nearly twice that of normotensive men (Mantel-Haenszel pooled estimate of odds ratio 1·79; 95% confidence interval 1·53 to 2·09). In treated hypertensive men the Mantel-Haenszel pooled estimate of odds ratio for the age adjusted relative risk was 2·63 (95% confidence interval 2·23 to 3·10).

TABLE IV—*Age adjusted prevalence of history of kidney stones in relation to hypertension*

	Age adjusted % with history of stones
Normotensive subjects (n=509)	14
Untreated hypertensive subjects (n=118)	18
Treated hypertensive subjects (n=61)	33

F=4·54; p<0·011 (analysis of covariance).

Discussion

This population based survey provides evidence of a clinical association between kidney stone disease and arterial hypertension and of the independence of this association from such potential confounders as age, body mass index, hyperuricaemia, and hypercalcaemia. Although a history of kidney stones was definitely related to the age of the subjects at the time of interview, the association of such a history with arterial hypertension remained highly significant after controlling for age. This agrees with a preliminary report from a similar study in central Italy.[23]

The study also indicates that hyperuricaemia is not a major factor in the higher prevalence of urolithiasis in hypertension. Though these patients may have a higher serum concentration[24,25] and an increased filtered load[26] of uric acid, they also have an enhanced reabsorption of urates in the proximal tubule.[26]

The prevalence of urolithiasis in our population increased stepwise from the normotensive state to the untreated hypertensive state and to the treated hypertensive state. This feature is consistent with the hypothesis that an as yet undetermined pathogenic factor linking high blood pressure and kidney stones was operating in relation to the severity of the hypertension (or was more prevalent in hypertension of severe degree). That the hypertension was more severe in the treated group than in the untreated group was plainly evidenced by the similar mean blood pressures in the two groups (that is, despite treatment).

What, then, might be the pathogenetic factor linking urolithiasis with hypertension? Hypercalciuria represents the most important risk factor for urolithiasis in adults.[14,15] We first reported increased 24 hour urinary calcium excretion and a higher prevalence of "hypercalciuria" in patients with essential hypertension[13] after McCarron *et al* had found increased calcium output in "spot" urine specimens.[27] We also found a reduced urinary magnesium to calcium ratio in hypertensive patients[28] and showed that urinary calcium excretion was higher in these patients at any value of serum ionised calcium, suggesting a primary renal calcium leak as the cause of the hypercalciuria, as also confirmed by higher serum parathyroid hormone concentrations.[13,27] The hypothesis that this renal abnormality was the mechanism linking hypertension with urolithiasis is attractive, especially given the exclusion of most other confounding factors. But cause and effect relations are not proved by statistical associations, and, moreover, the possibility that renal damage caused by stones might contribute to hypertension in some cases, though unlikely, cannot definitely be ruled out.

There is need for a prospective investigation to determine the incidence of urolithiasis and identify specific risk factors for this complication in hypertensive patients. Identifying predisposed patients and implementing preventive measures might substantially reduce the social costs of the disease.

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1 Wexler BC, McMurtry JP. Kidney and bladder calculi in spontaneously hypertensive rats. *Br J Exp Pathol* 1981;**62**:369-74.
2 Tibblin G. High blood pressure in men aged 50. A population study of men born in 1913. *Acta Med Scand* 1967;suppl 470:1-84.
3 Larsen JF, Phillip J. Studies on the incidence of urolithiasis. *Urol Int* 1962;**13**:53-4.
4 Ljunghall S, Hedstrand H. Epidemiology of renal stones in a middle-aged male population. *Acta Med Scand* 1975;**197**:439-45.
5 Currie WJC, Turner P. The frequency of renal stones within Great Britain in a gouty and non-gouty population. *Br J Urol* 1979;**51**:337-41.
6 Johnson CM, Wilson DM, O'Fallon WM, *et al*. Renal stone epidemiology: a 25-year study in Rochester, Minnesota. *Kidney Int* 1979;**16**:624.
7 Bengtsson C, Lennartsson J, Lindqvist O, *et al*. Renal stone disease—experience from a population study of women in Gothenburg, Sweden. *Scand J Urol Nephrol* 1980;**14** (suppl 53):39-43.
8 Churchill DN, Maloney CM, Bear J, *et al*. Urolithiasis—a study of drinking water hardness and genetic factors. *J Chronic Dis* 1980;**33**:727-31.
9 Tschope W, Ritz E, Haslback M, *et al*. Prevalence and incidence of renal stone disease in a German population. *Klin Wochenschr* 1981;**59**:411-2.
10 Hiatt RA, Dales LG, Friedman GD, *et al*. Frequency of urolithiasis in a prepaid medical care program. *Am J Epidemiol* 1982;**115**:255-65.
11 Vahlensieck EW, Bach D, Hesse A. Incidence, prevalence and mortality of urolithiasis in the German Federal Republic. *Urol Res* 1982;**10**:161-4.
12 Robertson WG, Peacock M, Baker M, *et al*. Studies on the prevalence and epidemiology of urinary stone disease in men in Leeds. *Br J Urol* 1983;55:595-8.
13 Strazzullo P, Nunziata V, Cirillo M, *et al*. Abnormalities of calcium metabolism in essential hypertension. *Clin Sci* 1983;**65**:137-41.
14 Van Den Berg CJ. Urolithiasis. In: Knox FG, ed. *Textbook of renal pathophysiology*. New York: Harper and Row, 1978:262-82.
15 Pak CYC. Pathophysiology of calcium nephrolithiasis. In: Seldin DW, Giebish G, eds. *The kidney physiology and pathophysiology*. New York: Raven Press, 1985:1365-79.
16 Lewis B, Chait A, Sigurdsson G, *et al*. Serum lipoproteins in four European communities: a quantitative comparison. *Eur J Clin Invest* 1978;**8**:165-73.
17 Strazzullo P, Trevisan M, Farinaro E, *et al*. Characteristics of the association between salt intake and blood pressure in a sample of male working population in southern Italy. *Eur Heart J* 1983;**4**:608-13.
18 Strazzullo P, Cappuccio FP, Trevisan M, *et al*. Association between blood pressure, dietary salt intake and family history of hypertension in a five year follow-up study. *J Hypertens* 1983;**1**(suppl 2):159-61.
19 Cappuccio FP, MacGregor GA, Strazzullo P, *et al*. Characteristics of the distribution of plasma atrial natriuretic peptides in a cross-sectional study of middle-aged untreated male workers. *J Cardiovasc Pharmacol* 1989;**13** (suppl 6):51-4.
20 Strazzullo P, Cappuccio FP, Trevisan M, *et al*. Erythrocyte sodium-lithium countertransport and renal lithium clearance in a random sample of untreated middle-aged men. *Clin Sci* 1989;**77**:337-42.
21 Morris JA, Gardner MJ. Calculating confidence intervals for relative risks (odds ratios) and standardised ratios and rates. *Br Med J* 1988;**296**:1313-6.
22 Kleinbaum DG, Kupper LL, Morgenstern H. *Epidemiologic research. Principles and quantitative methods*. New York: Van Nostrand Reinhold, 1982:320-76.
23 Cirillo M, Laurenzi M. Elevated blood pressure and positive history of kidney stones: results from a population-based study. *J Hypertens* 1988;**6**(suppl 4):485-6.
24 Dollery CT, Duncan H, Schumer B. Hyperuricaemia related to treatment of hypertension. *Br Med J* 1960;iii:832-5.
25 Breckenridge A. Hypertension and hyperuricaemia. *Lancet* 1966;i:15-8.
26 Strazzullo P, Cappuccio FP, Trevisan M, *et al*. Red blood cell sodium-lithium countertransport, blood pressure and uric acid metabolism in untreated healthy men. *Am J Hypertens* 1989;2:634-6.
27 McCarron DA, Pingree PA, Rubin RJ, Gaucher SM, Molitch M, Krutzik S. Enhanced parathyroid function in essential hypertension: a homeostatic response to a urinary calcium leak. *Hypertension* 1980;2:162-8.
28 Cirillo M, Siani A, Nunziata V, Cappuccio FP, Mattioli PL, Strazzullo P. Reduced urinary ratio Mg:Ca and kidney stone risk in essential hypertension. *Minerva Nefrologica* 1983;**30**:213-6.

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Correction

Is uterine growth retardation with normal umbilical artery blood flow a benign condition?

An editorial error occurred at the proof stage in the abstract of this paper by Dr Gerard Burke and others (21 April, p 1044). The first part of the second sentence of the results section should read "Among 55 women with abnormal flow there were two midtrimester abortions, three perinatal deaths, and one case of cerebral irritation in physically normal fetuses."