Hepatitis B
Lentivirus humimdef1

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Citywide HIV rounds

January 13, 2024

Disclosures

- Clinical trials
  - Takeda: SiRNA for PiZZ Alpha-1-antitrypsin deficiency
  - GSK: SiRNA for alcohol related liver disease
  - Physician initiated
    - HDV-HBV co-infection
    - Functional cure of chronic HBV infection
- New/investigational concepts
  - qHBsAg
    - What anti-HBs means clinically
  - Functional cure

Outline

- Review where we have been
  - New tests: qHBsAg
  - New goals: Functional cure
- Where we are
- Where we are going

Changing landscape

	HIV-HBV	HBV
Where we were	Treat everyone	Treat some
Where we are	New regimens without HBV	Functional cure qHBsAg
Where we are going	Acute HBV, HBV reactivation	Treat everyone

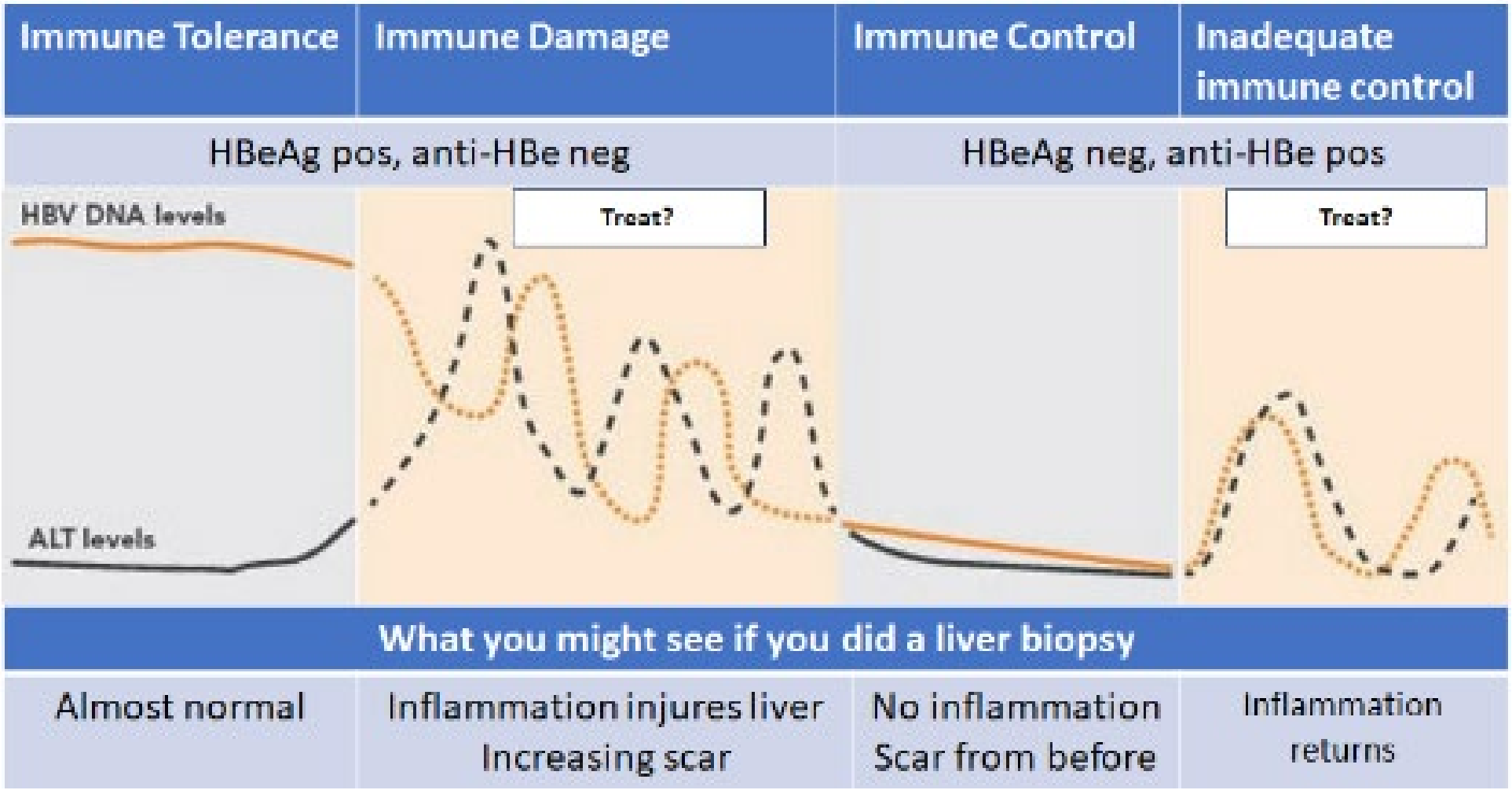
Different strategies to managing HBV

- Treat all
  - Rights of the many outweigh the rights of the few (many)
- Treat some
  - Rights of the few/individuals are acknowledged

The only rule of HBV

- For every rule, there is an exception

Immunopathogenesis of HBV



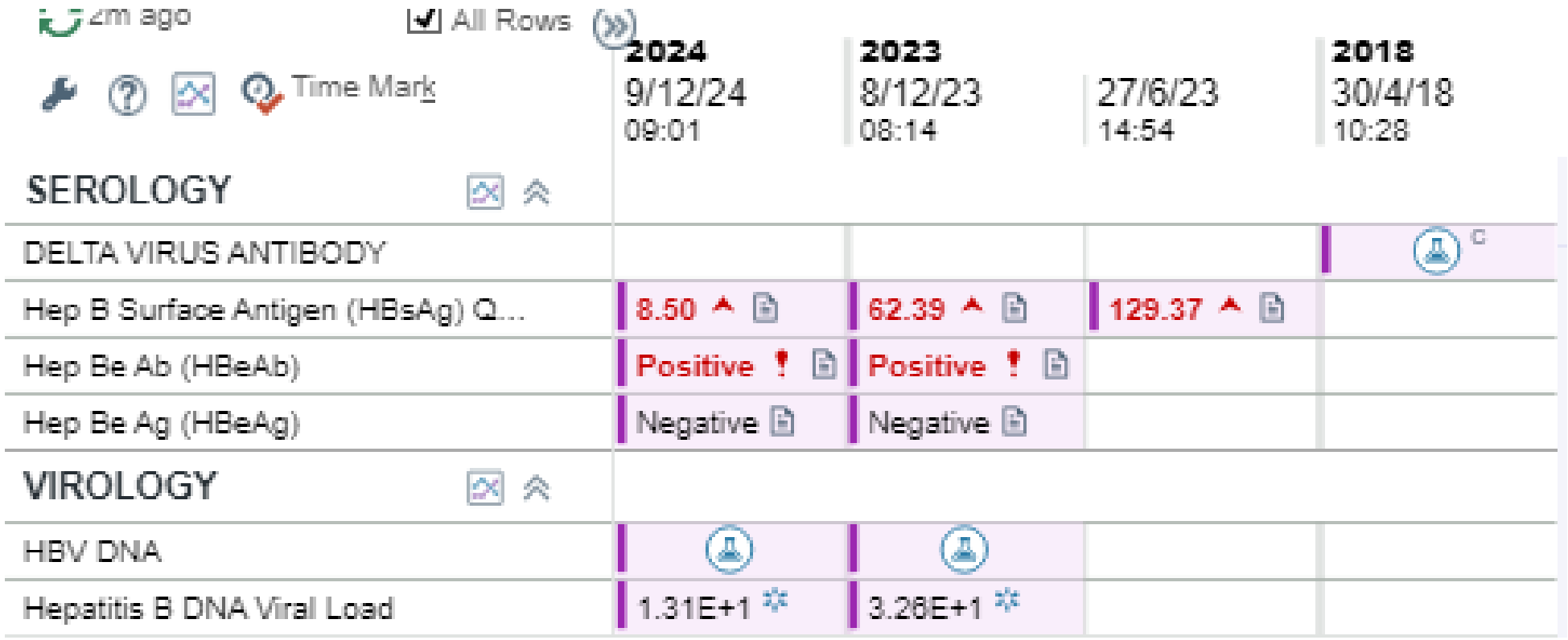
New concepts

- Functional cure
  - After documented chronic HBV infection > 6 months
    - HBsAg negative
    - Anti-HBs probably not important
    - HBV DNA negative (unclear if needs to be checked)
- Immunologically T cells are closer to ongoing chronic HBV infection
  - Unlike acute infection/resolved
  - HBV not in liver but not in blood
  - Implications for risk of HBV reactivation
    - Treat like HBsAg remains positive?

HBsAg

- At UHN
  - HBsAg (qual)
    - To screen for infection
    - “non-donor screening”
    - Reported to Public Health if positive
      - May get paged by lab for positive test
  - qHBsAg
    - Monitoring annually
    - Falling levels predict functional cure
    - Most on antiviral therapy have stable values
      - HBsAg loss on therapy is very rare
    - Rising titer off therapy is perhaps sign that they need to go back on treatment

qHBsAg examples: untreated



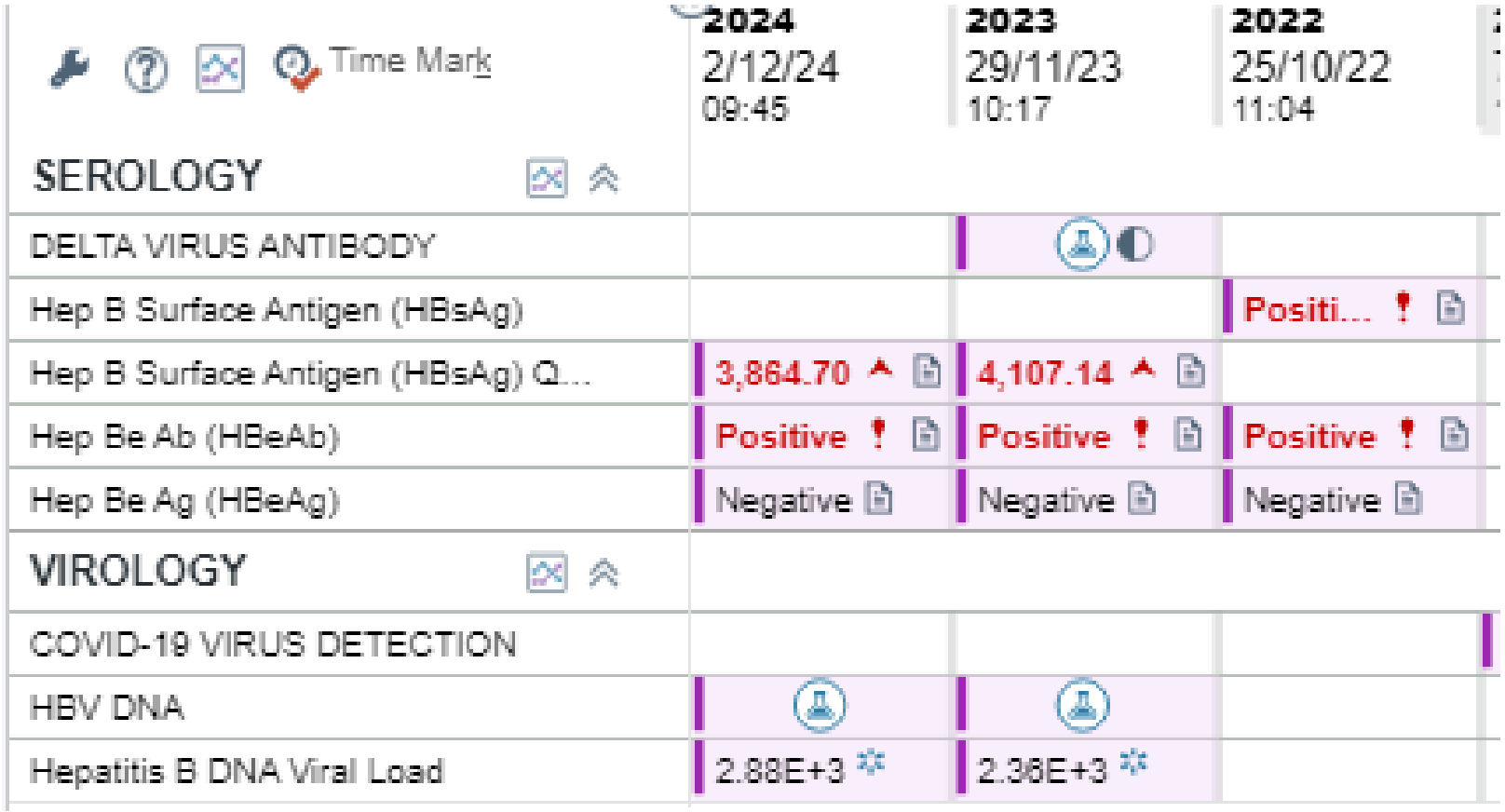
2m ago

All Rows

Time Mark

	2024 9/12/24 09:01	2023 8/12/23 08:14	27/6/23 14:54	2018 30/4/18 10:28
SEROLOGY				
DELTA VIRUS ANTIBODY				C
Hep B Surface Antigen (HBsAg) Q...	8.50	62.39	129.37	
Hep Be Ab (HBeAb)	Positive	Positive		
Hep Be Ag (HBeAg)	Negative	Negative		
VIROLOGY				
HBV DNA				
Hepatitis B DNA Viral Load	1.31E+1	3.26E+1		

qHBsAg examples: untreated

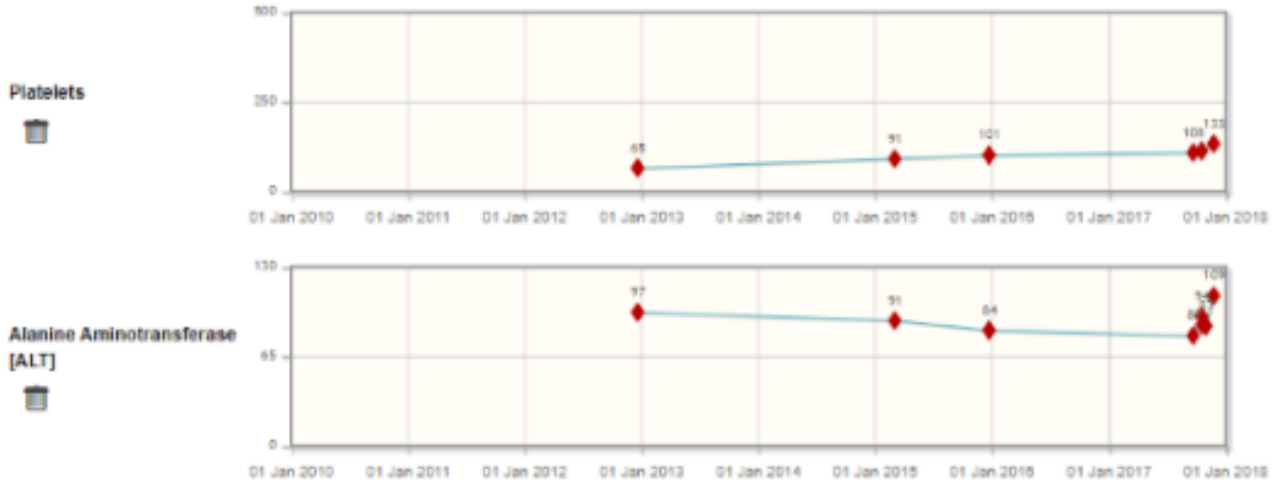


Time Mark	2024 2/12/24 09:45	2023 29/11/23 10:17	2022 25/10/22 11:04
SEROLOGY			
DELTA VIRUS ANTIBODY			
Hep B Surface Antigen (HBsAg)			Positi...
Hep B Surface Antigen (HBsAg) Q...	3,864.70	4,107.14	
Hep Be Ab (HBeAb)	Positive	Positive	Positive
Hep Be Ag (HBeAg)	Negative	Negative	Negative
VIROLOGY			
COVID-19 VIRUS DETECTION			
HBV DNA			
Hepatitis B DNA Viral Load	2.88E+3	2.36E+3	

Testing outweighs history

Everyone was talking about HCV – I thought I had HCV

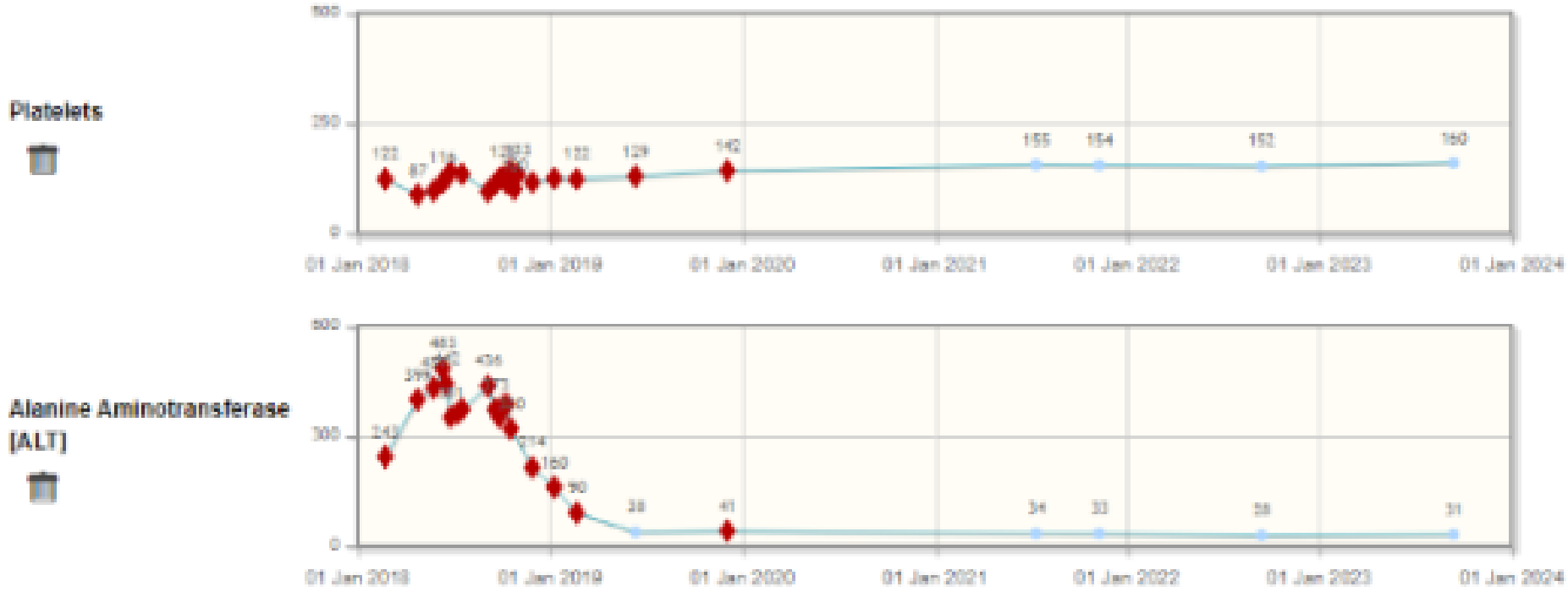
Risk for nodular regenerative hyperplasia: AZT (anemia requiring transfusion), D drugs until early 2000s.
2002 to 2008 on TDF then switched to DRV-EFV-RTG (T20 eventually stopped)



Oct 2017: HBsAg positive, HBeAg positive, HBV DNA >8 log IU/mL. ALT 80-94

HBV suppression can take a long time Hepatitis if HBV DNA <3-4 logs

Nov 2017: Tenofovir added back (FTC-TAF-RPV-DTG-DRV/cobi) but ALT 109-431

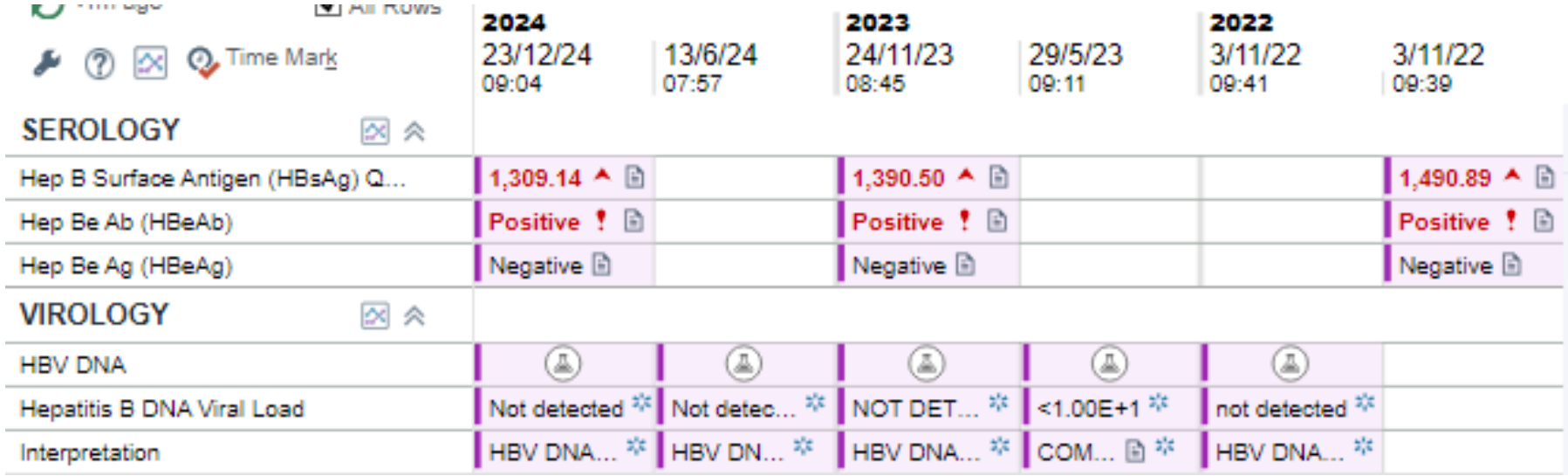


July 27, 2018: DTG stopped (FTC-TAF-RPV-DRV/cobi).

Lesson 1

- We used to stress a history for risks for infection to determine if we should test
  - Test is more reliable than history
- Anti-HBs may have no clinical significance
  - Positive test does NOT exclude chronic infection
    - HBsAg/anti-HBs double-positive
  - Positive test does NOT preclude acute infection in the future
    - HBV vaccine 10 years ago
    - HIV diagnosed, anti-HBs pos at baseline
    - Acute HBV 4 years later
  - Test HBsAg!!

qHBsAg on NUC



	2024		2023		2022	
	23/12/24 09:04	13/6/24 07:57	24/11/23 08:45	29/5/23 09:11	3/11/22 09:41	3/11/22 09:39
SEROLOGY						
Hep B Surface Antigen (HBsAg) Q...	1,309.14 ▲		1,390.50 ▲			1,490.89 ▲
Hep Be Ab (HBeAb)	Positive !		Positive !			Positive !
Hep Be Ag (HBeAg)	Negative		Negative			Negative
VIROLOGY						
HBV DNA						
Hepatitis B DNA Viral Load	Not detected	Not detec...	NOT DET...	<1.00E+1	not detected	
Interpretation	HBV DNA...	HBV DN...	HBV DNA...	COM...	HBV DNA...	

31M from Brazil

- No labs in Connecting Ontario

Past Medical History

Diagnosis	Date	Age	Comment	Src.
Acute hepatitis B	08/2024	31 y.o.		
Anxiety				
Asthma			Last ER visit 2010	
HIV (human immunodeficiency virus infection)	2017	23 - 24 y.o.	May 29, 2024 Switch to Cabotegra...	
Vaccination failure			HBV vaccine x 2	

Pertinent Negatives

Diagnosis	Date Noted	Comment	Src.
Hepatitis A	29/03/2022	Anti-HAV pos	
Hepatitis C	29/08/2024	HCV PCR neg	

Acute hepatitis B

- Did not test for HBV because history of HBV vaccination?
  - Anti-HBs pos (titer 857 IU/mL)
- HBsAg neg, IgM anti-HBc pos

Hepatitis B vaccine x 2, last in 2023 (anti-HBc neg in March 2022).
New medication: Cabotegravir/rilpivirine started May 29, 2024 - received 3 doses
Liver enzymes normal to Nov 2023, abnormal on next test Aug 15, 2024

Date	ALT	AST	ALP	T Bili	INR	Creat
15-Aug-24	4326	2196	113	103	1.23	89
16-Aug-24	3101	1036	102	79		
29-Aug-24	127		115	16	1.0	87
04-Sep-24	62	41				

Lesson 2

- HBV vaccination does not always prevent acute HBV infection
- Anti-HBs positive does not rule out recent acute HBV infection

Case 3 – 63M

- Complicated history:

Past Medical History

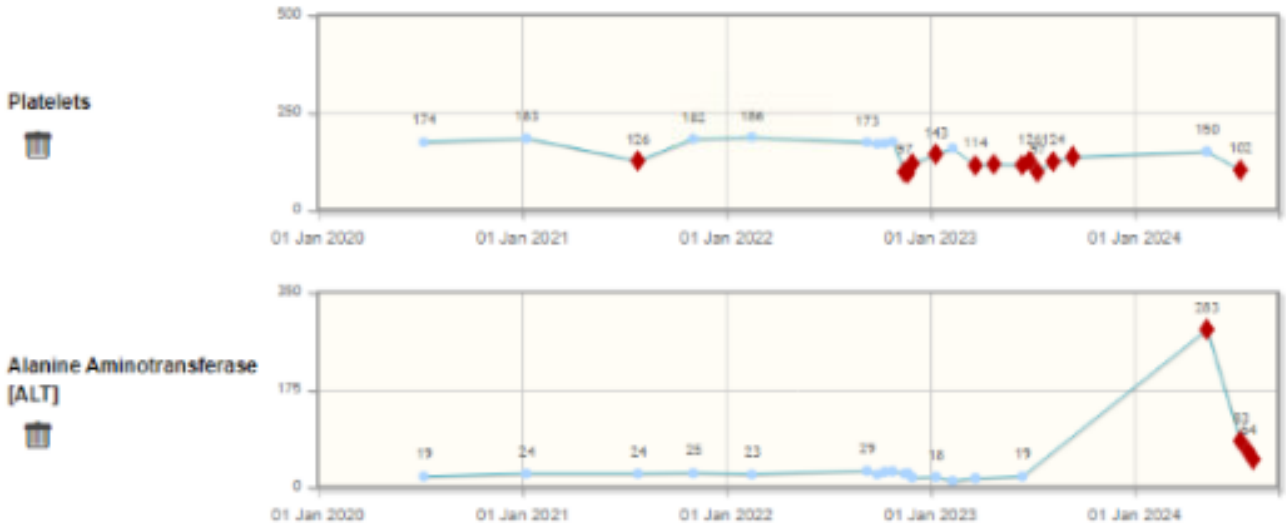
Diagnosis	Date	Age	Comment	Src.	F
Acute hepatitis B	09/05/2024	60 y.o.			
Bowel perforation			Colostomy 1990 secondary to bow…		
Cirrhosis			Seen in the chart. Patient does not…		
CKD (chronic kidney disease)	20/10/2023	60 y.o.			
Epididymitis			At least 2 episodes in the past - re…		
Epilepsy			Diagnosed age 9, in remission. No…		
Hepatitis B					
History of hepatitis C			Treated Jan 2016		
HIV disease	1988	24 - 25 y.o.	nadir CD4 in the low 100s. Manag…		
Kaposi sarcoma			R. leg, 2010 - Documented in histo…		
Neurosyphilis			Treated in 2014		
Polyarthritis			Patient states he had a reactive art…		
Squamous cell cancer of skin of scrotum			Initially excised Aug 2022 - SCC e…		
Squamous cell carcinoma of anal canal					

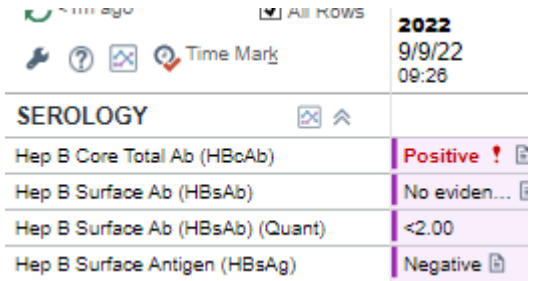
Pertinent Negatives

Diagnosis	Date Noted	Comment	Src.
Hepatitis A	08/07/2024	Anti-HAV pos	
Hepatitis C	09/05/2024	Jan 2016 Rx Sofosbuvir-Ledipasvir	

Aug 2, 2012: HBsAg neg, anti-HBc pos, anti-HBs neg

No TDF/TAF containing regimen from 2016 to 2024





Sep 9, 2022: HBsAg neg

Jul 8, 2024: HBsAg pos

HBeAg/anti-HBe not tested

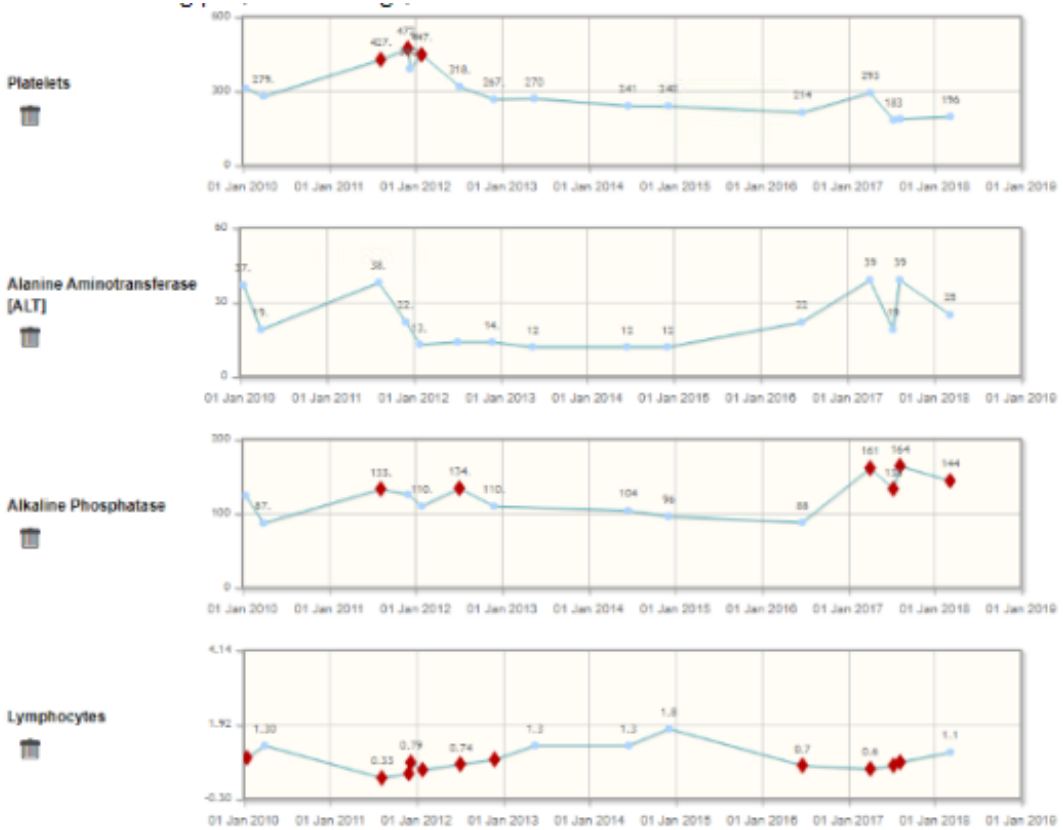
July 22, 2024: HBV DNA 1.87E8 IU/mL. IgM anti-HBc pos

IgM anti-HBc signal was done three times: 5.22, 5.01, 4.75 (<0.8 is neg, 0.8-0.99 is indeterminate, >1 positive)

Lesson 3

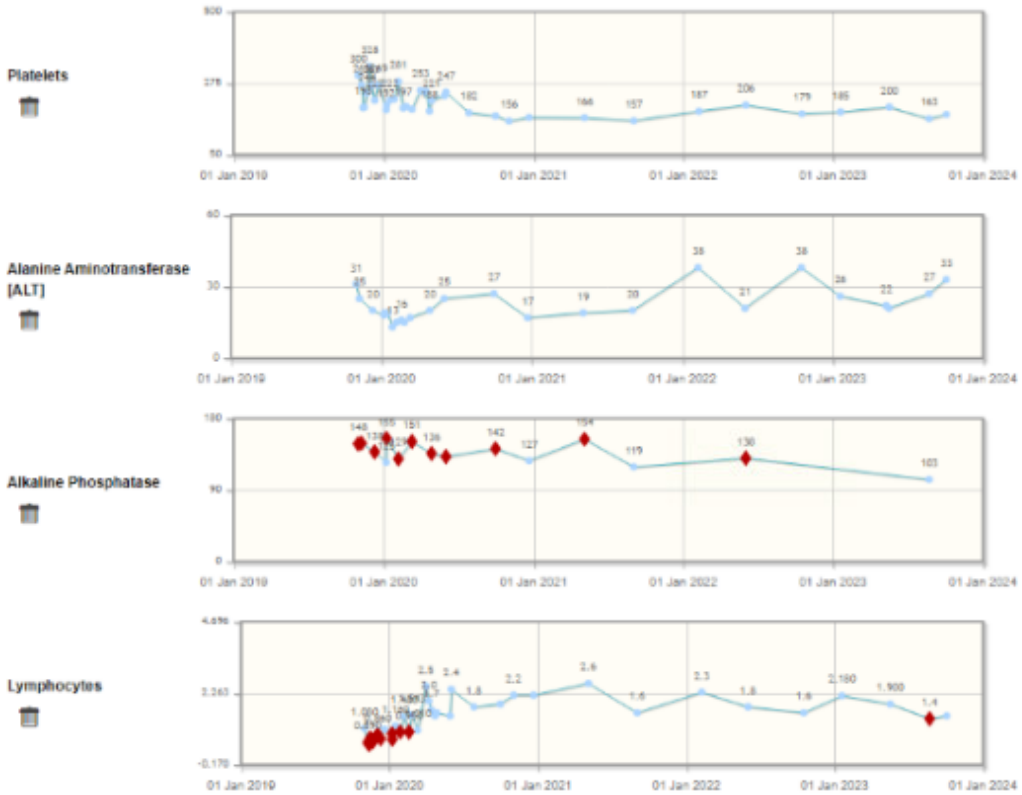
- It is very hard to distinguish between acute HBV and HBV reactivation
- Prior serology is most reliable
  - Can you have a second acute HBV if you previously had acute HBV infection that resolved?
  - IgM anti-HBc titer is higher in acute vs chronic
    - Not reported but can ask for optical density
    - Problem is interpretation – what is high?
- HBV reactivation: main risk is B cell depleting agents
  - What about HIV? CD4?

Case 4: 68 Chinese man with HBV-HIV



HBV viral loads >7 logs generally, down to 3-4 logs (surrogate for when he is on HIV Rx) in Dec 2014, Mar 2018,
HIV viral loads 4-5 logs (not on HIV Rx) in Jun 2016, Apr 2017
HBV viral loads >7 logs generally, down to 3-4 logs (surrogate for when he is on Tenofovir based HIV Rx) in Jun 2019, Jul 2019
HIV viral loads 4-5 logs (not on HIV Rx) in July 2017
HBV high in untreated range > 7-8 logs in Jun 2016, Apr 2017, Jul 2017, Aug 2017, Jun 2020
Adherence poor because of GI upset.

Better off TDF



	2024 23/10/24 10:28	21/2/24 10:55	2023 23/8/23 10:27
SEROLOGY			
DELTA VIRUS ANTIBODY			
Hep B Surface Antigen (HBsAg) Q...	2,911.53 ▲	2,421.56 ▲	2,872.47 ▲
Hep Be Ab (HBeAb)	Positive !	Negative	Positive !
Hep Be Ag (HBeAg)	Negative	Negative	Positive !
VIROLOGY			
HBV DNA			
Hepatitis B DNA Viral Load	3.06E+6	3.35E+6	

Aug 2022 stopped TDF based regimen, switch to Cabenuva

Fibroscan Aug 2023 was 7.8 kPa, Feb 2024 was 12.7 kPa, consistent with F2-3 (moderately advanced) liver fibrosis.

Lesson 4

- People will suffer from strict adherence to guidelines
- Immune control of HBV is possible
- Resistance to drugs
  - M204 (M184 YMDD): Lamivudine (3TC, FTC)
  - Compensatory mutations can lead to high HBV viremia
- TDF for YMDD
  - Renal issues, GI upset rare but possible
  - TAF works, risk of GI upset unclear to me
  - Entecavir an option if HBV DNA suppressed when switching
    - High risk of ETV failure if prior M204 AND HBV not suppressed after 6 months Rx

The rights of the few need to be considered

- Treat all
  - Rights of the many outweigh the rights of the few (many)
- Treat some
  - Rights of the few/individuals are acknowledged