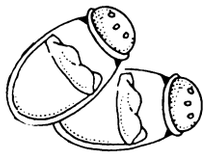
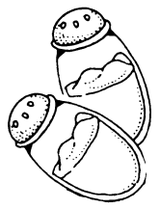
The African Gene?

Searching through history for the roots of black hypertension

By KATHY A. FACKELMANN






When Byllye Avery took the microphone last month at a meeting in Washington, D.C., the statistics on hypertension suddenly coalesced into a painful reality faced by one black American family.

"Twenty-one years ago, my husband died of a massive heart attack," she said in a soft, determined voice. "He was 33 years old. He was hypertensive and we didn't know it."

Avery, founding president of the National Black Women's Health Project in Atlanta, recounted her experience at a Sept. 19 editors' seminar on cardiovascular disease in black Americans, organized by the Dallas-based American Heart Association (AHA).

Blacks in the United States run a hypertension risk twice as great as that of Caucasians, but scientists still don't know why. One controversial hypothesis, proposed in 1988 by hypertension researcher Clarence E. Grim, traces the disparity back to the 16th century, when European slave traders began shipping captured Africans to plantations in the New World. According to this scenario, blacks living in the United States today may owe their high hypertension rate to a genetic trait that helped their ancestors survive the grueling conditions of slavery. That trait is an inherited tendency to conserve salt within the body, says Grim, director of the Drew/UCLA Hypertension Research Center at the Charles R. Drew University of Medicine and Science in Los Angeles.

Now Grim reports new research findings that strengthen the slavery hypothesis. His results, which remain controversial and unconfirmed, hint that physicians might one day be able to use genetic testing to identify blacks, and perhaps others, with a particularly high risk of hypertension, so that preventive measures can begin at an early age. Grim presented the new findings at the AHA's 45th annual scientific sessions on high blood pressure, held in Chicago the week after the Washington meeting.

U.S. blacks afflicted with hypertension run a greater risk of its life-threatening complications than whites. Elevated blood pressure puts extra strain on blood vessels and can damage the vessel walls, increasing the risk of stroke if a clot blocks the brain's blood supply. And, if left untreated, years of high blood pressure can inexorably damage the heart and kidneys, raising the very real possibility that these crucial organs will fail. Among hypertensives in the United States, blacks are 10 to 18 times more likely than whites to suffer kidney failure, and three to five times more likely to develop chronic heart failure, notes Edward S. Cooper of the University of Pennsylvania in Philadelphia, who spoke at the Washington conference.

High blood pressure is defined as systolic (heart-pumping) pressure of at least 140 millimeters of mercury (mm Hg) and diastolic (heart-resting) pressure of at least 90 mm Hg. Several factors can boost a person's risk of developing the condition, including stress, advancing age, obesity, lack of exercise, alcohol use, salty diet and family history of hypertension. But in nine out of 10 cases, physicians cannot pinpoint the cause. And scientists can only speculate about what makes black Americans particularly vulnerable to this potentially deadly condition.

Some researchers have suggested that socio-economic differences may underlie the chronically elevated pressures that predispose U.S. blacks to hypertension (SN: 2/16/91, p.111). For one thing, they note, the high cost of medical care and lack of insurance can prevent low-income patients from getting regular examinations or treatment. In addition, the stress of poverty or racism may evoke a hormonal "fight or flight" response that boosts heart rate and blood pressure, says Curtis G. Hames of the Medical College of Georgia in Augusta. In earlier times, these metabolic changes helped people escape physical danger, Hames says, but today's artery-pounding pressures may spring instead from inescapable stresses of modern life.

There's no doubt that environmental factors such as stress enter into the black hypertension puzzle. However, new data gathered by Grim and a colleague suggest that a genetic component may also heighten the risk faced by so many black Americans.

Grim theorizes that Africans with a salt-conserving gene or genes were less likely to die of dehydration during the long, parched voyage across the Atlantic. The ability to hold onto salt — and thus water — also helped them weather the harsh conditions they encountered in the New World, Grim suggests. But the same trait that conferred a survival advantage upon certain African slaves may prove deadly to their modern-day descendants.

"The long-term goal of our research is to look for evidence for selective survival during slavery and its effect on health today," says Grim, who conducted the new study with Thomas W. Wilson, a medical historian and epidemiologist formerly at Drew University.

Although the historical hypothesis has provoked heated debate, some researchers think Grim and Wilson are headed in the right direction. "I think Dr. Grim has his finger on the most important aspect of hypertension in blacks," says Cooper, who believes that research into the underlying cause of hyperten-

sion's racial differences will ultimately help physicians prevent the disease.

The Caribbean island of Barbados may seem an unlikely place to look for answers to a health problem suffered by U.S. blacks. Yet the history of Barbados includes a period in which landowners imported African slaves to work on the island's sugar plantations. And previous studies have shown that black Barbadians today suffer from the same hypertension rates as U.S. blacks, Grim says.

Unlike the United States, the island's black population is in the majority and has ready access to health care. Grim and Wilson speculated that Barbados blacks might not experience as much stress as their U.S. counterparts. They reasoned that a Caribbean study might help factor out some of the environmental triggers of hypertension among U.S. blacks.

Thus, the researchers traveled to Barbados where they recruited 50 healthy individuals aged 20 to 60. All participants identified themselves as black, but to get a more accurate picture of their African heritage, the researchers turned to a test that looks for DNA of African origin. They collected blood samples from each volunteer and isolated the white blood cells, focusing on the tiny mitochondria within the cells. These energy-producing structures contain DNA inherited from an individual's mother.

When an egg and sperm unite, the sperm tail, which contains the paternal mitochondria, drops off, Wilson explains. Thus, mitochondrial DNA analysis can show an unbroken line of African DNA on the maternal side of the family. While the test doesn't look at the contribution from the father, it provides a stronger marker of African heritage than skin color, Grim notes. Previous hypertension research had relied on skin color as an indication of African lineage.

Among study participants whose mitochondrial DNA suggested purely African maternal lineage, systolic blood pressures averaged 122 mm Hg. By contrast, those whose mitochondria showed non-African DNA had average systolic pressures of 115 mm Hg. The researchers discovered the highest pressures among blacks with the African marker, which suggests they may run a greater risk of developing high blood pressure later in life.

To control for nongenetic factors that might confound the results, the researchers factored in age, body mass and years of schooling (a measure of socioeconomic status). Even then, the link between maternal African DNA and higher blood pressures remained.

These findings, although very preliminary, suggest that the DNA test one day may serve as a "strong predictor" of hypertension risk, Wilson says. Grim cautions, however, that before physicians use mitochondrial DNA to forecast risk, the researchers need to follow all participants to find out who will ultimately develop blood pressures that soar into the danger zone.

The team also plans to test for paternal African DNA, perhaps by looking at the Y chromosome, present only in males, Grim says. Together, the Y chromosome and mitochondrial data might provide a more sensitive indicator of hypertension threat, he says.

The data from Barbados tell only part of the story of hypertension, genes and slavery. To get the rest of the picture, the researchers traveled to West Africa, where the forced diaspora of Africans began.

The team focused on rural Obodo-Ahiara. This agricultural center of about 6,000 people has no running water or electricity, but it lies in an area of Nigeria that was home to many ancestors of present-day black Americans, says Wilson, who is now at the Western Consortium for Public Health in Berkeley, Calif.

He and Grim conducted a preliminary study to determine whether hypertension rates in the village matched those of blacks in the United States and Barbados. Their findings, presented Aug. 1 in Brazil at the Sixth Annual International Conference on Hypertension in Blacks, revealed very low rates of hypertension despite a relatively salty diet.

The researchers began by recruiting 140 men aged 20 to 60. They measured the men's blood pressures and asked them to collect their urine for 24 hours.

Analyses of the urine samples showed that the men ate relatively salty diets: The average 24-hour sodium excretion (an indicator of dietary salt) logged in at 7.3 grams of sodium per day.

While blacks in Nigeria and in the U.S. share a penchant for salt, there was a "striking" difference in blood pressures between the two groups. Despite their high-salt diet, only 12 percent of the Nigerian men had systolic pressures of 140 mm Hg or greater. By contrast, about 32 percent of U.S. adult blacks show such elevated pressures, Wilson notes.

Moreover, age did not significantly increase blood pressures among the Africans, whereas 60 percent of U.S. blacks aged 50 or older suffer from dangerously elevated blood pressure.

The men of Obodo-Ahiara don't appear to show salt sensitivity – a finding that supports the theory that U.S. blacks owe their high hypertension rates to selective survival, perhaps during the slavery period. But the researchers say they have a long way to go before they can prove that such selection occurred.

"The survival hypothesis is only a hypothesis," says Grim, who notes that no one has yet found a salt-retaining gene or genes that would predispose a person to hypertension.

Richard S. Cooper (no relation to Edward Cooper), a hypertension researcher at Loyola University in Maywood, Ill., is among the many critics of the slavery hypothesis. "I think it's a crock," he says. "To attribute that magnitude of evolutionary change to a fairly brief period is a kind of fantasy."

Wilson counters that 70 percent of African slaves died within four years of their capture. If those with salt-conserving genes survived more often, it's not unreasonable to expect the second generation to exhibit this salt-hoarding trait, he argues. "It's a real myth to say that evolution must take millions of years," Wilson says.

John M. Flack, an epidemiologist at the University of Minnesota in Minneapolis, brings up another criticism: The slavery hypothesis, he says, is reminiscent of controversial arguments – largely rejected by the scientific community – that genes render blacks intellectually inferior to whites.

The theory has also fueled a long-standing debate over the relative importance of genes versus environmental influences.

"Obviously, what we're looking at is a gene/environment interaction," Grim says. "We think there are people who inherit the ability to store salt well, and that this tendency leads to high blood pressure in a high-salt environment."

Indeed, Grim believes thinks salt-conserving genes may contribute to hypertension in some whites as well as in blacks.

Others doubt that genes play much of a role at all in the development of hypertension. "We know that there are powerful environmental factors that could by themselves explain all the racial differences," Richard S. Cooper says. "Whether there are genetic factors as well remains to be discovered."

Hypertension researchers do agree on one thing, however: They need more data to tease out the complex factors leading to elevated blood pressure in U.S. blacks. And until scientists solve the mystery underlying hypertension, most cardiologists advise all U.S. blacks to get their blood pressure checked regularly. For those with high pressures, doctors often recommend a low-salt diet and in some cases, medication aimed at bringing dangerously high pressures down. And because U.S. blacks face such a high risk of this deadly condition, Grim suggests a low-salt diet and plenty of exercise as a preventive strategy.

His recommendation remains a safe bet for Americans of all colors in the battle against this killer disease. □