

Wonder drug fights gene linked to king's madness

Chris Smyth Health Editor

A gene-silencing drug has transformed the lives of people with an illness often linked to the madness of King George III.

Patients with porphyria saw attacks of crippling pain reduced by 90 per cent on average with half spared them entirely, a final-stage trial found. Hundreds of people in Britain could benefit from the "amazing" drug givosiran, which could be approved within a year.

Porphyria is an inherited disorder which means people cannot produce haem, a vital component of blood, and suffer a painful build-up of chemicals called porphyrins.

In the 1960s psychiatrists suggested that the illness might explain the mania suffered by George III, based on evidence that he had the purple urine which is a hallmark of the condition. The suggestion formed the basis of the Alan Bennett play *The Madness of George III*, starring Nigel Hawthorne, although recent research has cast doubt on the belief.

David Rees, of King's College London, who oversaw the UK arm of the trial, said that the condition was long misunderstood, not least as female sufferers often had symptoms triggered by their menstrual cycles. "Women used to go to hospital complaining of abdominal pain and no one could

find a reason so they were classed as hysterical and locked away in asylums," he said.

"There is a direct toxic effect on the brain beyond the pain so people might be more paranoid and anxious."

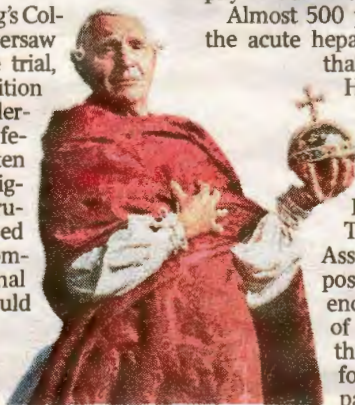
Today patients are given strong painkillers and a drug to blunt attacks, but Professor Rees said the condition is often missed. "The feeling is it's underdiagnosed and there are lot of people who go to hospital with severe pain and never find out [they have it]," he said.

Givosiran is a monthly injection that inhibits a defective gene from producing a key enzyme that leads to a harmful build-up of porphyrins. Results of a final-stage trial of 94 patients presented to the International Liver Congress in Vienna today showed that the drug reduced median attacks by 90 per cent compared with a placebo. Half of patients on the drug were attack-free compared with 16 per cent on placebo. Professor Rees said givosiran appeared to be "an amazing drug", adding: "It's still early days but for patients with porphyria it could be truly transformative."

Almost 500 people in Britain have the acute hepatic form of porphyria that is likely to respond.

However, the drug could cost tens of thousands of pounds a year and this will decide how widely the NHS recommends it.

The British Porphyria Association said: "The positive findings are an encouraging indication of the immense impact that givosiran could have for acute porphyria patients."



Nigel Hawthorne as George III, who may have had porphyria

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