Flaws of the Heart

Sudden death in athletes is often caused by cardiac defects

By KATHLEEN FACKELMANN

On Nov. 29, 1995, two-time gold medalist Sergei Grinkov collapsed suddenly while training at an ice rink in Lake Placid, N.Y. He died later that day. The 28-year-old had suffered a fatal heart attack.

Grinkov's death represents a tragedy for his family, friends, and the many fans of his elegant skating style. Yet like the sudden deaths of other famous athletes, it has focused attention on a killer that stalks people in the prime of life.

Sudden cardiac death kills an estimated 250,000 people in the United States each year, making it a public health problem of enormous magnitude.

As the summer games play out in Atlanta, several research teams are reporting discoveries about this heart hazard. One group recently identified a genetic flaw that played a role in Grinkov's untimely death. Another concluded that, in most cases, sudden death in athletes can be blamed on the heart—specifically, on one of several structural abnormalities.

Grinkov probably suffered no pain on that fateful morning last November. In medical terms, he suddenly went into ventricular fibrillation, a life-threatening quivering of the heart. A medical technician at the ice rink started cardiopulmonary resuscitation, and Grinkov was rushed to the emergency room at the Adirondack Medical Center in Lake Placid.

By the time Grinkov got to the hospital, his heart had stopped. Physician Joshua Schwartzberg and other staff members there nonetheless tried for more than an hour to bring him back to life. An autopsy revealed that Grinkov had suffered from severely clogged coronary arteries, the vessels that supply the heart with blood.

Although he was an elite athlete, Grinkov had the coronary arteries of a 70-year-old man with atherosclerosis. His widow and skating partner, Ekaterina Gordeeva, told Schwartzberg that her husband had never complained of chest pain or any other symptoms of heart disease. The only foreshadowing of the impending disaster had been his father's death at age 52 of a sudden heart attack.

Pascal J. Goldschmidt of Johns Hopkins University in Baltimore read an account of Grinkov's death in the New York Times. Goldschmidt, Paul F. Bray, also at Hopkins, and their colleagues had just described a genetic flaw that heightens the risk of early heart attack. He wondered if Grinkov had the trait.

Routine physical exams often don't turn up a cardiac condition in young athletes.

So Goldschmidt put in a call to the Adirondack Medical Center. He got lucky: The pathologist had saved a sample of Grinkov's blood and would ship the frozen vial to Baltimore.

When the vial arrived, the Hopkins team first extracted DNA from white cells in the blood sample. Then they searched for a particular version of the platelet antigen gene, which codes for a protein known to play a key role in the blood-clotting process. The group had reported on a link between a variation of this gene and heart attacks in the April 25 NEW ENGLAND JOURNAL OF MEDICINE.

The platelet antigen gene comes in two forms—Pl^{A1} and Pl^{A2}. The only difference between them is a slightly altered sequence of nucleotides, the building blocks of DNA. The Hopkins team had fingered Pl^{A2} as the villain in early heart attacks.

The researchers had studied 71 people with a heart attack or severe symptoms of heart disease. They compared those people to 68 people who had no known heart problems. Their investigation revealed that the heart patients were twice as likely to have inherited at least one Pl^{A2} gene as the controls.

Grinkov's blood sample revealed that he, too, had inherited one Pl^{A2} gene, presumably from his father. Goldschmidt, Bray, and Schwartzberg published their findings on Grinkov's death in the June 29 LANCET. The team believes that just one Pl^{A2} gene is enough to confer a heart risk.

Both Pl^{A} genes code for protein receptors on the surface of platelets, the disk-shaped cells active in the clotting process. Those receptors bind to molecules in the blood that form a bridge between platelets, Bray says. The resulting mesh of platelets forms the familiar gelatinous blood clot. However, Pl^{A2} codes for a protein that may be overly efficient when it comes to clotting, he says.

The Hopkins researchers think they know what happened to Grinkov on that fateful day in November. They speculate that a piece of the fatty debris on artery walls broke off and left a hole. Grinkov's Pl^{A2} swung into action, but instead of forming just a small clot to plug the injury, the protein receptor overdid it. A massive clot blocked the entire coronary artery and stopped blood flow to the heart.

Although Pl^{A2} seems to be the proximate cause of Grinkov's collapse, researchers wonder whether it also plays a role in the slow process of atherosclerosis. Goldschmidt notes that this same protein receptor shows up on the endothelial cells lining the interior walls of blood vessels. Something about this protein may increase the likelihood that cholesterol and other fats will cling to the wall, he says.

About 20 percent of the U.S. population has the Pl^{A2} gene, the researchers estimate. "It could be a major player in the generation of a heart attack," Goldschmidt says. It is not a death sen-

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tence, however. "This does not mean that being PI^{A2}-positive guarantees that you will have a heart attack," Bray says.

Researchers believe, however, that the gene may, in combination with other risk factors, put people in greater jeopardy of suffering a heart attack. If future research proves this theory, people with a family history of early heart disease may be able to get a blood test that looks for the gene variant. If they get a positive test, they could take steps to lower their risk.

An aspirin a day might be such a step. Aspirin is known to inhibit blood clotting, so people with a tendency to form clots could take this drug to offset their risk, Goldschmidt says. People with a higher-than-average risk could also cut down on their intake of fatty foods, a factor known to contribute to atherosclerosis.

Grinkov was only the most recent champion to collapse suddenly and die. Such deaths have struck athletes ranging from high school team members to professional basketball players. In the largest investigation of sudden death in athletes to date, cardiologist Barry J. Maron of the Minneapolis Heart Institute Foundation and his colleagues have found that most die from one of several heart abnormalities, only some of which have known genetic links.

Most are young athletes who harbor one of these cardiovascular defects from birth, Maron said at a New York press briefing held by the American Medical Association. Such defects "usually cause no symptoms prior to the catastrophe," he added. Maron and his colleagues detail their findings in the July 17 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION (JAMA).

They collected information on sudden deaths in athletes from 1985 through 1995. The probe turned up 158 such deaths, 134 of them with a cardiovascular origin.

The athletes ranged in age from 12 to 40. The largest group, 83 of the 134, was competing in high school sports. However, the series included 16 athletes who had achieved national or international fame in their sport. Sudden death felled the greatest number of young athletes in basketball and football. It also struck track, soccer, and baseball players and a few in eight other sports.

The most common cardiovascular disease identified as responsible for sudden death was an inherited condition known as hypertrophic cardiomyopathy (HCM), a finding in line with previous research. In this disorder, caused by any one of several mutated genes, the heart's main pumping chamber, the left ventricle, is abnormally thick.

The researchers were surprised to find that HCM was responsible for 48 percent of the sudden deaths in black athletes and just 26 percent of the deaths in white athletes. Earlier medical studies of HCM suggested that blacks rarely suffer from it. Maron thinks it possible that blacks with this genetic condition don't get a correct diagnosis as often as their white counterparts.

Other causes of sudden cardiac death in this series include birth defects and other abnormalities of the coronary arteries; aneurysm, or ballooning of the aorta; and myocarditis, a disease that begins with an infection that leads to changes in the heart muscle. A small number of athletes—like Grinkov—suffered from premature clogging of their coronary arteries.

At the press briefing, Maron said that in many cases, physical exertion appeared to trigger sudden death. The researchers found that 90 percent of the athletes collapsed during or immediately after a training session or competition.

How does exertion magnify the risk of a heart attack? That depends on the underlying cardiac condition, Maron says.

For people with HCM, strenuous activity increases the chance that the heart will develop arrhythmias, abnormal rhythms that can cause death, Maron points out. For athletes with aneurysms, exertion increases the likelihood that the weakened artery wall will burst.

In the JAMA study, only 24 of the 134 athletes had reported symptoms of cardiovascular disease, such as chest pain or fainting spells, in the 3 years before their fatal episode. Grinkov, who had never complained of chest pain, had apparently been having a heart attack for hours before he collapsed, Schwartzberg said.

Routine physical exams often don't turn up a cardiac condition in young athletes, that study shows. Of the 134 athletes who died of heart problems, 115 had received a standard screening. Doctors suspected only 4 of the 115 had cardiovascular disease. Just one case received a firm diagnosis of a heart condition, the authors note.

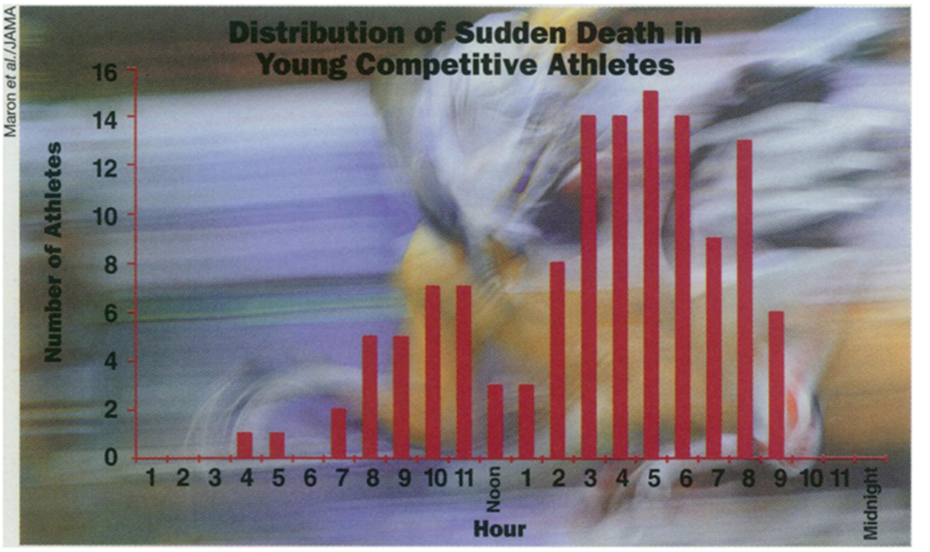
Unfortunately, there's no simple test to detect the variety of cardiovascular ills that may put an athlete in jeopardy, Maron says. "Some are virtually impossible to detect with a routine exam," he says. He favors standardizing the screening process so that more at-risk young people are identified.

So does Christine E. Seidman, an HCM researcher with the Howard Hughes Medical Institute at Brigham and Women's Hospital in Boston. Seidman believes researchers will someday develop blood tests capable of identifying the genetic mutations responsible for HCM and some other disorders that cause sudden death. Until then, physicians evaluating youngsters for competitive sports must use the tools at hand, including family histories, to find clues to cardiac risk.

Indeed, a more aggressive approach to screening might be in order for athletes with a family history of sudden cardiac death, Maron adds. Such athletes may want to consult a cardiologist before signing up for competitive sports. Heart specialists can more easily detect subtle symptoms of a heart disorder, he adds.

A young athlete who does get diagnosed with a cardiac flaw may find the prescription tough to take. For someone with HCM, for example, withdrawal from sports is the only way to reduce the risk, Maron says. Even that course of action is "no guarantee of a normal life expectancy," he adds.

No one knows how many young athletes harbor a silent defect of the heart. Scientists hope that Sergei Grinkov's highly publicized death will leave a lasting legacy in the form of research to improve detection and reduce the risk of sudden cardiac arrest. □



Maron's research shows that most athletes die in the afternoon—the time of day when training and athletic events usually occur. The finding suggests that exertion may precipitate sudden cardiac death in certain people.