Patient Evaluation Before Initiating HIV PrEP

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Disclosures

Jorge Mera has no actual or potential conflict of interest in relation to this program/presentation.

Outline

Case Presentation: Mr. P

Clinical/Laboratory evaluation

- Rationale for labs
- Interpretation of HIV and HBV serology
- Screening for STIs
- Kidney function evaluation prior to PrEP delivery
- Osteoporosis evaluation Prior to Starting PrEP

Treatment considerations

Counseling the Patient

Mr. P

HPI: Mr. P is a 32-year-old MSM who is requesting PrEP. He mentions he heard about PrEP from a friend and thinks he may be a candidate. He is feeling well, experienced a gonococcal urethritis 5 months ago that was treated and has been asymptomatic since then.

Sexual History: He does not have a stable sexual partner, uses condoms 50% of the time and engages in receptive anal intercourse. Has had 5 different sexual partners in the last 6 months of which 4 have reported to him that their HIV status is negative and 1 is unknown. He does not use drugs during sex. His last condom less receptive anal sexual encounter was 8 days ago. The HIV status of his partner in the last encounter is unknown.

PMH: Gonococcal urethritis treated 5 months ago. Otherwise, unremarkable

PE: Vital signs are normal, weight 70 kg, height 175 cm, BMI 23, otherwise normal.

Mr. P: Labs

HCV antibody

- Negative

HIV1/2 Antigen/Antibody Immunoassay

- Negative

GC/Chlamydia in urine, oropharynx and rectum

- Negative

HBsAg, HBsAb, HBcAb

- **HBsAg and HBcAb reactive. HBsAb not detectable**

HBV viral load

- 40,000 international units/mL

Complete Blood Count:

- Normal

Comprehensive Metabolic Panel

- MP: **ALT 72 IU/L, AST 45 IU**/, creatinine 0.9 mg/dL, GFR 116 ml/min, albumin 4.5 g/dL, total bilirubin 0.7 mg/dL, INR 1.0.

Which of the following statements are true for Mr. P?

a) Meets criteria for PrEP but needs counseling for Hep B

b) Will need an HIV RNA after day 10 of last sexual exposure or a repeat 4th generation HIV Assay within 3 weeks

c) Will need Hep B treatment before he can start PrEP

d) A and B are true

e) B and C are true

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Lab Workup Before Prescribing HIV PrEP

HIV:

- HIV1/2 Antigen/Antibody Immunoassay (4^{th} generation assay)
- ***HIV-1/HIV2 antibody differentiation immune assay***
- ***Nucleic Acid Test (NAT)***

HBV serologies:

- HBsAb: Surface antibody
- HBsAg: Surface antigen
- HBcAb: Total core antibody

HCV antibody

- If previously treated substitute for HCV RNA

Renal function

- Creatinine/GFR, Microalbumin/creatinine ratio

STI screening

- RPR
- **GC/*Chlamydia* (**Oral, anal and urine/vaginal)

Pregnancy screening

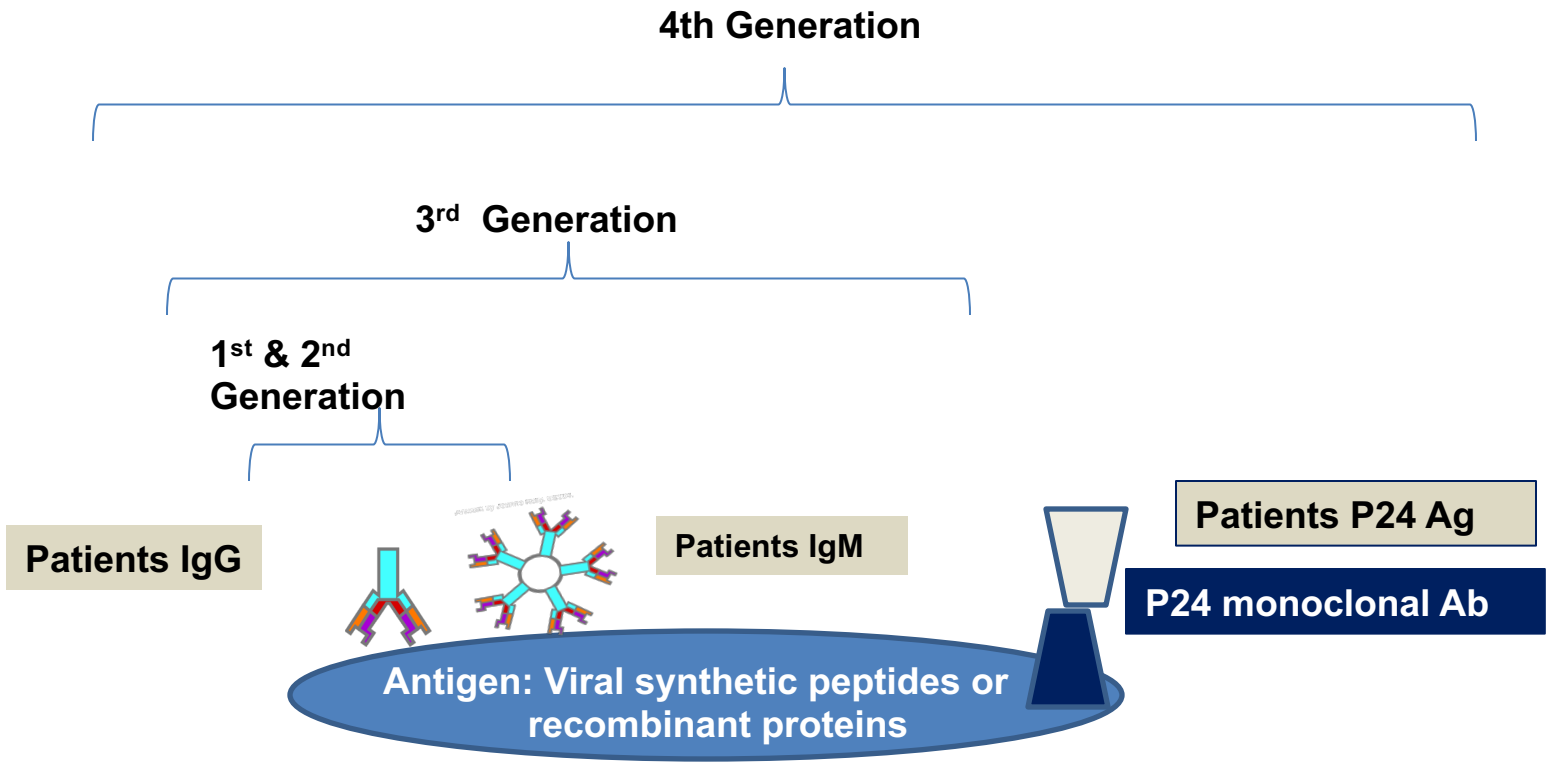
"4^{th} Generation Assays should be used for screening"

"Patients with Chronic HB need to be counseled for the risk of reactivation if PrEP is discontinued"

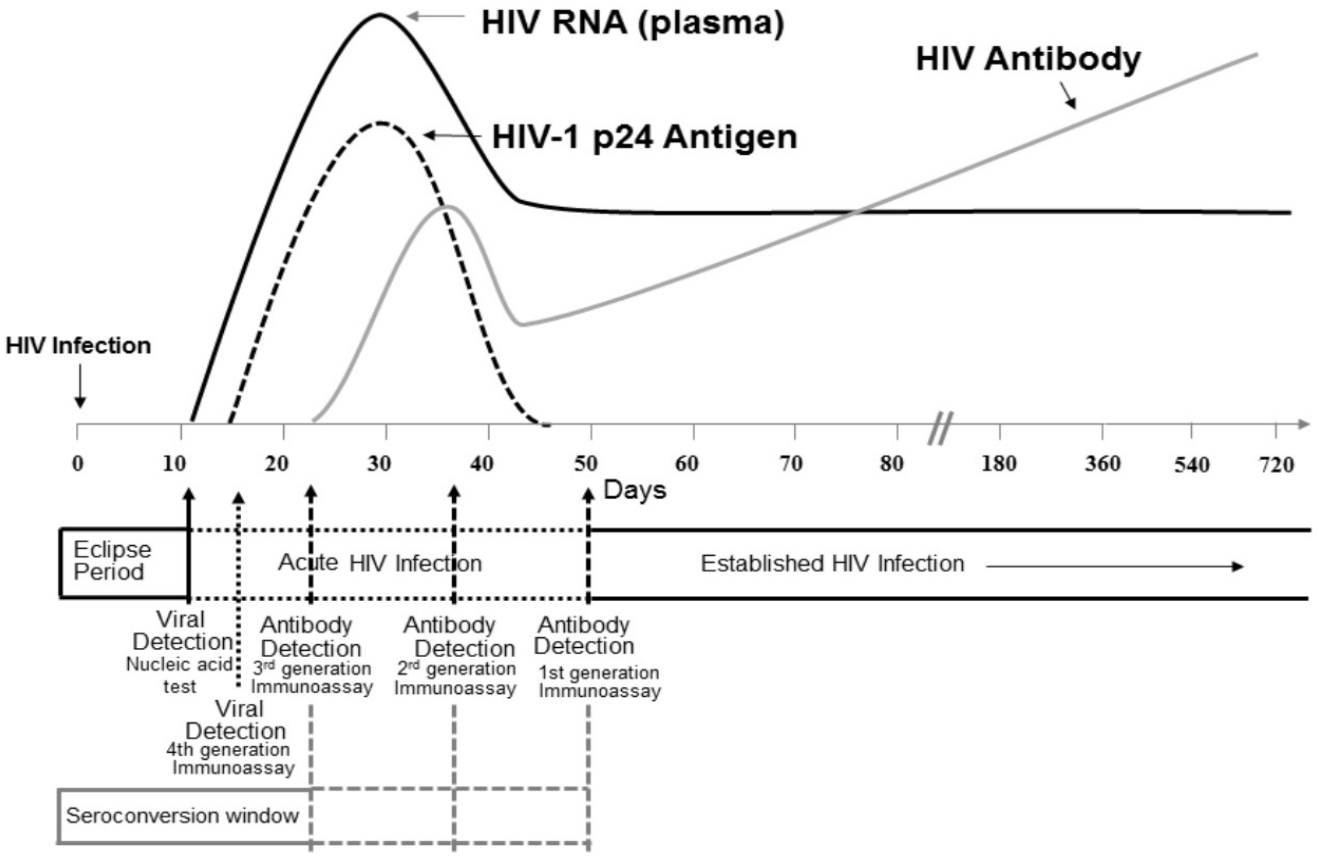
"STI self-reported risk is not always reliable"

"Pregnancy is not a contraindication for PrEP"

HIV Diagnostic Tests
ELISA



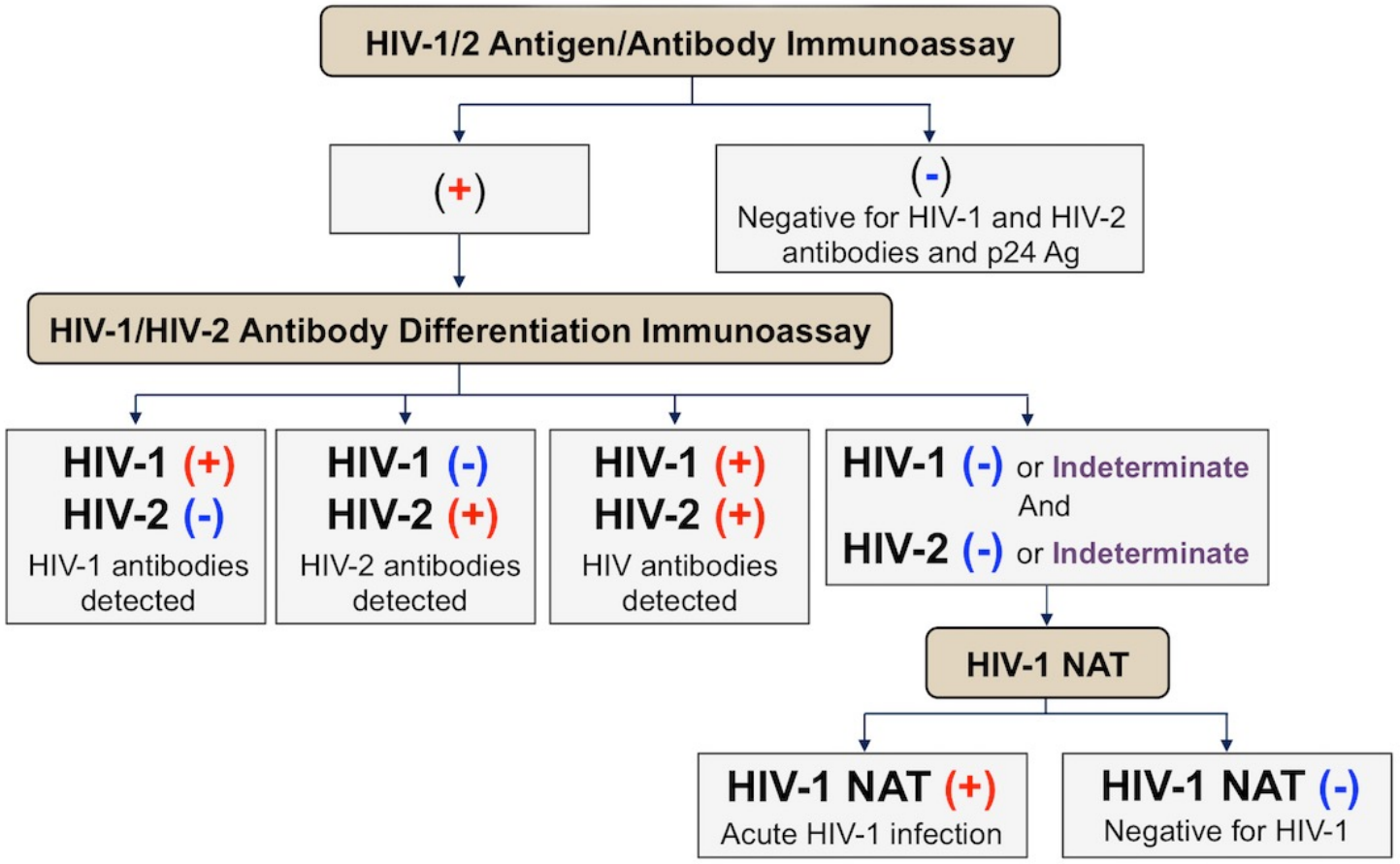
Sequence of Appearance of Laboratory Markers for HIV- Infection



Time to positivity		
3rd Generation	IgG and IgM Antibody	20-30 days
4th Generation	IgG and IgM Antibody & P24 Ag	15-20 days
HIV RNA	RNA	10-15 days
Ultrasensitive HIV RNA	RNA	5 days

Laboratory testing for the diagnosis of HIV infection : updated recommendations
June 27, 2014 http://dx.doi.org/10.15620/cdc.23447

CDC and APHL Recommended Laboratory Testing for the Diagnosis of HIV Infection



David H Spach, MD. HIV Diagnostic Testing. National HIV Curriculum, University of Washington
Laboratory testing for the diagnosis of HIV infection : updated recommendations
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HIV Testing Summary

The preferred HIV screening test is a fourth-generation antigen/antibody assay.

- A third-generation assay is acceptable if an antigen-antibody test is not available, and the clinical history suggests that acute HIV infection is unlikely.
- Rapid tests that use oral fluid should not be used
  - 12% false negatives rates in acute HIV

HIV RNA should be performed prior to initiating PrEP in the following groups of patients

- Patients with signs or symptoms suggestive of acute HIV infection within the previous four weeks.
- Patients with an indeterminate antigen/antibody test.
- Patients who report a high-risk exposure within four weeks of starting PrEP, regardless of symptoms.

You may start “Rapid PrEP” but will need to repeat HIV testing within 4 weeks

- Depending on initial test used and clinical history

Symptoms of Acute HIV

Table 8: Clinical Signs and Symptoms of Acute (Primary) HIV Infection[75]

Features	Overall (n = 375) %	Sex		Route of transmission	
		Male (n = 355) %	Female (n = 23) %	Sexual (n = 324) %	Injection Drug Use (n = 34) %
Fever	75	74	83	77	50
Fatigue	68	67	78	71	50
Myalgia	49	50	26	52	29
Skin rash	48	48	48	51	21
Headache	45	45	44	47	30
Pharyngitis	40	40	48	43	18
Cervical adenopathy	39	39	39	41	27
Arthralgia	30	30	26	28	26
Night sweats	28	28	22	30	27
Diarrhea	27	27	21	28	23

These Symptoms Should be Absent 30 days prior to starting PrEP!!!

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

Same-Day HIV Pre-Exposure Prophylaxis (PrEP) Initiation During Drop-in Sexually Transmitted Diseases Clinic Appointments Is a Highly Acceptable, Feasible, and Safe Model that Engages Individuals at Risk for HIV into PrEP Care

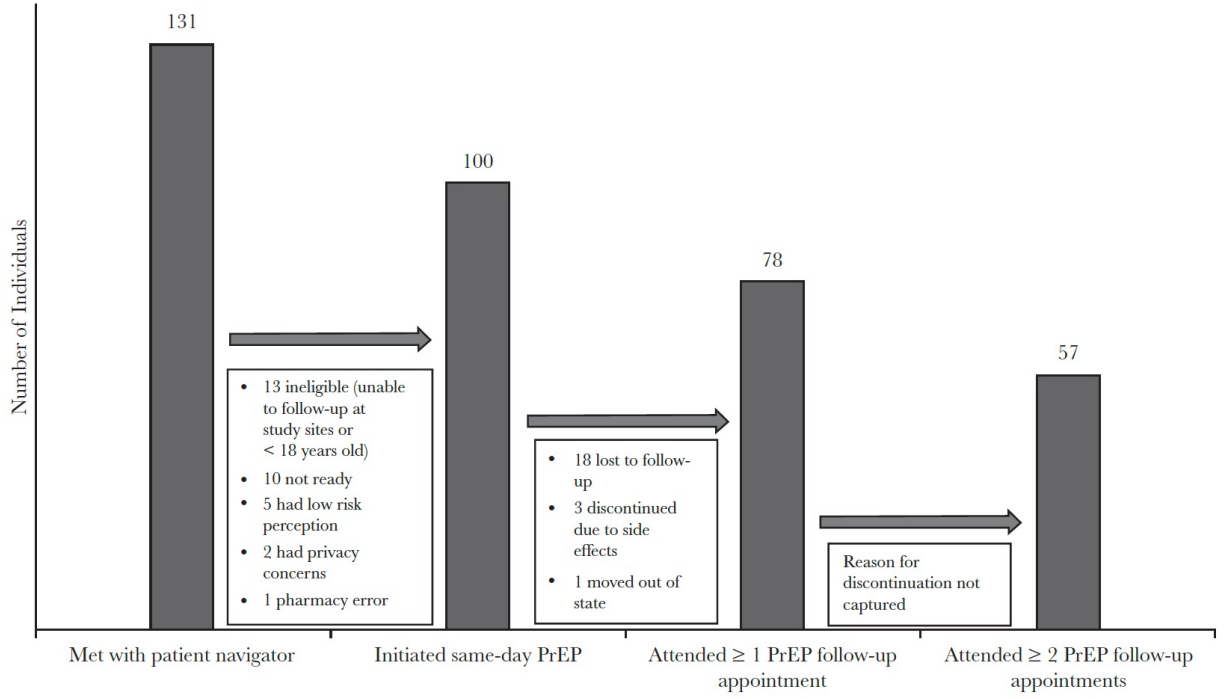
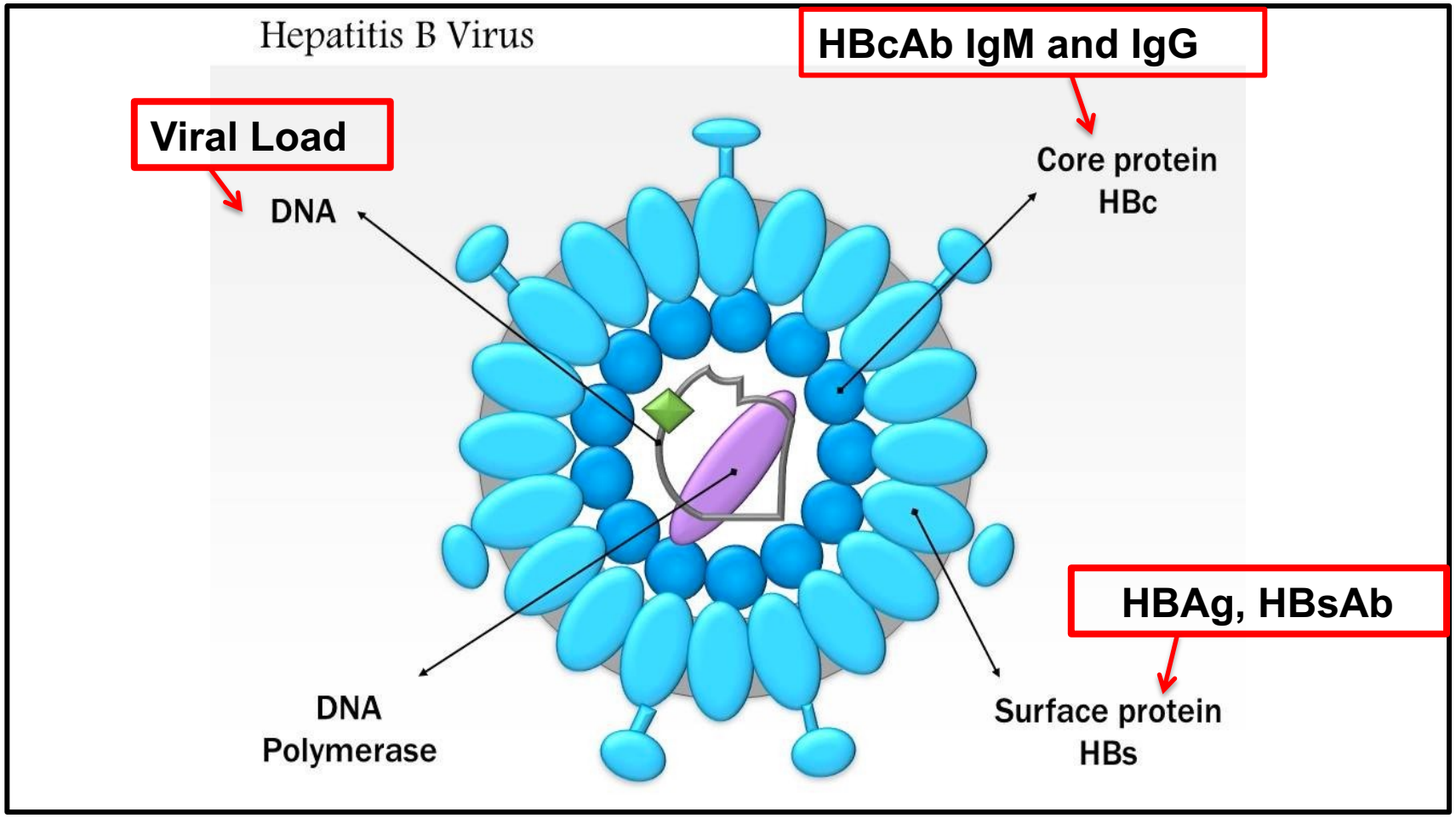


Figure 1. Follow-Up PrEP Care Cascade After Same-Day Initiation

Hepatitis B Viral Structure



HBV Diagnostic Markers

Serologic Marker Results

HBsAg	Total Anti-HBc	IgM Anti-HBc	Anti-HBs	Interpretation
-	-	-	-	Never infected and no evidence of immunization
+	+	+	-	Acute infection
+	+	-	-	Chronic infection
-	+	-	-/+	"Recovered" from past infection and not immune, low level carrier
-	-	-	+	Immune (immunization)

HBeAg- High infectivity

HBeAb- Low infectivity

Weinbaum CM, et al. *MMWR Recomm Rep.* 2008;57(RR-8):1-20.

Isolated HBc

- What do you do?
  - HBV DNA (Viral Load)
  - HBeAb and HBeAg
  - If all are negative, may consider vaccination

Window period of acute hepatitis B

Anti-HBs has fallen to undetectable levels many years after recovery from acute hepatitis B

HBsAg titer has fallen below the cutoff level for detection in those with chronic hepatitis B

- Approximately 0.5 percent per year

HBsAg mutations (false negative)

False-positive test result.

- An individual at low risk for disease

Screen for STIs

If not already done in prior 3-6 months:

- ❑ RPR for syphilis
- ❑ Gonorrhea and chlamydia
  - NAA testing preferred
  - **Extragenital sites too!**

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

Renal Function Evaluation

Serum creatinine will determine the candidacy and selection of an agent for PrEP.

- Individuals with a eGFR <30 ml/min/1.73 m^2 are not candidates for PrEP with either TDF-FTC or TAF-FTC
- Individuals with an eGFR <60 mL/min/1.73 m^2 are not candidates for PrEP with TDF-FTC.

For patients with an eGFR >60 mL/min/1.73 m^2, but with risk factors for renal disease (eg, diabetes, hypertension, older age [eg, >40 years], nephrotoxic medications)

- Obtaining baseline proteinuria and glycosuria is prudent (Not recommended by Guideline Panels)

In general, the risk of kidney injury with PrEP is low in patients without HIV taking TDF-FTC.

- In a meta-analysis the odds ratio of i creatinine elevations in patients who received TDF-based PrEP compared with placebo was 1.36 and only 6% of these patients had creatinine elevations that were greater than 1.3 times the upper limit of normal

Certain risk factors have been associated with declines in renal function:

- Baseline eGFR <90 mL/min/1.73 m^2
- Age greater than 40

Renal effects appear to be even less frequent with TAF-FTC than TDF-FTC.

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Osteoporosis Screening

Importance of osteoporosis history, risk factors or presence of osteopenia

- It informs our regimen selection for PrEP
- If only TDF-FTC is available discuss with patient risk of osteoporosis vs HIV

Bone loss appears to be greatest during the first six months, and then stabilizes

The need for routine bone density screening prior to initiating PrEP is unclear

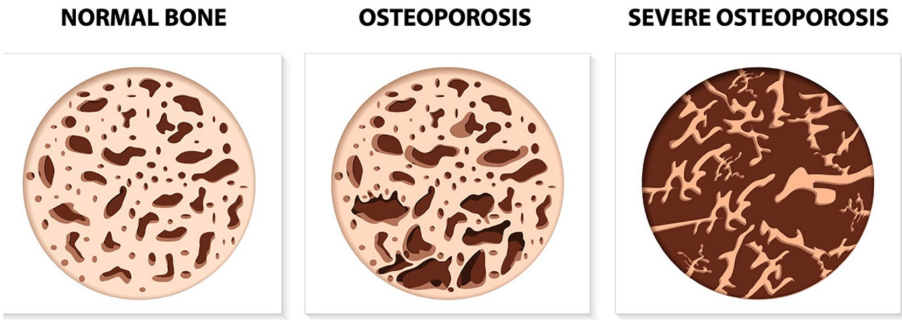
Consider obtaining a baseline DXA scan in:

- Patients who have a history of osteoporosis
- Those who are at high risk for osteoporosis

Patients on TDF-FTC may have decrease in bone mass

- But no differences in the rate of fractures have been reported
- The bone loss seen with TDF may be of more concern in adolescent MSM

There are no proven strategies to attenuate bone loss in patients taking PrEP.



DXA: Dual energy X-ray Absorptiometry

Preferred PrEP Regimens

For the Majority of patients TDF-FTC rather than TAF-FTC.

- Due to greater experience
- TAF has been associated with mild but greater weight gain and slight changes in lipid parameters that are less favorable compared with TDF-FTC

When is TAF/FTC a consideration

- MSM and transgender women with bone and renal disease
- Adolescents
  - Pros of using it: They appear to be at higher risk for loss of bone mineral density
  - Cons of using it: Not well studied in this population

Women and Transgender Men

If risk is mainly through vaginal sex avoid TAF-FTC.

- The DISCOVER trial, which compared TAF-FTC and TDF-FTC for PrEP, only evaluated those who engaged primarily in anal-receptive sex

For patients with eGFR is <60 mL/min/1.73 m^2

- Consider deferring PrEP if other alternatives for prevention can be sustained.
- TAF-FTC is the only option if PrEP is used with the uncertainty of efficacy

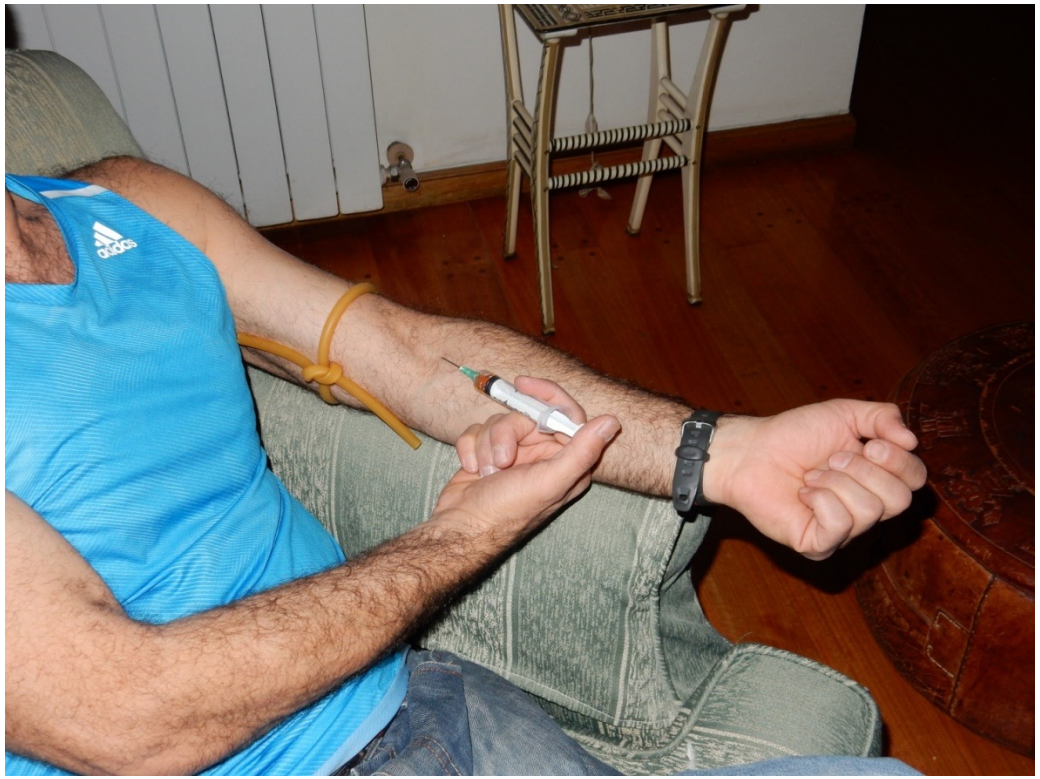
For those with eGFR ≥60 mL/min/1.73 m2 but have have risk factors for renal disease

- A trial with TDF-FTC and close monitoring is warranted

For those with or at risk of osteoporosis

- Weigh the the risk of HIV with the potential risk of exacerbating bone disease with the uncertainty of TAF vs TDF

Persons who inject drugs



Always maximize other harm reduction strategies

- Use of sterile needles/syringes and non sharing paraphernalia practices

TDF-FTC is the best option if feasible

TAF-FTC not studied when IDU is the only HIV risk factor, but it is an option for those patients with renal disease and osteoporosis:

- TAF achieves higher peripheral blood mononuclear cell concentrations than TDF

Counseling the Patient

Establish ground rules	Quarterly visit No HIV test: NO PRESCRIPTION!!!! First follow-up could be in 1 month
Discuss common side effects	Flatulence, nausea, GI upset, headache Usually resolve in 30 days
Discuss potential risks	Bone demineralization Nephrotoxicity
Discuss Adherence Strategies	

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