FSG 1000-01
NEPHROLITHIASIS IN AIRCREW

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REFERENCES:

A. AMA 100-01 Medical Standards for CF Aircrew
B. CFP 154 – Medical Standards for the Canadian Forces

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EPIDEMIOLOGY

1. Nephrolithiasis is common, with a lifetime risk of up to 12% in North American men at a peak age of 30 years. The male: female ratio is 1.5:1 and the incidence of nephrolithiasis is increasing in both sexes in conjunction with changes in dietary habits. The incidence of stone disease is further increased in aircrew compared with the general population presumably due to dehydration related to dry cabin environment, reduction in fluid intake when flying and potentially austere living conditions in arid climates. A family history of nephrolithiasis increases risk threefold. One third of asymptomatic stones become symptomatic within 3 years and the risk of a recurrent symptomatic stone is 15% at one year, 50% within 5 years and up to 80% lifetime.

AEROMEDICAL IMPLICATIONS

2. Renal tract stones may present suddenly and have a significant potential for incapacitation and/or mission compromise. From a Risk Matrix perspective (ref A), renal colic is a Class 2 Medical Event – likely to result in mission abort and/or compromised effectiveness; requires urgent medical attention. It is, therefore, imperative that management in aircrew be thorough and intensive in order to minimize flight safety risk and to allow return to productive employment with the minimum of restrictions and delay.

3. Unfortunately, prognostication of the occurrence or recurrence of stone disease is complex and depends upon factors such as stone size, location and type as well as the interaction of underlying genetics and environment. Consequently, decision making will remain on a case by case basis and require specialist input in most cases.

4. Aircrew selection is also impacted by the rising incidence of stone disease.

PATHOPHYSIOLOGY

5. Regardless of stone type, certain predisposing factors (See Table 1), especially low urine volume, excessive salt intake and the metabolic syndrome, are clearly recognized. Recent research has increased our understanding of the genetics and pathophysiology of nephrolithiasis.

6. It is now well established that hyperuricosuria and abnormally acidic urine with reduced citrate excretion are found in both Type 2 Diabetes and the Metabolic Syndrome and are related to changes in insulin signaling in the kidney. More than half of stone disease relates to these factors. Hypertension, gout and nephrolithiasis are also closely correlated with these abnormalities. Hyperuricosuria predisposes not only to uric acid stones, but also to those of calcium oxalate through formation of a uric acid nidus.

7. Increased urinary concentration of chemical constituents may be caused by either low urine volume or by increased urinary excretion of calcium, uric acid, oxalate or cystine (See Table 2). Decreased urinary solubility arises with abnormal urine pH.

8. Lifestyle and diet play an important role in nephrolithiasis. In a multivariate analysis of 7500 twin pairs discordant for kidney stones a protective dose-response pattern was identified for coffee and milk consumption. Those who drank 5 or more cups of coffee or at least 1 cup of milk per day were half as likely to develop stones. Increasing number of cups of tea and frequent consumption of fruit and vegetables was also protective. Factors such as the use of calcium supplements, consumption of solid dairy products, and alcohol were not significantly related to kidney stones.

Table 1 – Major Risk Factors for Calcium Stones

Urinary	**Other Medical Conditions**
• Lower volume	• Primary hyperparathyroidism
• Higher calcium	• Gout
• Higher oxalate (CaOx stones)	• Obesity
• Lower citrate	• Diabetes Mellitus
• Higher pH (CaP stones)	**Anatomic**
Diet	• Medullary sponge kidney
• Lower fluid intake	• Horseshoe kidney
• Lower dietary calcium	
• Higher oxalate	
• Lower potassium	
• Higher animal protein	
• Higher sodium	
• Higher sucrose	
• Lower phytate	
• Higher vitamin C	

Table 2 – Composition and Major Features of Urinary Calculi

STONE COMPOSITION	% OF CALCULI	MAJOR FEATURES
Calcium Oxalate	70	Majority due to idiopathic hypercalciuria, 30% hyperuricosuria, 5% hyperparathyroidism
Calcium Phosphate	15	As above
Pure Uric Acid	10	Hyperuricosuria (Diabetes and MetS) and increased urine acidity, radiolucent on plain radiographs
Struvite (Magnesium Ammonium Phosphate)	3	Urease producing bacteria, large "staghorn" stones (Pseudomonas, Proteus, Klebsiella, Enterococci)
Cystine	2	Hypercystinuria, rare congenital renal defect associated with alkaline pH, renal failure

PRESENTATION OF NEPHROLITHIASIS

9. Nephrolithiasis may present in several ways and the aeromedical implication of each will vary. Many stones are asymptomatic and detected incidentally. Stones that are retained within the renal parenchyma, in cysts or calyceal diverticula are unlikely to migrate into the collecting system and should neither lead to symptoms, grounding or medical category. Stones in the collecting system and ureter typically cause pain that onsets gradually and in aircrew may give sufficient warning to abort a flight. Stones < 5 mm should pass spontaneously, whereas those > 10 mm rarely do. Proximally located stones (pelvis of kidney and proximal ureter) are less likely to pass than those at the ureterovesical junction. The majority of stones that pass spontaneously do so within 30 days.

DIAGNOSIS

10. The foundations of diagnosis of acute stone disease (renal colic) include clinical assessment, urinalysis, and imaging. Ninety percent of those presenting to an emergency room will have the triad of unilateral flank pain, hematuria (either gross or microscopic) and positive imaging. Non-contrast thin- slice CT is the preferred imaging modality. Ultrasound and IVU (intravenous urography) can be considered if CT is unavailable. However, ultrasound may miss small stones and those in the ureter.

Acute

11. The most recent Cochrane Review (2005) showed no evidence for the use of fluids or diuretics for treatment of acute ureteric colic. Standard of practice includes adequate analgesia with NSAIDs, opiates or a combination of the two as well as MET (Medical Expulsive Therapy). Both the calcium channel blocker nifedipine and the alpha antagonist tamsulosin have been studied and are associated with more frequent and earlier stone passage, and fewer hospitalizations/procedures for failed stone passage. The alpha

blockers may be the preferred agents and are given for 4 weeks to those with stones < 10 mm.

12. Referral to a urologist is indicated for those with:

a. colic complicated by sepsis or underlying urinary tract abnormalities;

b. uncontrolled pain or other symptoms;

c. stones > 9 mm; and

d. stones that fail to pass after conservative management including MET.

13. Options for management of retained symptomatic stones include Shock Wave Lithotripsy (SWL), ureteroscopic lithotripsy with electrohydraulic or laser probes, percutaneous nephrolithotomy or laparoscopic stone removal. SWL is effective in up to 75%, especially for stones located in the renal pelvis and upper ureter. Another Cochrane Review (2007) concluded that ureteroscopy achieved a higher stone-free state but was associated with increased complications and longer hospital stays. Nevertheless, this approach is preferred for most aircrew since residual stones may lead to flight restriction.

Post Stone Passage

14. Urinalysis may be diagnostic of stone type:

a. urine pH > 7 and presence of phosphate crystals suggests calcium phosphate or struvite stones; or

b. hexagonal cystine crystals is cystinuria.

15. Stone retrieval and analysis is essential along with biochemical analysis of urine and blood. Two 24 hour urine collections and serum biochemistry panels, taken a week apart, when asymptomatic and on a customary diet and exercise regimen is required for all aircrew with an episode of renal colic (See Annex A). Urine supersaturation testing (and targeted intervention to reduce it) may become the standard of practice but is currently controversial and the testing is not universally available.

16. In first time or single stone formers, with a finding of abnormal urinary pH or metabolite excretion, and/or metabolic syndrome, diet and lifestyle modification for 4 – 6 months may suffice. For most this includes:

a. fluid intake to achieve a minimum of 2 L of urine output daily (preference for coffee, milk and tea but avoidance of grapefruit juice that may increase stone formation). Patient monitoring with reagent strip to maintain urine specific gravity between 1.005 – 1.010 can be considered;

b. normal calcium diet;

c. low animal protein diet;

d. low sodium diet; and

e. low calorie diet and exercise to produce a 7 - 10% body weight loss in those with metabolic syndrome.

17. Repeat serum and urine biochemistries must be done to confirm resolution of documented abnormalities. Repeat imaging is also indicated to assess for residual stone disease.

18. In the setting of multiple stones, or active stone disease (increasing numbers or size of stones) long-term medical management is indicated and is best managed by specialists. Drug therapies include high-dose hydrochlorothiazide to reduce urinary calcium excretion, allopurinol to reduce uricosuria, supplemental calcium taken with meals to reduce oxalate absorption, and potassium citrate to increase urinary citrate excretion and pH.

AEROMEDICAL DISPOSITION

19. With acute renal colic aircrew should be grounded pending initial treatment, investigation and institution of long-term management.

20. Upon resolution of the acute episode, and in the absence of additional high-risk stones or medication requirement, aircrew may be returned to flying duties expeditiously. Discussion with ASCS and/or AUMB is required and a referral visit to CFEME/Medical Consult Services may be requested at that time. Annex A must also be completed and forwarded to AUMB.

21. If pharmacological treatment is instituted, aircrew should not be returned to flying duties until it is deemed that the medication is efficacious (normalization of documented abnormal serum or urine parameters) and without adverse effects. Consultation with a urologist or nephrologist is required.

22. Aircrew with retained calculi, or who have a recurrence of renal colic must be grounded and will be assessed on an individual basis. Referral to a urologist or other specialist with particular expertise in stone management (e.g. nephrologist or internist) is required, and discussion with AUMB is recommended from the outset. A return to flying status will depend on:

a. location and size of the retained stone(s);

b. probability of recurrence of renal colic;

c. use and efficacy of long-term stone prevention therapies;

d. aircrew role/position; and

e. potential impact on flight safety and mission effectiveness.

23. Aircrew with recurrent renal colic or with retained calculi with a high probability of recurrent colic are likely to be permanently grounded. For recurrent renal urolithiasis, D Med Pol requirement for *G3 – at risk of experiencing a recurrence of a chronic medical condition for which medical care (by PA/NP or MO) may be required within 3 days, and O3 – should avoid dehydration as this may exacerbate a chronic medical condition (ref B).*

24. Aircrew with retained calculi or with a past history of stones status unknown should undergo renal ultrasound at the time of two consecutive medicals in order to establish their natural history and stability.

25. Initial aircrew applicants will be considered only if there are no retained calculi or, in the presence of a positive personal history of urolithiasis, a metabolic work-up comparable to that of Annex A is negative and a year has passed since stone passage.

ANNEX A - NEPHROLITHIASIS: METABOLIC WORK-UP CHECKLIST

Date: _____ Name & Init: _____ SN: _____ DOB: _____ Weight: ____kg Girth _____cm

FAMILY HISTORY OF STONES: _____

METABOLIC SYNDROME SCREEN: (as per FSG 900-01)
Abdo. Obesity ____ Hypertension ____ Low HDL ____ High TG ____ Dysglycemia _____

METABOLIC WORKUP: Collect **TWO** sets of serum/urine chemistries, at weekly intervals, while asymptomatic and on customary diet/exercise regimen.

URINALYSIS (TWO samples separated by a week or more; should be same dates as urine chemistry, below)**:**

	Date	Microsopic	Protein	Glucose	pH	Spec Grav
Sample #1						
Sample #2						

SERUM CHEMISTRY (TWO samples separated by a week or more; should be same dates as urine chemistry, below):

	Sample #1	**Sample #2**	**Normal Values**
	Date:	**Date:**	
Calcium			2.2 – 2.6 mmol/L
PTH (if first Ca++ >2.5 or urine Ca++ excretion increased			(depends on lab)
Uric Acid			< 450 umol/L
Creatinine			< 110 umol/L
eGFR			> 90 ml/min/1.73 m^2 (i.e., > 60 ml/min for avg size adult)
Electrolytes			normal limits

24 HOUR URINE CHEMISTRY (TWO samples separated by a week or more; same dates as serum chemistry, above):

	Sample #1	**Sample #2**	**Normal Values** (per 24 hr)	
	Date:	**Date:**	Male	Female
Creatinine			> 0.18 mmol/kg	> 0.14 mmol/kg
Phosphate			29 – 77 mmol (both genders)	
Calcium			< 7.5 mmol	< 6.25 mmol
Uric acid			< 4.8 mmol	< 4.5 mmol
Oxalate			< 0.5 mmol (both genders)	
Citrate			>1.67 mmol (> 320 mg)	>1.67 mmol (> 320 mg)

IMAGING RESULTS: _____ Date _____

STONE ANALYSIS: _____ Date _____