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Uric Acid Levels in Southern Germany in 1989

A Comparison with Studies from 1962, 1971, and 1984

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Summary. Since 1962 our group has performed four studies on uric acid values in blood donors in southern Germany (Bavaria). Uric acid levels in men have increased over the years, from 4.86 mg/dl in 1962 to 6.00 mg/dl in 1971, 5.60 mg/dl in 1984, and 5.90 mg/dl in 1989. Levels in women have increased slightly, from 4.05 mg/dl in 1962 to 4.35 mg/dl in 1971, 4.10 mg/dl in 1984, and 4.16 mg/dl in 1989. Women aged 51 to 60 years had significantly higher uric acid levels than those in the fourth decade. In women treated with oral contraceptives uric acid levels were significantly lower than in other women of the same age.

Hypouricemia (uric acid levels ≤ 2.0 mg/dl) was observed in three women, none of whom had a history of medication.

Hyperuricemia exists when uric acid levels are ≥ 6.5 mg/dl. In 1989 2.6% of the female blood donors and 28.6% of the males were hyperuricemic, with an increased risk of gout, nephrolithiasis, and nephropathy.

Key words: Blood donors – Epidemiology – Hyperuricemia – Hypouricemia – Uric acid

The normal value of uric acid can be defined biochemically by its solubility in plasma water, calculated to be 6.4 mg/dl at 37° C and pH 7.4 in the presence of 130 mmol/l natrium in vitro [18]. Elevated serum uric acid (urate) levels have been shown to correlate with increased incidence and prevalence of gouty arthritis and urolithiasis [9, 27].

During the past 30 years uric acid levels have been examined in many populations; an increase ascribed to nutritional changes has been observed in different studies (Table 1). Changing nutritional habits, particularly increased consumption of meat products, were thought to be responsible.

Between 1962 and 1984 Zöllner and/or his coworkers [28, 7, 14] performed three studies on the values of serum/plasma uric acid levels in Bavarian blood donors. Whereas the uric acid levels in women rose only slightly, from 4.05 mg/dl in 1962 and 4.35 mg/dl in 1971 to 4.10 mg/dl in 1984, in men they increased from 4.86 mg/dl in 1962 to 6.00 mg/dl in 1971, and then dropped to 5.60 mg/dl in 1984. Since purine consumption in Germany has not noticeably decreased during the last ten years, we decided to perform a new study in blood donors in 1989, after an interval of 5 years.

Material and Methods

In autumn 1989 blood was drawn from 3200 healthy donors (1103 women and 2097 men) from the Bavarian Red Cross Blood Transfusion Service. Persons between 18 and 65 years of age were admitted to blood donation and included in this study. According to the regulations of the transfusion service only healthy persons fulfilling the following criteria were included: temperature buccal < 37.5° C, hemoglobin > 12.5 mg/dl, systolic blood pressure 100–180 mmHg, diastolic blood pressure 50–100 mmHg, pulse 50–100/min, weight > 50 kg. Age, sex, blood group, and details about history and medication were registered. The mean age was 35.8 ± 12.6 years in women and 37.5 ± 12.1 years in men.

Blood samples were collected in polypropylene tubes, refrigerated, and transported to the Blood Center. Serum was separated from the clotted blood samples and stored at minus 22° C until uric acid assays could be performed.

Dedicated to Prof. Walter Seitz on the occasion of his 85th birthday

Table 1. Uric acid levels in different countries and years. The values are given as mean ± standard deviation. The figures in parentheses indicate the number of persons studied. Question marks indicate figures not to be found in the respective publication

Country Year,* authors	Population	Uric acid levels (mg/dl)	
		Men	Women
West Germany			
1962, Zöllner (1963)	blood donors	4.86 ± 1.32 (265)	4.05 ± 1.29 (119)
1969, Haug et al. (1972)	hospital-patients	6.02 ± 1.38 (5.656)	4.62 ± 1.06 (5.248)
1971, Griebsch and Zöllner (1973)	blood donors	6.00 ± 1.38 (662)	4.35 ± 1.18 (337)
1984, Löffler et al. (1989)	blood donors	5.60 ± ? (739)	4.10 ± ? (337)
1989, Gresser et al. (present study)	blood donors	5.90 ± 1.16 (2.097)	4.16 ± 0.96 (1.103)
East Germany			
1969, Thiele and Schröder (1980)	blood donors	4.2 ± ? (495)	3.4 ± ? (550)
1971,		4.8 ± ? (566)	3.7 ± ? (633)
1973,		5.5 ± ? (375)	4.4 ± ? (337)
1977,		6.2 ± ? (687)	4.6 ± ? (313)
1980, Thiele and Schröder (1982)	blood donors	6.3 ± ? (?)	5.2 ± ? (?)
Switzerland			
197?, Bräuer et al. (1986)	patients in general practice	5.6 ± ? (104)	4.5 ± ? (317)
France			
1965, Zalokar et al. – 1967, (1972)	male employees	5.88 ± 1.19 (23.923)	–
England			
1978, Cook et al. – 1980 (1986)	male patients in general practice	5.9 ± 1.15 (7.730)	–
USA			
195?, Hall et al. – ? (1967)	population Framingham	5.12 ± 1.11 (2.062)	4.0 ± 0.94 (2.489)
1961, Glynn et al. – 1963, (1983)	male population	5.77 ± 0.87 (1.141)	–
1975 – 1978	Boston	6.53 ± 1.15 (1.141)	–
Canada			
1970, Munan et al. – 197? (1976)	population Sherbrooke	5.80 ± 1.32 (558)	4.74 ± 1.10 (663)
Guayana			
197?, Bois and Feingold (1972)	3 tribes	6.2 ± 1.3 (22)	5.6 ± 1.3 (18)
Japan			
1973, Okada et al. – 1974 (1980)	population Hisayama	5.31 ± 1.08 (861)	4.74 ± 1.10 (1.147)
Samoa			
1978, Jackson et al. (1981)	rural population	6.87 ± 1.18 (356)	5.46 ± 1.13 (319)
	urban population	6.72 ± 1.43 (384)	5.27 ± 1.23 (415)

* In this table "year" means the year of uric acid determination

Table 2. Serum uric acid levels in male and female blood donors from Bavaria in 1989

Uric acid (mg/dl)	Men		Women	
	(*n*)	(%)	(*n*)	(%)
≤1	0	0	1	0.1
1.1 –2	0	0	2	0.2
2.1 –3	6	0.3	88	8.0
3.1 –4	69	3.3	455	41.2
4.1 –5	419	20.0	399	36.2
5.1 –6	750	35.8	109	9.8
6.1 –7	530	25.3	35	3.2
7.1 –8	241	11.5	10	0.9
8.1 –9	62	2.9	2	0.2
9.1–10	16	0.8	1	0.1
10.1–11	1	0.0	0	0.0
11.1–12	1	0.0	1	0.1
12.1–13	0	0.0	0	0.0
≥13	2	0.1	0	0.0
Total	2097	100.0	1103	100.0

Uric acid levels were determined enzymatically, through reactions catalyzed by uricase and peroxidase (Boehringer, Mannheim).

Results

Uric acid levels of 3200 blood donors (1103 women and 2097 men) were determined. The mean value was 5.30 ± 1.37 mg/dl. The frequency of different uric acid levels in men and women is shown in Table 2 and Fig 1. Figure 2 shows the cumulated frequencies of uric acid levels in men and women.

Uric Acid Levels and Sex

In the 1103 women the mean uric levels ($x \pm s$) were 4.16 ± 0.96 mg/dl. Therefore, the range ($x \pm 2s$) in women is 2.25–6.08 mg/dl. Twenty women were taking oral contraceptives; their uric acid levels ($x = 3.75$ mg/dl, $s = 0.15$ mg/dl) were significantly lower ($p < 0.01$) than those of all women in the same age group.

In 2097 men the mean value ($x \pm s$) of uric acid was calculated to be 5.90 ± 1.16 mg/dl and the range ($x \pm 2s$) 3.57–8.22 mg/dl. The difference between men and women was statistically significant here and in each subgroup listed below.

Uric Acid Levels and Age

Uric acid levels in women aged 18 to 20 years were significantly higher than in the group aged 21 to 30 years. The levels in women between 51 and 60 years were significantly higher than in women between 41 and 50 (Fig. 3). In men (Fig. 3) uric acid levels did not differ significantly by age group.

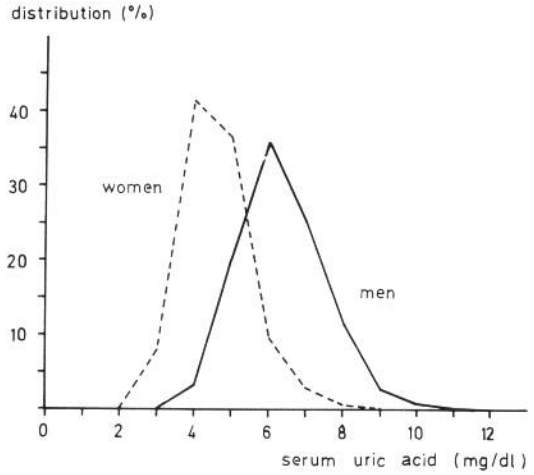

Fig. 1. Distribution of serum uric acid levels in 2097 male and 1103 female blood donors in Bavaria in 1989

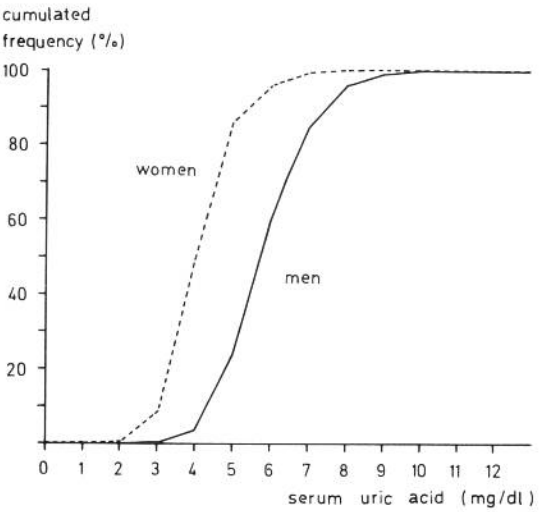

Fig. 2. Cumulated frequencies of serum uric acid levels in 2097 male and 1103 female blood donors in Bavaria in 1989

Uric Acid Levels and Blood Group

The distribution of uric acid levels in relation to the blood groups of the ABO system is shown in Table 3. Levels did not differ significantly with respect to blood groups in either men or women.

Uric Acid Levels in Different Regions of Bavaria

Comparison of serum uric acid levels in populations from different regions of Bavaria showed no significant differences in female blood donors (Ta-

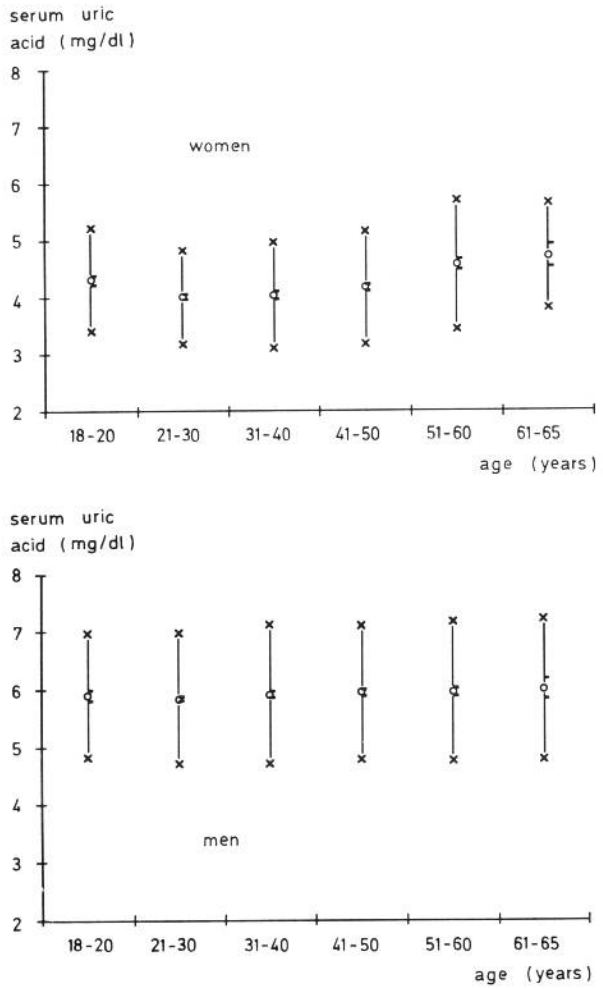

Fig. 3. Relation of serum uric acid levels to different age groups in female and male blood donors in 1989 (o = mean, x = standard deviation, – = standard deviation of the mean)

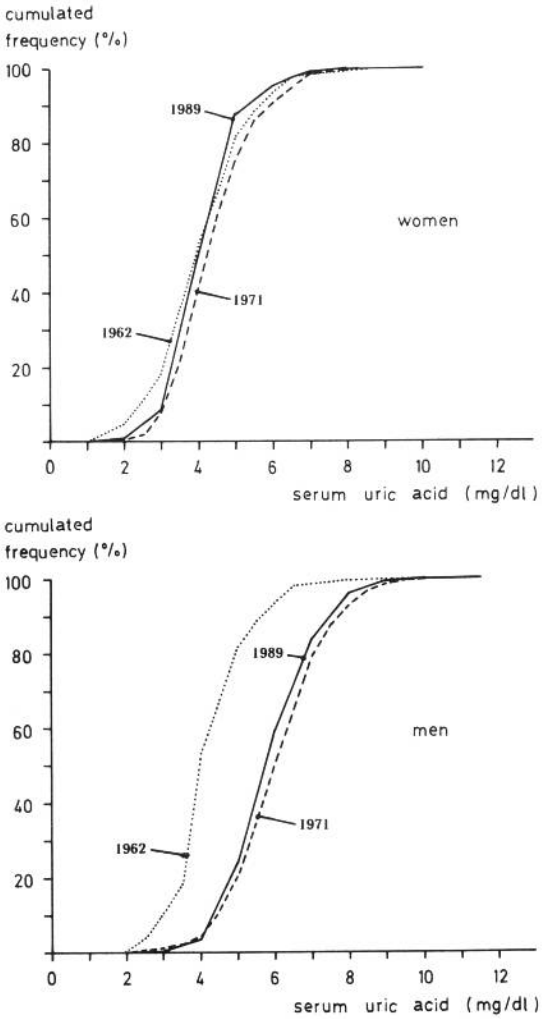

Fig. 4. Cumulated frequencies of uric acid levels in female and male blood donors in Bavaria in 1962, 1971, and 1989. Data for this figure was extracted from publications [28] and [7]

Table 3. Serum uric acid levels in blood donors from Bavaria in relation to blood groups, 1989. The values are given as mean ± standard deviation

Blood group (Number of blood donors)	Serum uric acid levels (mg/dl)	
	Men	Women
0 (1456)	5.91 ± 1.20	4.17 ± 1.02
A (1231)	5.89 ± 1.14	4.19 ± 0.92
B (357)	5.87 ± 1.13	4.08 ± 0.90
AB (156)	5.96 ± 1.07	4.15 ± 0.73

Table 4. Serum uric acid levels in blood donors from different regions of Bavaria, 1989. The values are given as mean ± standard deviation

Region (Number of blood donors)	Serum uric acid levels (mg/dl)	
	Men	Women
Regensburg/Bayerischer Wald (419)	6.06 ± 1.09	4.19 ± 0.93
München/Oberbayern (1103)	5.84 ± 1.17	4.11 ± 0.93
Augsburg/Schwaben (1678)	5.90 ± 1.17	4.20 ± 0.98

ble 4), but men from Regensburg and the Bayerischer Wald showed higher values than donors from the München or Augsburg area; this difference reached a threshold significance only in comparison to München/Oberbayern.

Uric Acid Levels in the Past 28 Years

The mean values of uric acid levels between 1962 and 1989 are shown in Table 1. Figure 4 shows the cumulated frequencies of uric acid levels,

drawn from the data published [28, 7] in comparison to the present study. Between 1962 and 1989 uric acid levels rose by 0.11 mg/dl to 4.16 mg/dl in women and by 1.01 mg/dl to 5.90 mg/dl in men (details in Table 1 and Figure 4). In both men and women the highest uric acid levels were measured in 1971, and those obtained in 1984 were intermediate between 1971 and the present values.

Discussion

Mean serum uric acid levels of 5.90 mg/dl for men and 4.16 mg/dl for women as determined by us in 1989 are in agreement with other recent studies in Europe and North America (Table 1), where uric acid levels between 5.6 mg/dl and 6.3 mg/dl in men and between 4.6 mg/dl and 5.2 mg/dl in women were reported. In two Pacific populations from Samoa uric acid levels were higher. In Bavaria significantly higher uric acid levels were measured in both male and female blood donors in 1989 than in 1962. A comparable rise in uric acid levels has been observed in other populations, e.g., in East Germany [23, 24] and in the United States [6]. An increase in nutritional purine was considered responsible by all authors. In Germany [5] purine intake has increased by 35% since 1962; the drop in the present uric acid levels in comparison to 1971 is not in accordance with that increase. However, nutritional influences on serum uric acid levels are caused not only by dietary purine as a whole. Purines contained in DNA exert less influence on serum uric acid than RNA or free nucleotides [29]. On the other hand, dietary protein exerts a uricosuric effect, lowering serum uric acid, and the same is the case for water diuresis, whereas alcoholic beverages inhibit uric acid excretion [15].

Also, it should not be overlooked that food tables for purines must be revised. Recent analyses quoted by Zöllner and Wolfram [30] give more reliable figures, which in most foods are higher than the old ones, but the ratio of new to old values differs considerably from one type of food to another. Finally, surveys on food consumption are usually based on the quantities purchased, which are not necessarily the quantities eaten. Therefore, much as one may consider the increase in serum uric acid levels from the post-war period to the present as a consequence of increased dietary intake of purines, no conclusions may be drawn from minor changes in serum uric acid levels.

In agreement with all other studies (Table 1) there are significant differences in uric acid levels between men and women in all subgroups of the population. Women using oral contraceptives had slightly but significantly lower uric acid levels than other women of the same age group. This confirms findings of the 1971 study [7].

With respect to age and uric acid levels, different results have been reported. Dodge [5a], Reuter and Sauer [21], and our group in the first study [28] saw not significant differences in uric acid levels in different age groups in men and women. This is possibly due to the same reasons also responsible for the lower serum uric acid levels in the male population, namely the lower dietary purine intake. A significant age-related increase of uric acid levels in both men and women has been reported by Bräuer et al. [3] and Zalokar et al. [27]. Okada et al. [17] reported an age-related increase of uric acid levels in women but not in men, and attributed their observation to a decrease in estrogen levels associated with menopause. Bengtsson and Tibblin [1] found in their investigation on uric acid levels in women an increase related to weight but not to menopause. In our present study we observed no age-related increase of uric acid levels in men. The levels of women between 51 and 60 years were significantly higher than those of younger women, but still significantly lower than those of men in the same age group. We also observed higher uric acid levels in the 18- to 20-year-olds than in the 21- to 30-year-olds (statistically significant only in women). Very few data on uric acid levels in children and young adults have been published. Schröder et al. [22] reported the highest uric acid levels in girls between 10 and 16 years. In boys they observed a steady age-related rise in uric acid levels. Possibly our observation of higher uric acid levels in young women between 18 and 20 years of age reflects the same phenomenon.

In this study we did not observe significant differences in uric acid levels in the subpopulations of different blood groups. This is in agreement with another more recent study [13]. A relationship between uric acid levels and blood groups of the ABO system had been described in some older studies.

Other studies have observed differences in uric acid levels between rural and urban populations (Table 1). This differentiation was not possible in the present study, since the blood was collected mostly in rural areas. In our subpopulations in Upper Bavaria (including Munich), Schwabia (including Augsburg), and the Bavarian Forest (including Regensburg), we observed a difference of treshold significance in uric acid levels only when comparing men from Upper Bavaria with those of the Bavarian Forest, who showed higher levels (Table 4). This finding may possibly be explained

Table 5. Prevalence of hyperuricemia in different populations. Question marks indicate figures not contained in the respective publication. In the column "uric acid levels" fields were left blank when the information was not given in the publication. In Samoa different populations with different uric acid levels were examined

Country year,* authors	Persons (%) with uric acid levels (mg/dl) above							
	6.0		6.5		7.0		8.0	
	♂	♀	♂	♀	♂	♀	♂	♀
West Germany								
1962, Zöllner (1963)			8.0	4.0				
1971, Griebsch and Zöllner (1973)	48.4	9.0	32.2	5.9	20.3	3.6	7.2	0
1989, Gresser et al. (present study)	40.7	4.4	28.6	2.6	15.4	1.3	3.9	0.4
East Germany								
1969, Thiele and Schröder (1980)		1.8			2.4			
1980, Thiele and Schröder (1982)		19.7			29.0			
Switzerland								
197?, Bräuer et al. (1986)	34.4	20.0	28.8	10.1	19.2	9.3	6.7	3.8
France								
1965, Zalokar et al. –1967, (1972)	43.2		28.4		17.6		5.4	
USA								
195?, Hall et al. (1967)	22.0	3.3			4.8	0.5	1.0	0
1975, Glynn et al. –1978, (1983)							11.3	
Canada								
1970, Munan et al. –197?, (1976)	44.0	14.2	26.3	6.6	16.9	3.3	6.3	1.2
Guayana								
197?, Bois and Feingold (1972)		40.7			22.8			
Samoa								
1978, Jackson et al. (1981)		23.3 to 29.5			36.4 to 43.3			

* In this table "year" means the year of uric acid determination

by a higher consumption of purines, especially beer, for which this area is said to be known.

In this study three women were hypouricemic (uric acid level ≤ 2.0 mg/dl), representing 0.27% of the females and 0.09% of the total population examined. Other studies [11, 19, 20, 25] observed higher prevalences between 0.40 and 1.05%, but they examined populations (e.g., hospital patients) possibly taking medications leading to secondary hypouricemia.

As shown in Table 5, in this study 28.6% of the men and 2.6% of the women were by definition hyperuricemic. The results are in good agreement with more recent studies in Europe and North America (Table 5). Thus, a considerable percentage of persons in a healthy population today is at increased risk for gout, nephrolithiasis, and nephropathy. Determination of the uric acid level should be part of any routine checkup in internal medicine. In case of hyperuricemia, dietary and pharmaceutical intervention should follow as described elsewhere [8, 30].

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