



## Is the Sense of Smell Impaired in Gout Patients?

Naomi Schlesinger<sup>1\*</sup>, Mariam Alikhan<sup>1</sup> and Richard L Doty<sup>2</sup>

<sup>1</sup>Department of Rheumatology, Rutgers-Robert Wood Johnson Medical School, USA

<sup>2</sup>Department of Otorhinolaryngology, Perelman School of Medicine, University of Pennsylvania, USA

### Abstract

**Objective:** Patients with gout, the most common inflammatory arthritis, frequently have multiple associated comorbidities, affecting many organs and aspects of one's health. Do gout patients have an impaired sense of smell?

**Methods:** The 40-item University of Pennsylvania Smell Identification Test (UPSIT), commercially known as the Smell Identification Test, was applied to the first 30 gout patients who had received care at an academic rheumatology practice between July 15, 2017 and May 25, 2018. The UPSIT scores were compared, using a paired t-test, to age and sex-matched controls from a normative database maintained at the University of Pennsylvania Smell and Taste Center.

**Results:** Gout patients ranged in age from 31 to 86 years (mean: 59 years) and included 26 men and 4 women. The duration of gout ranged from 1 to 43 years (mean: 9 years), with 19 having gout for >5 years. Visible tophi were observed in 6 patients (33%). C-reactive protein was within normal range except in one gout patient. Serum urate levels ranged from 5.1 mg/dL to 12 mg/dL (mean: 6.29 mg/dL).

The mean UPSIT scores of the two groups did not differ significantly [respective patient and control means (SDs)=31.40 (5.79) and 31.80 (4.37);  $t_{29}=-0.342$ ,  $p=0.74$ ].

**Conclusion:** This is the first study to examine quantitatively whether the sense of smell is impacted by gout. Despite being an inflammatory disorder with multiple associated comorbidities, we did not find a statistically significant effect of gout on smell function using a well-validated olfactory test.

**Keywords:** Gout; Smell

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#### \*Correspondence:

Naomi Schlesinger, Department of Rheumatology, Rutgers-Robert Wood Johnson Medical School, USA, Tel: 732 235 8378;  
E-mail: schlesna@rwjms.rutgers.edu

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### Introduction

The sense of smell is sensitive to hundreds of thousands of odorants. Smell sensations are mediated by specialized smell receptor cells in the upper recesses of the nasal cavity [1]. Smell receptors, unlike the receptors of most sensory systems, are directly exposed to the outside environment, except for a thin protective layer of mucus, making them relatively susceptible to damage from such exogenous agents as viruses, bacteria, pollutants, and airborne toxins.

Smell disorders significantly compromise the quality of life. A National Health and Nutrition Examination Survey (NHANES) 2013-2014 survey among US population aged 40 years of age and older years found smell dysfunction in ~20.5 million (13.5%) of Americans [2]. Prevalence of smell dysfunction increases with age [2,3]. Other factors influencing the sense of smell include ethnicity, smoking, medications, head trauma, chronic sinusitis, and upper respiratory tract infections. Other less common causes of smell loss include alcoholism and Neurological Disorders such as Epilepsy, Multiple Sclerosis, Alzheimer's disease, and Parkinson's disease.

The University of Pennsylvania Smell Identification Test (UPSIT) is a well-validated test of olfactory function that correlates with odor detection and other quantitative measures of olfaction [4]. This test has become the 'gold standard' for olfactory testing. The UPSIT is comprised of four booklets, each of which contains 10 pages. An odorized "scratch & sniff" label is present on each page of each booklet. The subject scratches the label and then indicates which of four response alternatives best matches the perceived smell. Examples of odors are chocolate, strawberry, smoke, leather, soap, grape, onion, and natural gas (mercaptan). The major advantage of UPSIT is that there is already a wealth of data on the results and due to its design it has strong internal consistency reliability [5]. It is also able to be easily self-administered.

Patients with gout, the most common inflammatory arthritis, frequently have multiple

associated comorbidities, affecting many organs and aspects of health. We questioned whether gout effects the sense of smell since the sense of smell is altered in a variety of Rheumatic disorders, including Sjogren's syndrome and fibromyalgia and comorbidities commonly associated with gout such as advanced age and alcoholism.

## Objective

To determine whether gout patients have an impaired sense of smell.

## Methods

This was a cross-sectional prospective study of gout patients seen in our rheumatology clinic. The first 30 clinic patients were recruited during the period 7/15/17 to 5/25/18.

Each patient was administered the 40-item UPSIT. For a given item, the patient releases an odor by scratching the microencapsulated pad with a pencil tip, smells the pad, and indicates the odor quality from four alternatives. Using a paired t-test, the UPSIT scores were compared to age- and sex-matched controls obtained from a normative database of nearly 4,000 normal individuals located at the University of Pennsylvania Smell and Taste Center. Both measures the absolute smell function (i.e., normosmia, mild hyposmia, moderate hyposmia, severe hyposmia, total anosmia) and relative function based on a percentile rank for each age and gender group.

Ethics board approval for this study was obtained from the Rutgers, New Brunswick Health Sciences review board (Approval No.Pro20170000756).

## Results

Gout patients ranged in age from 31 to 86 years (mean: 59 years); 26 (87%) of patients were  $\geq 40$  years old and included 26 men and 4 women. The duration of gout ranged from 1 to 43 years (mean: 9 years), with 19 having gout for  $>5$  years. Visible tophi were observed in 6 patients (33%). C-reactive protein was within normal range except in one gout patient. Serum urate levels ranged from 5.1 mg/dL to 12 mg/dL (mean: 6.29 mg/dL).

Two patients (12% of those with macrosomia) were current smokers; both had microsomia. No patients had head trauma, chronic sinusitis, upper respiratory tract infections, alcoholism or neurological disorders.

The mean UPSIT scores of the two groups did not differ significantly [respective patient and control means (SDs)=31.40 (5.79) and 31.80 (4.37);  $t_{29}=-0.342$ ,  $p=0.74$ ].

## Discussion

Smell disorders significantly compromise the quality of life. Prevalence of smell dysfunction increases with age and is affected by comorbidities often associated with gout such as alcoholism, smoking and sleep apnea.

Alzheimer's disease and Parkinson's disease are known to impact the sense of smell; whereas, gout is inversely associated with the risk

of developing Alzheimer's disease and Parkinson's disease, possibly due to neuroprotective effects of uric acid [6].

Using the 40-item UPSIT, an effective instrument with strong internal consistency reliability, we found no evidence that gout impacted smell function when individually compared to scores from age- and sex-matched members of large normative database. Could neuroprotective effects of uric acid be preventing loss of smell in gout patients?

## Conclusion

This is the first study to examine quantitatively whether the sense of smell, which is very sensitive to a range of diseases, is impacted by gout. Despite being a systemic inflammatory disease, we found no evidence that gout impacted scores on the UPSIT, a well-validated and reliable test of smell function. Could neuroprotective effects of uric acid be preventing loss of smell in gout patients? Future studies may wish to address this issue in larger samples as well as to focus on the ability to taste, i.e., sweet, sour, salty and bitter perception, to more fully explore potential chemosensory influences of gout.

### Take Home messages

- Smell disorders significantly compromise the quality of life.
- Patients with gout frequently have multiple associated comorbidities, affecting many organs and aspects of one's health.
- We did not find a statistically significant effect of gout on smell using the UPSIT olfactory testing we did not find a statistically significant effect of gout on smell function using a well-validated olfactory test.

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