

From Data to Action: Advances and Evolving Strategies in HIV and STI Prevention



Aniruddha Hazra, MD
Associate Professor of Medicine
University of Chicago
Chicago, IL



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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Hazra reported serving as a consultant to Abbott Laboratories, Gilead Sciences, Inc, and ViiV Healthcare. He reported receiving research grant funding from Gilead Sciences, Inc. (Updated October 29, 2025)

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Learning Objectives

After attending this presentation, learners will be able to:

- Analyze the current HIV preexposure prophylaxis (PrEP) landscape and differentiate between available prevention options
- Evaluate real-world outcomes and implementation considerations for long-acting PrEP in key populations
- Describe available evidence on and public health implications of doxycycline postexposure prophylaxis
- Assess emerging strategies for biomedical prevention of sexually transmitted infections

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The PrEP Landscape in 2025

	Daily FTC/TDF
Men who have sex with men	FDA approved, guideline recommended ¹⁻⁴
Transgender women	
Heterosexual men	
Heterosexual women	
Transgender men	
Persons Who Inject Drugs	

¹FTC/TDF PI, ²Genvi, ³JAMA, 2024, ⁴WHO implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection, 2024, ⁵CDC PrEP guidelines, 2021, ⁶FTC/TAF PI, ⁷CAB extended-release injectable suspension PI, ⁸LENPI, ⁹Amviro, ¹⁰JAMA, 2025, ¹¹CDC LEN PrEP guidelines, ¹²MMWR, 2025, 2024

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F/TAF in Cisgender Woman

- Subanalysis PURPOSE-1, HIV incidence in F/TAF arm not statistically different than background incidence or F/TDF
- Examined adherence through DBS TFV-DP concentration in F/TAF and F/TDF arms
 - ≥2 doses/wk 67% at week 8 down to 16% at week 52
- DBS data available in 37 of 39 incident cases in F/TAF group
 - 35/37 had low adherence (<2 doses/wk)
 - women with ≥2 doses/wk significantly lower likelihood of acquiring HIV

F/TAF was effective for PrEP in cisgender women with consistent adherence

Adherence
 High (≥4 doses/week)
 Medium (2-3 doses/week)
 Low (<2 doses/week)
 Missing data (n=7)
 HIV diagnosis (time diagnosis of HIV-1 RNA by quantitative testing)

Adherence^a
 High (≥4 doses/week)
 Medium (2-3 doses/week)
 Low (<2 doses/week)

People Who Acquired HIV n=37
Matched Control n=159

Kouyama PM, et al. CROI 2025. Abstract 154
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Optimizing On-Demand Oral F/TDF for Women

- On-demand oral PrEP data needed in women
 - Prior modeling studies suggest 2-1-1 PrEP provides protective drug levels in FGT for 5 days post-sex
 - Need for additional on-demand regimens for extended protection (5-10 days) in women
- PK/PD modeling used to predict drug concentrations in the FGT of various on-demand regimens
 - Protection levels assessed at 5, 7, and 10 days post-sex
- Key findings
 - >80% protection at 5 days for all regimens
 - Adding a 4th day boosts 7-day protection
 - No regimen sustained protection for 10 days
 - Clinical studies on 2-2-2, 2-1-1-1, 2-2-1-1 regimens in women are sorely needed

Key Takeaways:
 Adding 1 day of dosing ↑ protection by 8-15% for the same total dose

Key Takeaways:
 All 4 Day >80% at 7 days
 2-2-2-2 >90% at 7 days

Confield ML, et al. CROI 2025. Abstract 157
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LEN FDA Approval and Guideline Updates

THE NEW ENGLAND JOURNAL OF MEDICINE

ISSN 0028-2728

Volume 382, Number 10 • May 19, 2020

Twice-Yearly Symposium on Daily HIV for HIV Prevention in Cisgender Women

JAMA

Volume 323, Number 10 • May 19, 2020

Consent & Recourse

Preoperative Prophylaxis for HIV

Updated Recommendations From the 2024 International Antiviral Society-USA Panel

Editorial: HIV and the COVID-19 Pandemic

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THE NEW ENGLAND JOURNAL OF MEDICINE

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Twice-Yearly Symposium on Daily HIV for HIV Prevention in Men and Gender-Diverse Persons

MMWR

Weekly and Monthly Morbidity and Mortality Reports

Volume 69, Number 10 • May 15, 2020

Consent & Recourse

Preoperative Prophylaxis for HIV

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Bioscience Resource Project

Volume 1, Number 1 • May 19, 2020

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HIV Acquisition on LEN PrEP (PURPOSE 1 & 2)

5 seroconversions across PURPOSE 1 & 2 studies

PURPOSE 1

- 2 new seroconversions post-primary analysis
 - Case 1: Occurred after LEN discontinuation with sub-therapeutic drug levels; no capsid inhibitor mutations
 - Case 2: Low-level viremia, target LEN levels, genotype unsuccessful

A line graph titled 'HIV-1 RNA copies/mL' on the y-axis (log scale from 100 to 100,000) and 'Time (weeks)' on the x-axis (0 to 12). Two data series are plotted: Patient 1 (green line) and Patient 2 (purple line). Patient 1 starts at ~10,000 copies/mL at week 0, drops to ~1,000 copies/mL at week 4, and remains low through week 12. Patient 2 starts at ~10,000 copies/mL at week 0, drops to ~1,000 copies/mL at week 4, rises to ~10,000 copies/mL at week 8, and remains elevated through week 12.

PURPOSE 2

- 2 seroconversions on study
 - On-time injections, target concentrations
 - N74D capsid mutations detected in both
- 1 additional case (post-primary analysis):
 - On-time injections, target concentrations
 - Q67H / K70R capsid mutations detected

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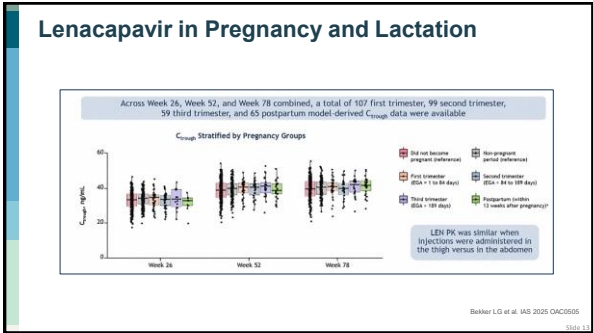
Lenacapavir in Pregnancy and Lactation

Participants and Pregnancies*	LEN n = 113	F/TAF n = 216	F/TDF n = 98
Confirmed pregnancies	193	214	98
Participants with confirmed pregnancies†	184	208	95
Pregnancy status, n (%)			
Completed	186 (96.4)	207 (95.0)	97 (99.0)
Unknown	7 (3.6)	11 (5.0)	1 (1.0)
Live births, n (%)‡	128 (66.3)	119 (54.6)	56 (57.1)
Pregnancy losses, n (%)	40 (21.1)	89 (45.8)	41 (41.8)
Stillbirth	5 (2.4)	6 (2.8)	3 (3.1)
Induced abortion	35 (18.1)	50 (22.9)	23 (23.5)
Spontaneous miscarriage§	20 (10.4)	33 (15.1)	15 (15.3)

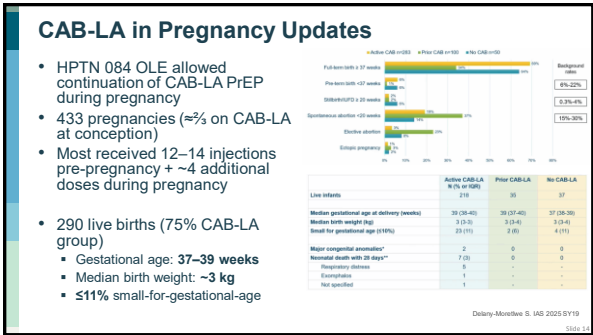
* In total, 10 congenital abnormalities were reported (six in LEN arm; four in F/TAF arm)*

Baskler LG et al. *IAS 2020 CAC0505*

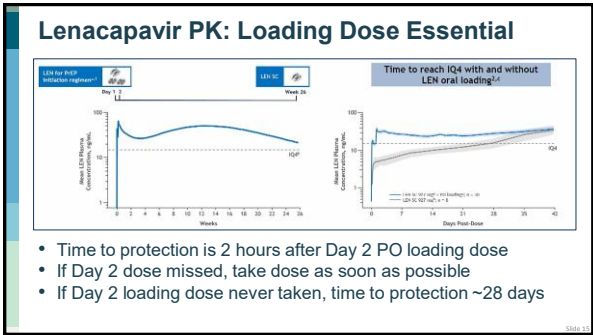
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Lenacapavir Drug-Drug Interactions

- LEN is substrate of P-gp, UGT1A1, CYP3A and **inhibits CYP3A**
- Contraindicated meds: phenytoin, carbamazepine, oxcarbazepine, phenobarbital, rifamycin, St. John's wort
- No increase on common AEs associated with PDE5 inhibitors nor statins in PURPOSE 2**

Figure 1. LEN is a Moderate Inhibitor of CYP3A. May Increase Blood Levels of Co-administered Drugs That Are CYP3A Substrates^{1,2}

Figure 2. PDE5 Inhibitors and Statins That Are Metabolized by CYP3A^{1,2}

Abbington A et al. EACS 2025.

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Substance Use and LEN for PrEP

- More than a third of PURPOSE 2 participants receiving LEN reported any substance use
- Over 40% of participants reported monthly or more frequent binge drinking episodes
- Approximately 37% reported any substance use
- Substance use did not impact adherence to SC LEN injections
- Low clinical interactions predicted between SC LEN and fentanyl

Figure 1. Substance Use and LEN for PrEP

Figure 2. AUC Ratio of Fentanyl in Presence of CYP3A4 Inhibitor to Fentanyl alone

Clark J et al. IDWeek 2025 Abstract 392

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3-Month vs 6-Month STI Screening With PrEP

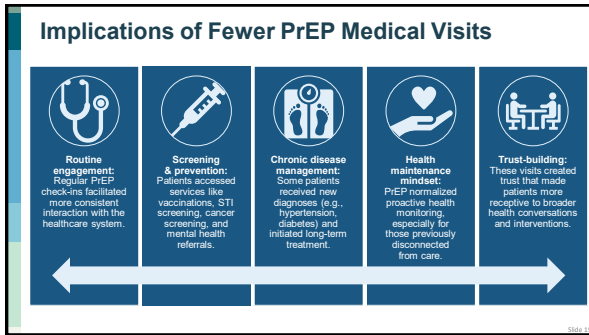
- 428 MSM on PrEP randomized to 6- vs. 3-monthly STI screening in the Netherlands
- 6-monthly group had fewer total visits, but more additional STI visits
- No difference in STI positivity between groups (29.1% vs. 25.6%)
- Suggests 6-monthly monitoring may be safe and cost-efficient for PrEP care

STI positivity by monitoring frequency

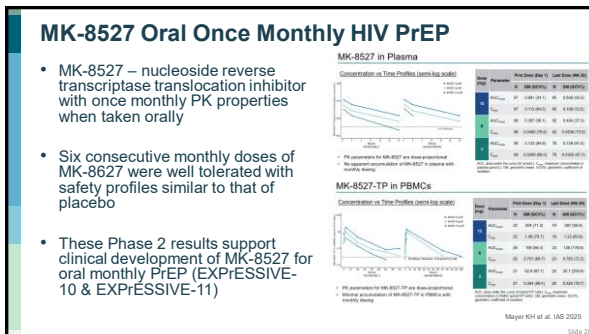
STI positivity by monitoring frequency

Bouwers et al. AIDS 2024 Abstract 04030

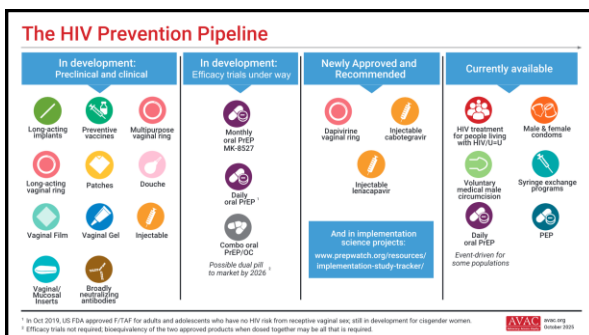
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Sexually Transmitted Infections Surveillance, 2024



More than 2.2 million STIs were reported in the U.S., but signs of progress continue.

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Doxycycline (any formulation) 200 mg taken as soon as possible within 72 hours of oral, vaginal, or anal sex has been shown to reduce syphilis and chlamydia infections by >70% and gonococcal infections by approximately 50% in MSM and TGW

Molina JM, et al. *Lancet Infect Dis*. 2019.
Ludwigsson AF, et al. *N Engl J Med*. 2020.
Molina JM, et al. *Lancet Infect Dis*. 2024.

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Completed Doxycycline Prophylaxis Studies				
Study	Sample Size and Population	STI Rate or Outcome		Reduction in Relative Risk
		Doxycycline PPK	No Doxycycline PPK	
DoxyPEP Pilot (Los Angeles, USA, 2011-2012)	Men with HIV (n=30)	12.3 per 100 PY	33.2 per 100 PY	73% (p=0.02)
ANRS IPERGAY (Paris, France, 2015-2016)	Men on HIV PHEP (n=232)	37.7 per 100 PY	69.7 per 100 PY	47% (p<0.001)
DoxyPEP (Seattle and San Francisco, USA, 2020-2022)	Men with HIV (n=174)	11.8% per quarter	30.6% per quarter	NNT: 5.3
	Men on HIV PHEP (n=527)	10.7% per quarter	31.9% per quarter	66% (p<0.001); NNT: 4.7
DOXYVAC (Paris, France, 2021-2023)	Men on HIV PHEP (n=502)	8.8 per 100 PY*	53.2 per 100 PY*	83% (p<0.0001)
DuDS (Vancouver, Canada, 2019-2020)	Men on HIV PHEP (n=62)	0 per 100 PY**	81.6 per 100 PY**	82% (p=0.011)
DuDS (Toronto and Vancouver, Canada, 2020-2023)	Men with HIV (n=52)	23.7 per 100 PY	119.4 per 100 PY	80% (p<0.001)
PEP (Kisumu, Kenya, 2020-2022)	Women on HIV PHEP (n=449)	25.1 per 100 PY	29.0 per 100 PY	12% (p=0.51)
DoxyPEP Pilot (Tokyo, Japan, 2022-2023)	Women sex workers (n=40)	79.2 per 100 PY	232.3 per 100 PY	67% (p=0.02)
DoxyPEP Pilot (Kisumu, Kenya, 2024-2025)	Women on HIV PHEP (n=60)	11.2 per 100 PY	29.6 per 100 PY	61% (p=0.11)

*Point estimates are for CT and syphilis only. **Point estimates are for CT only. Slide adapted from Hertz et al. *Clin Infect Dis*.

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BOX 1. CDC recommendations for use of doxycycline as postexposure prophylaxis for bacterial sexually transmitted infections prevention	
Recommendation*	Strength of recommendation and quality of evidence ¹
Providers should counsel all gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW) with a history of at least one bacterial sexually transmitted infection (STI) (specifically, syphilis, chlamydia or gonorrhea) during the past 12 months about the benefits and harms of using doxycycline (any formulation) 200 mg once within 72 hours (not to exceed 200 mg per 24 hours) of oral, vaginal, or anal sex and should offer doxycycline postexposure prophylaxis (doxy PEP) through shared decision-making. Ongoing need for doxy PEP should be assessed every 3–6 months.	AI High-quality evidence supports this strong recommendation to counsel MSM and TGW and offer doxy PEP.
No recommendation can be given at this time on the use of doxy PEP for cisgender women, cisgender heterosexual men, transgender men, and other queer and nonbinary persons.	Evidence is insufficient to assess the balance of benefits and harms of the use of doxy PEP
*Although not directly assessed in the trials included in these guidelines, doxy PEP could be discussed with MSM and TGW who have not had a bacterial STI diagnosed during the previous year but will be participating in sexual activities that are known to increase likelihood of exposure to STIs. ¹See Table.	
5 US Department of Health and Human Services Centers for Disease Control and Prevention MMWR June 6, 2024 Vol. 73 No. 2	

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Citywide Impact of DoxyPEP Guidelines — San Francisco, 2022–2023

- Interrupted time-series analysis
- Comparison of monthly STI cases before (Jul 2021–Oct 2022) vs. after (Nov 2022–Nov 2023) guideline release
- Citywide doxyPEP rollout was associated with major declines in chlamydia and syphilis, but not gonorrhea.
- Highlights potential population-level STI prevention impact, while underscoring need for ongoing resistance monitoring.

Sanikaran M, et al. JAMA Int Med 2025. Page 77

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High Sustained Effectiveness of Doxycycline PEP for STI Prevention After Clinical Implementation

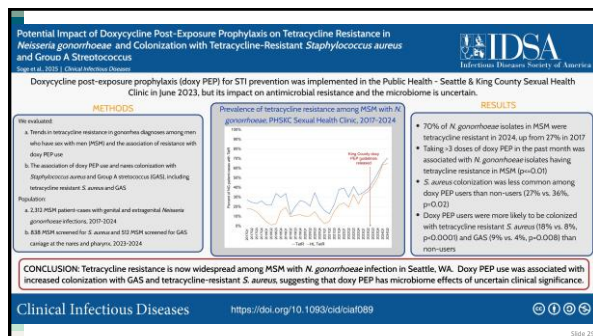
- Retrospective analysis of 4,149 clients at a San Francisco sexual health clinic
 - 2,419 used DoxyPEP users vs 1,730 non-users
 - Up to five quarters before and after DoxyPEP initiation
 - Median age 30–39
 - 89% cisgender men
 - 33% White, 24% Hispanic/Latinx, 17% Asian, 13% multiracial, 7% Black
- Before DoxyPEP initiation, users had a higher STI risk compared to non-users (OR=5.33).
- Post-initiation, STI rates among DoxyPEP users declined significantly – Overall: 72% reduction (OR=0.28)
 - Chlamydia: 95% reduction (OR=0.05)
 - Gonorrhea: 55% reduction (OR=0.45)
 - Syphilis: 34% reduction (OR=0.16)
- Interrupted time series analysis indicated a sustained decline in STI rates over time among users
- Key findings
 - DoxyPEP guideline led to a substantial and sustained decrease in bacterial STIs

STI	OR	95% CI	P-value
Chlamydia	0.05	0.01–0.42	<.001
Gonorrhea	0.45	0.14–1.39	<.001
Syphilis	0.16	0.03–0.84	<.001

STI	OR	95% CI	P-value
Chlamydia	5.33	3.89–7.36	<.001
Gonorrhea	5.33	3.89–7.36	<.001
Syphilis	5.33	3.89–7.36	<.001

Scott H, et al. CROI 2025. Abstract 163. Page 23

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Other Resistance Concerns

- Widespread use of doxyPEP will select for tetracycline-resistant gonorrhea
- Limited long-term benefit for extragenital GC
- DoxyPEP will **not** be our answer to reducing GC infections
- Theoretical risk of selective dual-resistance GC isolates (bacteria resistant to TCN as well as cephalosporin)

We must weigh these real AMR concerns with the significant reductions seen in syphilis and chlamydia infections

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Syphilis Diagnostics in the DoxyPEP Era

- Delayed seroconversion — may extend >2 weeks after ulcer onset
- Potential impact of DoxyPEP on syphilis diagnostic algorithms warrants monitoring

Seattle Sexual Health Clinic, 2023–2024 (n = 1,777 PrEP patients)

- Median RPR titer: 1:8 in DoxyPEP users vs. 1:32 in non-users
- Early syphilis: 12% among users vs. 88% among non-users
- Possible explanations:
 - Attenuated or delayed antibody response from recent doxycycline use
 - Higher prevalence of past treated infections among DoxyPEP users

Raccagni AR et al. 2024
Cannon C et al. ISSTD 2025

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So where do we go from here?

Striking similarities between HIV PrEP and DoxyPEP

- Novel biomedical intervention w/ significant impact in priority populations
- Concerns of anti-microbial resistance/misuse
- Equity concerns regarding utilization and uptake
- Data in cisgender women are lacking

So, what's different now?

- Signals of higher interest in Black and Hispanic/Latinx men
- **WE SHOULD KNOW AND DO BETTER**

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Weekly DoxyPEP Among Cisgender Women in Kenya (dPEP Kenya Study)

- Open-label, single-arm pilot study
- Intervention: **Doxycycline 200 mg once weekly**
 - Combines elements of PEP + PrEP (see next slide)
- **60** nonpregnant cisgender women (ages 18–30)

Key Findings to date

- **91%** adherence to weekly dosing
- **61% reduction** in chlamydia incidence

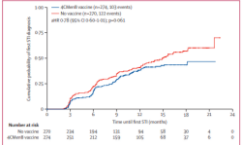
Stewart J et al. ISSTD 2025

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DoxyVAC Results – 4CMenB Vaccine

- Data for MenB vaccination to prevent GC was inconclusive
- Small benefit (~20-30%) possible
- Similar rates of cumulative as well as symptomatic infections
- Phase 3 trial of gonorrhea specific vaccine completed August 2025
- In meantime UK's NHS has endorsed 4CMenB vaccination in sexual-health clinics August 2025



GOV.UK

Press release
NHS begins roll-out of world-first gonorrhoea vaccine programme

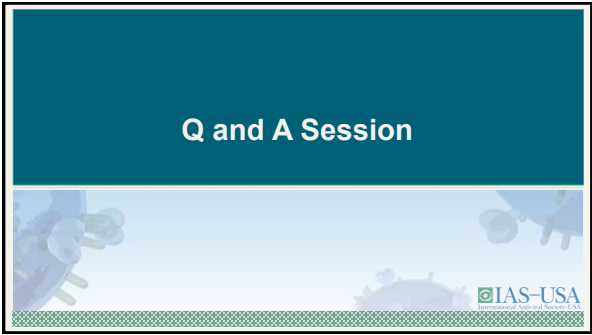
NHS and local authorities begin roll-out of world-first gonorrhoea vaccination programme across the country.

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The IAS–USA Annual Update on HIV Management in Chicago, Illinois, November 18, 2025

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