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## **'Rotten eggs' gas and inflammation in arthritic joints**

**Latest research shows for the first time that hydrogen  
sulfide is present in the fluid inside the human knee  
joint (synovial fluid) and may protect against  
inflammation**

Hydrogen sulfide (H<sub>2</sub>S) is a gas more commonly associated with the smell of 'rotten eggs' and blocked drains. However, it has now been shown to be present naturally in our bodies and reside in knee joint synovial fluid, the protective fluid found in the cavities of joints that reduces friction between the cartilage of joints during movement. Synovial fluid H<sub>2</sub>S may play a role in reducing inflammation in joints.

The research, carried out by scientists at the Peninsula Medical School and rheumatologists at the Royal Devon & Exeter NHS Trust in Exeter and funded by the local Northcott Medical Research Foundation, was presented at the New York Academy of Sciences' 4th International Conference on Oxidative/Nitrosative Stress and Disease and is published in the current issue of the prestigious *Annals of the New York Academy of Sciences*.

The study compared H<sub>2</sub>S in blood samples and knee-joint synovial fluid from patients with rheumatoid arthritis, osteoarthritis and healthy individuals. Patients with rheumatoid arthritis were found to have higher concentrations of H<sub>2</sub>S in their synovial fluid compared to controls and up to four fold higher levels than in blood samples from the same patients. Higher H<sub>2</sub>S levels were associated with disease activity and lowered counts of inflammatory cells suggesting H<sub>2</sub>S may be a novel mediator made by the body to

control inflammation. This is the first time that H<sub>2</sub>S has been shown to be present in the synovial fluid of joints.

As a result, the way is open for further study into how H<sub>2</sub>S could be used as a therapeutic and possibly 'natural' option for patients with chronic inflammatory diseases.

In 2008 the same research team from the Peninsula Medical School synthesised a new molecule that release very low amounts of H<sub>2</sub>S in a controlled manner. This was a major breakthrough because until then H<sub>2</sub>S could only be delivered in one go via a gas cylinder or through the use of sulfide salts. Both of which are administered as a large bolus to generate instant H<sub>2</sub>S and are generally highly toxic, in addition to being foul smelling.

The results of the research that shows a clear correlation between levels of H<sub>2</sub>S in synovial fluid and inflammation in joints, combined with the earlier synthesis of a molecule that can release H<sub>2</sub>S safely, indicates that the development of H<sub>2</sub>S-based therapeutic intervention in human chronic inflammatory diseases such as rheumatoid arthritis deserves further study.

The team has recently received a grant of £140,000 over three years from the Wellcome Trust to pursue further study in this field.

Dr. Matt Whiteman, who led the study from the Peninsula Medical School in Exeter commented:

"Chronic inflammatory diseases are by their very nature debilitating, and current pharmaceutical interventions can occasionally exacerbate patients' discomfort - traditional anti-inflammatory drugs are very potent and safe, but they can sometimes damage the stomach lining in some individuals leading to further complications. By identifying a clear link between levels of H<sub>2</sub>S in synovial fluid and inflammation we can apply our earlier synthesis of a new molecule to control the delivery of H<sub>2</sub>S more effectively, we leave the way open for the development of H<sub>2</sub>S-based therapies that provide the benefits of traditional anti-inflammatory drugs without their unpleasant side effects."

Dr. Whiteman added, "We are only just starting to unravel what H<sub>2</sub>S does in the body and how to manipulate it. Since H<sub>2</sub>S is naturally produced in our bodies by enzymes which use predominantly sulfur-containing amino acids such as cysteine, methionine and homocysteine, it may be possible to manipulate the activity of these enzymes to increase their activity, possibly by dietary means, to boost the body's ability to deal with inflammation and tissue damage. "

According to statistics from Arthritis Research UK, around 20,000 new cases of rheumatoid arthritis are diagnosed in the UK each year. Almost 400,000 adults in the UK suffer from the disease, which is more prevalent in women than men. Up to four out of ten working people with rheumatoid arthritis lose their jobs within five years of diagnosis – one in seven give up work within one year.

Ten million working days were lost in 2006/7 due to musculoskeletal conditions with a cost to the UK of £5.7 billion annually. More than 10 million adults consult their GP each year with arthritis and related conditions and around 15,000 children in the UK have ongoing problems with juvenile idiopathic arthritis and similar conditions.