I guess that's why they call it the Hughes

How one man's sleuthing has led to the most important medical breakthrough you've never heard of

BY SUSANNAH HICKLING

Frances Krarup had come to believe she would never have a child. In six years the 40-year-old from Hastings had suffered nine miscarriages.

Then her obstetrician announced he'd discovered the reason: Frances was suffering from Hughes Syndrome. Like most people, Frances had never heard of Hughes. Yet the diagnosis was a breakthrough. The next time Frances got pregnant, she took aspirin and injected the blood-thinning drug heparin every day. When Jessica was born by Caesarean at 34 weeks in November 2007, both Frances and her doctors were ecstatic. "She's alive,

PHOTOGRAPHED BY PETER DENCH

Something in the blood: after being diagnosed with Hughes syndrome, Frances Krarup finally gave birth to Jessica, now almost two

she's alive!" cried Frances when she saw her daughter.

With one in five babies lost to Hughes, it is now recognised as the single biggest cause of treatable miscarriage. But it is also responsible for one in five strokes in the under-45s, one in five cases of deep vein thrombosis and one in five heart attacks in young women.

In Britain, as many as one person in a hundred may have Hughes. Yet it was discovered only in the 1980s—and even now many doctors are not fully aware of it. In 2004 the dean of the Barcelona Faculty of Medicine, Miguel Vilardell, said there were only two new diseases in the late 20th century—Aids and Hughes Syndrome.

Professor Graham Hughes is the former head of the lupus unit at St Thomas' Hospital in London and now, at 67, runs the London Lupus Centre at the private London Bridge Hospital. Small, dapper, courteous and jovial—the essence of self-effacing charm—he certainly does not fit the stereotype of a detective. Yet it was he who doggedly pieced together a medical puzzle that had eluded doctors for decades.

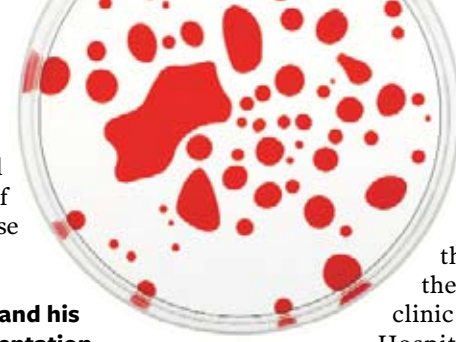
Hughes's specialty, lupus, is an autoimmune condition where the body's defences turn on itself—a sort of "self allergy". It can cause rashes, inflammation, organ or joint problems, and even death.

But it was a one-year secondment to Jamaica in the mid 1970s—considered by some an unwise career move—that provided Hughes with the first clue to a new syndrome. Working as a general doctor at a Kingston hospital, he was intrigued by the large number of patients, many of them women, confined to wheelchairs and suffering from a mysterious paralysis known as Jamaican neuropathy.

Hughes wanted to find out what caused it. Blagging a key to a lab in a gleaming new suite reputedly funded by the World Bank but apparently mothballed, he and his colleagues conducted blood tests. As a result, he discovered that these patients had an antibody (aPL) in the brain that was directed against phospholipid, a major component of cell membranes.

Hughes returned to the lupus clinic he had set up at Hammersmith Hospital and, as the newly appointed head of rheumatology, had his team start testing for antiphospholipids. On his ward rounds, in his clinics and in staff meetings in a small room overlooking Wormwood Scrubs prison, he was struck by how many patients with positive aPL tests had thrombosis in veins or arteries and recurrent miscarriages. He was also seeing neurological problems in these patients—not only Jamaican neuropathy but also migraines, strokes, epilepsy, memory loss and even the jerky, uncontrollable movements known as St Vitus's dance.

Increasingly Hughes believed he had come across a syndrome that was frequent in patients with lupus—but distinct from it. Could the aPL antibody somehow cause the blood to sludge, causing clots to form in different parts of the body? If the blood vessels feeding the placenta silted up, for example, it would starve a baby of oxygen and so cause a miscarriage.



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In 1982, Hughes and his team gave a presentation of their initial findings at Hammersmith. The first patient Hughes had treated with anti-clotting drugs, a woman who had had multiple miscarriages, travelled to London from her home in Lockerbie—bringing her new baby.

Sitting quietly next to Hughes in the front row of the auditorium was the professor of surgery. "Graham," he said, turning to his colleague, "my first wife died of this." Both men now knew she could have been saved.

IN BRITAIN, AS MANY AS ONE PERSON IN A HUNDRED MAY HAVE HUGHES SYNDROME

Graham Hughes

But still nobody had an idea of the full effects of Hughes Syndrome—also known as antiphospholipid syndrome (APS) or "sticky blood". By now obsessed, Hughes turned to other hospital departments. "You go and work with the platelet doctors," he said to one research fellow. "You're going to work in obstetrics," he instructed another. Had doctors in other specialties come across similar symptoms?

Colleagues in obstetrics said yes, they certainly saw women who suffered from migraines, DVT and other problems, as well as recurrent miscarriage. Testing revealed one in five had aPL in their blood. It was the same in the liver clinic at King's College Hospital, in the kidney clinic, in neurology.

Hughes felt he and his colleagues had arrived when in November 1983 their article on the new syndrome was accepted by the prestigious medical journal *The Lancet*. There were eminent doubters—at an American College of Rheumatologists meeting, a Mexican lupus expert refused to believe APS was a separate disease. But within a year, he too was testing for the antibody at his clinic in Mexico City.

Despite his successes, Hughes's biggest problem was funding: pharmaceutical companies could see little commercial potential in a disease treated by existing drugs. Nevertheless the team continued to work at a furious pace, transferring to St Thomas' Hospital in 1985.

It has become clear that while 20 per cent of lupus sufferers also have Hughes Syndrome, it is widespread in the rest of the population too. In fact there are now more Hughes than lupus patients coming to the London lupus clinics.

"It is rippling into all specialties,"

CLUES TO HUGHES

says Hughes. Research from Italy has shown that one in five people who develop epilepsy unexpectedly as a teenager test positive for Hughes. Seizures occur when small clots choke the blood supply in their brains. "If the brain doesn't get enough oxygen you can get headaches or memory problems or balance problems or epilepsy."

Others fear they have Alzheimer's when they become forgetful. During memory tests by a psychiatrist at St Thomas', one woman scored just 14 per cent on word recall. But after three weeks taking anticoagulants, the "fog" lifted and she achieved 100 per cent.

Often, members of the same family will suffer different symptoms—one with MS, say, one with epilepsy, another with migraines and another with thyroid problems. All will test positive for Hughes. The diagnostic tests are becoming more sensitive; sufferers can now do a regular pinprick test to monitor the thickness of their blood and adjust their medication accordingly.

In recent years the spotlight has been on multiple sclerosis. When Hughes asked his patients if doctors had ever suspected them of having MS, 32 per cent said yes. One woman was totally disabled, but when Hughes treated her with the anticoagulant warfarin she was able to walk again.

Hughes is now on a mission to spread the word among GPs and the public. "Strokes cost £7 billion a year," he points out. "If one in five strokes in under-45s is preventable, that would be an amazing saving." He also predicts the syndrome will prove the "missing link" between stroke and migraine—it is already well documented that some stroke victims are migraine sufferers.

While blood tests will in most cases bring the correct diagnosis, many who have been helped by Professor Hughes are struck by his keenness to listen, when perhaps other doctors have not. By the time Deborah Meanley, 69, came to him in 2003, she had seen 12 doctors over 22 years. In that time she suffered joint pain, migraines, mini-strokes, memory loss, balance problems and temporary blindness. She had to switch career from GP to psychiatrist before being forced to give this up too. In the end, she was spending up to five hours a day in bed, exhausted. Yet doctors put her problems down to anxiety, an inner-ear condition or dementia.

Finally, she got a referral to Hughes. He listened intently to Deborah for 15 minutes before saying, "I think you've got Hughes Syndrome." Studying test results that other doctors had ignored confirmed his suspicion.

After three or four days on warfarin she was up and about and her cognitive function improved. "I was able to rejoin an orchestra and two string ensembles as a violinist," she says. "It has brought back my quality of life."

Do you know someone who's been diagnosed with Hughes Syndrome? Email readersletters@readersdigest.co.uk.

Have you suffered from one or more of the following?

- Headaches or migraines.
- Memory loss.
- Mental "fogginess".
- Giddiness.
- Pregnancy problems, including multiple miscarriage and infertility.
- Visual disturbance, such as flashing lights, double or sudden loss of vision.
- Skin problems, in particular blotchy arms and legs, or ulcers.
- DVT or thrombosis in kidney or liver.
- Stroke, mini-strokes or heart attack under the age of 45.
- MS-like features, including numbness, pins and needles or problems walking.
- Gastro-intestinal disorders.
- Fatigue.
- Epilepsy.

If so, ask your GP to test you for Hughes. This involves two universally available blood tests—aCL and LA. For more information, go to hughes-syndrome.org.

IT'S A RIGHT ROYAL RUMBLE

We're all aware that King John signed the Magna Carta and that Harold was killed at the Battle of Hastings. But what we really want to know about our monarchs is stuff like which one sired the most bastard children. In "How Fat Was Henry VIII?" (The History Press), Raymond Lamont-Brown unearths this and other important royal facts.

l Henry VIII was very, very fat. Towards the end of his life, he had to be carried round in velvet-and-gold chairs and his armour cut open to accommodate his legs. In one year, his courtiers consumed 1,240 oxen, 8,200 sheep, 2,330 deer, 760 calves, 1,870 pigs, 53 wild boar, numerous fish species from cod to whale, washed down with 600,000 gallons of ale.

l The last British king to lead his troops into battle was George II. It was in Dettingen, Bavaria, in a 1743 dispute with the French. "Fire and behave bravely," he stirred his men, "and the French will soon run." His horse promptly bolted.

l Queen Victoria sought respite from the glare of public scrutiny by pretending she was invisible. If courtiers happened upon her while she was out walking on the Balmoral Estate, it was protocol to act as if they couldn't see her.

l Henry I (1100–35) claims the title of most prodigious royal lech, with 25 illegitimate kids. Charles II wasn't far behind, with 16 by eight mistresses.

l A mole was indirectly responsible for the death of William III. William of Orange, as he was otherwise known, was riding towards Hampton Court in February 1702 when his horse stumbled on a molehill. He fell off, broke his collarbone and contracted a fever that exacerbated his underlying pleurisy. Pneumonia followed and he died a few days later.