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Metabolic evaluation

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GUIDELINES

No recommendations possible based on Level I or II evidence

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)
Suggestions are based on opinion and other guidelines. Clinical assessment is important to determine whether stones might be secondary to gastrointestinal disorders (i.e. malabsorption, Crohn's disease or following surgical bowel resection or bypass), other medical conditions (e.g. sarcoidosis) or medications (e.g. indinavir, triamterene). The investigations suggested below are to help to detect other important secondary causes of stones (e.g. hypercalcaemia, urinary infection) and possible complications of stones (e.g. impaired kidney function).

Extensive investigations have not been recommended in people presenting with their first stone as these are unlikely to change management. Urinary metabolic testing can be performed in people who are being considered for prophylactic medical therapy, if the therapy is to be tailored to the specific abnormality found. This includes those who are forming recurrent stones and others who are at high risk of complications if they develop further stones (e.g. single kidney or renal impairment). In people presenting with idiopathic stones (i.e. no identifiable underlying medical condition such as infection stones, malabsorption, cystinuria, etc.), metabolic testing does not appear to be able to accurately predict who will go on to develop stones in the future.

There is limited evidence that metabolic testing should be deferred for at least 3 months after an episode of acute renal colic in order to allow dietary and fluid intake to return to normal, allowing more accurate assessment of any abnormalities.[1]

Following the formation of a single stone:
- **Blood – electrolytes, bicarbonate, urea, creatinine, calcium**
- **Spot urine – pH, blood, leucocytes, microscopy, culture**
- **Imaging – can use x-ray, ultrasound or CT. Unenhanced helical CT is the imaging modality of choice for suspected acute renal colic. See the imaging guideline for further information.**
- **Stone analysis if possible**
- **Consider urinary cystine if stone composition unknown**
- **Parathyroid hormone in those with hypercalcaemia**

For recurrent stone formers or complicated stone disease:
- **Blood uric acid**
- **24 h urine volume, creatinine, calcium, uric acid, oxalate, citrate, cystine (other possible tests include sodium, potassium, magnesium, phosphate, chloride and urea).**

BACKGROUND

People who form kidney stones require investigations to identify underlying medical conditions and to detect other predisposing metabolic abnormalities. The results of these investigations can also be used to help guide therapy to prevent future stone formation. The extent of testing required depends on several factors including age and medical history of the person and the number and frequency of stones. This guideline aims to provide a brief review of available evidence regarding which investigations are required to assist in the management of people with kidney stones. This is supplemented with the Suggestions for Clinical Care section and recommendations from other international guidelines.

SEARCH STRATEGY

Databases searched: Medline (1966 to July Week 3, 2004). MeSH terms and text words for kidney stones were combined with MeSH terms and text words for metabolic work-up (e.g. serum calcium, serum phosphate, pH level, etc.). The results were then combined with the Cochrane search strategy for cohort and prognostic studies.
Date of searches: 17 January 2005.

WHAT IS THE EVIDENCE?

No trials have studied which investigations are required in first-time stone formers in order to detect underlying or contributing medical conditions.

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Several randomized controlled trials of medical therapies have only included recurrent stone formers with specific metabolic abnormalities (e.g. hypercalcaemia, hyperuricosuria). Therefore, quantification of these parameters is required if people are to be treated according to the results of these trials (see Guidelines for each stone type for trial details).

The value of metabolic testing to give prognostic information has been studied in a number of studies. In retrospective studies, people who form stones are more likely to have urinary metabolic abnormalities (e.g. hypercalcuria)[2–7] and those who form recurrent stones tend to have more significant metabolic abnormalities than those with single stones.[7–13] Furthermore, those who have improvement in urinary metabolic abnormalities during therapy are less likely to develop subsequent stones.[14] However, in prospective studies of people presenting with kidney stones, the overlap in the urinary metabolic results is so great that those who will go on to develop stones in the future cannot prospectively be separated from those who will not.[9,15,16]

Interpretation of urinary metabolic results is further complicated by the fact that many results are continuous variables and the distinction between normal and abnormal is arbitrary. This can mean that many normal people without a history of stones have abnormal urinary results.[4,17] Furthermore, people with previous stones whose urinary excretion of several salts is high in the normal range can be at significant risk of recurrent stones.[7]

SUMMARY OF THE EVIDENCE

There are no randomized controlled trials on this topic.

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality Initiative: No recommendation.
UK Renal Association: No recommendation.
Canadian Society of Nephrology: No recommendation.
European Best Practice Guidelines: No recommendation.

INTERNATIONAL GUIDELINES

National Institutes of Health Kidney Stones Consensus Conference:[18]

- Collect and analyse the stone in all patients
- Urinalysis; culture if clinically indicated
- Blood electrolytes, creatinine, calcium, phosphate, uric acid
- Urinary cystine if stone composition is unknown
- Parathyroid hormone (PTH) in hypercalcaemic patients
- Kidney ureter bladder x-ray (KUB) and intravenous pyelography in all patients unless contraindicated
- In recurrent stone formers (and all children), additional investigations should include a 24 h urine test for volume, pH, calcium, phosphorus, sodium, uric acid, oxalate, citrate and creatinine

European Association of Urology, Working Party on Lithiasis[19]

- Stone composition in every patient
- Blood – calcium, albumin, creatinine, ± uric acid
- Early morning sputum
  - Dipstick pH, leucocytes, bacteria
  - Culture if bacteria
  - Cystine test if cystinuria not excluded by other means
- Complicated stone formers – 24 h urine for calcium, oxalate, citrate, urate, creatinine, volume, magnesium, phosphate, urea, sodium, chloride, potassium

IMPLEMENTATION AND AUDIT

No recommendations.

SUGGESTIONS FOR FUTURE RESEARCH

No recommendations.

CONFLICT OF INTEREST

Peter Hughes has no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.

REFERENCES

1. Norman RW, Bath SS, Robertson WG *et al*. When should patients with symptomatic urinary stone disease be evaluated metabolically? *J. Urol.* 1984; **132**: 1137–9.
2. Wasserstein AG, Stolley PD, Soper KA *et al*. Case–control study of risk factors for idiopathic calcium nephrolithiasis. *Miner Electrolyte Metab.* 1987; **13**: 85–95.
3. Leonetti F, Dussol B, Berthezene P *et al*. Dietary and urinary risk factors for stones in idiopathic calcium stone formers compared with healthy subjects. *Nephrol. Dial. Transplant.* 1998; **13**: 617–22.
4. Curhan GC, Willett WC, Speizer FE *et al*. Twenty-four-hour urine chemistries and the risk of kidney stones among women and men. *Kidney Int.* 2001; **59**: 2290–98.
5. Strazzullo P, Gianvincenzo B, Vuotto P *et al*. Past history of nephrolithiasis and incidence of hypertension in men: A reappraisal based on the results of the Olivetti Prospective Heart Study. *Nephrol. Dial. Transplant.* 2001; **16**: 2232–5.
6. Cirillo M, Stellato D, Panarelli P *et al*. Cross-sectional and prospective data on urinary calcium and urinary stone disease. *Kidney Int.* 2003; **63**: 2200–206.
7. Robertson WG. A risk factor model of stone-formation. *Front. Biosci.* 2003; **8**: S1330–38.
8. Strauss AL, Coe FL, Deutsch L *et al*. Factors that predict relapse of calcium nephrolithiasis during treatment. A prospective study. *Am. J. Med.* 1982; **72**: 17–24.
9. Ljunghall S, Danielson BG. A prospective study of renal stone recurrences. *Br. J. Urol.* 1984; **56**: 122–4.
10. Cupisti A, Morelli E, Lupetti S *et al*. Low urine citrate excretion as main risk factor for recurrent calcium oxalate nephrolithiasis in males. *Nephron* 1992; **61**: 73–6.
11. Di Silvero F, D'Angelo AR, Gallucci M *et al*. Incidence and prediction of stone recurrence after lithotripsy in idiopathic calcium stone patients: A multivariate approach. *Eur. Urol.* 1996; **29**: 41–6.

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12. Yagisawa T, Chandhoke PS, Fan J. Metabolic risk factors in patients with first-time and recurrent stone formations as determined by comprehensive metabolic evaluation. *Urology* 1998; **52**: 750–55.
13. Tiselius HG. Factors influencing the course of calcium oxalate stone disease. *Eur. Urol.* 1999; **36**: 363–70.
14. Tiselius HG, Sandvall K. How are urine composition and stone disease affected by therapeutic measures at an outpatient stone clinic? *Eur. Urol.* 1990; **17**: 206–12.
15. Trinchieri A, Ostini F, Nespoli R *et al.* A prospective study of recurrence rate and risk factors for recurrence after a first renal stone. *J. Urol.* 1999; **162**: 27–30.
16. Siener R, Glatz S, Nicolay C *et al.* Prospective study on the efficiency of a selective treatment and risk factors for relapse in recurrent calcium oxalate stone patients. *Eur. Urol.* 2003; **44**: 467–74.
17. Curhan GC, Willett WC, Speizer FE *et al.* Intake of vitamins B6 and C and the risk of kidney stones in women. *J. Am. Soc. Nephrol.* 1999; **10**: 840–45.
18. Consensus Conference. Prevention and treatment of kidney stones. *JAMA* 1988; **260**: 977–81.
19. Tiselius HG, Ackermann D, Alken P et al. Working Party on Lithiasis, European Association of Urology. Guidelines on urolithiasis. *Eur. Urol.* 2001; **40**: 362–71.

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