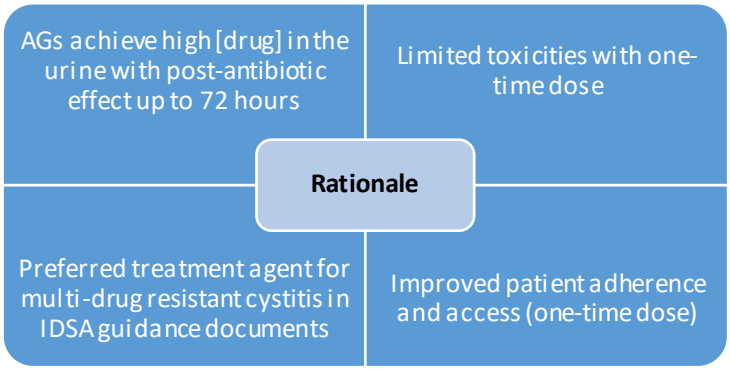
DUHS Adult Urinary Tract Infection (UTI): Single-Dose Aminoglycoside Guidance Document

Aminoglycosides (AG):

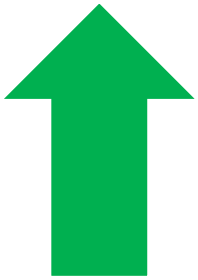
- Due to increasing resistance among various antibiotic classes used to treat UTIs (*e.g.* fluoroquinolones, SMX/TMP), alternative agents with activity against multidrug resistant (MDR) bacteria are required
- AGs have retained excellent activity against MDR urinary pathogens (*e.g.* ESBL *Escherichia coli*) and may be a suitable monotherapy option as a one-time dose for cystitis



	Gentamicin⁺	Tobramycin	Amikacin
Dose*	5 mg/kg IV/IM once	5 mg/kg IV/IM once	15 mg/kg IV/IM once
Administration	**IM:** undiluted 40 mg/mL vial (may require multiple injections depending on weight) **IV**: Dilute in 50 to 200 mL of NS, LR, or D5W and infuse over 30 min to 2 h	**IM:** use undiluted 80 mg/2 mL vial (may require multiple injections depending on weight) **IV:** Dilute in 50 to 100 mL of NS, LR or D5W and infuse over 20 min to 60 min	**IM:** use undiluted 500 mg/2 mL vial **IV:** Dilute in 100 to 200 mL of NS, LR, or D5W and infuse over 30 min to 60 min
Adverse Effects	- **Nephrotoxicity (low risk)** ○ 0.5% (63/13,804) in one systematic review ○ Transient rise in serum creatinine: 10% (2520/24,107) in another systematic review ○ All cases of acute kidney injury were reversible - **Ototoxicity (low risk)** ○ No reports in of ototoxicity two systematic reviews		

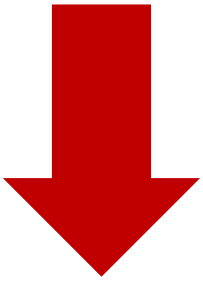
*Appropriate weight: if underweight (TBW < IBW): use TBW; if non-obese (TBW 1-1.25x IBW): use IBW; if obese (TBW >1.25x IBW): use AdjBW

When to use single-dose aminoglycosides for UTI?



Consider Using:

- Lower urinary symptoms only
- Medication adherence or access issues
- Multiple antibiotic allergies
- Unable to take oral medications
- Known history of or current UTI due to MDR organism



Avoid Use:

- Urinary tract abnormalities
- Systemic signs of infection (bacteremia, sepsis, fever)
- Upper tract infection (pyelonephritis)

Review of the Literature:

Article	Goodlet et al (Efficacy)	Hayward et al (Safety)
Design	Systematic review (n=13,804 patients across 13 studies published from 1978 to 1991)	Systematic Review (n = 24,107) across 36 studies) to evaluate safety of gentamicin

Patient Population	- **Age:** 2 weeks to >70 years
	  ○ 53% of studies with only children
	- **Setting:** Inpatient and outpatient
	- **Demographic:** female (79.5%) with acute uncomplicated cystitis with normal renal function
	  ○ 2 studies included pyelonephritis none with sepsis/bacteremia
	- **Pathogens:** 72% of isolates were E. coli
		- **Age:** ≥16 years of age (ranged from 18-95 years)
		- **Demographic:** 11,107 female and 11,332 male

Intervention	- **Therapy:** Single-dose aminoglycoside monotherapy
	  ○ Netilmicin = most common AG > gentamicin >amikacin
	- 7 studies with a comparator arm:
	  ○ Single dose oral fosfomycin
	  ○ TMP/SMX
	  ○ Amoxicillin or cephalosporin x 5-10 d
		- **Therapy:** Gentamicin 1 mg/kg x 1 to 480 mg per dose
		  ○ Given either IV or IM
		- **Indications:**
		  ○ **Prophylaxis:** surgery (n=20), cystogram (n=1) or transrectal prostate biopsy (n=1)
		  ○ **Treatment:** sepsis (n=1), gonorrhea (n=3) and UTI (n=2)

Outcomes	- **Microbiologic Cure Rate:** 94.5% ± 4.3%
	  ○ No differences between pediatrics vs. adults or between AG vs. comparator arms
	- **Sustained cure with anatomical abnormalities vs. no abnormalities:** 57.3% vs 87.5% (p<0.001)
	- **Recurrence:** 19% (84/443) 30-day recurrence rate
	- **Adverse effects:** 0.5% (64/13,804); most common vestibular toxicity (n = 53) and nephrotoxicity (n = 7)]
		Safety in Patients Receiving Gentamicin
		- **Nephrotoxicity:** 2520 participants
		  ○ Majority of cases were reversible.
		- **Ototoxicity:** None

Limitations	- Comparisons not against commonly used agents (ceftriaxone/nitrofurantoin)
	- Symptom data not reported
	- Limited generalizability:
	  ○ Many studies with pediatric patients (8 studies), 3 studies adult only
	  ○ Few studies with pyelonephritis and none with sepsis or bacteremia
	  ○ Few studies with renal impairment
	- None of the studies were blinded
		- Heterogeneity between studies (unable to perform meta-analysis)
		- Potential confounding factors for renal injury (ex: orthopedic surgeries, concomitant medications, old age)
		- Cohort studies contributed the most to the systematic review

References:

1. Nicolle LE, Gupta K, Bradley SF, et al. Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of Americaa. *Clinical Infectious Diseases*. Published online March 21, 2019. doi:10.1093/cid/ciy1121
2. Goodlet KJ, Benhalima FZ, Nailor MD. A Systematic Review of Single-Dose Aminoglycoside Therapy for Urinary Tract Infection: Is It Time To Resurrect an Old Strategy? *Antimicrob Agents Chemother*. 2019;63(1):e02165-18. doi:10.1128/AAC.02165-18
3. Hayward RS, Harding J, Molloy R, et al. Adverse effects of a single dose of gentamicin in adults: a systematic review: Review of adverse effects of single-dose gentamicin. *Br J Clin Pharmacol*. 2018;84(2):223-238. doi:10.1111/bcp.13439
4. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC β-lactamase-Producing Enterobacterales, Carbapenem-Resistant Acinetobacter baumannii, and Stenotrophomonas maltophilia Infections. Clin Infect Dis. 2021 Dec 5:ciab1013. doi: 10.1093/cid/ciab1013
5. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America 2022 Guidance on the Treatment of Extended-Spectrum β-lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR-P. aeruginosa). Clin Infect Dis. 2022 Apr 19:ciac268. doi: 10.1093/cid/ciac268.