DISCIPLINE OF VIROLOGY

QUARTERLY NEWSLETTER Q2 OF 2022

NATIONAL HEALTH LABORATORY SERVICE

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

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NEWSLETTER

This issue of the newsletter was edited by Dr Kerusha Govender. Please email questions or comments to: govenderk7@ukzn.ac.za

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MESSAGE FROM OUR HOD

In this newsletter we shine the spotlight on viral hepatitis.

The World Health Organization (WHO) declared 28 July 2022 as **World Hepatitis Day.** The date is set aside each year to observe and raise awareness of viral hepatitis, which causes inflammation of the liver that leads to severe disease and liver cancer. There are 5 types of viral hepatitis viruses: namely A, B, C, D and E. Hepatitis B, C & D are responsible for chronic viral hepatitis.

The theme of this year's World Hepatitis Day was: "**Bringing hepatitis care closer to you**". The aim is to raise awareness about the need to simplify and bring hepatitis care to primary health facilities, community-based venues and locations beyond hospital sites, so that care is closer to communities and people wherever they are. In 2016, WHO released the first **Global Health Sector Strategy on Viral Hepatitis, 2016–2021**. The goal of the strategy is to eliminate viral hepatitis as a major public health threat by 2030.

So where are we now and what will it take to achieve this ambitious target?

1. WHO estimates that **296 million** people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year.
2. In 2019, hepatitis B resulted in an estimated **820 000 deaths**, mostly from cirrhosis and hepatocellular carcinoma.

What are the key challenges?

1. Data suggest that only 43% of infants receive the birth dose of the HBV vaccine globally
2. For HBV, only 22% of patients diagnosed are on treatment.

MESSAGE FROM OUR HOD

continued

3. For HCV, only 62% of patients diagnosed are treated. HCV is curable

4. The global prevalence of HBV infection in HIV-infected persons is 7.4%. This is higher in SA.

What are the short to intermediate plans to move closer to realizing elimination targets?

1. **Integration** of care and services. The new global strategy now calls for integration of HIV, hepatitis and STI services and care.

2. At least 60% of people living with hepatitis B and C must be **diagnosed** and at least 50% eligible for treatment must be cured (for HCV) or receiving **treatment** (for HBV) by 2025.

3. All infants must be given the **birth dose** of the HBV vaccine.

What is the status quo in South Africa and what programmes exist to respond to the viral hepatitis challenge?

1. Although studies conducted in South African show variable HBV & HCV prevalence in different groups and communities, the country is considered to have **high intermediate endemicity** for HBV.
2. HIV and HBV co-infection remains a challenge in our setting and requires a renewed focus in **integrating care** so that we can improve the number of people with HIV/HBV coinfection who are diagnosed, started on treatment and adequately monitored to ensure viral suppression for both infections.

3. The **2019 South African guidelines** for the management of viral hepatitis provide a comprehensive and detailed approach to managing viral hepatitis, but implementation in practice still lags behind.

In response to the WHO call for scaling up of screening, care and treatment services. We remind colleagues of diagnostic services available in our virology laboratories to offer both serological screening and monitoring using nucleic acid based quantitative assays for patients who have been diagnosed and are on treatment for chronic viral hepatitis.

We hope this brings the topic of viral hepatitis back into our present consciousness and we each play our part towards eliminating viral hepatitis as a public health threat by 2030.

Until next time.

Dr Khanyi Msomi

Key references & resources

1. *Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030: WHO Geneva (June 2022). https://www.who.int/publications/m/item/global-health-sector-strategies-on-respectively--hiv-viral-hepatitis-and-stis-for-2022-2030*
2. *Hepatitis B fact sheet-June 2022 https://www.who.int/news-room/fact-sheets/detail/hepatitis-b*
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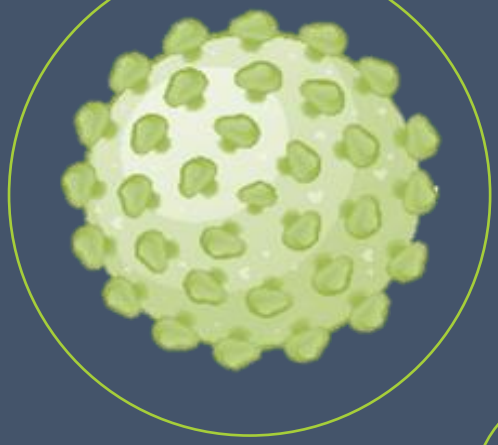
WHO aims to achieve hepatitis elimination by 2030



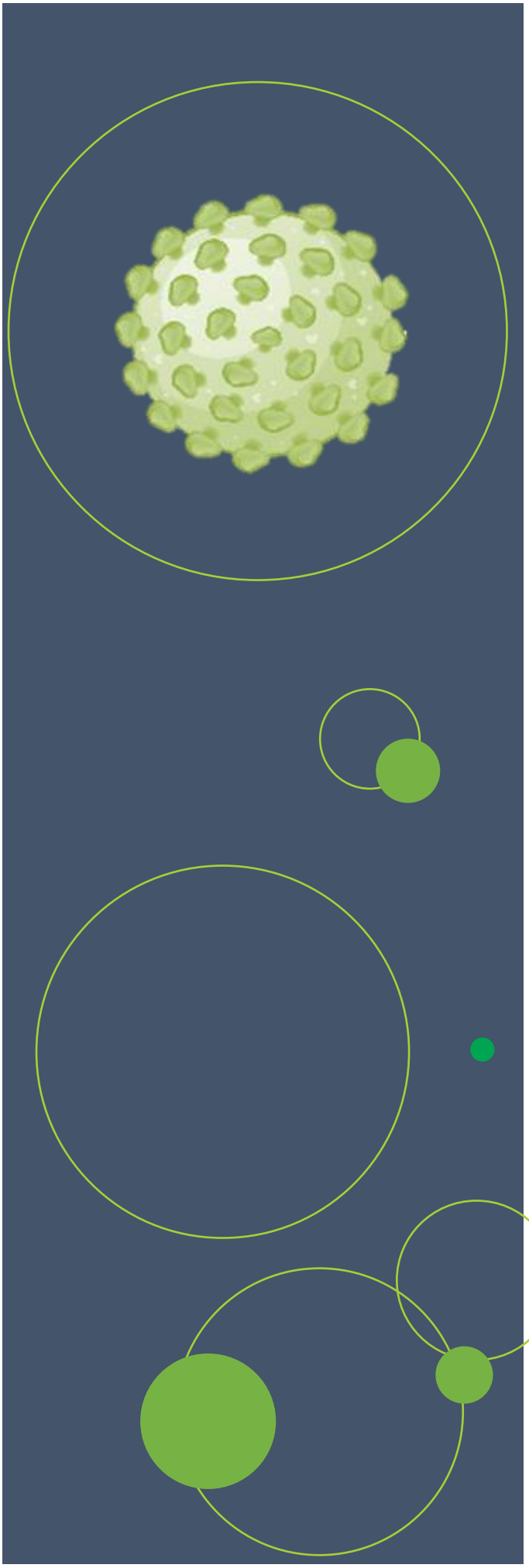
FOCUS ON HEPATITIS B VIRUS

This section is a synopsis of an interdepartmental update about Hepatitis B virology and diagnosis. The update was done by Dr Kerusha Govender at the UKZN Department of Internal Medicine on 15 August 2022.

The seroprevalence of HBsAg (a marker of Hepatitis B virus infection) in South Africa is approximately 6.7%, which is considered high intermediate endemicity. [1] The predominant mode of transmission in sub-Saharan Africa is thought to be "horizontal" **childhood transmission**, through close contact e.g., household contact, which contrasts with perinatal and parenteral transmission in other parts of the world. [1] Genotypes **A and D** predominate in South Africa, and the former is notably associated with a higher risk of hepatocellular carcinoma than other genotypes. [2]

There are multiple events in the Hepatitis B virus (HBV) replication cycle with meaningful clinical relevance. The cell receptor which engages with HBsAg and is crucial for cell entry is NTCP (Sodium-taurocholate co-transporting polypeptide (Ntcp)).[3] This bile acid transporter molecule is what determines the restricted host and **tissue tropism**, confining viral replication to the liver. The HBV polymerase enzyme enables the conversion of an incomplete HBV circular genome into a completely closed circular genome (i.e., **cccDNA**) which enables the virus to persist in true latency within the host cell nucleus, or persist through low level replication.[4] This is a key factor in the inadequacy of current strategies, such as nucleoside analogs, to **cure** HBV as these largely act upon replicating viruses rather than latent viruses. The secretion of the enveloped HBV viral particle via the endoplasmic reticulum out of the cell is a non-cytopathic process, meaning that the liver damage is **immune-mediated** instead of virus-mediated.

The natural history of chronic HBV is **phasic**, characterized by periods of active hepatitis and periods without minimal liver damage, over many years. Over time, the infection converts from one that is eAg positive (i.e., a marker of active replication and infectivity) to **eAg negative**. The ups and downs of transaminases, and viral activity means that the range of biomarkers (such as ALT, HBsAg, HBsAb, HBeAg, HBeAb, HBcAb (total), HBcAb (IgM) and HBV DNA) need to be interpreted with a deep understanding of the various phases of infection and disease. Further to this, catching a patient at the tail end of a phase (e.g., during the resolution of acute infection) may yield a set of results which is difficult to interpret. The phenomenon of occult hepatitis B, in which the classical marker of



FOCUS ON HEPATITIS B VIRUS

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infection, HBsAg, is unexpectedly negative, occurs with varying frequency in different subsets of the population, and screening at-risk patients may require HBV PCR.[5]

Future prospects for HBV biomarkers revolve around the newer curative pharmaceuticals which are being developed. Quantifying not just viral DNA, but also HBsAg, HBV RNA and HBcrAg (i.e., core-related antigen) may hold the key to measuring cccDNA, and confirming the attainment of cure.

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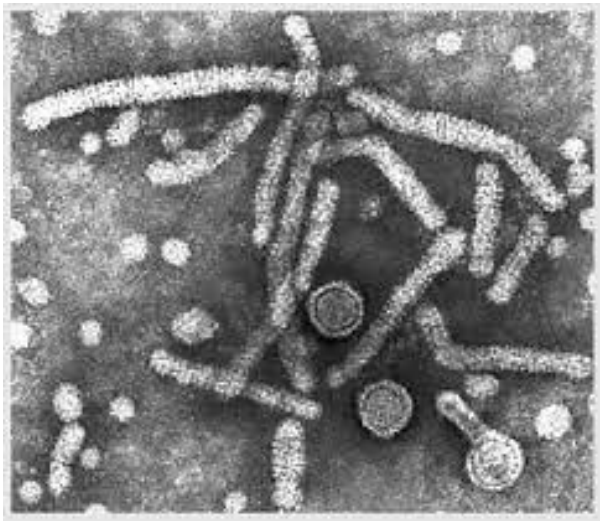
1. *Schweitzer, Aparna, et al. "Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013." The Lancet 386.10003 (2015): 1546-1555.*
2. *Kramvis, Anna, and Michael C. Kew. "Epidemiology of hepatitis B virus in Africa, its genotypes and clinical associations of genotypes." Hepatology Research 37 (2007): S9-S19*
3. *Naggie, Susanna, and Anna S. Lok. "New therapeutics for hepatitis B: the road to cure." Annual Review of Medicine 72 (2021): 93-105.*
4. *European Association For The Study Of The Liver. "EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection." Journal of hepatology 67.2 (2017): 370-398.*
5. *National guidelines for the management of viral hepatitis 2019.*



NEWS

1. Appointment of medical officer

The department has appointed a medical officer for the first time. A big welcome to Dr Shimon Barit who is currently assisting with operational activities in the department, such as the release of diagnostic results**.**

2. Training

Dr Lili Gounder attended a Statistical Computing Bootcamp in May 2022 which was facilitated by Dr. Elphas Okango and held by University of KwaZulu Natal, Heidelberg institute of Global Health and Harvard School of Public Health. The bootcamp was an introduction to the basics of programming languages and techniques for data manipulation. It was a preparation for the Statistical Computing for Data Science course which was held in June 2022. This course included concepts from Statistics, Computer Science and Software Engineering. Dr Gounder found these courses valuable for her current and future research projects.

Dr Kerusha Govender attended an Exploratory Data Analysis Workshop in August 2022, which focused on data analysis and modelling techniques in R. The course was hosted at Nelson R Mandela School of Medicine, by UKZN, Harvard Medical School and Washington University.

The ability to clean, analyze and visualize data will be crucial for implementing Next Generation Sequencing in the department.

3. Plans for the department

Our department plans to improve the viral hepatitis testing repertoire. This will include sensitizing clinicians to the availability of HBV and HCV PCR and Viral loads, and drug susceptibility testing. It is planned that these soon be offered in-house, reducing the need for referring the tests out, thus reducing the turn-around-time.

We are in the process of reviving our cell culture laboratory, and viral isolation diagnostic methods for both training and research purposes. Collaborative projects in this respect are welcomed.

4. Upcoming graduations

Mr Sontaga Manyana completed his MMedSci (Virology) summa cum laude during this quarter. His research project was about HIV-1 drug resistance in adults and adolescents on protease inhibitor-based antiretroviral therapy. He was supervised by Dr Ben Chimukangara. Dr Kerusha Govender completed her PhD (Virology), supervised by Dr Raveen Parboosing. Her thesis was entitled "Cytomegalovirus pneumonia in infants in KwaZulu Natal."

NEWS

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5. Provision of a training workshop

The department held a 2-week training workshop in July 2022 for medical technology students from all over the country. The purpose of the workshop was to help prepare students for their upcoming board examinations. The format was interactive, listening to lectures from our department section supervisors and doctors. Small group sessions were held, approaching difficult concepts and past examination questions.

A group picture of our students with their facilitators: Front row: Joseph, Sinovuyo, Kagiso, Nomfundo, Cherise, Nelisiwe, Naadira, Ingithandile, Siphosenkosi. Back row: Aishat, Branzy (Palesa), Morwesi

Facilitators Tshepiso, Nelisiwe, Penny, Zandy and Pravi working with their students. Inset: Students, Siphosenkosi and Kagiso hard at work

RESEARCH

NEW RESEARCH GRANTS AWARDEES

Mrs Subitha Govender has received an NHLS Research Trust Grant award for the completion of her MMedSci (Virology) research project

RECENT PUBLICATIONS

1. Houriiyah Tegally, Monika Moir, Josie Everatt, Marta Giovanetti, Cathrine Scheepers, Eduan Wilkinson, Kathleen Subramoney, Zinhle Makatini, Sikhulile Moyo, Daniel G. Amoako, Cheryl Baxter, Christian L. Althaus, Ugochukwu J. Anyaneji, Dikeledi Kekana, Raquel Viana, Jennifer Giandhari, Richard J. Lessells, Tongai Maponga, Dorcas Maruapula, Wonderful Choga, Mogomotsi Matshaba, Mpaphi B. Mbulawa, **Nokukhanya Msomi**, NGS-SA consortium, Yeshnee Naidoo, Sureshnee Pillay, Tomasz Janusz Sanko, James E. San, Lesley Scott, Lavanya Singh, Nonkululeko A. Magini, Pamela Smith-Lawrence, Wendy Stevens, Graeme Dor, Wolfgang Preiser, Derek Tshiabuila, Nicole Wolter, Florette K. Treurnicht, Marietjie Venter Caitlyn McIntyre, Aine O'Toole, Georginah Chiloane, Christopher Ruis, Thomas P. Peacock Cornelius Roemer, Sergei L. Kosakovsky Pond, Carolyn Williamson, Oliver G. Pybus, Jinal N. Bhiman Ben Jackson, Andrew Rambaut, Allison Glass, Darren P. Martin, Oluwakemi Laguda-Akingba, Simani Gaseitsiwe, Anne von Gottberg and Tulio de Oliveira. Emergence of SARS-CoV-2 Omicron lineages BA.4 and BA.5 in South Africa : Nature Medicine June 2022 https://doi.org/10.1038/s41591-022-01911-2

2. **Msomi N, Parboosing R**, Wilkinson E, Giandhari J, **Govender K**, **Chimukangara B**, Mlisana KP. Persistent Hepatitis B Viraemia with Polymerase Mutations among HIV/HBV Co-Infected Patients on HBV-Active ART in KwaZulu-Natal, South Africa. Viruses. 2022 Apr 10;14(4):788. https://doi.org/10.3390/v14040788

3. Moshabela M, **Msomi N**, Kalla GC, Maimela G, Yombi JC, Mbopi-Keou FX. Hosting ICASA 2021 in South Africa amidst the global Omicron scare. The Pan African Medical Journal. 2022;41.

4. Tongai G Maponga, Montenique Jeffries, Houriiyah Tegally, Andrew Sutherland, Eduan Wilkinson, Richard J Lessells, **Nokukhanya Msomi**, Gert van Zyl, Tulio de Oliveira and Wolfgang Preiser. Persistent Severe Acute Respiratory Syndrome Coronavirus 2 Infection With accumulation of mutations in a patient with poorly controlled Human Immunodeficiency Virus infection. Clin Infect Dis 2022 Jul 6;ciac548. Online ahead of print https://doi:10.1093/cid/ciac548

5. J C Y Nyasulu, R Maphoto, M G S Kamupira, **N Msomi:** South Africa regains polio-free status: Processes involved and lessons learnt. South African Journal of Child Health 2022;16(2):58.

6. **Kerusha Govender, Raveen Parboosing,** Salvatore Camiolo, Petr Hubáček, Irene Görzer, Elisabeth Puchhammer-Stöckl, and Nicolás M. Suárez. "Complexity of Human Cytomegalovirus Infection in South African HIV-Exposed Infants with Pneumonia." Viruses 14, no. 5 (2022): 855.

RESEARCH

RECENT PUBLICATIONS

continued

7. **Serumula W,** Fernandez G, Gonzalez VM, **Parboosing R.** Anti-HIV Aptamers: Challenges and Prospects. Current HIV Research. 2022 Jan 1;20(1):7-19.

8. Ncobeni N, de la Torre BG, Albericio F, Kruger HG, **Parboosing R**. Active targeting of CD4+ T lymphocytes by PEI-capped, peptide-functionalized gold nanoparticles. Nanotechnology. 2022 Jul 11;33(40):405101.

9. Maduray K, Moodley R, Ramdhani S, **Parboosing R**. The anti-HIV activity of biogenic silver nanoparticles synthesized from Centella asiatica extracts. Journal of Herbal Medicine. 2022 Aug 5:100592.

10. Brijkumar J, Edwards JA, Johnson BA, Ordonez C, Sunpath H, Lee M, Dudgeon MR, Rautman L, Pillay S, **Moodley P**, Sun YV. Comparing effectiveness of first‐line antiretroviral therapy between peri‐urban and rural clinics in KwaZulu‐Natal, South Africa. HIV medicine. 2022 Jan 12.

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A. Edwards Claudia E. Ordonez, Mathew R. Dudgeon, Henry Sunpath, Selvan Pillay, **Pravi Moodley,**

Daniel R. Kuritzkes, Mohamed Y. S. Moosa, Dean P. Jones, Vincent C. Marconiand Yan V. Sun. Crosstalk between Host Genome and Metabolome among People with HIV in South Africa. Metabolites. 2022 Jul;12(7):624.

NEW COLLABORATIONS

The department is collaborating on a study entitled: Evaluation of Vukuzazi LiVEr disease - Hepatitis B **(EVOLVE-HBV).** This study aims to determine the prevalence and characteristics of chronic hepatitis B virus infection in the Vukuzazi population to inform interventions for diagnosis, treatment and prevention. The principal investigator is Dr Philippa Matthews of University College London.

We will also be participating as a co-lead applicant in a grant for the **SAPRIN** - DSI/ SAMRC South African Population Research Infrastructure Network. This is a long-term investment into a national research infrastructure, funded by the National Department of Science and Innovation (DSI) and hosted by the South African Medical Research Council. The eThekwini node of SAPRIN is **USINGA**.

RESOLVE is a randomized clinical trial to evaluate solutions for the management of virologic failure for individuals on TLD in Sub-Saharan Africa. The PI is Dr Susanne McCluskey of Harvard Medical School.