AETC AIDS Education & Training Center Program Pacific

Post-Exposure Prophylaxis (PEP)

Larry York, PharmD, BCIDP, BCPS, AAHIVP
Sascha Bianchi, MPH

Some slides adapted from John Leander Po, MD, PhD

Disclaimer

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Objectives

By the end of this discussion, you will be able to understand and discuss:

1. The research related to Post-Exposure Prophylaxis for HIV
2. How to initiate and manage PEP care
3. The PEP delivery methods via telemedicine

What is PEP?

- Regimen to reduce risk of contracting HIV if exposed
- "Plan B" of HIV
  - 72 hour window of efficacy from moment of possible exposure
- Typically consists of Truvada 200/300 mg plus another agent
  - Unlike PrEP, PEP is a complete antiretroviral regimen against HIV

HIV ACQUISITION RISK GROUPS

HIV Occupational PEP (oPEP)

- Exposures common
- 58 **documented** cases of health care workers contracting HIV from exposures as of 2010;
  - **No new documented cases** since 1999
  - 150 other possible cases (1981-2010)
- Area of considerable concern but little data

Source:
https://www.cdc.gov/hai/organisms/hiv/surveillance-occupationally-acquired-hiv-aids.html

HIV Non-Occupational PEP (nPEP)

- Includes all exposures outside of a healthcare setting
- Underutilized resource to potentially prevent HIV spread
- More difficult to obtain medicine

Which fluids are potentially infectious for HIV?

- blood?
- saliva?
- sweat?
- feces?
- semen?
- vaginal secretions?
- cerebrospinal fluid?
- breastmilk?
- synovial fluid?
- pleural fluid?
- peritoneal fluid?
- pericardial fluid?
- amniotic fluid?
- pus?
- urine?
- vomitus?

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Exposure Risks (average, per episode, involving HIV-infected source patient)

Exposure	Risk
Percutaneous (blood)[1]	0.3%
Mucocutaneous (blood)[2]	0.09%
Receptive anal intercourse[3]	1 - 2%
Insertive anal intercourse[4]	0.06%
Receptive vaginal intercourse[5]	0.1 – 0.2%
Insertive vaginal intercourse[6]	0.03 – 0.14%
Receptive oral (male)[7]	0.06%
Female-female orogenital[8]	4 case reports
IDU needle sharing[9]	0.67%
Vertical (no prophylaxis)[10]	24%

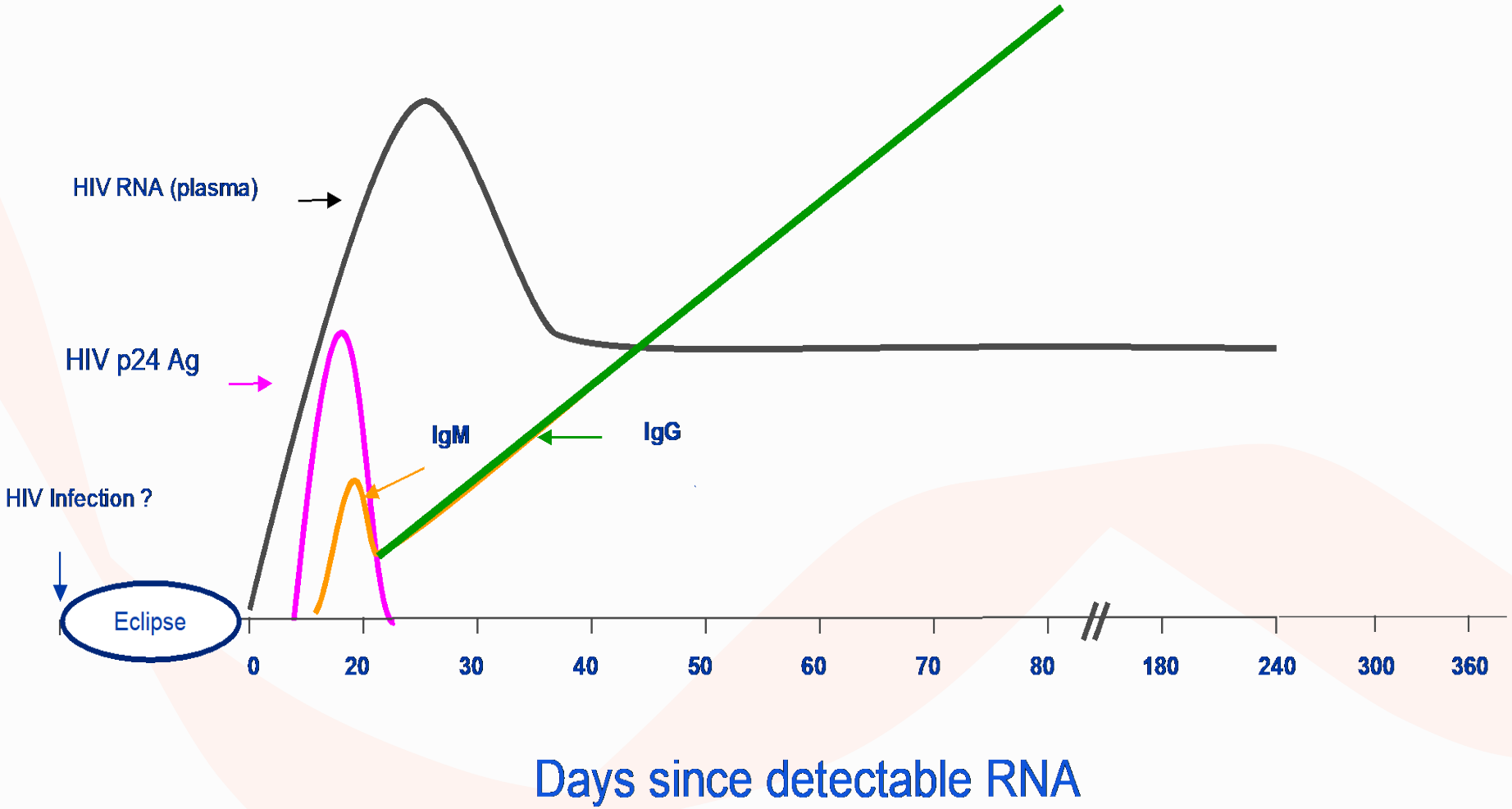
Other Risk Factors to Consider

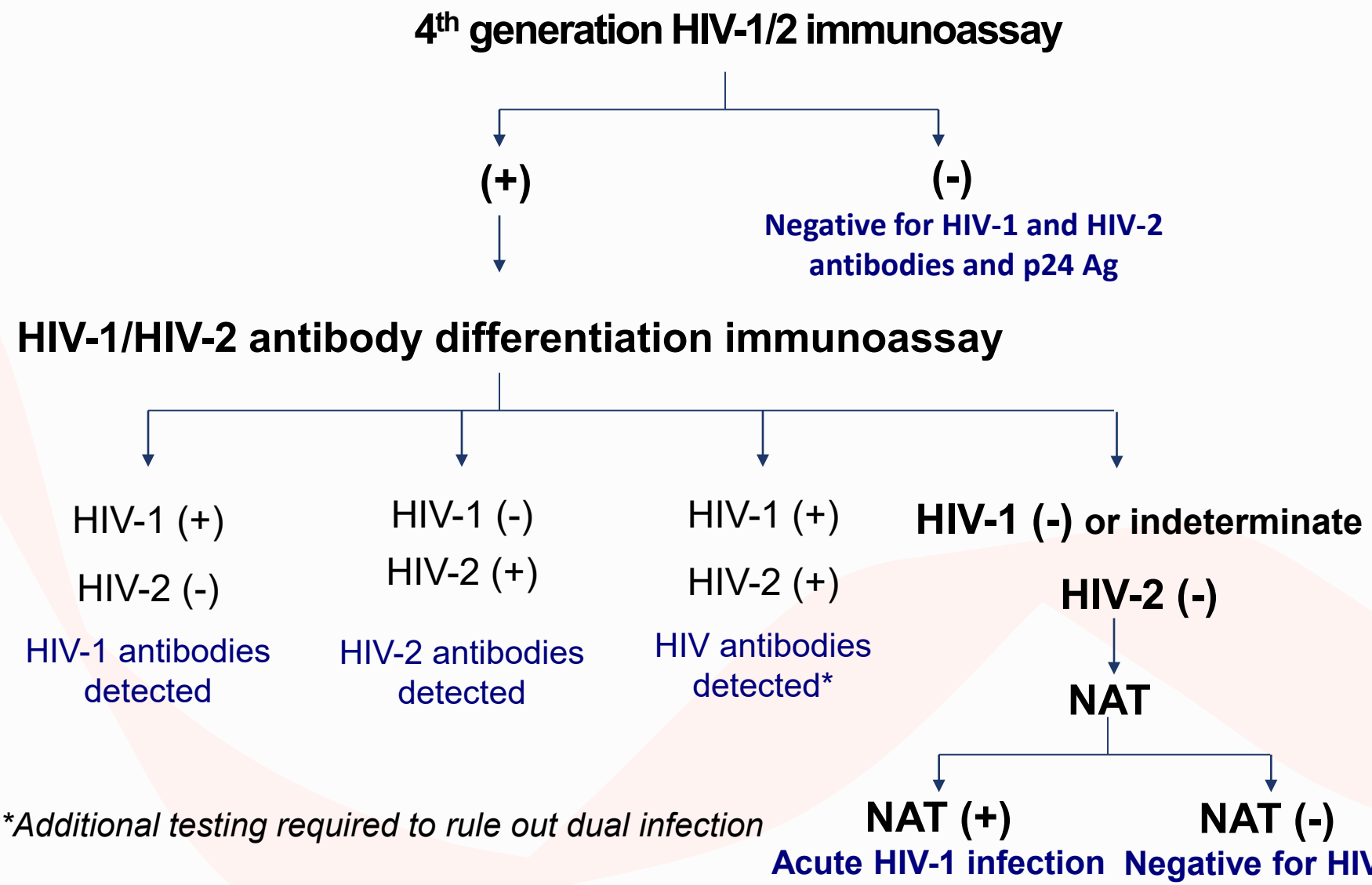
- Viral load of source patient

- Considerations for needlesticks:
  - Glove use
  - 50% decrease in volume of blood transmitted
  - Hollow bore vs solid bore
    - Large diameter needles weakly associated with increased risk
    - Drying conditions
    - Tenfold drop in infectivity every 9 hours

HIV TESTING AND ACUTE HIV

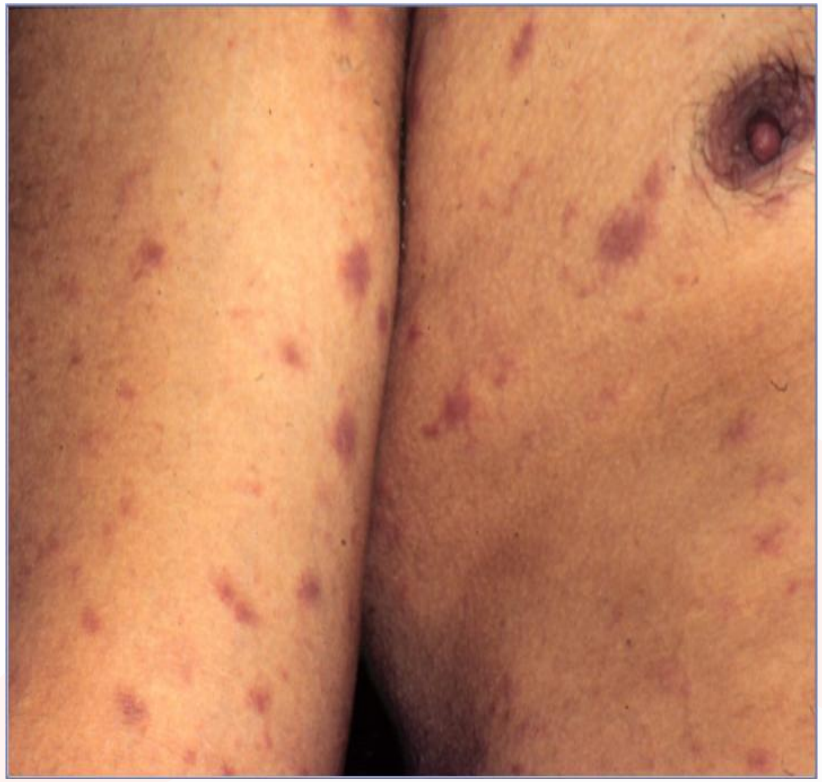
Laboratory Markers of HIV Infection




4th generation HIV-1/2 immunoassay
(+)
(-)
Negative for HIV-1 and HIV-2 antibodies and p24 Ag
HIV-1/HIV-2 antibody differentiation immunoassay
HIV-1 (+)
HIV-2 (-)
HIV-1 antibodies detected
HIV-1 (-)
HIV-2 (+)
HIV-2 antibodies detected
HIV-1 (+)
HIV-2 (+)
HIV antibodies detected*
HIV-1 (-) or indeterminate
HIV-2 (-)
NAT
NAT (+)
Acute HIV-1 infection
NAT (-)
Negative for HIV-1
*Additional testing required to rule out dual infection

Acute Retroviral Syndrome Signs/Symptoms

- Fever
- Malaise
- Myalgia
- Rash
- Headache
- Sore throat
- Lymphadenopathy

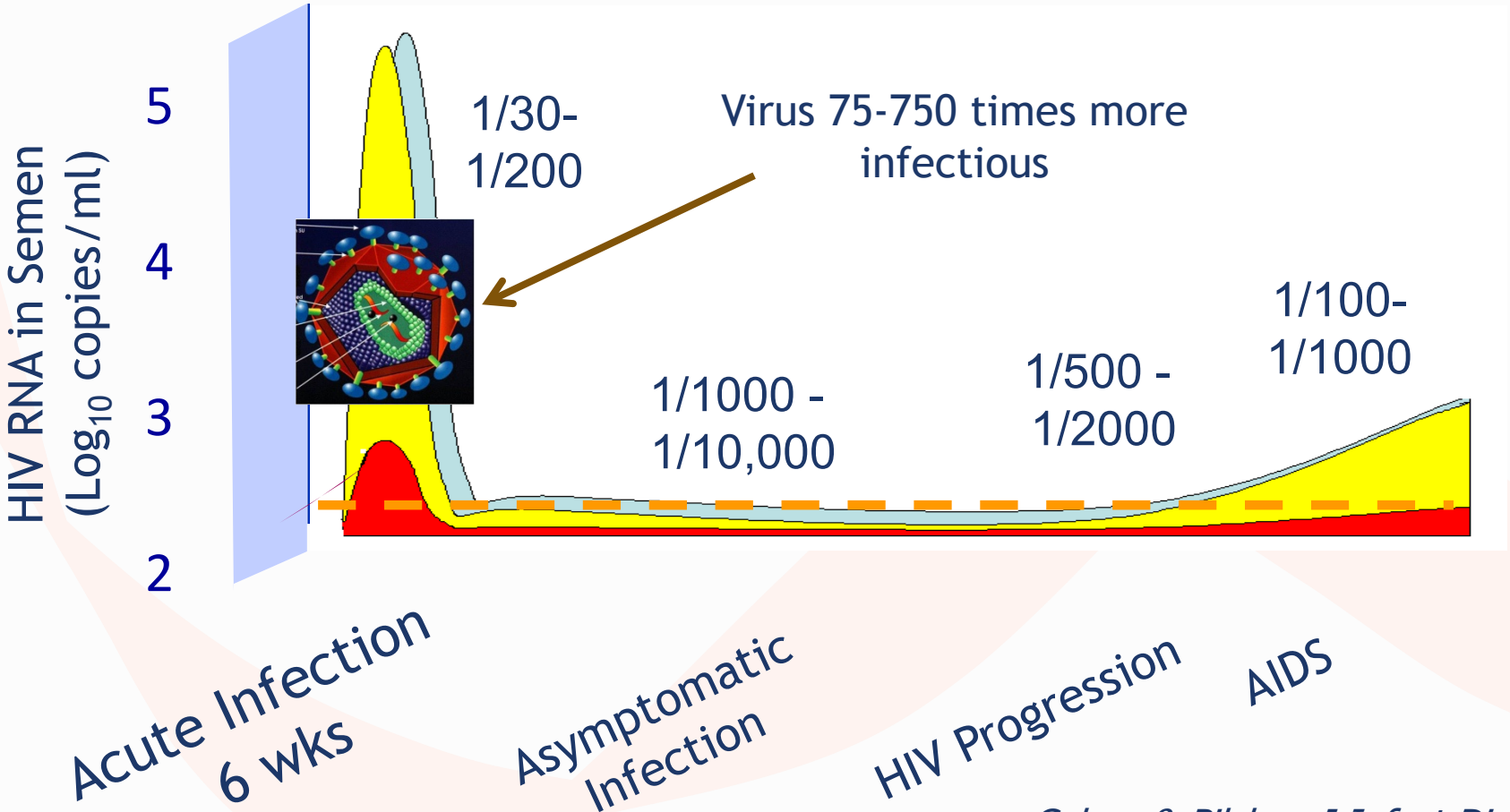


Acute Retroviral Syndrome Presentation

- Most patients who contract HIV are symptomatic with seroconversion[1]
- Flu-like or mono-like illness often accompanied by a rash[2]
- Onset typically 2-6 weeks following exposure, but high variability[1]
- Treatment of acute HIV with antiretroviral therapy may have significant long-term benefit[3]

1. Schacker T et al. Ann Int Med 1996;125:257-64.
2. Kahn JO, Walker BD. N Engl J Med. 1998;339:33-39.
3. Walker B. State of the Art Lecture and Summary. 8th CROI, Session #37.

Increased Risk of Sexual Transmission of HIV



Cohen & Pilcher, J Infect Dis. 2005

PEP ANTIRETROVIRALS AND THEIR MANAGEMENT

Key Points of PEP Regimens

- Duration is always 28 days
- COMPLETE regimen against HIV
- Timing is critical
  - Begin AS SOON AS POSSIBLE

Preferred PEP Regimens

- Integrase-based regimens preferred:
  - Truvada 200/300 mg + Isentress (raltegravir) 400 mg twice daily
  - Truvada 200/300 mg + Tivicay (dolutegravir) 50 mg once daily
- Total duration is always 28 days

Truvada (FTC/TDF)

- Single pill containing two medications
  - Emtricitabine (FTC) 200 mg
  - Tenofovir disoproxil (TDF) 300 mg
- Can be taken with or without food
- Both agents have renal adjustments
  - These adjustments have NOT been studied for PEP

Side Effects of Truvada

- May experience nausea, bloating upon initiation
  - Usually resolves within 2-3 weeks
- Headache
- Increased risk of decreased renal function
  - Uncommon but known adverse effect from TDF
  - Renal function usually returns to normal if TDF stopped
- Increased risk of decreased bone mineral density

When NOT to use Truvada

- Do not begin Truvada if CrCl < 60 mL/min
- If CrCl declines to < 50 mL/min, alternative recommended
  - Definite recommended point for renal dose adjustments

Truvada and Chronic HBV

- FTC and TDF both active against HBV
  - Sudden withdrawal may lead to acute HBV flares

- Critical to know HBV status of PEP patient to assess risk
  - May consider continuing Truvada or TDF beyond 4 week period
  - Assess by reviewing HBsAb, HBcAb, HBsAg

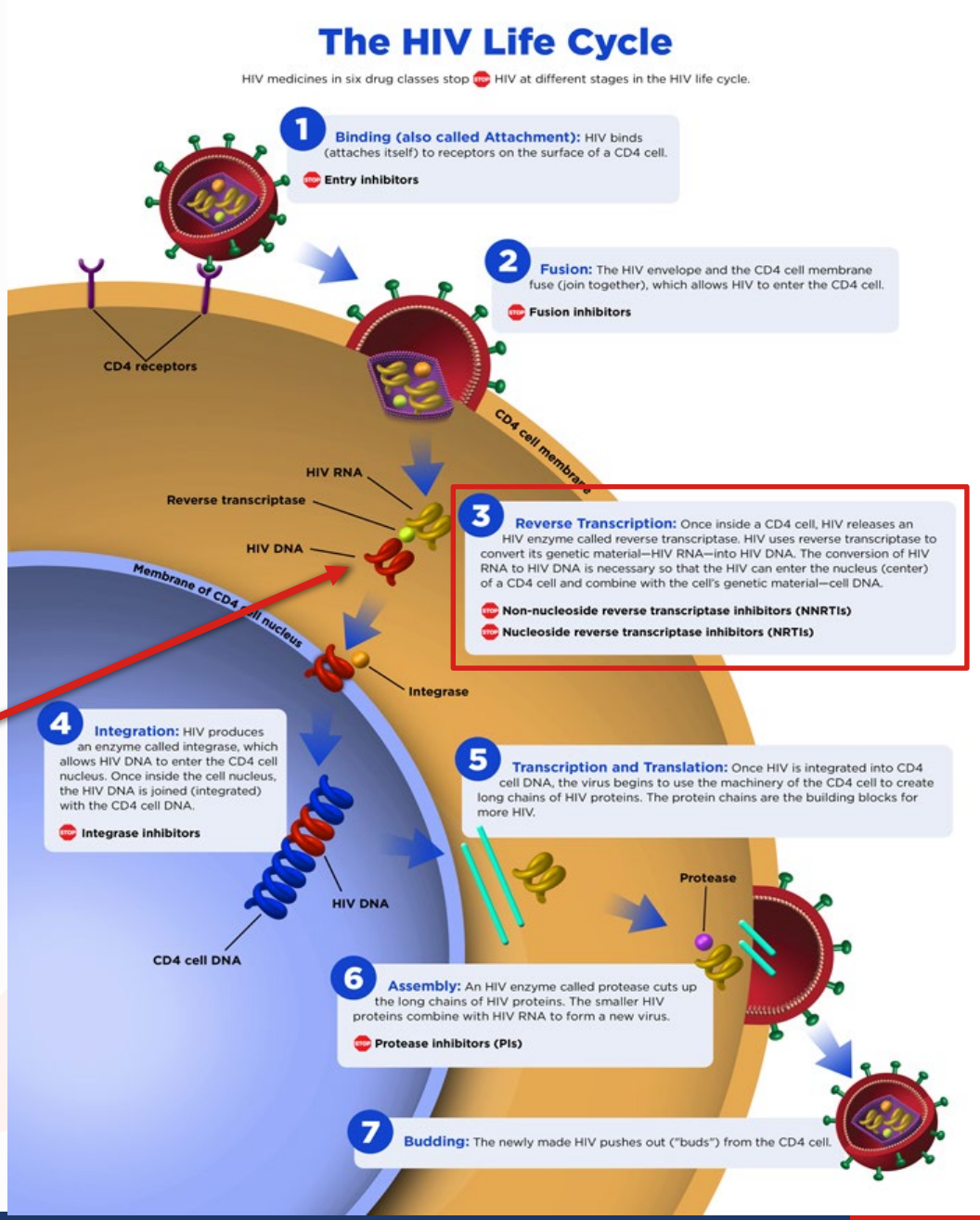
Critical Issues in PEP Treatment

- Timing is key
  - Efficacy decreases continuously after initial exposure
  - Beyond 72 hours, PEP generally no longer recommended
- Treatment duration is 4 weeks
- If source patient has known HIV resistance:
  - Optimize regimen to treat the resistant virus

NRTIs

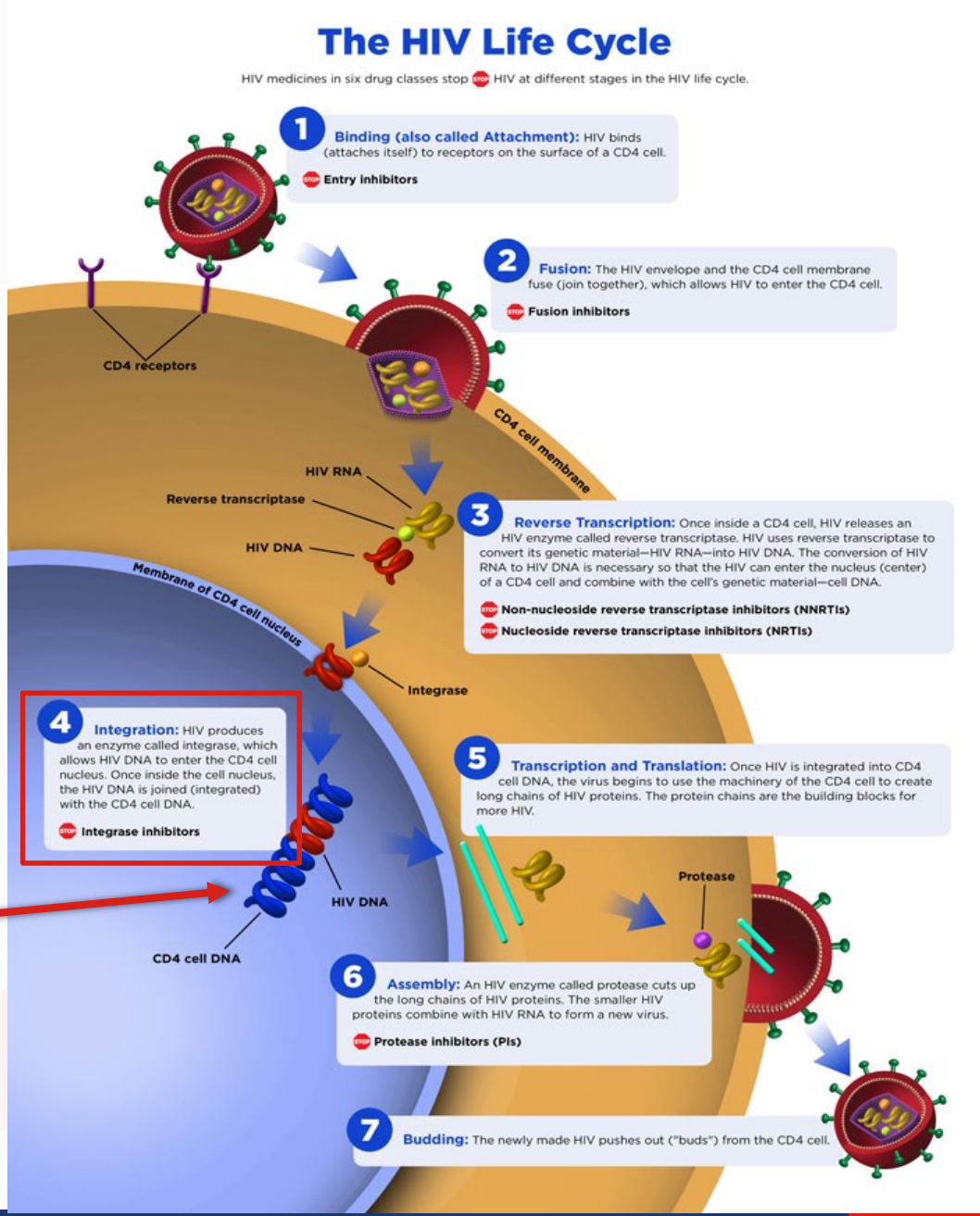
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

Indirectly inhibits enzyme required to copy viral RNA to DNA.



INSTIs
Integrase Inhibitors

Inhibits strand transfer of viral DNA to host cell DNA by the integrase enzyme.



Side Effects of INSTI-Based PEP

- Increased incidence of headaches
- Sleep disturbance
  - Insomnia more prevalent in drug studies

Isentress (RAL)

Advantages

- Well-tolerated
- Data for use in pregnancy
- Very low risk of drug interactions

Disadvantages

- Twice-daily dosing
- Lower barrier to HIV resistance

Tivicay (DTG)

Advantages

- Well-tolerated
- Once-daily dosing
- Very high barrier to HIV resistance

Disadvantages

- Neural tube defects?

Dolutegravir and Neural Tube Defects?

- Recent study from Botswana suggested this connection
  - Has not been observed in studies or through US pregnancy registry
- Incidence of NTDs comparatively higher in Botswana
- More recent data from this study did not find a statistically significant increase in neural tube defects

Drug Interactions of INSTI-Based PEP

- RAL and DTG can chelate polyvalent cations and lose efficacy
  - Give 2 hours before or 6 hours after Ca/Mg/Fe/Al/Zn supplements
- Not recommended with select anticonvulsants
  - Phenytoin, phenobarbital, carbamazepine diminish INSTI levels
- DTG can increase metformin levels
  - Monitor closely
  - Consider metformin 1,000 mg/day max during duration

Alternative PEP Regimens

- For renal dysfunction/kidney disease (CrCl ≤ 60 mL/min):
  - Dose-adjusted lamivudine and zidovudine 300 mg twice daily
    - Combivir includes both lamivudine and zidovudine at full dose
  - Preferred 3rd agent (raltegravir, dolutegravir)

- For alternative to raltegravir or dolutegravir:
  - Darunavir 800 mg daily + ritonavir 100 mg daily
    - If pregnant, darunavir 600 mg + ritonavir 100 mg both twice daily

- Consult with specialist for further regimens
  - Particularly if source patient has known resistance

Zidovudine

Advantages

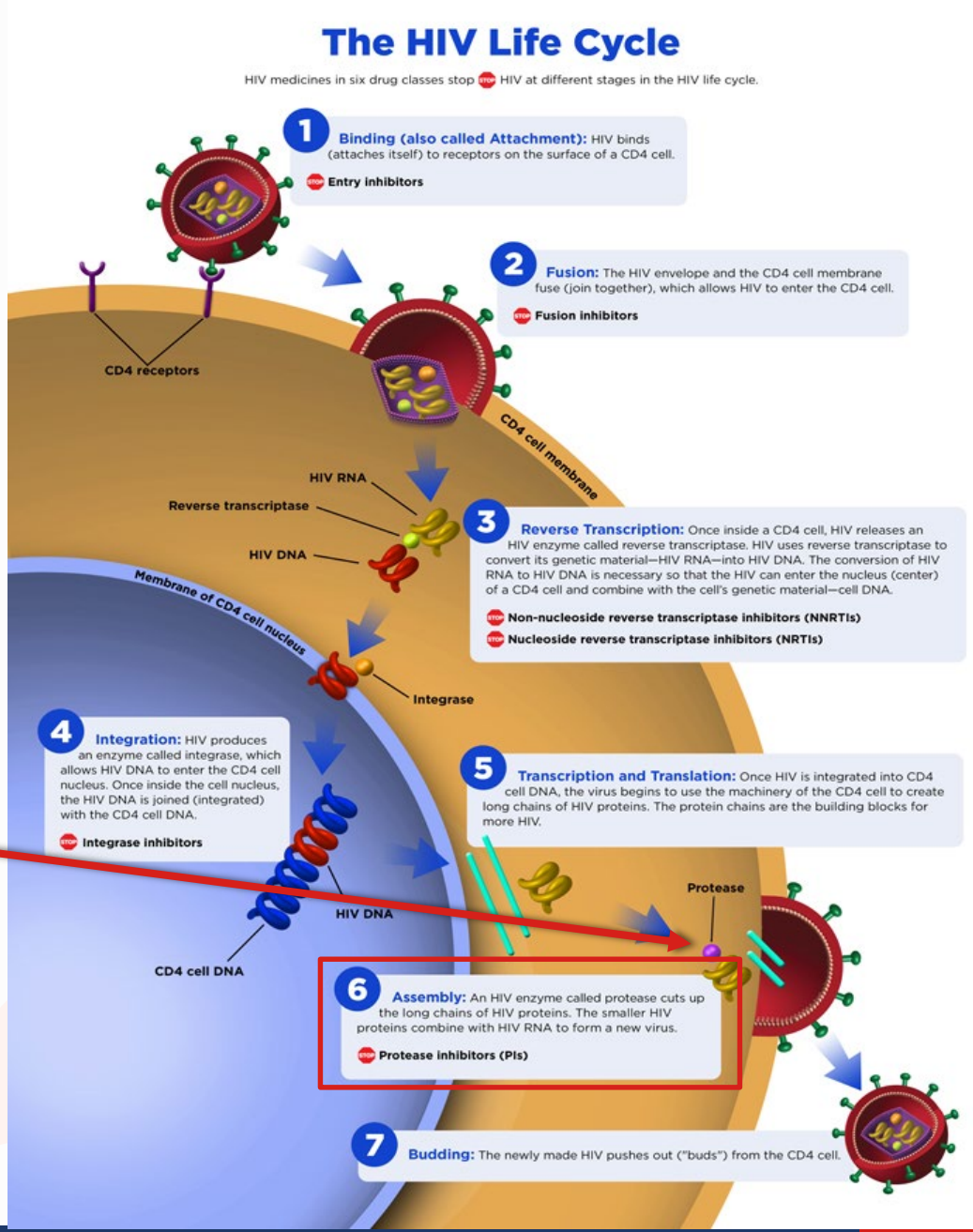
- Well-studied against HIV

Disadvantages

- Twice-daily dosing
- Numerous adverse effects
- Tolerability concerns

PIs
Protease Inhibitors

Inhibits protease, the enzyme that cuts HIV protein into smaller strands used to assemble a new virus.



Prezista (darunavir) + Norvir (ritonavir)

Advantages

- Very high barrier to HIV resistance
- Better tolerated than other PIs

Disadvantages

- At least two pills once daily
- Numerous drug interactions
- Metabolic/liver/lipid effects

Occupational PEP Testing

- Baseline:
  - HIV screening
  - Renal and hepatic function tests
  - Complete blood count (CBC)
- Repeat renal/hepatic testing and CBC 2 weeks post-exposure
- Repeat HIV testing at 6 weeks, 12 weeks, and 6 months
  - If 4th gen testing used, can retest at 6 weeks and 4 months

HBV/HCV Retesting

- Warranted at 4-6 months if source patient known or suspected to have either HBV or HCV
- Only retest HBV if susceptible at baseline
  - Include HBsAb, HBcAb, HBsAg to fully assess status
- HCV/HIV coinfection may delay HIV antibody response
  - If concerned, recheck both at 4-6 months

Non-Occupational PEP Testing

Table 2. Recommended schedule of laboratory evaluations of source and exposed persons for providing nPEP with preferred regimens

Test	Source	Exposed persons			
	Baseline	Baseline	4–6 weeks after exposure	3 months after exposure	6 months after exposure
		For all persons considered for or prescribed nPEP for any exposure			
HIV Ag/Ab testing[a] (or antibody testing if Ag/Ab test unavailable)	✓	✓	✓	✓	✓[b]
Hepatitis B serology, including: hepatitis B surface antigen hepatitis B surface antibody hepatitis B core antibody	✓	✓	—	—	✓[c]
Hepatitis C antibody test	✓	✓	—	—	✓[d]
		For all persons considered for or prescribed nPEP for sexual exposure			
Syphilis serology[e]	✓	✓	✓	—	✓
Gonorrhea[f]	✓	✓	✓[g]	—	—
Chlamydia[f]	✓	✓	✓[g]	—	—
Pregnancy[h]	—	✓	✓	—	—
		For persons prescribed tenofovir DF+ emtricitabine + raltegravir or tenofovir DF+ emtricitabine + dolutegravir			
Serum creatinine (for calculating estimated creatinine clearance[i])		✓	✓	—	—
Alanine transaminase, aspartate aminotranferase		✓	✓	—	—
	For all persons with HIV infection confirmed at any visit				
HIV viral load	✓	✓[j]			
HIV genotypic resistance	✓	✓[j]			

Source: https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf

nPEP Testing Footnotes

Abbreviations: Ag/Ab, antigen/antibody combination test; HIV, human immunodeficiency virus; nPEP, nonoccupational postexposure prophylaxis; tenofovir DF, tenofovir disoproxil fumarate.

[a] Any positive or indeterminate HIV antibody test should undergo confirmatory testing of HIV infection status.

[b] Only if hepatitis C infection was acquired during the original exposure; delayed HIV seroconversion has been seen in persons who simultaneously acquire HIV and hepatitis C infection.

[c] If exposed person susceptible to hepatitis B at baseline.

[d] If exposed person susceptible to hepatitis C at baseline.

[e] If determined to be infected with syphilis and treated, should undergo serologic syphilis testing 6 months after treatment

[f] Testing for chlamydia and gonorrhea should be performed using nucleic acid amplification tests. For patients diagnosed with a chlamydia or gonorrhea infection, retesting 3 months after treatment is recommended.

- For men reporting insertive vaginal, anal, or oral sex, a urine specimen should be tested for chlamydia and gonorrhea.
- For women reporting receptive vaginal sex, a vaginal (preferred) or endocervical swab or urine specimen should be tested for chlamydia and gonorrhea.
- For men and women reporting receptive anal sex, a rectal swab specimen should be tested for chlamydia and gonorrhea.
- For men and women reporting receptive oral sex, an oropharyngeal swab should be tested for gonorrhea. (http://www.cdc.gov/std/tg2015/tg-2015-print.pdf)

[g] If not provided presumptive treatment at baseline, or if symptomatic at follow-up visit.

[h] If woman of reproductive age, not using effective contraception, and with vaginal exposure to semen.

[i] eCrCl = estimated creatinine clearance calculated by the Cockcroft-Gault formula; eCrClCG = [(140 − age) x ideal body weight] ÷ (serum creatinine x 72) (x 0.85 for females).

[j] At first visit where determined to have HIV infection.

Source:
https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf

Counseling at time of exposure and follow-up appointments

- Use condoms
- Avoid blood or tissue donations
- Avoid pregnancy & breastfeeding (if possible)
- Possible drug side effects
- Possible drug interactions
- Importance of adherence to PEP regimen
- Consider re-evaluation of exposed health care professional (HCP) 72 hours post-exposure, especially after additional information about the exposure or SP becomes available.

PEP in Pregnancy

- Considerations similar to those of non-pregnant exposed persons.
  - The pregnant exposed person *and* her fetus are at risk for HIV acquisition.
  - Most PEP regimens, benefits outweigh the risk of infant (and maternal) exposure to ARVs.
  - Based on limited data, use of ARVs in pregnancy does not appear to increase the risk of birth defects compared to the general population.
  - Toxicities from currently recommended PEP medications are not thought to be significantly increased in pregnancy.

PEP and Lactation

- Breastfeeding is not a contraindication for PEP.
- The decision to take PEP and/or continue breastfeeding is complex and individualized, and expert consultation is recommended
- Considerations:
  - Acute HIV in a breastfeeding mother greatly increases the risk of HIV transmission to her infant.
  - Pump and discard
  - Pumping and storing while waiting on SP's HIV test results
  - Limited data on PEP medications in breastmilk

Conclusion

- PEP a valuable resource that may be underutilized
  - Well-tolerated agents available for use
  - Efficiency in prescribing and taking PEP critical to success

Cheat Sheet Part 1

- Preferred regimens:
  - Truvada 200/300 mg daily + Tivicay 50 mg daily

  Or
  - Truvada 200/300 mg daily + Isentress 400 mg BID

- CrCl < 60 mL/min regimens:
  - Combivir 150/300 mg BID + an above INSTI
    - May administer zidovudine and dose-adjusted lamivudine separately in place of Combivir
    - Full-dose lamivudine safe down to as low as CrCl ≥ 30 mL/min

Cheat Sheet Part 2

- If pregnant:
  - Truvada 200/300 mg daily + Isentress 400 mg BID
  - Truvada 200/300 mg daily + Tivicay 50 mg daily
- If INSTI-intolerant:
  - Truvada 200/300 mg daily + Prezista 800 mg daily + Norvir 100 mg daily
- If INSTI-intolerant and pregnant:
  - Truvada 200/300 mg daily + Prezista 600 mg BID + Norvir 100 mg BID

PEP: Special Cases

- Known or suspected resistance of the source virus to antiretroviral agents
- Delayed exposure report (after 72 hours)
- Exposed person has serious illness (eg, renal disease)

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PEP: Post-Exposure Prophylaxis

Timely answers for urgent exposure management

Get rapid, expert guidance in managing healthcare worker exposures to HIV and hepatitis B and C, including recommendations on when and how to initiate PEP through our online Quick Guide for urgent occupational PEP decision-making, or from experienced clinicians on our telephone consultation service. Note that our hours have changed because of funding limitations. ***We cannot accept calls from unknown numbers. Please unblock your phone prior to calling the PEPline.***

Hours of operation for occupational PEP consultation are **11 a.m. – 8 p.m. ET (seven days a week)**. If you are trying to reach us regarding an occupational PEP question outside of these hours, please check out our PEP Quick Guide for Occupational Exposures.
Hours of operation for non-occupational PEP consultation are **9 a.m. – 8 p.m. ET Monday – Friday**, and **11 a.m. – 8 p.m. ET on weekends & holidays**.
(888) 448-4911

CALL

See our PEP Quick Guide for answers to the most frequently asked questions.

nccc.ucsf.edu

PEP PATIENT NAVIGATION IN THE ERA OF COVID-19

PEP Navigation Process Overview

Evaluating Provider

Initiate PEP within 72 hours.

Conduct baseline testing.

Ensure patient can access at least 3 days of medication.

PEP Clinic

Ensure patient accesses remainder of medication.

Follow-up within 1 week.

Follow-up at 4-6 weeks.

Ensure patient can access at least 3 days of medication while setting up remainder

- Preplanned billing options in case of insurance issues
- Trusted pharmacies that have training on PEP
- Complete PAs, if needed, enroll in manufacturers' assistance

Copay Assistance/Free Medications Available!

https://www.gileadadvancingaccess.com/

https://www.viivconnect.com/patient-assistance-program/

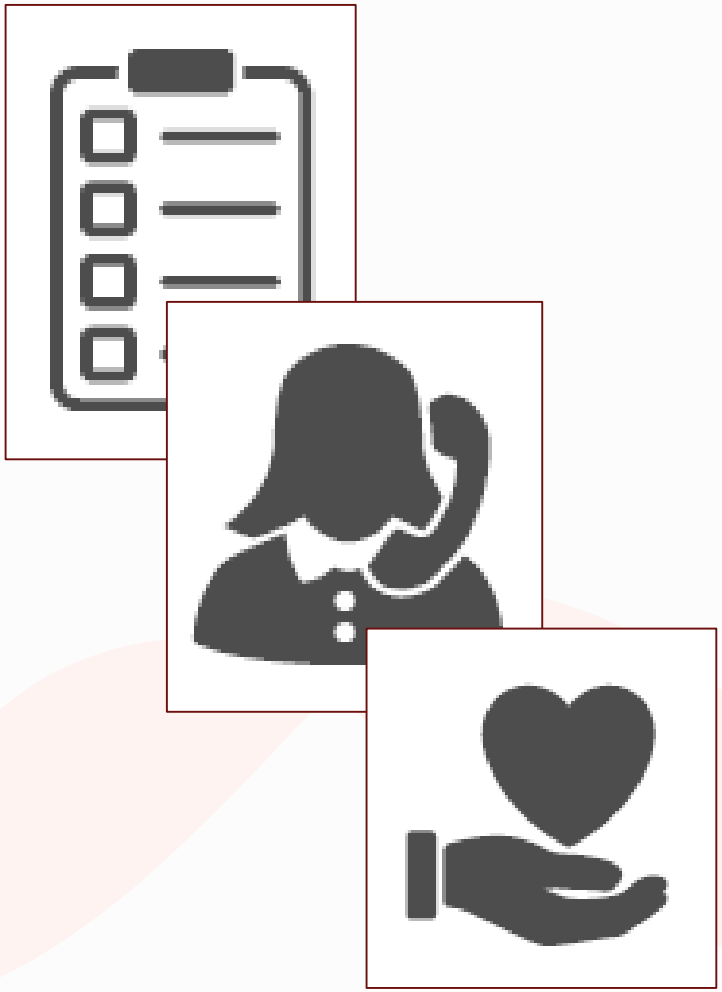
https://www.isentress.com/#

https://www.patientadvocate.org/

https://www.panfoundation.org/

Intake via Telemedicine

- Have a pre-planned process for collecting important information and communicating it with provider
- Have an assigned person that the patient/pharmacy can reach **when** problems arise
- Important messages should be repeated often due to trauma associated with PEP

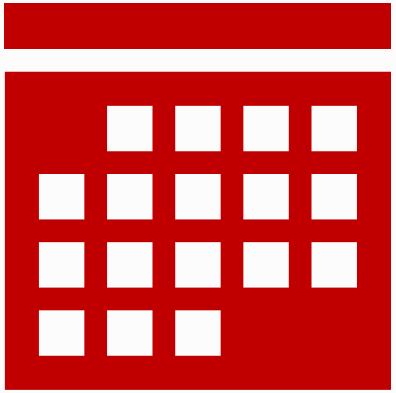


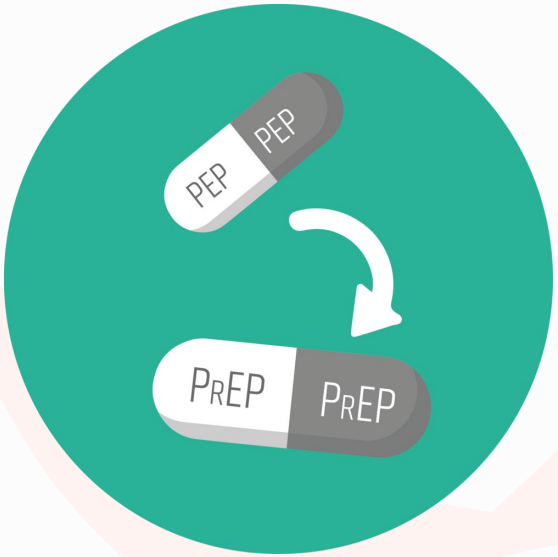
Follow-up within 1 week

- Providers who understand the urgency and are willing to double book
- Multiple options for patients, video visit, phone visit, in-person
- Complete any missing baseline labs
- Ensure patients have access to full 28 days of medication

Follow-up

- Follow-up at 4-6 weeks
- Complete follow-up labs





- Transition to PrEP if patient desires
- Labs completed on day 25, PrEP started immediately on day 29

Additional Considerations in the Era of COVID-19

- Emergency rooms are overwhelmed
  - Preferable to directly see patients same day
- Schedule lab visits later in the day to avoid crowds
- Have mental health linkages to care on hand
- Work with pharmacies able to deliver medication

Virtual Visits

Patient Access:

- Telephone needed for phone consults
- Smartphone or computer with working camera needed for video consults

Telemedicine Coordination:

- Confirm patient's appointment type
- Coordinate necessary lab work and access to virtual consults
- Make sure patient has a clear understanding of follow-up plan, provide in writing if possible
- Make sure patient has access to all necessary testing, including STI swabs

Telemedicine Best Practices

Tips for Coordinators:

-Have a back-up plan if technology fails

-Determine what information is necessary

-Call patient ahead of time to practice using telehealth systems

Tips for Providers:

-Determine what information is necessary

-Many additional services can be provided without requiring a face-to-face visit including vaccinations, STI treatments, emergency contraception

Conclusion

- The practice of PEP is straightforward
  - Supporting PEP management, however, can take considerable work
- Telemedicine a perfect avenue to deliver PEP care
- Research still ongoing in simplifying PEP management

THANK YOU