

Department of Pathology, Faculty of Medicine, University of Ruhuna

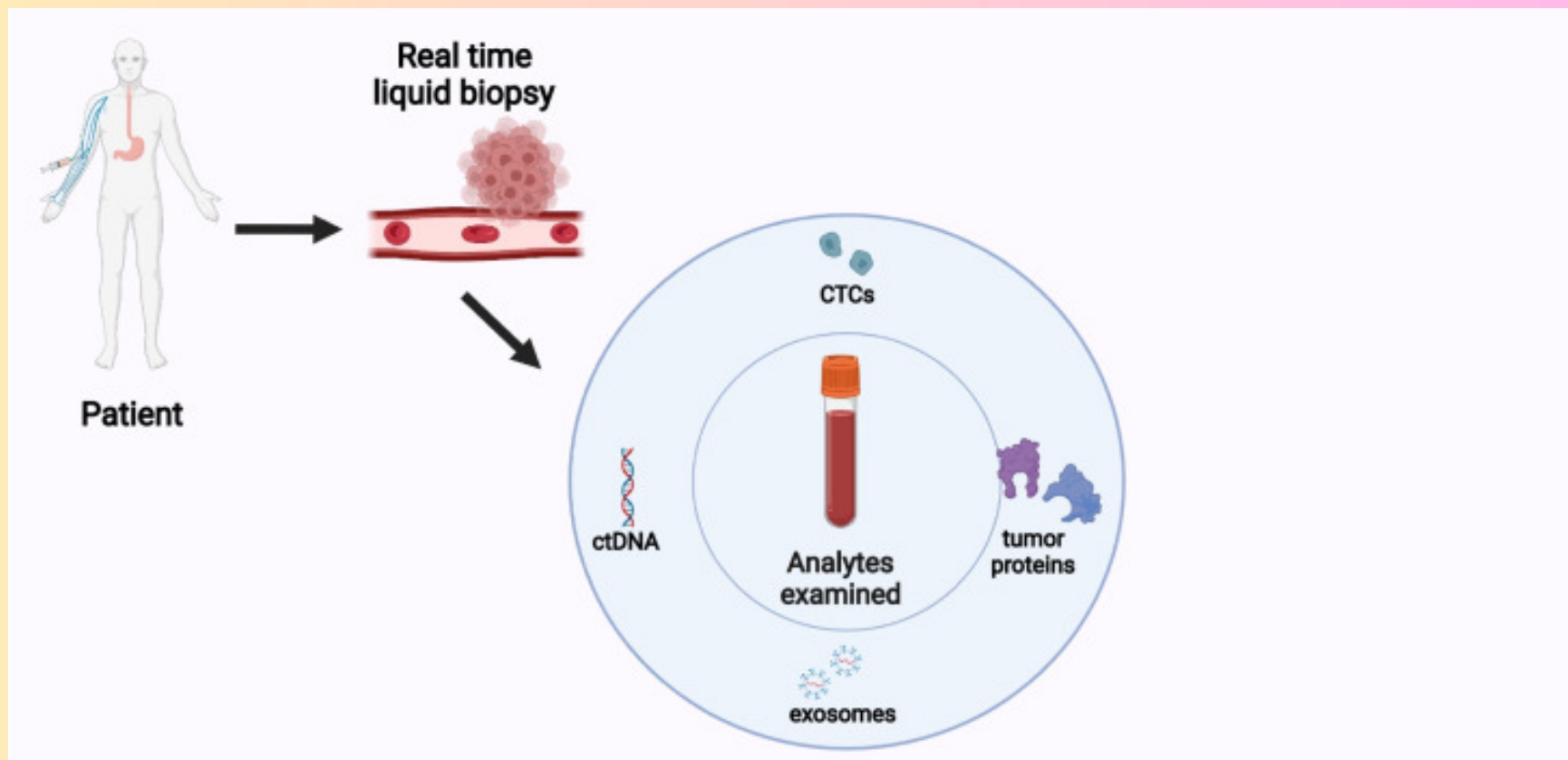


Figure 1. Entities analyzed in liquid biopsies and their application (Loan *et al.*, 2022).

“Breathing Myths to Life: Ondine's Curse Unveiled in the Tapestry of Respiratory Medicine”

One of the most captivating myths in medicine is the story of Ondine's curse. Once she fell in love, married, and had a child, the immortal water spirit Ondine transformed into a human being. According to one version of the story, she cursed her husband to stay awake so he could regulate his own breathing after discovering him having an affair. The unusual syndrome known as "Ondine's curse" was termed so ingeniously during the 19th century. It is characterized by the lack of autonomic breath control while voluntary respiration is preserved. Although congenital central hypoventilation syndrome is now commonly linked to the term "Ondine's curse," it also refers to a number of other respiratory conditions in medical research. The term "Ondine's curse" has been defined to a variety of respiratory dysfunction diseases in the medical literature; nevertheless, knowledge of it allows for early diagnosis and treatment, particularly to avoid abrupt death in infants.

(Demartini *et al.*, 2020)

Editorial Board

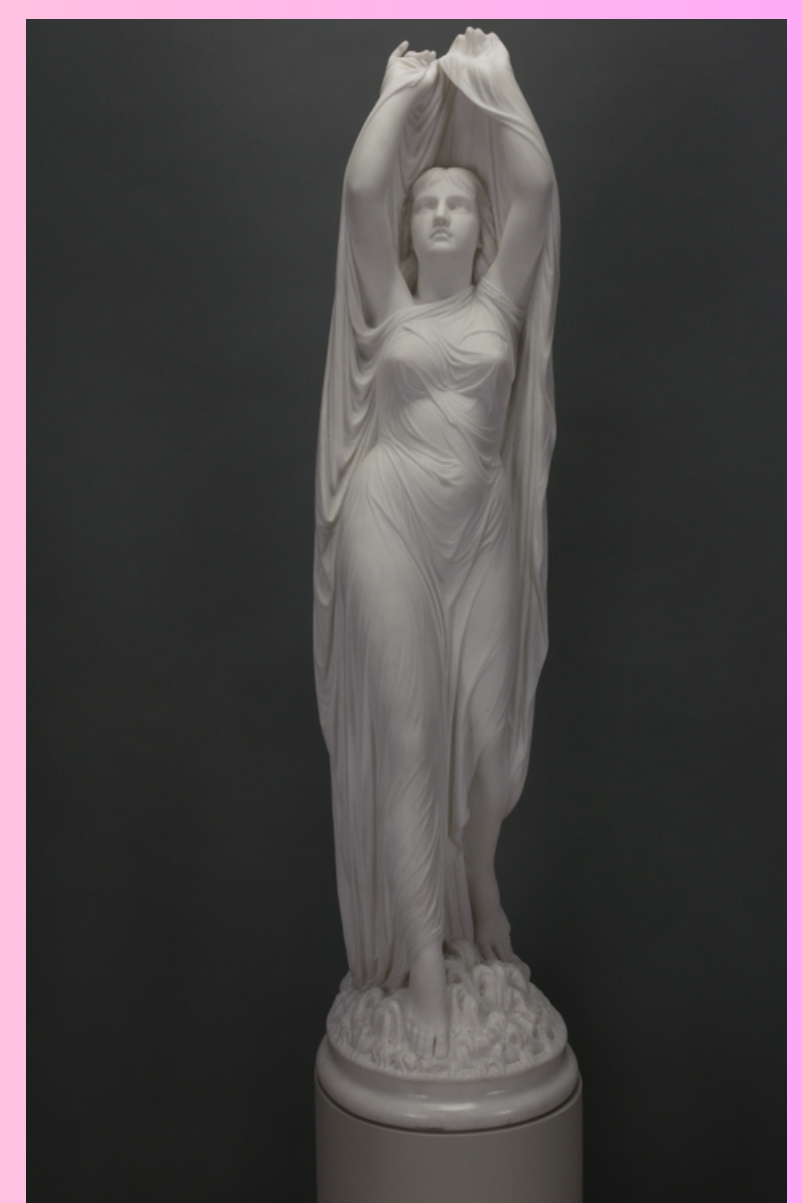
- Dr. Thusharie Liyanage
- Dr. T.W. Wijesiri
- Ms. W.G. Dinushi
- Ms. P.V. Vihanga Ranmini



(Medvision, 2019)

Contents:

01. Analysis of Physicochemical Parameters of Bee Honey	02
02. Aspartame in Food and its Health Implications	02
03. Are 'Night Owls' at Greater Risk of Type 2 Diabetes and Heart Disease than 'Early Birds'	03
04. Liquid Biopsy-Revolutionizing Cancer Detection and Monitoring	03
05. Risk Based Quality Improvement: Part 2	04
06. Exosomes for Diagnostic and Therapeutic Approach	04



(Chauncey Bradley, 2019)

Analysis of Physicochemical Parameters of Bee Honey

-Ms. W.G. Dinushi-

The primary constituents of bee honey, making up approximately 95% of its dry weight, are sugars. Interestingly, despite this high sugar content, bee honey has a lower glycemic index of 58 when compared to table sugar's index of 65. Consequently, consuming bee honey does not lead to rapid spikes in blood sugar levels, highlighting its potential as a healthier alternative to table sugar. This study aimed to explore the sugar composition and other physicochemical parameters of bee honey sourced from various geographical regions in Sri Lanka, selected based on their suitability for beekeeping. The analysis focused on parameters such as reducing sugars, apparent sucrose, the fructose-to-glucose ratio, and solid content. Statistical analysis, employing normality testing and LS-means separation within a General Linear Model framework, revealed significant variations in these parameters attributable to climate and floral origins in different locations. The findings underscore the importance of understanding honey's diverse profiles based on its origin, shedding light on the multifaceted benefits of substituting bee honey for table sugar. Furthermore, various properties like pH, conductivity, moisture content, acidity, and color intensity were assessed using established methodologies from the SLS institution. These properties also exhibited variations linked to geographical disparities, stemming from differences in floral sources, climate patterns, and agroecological zones. The findings underscore the importance of understanding honey's diverse profiles based on its origin, shedding light on the multifaceted benefits of substituting bee honey for table sugar. These findings are beneficial into increase the pharmaceutical and market value of bee honey.

Key References:

- de Sousa JM, de Souza EL, Marques G, de Toledo Benassi M, Gullón B, Pintado MM, Magnani M. Sugar profile, physicochemical and sensory aspects of monofloral honeys produced by different stingless bee species in Brazilian semi-arid region. *LWT-Food Science and Technology*. 2016 Jan 1;65:645-51.
- Dżugan M, Sowa P, Kwaśniewska M, Wesółowska M, Czernicka M. Physicochemical parameters and antioxidant activity of bee honey enriched with herbs. *Plant foods for human nutrition*. 2017 Mar;72:74-81

Aspartame in Food and Its Health Implications

-Ms. Vihanga Ranmini-

Aspartame, an artificial sweetener 200 times sweeter than sugar, is a common ingredient in various food and beverage products. Composed of two amino acids, aspartic acid and phenylalanine, it also yields a small amount of methanol during digestion. While widely used, aspartame has specific considerations. It loses sweetness at high temperatures, limiting its use in baking. The FDA has established an acceptable daily intake (ADI) of 50 mg/kg, but individuals with phenylketonuria (PKU) should restrict their aspartame consumption due to phenylalanine buildup. Health implications of aspartame include the risk to PKU sufferers, who can develop intellectual disabilities and other health problems from phenylalanine accumulation. Allergic reactions and sensitivities, manifesting as headaches or gastrointestinal disturbances, may occur. Neurological and psychological effects such as mood changes, cognitive issues, and headaches have also been reported. Recent concerns revolve around the potential carcinogenicity of aspartame. The World Health Organization (WHO) declared it a "possible" carcinogen based on limited evidence, specifically for hepatocellular carcinoma. While it falls under WHO's Group 2B classification ("possibly carcinogenic to humans"), the evidence remains inconclusive. WHO recommends a daily maximum of 40 mg/kg for aspartame but does not confirm it as a carcinogen. Consumers need not cease aspartame consumption but should be mindful of their intake. This abstract highlights the importance of informed choices regarding aspartame consumption and its potential health effects.

Key References:

- Aspartame hazard and risk assessment results released [Internet]. World Health Organization; 2023 [cited 2023 Oct 9]. Available from: <https://www.who.int/news/item/14-07-2023-aspartame-hazard-and-risk-assessment-results-released>
- Butchko HH, Stargel WW, Comer CP, Mayhew DA, Benninger C, Blackburn GL, de Sonneville LM, Geha RS, Hertelendy Z, Koestner A, Leon AS. Aspartame: review of safety. *Regulatory Toxicology and Pharmacology*. 2002 Apr 1;35(2):S1-93.

Are 'Night Owls' at Greater Risk of Type 2 Diabetes and Heart Disease than 'Early Birds'?

-Dr. Isuri Yasara-

Night Owls, individuals with delayed circadian rhythms who prefer staying up late, may face greater health risks compared to Early Birds with advanced circadian rhythms. Several factors contribute to these risks. Firstly, disrupted circadian rhythms in Night Owls can lead to irregular sleep patterns, potentially increasing the risk of metabolic disorders like Type 2 diabetes and obesity. Chronic sleep deprivation, often experienced by Night Owls due to societal demands favoring early waking times, can contribute to insulin resistance, a Type 2 diabetes risk factor, and other factors associated with heart disease. Unhealthy lifestyle factors, including dietary choices, physical activity levels, and stress, can also be influenced by night-oriented schedules. Additionally, exposure to artificial light at night disrupts melatonin production, affecting sleep quality and potentially contributing to metabolic disturbances. Genetic factors play a role in determining one's sleep pattern, with some genetic variations associated with both sleep patterns and an increased risk of metabolic conditions. Studies, such as "Association of Chronotype With Mental Health Disorders and Chronotype Genetic Instrument" and "Circadian Misalignment Increases Diabetes Risk," support a link between being a Night Owl and an increased risk of Type 2 diabetes. Factors like sleep deprivation, unhealthy lifestyle choices, and inflammation contribute to the higher risk of heart disease associated with Night Owls. To mitigate these risks, individuals should prioritize sleep, maintain a consistent sleep schedule, make healthy lifestyle choices, limit light exposure at night, and consider consulting a healthcare professional for personalized guidance.

Key References:

- Chantigian D. Night Owls Have Higher Chance for Type 2 Diabetes, New Study Finds Night Owls Have Higher Chance for Type 2 Diabetes, New Study Finds.
- Adams C. Night Owls Tend to Die Sooner, Suffer More Disease.

Liquid Biopsy-Revolutionizing Cancer Detection and Monitoring

-Dr. Madavi Baduraliyage-

Liquid biopsy is an emerging revolutionary non-invasive diagnostic tool in the field of medicine. This technique involves analysing specific biomarkers present in bodily fluids, primarily blood, for detecting and monitoring diseases. Currently, it has a primary focus on cancer. Unlike traditional tissue biopsies, liquid biopsies offer numerous advantages, including obtaining serial samples during treatment, providing valuable insights into tumour genomics, and offering a potentially more cost-effective alternative to tissue biopsy. Liquid biopsy's strength lies in its capacity to overcome the limitations of single-tissue biopsies. It offers a comprehensive view of tumour heterogeneity, a crucial factor in cancer progression and treatment response. It mainly analyses circulating cell-free DNA (cfDNA/ctDNA), circulating tumour cells (CTCs), and exosomes. Liquid biopsy provides a more dynamic and less invasive method for identifying tumour markers, monitoring treatment responses and detecting minimal residual disease. However, challenges include the potential to miss certain tumour biomarkers, test variability, and a need for more consensus in technical approaches. Nevertheless, the liquid biopsy field is rapidly evolving, with emerging technologies like single-cell analysis, digital PCR, and advanced sequencing platforms promising improved sensitivity, specificity, and overall performance. Moreover, the potential applications of liquid biopsy extend beyond cancer, encompassing infectious diseases, prenatal screening, and other medical conditions. So, in the near future, liquid biopsy will play a pivotal role in early disease detection and personalised medicine.

Key References:

- Lone SN, Nisar S, Masoodi T, Singh M, Rizwan A, Hashem S, El-Rifai W, Bedognetti D, Batra SK, Haris M, Bhat AA. Liquid biopsy: A step closer to transform diagnosis, prognosis and future of cancer treatments. *Molecular cancer*. 2022 Mar 18;21(1):79.

Risk Based Quality Improvement: Part 2

-Prof. K.A.C. Wickramaratne-

Here we focus more on Failure mode and effects analysis (FMEA) further. Indeed FMEA is useful even in day to day activities. Reflecting how a student can fail would enable him or her to focus on most important issues which is critically affecting performance at the examination. The same manner, the laboratories can explore how things can go wrong in all its processes which affect quality of results and consequences thereof. Laboratories can list all the key processes in its operations. E.g: Pre examination, examination, post examination, purchasing, environment maintenance, and waste management. The pre examination includes collecting, transporting and processing of samples. The “bad in bad out – good in good out” is fully applicable to testing. In FMEA, we should list how poor quality samples are generated. 70% laboratory errors are pre analytical. In histopathology, formal saline is required for specimen transport. Transport and storage of biopsies in normal saline is a major failure in pre analytical process. That causes deterioration of biopsy. Thus, even though likelihood of transport of biopsy in normal saline is infrequent, the consequences are serious. Inadequate awareness, and absence of formal saline supplies to the operating theatres are known to cause such mishaps. The laboratory can prevent it by providing sample containers filled with formal saline thus risk is eliminated. If laboratory provides formal saline solution uninterrupted to the theatre, a simple check list with few questions such as; have you filled the biopsy container with formal saline provided by the lab, is it the correct volume, is the biopsy totally immersed, and is the volume adequate will enable adherence to correct procedure and minimizing risk. Yet, we should be vigilant, and alert on potential mishaps thus management is a continuous process and indeed a brain work!

Key References:

- Key References: 1. ISO 15189:2022
- EP 23-A A practical guide for laboratory Quality Control Based on Risk Management
- EQUIP 7 ACHSi risk assessment and control

Exosomes for Diagnostic and Therapeutic approach

-Dr. S.D.M. Jayawardhana-

Exosomes, a subtype of extracellular vesicles (EVs), are gaining attention as promising tools for diagnostics and clinical applications. EVs, including exosomes, are nanosized lipid membrane vesicles released by cells into the extracellular space. They play crucial roles in intercellular communication, immune regulation, and disease progression. EVs are found in various bodily fluids, making them potential sources for disease biomarkers. Isolating EVs presents challenges due to their heterogeneity and the risk of contamination. Common isolation methods include ultracentrifugation, size-exclusion chromatography, tangential flow filtration, immunoaffinity, and precipitation. Each method has its advantages and drawbacks, making the choice of technique context-dependent. Exosomes have already shown promise in diagnostics, with a clinically approved test for high-grade prostate carcinoma. This non-invasive urine-based test relies on exosomal RNA isolation to create an EPI risk score. The precision medicine field also sees potential in EVs as biomarkers for monitoring disease microenvironments and assessing drug efficacy. Additionally, EVs hold therapeutic potential, with ongoing clinical trials for conditions like acute respiratory distress syndrome (ARDS). EVs can be engineered for drug delivery, improving precision and biodistribution, while their use in imaging applications enables the visualization and tracking of EVs in vivo, overcoming detection challenges. While there are still challenges to address, exosomes and EVs are emerging as valuable tools with a wide range of diagnostic and therapeutic applications.

Key References:

- Pegtel DM, Gould SJ. Exosomes. Annual review of biochemistry. 2019 Jun 20;88:487-514.
- Kalluri R, LeBleu VS. The biology, function, and biomedical applications of exosomes. Science. 2020 Feb 7;367(6478):eaau6977.