Appendix C. Table 5. Evidence table: Acetohydroxamic acid (AHA) trials for recurrent nephrolithiasis

| **Study/Region/****Funding Source** | **Inclusion/Exclusion Criteria** | **Patient Characteristics (expressed in means unless otherwise noted)** | **Baseline Stone Characteristics/****Biochemistry** | **Intervention/Duration** | **Study Quality** |
| --- | --- | --- | --- | --- | --- |
| Griffith, 199126Location: USAFunding Source: Government | Inclusion Criteria: * presence or history of infection calculi in association with chronic, urea-splitting urinary infection that was recalcitrant to permanent eradication by antimicrobial agents;
* serum creatinine <2.5 mg/dL (225 μmol/L);
* not suitable for surgical removal of calculi and antimicrobial therapy

Exclusion Criteria: NR | N=94Age (yr): 79% in age range 25-75y Gender (Male %): 51Race/Ethnicity (%): NRSpinal cord injury: 50%BMI, weight, or percent with obesity: NR Previous bariatric surgery (%): NRChronic kidney disease (%): NRSerum creatinine (mg/dL): NREstimated GFR (ml/min/1.73m2): NRSolitary kidney (%): NRHistory of renal transplant (%): NRUrinary tract anatomic abnormality (%): 64% with prior urinary diversion (ileal conduits) Pregnancy: NRHistory of CAD: NRHistory of DM: NRHistory of HTN: NR | Stone type: Struvite 100%Past stone episodes: multiple 100%Residual stones/ fragments: 89% by X-ray. Urine analysis: Hypercalciuria NR; hypocitraturia NR; hyperuricosuria NR; hyperoxaluria NR; mixed NR; no metabolic disorder NRBlood analysis:Hyperuricemia NRDiet characteristics: NR | 1. AHA 15 mg/kg/d every 6-8 hours (n=45)2. Placebo (n=49)Other: Antibiotics were prescribed according to the physicians as clinically indicated Follow up period: 6-32 mosStudy withdrawals (%): * overall 65 (69)
* due to adverse events 15 (15.9)
* due to loss to follow-up 11 (11.7)

Assessment of compliance and adherence to treatment: Overall > 80% medication compliance as assessed by study nurse Setting (e.g., medicine, urology): NRFollow up biochemical measures collected: (y/n): NR | 1. Allocation Concealment: unclear, not specified2. Blinding: double blind and radiologist who reviewed radiographs3. Intention to Treat Analysis: yes4. Withdrawals/Dropouts adequately described: yes*Quality of harms reporting:*1. Harms predefined: No2. Harms specified as ALL events collected: No3. Number of participants that withdrew/lost to follow up adequately described: Yes4. Total number of participants affected by harms specified for each study group: Yes5. Number for each type of harm event specified for each study group: Yes |

| Appendix C. Table 5. Evidence table: Acetohydroxamic acid (AHA) trials for recurrent nephrolithiasis (continued) |
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| **Study/Region/****Funding Source** | **Inclusion/Exclusion Criteria** | **Patient Characteristics (expressed in means unless otherwise noted)** | **Baseline Stone Characteristics /****Biochemistry** | **Intervention/Duration** | **Study Quality** |
| Griffith, 198827Location: USAFunding Source: Government | Inclusion Criteria: * non-progressive spinal cord injury
* chronic urinary tract infection with urea-splitting organisms
* serum creatinine < 3 mg/dL
* acceptance of the logistical requirements of 3-month follow up visits for 2 years
* acceptance of the double-blind investigational format.

Exclusion Criteria: * progressive neuropathy
* candidates for surgical lithotomy
* nonfunctioning stone-containing kidneys
* major coexistent medical problems; having social, economic and logistical problems that would hinder compliance and/or follow up
 | N=210Age (yr): 49Gender (Male %): 100Race/Ethnicity (%): NRSpinal cord injury: 100%Weight (mean, kg): AHA 79.1, placebo 72.6Previous bariatric surgery (%): NRChronic kidney disease (%): NRSerum creatinine (mg/dL): 1.0Estimated GFR (ml/min/1.73m2): NRSolitary kidney (%): NRHistory of renal transplant (%): NRUrinary tract anatomic abnormality (%): NRPregnancy: NRHistory of CAD: NRHistory of DM: NRHistory of HTN: NR | Stone type: Struvite 100%Past stone episodes: single NR, multiple NRResidual stones/ fragments: 88% by excretory urogram. Urine analysis: Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR; mixed NR; no metabolic disorder NRBlood analysis:Hyperuricemia NRDiet characteristics: NR | 1. Acetohydroxamic acid 0.5-1.0 gm/d (n=121)2. Placebo (n=89)Follow up period: up to 24 mosStudy stated that no attempt was made to control antibiotic use during the study.Study withdrawals (%): 103 (49) Study withdrawals (%): * AHA 62%, placebo 31%
* due to adverse events AHA 20%, placebo 5% (severe reactions)
* due to loss to follow-up NR

Assessment of compliance and adherence to treatment: Pill count (at least 80% of pills at previous visit),79-91% in AHA and 84-94% in placebo groupSetting (e.g., medicine, urology): NRFollow up biochemical measures collected: (y/n): Yes | 1. Allocation Concealment: adequate2. Blinding: double and radiologist who reviewed radiographs. Results reviewed by independent monitoring body.3. Intention to Treat Analysis: No4. Withdrawals/Dropouts adequately described: Yes*Quality of harms reporting:*1. Harms predefined: No2. Harms specified as ALL events collected: No3. Number of participants that withdrew/lost to follow up adequately described: Yes4. Total number of participants affected by harms specified for each study group: NR5. Number for each type of harm event specified for each study group: NR |
| Williams, 198428Location: USAFunding Source: Government and non industry | Inclusion Criteria: * Documented struvite nephrolithiasis concomitant with infection with a urea-splitting organism
* > 18 years of age
* serum creatinine <3mg/dL
* hematocrit > 25%
* patients on the phosphate depleting Shor regimen were continued on it

Exclusion Criteria: * participants unable to understand the protocol
* pregnancy
* lactation
* oral contraceptive use
* history of varicose veins, phlebitis or pulmonary embolism.
 | N=39Age (yr): AHA 52, placebo 44 Gender (Male %): 17.9Race/Ethnicity (%): NRBMI, weight, or percent with obesity: NR Previous bariatric surgery (%): NRChronic kidney disease (%): NRSerum creatinine (mg/dL): NREstimated GFR (ml/min/1.73m2): NRSolitary kidney (%): NRHistory of renal transplant (%): NRUrinary tract anatomic abnormality (%): AHA 20% and placebo 15.7% had supra vesical dversions (17.9% overall); AHA 5% and placebo 10% had neurogenic bladders (7.7% overall)Pregnancy: 0%History of CAD: NRHistory of DM: NRHistory of HTN: NR | Stone type: Struvite 100%Past stone episodes: multiple 100%Residual stones/ fragments: NR for all but 7 placebo patients had stones that doubled in area versus 0 for AHA patients (determined by X-ray). Urine analysis: Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR; mixed NR; no metabolic disorder NRBlood analysis:Hyperuricemia NRDiet characteristics: NR | 1. Acetohydroxamic acid 15 mg/kg/d (n= 20)2. Placebo (n=19)Other: Both groups treated with suppressive antibiotics throughout study.Follow up period: overall mean 18 (up to 30 mos), mean AHA 15.8, mean placebo 19.6Study withdrawals (%): * overall 6 (15.3)
* due to adverse events AHA 2 (10)
* due to loss to follow-up NR

Assessment of compliance and adherence to treatment:Assessed by pill counts and urine AHA screening; participants determined by either measure to be taking <50% of medication were withdrawn from the study. 16% of AHA group and 5% of placebo group excluded from 7 to 10 months analysis for noncompliance, but compliance not reported over full study duration.Setting (e.g., medicine, urology): NRFollow up biochemical measures collected: (y/n): NR | 1. Allocation Concealment: adequate2. Blinding: double and radiologist who reviewed radiographs3. Intention to Treat Analysis: no4. Withdrawals/Dropouts adequately described: yes*Quality of harms reporting:*1. Harms predefined: No2. Harms specified as ALL events collected: No3. Number of participants that withdrew/lost to follow up adequately described: Yes4. Total number of participants affected by harms specified for each study group: Yes5. Number for each type of harm event specified for each study group: Yes |