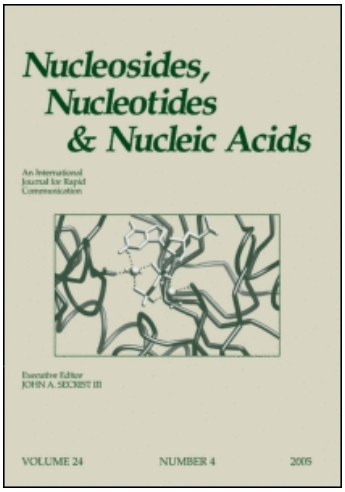

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Analysis of Excretion Fraction of Uric Acid

B. Stibůrková[a]; E. Pospíšilová[a]; S. Kmoch[b]; I. Šebesta[c]
[a] Institute of Inherited Metabolic Disorders, Charles University 1st School of Medicine, Prague, Czech Republic [b] Center for Applied Genomics, Charles University 1st School of Medicine, Prague, Czech Republic [c] Institute of Inherited Metabolic Disorders and Institute of Chemical Biochemistry and Laboratory Diagnostics, General University Hospital and Charles University 1st School of Medicine, Prague, Czech Republic

To cite this Article Stibůrková, B. , Pospíšilová, E. , Kmoch, S. and Šebesta, I.(2006) 'Analysis of Excretion Fraction of Uric Acid', Nucleosides, Nucleotides and Nucleic Acids, 25: 9, 1301 — 1304
To link to this Article: DOI: 10.1080/15257770600893917
URL: http://dx.doi.org/10.1080/15257770600893917

Nucleosides, Nucleotides, and Nucleic Acids, 25:1301–1304, 2006

ISSN: 1525-7770 print / 1532-2335 online
DOI: 10.1080/15257770600893917

Taylor & Francis
Taylor & Francis Group

ANALYSIS OF EXCRETION FRACTION OF URIC ACID

B. Stibůrková and E. Pospíšilová □ *Institute of Inherited Metabolic Disorders, Charles University 1st School of Medicine, Prague, Czech Republic*

S. Kmoch □ *Center for Applied Genomics, Charles University 1st School of Medicine, Prague, Czech Republic*

I. Šebesta □ *Institute of Inherited Metabolic Disorders and Institute of Chemical Biochemistry and Laboratory Diagnostics, General University Hospital and Charles University 1st School of Medicine, Prague, Czech Republic*

□ *Excretion fraction of uric acid (EF_{UA}), is one of the most important hallmarks for diagnosis of familial juvenile hyperuricemic nephropathy (FJHN) and hereditary renal hypouricemia. EF_{UA} was measured in 20 patients with FJHN. However, low excretion fraction (<6%) was found also in healthy FJHN family members and healthy controls (ref. ranges EF_{UA}: men 6–12%, women 6–20%). Similar finding of low EF_{UA} was reported recently. Distribution of EF_{UA} was further studied in 2,416 healthy controls, which were selected from 6,000 samples and divided according to age. In conclusion, finding of low EF_{UA} in family members is a risk factor for renal damage and indication for purine metabolic investigations with subsequent molecular biology analysis. As EF_{UA} could be found also in healthy controls—it should be interpreted with care and other features of FJHN (such as hyperuricemia, progressive renal disease in family) should be taken to account.*

Keywords Excretion fraction; Familial juvenile hyperuricemic nephropathy; Uric acid

INTRODUCTION

It has been well documented that the most important single test in the hyperuricemic patient is determination of urinary urate excretion.[1] It allows to identify under- and overexcretors of uric acid. Excretion fraction of uric acid (EF_{UA}—expressed as ratio of uric acid clearance and creatinine clearance), is one of the most important hallmarks for diagnosis of familial juvenile hyperuricemic nephropathy (FJHN) and hereditary renal

This study was supported by a grant VZ MSM 0021620806, Czech Republic.
Address correspondence to I. Šebesta, Institute of Clinical Biochemistry and Laboratory Diagnostics, 4 Nemocnice 2, 128 01 Prague 2, Czech Republic. E-mail: isebes@lf1.cuni.cz

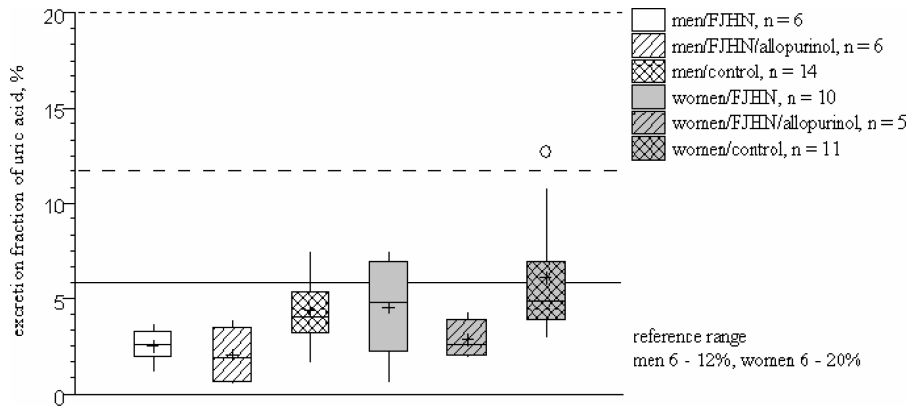

FIGURE 1 Levels of excretion fraction of uric acid in FJHN patients. The control men and women are healthy and unrelated family members.

hypouricemia. FJHN is a dominant disorder with high penetrance, hyperuricemia, low EF_{UA} and progressive renal disease. Gout and hypertension are inconsistent features.[2] Hereditary renal hypouricemia is characterized by abnormal elevation of EF_{UA}. Novel identification of the urate transporter in the kidney (URAT1) led to the molecular elucidation of this idiopathic renal hypouricemia.[3] In consideration of our finding of low EF_{UA} in healthy controls and in family members of FJHN, found also in a recent report,[4] we have performed, therefore, detailed analysis of EF_{UA} in a larger number of patients with FJHN and healthy controls.

MATERIALS AND METHODS

Uric acid in serum and urine was measured by a specific enzymic method. Creatinine in plasma and urine was measured by the Jaffé reaction adapted to the autoanalyser. Excretion fraction of uric acid was evaluated as uric acid clearance factored by creatinine clearance $\times$ 100. EF_{UA} was measured in 20 patients with FJHN and in 2,416 healthy controls selected from 6,000 samples. Normal renal function was defined as a creatinine clearance of glomerular filtration rate greater than 80 ml/min per 1.73 m^2. Diagnosis of FJHN was based on family history with progressive renal disease with autosomal dominant mode of inheritance, detailed purine metabolic, and molecular biology investigations. Linkage analysis in our FJHN families have been described in detail previously.[5]

RESULTS AND DISCUSSION

The values of EF_{UA} in patients with FJHN are presented on the Figure 1. The mean, median, range, S.D., and S.E.M. are shown. Low excretion

TABLE 1 Measured New Reference Range of EF_{UA}

Age, sex	n	Median	Average ± SD	Range
0–6 weeks	63	27.2	29.1 ± 11.7	17.4–40.8
6 weeks–1 year	744	22.0	23.9 ± 10.4	13.5–34.3
1–3 years	373	14.0	15.2 ± 6.2	9.0–21.4
3–13 years	961	11.3	12.2 ± 5.5	6.7–17.7
>13 men	145	7.1	8.0 ± 3.7	4.3–11.7
>13 women	130	9.9	10.3 ± 4.2	6.1–14.5

fraction (<6%) was found also in healthy and unrelated FJHN family members. Similar finding was reported.[4] Therefore, distribution of EF_{UA} according to age in large group of 2,416 samples of healthy controls was further studied and is given at the Table 2. Low excretion fraction was found in a part of healthy men. Value EF_{UA} of 8.0% ± 3.7 was found in collection of men older then 13 years; value of 10.3% ± 4.2 was found in women (>13 years). These results are in accord with excretion fraction of urate in healthy UK population, in men being 8.1% ± 3.2; in women being 12.8 % ± 2.9.[6]

The evaluation of uric acid levels in blood and urine is essential for recognizing overproduction or underexcretion in several rare metabolic disorders of purine metabolism. Moreover, recent studies in both humans and experimental animals have led to renewed interest in uric acid and its association with frequent diseases such as cardiovascular events, hypertension, and renal disease progression.[7] It was found that soluble uric acid has important biological roles. There is evidence that uric acid has pro-inflammatory and proliferative effects on vascular smooth muscle cells, and causes dysfunction of endothelial cells. This cellular mechanism may translate into why uric acid has a role as a true cardiovascular risk factor, particularly for the development of hypertension and renal disease.[8] Therefore, assessment of blood and urinary concentrations of uric acid will be more important then previously thought. The proper evaluation of EF_{UA} could be a first and easy step in diagnosis of new patients with under—or overexcretion of uric acid.

The primary cause of low EF_{UA} found in healthy subjects seems to be unknown and further studies are needed. Different values in patients with FJHN are probably due to genetic heterogeneity of this disease. In conclusion, finding of low EF_{UA} in family members is a risk factor for renal damage and indication for purine metabolic investigations with subsequent molecular biology analysis. As low EF_{UA} could be found also in healthy controls—it should be interpreted with care and other features of FJHN (such as hyperuricemia, progressive renal disease in family, and eventually gout) should be taken to account.

REFERENCES

1. Cameron, J.S.; Moro, F.; McBride, B.; Simonds, H.A. Inherited disorders of purine metabolism and transport. *In* Oxford Textbook of Clinical Nephrology. Davison, A.M.; Cameron, J.S.; Grűnfield, J.-P.; Kerr, D.N.S.; Ritz, E.; Winearls, C.G., Eds., 2nd ed., Oxford University Press: Oxford, **1997**, 2469–2482.
2. Fairbanks, L.D.; Cameron, J.S.; Venkat-Raman, G.; Rigden, S.P.A.; Rees, I.; Vanát Hoff, W.; Mansell, M.; Pattison, J.; Goldsmith, D.J.A.; Simonds, H.A. Early treatment with allopurinol in familial juvenile hyperuricaemic nephropathy (FJHN) ameliorates the long-term progression of renal disease. *Q. J. Med.* **2002**, 95, 597–607.
3. Ichida, K.; Hosoyamada, M.; Hisatome, I.; Enomoto, A.; Hikita, M.; Endou, H. et al. Clinical and molecular analysis of patients with renal hypouricemia in Japan: influence of URAT 1 gene on urinary urate excretion. *J. Am. Soc. Nephrol.* **2004**, 15, 164–73.
4. Bleyer, A.J.; Woodard, A.S.; Shihabi, Z.; Sandhu, J.; Zhu, H.; Satko, S.G.; Weller, N.; Deterding, E.; McBride, D.; Gorry, M.C.; XU, L.; Ganier, D.; Hart, T.C. Clinical characterization of a family with a mutation in the uromodulin (Tamm-Horsfall glykoproteinprotein) gene. *Kidney Int.* **2003**, 64, 36–42.
5. Stibůrková, B.; Majewski, J.; Sebesta, I.; Zhang, W.; Ott, J. Familial juvenile hyperuricaemic nephropathy: localization of the gene on chromosome 16p11.2-and evidence for genetic heterogeneity. *Am. J. Hum. Genet.* **2000**, 66, 1989–94.
6. McBride, M.B.; Rigden, S.; Haycock, G.B.; Dalton, N.; Vanát Hoff, W.; Rees, L.; Raman, G.V.; Moro, F.; Ogg, C.S.; Cameron, J.S.; Simmonds, H.A. Presymptomatic detection of familial juvenile hyperuricaemic nephropathy in children. *Pediatr. Nephrol.* **1998**, 12, 357–64.
7. Kanneli, J.; Feig, D.I.; Johnson, R.J. Does asymptomatic hyperuriceamia contribute to the development of renal and cardiovascular disease?. *Nephrology* **2004**, 9, 394–399.
8. Kang, D.H.; Han, L.; Ouyang, X.; Kahn, A.M.; Kannellis, J.; Li, P.; Feng, L.; Nakagawa, T.; Watanabe, S.; Hosoyamada, M.; Endou, H.; Lipkowitz, M.; Abramson, R.; Mu, W.; Johnson, R.J. Uric acid causes vascular smooth musle proliferation by entering cells via functional urate transporter. *Am. J. Nephrol.* **2005**, 25, 425–433.