Hepatitis B Reactivation and Hemodialysis-Related Transmission

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Hepatitis B Virus (HBV)

- **Acute HBV**
  - 2,890 reported cases in U.S. (2011)
  - 74 reported cases in NC (2013)
  - Many asymptomatic or never reported
  - Incidence highest among adults, especially males 25–44 years
- **Chronic HBV**
  - ~800,000–1.4 million people in U.S.
  - ~25,000-43,000 people in NC

http://www.cdc.gov/hepatitis/HBV/HBVfaq.htm

Acute HBV: Surveillance Case Definition

- **Clinical: Acute illness with discrete onset of sign or symptom* consistent with acute viral hepatitis, and either**
  - Jaundice, or
  - ALT >100 IU/L
- **Laboratory:**
  - Hepatitis B surface antigen (HBsAg) positive, and
  - Immunoglobulin M (IgM) antibody to hepatitis B core antigen (IgM anti-HBc) positive (if done)

*A documented negative HBsAg result within 6 months prior to a positive test for HBsAg, hepatitis B "e" antigen (HBeAg), or HBV DNA does not require acute clinical presentation to meet surveillance case definition

http://wwwn.cdc.gov/NNDSS/script/casedef.aspx?CondYrID=711&DatePub=1/1/2012%2012:00:00%20AM

Chronic HBV:
Surveillance Case Definition

- **Clinical: No symptoms required**
- **Laboratory:**
  - IgM anti-HBc negative AND a positive result on one of the following tests:
    - HBsAg, or
    - Hepatitis B e antigen (HBeAg), or
    - Nucleic acid test for HBV DNA

  OR

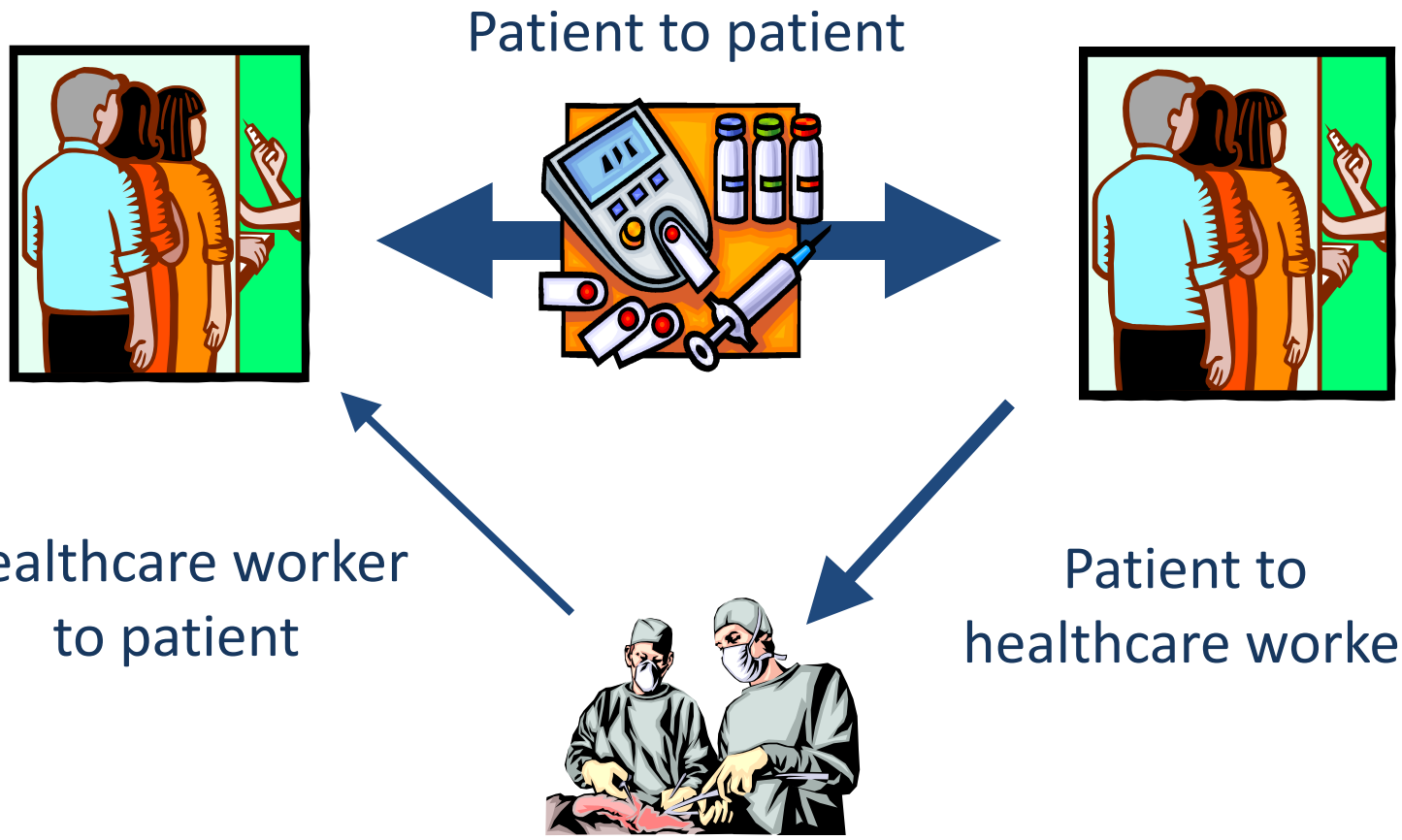
  - HBsAg positive or nucleic acid test for HBV DNA positive or HBeAg positive 2 times at least 6 months apart

http://wwwn.cdc.gov/NNDSS/script/casedef.aspx?CondYrID=715&DatePub=1/1/2012%2012:00:00%20AM

Healthcare-Associated Transmission of Viral Hepatitis

- **Common exposures**
  - Unsafe injection practices
    - Syringe reuse
    - Misuse of single-dose/single-use vials
    - Failure to use aseptic technique
  - Unsafe diabetes care
  - Other lapses in infection control
- **35 healthcare-associated hepatitis outbreaks reported to CDC (2008–2012)**
  - 33 (94%) in non-hospital settings
    - Assisted living and skilled nursing facilities
    - Dental clinic
    - Outpatient clinics
    - Hemodialysis (HD) facilities

Routes of Viral Hepatitis Transmission in Healthcare Settings



Williams et al. Viral hepatitis transmission in ambulatory health care settings. CID 2004; 38:1592–8.

Viral Hepatitis in HD Setting

- **Repeated opportunities for transmission**
- **Can be transmitted despite no visible blood**
- **Hepatitis B and C viruses survive on surfaces**
  - HD chairs
  - HD machines

HBV in HD Setting

- **Present in high titers in blood**
- **Environmental contamination**
- **HBV-infected patients dialyze in isolation**
  - Separate room, machine, equipment, and supplies
  - Designated staff

Transmission of HBV in HD Setting

- Failure to isolate infected patients
- Sharing staff, equipment, and supplies
- Failure to vaccinate susceptible patients

Reported HBV Transmission Events in HD Setting, United States

Location	Time period	Likely mode(s) of transmission
Nebraska	March–June 1994	• Shared staff
Texas	April–May 1994	• Inadequate hand washing and glove changing • Adjacent clean and contaminated supply areas
California (1)	April–June 1994	• Multidose vials
California (2)	June–August 1994	• Undetermined
California (3)	June–August 1994	• Shared staff, equipment, and supplies
Pennsylvania	December 1995–May 1996	• Shared supplies • Multidose vials

CDC. Outbreaks of hepatitis B virus infection among hemodialysis patients—California, Nebraska, and Texas, 1994. MMWR 1996;45,14.
Hutin, et al. An outbreak of hospital-acquired HBV infection among patients receiving chronic hemodialysis. Infect Cont Hosp Ep 1999;20:731-735.
Lanini, et al. Patient to patient transmission of HBV: a systematic review of reports on outbreaks between 1992 and 2007. BMC Med 2009;7:15.

Guidelines for HBV Testing in HD Setting

- **On admission:**
  - HBsAg
  - Anti-HBc
  - Anti-HBs
- **HBV-susceptible (including nonresponders):**
  - HBsAg – Monthly
- **Anti-HBs positive (>10 mIU/mL) and anti-HBc negative:**
  - Anti-HBs – Annually
- **Anti-HBs positive and anti-HBc positive:**
  - No additional HBV testing

CDC. Recommendations for preventing transmission of infections among chronic hemodialysis patients. MMWR 2001;50,RR-5.

HBV Vaccine Schedule for HD Patients

TABLE 3. Doses and schedules of licensed hepatitis B vaccines for hemodialysis patients and staff members

Group	Recombivax HB™*			Engerix-B®†		
	Dose	Volume	Schedule	Dose	Volume	Schedule
Patients aged ≥20 years						
Predialysis§	10 µg	1.0 mL	0, 1, and 6 months	20 µg	1.0 mL	0, 1, and 6 months
Dialysis-dependent	40 µg	1.0 mL¶	0, 1, and 6 months	40 µg	2–1.0 mL doses at one site	0, 1, 2, and 6 months
Patients aged <20 years**	5 µg	0.5 mL	0, 1, and 6 months	10 µg	0.5 mL	0, 1, and 6 months
Staff members aged ≥20 years	10 µg	1.0 mL	0, 1, and 6 months	20 µg	1.0 mL	0, 1, and 6 months

* Merck & Company, Inc., West Point, Pennsylvania.
† SmithKline Beecham Biologicals, Philadelphia, Pennsylvania.
§ Immunogenicity might depend on degree of renal insufficiency.
¶ Special formulation.
** Doses for all persons aged <20 years approved by the U.S. Food and Drug Administration; for hemodialysis patients, higher doses might be more immunogenic.
Note: All doses should be administered in the deltoid by the intramuscular route.

CDC. Recommendations for preventing transmission of infections among chronic hemodialysis patients. MMWR 2001;50:RR-5.

Nonresponders to HBV Vaccination

- **Anti-HBs (≤10 mIU/mL)**
- **After 2 courses, additional doses not likely to induce antibody response**

CDC. Epidemiology and Prevention of Vaccine-Preventable Disease, 12th Edition. 2012.
CDC. Recommendations for preventing transmission of infections among chronic hemodialysis patients. MMWR 2001;50:RR-5.

Maintaining Protective Levels of anti-HBs

- **Booster doses when anti-HBs levels <10 mIU/mL**
- **No documented HBV infections among vaccinated HD patients with protective anti-HBs levels**
- **Outbreaks among unvaccinated and under-vaccinated HD patients can occur**

CDC. Recommendations for preventing transmission of infections among chronic hemodialysis patients. MMWR 2001;50:RR-5.

HBV Reactivation

- HBV persists in hepatocytes, even in patients with resolved infection
- Moderate immunosuppression may lead to renewed HBV replication in persons with inactive chronic infection
- Severe immunosuppression may lead to reactivation of HBV replication in persons with resolved infection

- HBV reactivation and subsequent transmission in U.S. HD setting not previously described

Immunosuppression and HBV Testing

- **2008 CDC guidelines recommend HBV testing in immunosuppressed patients**
  - Transplant patients
  - Patients receiving immunosuppressive therapy
  - HIV-positive patients

Public Health Notification

- **March 27, 2013**
- **Guilford County Health Department notified via electronic laboratory report of new HBV infection**
  - HD patient with no other identified risk factors
- **Epidemiologic investigation began…**

Objectives

- Establish source of HBV infection
- Identify other exposed patients
- Prevent additional infections

Methods

- Reviewed medical and laboratory records
- Interviewed index patient (Patient 1)
- Observed infection control practices at HD facility
- Performed HBV molecular testing
- Requested additional laboratory testing of some patients

Patient 1

- **81 year-old woman**
- **Risk factors for acute HBV infection:**

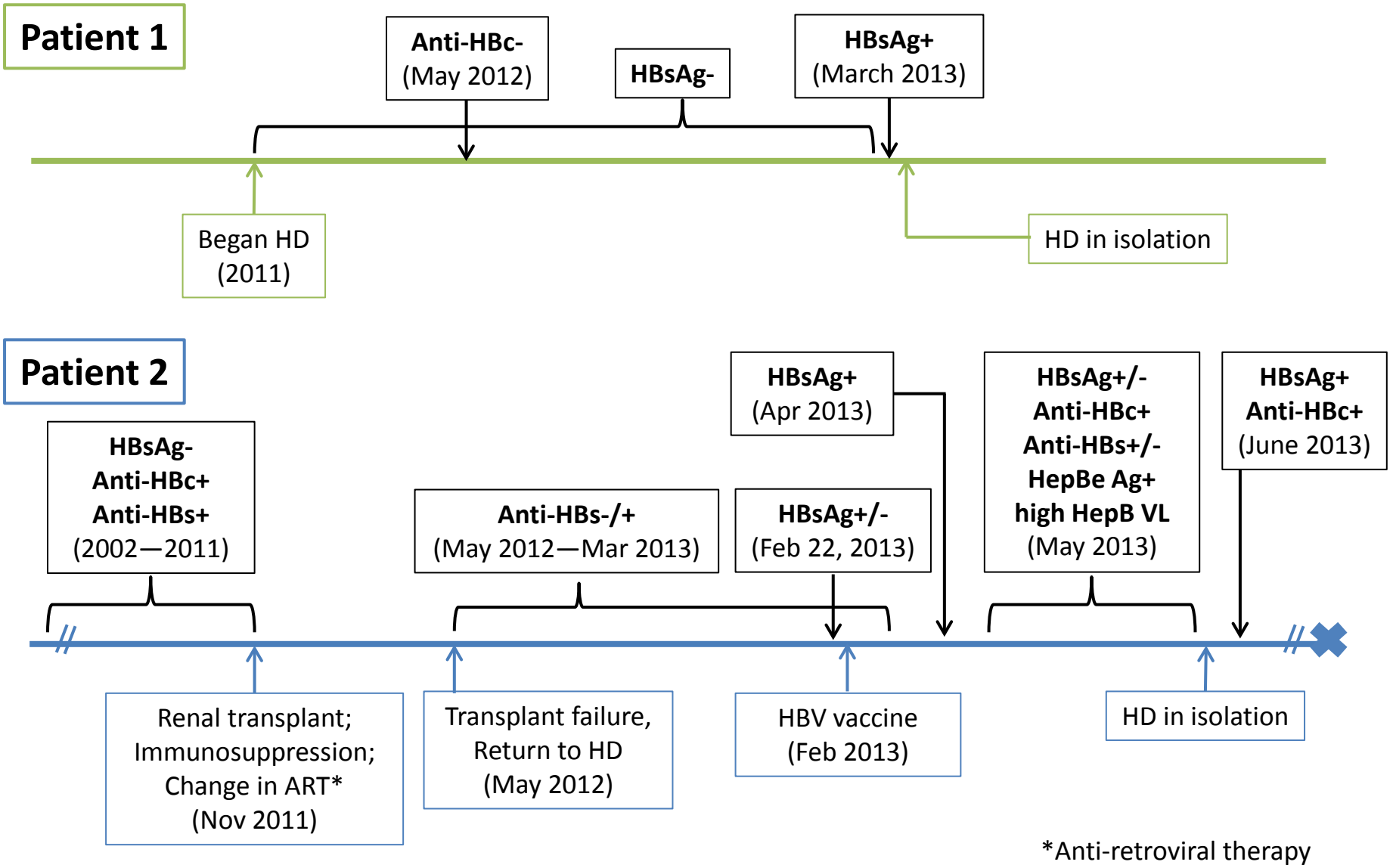
Present	Absent
Hemodialysis	Injection drug use
	Tattoo or piercing
	Contact with HBV-infected
	Communal living

- **Non-responder to HBV vaccination**
- **Anti-HBc negative**
- **HBsAg negative**

Patient 2

- **46 year-old man**
- **Diagnosed with acute HBV in 1989**
  - Serologic evidence of resolution and immunity
- **Diagnosed with HIV in 1997**
  - Antiretroviral therapy (ART) since 1999

Timelines of HBV serology results



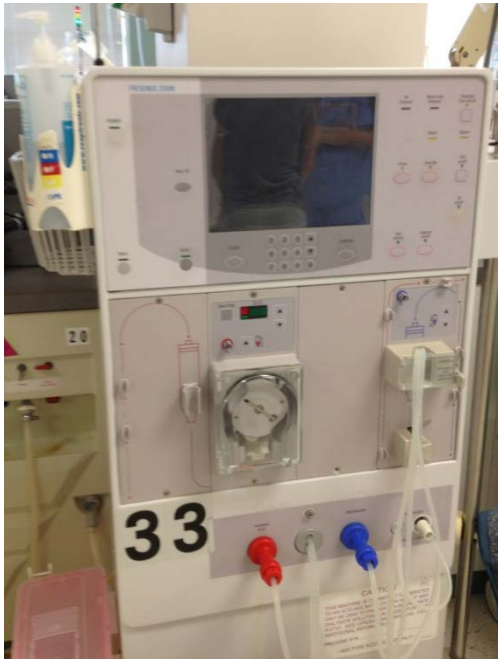
*Anti-retroviral therapy

Case Finding

- **HBV serology identified no new infections among other patients during the risk period, May 2012-May 2013**
- **Only Patients 1 and 2**

Infection Control Observations

- HD stations not thoroughly disinfected
- Materials carried from HD station to station
- Medication preparation cart close to HD stations



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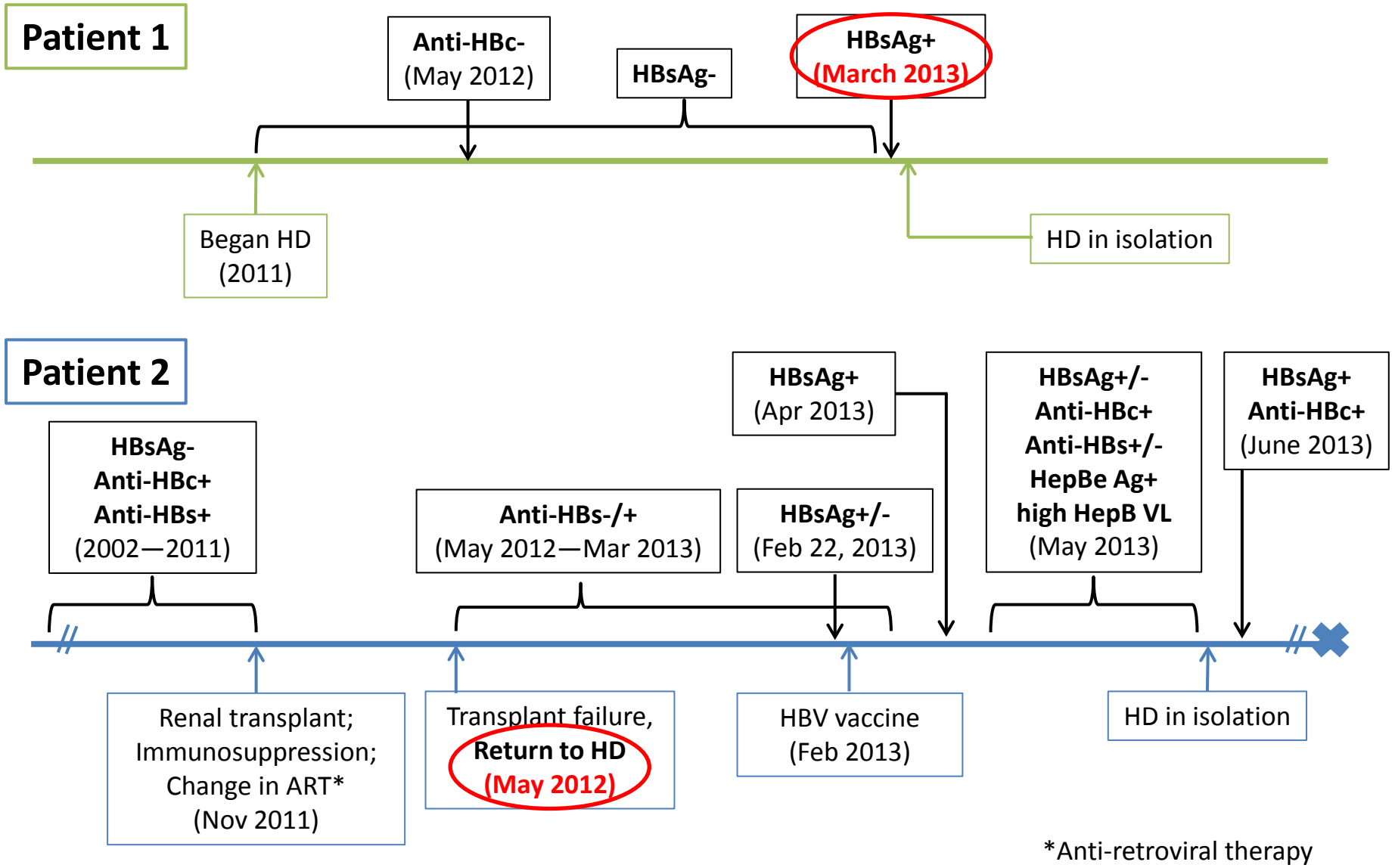


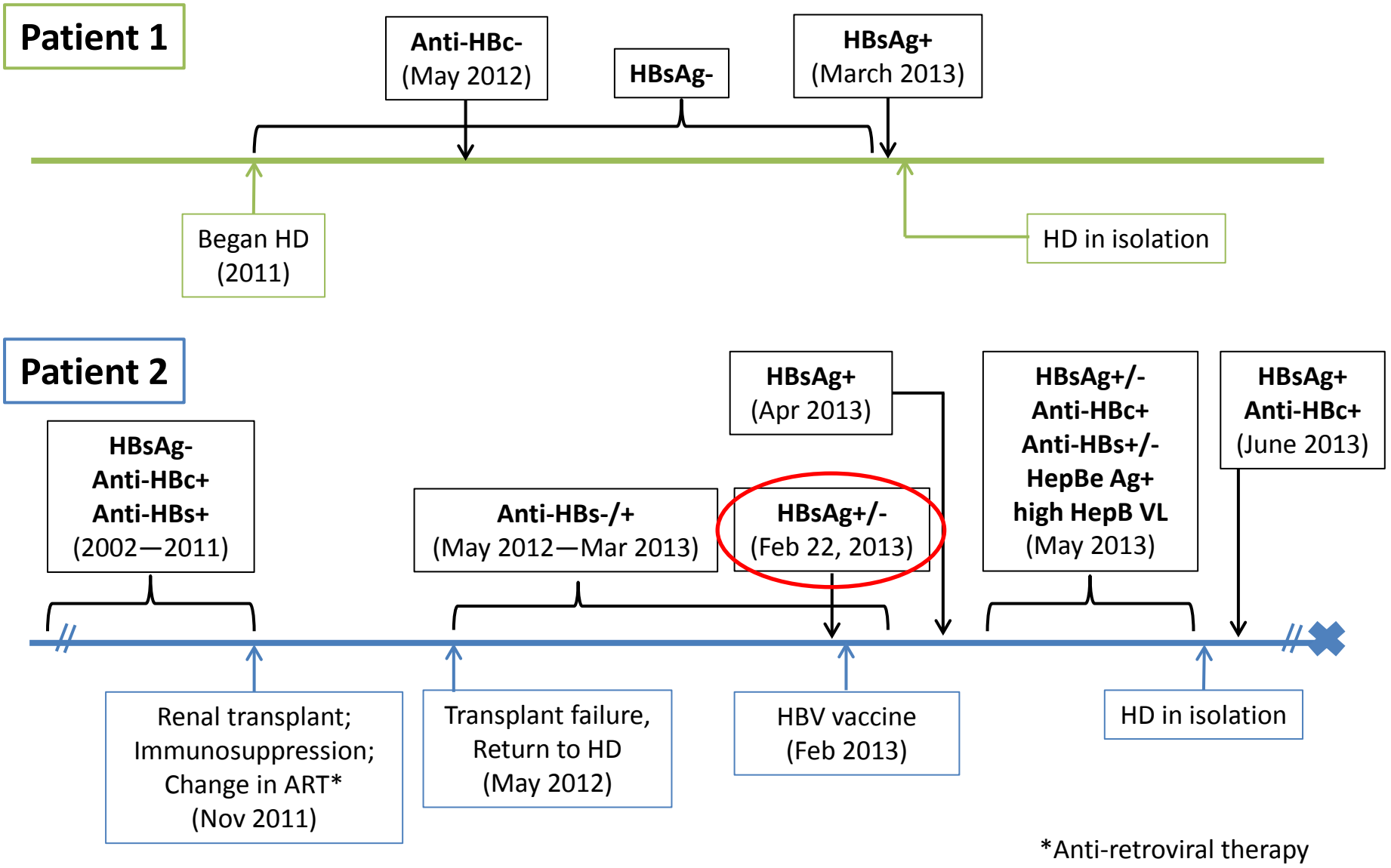
Molecular testing of HBV from Patients 1 and 2

- July 2013
- Viral loads >110,000,000 IU/ml
- Whole genome sequences indicated 99.9% genetic homology

Limitations

- **Observations at site visit might not fully reflect practices**
- **Not able to precisely determine HBV transmission time interval**

Timelines of HBV serology results



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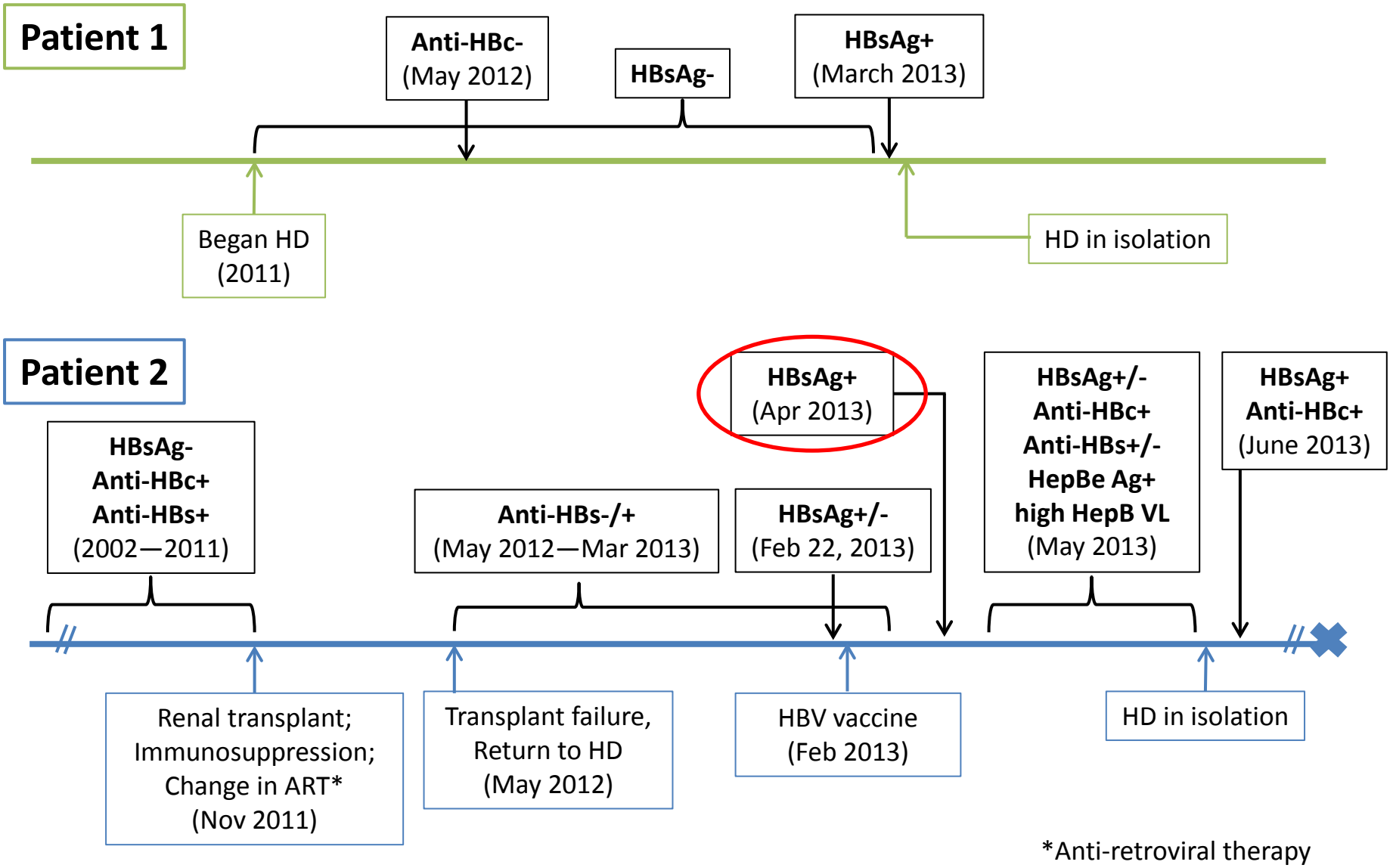

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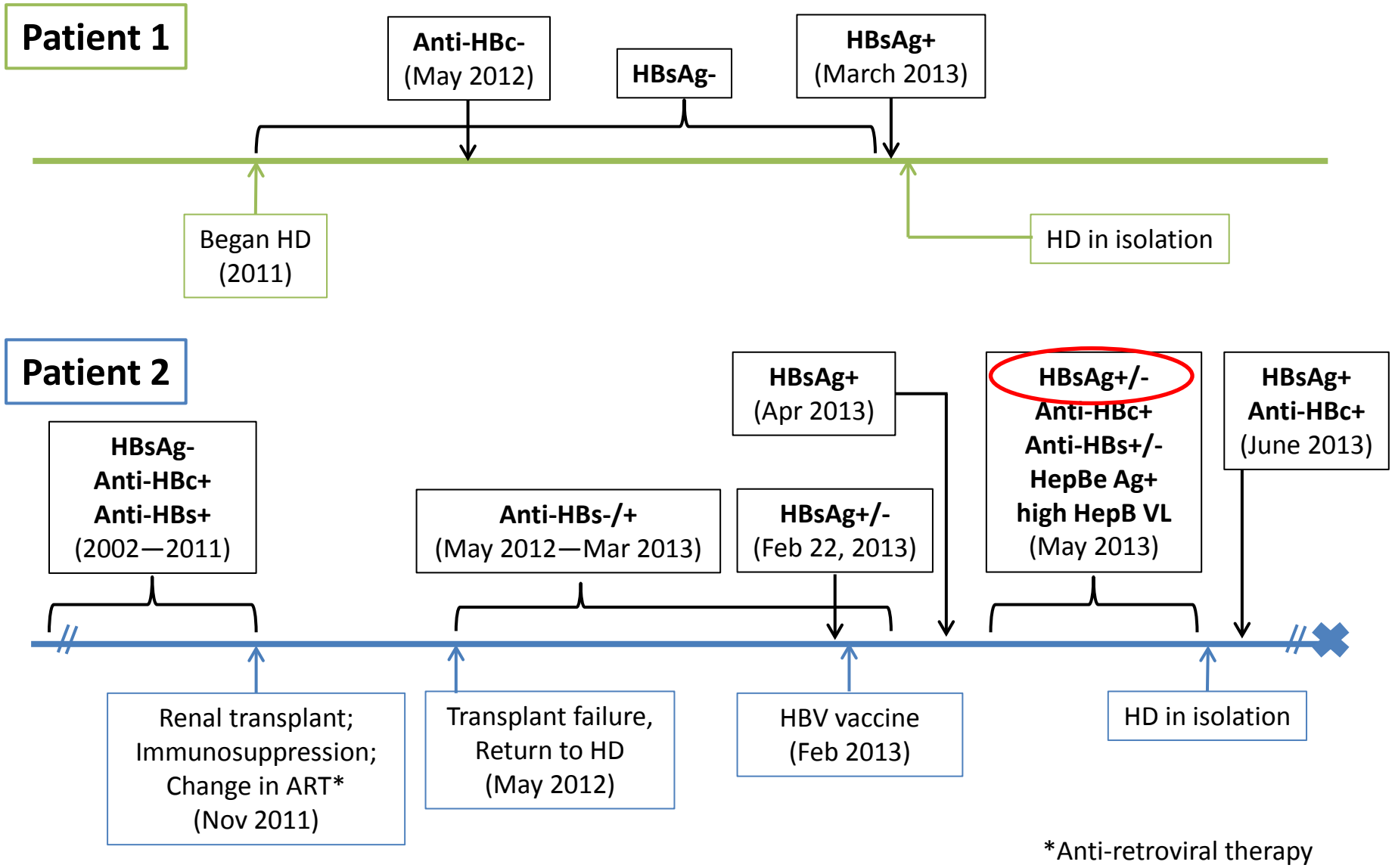

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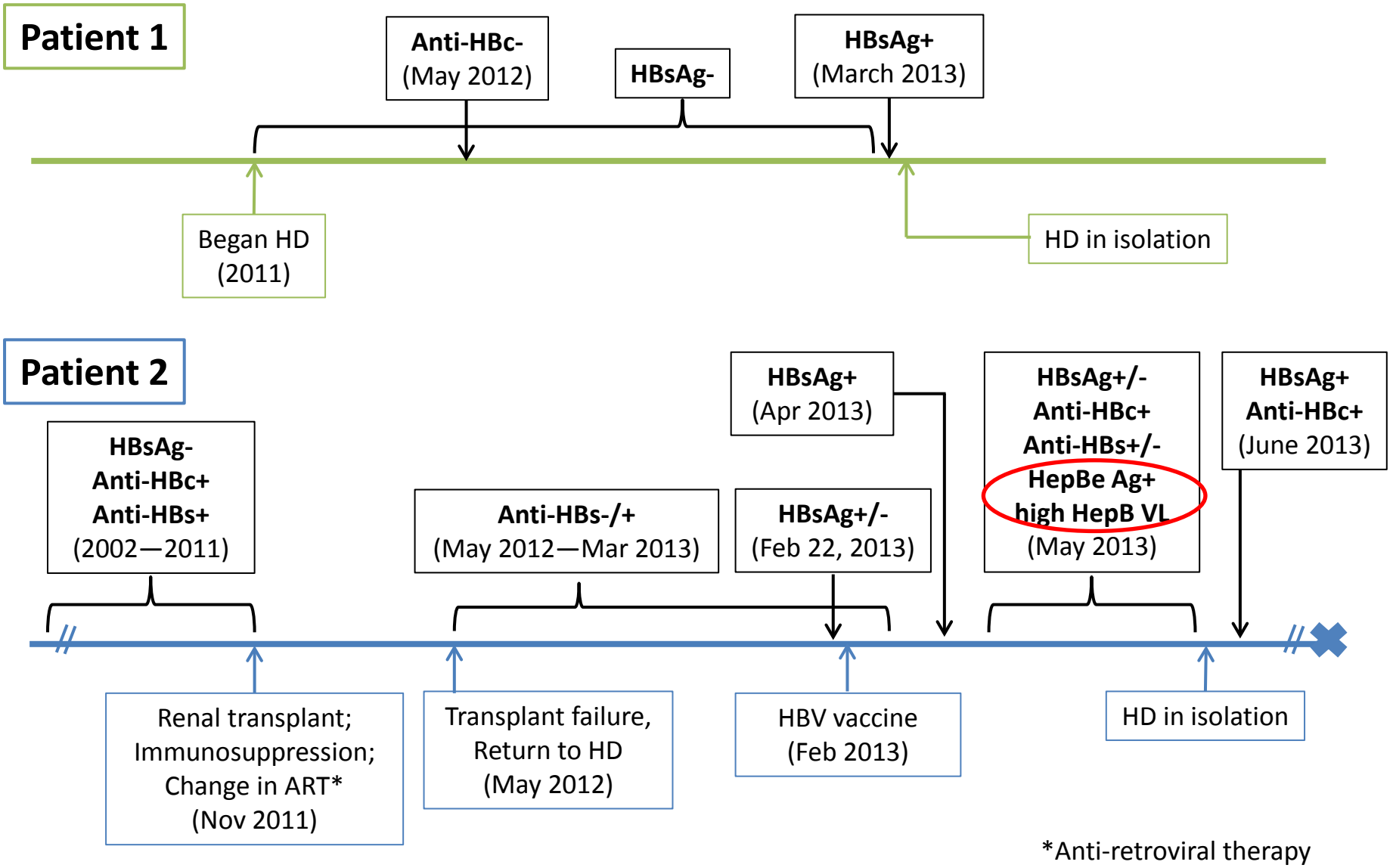

Conclusions

- **HBV transmission occurred after reactivated infection**
- **1st reported HD-related HBV transmission in U.S. since 1996**
- **Only reported HD-related transmission due to HBV reactivation**

Discussion

- Challenges in identification and isolation of HD patients with reactivated HBV infection
- Consideration of frequent monitoring for HBV reactivation if severe immunosuppression occurs