Clinic in Magdeburg, a city of about 230,000 in Germany. Reppin estimates that ten percent of patients in the region have a drinking problem. That estimate is echoed by Jos P. M. Wielders, PhD, who works at the Meander Medical Center in Amersfoort, the second largest city in the Dutch province of Utrecht, with a population of about 150,000. The Meander Medical Center is among the 20 most prestigious hospitals in the country,



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Jos P. M. Wielders, PhD,  
Department of Clinical Chemistry,  
Meander Medical Center,  
Amersfoort, Netherlands



Because the samples are bar-coded, different patient tubes with different plasma protein requests can be measured simultaneously.

...serving about 300,000 people in the area. Wielders puts the percentage of alcoholics in the regional population and at the hospital at the same figure: ten percent. Wielders, head of general and special chemistries at the facility’s Department of Clinical Chemistry, reports that alcohol abuse has different effects within hospitals’ various clinical departments: “When we talk about risk, for some types of trauma surgery, alcohol is reported to be involved in up to 70 percent of the cases.” Up to 25 percent of internal medicine cases are attributable to alcohol problems, along with up to 30 percent in psychiatry, Wielders says. While a general practitioner, who knows his patients well, can estimate whether his or her patient is at risk with a few standard questions, there are published questionnaires (like AUDIT) available to

ask patients about their alcohol use. The risk, however, that respondents will underestimate their alcohol problems – deliberately or unconsciously – is high. Anyone who drinks more than 60 grams of alcohol daily, equivalent to one bottle of wine or one-and-one-half liters of beer (about three 16-ounce cans or four 12-ounce cans), is at high risk. “A person with this kind of behavior, though, will vehemently deny it if someone says to him, ‘watch out, you’re on your way to becoming an alcoholic,’” says Reppin.

### Clear Biomarker, Reliable Test

However, medical laboratories have to offer doctors and psychiatrists reliable test methods that confirm alcohol abuse without any doubt. The carbohydrate-deficient transferrin (CDT) is the most specific marker to detect high alcohol

consumption, and the Siemens N Latex CDT Kit is a very specific assay to measure CDT<sup>3</sup>. In the late 1980s, Swedish researchers discovered that high alcohol consumption induces characteristic changes in the common serum protein transferrin, giving rise to molecular forms that are significant indicators for alcohol abuse, commonly known as CDT.

Reppin heads a working group that focuses on proteins and molecular biology methods, and she is especially pleased at this discovery. Now, lab professionals are not dependent on indicators that either take months for alcohol abuse detection or that are influenced by non-alcohol related causes. "The rare diseases that also raise CDT levels are easier to isolate," reports clinical chemist Reppin. CDT concentrations in the blood represent the average intake of two to three weeks, and it takes about two weeks of abstinence to return to a basic level again, says Wielders. One night of excessive drinking is not enough to send CDT values into the critical range.

Based on these research findings, the nephelometric N Latex CDT testing method was developed. Wielders was involved in evaluating the N Latex CDT Kit at an early stage of development. The mechanism underlying the test is an antigen-antibody reaction. The reagent used in the test contains monoclonal antibodies and CDT-like antigens on Latex particles. "If CDT was not present in the sample, the antibody would agglutinate only with the CDT-like antigen. CDT from the sample inhibits this agglutination. Even without drinking, some CDT is always present, so results will never be zero," explains Wielders. This reaction can be measured with the BN™ II or BN ProSpec® System quickly and accurately. This method determines, with high specificity, whether a test subject has elevated levels of CDT in his or her blood, but that is not its only virtue. It is also easy to use and robust. The only immunoassay CDT method on the market, samples do not have to be pretreated to undergo N Latex CDT testing, and with the BN system all measurements and analyses are automated. After just 18 minutes, it delivers the first results. Because the

sample tubes and reagents are bar-coded, different plasma proteins can be analyzed simultaneously. A broad plasma protein test menu of more than 60 tests is available for determinations from serum, plasma, urine, and cerebrospinal fluids.

### Proven in Internal Routines, Acknowledged Externally

The lab in Magdeburg performs about 2,000 CDT analyses each year, requested



**“We run CDT for the university clinic’s emergency room, psychiatry, and gastroenterology departments. CDT is fully automated on the BN system and samples do not require pretreatment.”**

Regina Reppin, PhD,  
Institute for Clinical Chemistry and Pathobiochemistry,  
University Clinic, Magdeburg, Germany

## Organ Imaging Options for Damage Associated with Alcohol

Alcohol affects the entire body. The immunological and metabolic changes caused by chronic alcohol abuse can trigger both acute and chronic diseases. Hardly a single organ in the body is immune to the ill effects of alcohol abuse. From head to foot, the entire body is at risk. Alcohol adversely affects the mucous membranes, for instance, starting in the mouth and passing through the throat and esophagus before affecting the entire digestive tract. If the inflammation caused by constant, risky consumption of alcohol lasts for many years, cell damage can result in precancerous conditions and potentially in malignant tumors. In addition to lab findings and clinical examinations, imaging processes should help detect these developments early on or locate manifestations of these effects and determine their extent.

In the gastrointestinal tract, pathological changes are often detected via endoscopy. If further examination is advisable, tissue samples are taken during this process. Depending on the suspected diagnosis, but also according to the medical center's specialization, scintigraphy, magnetic resonance imaging (MRI), and computed tomography (CT) imaging methods are also used. Alcohol-related liver diseases such as fatty liver, alcoholic hepatitis, and cirrhosis are as widely known as

they are widespread. The imaging repertoire for these includes ultrasound, MRI, and CT. Ultrasound is usually applied first in detecting dilated bile ducts and to confirm diagnosis of fatty liver. Conventional ultrasound, however, cannot detect fibrotic changes until cirrhosis is already present.

Major progress in this regard is offered by Strain Imaging, a simple ultrasound application that enables a real-time assessment of the stiffness or elasticity of the tissue. Siemens' unique Virtual Touch™ Tissue Imaging and Quantification\* technology, which demonstrates and measures the stiffness of tissue, helps physicians better assess the need for biopsy. Another emerging application in the field of elasticity imaging is MRI elastography.

The nervous system can be directly damaged by toxic acetaldehyde, which is a product of alcohol metabolism, with consequences including disruptions in eye movement, unsteady gait, and disorientation. The diminution of brain mass that commences in alcoholics can lead to, for example, dementia, which can be visualized using CT and MRI. The good news: If a patient abstains, the body can balance out the loss of nerve cells.

\* Not available in the U.S.

by the university clinic's emergency room and by its psychiatry and gastroenterology departments. In the case of emergency room patients who are unresponsive due to factors such as delirium or a traffic accident, the speed of the N Latex CDT method pays off. In gastroenterology patients, the aim is often to use CDT to differentiate between alcohol-induced and non-alcohol-induced liver diseases. In these cases, the tests are often accompanied by imaging procedures such as sonography, which detect factors such as changes in the liver caused by cirrhosis indicating alcohol abuse. With CDT tests, alcohol abuse can be ruled out and the basic cause of the liver disease can be treated in the early stages.

Reppin is a fan of the nephelometric measurement with the BN systems and the use of monoclonal antibodies, saying, "Everything I can measure here with a monoclonal antibody, I measure without disruptive factors." The less a person needs to intervene in the test, the more precise its results are. This test's very high reliability is also not affected by variations in the samples. As the expert in Magdeburg explains, lab tests conducted in Germany undergo not only internal quality control, but also external reviews. To this end, the German INSTAND Society for Promotion of Quality Assurance in Medical Laboratories regularly conducts interlaboratory tests. In the four years since the lab in Magdeburg began work-

ing with the N Latex CDT Kit, it has passed all of the external performance tests conducted.

Within the department where Wielders works, 4,000 to 5,000 N Latex CDT tests are performed each year. Tests ordered by general practitioners who need the results in order to confront patients about their alcohol problems are the minority. Three-quarters of the tests are performed for legal issues, particularly when it comes to withdrawal and regranting of driver's licenses that have been suspended for alcohol abuse. In the Netherlands, psychiatrists commissioned by the government's Driving Test Organization are responsible for the medical judgement of the clients' driving ability. The depend-

able CDT immunoassay test is a valuable and acknowledged part of the highly regulated procedures of withdrawal and regranting. "The psychiatrists say that the CDT test is the most valuable contribution in the whole report. They hesitate very much to say someone is drinking with a normal lab test, and especially with a normal CDT result. Meanwhile, the CDT test is the cornerstone of the psychiatrists' report about chronic alcohol abuse and an essential part of the official guideline on the subject," Wielders reports with some satisfaction. After all, he has been championing the evaluation of this test, along with standardization of reliable test procedures for legal purposes for many years.

Among his other activities, Wielders is the Chairman of the CDT Committee of the Dutch Society of Clinical Chemistry and a member of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) working group on CDT standardization. His department is named as a reference lab for the IFCC. This IFCC working group has made a major contribution to ensuring that HPLC is acknowledged as a reference method at the international level. CDT testing with the N Latex CDT Kit and the BN systems has a relative specificity of 97 percent compared to the HPLC reference method.<sup>3</sup> For Reppin and Wielders, the CDT test has become an essential method in diagnosing chronic alcohol abuse.

**Matthias Manych**, a biologist, is a freelance scientific journalist, editor, and author specializing in medicine. His work appears primarily in specialized journals, but also in newspapers.

<sup>1</sup> National Institute on Alcohol Abuse and Alcoholism (NIAAA), Strategic Plan 2001–2005.

<sup>2</sup> <http://www.euro.who.int/en/what-we-do/health-topics/disease-prevention/alcohol-use/facts-and-figures>.

<sup>3</sup> Delanghe, J. et al; Development and Multicenter Evaluation of the N Latex CDT Direct Immunonephelometric Assay for Serum Carbohydrate-Deficient Transferrin, *Clinical Chemistry*, 53:6 1115–1121 (2007).



Samples do not have to be pretreated to undergo N Latex CDT testing, and with the BN ProSpec System all measurements and analyses are automated.

## Summary

### Challenge:

- Health risks, social and economic strain caused by chronic alcohol abuse
- Forensic and clinical decisions require clear-cut test results
- Biomarkers and test methods must work dependably and robustly
- Test method must improve workflow

### Solution:

- CDT: highly specific biomarker to detect chronic alcohol abuse
- N Latex CDT with monoclonal antibodies: clear reactions
- Reliable measurements via nephelometry
- BN II and BN ProSpec Systems offer automated workflows
- BN systems: fast results for a broad menu of plasma proteins
- N Latex CDT and BN systems in combination deliver accurate results with no sample prep

### Result:

- CDT: the most reliable biomarker for chronic alcohol abuse<sup>3</sup>
- N Latex CDT Kit achieves nearly 97 percent relative specificity to the HPLC reference method<sup>3</sup>
- Improved workflow throughout the testing process
- Automated method with bar-code detection for various sample materials
- Robust, validated test results in 18 minutes
- High sample throughput of up to 130 tests/hour with the BN II System

## Further Information

[www.siemens.com/cdt](http://www.siemens.com/cdt)