



Blood test warns of heart failure

To keep the motor running

It is not just the elderly who suffer from congestive heart failure; even young people's "engines" can start to stutter. Usually they are not even aware of it, since they rarely notice any symptoms. And yet the consequences can be fatal. Bayer has launched a blood test to help doctors detect this life-threatening disease at an early stage. After all, if treated in time, the old ticker will keep working for longer.

This stained X-ray shows up a constriction (left) of the artery that supplies the heart muscle with oxygen-enriched blood – which could be lethal for the patient.



Rich Molloy collects the substances that will serve as "raw materials" for diagnosis with the ADVIA Centaur® system.

If it feels like climbing a mountain when all you are doing is walking up three flights of stairs, or if you tend to get out of breath, with your heart racing and your knees giving way, then you should get yourself checked out thoroughly, no matter what age you are. The diagnosis is likely to be advanced congestive heart failure. This condition is by no means simply part of the normal aging process of the heart; it is a serious and prevalent disease in the industrial nations of the West – albeit one that can be effectively treated.

"Confirming a suspected case of heart failure is a complex process, however, and cannot be done everywhere," says Dr. Rainer Neumann from Bayer HealthCare's Diagnostics Division, European Scientific Affairs, in Leverkusen. "The symptoms are often either not apparent or are ignored by the patient." Congestive heart failure (CHF) is the third most common cause of death in Germany, where some 1.6 million people are currently undergoing treatment for heart failure. Since so many cases go undetected, however, the true number of people affected by this condition in Germany is estimated at up to four million.

Advanced heart failure, with classic symptoms like difficult breathing and edema (swelling) of the legs and arms, is the most common reason for hospitalization in those over 65. It is six to nine times more likely to end in death than any other disease. "Life expectancy is increasing all the time, but

people's hearts aren't getting any younger," explains Neumann. And yet we can delay the weakening of the heart muscles - by making lifestyle changes or taking blood pressure-lowering drugs (called antihypertensives) such as beta-blockers and ACE inhibitors. The New York Heart Association defines four classes of congestive heart failure, from Class I with virtually no symptoms to Class IV when patients complain of breathing difficulties even at rest.

The sooner the doctor identifies a heart problem, the sooner he can take measures to counteract it. In order to allow a clear diagnosis as early as possible, Bayer HealthCare researchers have developed a blood test for the fully automated ADVIA Centaur® diagnostics system, which can help to confirm heart failure as early as Class I.

Heart-muscle protein indicates risk of disease

Neumann, who is an expert in diagnostics, explains the principle as follows: "The test allows us to detect a specific protein in the blood that is produced almost exclusively by the heart muscle and is a very good indicator of cardiac stress." This protein, which experts call BNP (brain natriuretic peptide), is secreted in particular when the heart muscle is severely stretched. High BNP levels correlate with an increase in the muscular mass of the heart's left ventricle and are associated with an elevated risk of po-

Four classes of heart failure

The New York Heart Association defines four classes of heart failure. The disease usually goes unnoticed in the first two stages.

No symptoms (Class I)

People affected do not yet notice that their heart muscle has become weaker.

First symptoms (Class II)

Any unusually strenuous exertion causes shortness of breath, sweating, an increased pulse rate or slight dizziness. Mountaineers are completely out of breath.

Clear symptoms (Class III)

Even minor physical activities, like climbing steps, are suddenly difficult. The heart races. The person experiences a feeling of tightness in the chest and breathing difficulties. The ankles swell. By now patients are comfortable only at rest.

Manifest heart failure at rest (Class IV)

Patients have symptoms even at rest. They experience breathing difficulties particularly at night, when the symptoms can only be alleviated by sitting up. Patients are severely restricted in their activities.



Diagnostics expert
Dr. Rainer
Neumann from
Bayer HealthCare.

tentially fatal cardiovascular events, such as myocardial infarction or stroke. Thanks to the BNP blood test, doctors can spot signs of heart failure even before the patient notices anything wrong. They can also get a good idea of the severity of the disease. Another advantage, according to various publications, is that the test results allow doctors to optimize the patient's therapy.

The blood test is inherently reliable: "When we were developing the test, we decided to focus on the active BNP molecule," explains Margit Czup from the marketing department of Bayer HealthCare's Diagnostics Division in Fernwald near Giessen, Germany. Like insulin, the BNP protein generally occurs in the human body in the pro-molecule form. Pro-BNP is found in the heart cells and is released into the

bloodstream in higher quantities when there is an increase in volume or pressure. It is then broken down to form biologically active BNP and an inactive product called NT-pro-BNP. "Other tests use NT-pro-BNP as an indicator of heart failure. Many of the current studies assume that the NT-proBNP value is more dependent on Kidney failure than this applies to the BNP value, says Czup. She also emphasizes that active BNP has a shorter half-life in the body. Therefore BNP measurement includes less molecules which are solely accumulated but may not be direct effect of the current condition of the heart.

Professor Norbert Katz, Head of the Institute of Clinical Chemistry and Pathobiochemistry at the University of Giessen, has been examining the relationship between BNP blood levels and heart disease for years. "In addition to regular blood-pressure checkups, people aged 60 and above should have their BNP levels measured about every five years," Katz says.

The body's own early warning system facilitates diagnosis

Congestive heart failure can have various causes, such as high blood pressure, narrowing of the coronary arteries, atherosclerosis, myocarditis (inflammation of the heart muscle), heart valve disease or even myocardial infarction, and can affect different parts of the heart. In most cases, the heart muscles are weakened by damage to

the muscle wall as a result of an increase in blood pressure. This causes breathlessness or a build-up of fluid in the feet. The most common cause of heart failure is over-exertion of the heart's left ventricle, which supplies the body with oxygen-enriched blood. But the right ventricle, which pumps blood through the lungs, can also incur damage.

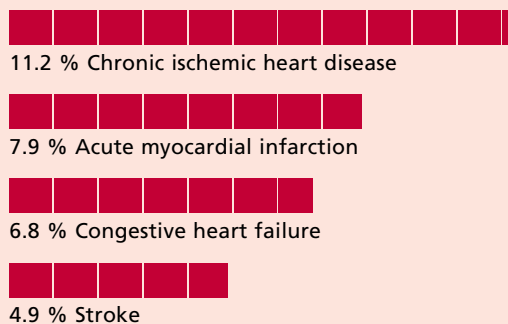
Up to now, it was always quite difficult to diagnose heart failure, even when the patient had pronounced symptoms. This is because experts were previously unable to identify appropriate substances, called diagnostic markers, which occur in the patient's blood and help indicate disease progression. The relevant markers for myocardial infarction or angina pectoris, on the other hand, were pinpointed a long time ago. This kind of early warning system is now becoming more and more important for other cardiovascular diseases.

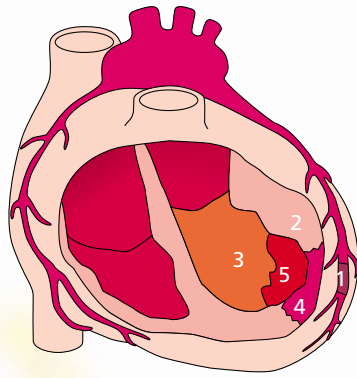
"In the past, very few general practitioners were able to establish a definite diagnosis of heart failure without using serum markers," points out Dr. Christian Schneider from the University of Cologne. In cases of suspected heart failure, they had to either rely on their own experience to rule out other causes – like lung disease in patients with breathing difficulties – or, if still in doubt, refer the patient to a specialist.

Now the ADVIA Centaur® diagnostics system can give doctors more certainty. Studies show, for example, that for

A dubious honor

Cardiovascular diseases top the list of the most common causes of death in Germany.





Engine trouble

The "human engine" can be damaged in many different ways. This illustration of the heart shows a healthy ventricle (on the left) compared with a damaged one (on the right). The coronary artery may be completely occluded (obstructed) (1), the heart muscle may have thickened (2), the ventricle may be enlarged (3) or there may have been a myocardial infarction (4) with the gradual build-up of a thrombus or clot (5). Whatever the case, the person affected frequently only notices these problems when it is far too late.

Heart failure

patients who go to the doctor for the first time with symptoms of heart failure, a negative BNP test result can rule out heart failure with around 98 percent certainty, while raised levels confirm the need for treatment.

Even the most minor cardiac damage is detected

Schneider, a heart specialist, can already draw on his own valuable experience involving several thousands of these tests, and he sees the findings of international studies confirmed on a daily basis in his work. One of these studies was led by Professor Alan S. Maisel from the University of California, San Diego. He and his colleagues examined more than 1,500 patients with acute dyspnea (shortness of breath) and found that the BNP value closely correlated with the severity of CHF.

At Cologne University Hospital, Schneider also believes in treatment based on BNP monitoring: "It has proven extremely useful in everyday practice." According to Bayer expert Neumann, the serum marker assay has given doctors not only a very valuable tool for perfecting the drug regimen, "but also a means of long-term monitoring, allowing them to adjust the treatment on a continuous basis for the best possible results."

Bayer's BNP test is an excellent addition to the other cardiac serum markers that have been available with the fully automated ADVIA Centaur® sys-



tem for some time. With the help of the troponin I test, for example, doctors can identify even the slightest damage to the heart and subsequently prevent myocardial infarction with the appropriate therapy. Levels of troponin, myoglobin and CKMB are used to diagnose acute myocardial infarction, and two general markers for heart disease have been added to Bayer's range of tests: homocysteine for the Centaur system and C-reactive

protein (CRP) for the ADVIA 1650 or 2400. These markers help doctors assess inflammatory processes such as atherosclerosis or coronary heart disease. Increased levels of homocysteine occur, for example, because of enzyme defects or a deficiency of folic acid or vitamin B6 and B12. Excessive levels of homocysteine have a toxic and destructive effect on the vascular endothelium, the "plasterwork" that lines the inner walls of the blood

Test samples ready to be put through Bayer's ADVIA Centaur® system.



For ease of use, each key represents a different test substance.



Helga Kröck (left) and Yvett Oberhoffner at the ADVIA Centaur® unit in the Diagnostics Division's training center in Fernwald.

vessels. This impedes blood flow and ultimately clogs up the blood vessels. The link between homocysteine levels and premature atherosclerosis was discovered more than 30 years ago.

The CRP value also increases if the patient already has atherosclerosis, since this protein always coincides with inflammation. In the United States, CRP is now considered the number one indicator of cardiac health. Hundreds of thousands of Americans regularly have their CRP levels checked out.

"Many cardiologists in Germany have long been using the CRP test on all patients already affected by coronary heart disease," points out Neumann.

He warns against attaching too much importance to raised levels without a full investigation: "You will also find a lot of CRP in the blood if you just have an inflamed wound." The BNP test has now been registered by the FDA (Food and Drug Administration) in the United States, and it is also available in Europe, Latin America and in the Asia-Pacific area.

www.acc.org/media/patient/chd/chf.htm

The website of the American College of Cardiology Foundation provides further information on cardiovascular disease.

Protection and prevention for the heart

Bayer HealthCare already markets a number of drugs for treating cardiovascular diseases, and it has others in the pipeline.

Use	Drug	Mode of action
Blood pressure	Kinzal®	Inhibits uptake of the blood pressure-raising hormone angiotensin II.
	Kinzalplus®	Decreases fluid and blood volume. Blood pressure is lowered.
	Adalat® Baymycard®	Reduce calcium uptake into the vascular muscles. The vessels relax and the blood pressure lowers.
Diabetes	Glucobay®	Inhibits the development of type II diabetes. Reduces the rate of cardiac incidents by nearly 50 percent.
Blood platelets	Aspirin protect®	Prevents the activation and accumulation of blood platelets in the blood vessels. Reduces the risk of myocardial infarction by 34 percent.
Blood coagulation	Factor Xa inhibitor	Prevents thromboembolic events.

Joining forces to help the heart

Modern medicines strike at the very root of cardiovascular disease, tackling blood glucose levels, vascular occlusion and levels of fats such as cholesterol. Now researchers at Bayer HealthCare are also aiming to reduce the pressure on the "blood pipelines". After all, high blood pressure (hypertension) is a major risk factor, especially in Europe.

"This is why drugs that treat high blood pressure are a top priority for cardiovascular concerns," explains Dr. Eva Muehlhofer from the Pharmaceuticals Division of Bayer HealthCare. Bayer's two latest drugs for preventing cardiovascular disease, Kinzal® and Kinzalplus®, were launched in the spring of this year. Diabetes is another risk factor for heart disease. It can be warded off not just by a healthy diet with plenty of vitamins, but also by Bayer's many active ingredients that help protect the heart.

Dr. Josef Schönesseiffen from Bayer HealthCare's Pharmaceuticals Division in Wuppertal promises that there are more drugs on the way: "For diabetics, for example, we have drugs in the pipeline that regulate both blood sugar levels and a lipid metabolism disorder in one."