1

NZIMLS
THE NEW ZEALAND INSTITUTE OF MEDICAL LABORATORY SCIENCE

ISSN 1171-0195 VOLUME 78 • NUMBER 01 MARCH 2024

New Zealand Journal of Medical Laboratory Science

Official Publication of
The New Zealand Institute of
Medical Laboratory Science Incorporated

Nikon

ECLIPSE Ui

DIGITAL IMAGING MICROSCOPE

A Real Solution for Digital Pathology

LIVE ON-SCREEN OBSERVATION

Nikon's new ECLIPSE Ui Digital Upright Microscope provides accurate microscopy-based observation imaging. View and share high quality images in real time with easy-to-use software for a more streamlined workflow.

VIEW
Display high quality images in real time

FAST
Fast imaging for quicker workflow

USABILITY
User-friendly and simple for operational efficiency

NETWORK ACCESS
Digital medical system compatible with network for remote viewing and data sharing

EASY TO USE ON A DAILY BASIS
Functions to support multiple use cases and applications

Eclipse Ci-L Plus

Upright
Clinical
Microscope

Also available at
Abacus dx

Distributed by Abacus dx:
0800 222 170 | info@abacusdx.com | www.abacusdx.com

abacus dx
a partner you can count on

Editor
Lisa Cambridge, NZCS DipQA B.ApplManagement, MNZIMLS, NZIMLS, Rangiora

Deputy Editors
Michael Legge, PhD MRSB FIBMS FNZIMLS FFSc(RCPA), University of Otago, Dunedin
Holly Perry, DipMLS MAppSc(Hons) PhD MNZIMLS, University of Otago

Emeritus Editor
Rob Siebers, PGCertPH FNZIC FNZIMLS FRSB HonFNZAP, Wellington

Editorial Board
Paul Austin, MSc(Hons) DipMLT MNZIMLS, LabPlus, Auckland
Jillian Broadbent, FNZIMLS, NZIMLS, Rangiora
Julie Creighton, DipMLS, FNZIMLS, Canterbury Health Laboratories, Christchurch
Sujata Hemmady, PGDipMLSc, MMLSc, MNZIMLS, LabPlus, Auckland
Chris Kendrick, GradDipSci MSc MNZIMLS, Massey University, Palmerston North
Craig Mabbett, BMLSc PGDipHSM, LabCare Pathology, New Plymouth
Holly Perry, DipMLS MAppSc(Hons) PhD MNZIMLS, University of Otago
Mohd. Shahid, MBBS MD PhD FNZIMLS, PGDipHSM, Arabian Gulf University, Bahrain
Terry Taylor, BSc DipMLS MNZIMLS, Southern Community Laboratories, Dunedin
Sharon Tozer, DipBis Stud, AT CAANZ, NZIMLS, Rangiora
Robyn Wells, BApllSci(MT) GradCert Haem, Milton, Australia

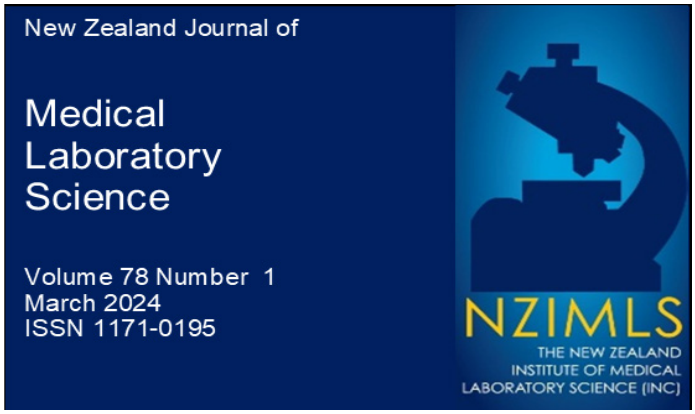
Formatting
Sharon Tozer, AT DipBusStud, Executive Office NZIMLS, Rangiora

About the Journal
The New Zealand Journal of Medical Laboratory Science (the Journal) is the official publication of the New Zealand Institute of Medical Laboratory Science (NZIMLS). The Journal is peer reviewed and publishes original and review articles, case studies, technical communications, and letters to the Editor on all subjects pertaining to the practice of medical laboratory science. The Journal is open access (www.nzimls.org.nz/nzimls-journal) and is published three times per year in March, July, and November. Hard copies are circulated to all NZIMLS members and universities and research units in New Zealand and overseas. Current circulation is about 2,800 copies per issue. Printing is by Blueprint Ltd, Christchurch on environmentally responsible paper using elemental chlorine free third party certified pulp sourced from well managed and legally harvested forests and manufactured under the strict ISO14001 Environmental Management System. The Journal is indexed by CINAHL, EMBASE, SCOPUS, Informit, Thomson Gale, EBSCO and Biosis Citation Index, and the Journal Editors are members of the World Association of Medical Editors (www.wame.org).

Brief instructions to authors
The Journal accepts original submissions from anyone and anywhere. Comprehensive instructions can be found on the NZIMLS website (www.nzimls.org.nz/instructions-to-authors.html). All submissions will undergo single-blind peer review and possibly plagiarism checking with iThenticate™ software. If accepted for publication, copyright is vested in the author(s) under terms of the Creative Commons Attribution License (www.creativecommons.org/licenses/by/2.5/legalcode). The authors are responsible for the scientific content and views. Opinions expressed in the Journal are not necessarily those of the Editors, Editorial Board, or Council of the NZIMLS.

Advertising and subscription
Advertisement bookings and enquiries should be addressed to the NZIMLS Executive Officer, Sharon Tozer: sharon@nzimls.org.nz. Phone +64 3 313 4761.

Journal cover © Joseph Manieda, Te Whatu Ora Hawke's Bay



In this issue

For the first issue of 2024, we have an absolute star cast of New Zealand authors and articles from New Zealand Medical Laboratories as well as news and events from within the profession and around the country.

I share my thoughts on sustainability initiatives in the New Zealand healthcare sector in the Editorial, looking to understand how government legislation is being interpreted by the healthcare providers and question what can be done to support the implementation of green initiatives into clinical laboratories.

New information about blood group systems and antigens are presented regularly in the literature but not collated into a single text resource. Natalya Clark and Holly Perry from the University of Otago developed a review collection of 122 blood group antigens and 17 blood group systems that have been described in the past 20 years (2003-2023), including genetic basis of variants and the clinical significance of their antibodies where known. Reports showed that blood group systems have a high degree of polymorphism in a large and heterogenous human population, with new variants appearing on a continuous basis. These descriptions, carefully tabled, together with an extensive literature review and an emphasis on clinical practice, provide a useful resource for practising transfusion scientists.

In our second blood group system article, Rei Miyamoto, from the University of Otago and a NZIMLS top student award winner for 2023, reviews the MNS blood group system in the context of transfusion science. This large and important system of polymorphic, high and low frequency antigens are formed through genetic recombination, unequal crossing over, gene conversion and SNPs, as well as the interesting phenotypic frequencies among population groups. In transfusion science, many of the human blood group systems have alloantibodies that are clinically significant with the potential to cause adverse events during blood transfusions. Miyamoto describes the diverse molecular and immunological properties that the MNS blood group system exhibits and emphasizes the importance of matching MNS blood groups for patients requiring blood transfusion in whom atypical clinically significant alloantibodies of the MNS system have been encountered and can cause transfusion reactions or hemolytic transfusion disease (HTR) of the fetus and newborn (HDFN).

Leptospirosis is an illness caused by infection with pathogenic spirochaetes of the Leptospira genus and a notifiable disease in New Zealand. Hall and colleagues from Pathlab, and ESR in the Waikato present a review of ten years of Leptospira serology and PCR testing within New Zealand to identify and report the most sensitive testing strategy. A typically zoonotic transmission, Leptospirosis causes a biphasic illness with a range of presentations that are nonspecific and variable, making the infection difficult to identify by clinical presentation alone. Using a retrospective review of serology and PCR results over a ten period, analysing Leptospira IgM and PCR test data from 3,344 patients they determined the utility and value of the different tests available to determine what strategies have been the most effective in detecting leptospirosis. Results of this study recommend a combination of PCR and well-timed serology to be the most effective testing strategy as no one test captures all clinical cases.

Can the use of triglyceride to glucose and triglyceride to high density lipoprotein ratios indicate metabolic syndrome in the spinal cord injured male? This is the question posed by Jones and Legge from the School of Physical Education and Department of Biochemistry at the University of Otago in an original study. Spinal cord injury resulting in paralysis causes significant changes in body composition below the lesion, loss in motor function leads to skeletal muscle wasting and fat mass increase above and below the lesion and contributes to major metabolic changes strongly associated with cardiovascular disease and the development of factors associated with metabolic syndrome including, glucose intolerance, hyperinsulinaemia, insulin resistance and dyslipidaemia. The investigation of TyG:G and TyG:HDL ratios in twenty matched controls and twenty spinal cord injured males identified significant differences between spinal cord injured complete and spinal cord injured incomplete, concluding that the level of de-innervation has a significant role in the onset of metabolic syndrome in the spinal cord injured.

Dennis Mok from Australia and his global colleagues report on the implementation and International Standard (ISO) requirements of laser warning markings for equipment and instruments in the New Zealand diagnostic laboratory. The objective in their scientific letter is to enhance the awareness of requirements related to risk control measures and present the accepted warning markings for Class1 to Class 4 laser equipment that must be clearly visible. Images of the warning markings can be found in the supplementary material on the Journal website.

Michael Legge shares his book review for; “Most delicious poisons: the story of nature’s toxins from spices to vices” by evolutionary biologist, Noah Whiteman.

A briefing for the incoming minister and associate ministers was prepared by the NZIMLS Council in November 2023 and was submitted to the incoming government ministers of health as a way of directly communicating and outlining issues in the profession. This briefing is republished in this issue for NZIMLS members.

NZIMLS President, Tony Barnett, remembers Paul McLeod, a past NZIMLS president, long-serving Medical Laboratory Scientist and life member, who passed away in June 2022.

Convenors report on Special Interest Group seminars (SIG) held and enjoyed around the country in October and November 2023. Meetings included; Anatomical Pathology, AACB/Biochemistry, Molecular Diagnostics, Microbiology, and Preanalytical, with topics presented by members and invited guests. Participants enjoyed interesting presentations, discussions, catching up with colleagues over the sharing of food.

As well as our regular features; Science Digest, Recent Reviews, Journal Citations and the Pacific Way we share interesting interviews with the three recipients of the NZIMLS Top Student Award for 2023, Alejandra Walker, Lillian Birkett and Rei Miyamoto. These graduates are an inspiration to the profession, with wonderful enthusiasm and energy that will be welcomed wherever they land.

Lisa Cambridge
Editor

Sustainability and green laboratory practices

Lisa Cambridge

Healthcare systems contribute an estimated 4-5% of greenhouse emissions globally, in New Zealand this figure has been reported at between 3-8% and is the largest emitter (excluding transport) in our public sector (1). Healthcare facilities operate 24/7 with a large footprint that impacts the environment, generating large quantities toxic and non-biodegradable waste, consuming high amounts of energy, emitting greenhouse gases and consuming vast quantities of water (Table 1).

Table 1. Laboratory-attributed emissions

Energy & greenhouse gas emission	Water consumption
– Cold storage, refrigerants – Transport – Equipment – Climate control, air conditioning, insulation – Lighting – Computers, systems hardware and storage – Medical gases *Labs consume 5-10x more energy than Equiv. sized office**	– Heating and cooling equipment – Washing, cleaning – Reagents *Up to 60% of water usage in buildings by laboratories* autoclaves can use up to 227L water per cycle⁺*
Chemicals & materials	**Waste**
– Reagents – Catalysts – Washing, cleaning and flushing – Gases, metals – Paper and printing supplies *Implications for wider pollution of air, water and soil*	– Single-use plastics (e.g. gloves, syringes, pipette-tips, culture plates) – Biological, medical waste – Packaging *Biological, medical or agricultural research waste est. ~5.5Mt of lab plastic waste/year or 2% total global plastic waste**

*Royal Society of Chemistry (6), ⁺ My Green Lab (5), Mt = metric tonne

Unequivocal scientific evidence on the detrimental impact of human activity on the planet and the critical environmental tipping points (2), shows that the planet may never recover. On a global scale, conversations, policy and government-initiated projects for reducing emissions have gained significant momentum since the 196 countries, including New Zealand, signed the Paris Agreement (2015) at the UN Climate Change Conference (COP21). As part of this agreement, the New Zealand government committed to reducing our greenhouse gas emissions to 30% below 2005 levels, by 2030 and amending legislation and establishing a Climate Change Commission. Climate-related Disclosures and Other Matters Amendment Act (2021), requires mandatory climate-related reporting and disclosure by publicly listed companies, such as insurers and banks. The Ministry of Health requires the healthcare sector to report its sustainability actions and goals in annual planning and budgeting to meet the Climate Change Response (Zero Carbon) Amendment Act (2019) legislation.

Te Whatu Ora released its baseline Greenhouse Gas Emissions Inventory Report in September 2023 (1), quantifying emissions including; gas (medical and industrial), electricity, transport and waste directly attributed to their operations and reporting a 10.3% decrease in CO_2 emissions between 2019 and 2020. However, they did not provide a breakdown of emissions attributed to clinical laboratories in its charge nor address laboratories specifically in their guidance material (3), released in September 2023 as a; “guide to support and encourage the New Zealand health sector to take an active role in implementing sustainability as integral part of its practice.”

How many of these types of reports and guidelines are paying lip-service to the Acts without taking practical steps towards sustainability for the planet? Or provide the teeth to make decisions, offer effective solutions, resources and assistance to clinical laboratories to meet these initiatives?

Is it too little too late? Afterall we are a mere six years away from this committed target. Statistics NZ reported in 2020 that New Zealand’s gross greenhouse emissions showed no sustained reduction when compared with 2005 figures (4). Has sustainability been given the sense of urgency and priority that it deserves?

The guidelines only serve to put the onus back on hospitals, laboratories and primary healthcare providers to do all the heavy lifting. As we dive into 2024, the medical laboratory profession and healthcare services in New Zealand remain in crisis. Any management plans to minimise emissions, reduce waste and implement green practices, will ultimately fail, if they compound upon already untenable workloads and pressure for the current healthcare workforce, without providing sufficient and additional resourcing and opportunities.

The creation of sustainable and green practices in laboratories requires a multidisciplinary approach that cannot be undertaken solely by the laboratories and quality managers but involves sweeping changes to company culture from the top down. Healthcare management must provide the influence, financial support and provision of dedicated resources. Organisations need to establish networks across different business sectors (e.g. construction (energy efficient building /laboratory design), transport, supply chains, suppliers and manufacturers), coordinate rollout of new technologies, advocate for change across healthcare professions and researchers, promote and recognise achievement by rewarding laboratories for their sustainability initiatives, negotiating shared spaces and pooling resources, securing public funding for green initiatives and offering sustainability education in academic degree courses.

There are established certification routes, for example; Liggins Institute Laboratory, at the University of Auckland, is the first university research laboratory in New Zealand to achieve ‘My Green Lab’ certification (5) in 2022. In March 2022, the Awanui pathology group obtained Carbon Reduce Certification *(emissions to ISO14064-1 requirements)* from Toitū Envirocare (www.toitu.co.nz). But for most laboratories, it is more practical to develop steps, targets and measures to reduce energy

emissions, chemical and material use, waste and water usage as they apply to their own workflows. Multiple online resources provide tips, tools, networking and interactive guides to get the green ball rolling, including, My Green Lab (5), the Royal Society of Chemistry (6) and labconscious (www.labconscious.com). Literature also provides an increasing number of studies and commentaries for clinical laboratories, for example, Lopez (7) presented methods to review current lab operation and introduce sustainable practices using the quality improvement model PDCA tools to develop key targets and actions.

There is wide agreement and good-will amongst laboratory and healthcare workers to reduce the impact of their work on the environment. Healthcare professionals are astutely aware of the barriers and challenges for a working clinical laboratory and the compromises between implementing sustainability actions and ensuring the health and safety of workers, patients and the public, and maintaining testing efficacy, quality and throughput. Consultation across and up and down the sector during planning and implementation is crucial, as will buy-in and participation in any decision-making and implementation.

In the same way that confusing and inconvenient recycling instructions imposed by local government are causing green or recycling fatigue that threaten our eco-friendly behaviour in the community, overly complex measures, under resourcing, impossible targets and poor management will only serve to further erode the goodwill of the profession and fail to implement sustainable and green practices that the healthcare sector and the planet cannot afford to lose.

Author information: Lisa Cambridge, B.Appl.Management, DipQA, NZCS, MNZIMLS, Editor, NZIMLS.
Email: editor@nzimls.org.nz

REFERENCES

1. Geesink M, Te Whatu Ora - Health New Zealand. Greenhouse gas emissions inventory report – FYI2022/23 baseline year. Te Whatu Ora 2023. Available from: https://www.tewhatuora.govt.nz/publications/greenhouse-gas-inventory-report/
2. Lenton TM, McKay D, Loriani S et al (eds.) The global tipping points report. University of Exeter, Exeter, 2023. Available from: www.global-tipping-points.org/
3. Te Whatu Ora – Health New Zealand. Sustainability and the health sector: a guide to getting started. Te Whatu Ora, Wellington, 2023. ISBN:9781991067616.
4. Stats NZ. New Zealand greenhouse gas emissions. Stats NZ, Wellington 2022. [cited January 2024] Available from: www.stats.govt.nz/indicators/new-zealands-greenhouse-gas-emissions
5. My Green Lab. [cited January 2024] www.mygreenlab.org
6. Royal Society of Chemistry. Sustainable laboratories: a community-wide movement toward sustainable laboratory practices. [cited January 2024] Available from: www.rsc.org/policy-evidence-campaigns/environmental-sustainability/sustainability-reports-surveys-and-campaigns/sustainable-laboratories/
7. Lopez JB, Jackson D, Gammie A and Badrick T. Reducing the environmental impact of clinical laboratories. *Clin Biochem Rev* 2017: 38(1): 3-11.

Copyright: © 2024 The author(s). This is an open-access article distributed under te terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

Call for nominations for Life Membership of the NZIMLS

The Council of the New Zealand Institute of Medical Laboratory Science (Inc.) (NZIMLS) is calling for nominations for suitable candidates for Life Membership. A Life Member is any member of the NZIMLS who the Council considers has given outstanding service to the Institute of Medical Laboratory Science (typically but not exclusively) who notwithstanding anything to the contrary in these rules shall retain the privileges of his/her previous category of membership.

Guidelines for Life Membership:
Worthy or notable services to our profession and/or Institute may be included but will be limited to any/some/all of the following:

- Leader and/or recognised expert in a scientific field or topic.
- Publications
  - preferably in the NZ Journal of Medical Laboratory Science
  - preferably of leading or educative articles
- Oral Presentations
  - preferably to share knowledge with colleagues in the fora of the ASM and SIG meetings.
- Voluntary contributions to Institute activities, e.g. Council, SIGs, Conferences etc.
- Special projects
  - technical
  - professional
- Other areas considered relevant by nominators.
- To be eligible for Life membership nominees will be financial members of the Institute. The length of membership service will be considered.

Nominations for Life Membership should be with the Executive Officer no later than 31 January for the current year.

Please email the Executive Officer for a nomination form: sharon@nzimls.org.nz or download from our website.

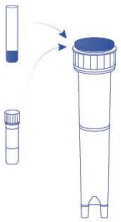
USTAR 优思达
Molecular Testing Anywhere

Quick Results - On Demand

Ustar's Point Of Care Testing (POCT) kits integrate
nucleic acid extraction, purification, amplification and test in an enclosed cartridge
to achieve a fast, accurate, simple and safe test with LOD≤200 copies/mL.

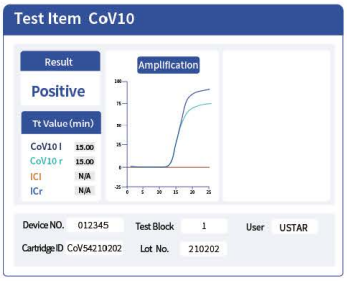
Testing Procedure

1 Load Sample



2 Insert Cartridge

3 Report Result



bio-strategy
Part of DKSH Group

Bio-Strategy Limited
T 0800 34 24 66 | sales.nz@bio-strategy.com
www.bio-strategy.com | shop.bio-strategy.com

REVIEW ARTICLE

Blood group systems and antigens described in the last 20 years: an update

Natalya J Clark and Holly E Perry

ABSTRACT

Objectives: New information about blood group systems and antigens appears frequently but has not been recently collated as a single text. Books such as the *Blood Group Antigen FactsBook* by Reid, Lomas-Francis and Olsson provide an excellent reference source. However, the last edition was released a decade ago, and much has been discovered since then. New information is used to review requirements for red cell antibody screening cells, maintain rare donor databases, monitor clinical events and educate practitioners. The aim of this study was to summarise information elucidated in the past 20 years, with emphasis on significance in clinical practice. We aimed to provide a resource that may be useful to practising transfusion scientists.

Methods: Information was gathered by literature search.

Results: 122 blood group antigens and 17 blood group systems were described in the past 20 years (2003 – 2023). 31 antibodies were either implicated in transfusion reactions or haemolytic disease of the fetus and newborn or were considered to have the potential to cause these events.

Conclusion: Discovery and elucidation of blood group systems continues. Due to the rarity of clinical events, the clinical significance of many of the newer antigens and antibodies described is not yet certain. Nevertheless, it is important for transfusion scientists to be aware of new blood groups and monitor the likelihood of antibodies to cause transfusion reactions and/or haemolytic disease of the fetus and newborn. This literature review provides an update for transfusion scientists.

Key words: Blood group antigen, Rare blood group antibodies

NZ J Med Lab Sci 2024; 78(1): 06:19

INTRODUCTION

Blood group antigens are inherited markers found on surfaces including the red blood cell membrane. Corresponding antibodies can have a range of clinical effects, including haemolytic transfusion reactions (HTR), haemolytic disease of the fetus and newborn (HDFN) and autoimmune haemolytic anaemia (AIHA).

The International Society of Blood Transfusion (ISBT) classifies all known blood group systems and antigens. It defines a blood group system as a genetically discrete system of "one or more blood group antigens that are related by one gene, or one complex of two or more closely linked genes that are homologous" (1). A homolog is a gene that has a very similar nucleotide sequence to another gene.

There are several blood group antigens that cannot currently be classified as a system based on ISBT requirements. These form the 700 series (low prevalence antigens found at a population frequency of <1%), the 901 series (high prevalence antigens found at a population frequency of >90%) and independent collections which contain antigens that are related, but not yet fully elucidated at a genetic level (1).

Blood group systems frequently arise from an ancestral gene coding for a protein on the red cell surface, and polymorphisms are the result of single nucleotide changes. For example, in the Duffy system, the gene is FY and the reference allele is FY*02 (Fy^b), which encodes 4 antigens on the Duffy glycoprotein, a receptor for chemokines. FY*01 (Fy^a) arises from a change at nucleotide 125, producing an amino acid (aa) change at aa42 (2). Single nucleotide polymorphisms (SNP) are responsible for most of the variation in blood groups.

Hybrid genes are responsible for the high degree of these polymorphism seen in the Rh and MNS blood group systems. These genetic variants occur at different frequencies around the world due to both selective pressures and geographic isolation. Null phenotypes (where no blood group structure in a system is present on the red cell) may be associated with a survival advantage. For example, Duffy null provides protection against some species of malaria; lacking the Duffy glycoprotein on the cell surface removes the ability of the parasite to bind and invade the red cell (2). Consequently, Duffy null is rare in countries where malarial parasites are absent, but common in malaria-endemic countries (3).

Advances in molecular technology in the past 20 years have greatly assisted the modern description of blood groups and allow classification of systems and antigens based on their exact genetic basis. As of December 2023, there were 49 genes determining 45 blood group systems and 360 blood group antigens, as well as 33 blood group antigens that have not yet been classified into a blood group system (1). Of these, 17 blood group systems and 122 blood group antigens were discovered in the last 20 years (2003 – 2023).

This report provides an update on the blood group antigens that have been described in the last 20 years, including genetic basis of variants and the clinical significance of their antibodies where known.

MATERIAL AND METHODS

A rigorous systematic literature search of the Wiley Online Library was performed, focusing on three journals: *Vox Sanguinis*, *Transfusion* and *Transfusion Medicine*. Information was also gathered from the Blood Group Antigens FactsBook (3rd ed.) and the Genome Aggregation Database (gnomAD) (4). ISBT nomenclature was used.

Data is presented in two sections: additions to systems and new systems. Data is tabulated throughout, with the column "clinical significance" referring to the reported potential of the antibody to the antigen described to cause haemolysis. The word "new" refers to antigens or systems described since 2003. Although some antigens described have been known for many years, the "year described" in tables refers to the year the antigen was fully elucidated at a genetic level. Where antigen frequencies are known to differ in different regions, more than one frequency is provided. When a single figure is given, it is assumed that antigen frequency is similar across many populations (4).

RESULTS

122 blood group antigens and 17 blood group systems were described in the past 20 years (2003 – 2023). Of these, the following have antibodies that are either clinically significant, or potentially clinically significant but infrequent: ENEV (MNS45), SARA (MNS47), P^k (P1PK3), CETW (RH63), VONG (KEL28), KEAL (KEL39), KHOZ (KEL41), DISK (DI22), YTGT (YT6), SCAN (SC7), SCAC (SC9), DOMR (DO7), GECT (GE13), INFI (IN3), PX2 (GLOB4), DSLK (RHAG3), Kg (RHAG5), THIN (RHAG7), Jr^a (JR1), Lan (LAN1), Vel (VEL1), At^a (AUG2), ATML (AUG3), ATAM (AUG4), Sd^a (SID1), MAM (MAM1), Emm (EMM1), Er3 (ER3), ERSA (ER4), ERAMA (ER5) and CD36.1. Anti-Kg, anti-Jr^a, anti-Lan, anti-Vel, anti-At^a and Anti-Sd^a were clinically significant antibodies seen in multiple clinical cases. These six antibodies were discovered more than 20 years ago, but the respective blood group systems were fully elucidated more recently.

Section 1. Additions to Blood Group Systems

002 - MNS

Table 1. New antigens in the MNS system (5-12)

Name	#	Year Described	Antigen frequency	Clinical significance
ENDA	44	2008	>99%	Unknown
ENEV	45	2010	>99%	Mild HTR
MNTD	46	2006	<1%	Unknown
SARA	47	2014	<1%	Severe HDFN
KIPP	48	2015	<1%	Unknown
JENU	49	2016	Most populations >99% Less frequent in Southeast Asians	Unknown
SUMI	50	2020	<1%	Unlikely

ENDA, KIPP and JENU are the result of hybrids between Glycophorin A (GYPA) and Glycophorin B (GYPB), while ENEV, MNTD, SARA and SUMI are the result of SNPs. One antithetical pair of antigens was discovered: ENDA with DANE (MNS32, previously described).

One antigen, SARA, was previously assigned 700.052, and moved to the MNS blood group system when its genetic basis was identified. It is a low prevalence antigen found in one Australian and one Canadian family, and its antibody has caused severe HDFN in one newborn (9).

003 - P1PK

Table 2. New antigens in the P1PK system (2, 13-14)

Name	#	Year Described	Antigen frequency	Clinical significance
P^k	3	2010	>99%	Probable
NOR	4	2012	<1%	Unknown

The P1PK system was renamed from P after the P and P^k antigens were found to be tied to the same gene - Alpha 1,4-Galactosyltransferase (*A4GALT*), which is found on 22q13.2 chromosome (2). During this change, P^k (P1PK3) was moved from the now obsolete Globoside collection into the P1PK system. Globoside is now a blood group system in its own right. (system 028, Table 18).

P^k (previously 209.002) is only expressed strongly on the cells of P_1^k and P_2^k individuals (2). Inactivating mutations in the B3GALNT1 gene cause an increase in expression of P^k. Rare inactivating mutations in *A4GALT* lead to the P^k negative null phenotype (p). Anti-P^k is usually found alongside anti-P and anti-P1 (anti-PP1P^k), which can cause severe transfusion reactions, spontaneous abortions and HDFN (2).

004 - Rh

Table 3. New antigens in the Rh system (15-22)

Name	#	Year Described	Antigen frequency	Clinical significance
CENR	56	2004	<1%	Unknown
CEST	57	2009	>99%	Unknown
CELO	58	2011	>99%	Unknown
CEAG	59	2015	>99%	Unknown
PARG	60	2017	<1%	Unknown
CEVF	61	2013	<1%	Unknown
CEWA	62	2012	>99%	Unknown
CETW	63	2021	<1%	HDFN

CENR, CEST, CELO, CEAG, PARG and CEVF are caused by hybrid RHCE alleles, while CEWA and CETW are the result of SNPs in *RHCE*. Two antithetical pairs of antigens were discovered: CEST and JAL (RH48), and CELO and Crawford (RH43).

Of the eight antigens recently assigned to the Rh blood group system, only CETW is known to be clinically significant, having caused HDFN in one indigenous Australian newborn (22).

005 - Lutheran

Table 4. New antigens in the Lutheran system (23-30)

Name	#	Year Described	Antigen frequency	Clinical significance
LURC	22	2009	>99%	Unknown
LUIT	23	2023	>99%	Unknown
LUGA	24	2023	>99%	Unknown
LUAC	25	2016	>99%	Unknown
LUBI	26	2016	>99%	Unknown
LUYA	27	2018	>99%	Unknown
LUNU	28	2019	>99%	Unknown
LURA	29	2019	>99%	Unknown
LUOM	30	2023	>99%	Unknown

All new antigens in the Lutheran blood group system are the result of SNPs in Basal Cell Adhesion Molecule (*BCAM).*

LUAC has some relevance to New Zealand, as its antibody was found in a Māori patient in Auckland (26). Its clinical significance is unknown.

006 - Kell

Table 5. New antigens in the Kell system (31-43)

Name	#	Year Described	Antigen frequency	Clinical significance
VONG	28	2003	<1%	Mild HDFN
KALT	29	2006	>99%	Unknown
KTIM	30	2006	>99%	Unknown
KYO	31	2006	Most populations <1% Japanese 1.5%	Unknown
KUCI	32	2013	>99%	Unknown
KANT	33	2013	>99%	Unknown
KASH	34	2010	>99%	Unknown
KELP	35	2010	>99%	Unknown
KETI	36	2011	>99%	Unknown
KHUL	37	2011	>99%	Unknown
KYOR	38	2012	<1%	Unknown
KEAL	39	2016	<1%	Severe HDFN
KHIZ	40	2022	>99%	Unknown
KHOZ	41	2022	<1%	HTR

All new antigens in the Kell blood group system are the result of SNPs in Kell metallo-endopeptidase (*KEL*); KELP is unique in that it is a result of two separate SNPs in *KEL*. Four pairs of antithetical antigens have been identified; VONG with VLAN (KEL25, previously identified), KYO with KYOR, KHUL with KEAL, and KHIZ with KHOZ.

010 - Diego

Table 6 New antigens in the Diego system (44,45)

Name	#	Year Described	Antigen frequency	Clinical significance
DISK	22	2010	>99%	Probable
DIST	23	2021	<1%	Unknown

Both new antigens in the Diego blood group system are the result of SNPs in Solute Carrier Family 4 Member 1 (*SLC4A1*). DISK is antithetical to Wu (DI9). Anti-DISK was found in an Irish proband after she miscarried, but its clinical relevance to the miscarriage was uncertain (44).

011 - Yt

Table 7. New antigens in the Yt system (46-48)

Name	#	Year Described	Antigen frequency	Clinical significance
YTEG	3	2017	>99%	Unknown
YTLI	4	2018	>99%	Unknown
YTOT	5	2018	>99%	Unknown
YTGT	6	2022	>99%	HTR

All new antigens in the Yt blood group system are the result of SNPs in *acetylcholinesterase (ACHE)*. Anti-YTGT was found in two unrelated Native American patients, one of whom experienced an acute HTR following transfusion (48).

013 - Scianna

Table 8 New antigens in the Scianna system (49-52)

Name	#	Year Described	Antigen frequency	Clinical significance
STAR	5	2005	>99%	Unknown
SCER	6	2005	>99%	Unknown
SCAN	7	2005	>99%	HTR
SCAR	8	2020	>99%	Unknown
SCAC	9	2022	>99%	Probable

All new antigens in the Scianna blood group system are the result of SNPs in Erythroblast Membrane Associated Protein (*ERMAP*).

In vitro tests suggest anti-SCAR is unlikely to be clinically significant, and there was no evidence of haemolysis after one SCAR negative proband received an antigen mismatched transfusion (51). However, the patient was receiving hydroxyurea at the time and may have otherwise developed anti-SCAR at high enough titres to be clinically significant.

014 - Dombrock

Table 9. New antigens in the Dombrock system (53-57)

Name	#	Year Described	Antigen frequency	Clinical significance
DOYA	6	2010	>99%	Unknown
DOMR	7	2010	>99%	Possible HDFN
DOLG	8	2011	>99%	Unknown
DOLC	9	2013	>99%	Unknown
DODE	10	2015	>99%	Unknown

All new antigens in the Dombrock blood group system are the result of SNPs in ADP-Ribosyltransferase 4 (*ART4*); DOMR is the result of two SNPs in *ART4*. Anti-DOMR caused a positive DAT, jaundice and reticulocytosis in a newborn (54).

015 - Colton

Table 10. New antigens in the Colton system (58)

Name	#	Year Described	Antigen frequency	Clinical significance
Co4	4	2010	>99%	Unknown

Co4 is the result of a SNP in Aquaporin 1 (*AQP1*).

016 - Landsteiner-Wiener

T**able 11.** New antigens in the Landsteiner-Wiener system (59)

Name	#	Year Described	Antigen frequency	Clinical significance
LWEM	8	2022	>99%	Unknown

LWEM is the result of a SNP in Intercellular Adhesion Molecule-4 (*ICAM4*).

020 - Gerbich

Table 12. New antigens in the Gerbich system (60-63)

Name	#	Year Described	Antigen frequency	Clinical significance
GEIS	9	2004	<1%	Unknown
GEPL	10	2008	>99%	Unknown
GEAT	11	2008	>99%	Unknown
GETI	12	2008	>99%	Unknown
GECT	13	2020	>99%	HTR
GEAR	14	2016	>99%	Unknown

All antigens in the Gerbich blood group system are the result of SNPs in Glycophorin C (*GYPC*).

021 - Cromer

Table 13. New antigens in the Cromer system (64-71)

Name	#	Year Described	Antigen frequency	Clinical significance
SERF	12	2004	>99%	Unknown
ZENA	13	2007	>99%	Unknown
CROV	14	2007	>99%	Unknown
CRAM	15	2007	>99%	Unknown
CROZ	16	2010	>99%	Unknown
CRUE	17	2012	>99%	Unknown
CRAG	18	2012	>99%	Unknown
CROK	19	2012	>99%	Unknown
CORS	20	2020	>99%	Unknown

All new antigens in the Cromer blood group system are the result of SNPs in Decay accelerating factor (*DAF)*. Anti-CRUE was found in Auckland in a Thai patient (68)

022 - Knops

Table 14. New antigens in the Knops system (72-76)

Name	#	Year Described	Antigen frequency	Clinical significance
KCAM	9	2005	Caucasians 98% West Africans 20%	Unknown
KDAS	10	2020	Europeans 39% Africans 95.8% South Asians 67.7%	Unknown
DACY	11	2020	Europeans 96% Africans 95% South Asians 82%	Unknown
YCAD	12	2020	Europeans 35% Africans 40% South Asians 67%	Unknown
KNMB	13	2023	>99%	Unknown

All new antigens in the Knops blood group system are caused by SNPs in Complement Component (3b/4b) Receptor 1 (*CR1*). KCAM and KDAS are antithetical antigens, as are DACY and YCAD.

023 - Indian

Table 15 New antigens in the Indian system (77-79)

Name	#	Year Described	Antigen frequency	Clinical significance
INFI	3	2007	>99%	Mild HDFN
INJA	4	2007	>99%	Unknown
INRA	5	2016	>99%	Unknown
INSL	6	2018	>99%	Unlikely

All new antigens in the Indian blood group system are caused by SNPs in *CD44.*

024 - OK

Table 16. New antigens in the OK system (80,81)

Name	#	Year Described	Antigen frequency	Clinical significance
OKGV	2	2003	>99%	Unknown
OKVM	3	2006	>99%	Unknown

Both new antigens in the OK blood group system are caused by SNPs in Basigin (*BSG*).

026 - John Milton Hagen

Table 17. New antigens in the John Milton Hagen system (82-86)

Name	#	Year Described	Antigen frequency	Clinical significance
JMHK	2	2006	>99%	Unknown
JMHL	3	2006	>99%	Unknown
JMHG	4	2006	>99%	Unknown
JMHM	5	2006	>99%	Unknown
JMHQ	6	2010	>99%	Unknown
JMHN	7	2019	>99%	Unknown
JMHA	8	2020	>99%	Unlikely

All new antigens in the JMHK blood group system are the result of SNPs in Semaphorin 7A (*SEMA7A*).

Section 2. New Systems

028 – Globoside (promoted from a collection to a system in 2003).

In 2003 the system contained one antigen P but new antigens have subsequently been added (Table 18). The Globoside blood group system is encoded by Beta-1,3-N-Acetylgalactosaminyltransferase 1 (*B3GALNT1*), which is found on 3q26 chromosome (2). The gene encodes an enzyme which transfers *N*-acetylgalactosamine onto the P^k antigen in the P1PK system to form P.

Table 18. New antigens in the Globoside system (87,88)

Name	#	Year Described	Antigen frequency	Clinical significance
PX2	4	2011	>99%	Probable
ExtB	5	2019	Caucasians 13% African Americans 24% Asians 31%	Unknown

Anti-PX2 is found in patients with the very rare Pk phenotype. This phenotype arises from inactivations of the B3GALNT1 gene. Usually, anti-PX2 is found alongside other antibodies (anti-P, anti-P1) so its clinical significance is hard to determine. PX2 is abundant on p cells (PPIPk negative) so patients with anti-PX2 have an incompatible crossmatch with cells from p individuals. ExtB is associated with the B antigen. Anti-ExtB is found in group O individuals, as well as group AB and B Pk individuals, and reacts with B cells that are PPIPk-.

030 - Rh-Associated Glycoprotein (RHAG) (promoted to a system in 2008).
Antigens described since 2003 are listed in Table 19.
The RHAG blood group system is encoded by Rh-Associated Glycoprotein (*RHAG*), which is found on 6p21.3 chromosome (2). The gene encodes a multi-pass membrane glycoprotein which is associated with RhD, RhCE, GPB, LW and CD47. This complex of molecules helps to maintain erythrocyte membrane integrity. RHAG is also involved in transporting some molecules and cations across the red cell membrane. It is expressed only on RBCs, but RHAG homologs can be found in other tissues.

Table 19. New antigens in the RHAG system (89-95)

Name	#	Year Described	Antigen frequency	Clinical significance
DUCLOS	1	2010	>99%	Unknown
Ol^{a}	2	2010	<1%	Unknown
DSLK	3*	2010	>99%	Probable
Kg	5	2020	<1%	Severe HDFN Probable HTR
SHER	6	2022	<1%	Unknown
THIN	7†	2023	<1%	HDFN
* “Provisional number assigned awaiting further examples of the DSLK− phenotype to confirm the polymorphism.” (1) † Provisional number assigned.				

All antigens in the RHAG blood group system are the result of SNPs in *RHAG*. One new pair of antithetical antigens were discovered: DSLK and Kg. Three of the antigens were identified more than 20 years ago but elucidated more recently: DUCLOS (previously 901.013), Ol^{a} (previously 700.043) and Kg (previously 700.045). Kg is present in approximately 0.2% of the Japanese population (90). Anti-Kg has caused two severe cases of HDFN that required exchange transfusion, and in vitro tests have suggested that it is capable of causing HTRs (90,93). In vitro tests suggest that the antibody to its antithetical antigen, DSLK, may also be clinically significant.

031 - FORS
The FORS blood group system is encoded by Globoside Alpha-1,3-N-Acetylgalactosaminyltransferase 1 (*GBGT1*), which is found on 9q34.2 chromosome (2). The gene encodes a glycosyltransferase, which catalyses the formation of Forssman glycolipids. These glycolipids are usually seen in animals and humans have corresponding naturally occurring antibodies.

Table 20. Antigens in the FORS system (96)

Name	#	Year Described	Antigen frequency	Clinical significance
FORS1	1	2013	<1%	Unknown

FORS1 is caused by a SNP in *GBGT1*.

032 - JR
The JR blood group system is encoded by ATP Binding Cassette Subfamily G Member 2 (*ABCG2*), which is found on 4q22.1 chromosome (97). The gene encodes an ATP-dependent transporter that can transport a wide specificity of substrates, particularly uric acid. It is expressed on a range of cells, including the placenta and epithelial cells.

Table 21. Antigens in the JR system (97-102)

Name	#	Year Described	Antigen frequency	Clinical significance
Jr^{a}	1	2012	>99%	Severe HDFN HTR

The null phenotype of Jr^{a} (previously 901.005) is caused by mutations in *ABCG2*. Jr(a-) has a prevalence of 0.03% in Japanese and <0.01% of most other populations. Anti-Jr^{a} is clinically significant, having caused severe and even fatal HDFN, and sometimes causes HTRs (98-102).

033 - LAN
The LAN blood group system is encoded by ATP-binding Cassette Subfamily B Member 6 (*ABCB6*), which is found on 2q36 chromosome (103). The gene encodes an ATP-dependent transport protein which transports heme and its precursors across the red blood cell membrane and outer mitochondrial membrane (104).

Table 22. New antigens in the LAN system (103,105)

Name	#	Year Described	Antigen frequency	Clinical significance
Lan	1	2012	>99%	Severe HDFN Probable HTR

The null phenotype of Lan (previously 901.002) is caused by inactivating mutations in *ABCB6*.

034 - Vel

The Vel blood group system is encoded by Small Integral Membrane Protein 1 (*SMIM1*), which is found on chromosome 1p36.32 (106). It encodes a transmembrane protein and is found in a range of tissues, particularly in the bone marrow, testes and kidney (107).

Table 23 Antigens in the Vel system (108-113)

Name	#	Year Described	Antigen frequency	Clinical significance
Vel	1	2013	>99%	HDFN Severe HTR AIHA

The null phenotype of Vel is caused by inactivating mutations in *SMIM1*. Anti-Vel is capable of causing AIHA, severe HTR and rarely HDFN (109-113).

035 - CD59

The CD59 blood group system is encoded by *CD59* which is found on 11p13 chromosome (114). The gene encodes a glycoprotein that has a role in complement regulation (inhibition of the MAC complex) (115). It is expressed on all blood cells, endothelial cells and epithelial cells. It is also present in tear fluid (116).

Table 24. Antigens in the CD59 system (117)

Name	#	Year Described	Antigen frequency	Clinical significance
CD59.1	1	2014	>99%	Unknown

Anti-CD59.1 was found in a patient with a CD59 deficiency. Very few cases of CD59 deficiency have been reported; seven as of 2014, and three distinct CD59-null alleles were implicated. Of several transfusions given to one proband, only one post-transfusion test revealed a transiently positive DAT with no clinical signs of HTR (117).

036 - Augustine

The Augustine blood group system is encoded by Solute Carrier Family 29 Member 1 (*SLC29A1*), which is found on 6p21.1 chromosome (118). The gene encodes the ENT1 protein, which may have a role in adenosine transport and erythroid differentiation, as well as being involved in regulating bone metabolism (119). This protein is found ubiquitously in human tissues.

Table 25. Antigens in the Augustine system (119-124)

Name	#	Year Described	Antigen frequency	Clinical significance
AUG1	1	2015	>99%	Unknown
At^{a}	2	2015	>99%	Moderate HDFN Severe HTR AIHA
ATML	3	2018	<1%	Severe HDFN
ATAM	4	2023	>99%	Probable

All antigens in the Augustine blood group system are the result of SNPs in *SLC29A1*, except for AUG1 whose loss is associated with the rare Augustine null phenotype. Anti-At^{a} has been found in a number of African American individuals. In vitro tests suggest that anti-At^{a} is clinically significant, and it has been implicated in cases of HDFN (one of which was moderate), HTRs (one of which was severe) and AIHA (120-122).

037 - KANNO

The KANNO blood group system is encoded by Prion Protein (*PRNP*), which is found on 20p13 chromosome (125). The gene encodes prion protein, a glycoprotein found in the brain and other tissues. It may have a role in copper transport and neuroprotection, as mutations are associated with Creutzfeldt-Jakob disease (126). Its function in RBCs is unknown

Table 26. Antigens in the KANNO system (125,127,128)

Name	#	Year Described	Antigen frequency	Clinical significance
KANNO1	1	2020	Most populations >99% Japanese 94.2% Southeast Asians 96%	Unknown

The clinical significance of anti-KANNO is unknown, but among 16 reported cases of pregnancy and 7 reported cases of transfusion there were no cases of HDFN or HTR, with only one newborn testing DAT positive (127).

038 - SID

The SID blood group system is encoded by Beta-1,4-N-Acetyl-Galactosaminyltransferase 2 (*B4GALNT2*), which is found on 17q21.32 chromosome (129). The gene encodes an enzyme which catalyses the formation of the carbohydrate determining the Sd^a antigen. This enzyme is absent on gastrointestinal cancer cells, suggesting it may play a role in eliminating metastasis. It is found in the kidney, colon and stomach, as well as human serum, milk, meconium and urine.

Table 27. Antigens in the SID system (130-133)

Name	#	Year Described	Antigen frequency	Clinical significance
Sd^a	1	2019	Most populations 91%	HTR

The loss of Sd^a is associated with mutations in the *B4GALNT2* gene. 91% of the population carries this antigen on red cells, but only 4% are Sd^a negative in all tissues and therefore capable of making anti-Sd^a (130). Anti-Sd^a can cause HTR, particularly when RBCs of the rare Cad (Sda++) phenotype are transfused, as these react more strongly with anti-Sd^a (132,133).

039 - CTL2

The CTL2 system is encoded by Solute Carrier Family 44 Member 2 (*SLC44A2*), which is found on 19p13.2 chromosome (134,135). The gene encodes the CTL2 glycoprotein, which has a role in choline transport and carries HNA-3 (human neutrophil antigen), the antibody of which causes severe and fatal transfusion-related acute lung injury (TRALI). CTL2 is found in a variety of tissues, notably blood cells, inner ear and lung endothelium (135).

Table 28. Antigens in the CTL2 system (136)

Name	#	Year Described	Antigen frequency	Clinical significance
VER	1	2019	>99%	Unknown
RIF	2	2019	>99%	Unknown

Anti-VER was found in one CTL2 null proband (136). RIF is the result of a SNP in *SLC44A2*.

040 - PEL

The PEL blood group system is encoded by ATP Binding Cassette Subfamily C Member 4 (*ABCC4*), which is found on 13q32.1 chromosome (137). The gene encodes an ATP-dependent transport protein which transports a variety of molecules and is involved in erythropoiesis (138). It is found in a variety of tissues, particularly the prostate and kidney (139).

Table 29. Antigens in the PEL system (140)

Name	#	Year Described	Antigen frequency	Clinical significance
PEL	1	2020	>99%	Unknown

The loss of PEL (previously 901.014) is caused by a deletion of *ABCC4*.

041 - MAM

The MAM blood group system is encoded by Epithelial Membrane Protein 3 (*EMP3*), which is found on 19q13.33 chromosome (141). The gene encodes the EMP3 protein, which has a role in tumour suppression (142). It is expressed in the ovary, rectum, liver, kidney and embryonic lung (142).

Table 30. Antigens in the MAM system (143,144)

Name	#	Year Described	Antigen frequency	Clinical significance
MAM	1	2020	>99%	Severe HDFN Probable HTR

The loss of MAM (previously 901.016) is caused by various inactivating mutations in *EMP3*. A total of eleven MAM negative probands have been described, including one in New Zealand (143). Anti-MAM causes severe and fatal HDFN, and in vitro tests suggest that anti-MAM is capable of causing HTR (141,144).

042 - EMM

The EMM blood group system is encoded by Phosphatidylinositol Glycan Anchor Biosynthesis Class G (*PIGG*), on 4p16.3 chromosome (145). The gene encodes an enzyme that has a role in glycosylphosphatidylinositol (GPI) anchor synthesis. Mutations in *PIGG* are associated with intellectual disability, seizures and hypotonia (146).

Table 31. Antigens in the EMM system (147-150)

Name	#	Year Described	Antigen frequency	Clinical significance
Emm	1	2021	>99%	HTR

The loss of Emm (previously 901.008) is caused by inactivating mutations in PIGG. Anti-Emm is thought to be a naturally occurring antibody in Emm negative individuals and has caused one acute HTR (148,149). In vitro tests suggest that a ti-Emm does not cause HDFN, and one recorded pregnancy was unaffected by anti-Emm, but this evidence is not conclusive (150).

043 - ABCC1

The ABCC1 blood group system is encoded by ATP Binding Cassette Subfamily C Member 1 (*ABCC1*), which is found on 16p13.11 chromosome (137). The gene encodes an ATP-binding cassette (ABC) transporter, which plays a role in protection of kidney epithelial cells. The protein is expressed ubiquitously in almost all human tissues (151).

Table 32. Antigens in the ABCC1 system (137)

Name	#	Year Described	Antigen frequency	Clinical significance
WLF	1	2020	>99%	Unknown

The rare null phenotype is caused by an intron deletion (137).

044 - Er

The Er blood group system is encoded by Piezo Type Mechanosensitive Ion Channel Component 1 (*PIEZO1*), which is found on 16q23-q24 chromosome (152). The gene encodes a red cell calcium channel, which helps change RBC volume in response to deformation (153). It is also expressed in the bladder, colon, lung and skin (154).

Table 33. Antigens in the Er system (155)

Name	#	Year Described	Antigen frequency	Clinical significance
Er^a	1	2022	>99%	Unlikely
Er^b	2	2022	<1%	Unknown
Er3	3	2022	>99%	Probable HTR
ERSA	4	2022	>99%	Severe HDFN
ERAMA	5	2022	>99%	Severe HDFN

All antigens in the Er blood group system are the result of a SNP in *PIEZO1*, except for Er3, whose loss is associated with the very rare Er(a-b-) phenotype. Er^a and Er^b are antithetical antigens.

In vitro tests suggest that anti-Er^a is unlikely to be clinically significant, and a small number of incompatible transfusions have been reported without complications. Results of in vitro tests performed to determine the clinical significance of anti-Er3 showed that incompatible RBCs were destroyed faster than normal, suggesting anti-Er3 may be capable of causing HTRs (156).

045 - CD36

The CD36 blood group system is encoded by *CD36*, which is found on 7q11.2 chromosome (156). The gene encodes a type B scavenger receptor with roles in cell signalling, fatty acid transport, and immune cell function (157). It is expressed in a range of immune and non-immune cells in the blood, including the endothelium (158).

Table 34. Antigens in the CD36 system (159)

Name	#	Year Described	Antigen frequency	Clinical significance
CD36.1	1	2023	Unknown	Possible HDFN

DISCUSSION

This report provides an update on what has been learnt about blood group antigens and systems over the last 20 years, and how their antibodies may affect patients in a clinical context. The results of this study had the potential to reveal limitations in our current ability to identify clinically significant antibodies and provide up to date information that will allow requirements of red cells used in red cell antibody screening to be reviewed.

The following blood group antigens produced antibodies that were either clinically significant or likely to be clinically significant: ENEV (MNS45), SARA (MNS47), P^k (P1PK3), CETW (RH63), VONG (KEL28), KEAL (KEL39), KHOZ (KEL41), DISK (DI22), YTGT (YT6), SCAN (SC7), SCAC (SC9), DOMR (DO7), GECT (GE13), INFI (IN3), PX2 (GLOB4), DSLK (RHAG3), Kg (RHAG5), THIN (RHAG7), Jr^a (JR1), Lan (LAN1), Vel (VEL1), At^a (AUG2), ATML (AUG3), ATAM (AUG4), Sd^a (SID1), MAM (MAM1), Emm (EMM1), Er3 (ER3), ERSA (ER4), ERAMA (ER5) and CD36.1.

There were some limitations in the information found during the literature search. Many antigens were only described in one study or abstract, and a few were only referenced by a secondary source. The coverage for each antigen varied; only a handful of studies gave a prediction of clinical significance, in some studies the quantity of antisera was limited, and therefore many studies were unable to estimate antigen or antibody frequency. The identification and classification of antigens is transitioning to molecular sequencing.

Future research could investigate antigen or allele frequencies in different populations as resources permit, as this can help us determine whether their antibodies are likely to appear more frequently. It could also focus on determining the clinical significance of antibodies, using such tests as the monocyte monolayer assay.

CONCLUSION

Blood group systems show a high degree of polymorphism in a large and heterogeneous human population and new variants appear on a continuous basis. Corresponding antibodies can have real-world consequences in transfusion, pregnancy and autoimmunity. This report described 122 blood group antigens and 17 blood group systems that were elucidated in the last 20 years.

AUTHOR INFORMATION

Natalya J Clark, BMLSc, Student[1]
Holly E Perry, PhD, MSc, MPHIL, Lecturer[2]

[1]University of Otago, Dunedin, New Zealand

[2]Department of Pathology, University of Otago, Dunedin, New Zealand

Correspondence: Natalya Clark
email: natalya.clark@protonmail.com

REFERENCES

1. ISBT. Red Cell Immunogenetics and Blood Group Terminology. Amsterdam, the Netherlands: International Society of Blood Transfusion; 2023 [cited 2023 April 1]. Available from: https://www.isbtweb.org/isbt-working-parties/rcibgt.html
2. Reid ME, Lomas-Francis C, Olsson ML. The Blood Group Antigen FactsBook, 3rd ed. Academic Press; 2012; 758.
3. Hodgson JA, Pickrell JK, Pearson LN et al. Natural selection for the Duffy-null allele in the recently admixed people of Madagascar. *Proc R Soc B* 2014; 281(1789): 20140930. Available from: https://doi.org/10.1098/rspb.2014.0930.
4. Karczewski KJ, Francioli LC, Tiao G, Cummings BB et al. The mutational constraint spectrum quantified from variation in 141,456 humans. *Nature* 2020; 581: 434-443.
5. Velliquette RW, Palacajornsuk P, Hue-Roye K, et al. Novel GYP(A-B-A) hybrid gene in a DANE+ person who made an antibody to a high-prevalence MNS antigen. *Transfusion* 2008; 45(12): 2618-2623.
6. Velliquette RW, Hu Z, Lomas-Francis C, et al. Novel single-nucleotide change in GYP*A in a person who made an alloantibody to a new high-prevalence MNS antigen called ENEV. *Transfusion* 2010; 50(4): 856-860.
7. Uchikawa M, Tsuneyama H, Ogasawara K, et al. Molecular basis for a novel low frequency antigen in the MNS blood group system. *Vox Sang* 2006; 91(s3): 133.
8. McBean RS, Hyland CA, Hendry JL, et al. SARA: a “new” low-frequency MNS antigen (MNS47) provides further evidence of the extreme diversity of the MNS blood group system. *Transfusion* 2014; 55(6): 1451-1456.
9. Towns D, Hannon J, Hendry J, et al. Hemolytic disease of the fetus and newborn caused by an antibody to a low-prevalence antigen, anti-SARA. *Transfusion* 2011; 51(9): 1977-1979.
10. Lopez GH, Wei L, Ji Y, et al. GYP*Kip, a novel GYP(B-A-B) hybrid allele, encoding the MNS48 (KIPP) antigen. *Transfusion* 2015; 56(2): 539-541.
11. Lopez GH, Wilson B, Liew YW, et al. An alloantibody in a homozygous GYP*Mur individual defines JENU (MNS49), a new high-frequency antigen on glycophorin B. *Transfusion* 2016; 57(3): 716-717.
12. Ito S, Kaito S, Miyazaki T, et al. A new antigen SUMI carried on glycophorin A encoded by the GYPA*M with c.91A>C (p.Thr31Pro) belongs to the MNS blood group system. *Transfusion* 2020; 60(6): 1287-1293.
13. Hagman JR, Hult AK, Westman JS, et al. Multiple miscarriages in two sisters of Thai origin with the rare Pk phenotype caused by a novel nonsense mutation at the B3GALNT1 locus. *Transfus Med* 2018; 29(3): 202-208.
14. Suchanowska A, Kaczmarek R, Duk M, et al. A single point mutation in the gene encoding Gb3/CD77 synthase causes a rare inherited polyagglutination syndrome. *J Biol Chem* 2012; 287(45): 38220-38230.
15. Westhoff CM, Storry JR, Walker P, et al. A new hybrid RHCE gene (CeNR) is responsible for expression of a novel antigen. *Transfusion* 2004; 44(7); 1047-1051.
16. Lomas-Francis C, Alcantara D, Westhoff C, et al. JAL (RH48) blood group antigen: serologic observations. *Transfusion* 2009; 49(4): 719-724.
17. Hipsky CH, Lomas-Francis C, Fuchisawa A, et al. RHCE*ceCF encodes partial c and partial e but not CELO, an antigen antithetical to Crawford. *Transfusion* 2011; 51(1): 25-31.
18. Westhoff CM, Vege S, Hipsky CH, et al. RHCE*ceAG (254C>G, Ala85Gly) is prevalent in blacks, encodes a partial ce-phenotype, and is associated with discordant RHD zygosity. *Transfusion* 2015; 55(11): 2624-2632.
19. Scharberg EA, Rink G, Roth S, et al. The RHCE*Ce(501A) allele encodes the PARG antigen (RH60). *Transfusion* 2017; 57(2): 484-486.
20. Westhoff CM, Vege S, Horn T, et al. RHCE*ceMO is frequently in cis to RHD*DAU0 and encodes a hrS–, hrB–, RH:–61 phenotype in black persons: clinical significance. *Transfusion* 2013; 53(11): 2983-2989.
21. Poole J, Grimsley S, Thornton N: A novel mutation in RHCE giving rise to the Rh:-51 phenotype and an antibody to a high frequency Rh antigen present on other Rh:-51 cells. Transfus Med. 2012;22(s1):56. Cited in: Storry JR, Clausen FB, Castilho L, et al. International Society of Blood Transfusion Working Party on Red Cell Immunogenetics and Blood Group Terminology: Report of the Dubai, Copenhagen and Toronto meetings. *Vox Sang* 2018; 114(1): 95-102.
22. Flower R, Wilson B, Davidson C, et al. A case of HDFN defines a novel low frequency Rh antigen associated with indigenous heritage and identified in a blood group genomic study. *Intern Med J* 2021; 51(s6): 6-9.
23. Crew VK, Thornton N, Burton N, et al. Two heterozygous mutations in an individual result in the loss of a novel high incidence Lutheran antigen Lurc. *Transfus Med* 2009; 19(1): 1-19.
24. Hustinx H, Lejon-Crottet S, Henny C, et al. LUIT: a novel high incidence antigen in the Lutheran blood group system. *Vox Sang* 2014; 107(s1): 172.
25. Floch A, Lomas-Francis C, Vege S, et al. A novel high-prevalence antigen in the Lutheran system, LUGA (LU24), and an updated, full-length 3D BCAM model. *Transfusion* 2023; 63(4): 798-807.
26. Crew VK, Laundy R, Bahashwan A, et al. Two novel high incidence antigens in the Lutheran blood group system (LUAC and LUBI). *Vox Sang*. 2016; 111(s1): 63.
27. Vrignaud C, Ramelet S, Amiranoff D, et al. Characterization of a Novel High-Prevalence Antigen in the Lutheran Blood Group System. *Transfusion*. 2018; 58(s2): 6A-254A.
28. Crew VK, Mayer B, Baglow L, et al. A novel high frequency antigen in the Lutheran blood group system (LUNU). *Vox Sang*. 2019; 114(s1): 5-240.
29. Yosephi L, Crew VK, Shinar E, et al. A Lutheran related antibody detected in a patient with a homozygous missense BCAM mutation indicating a novel antigen of the system. *Vox Sang*. 2019; 114(s1): 5-240.
30. Alsubhi S, Mankelow T, Crew VK et al. The expression of BCAM c.674G>A in K562 and HEK293T cell lines helps to define a novel Lutheran antigen LUOM. *Vox Sang* 2023; 118(S1): 6-118.
31. Grey D, Poole J, Martin P, et al: Haemolytic disease of the newborn caused by a new Kell antigen. *Transfus Med*. 2003; 13(1): 30. Cited in: Daniels GL, Fletcher A, Garratty G, et al. Blood group terminology 2004: from the International Society of Blood Transfusion committee on terminology for red cell surface antigens. *Vox Sang*. 2004; 87(4): 304-316.
32. Lee S, Debnath AK, Wu X, et al. Molecular basis of two novel high-prevalence antigens in the Kell blood group system, KALT and KTIM. *Transfusion*. 2006; 46(8): 1323-1327.
33. Boturão-Neto E, Bordin JO. Frequencies of KEL*29 (KALT) and KEL*30 (KTIM) alleles in blood donors and patients with hemoglobinopathies in Brazil. *Transfusion* 2007; 47(8): 1552.
34. Uchikawa M, Onodera T, Ogasawara K, Tsuneyama H, Toyoda C, Yabe R, Enomoto T, Satake M, Nakajima K. Molecular basis for a novel low-frequency antigen in the Kell blood group system, KYO. *Vox Sang* 2006; 91(s3): 136.
35. Velliquette RW, Hue-Roye K, Lomas-Francis C, et al. Molecular basis of two novel and related high-prevalence antigens in the Kell blood group system, KUCI and KANT, and their serologic and spatial association with K11 and KETI. *Transfusion* 2013; 53(11pt2): 2872-2881.
36. Crew VK, Poole J, Watson T, et al. KASH (KEL34): A novel high incidence antigen in the Kell blood group system. *Vox Sang* 2010; 99(s1): 357.

37. Crew VK, Poole J, Bullock T, et al. KELP (KEL35): A New High Incidence Antigen in the Kell Blood Group System Defined By Two Homozygous Missense Mutations in KEL. *Transfus Med* 2010; 20(s1): 30.
38. Crew VK, Poole J, Bullock T, et al. KETI, a novel high incidence antigen in the Kell blood group system: a serological and molecular study. *Vox Sang* 2011; 101(s1): 19.
39. Lomas-Francis C, Vege S, Velliquette RW, et al. Expansion of the Kell blood group system: two new high-prevalence antigens and two novel K0 (Kellnull) phenotypes. *Transfusion* 2013; 53(11pt2): 2887-2891.
40. Lomas-Francis C, Fuchisawa A, Uchikawa M, et al. A new high prevalence Kell antigen KYOR, antithetical to the low-prevalence antigen KYO, is the second trypsin-sensitive Kell antigen. *Transfusion* 2012; 53(s3):158A-159A.
41. Scharberg EA, Wieckhusen C, Luz B, et al. Fatal hemolytic disease of the newborn caused by an antibody to KEAL, a new low-prevalence Kell blood group antigen. *Transfusion* 2016; 57(1): 217-8.
42. Martin-Blanc S, Laget L, Babinet J, et al. Characterization of a novel high-prevalence antigen in the KEL blood group system. *Vox Sang* 2022; 117(s1): 56.
43. Hyland C, Buhariwala K, Lopez G et al. Intertwining roles for genomics and international data sharing defines a novel low prevalence Kell antigen in a blood donor. *Transfusion Medicine* 2022; 32(s3): 3-37.
44. Poole J, Thornton NM, Tilley L, et al. Novel high incidence antigen in the Diego blood group system (DISK) and the clinical significance of anti-DISK. *Vox Sang* 2010; 99(s1): 54-55.
45. Scharberg EA, Stürtzel A, Rothenberger-Mürb S, et al. A new low prevalence Diego blood group antigen found in a Caucasian blood donor. *Vox Sang* 2021; 116(s1): 29.
46. Laundy R, Crew VK, Davies H, et al. A novel high frequency antigen in the Yt blood group system. *Transfus Med* 2017; 27(s2): 42-43.
47. Crew VK, Laundy R, Walser P, et al. Serological and molecular characterisation of a novel high frequency antigen in the Yt blood group system. *Vox Sang* 2018; 113(s1): 63.
48. Van Buren NL, Gillen B, Lomas-Francis C, et al. YTGT: A new high-prevalence antigen in the Yt blood group system in two unrelated Native Americans and transfusion management. *Transfusion* 2022; 62(9): 1917-1922.
49. Hue-Roye K, Chaudhuri A, Velliquette RW, et al. STAR: a novel high-prevalence antigen in the Scianna blood group system. *Transfusion* 2005; 45(2): 245-247.
50. Flegel WA, Chen Q, Reid ME, et al. SCER and SCAN: two novel high-prevalence antigens in the Scianna blood group system. *Transfusion* 2005; 45(12): 1940-1944.
51. Srivastava K, Albasri J, Alsuhaibani OM, et al. SCAR: The high-prevalence antigen 013.008 in the Scianna blood group system. *Transfusion* 2020; 61(1): 246-254.
52. Floch A, Lomas-Francis C, Vege S, et al. Two new Scianna variants causing loss of high prevalence antigens: ERMAP model and 3D analysis of the antigens. *Transfusion* 2022; 63(1): 230-238.
53. Mayer B, Thornton N, Yürek S, et al. New antigen in the Dombrock blood group system, DOYA, ablates expression of Doa and weakens expression of Hy, Joa, and Gya antigens. *Transfusion* 2010; 50(6): 1295-1302.
54. Costa FPS, Hue-Roye K, Sausais L, et al. Absence of DOMR, a new antigen in the Dombrock blood group system that weakens expression of Dob, Gya, Hy, Joa, and DOYA antigens. *Transfusion* 2010; 50(9): 2026-2031.
55. Crew VK, Poole J, Marais I, et al. DOLG, a novel high incidence antigen in the Dombrock blood group system. *Vox Sang* 2011; 101(s1): 263.
56. Crew VK, Thornton N, Bullock T, et al. Serological and molecular characterisation of DOLC, a novel high incidence antigen in the Dombrock blood group system. *Vox Sang* 2013; 105(s1): 30.
57. Shakarian G, Vege S, Hue-Roye K, et al. A Dombrock System Antibody Detects a New High-Prevalence Antigen, DODE. *Transfusion* 2015; 55(s3): 35A-36A.
58. Arnaud L, Helias V, Menanteau C, et al. A functional AQP1 allele producing a Co(a–b–) phenotype revises and extends the Colton blood group system. *Transfusion* 2010; 50(10): 2106-2116.
59. Lopez GH, Wilson B, Millard GM, et al. A new high-prevalence LW antigen detected by an antibody in an Indigenous Australian homozygous for LW*A c.309C>A variant. *Vox Sang* 2022; 117(7): 958-965.
60. Yabe R, Uchikawa M, Tuneyama H, et al. Is: a new Gerbich blood group antigen located on the GPC and GPD. *Vox Sang* 2008; 87(s3): 79.
61. Poole J, Tilley L, Hudler P, et al. Novel mutations in GYPC giving rise to lack of Ge epitopes and anti-Ge production. *Vox Sang* 2008; 95(s1): 181.
62. Lomas-Francis C, Tahiri T, Vege S, et al. GECT: A New High-Prevalence Antigen in the GE Blood Group System in a SCD Patient with an Apparent Anti-GE2. *Transfusion* 2020; 60(s5): 13A.
63. Shakarian G, Ong J, Vege S, et al. A New Antibody in the Gerbich Blood System against a Novel High Prevalence Antigen Named GEAR. *Transfusion* 2016; 56(s4): 140A
64. Banks J, Poole J, Ahrens N, et al. SERF: a new antigen in the Cromer blood group system. *Transfus Med* 2004; 14(4): 313-318.
65. Suwanwootichai P, Phiancharoen S, Bejrachandra S, et al. Cromer system: SERF negative Thai patient with allo anti-SERF. *Vox Sang* 2022; 117(s1): 191.
66. Hue-Roye K, Lomas-Francis C, Belaygorod L, et al. Three new high-prevalence antigens in the Cromer blood group system. *Transfusion* 2007; 47(9): 1621-1629.
67. Crew VK, Poole J, Thornton N, et al. Two unusual cases within the Cromer blood group system: I) a novel hgh incidence antigen Croz and II) a novel molecular basis of Inab phenotype. *Transfus Med* 2010; 20(s1): 12.
68. Crew VK, Poole J, Mathlouthi R, et al. A novel Cromer blood group system antigen, CRUE, arising from two heterozygous DAF mutations in one individual with the corresponding anti-CRUE. *Vox Sang* 2012; 103(s1): 56.
69. Lomas-Francis C, Fuchisawa A, Hamilton J, et al. CRAG: A new high-prevalence antigen in the Cromer blood group system. *Vox Sang* 2012; 103(s1): 211.
70. Asher O, Finkel L, Yosephi L, et al. CROK (CROM19): A new high-prevalence antigen in the Cromer blood group system. *Transfusion* 2021; 61(11): E85-E87.
71. Vrignaud C, Chiaroni J, Durieux-Roussel E, et al. CORS (CROM20): A new high-prevalence antigen in the Cromer blood group system. *Transfusion* 2020; 60(11): E40-E42.
72. Moulds JM, Pierce S, Peck KB, et al: KAM: a new allele in the Knops blood group system. Transfusion 2005; 45:27A. Cited in: Daniels G, Flegel WA, Fletcher A, et al. International Society of Blood Transfusion Committee on Terminology for Red Cell Surface Antigens: Cape Town report. *Vox Sang* 2007; 92(3): 250-253.
73. Scharberg EA, Rink G, Schulz D, et al. KDAS, a new blood group antigen in the Knops blood group system antithetical to KCAM. *Transfusion* 2020; 60(8): E25-E27.
74. Grueger D, Zeretzke A, Habicht CP, et al. Two novel antithetical KN blood group antigens may contribute to more than a quarter of all KN antisera in Europe. *Transfusion* 2020; 60(10): 2408-2418.
75. Bugert P. Knops blood group system: A molecular view. *Vox Sang* 2023; 118(s1): 6-118.
76. Weinig E, Rink G, Stürtzel A, et al. KNMB, a novel Knops blood group antigen located in LHR-C. *Transfusion* 2023. Available from: https://doi.org/10.1111/trf.1754.
77. Poole J, Tilley L, Warke N, et al. Two missense mutations

in the CD44 gene encode two new antigens of the Indian blood group system. *Transfusion* 2007; 47(7): 1306-1311.
78. Jones B, Joshi S, Crew VK, et al. A new high incidence antigen of the Indian blood group system. *Transfus Med* 2016; 26(s2): 20-21.
79. Henny C, Thornton N, Crottet SL, et al. An antibody against a novel high incidence antigen in the Indian blood group system. *Vox Sang* 2018; 113(s1): 231.
80. Crew VK, Daniels G, Poole J. A New Variant in the OK Blood Group System. *Transfus Med* 2003; 13(s1): 32.
81. Crew VK, Thomas R, Gillen B, et al. A Novel Variant in the Ok Blood Group System. *Transfus Med* 2006; 16(s1): 41.
82. Seltsam A, Strigens S, Levene C, et al. The molecular diversity of Sema7A, the semaphorin that carries the JMH blood group antigens. *Transfusion* 2006; 41(1): 133-146.
83. Richard M, St-Laurent J, Perreault J, et al. A new SEMA7A variant found in Native Americans with alloantibody. *Vox Sang* 2010; 100(3): 322-326.
84. Tilley L, Laundy R, van der Mark-Zoet J, Folman C, de Haas M, Thornton N, Daniels G. Homozygosity for a Variant SEMA7A Allele Resulting in Loss of a Novel High Frequency JMH Antigen. *Transfus Med* 2014; 24(s2): 27-28.
85. Vrignaud C, Ramelet S, Herb A, et al. Characterization of a novel high-prevalence antigen in the JMH blood group system. *Vox Sang* 2019; 114(s1): 52-3.
86. Henny C, Thornton N, Laundy R, et al. An antibody against a novel high prevalence antigen in the JMH blood group system. Vox Sang . 2020; 115(s1): 231.
87. Westman JS, Benktander J, Storry JR, et al. Identification of the Molecular and Genetic Basis of PX2, a Glycosphingolipid Blood Group Antigen Lacking on Globoside-deficient Erythrocytes. *J Biol Chem* 2015; 290(30): 18505-18518.
88. Hagman JR, Barone A, Westman J, et al. β1,3GalNAc-T1-dependent extension of the human blood group B antigen results in a novel ABO-related glycolipid structure on erythrocytes. *Vox Sang* 2019; 114(s1): 53.
89. Tilley L, Green C, Poole J, et al. A new blood group system, RHAG: three antigens resulting from amino acid substitutions in the Rh-associated glycoprotein. *Vox Sang* 2010; 98(2): 151-159.
90. Tanaka M, Abe T, Minamitani T, et al. The Kg-antigen, RhAG with a Lys164Gln mutation, gives rise to haemolytic disease of the newborn. *Br J Haematol* 2020; 191(5): 920-926.
91. Ichikawa Y, Sato C, McCreary J, Lubenko A. Kg, a new low-frequency red cell antigen responsible for hemolytic disease of the newborn. *Vox Sang* 1989; 56(2): 98-100.
92. Kubo S, Takahashi J, Yoshizawa H, et al. Male newborn with anti-Kg antibody-induced hemolytic disease of the newborn. *Pediatr Int* 2009; 51(4): 582-584.
93. Tanaka M, Horikawa T, Kusumi T, et al. Anti-Kg antibodies induce monocyte phagocytosis of the red blood cells. *Transfusion* 2021; 61(10): 3050-3051.
94. Gonzalez-Santesteban C, Nogués N, Ruiz NB, et al. Identification of a new low prevalence antigen in the RHAG glycoprotein. *Vox Sang* 2022; 117(s1): 55-56.
95. Long S, Millard G, Liew YW. Haemolytic disease of the fetus and newborn caused by a novel RhAG antigen with c.140T>C (p.Phe47Ser) missense mutation. *Transfus Med* 2022; 32(s3): 3-37.
96. Svensson L, Hult AK, Stamps R, et al. Forssman expression on human erythrocytes: biochemical and genetic evidence of a new histo-blood group system. *Blood* 2013; 121(8): 1459-1468
97. Wieckhusen C, Rink G, Scharberg EA, et al. A new genetic background for the Jr(a–) blood group phenotype caused by the ABCG2*439T allele encoding a p.Arg147Trp change. *Transfusion* 2017; 57(12): 3063-3064.
98. Saison C, Helias V, Ballif BA, et al. Null alleles of ABCG2 encoding the breast cancer resistance protein define the new blood group system Junior. *Nat Genet* 2012; 44(2): 174-177.
99. Haer-Wigman L, Soussan AA, Ligthart P, et al. Molecular analysis of immunized Jr(a–) or Lan– patients and validation of a high-throughput genotyping assay to screen blood donors for Jr(a–) and Lan– phenotypes. *Transfusion* 2014; 54(7): 1836-1846.
100. Hundric Haspl HHZ, Jurakovic Loncar JLN, Tomicic TM, et al. The clinical significance of anti-Jr(a): mild or severe? *Vox Sang* 2007; 93(s1): 208-209.
101. Peyrard T, Pham BN, Arnaud L, et al. Fatal hemolytic disease of the fetus and newborn associated with anti-Jra. *Transfusion* 2008; 48(9): 1906-1911.
102. Kwon MY, Su L, Arndt PA, et al. Clinical significance of anti-Jra: report of two cases and review of the literature. *Transfusion* 2004; 44(2): 197-201
103. Helias V, Saison C, Ballif BA, et al. ABCB6 is dispensable for erythropoiesis and specifies the new blood group system Langereis. *Nat Genet* 2012; 44: 170-173.
104. Boswell-Casteel R, Fukuda Y, Schuetz JD. ABCB6, an ABC transporter impacting drug response and disease. *AAPS*; 20(1): 8.
105. Tanaka M, Yamamuro Y, Takahashi J, et al. Novel alleles of Lan− in Japanese populations. *Transfusion* 2014; 54(5): 1438-1439.
106. Cvejic A, Haer-Wigman L, Stephens JC, et al. SMIM1 underlies the Vel blood group and influences red blood cell traits. *Nat Genet* 2013; 45: 542-545.
107. SMIM1 small integral membrane protein 1 (Vel blood group) Homo sapiens (human). United States: National Library of Medicine, 2023. Available from: https://www.ncbi.nlm.nih.gov/gene/388588.
108. Cvejic A, Haer-Wigman L, Stephens JC, et al. SMIM1 underlies the Vel blood group and influences red blood cell traits. *Nat Genet* 2013; 45: 542-545.
109. Becton DL, Kinney TR. An infant girl with severe autoimmune hemolytic anemia: apparent anti-Vel specificity. *Vox Sang* 1986; 51(2): 108-111.
110. Herron R, Hyde RD, Hillier SJ. The second example of an anti-Vel auto-antibody. *Vox Sang* 1979; 36(3): 179-181.
111. Ferrer Z, Cornwall S, Berger R, et al. A third example of haemolytic auto-anti-Vel. *Rev fr transfus immuno hématol* 1984; 27(5): 639-644.
112. Levine P, White JA, Stroup M. Seven Vea (Vel) Negative members in three generations of a family. *Transfusion* 1961; 1(2): 111-115.
113. Van Gammeren AJ, Overbeeke MAM, Idema RN, et al. Haemolytic disease of the newborn because of rare anti-Vel. *Transfus Med* 2008; 18(3): 197-198.
114. Li XF, Lin FQ, Li JP. Identification of c.238 A>G (p.Arg80Gly) of CD59 blood group gene. *Transfusion* 2018; 58(12): 3033-3034.
115. Madjd Z, Pinder SE, Paish C, et al. Loss of CD59 expression in breast tumours correlates with poor survival. *J Pathol* 2003; 200(5): 633-639.
116. Cocuzzi E, Szczotka LB, Brodbeck WG, et al. Tears contain the complement regulator CD59 as well as decay-accelerating factor (DAF). *Clin Exp Immunol* 2001; 123(2): 188-195.
117. Anliker M, von Zabern I, Höchsmann B, et al. A new blood group antigen is defined by anti-CD59, detected in a CD59-deficient patient. *Transfusion* 2014; 54(7): 1817-1822.
118. Mikdar M, González-Menéndez P, Cai X, et al. The equilibrative nucleoside transporter ENT1 is critical for nucleotide homeostasis and optimal erythropoiesis. *Blood* 2021; 137(25): 3548-3562.
119. Daniels G, Ballif BA, Helias V, et al. Lack of the nucleoside transporter ENT1 results in the Augustine-null blood type and ectopic mineralization. *Blood* 2015; 125(23): 3651-3654.
120. Sweener JD, Holme S, McCall LA, et al. At(a−) phenotype: description of a family and reduced survival of At(a+) red

cells in a proposita with anti-Ata. *Transfusion* 1995; 35(1): 63-67.
121. Cash KL, Brown T, Sausais L, et al. Severe delayed hemolytic transfusion reaction secondary to anti-Ata. *Transfusion* 2002; 39(8): 834-837.
122. Culver PL, Brubaker DB, Sheldon RE, et al. Anti-Ata causing mild hemolytic disease of the newborn. *Transfusion* 1987; 27(6): 468-470.
123. Millard GM, McGowan EC, Wilson B, et al. A proposed new low-frequency antigen in the Augustine blood group system associated with a severe case of hemolytic disease of the fetus and newborn. *Transfusion* 2018; 58(5): 1320-1322.
124. Vrignaud C, Mikdar M, Duval R, et al. Molecular and structural characterization of a novel high-prevalence antigen of the Augustine blood group system. *Transfusion* 2023; 63(3): 610-618.
125. Omae Y, Ito S, Takeuchi M, et al. Integrative genome analysis identified the KANNO blood group antigen as prion protein. *Transfusion* 2019; 59(7): 2429-2435.
126. PRNP gene. Bethesda, United States: National Library of Medicine, 2014. Available from: https://medlineplus.gov/genetics/gene/prnp/
127. Ogasawara K, Omae Y, Ito S, et al. The new blood group system no, 37 - "Kanno". *Vox Sang* 2020; 115(s1): 59.
128. Bullock T, Folman C, van der Mark-Zoet J, et al. The first example of anti-KANNO found outside of Japan. *Vox Sang* 2015; 109(s1): 261.
129. Gassner C, Castilho L, Chen Q, et al. International Society of Blood Transfusion Working Party on Red Cell Immunogenetics and Blood Group Terminology Report of Basel and three virtual business meetings: Update on blood group systems. *Vox Sang* 2022; 117(1): 1332-1344.
130. Stenfelt L,Hellberg Å, Möller M, et al. Missense mutations in B4GALNT2 in Sd(a–) individuals with anti-Sda enable genotypic prediction of Sda deficiency and form the basis of a new blood group system. *Transfus Med* 2019; 29(s2): 21.
131. Veldhuisen B, Ligthart P, van der Mark-Zoet J, et al. Identification of a single homozygous mutation in the B4GALNT2 gene in individuals lacking the Sd(a) (SID) antigen on red blood cells. *Vox Sang* 2019; 114(s1): 193.
132. Reznicek MJ, Cordle DG, Strauss RG. A hemolytic reaction implicating Sda antibody missed by immediate spin crossmatch. *Vox Sang* 1992; 62(3): 173-175.
133. Peetermans ME, Cole-Dergent J. Haemolytic transfusion reaction due to Anti-Sda. *Vox Sang* 1970; 18(1): 67-70.
134. Santoso S. New insights into TRALI: activation of monocytes and endothelial cells as triggers of transfusion-related acute lung injury. *Vox Sang* 2012; 103(s1): 20.
135. Flesch BK, Wesche J, Berthold T, et al. Expression of the CTL2 transcript variants in human peripheral blood cells and human tissues. *Transfusion* 2013; 53(12): 3217-3223.
136. Vrignaud C, Mikdar M, Koehl B, et al. Alloantibodies directed to the SLC44A2/CTL2 transporter define two new red cell antigens and a novel human blood group system. *Transfusion* 2019; 59(s3): 18A.
137. Sugier H, Vrignaud C, Duval R et al. Null allele of ABCC1 encoding the multidrug resistance protein 1 defines a novel human blood group system. *Vox Sang.* 2020; 115(S1): 40-41.
138. Sassi Y, Lipskaia L, Vandecasteele G, et al. Multidrug resistance-associated protein 4 regulates cAMP-dependent signaling pathways and controls human and rat SMC proliferation. *J Clin Invest* 2008; 118(8): 747-757.
139. Reid G, Wielinga P, Zelcer N, et al. The human multidrug resistance protein MRP4 functions as a prostaglandin efflux transporter and is inhibited by nonsteroidal antiinflammatory drugs. *Proc Natl Acad Sci USA* 2003; 100(16): 9244-9249.
140. Azouzi S, Mikdar M, Hermand P, et al. Lack of the multidrug transporter MRP4/ABCC4 defines the PEL-negative blood group and impairs platelet aggregation. *Blood* 2020; 135(6): 441-448.
141. Baglow L, Tilley L, Crew VK, et al. A novel EMP3 null allele detected in a patient with the MAM- phenotype. *Vox Sang* 2021; 116(s1): 32-33.
142. Zhang N, Zhu HP, Huang W, et al. Unraveling the structures, functions and mechanisms of epithelial membrane protein family in human cancers. *Exp Hematol Oncol 2022* Oct 10;11:69.
143. Thornton N, Crew VK, Tilley L, et al. Disruption of the tumour-associated EMP3 enhances erythroid proliferation and causes the MAM-negative phenotype. *Nature Communication*s 2020; 11: 3569.
144. Montgomery Jr WM, Nance SJ, Donnelly SF, et al. MAM: a "new" high-incidence antigen found on multiple cell lines. *Transfusion* 2002; 40(9): 1132-1139.
145. PIGG phosphatidylinositol glycan anchor biosynthesis class G. United States, National Library of Medicine. 2023. Available from: https://www.ncbi.nlm.nih.gov/gtr/genes/54872/
146. Makrythanasis P, Kato M, Zaki MS, et al. Pathogenic Variants in PIGG Cause Intellectual Disability with Seizures and Hypotonia. *Am J Hum Genet* 2016; 98(4): 615-626.
147. McOmish C. A monthly roundup of key articles in other journals. *Transfusion* 2021; 62(1): 11-13
148. Daniels GL, Taliano V, Klein MT, McCreary J. Emm, a red cell antigen of very high frequency. *Transfusion* 1987; 27(4): 319-321.
149. Takahashi J, Date E, Kusumi T, et al. The first example of an acute hemolytic transfusion reaction due to anti-EMM and the first Japanese proband. *Vox Sang* 2013; 105(s2): 21.
150. Wagner MM, van Dunné FM, Kuipers I, et al. Anti-Emm in a pregnant patient - case report. *Vox Sang* 2013; 106(4): 385-386.
151. Jiye Y, Jianting Z. Multidrug resistance-associated protein 1 (MRP1/ABCC1) polymorphism: from discovery to clinical application. *Zhong Nan Da Xue Xue Bao Yi Xue Ban* 2011; 36(10): 927–938.
152. Andolfo I, Alper SL, De Franceschi L, et al. Multiple clinical forms of dehydrated hereditary stomatocytosis arise from mutations in PIEZO1. *Blood* 2013; 121(19): 3925-3935.
153. Antonelou MH. Tools and metrics for the assessment of post-storage performance of red blood cells: no one is left over. *Transfusion* 2022; 63(1): 1-6
154. Coste B, Mathur J, Schmidt M, et al. Piezo1 and Piezo2 are essential components of distinct mechanically-activated cation channels. *Science* 2010; 330(6000): 55-60.
155. Crew VK, Tilley LA, Satchwell TJ, et al. Missense mutations in PIEZO1, encoding the Piezo1 mechanosensor protein, define the Er red blood cell antigens. Blood. 2022. Cited In: McOmish C. A monthly roundup of key articles in other journals. *Transfusion* 2022; 63(1): 7-10.
156. Rać ME, Safranow K, Poncyljusz W. Molecular Basis of Human CD36 Gene Mutations. *Mol Med* 2007; 13: 288-296.
157. Chen Y, Zhang J, Cui W, Silverstein RL. CD36, a signaling receptor and fatty acid transporter that regulates immune cell metabolism and fate. *J Exp Med* 2022; 219(6): e20211314. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9022290/
158. van Schravendijk MR, Handunnetti SM, Barnwell JW, Howard RJ. Normal Human Erythrocytes Express CD36, an Adhesion Molecule of Monocytes, Platelets, and Endothelial Cells. *Blood* 1992; 80(8): 2105-2114.
159. Alattar AG, Storry JR, Olsson ML. Challenging the definition of a blood group: proposal to make CD36 a novel blood group system based on a case report and pre-existing genetic, proteomic and clinical data. *Vox Sang* 2023; 118(s1): 6-118.

Copyright: © 2024 The author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

REVIEW ARTICLE

The MNS blood group system: a review

Rei Miyamoto

ABSTRACT

In transfusion science, blood group systems are one of the significant factors that must be considered throughout the donation and transfusion processes. One of these blood group systems is the MNS system, which was discovered second only to the ABO system, in 1927. The system is comprised of a large group of polymorphic, high-frequency and low-frequency antigens, which have formed from genetic recombination, unequal crossing over, gene conversion, and single nucleotide polymorphisms (SNPs). Besides the genetic mechanisms, the phenotypic frequencies among population groups are interesting characteristics of this blood group system. The antigens are found on single pass sialoglycoproteins A and B on the red blood cell (RBC) membrane as well as the renal endothelium and epithelium. They are involved in many roles such as preventing RBC agglutination in blood vessels, complement regulation, transmembrane signalling, anion exchange, and binding cytokines. They are even thought to bind bacteria and malarial parasites, meaning that individuals with null phenotypes have resistance to some infectious diseases. The clinical significance of this blood group system in transfusion practice comes from the alloantibodies that can cause transfusion reactions or haemolytic disease of the fetus and newborn (HDFN).

This review aims to provide an informative and critical summary of the MNS blood group system in the context of transfusion science.

Keywords: MNS blood group system, sialoglycoproteins, red blood cell, transfusion reactions.

NZ J Med Lab Sci 2024; 78(1):20:23

INTRODUCTION

In transfusion science, many of the human blood group systems have alloantibodies that are clinically significant, with the potential to cause adverse events during blood transfusion (1). It is therefore important to understand the potential for adverse immunological events for each of the blood group systems and in this review the MNS blood group system will be considered.

Discovery

In the MNS blood group system, the major antigens are M, N, S, s, and U (2, 3). After the discovery of the ABO system, Landsteiner and Levine later discovered the M and N antigens in 1927. The letters of these antigens were taken from the word 'immune', as they discovered that rabbits became immunised to produce anti-M and anti-N, following exposure to human red blood cells (RBCs) (3-5). Later in 1947, Walsh and Montgomery discovered an antibody in a patient against a new antigen which they called S, named after 'Sydney ' in Australia where it was first found. The antithetical antigen of S was named s, following its discovery in 1951 (3-5). Genetic studies into several families showed that the loci of M/N and S/s were closely linked and that there was a high degree of polymorphism of this blood group system (6). The U antigen of the MNS system was later discovered in 1953 by Wiener, Unger, and Gordon, and stands for 'universal' based on its universal distribution as it is expressed in almost all Caucasians and Africans (3-5, 7, 8).

According to the most recent classifications by the International Society of Blood Transfusion (ISBT), there are a total of 50 antigens in the MNS blood group system (ISBT 002) (9). The frequencies of different MNS phenotypes in Caucasian and African populations are displayed in Table 1 (1, 4, 7, 10). Other than the main antigens, there are others of high prevalence, existing in over 90% of the population, or low prevalence, seen in less than 1% of the population (6).

Genetics

The genes encoding the MNS proteins are found on the long arm of chromosome 4 (2, 4, 5, 11). The two codominant alleles for the M (MNS1) and N (MNS2) antigens are found on the *GYPA* gene which encodes the glycophorin A (GPA) protein (2, 3, 11). It is thought that the *GYPA* gene duplicated and underwent cross-over between two chromatid strands, resulting in progenitor *GYPB* and *GYPE* segments that became independent genes (3, 4). This makes the *GYPA*, *GYPB*, and *GYPE* genes very similar (>95% homology) and closely linked, allowing further recombination to occur (3, 4). This confers the formation of a highly diverse group of antigens in this system that is much larger than in other blood group systems such as ABO, Kell, Duffy, and Kidd (2, 4, 9 12). The *GYPB* gene encodes for glycophorin B (GPB) and has an MNS3 allele for the S antigen, and an MNS4 allele for the s antigen, which are also co-dominantly expressed (2, 3, 11). The M and N alleles differ by three single nucleotide polymorphisms (SNPs) on the *GYPA* gene, leading to serine and glycine in the M antigen and leucine and glutamic acid in the N antigen at amino acid positions 1 and 5, respectively (Figure 1) (2-4, 7). On the other hand, the S and s alleles only have one SNP difference in the *GYPB* gene, leading to methionine on the S antigen and threonine on the s antigen at position 29 (Figure 1) (2-4, 7). The role of the *GYPE* gene is not well understood as its protein is not found on the RBC surface; however, it is thought to contribute to other MNS variants through gene rearrangement with *GYPB*. It has an identical genetic sequence to *GYPA*, so expression would result in M antigens on the RBC surface (3-5, 11).

Proteins and antigens

The M/N and S/s antigens are found on single pass sialoglycoproteins A and B, respectively, as displayed in Figure 1. They are found in the glycocalyx of the RBC membrane as well as the renal endothelium and epithelium (2-5). GPA is glycated by N-linked and O-linked oligosaccharides, while GPB only has N-glycosylation (4, 6). The sialic acid contributes to the negative charge on the RBC surface, preventing RBC agglutination for good blood flow in small blood vessels (2-5, 14). This glycation is also essential for the insertion and expression of GPA and GPB on the RBC surface (6). Other major functions include complement regulation, transmembrane signalling, facilitating anion exchange by band 3, and binding cytokines (2, 5, 6, 14). By interacting with band 3, the glycophorins provide physical support to the RBC cytoskeleton and assist with CO_2 exchange between tissues. This is reinforced by the fact that individuals with the Mur glycophorin variant with high band 3 expression were found to have a higher rate of CO_2 respiration (15). They also bind bacteria, viruses, and the *Plasmodium falciparum* parasite, due to the high abundance of glycophorins on RBCs and other cells (2, 3, 5). The MNS null phenotype of the system provides a selective advantage for resistance to some infections with some of the populations from African malaria-endemic countries having a relatively higher frequency of the S-s- and U- phenotypes (Table 1) (2, 4, 14, 16). It is thought that *P. falciparum* binds to band 3 and the sialic acid on GPA or some GPB to form a tight complex and invade the RBCs (17). Despite the overall low prevalence of S-s- phenotypes indicated by Table 1, some select African populations were found to have a S-s- frequency of up to 35%. Furthermore, a vast majority of these individuals also had the U- phenotype (18). A more recent study by Leffler *et al.* revealed that a rare MNS hybrid variant called Dantu, is present in East African populations which also confers

protection against severe malaria (16). This variant is thought to result in a hybrid between the extracellular domain of GPB and the transmembrane and intracellular domains of GPA, reducing the ability of *P. falciparum* to bind to band 3 (16, 17). Not only does the Dantu variant reduce the risk of severe malaria, it also reduces the morbidity of individuals once infected (17).

The GPA structure is thought to act as a receptor for bacteria such as pathogenic strains of *Escherichia coli*, causing urinary tract infections and possibly meningitis and septicaemia in neonates (19, 20). Several viruses have been reported to also use glycophorin structures for RBC invasion, including hepatitis A virus, reovirus, Influenza virus, and rotavirus. In contrast to *P. falciparum* infection, the presence of glycophorins on the RBC surface helps to protect individuals against these viruses, bringing viruses in the blood to sites of immune processing away from important target tissues via RBCs (21, 22).

As discussed earlier, the genetic linkage and high similarity between the genes result in a highly polymorphic and diverse group of antigens (5, 11). The main antigens M, N, S, s, and U are expressed on the cord RBC surface at birth (7). The U antigen is also present on the GPB structure and is distributed in high frequency along with other antigens such as En^a, as listed in Table 2 (2, 4, 11). Most U- individuals have associated S-s- phenotype due to the absence or alteration of the GPB protein overall (1, 5, 8). Similarly, En^a- is associated with the absence of the M and N antigens on GPA (14). The En^a antigen is present on GPA, close to the RBC surface and is part of the RBC envelope, where its name comes from (7).

Another interesting property of the MNS blood group antigens is their sensitivity to certain laboratory enzymes. For example, M and N antigens are cleaved from the glycophorin structures using ficin, papain, trypsin, and pronase, while the S and s antigens are sensitive to a-chymotrypsin and pronase with some sensitivity to both ficin and papain (2, 10). Their cleavage sites in the GPA and GPB structures are shown in Figure 1 (12). This characteristic is useful in the diagnostic identification of alloantibodies, as laboratory enzymes can destroy specific antigens and enhance the activity of others (e.g., ABO, Rh, Kidd, Lewis, P) (23). This fact also allows the differentiation of antibodies in a mixture of antibodies that respond differently to enzyme treatment (24). Some of the low frequency MNS antigens are enzyme resistant with the M variant antigen resistant to trypsin, papain, ficin, and bromelin (25).

Alloantibodies

Alloantibodies against the MNS blood group antigens have different characteristics and properties. Anti-M and anti-N are usually IgM and show a dosage effect, and some anti-M can have a partial IgG component. Alloantibodies can directly agglutinate M or N-positive RBCs due to the high expression of GPA (2, 3, 5, 11) in saline (8). Both anti-M and anti-N are more reactive and specific at a slightly acidic pH, around 6.5 (6). As they are cold-reactive, they can be detected at lower temperatures meaning they can often interfere in ABO grouping reactions, necessitating ABO grouping to be performed at 37°C (5, 11). Anti-M & N are naturally occurring alloantibodies, having been found in children without exposure to M or N antigens. As they are mostly reactive at body temperature, most are not clinically significant in blood transfusion (2-5, 11). Rare examples of anti-M and anti-N that are reactive at 37°C have been reported and have led to both immediate and delayed-type haemolytic transfusion reactions (HTR) bringing about extravascular red cell destruction (2, 4, 5, 8, 11). Anti-M rarely causes haemolytic disease of the fetus and newborn (HDFN) and neonatal RBC aplasia (2, 4-6, 8, 11). Anti-M is more common in young children, patients with bacterial infections, and pregnant women with an M+ fetus. Generally, anti-N is less often seen due to the structurally similar “N” antigen on GPB, preventing N- individuals from producing anti-N (10). On the other hand, anti-En^a are usually IgG and have caused severe HTR and HDFN reacting with the high-frequency epitopes on GPA. Because of the high prevalence of En^a epitopes in the population, it is difficult to find compatible donor units for En^a-patients with anti-En^a, who are usually also M-N- (2, 3, 5).

In contrast, antibodies against the S, s, and U antigens are generally IgG, though rare cases of IgM anti-S have been reported (2, 5, 10, 11). IgG class antibodies require the use of anti-human antiglobulin in the indirect antiglobulin test (IAT) alloantibody screen. Agglutination by anti-s can be enhanced by slightly reducing the pH to 6.0 from the buffered saline pH of 7.0 (5, 8, 10). The presence of these alloantibodies is more clinically significant than anti-M and anti-N, as they are reactive at body temperature and can cross the placenta. Anti-S and anti-s have been reported to cause delayed HTR and HDFN, in higher frequencies than anti-M or anti-N (1, 8, 14). Anti-U is rare but is known to be more severe or fatal in the event of transfusion reactions and must be considered in S-s- individuals due to the GPB-null phenotype (1, 3, 8). This means that S-, s-, or U- patients require transfusion with null phenotype blood to avoid adverse transfusion reactions (13).

Autoantibodies in this blood group system are rare, but some autoimmune diseases have been reported in the past (2, 14, 26). This includes auto anti-N in a dialysis patient using equipment that was disinfected by formaldehyde. Other examples of auto anti-N, auto anti-S, and auto anti-U have been reported to cause autoimmune haemolytic anaemia as well as warm autoantibodies against M, N, S, s, U, and En^a antigens (2, 6, 7, 26).

Genetics, Antigens, and Antibodies of Hybrid Variants

Many hybrid variants are formed through unequal crossing over, gene conversion, missense mutations, and splicing variants (4, 22, 27). New hybrid glycophorins are expressed following a repair of a defective splice site in exon III of the *GYPB* gene and this is the ‘hotspot’ of recombination between the homologous sequences (22, 27).The different hybrid types are named GYP(A-B) and GYP(B-A) caused by unequal crossing over; and GYP(A-B-A), GYP(B-A-B), GYP(A-E-A), and GYP(B-E-B) caused by gene conversion (4, 27, 28). Unequal crossing over between two chromatin strands results in different hybrid variant types based on the recombination site and arrangements as demonstrated in Figure 2. For instance, the GYP(A-B) strand is missing *GYPA* and *GYPB,* but the GYP(B-A) strand has both *GYPA* and *GYPB*. GYP(A-B-A) only has *GYPB* and GYP(B-A-B) has *GYPA*, by the replacement of defective splice sites (4, 27). Missense mutations or splicing variants are caused by SNPs present in the introns or exons and lead to a change in the amino acid sequence or splice site (4). Unequal crossing over as well as gene deletion are also responsible for null phenotypes such as M-N-En^a-, S-s-U-, and M^kM^k (lack of both M/N and S/s antigens) (5, 26).

MNS hybrid variants are more commonly seen in Asian populations (4). Most of the hybrid variants are low-prevalence antigens (Table 2); however, corresponding alloantibodies may be clinically significant for causing both immediate and delayed HTR and HDFN (4, 5). For example, the Mur glycophorin is common in China, Thailand, Taiwan, Singapore, Malaysia, and Vietnam, and exposure triggers an antibody response to Mi^a, Mur, MUT, and Hil antigens. The IgG class alloantibodies formed against these antigens have caused HTR and HDFN; however, some are naturally occurring and harmless (27). Alloantibodies against the Vw and Mi^a antigens on the Vw glycophorin are also common however they are clinically insignificant unless they are IgG (22, 27). Clinically significant IgG class anti-Vw examples are more common in European countries such as Switzerland, causing HDFN (22). In transfusion medicine, the identification of irrelevant IgM antibodies is avoided by using alloantibody screening cells without corresponding antigens (22). Conversely, new alloantibody screening cells or kodecytes have been developed to include specific blood group variant antigens for which antibodies may be more common and clinically significant in certain populations. For example, the epitopes of Mur and MUT peptides were successfully attached onto RBCs by KODE™ technology, without affecting the qualitiy of alloantibody screening or identification tests (30).

Table 1: MNS Phenotype Frequencies in Caucasians and Africans (1, 4, 7, 10)

MNS Phenotype	Caucasians (%)	Africans (%)
M+N-	30	25
M+N+	49	49
M-N+	21	26
S+s-	10	6
S+s+	42	24
S-s+	48	68
S-s-	0	2
U+	100	99
En^a+	100	100

Table 2. Other antigens in the MNS Blood Group System (4, 7)

Classification	Antigen (n=50)
Polymorphic	M, N, S, s
High prevalence	U, En^a, ENKT, "N", ENEP, ENEH, ENAV, ENDA, ENEV, JENU
Low prevalence	He, Mi^a, M^c, Vw, Mur, M^g, Vr, M^e, Mt^a, St^a, Ri^a, Cl^a, Ny^a, Hut, Hil, M^v, Far, s^D, Mit, Dantu, Hop, Nob, Or, DANE, TSEN, MINY, MUT, SAT, ERIK, Os^a, HAG, MARS, MNTD, SARA, KIPP, SUMI

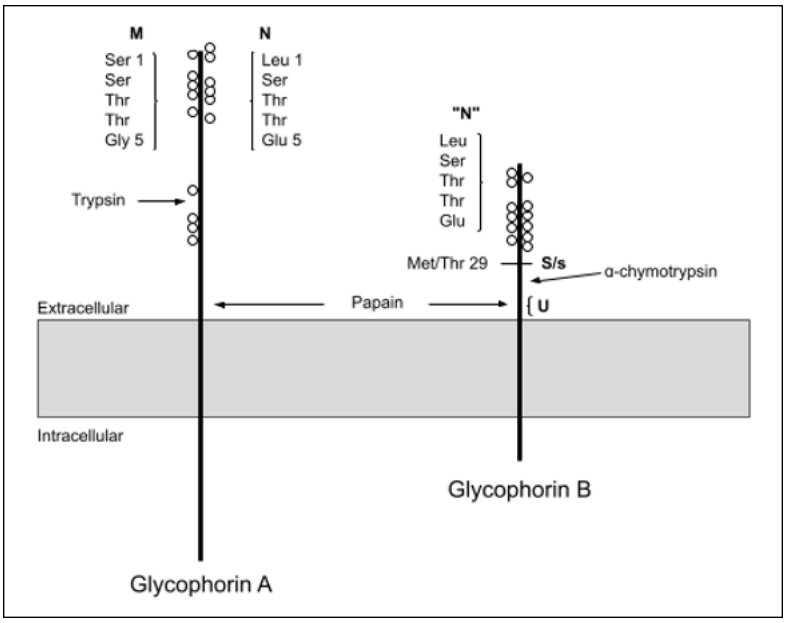


Figure 1. Structure of glycophorin A and glycophorin B adapted from (12)

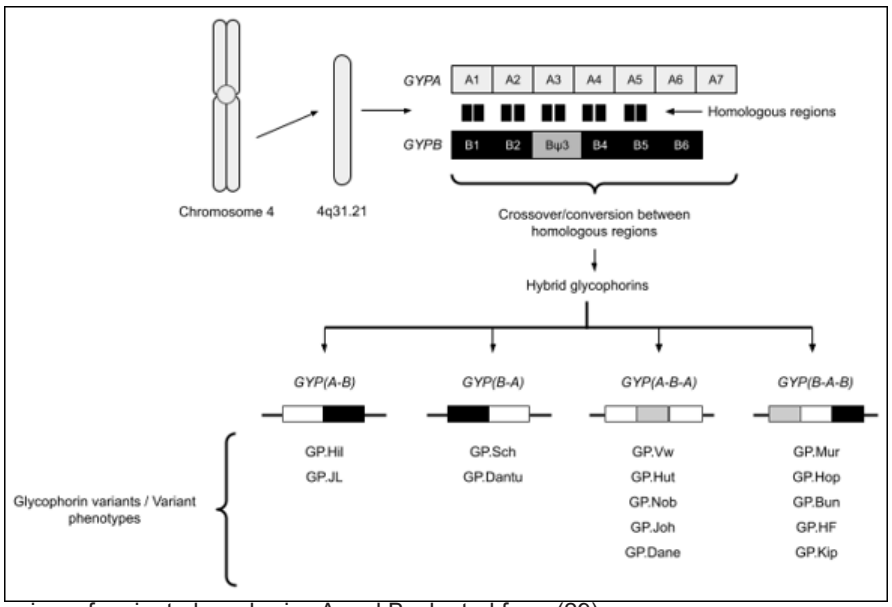


Figure 2. Genetic mechanism of variant glycophorins A and B adapted from (29)

CONCLUSION

The MNS blood group system exhibits diverse molecular and immunological properties. The genes, proteins, antigens, and corresponding alloantibodies can contribute to an individual's unique MNS blood group. This review emphasizes the importance of matching MNS blood groups for patients requiring blood transfusion in whom atypical clinically significant alloantibodies of the MNS system have been encountered and threaten HTR or HDFN. While some MNS blood group variations are rare or less clinically significant, each should be considered, as clinical consequences can be severe.

The understanding of the MNS system has been evolving since its discovery in 1927 and today, 50 antigens have been identified in this highly polymorphic system.

AUTHOR INFORMATION

Rei Miyamoto, BMLSc, Medical Laboratory Scientist, University of Otago.

Correspondence: Rei Miyamoto
email: rei1004miyamoto@gmail.com

REFERENCES

1. Stendahl K, Tormey CA, Baine IL. Methods of RBC Alloimmunization to ABO and Non-ABO antigens, and test methodologies. In: Maitta RW, eds. *Immunologic Concepts in Transfusion Medicine*. Elsevier, Philadelphia 2020; 15–33.
2. Aeschlimann J, Westhoff CM. MNS and duffy blood group systems. In: Shaz BH, Hillyer CD, Gil MR, eds. *Transfusion Medicine and Hemostasis: clinical and laboratory aspects.* Elsevier Science, Amsterdam 2019; 163–167.
3. Dean L. The MNS blood group. In: Beck B, eds. *Blood Groups and Red Cell Antigens*. National Center for Biotechnology Information, Bethesda 2005; 65-69.
4. Lopez GH, Hyland CA, Flower RL. Glycophorins and the MNS blood group system: a narrative review. *Annals of Blood* 2021; 6: 1-16.
5. Reid ME, Westhoff CM. Other blood group antigens and antibodies. In: Hillyer CD, Silberstein LE, Ness PM, et al, eds. *Blood Banking and Transfusion Medicine*. Churchill Livingstone/Elsevier, Philadelphia 2007; 96–111.
6. Daniels G. Human Blood Groups. 2nd ed. John Wiley & Sons, Incorporated, 2002.
7. Reid ME, Lomas-Francis C, Olsson ML. MNS Blood Group System. In: Reid ME, Lomas-Francis C, Olsson ML, eds. *The Blood Group Antigen FactsBook*. Academic, Oxford 2012; 53–134.
8. Knowles S, Regan F. Blood cell antigens and antibodies: erythrocytes, platelets, and granulocytes. In: Lewis SM, Bain BJ, Bates I, eds. *Dacie and Lewis Practical Haematology*. Churchill Livingstone/Elsevier, Philadelphia 2006; 481–522.
9. ISBT. 201 Table of blood group systems [Internet]. *International Society of Blood Transfusion* 2022; Available from: https://www.isbtweb.org/resource/tableofbloodgroupsystems.html
10. Castillo B, Dasgupta A, Klein K, et al. Red cell antigens and antibody. In: Castillo B, Dasgupta A, Klein K, et al, eds. *Transfusion Medicine for Pathologists*. Elsevier 2018; 69–112.
11. Quraishy N, Sapatnekar S. Advances in blood typing. In: Makowski GS, eds. *Advances in Clinical Chemistry*. Clinical Laboratory Partners, Newington 2016; 221–269.
12. Aeschlimann J, Westhoff CM. MNS and duffy blood group systems. *Transfusion Medicine and Hemostasis* 2019. Figure 28.1, Diagram of glycophorin A and glycophorin B; p. 163.
13. Hagman JR, Storry JR. Other protein blood groups. In: Simon TL, Gehrie EA, McCullough J, et al, eds. *Rossi's Principles of Transfusion Medicine*. Wiley-Blackwell, Chichester, 2022; 109–117.
14. Reid ME, Lomas-Francis C, Olsson ML. Section III. Other useful facts. In: Reid ME, Lomas-Francis C, Olsson ML, eds. *The Blood Group Antigen FactsBook*. Academic, Oxford 2012; 692–729.
15. Hsu K. Exploring the potential roles of band 3 and aquaporin-1 in blood CO2 transport–inspired by comparative studies of glycophorin B-A-B hybrid protein GP.Mur. *Front Physiol* 2018; 9: 1-10.
16. Leffler EM, Band G, Busby GBJ, et al. Resistance to malaria through structural variation of red blood cell invasion receptors. *Science* 2017; 356(6343): 1-31.
17. Jaskiewicz E, Jodłowska M, Kaczmarek R, Zerka A. Erythrocyte glycophorins as receptors for plasmodium merozoites. *Parasit Vectors* 2019; 12(1): 317. doi: 10.1186/s13071-019-3575-8
18. Lu YQ, Liu JF, Nagel RL, Blumenfeld OO. Erythrocyte membrane glycophorins of Central Africans and some hematological patients. *Chin Med J* 1987; 100(10): 787–794.
19. Parkkinen J, Rogers GN, Korhonen T, et al. Identification of the O-linked sialyloligosaccharides of glycophorin A as the erythrocyte receptors for S-fimbriated Escherichia coli. *Infect Immun* 1986; 54(1): 37–42.
20. Wright KJ, Hultgren SJ. Sticky fibers and uropathogenesis: bacterial adhesins in the urinary tract. *Future Microbiol* 2006; 1(1): 75–87.
21. Salas A, Marco-Puche G, Triviño JC, et al. Strong down-regulation of glycophorin genes: a host defense mechanism against rotavirus infection. *Infect Genet Evol* 2016; 44: 403–411.
22. Heathcote DJ, Carroll TE, Flower RL. Sixty years of antibodies to MNS system hybrid glycophorins: what have we learned? *Transfus Med Rev* 2011; 25(2): 111–124.
23. Castillo B, Dasgupta A, Klein K, et al. Blood bank testing. In: Castillo B, Dasgupta A, Klein K, et al, eds. *Transfusion Medicine for Pathologists*. Elsevier, 2018; 51–68.
24. Strobel E. Use of the enzyme method for antibody identification. *Clin Lab* 2004; 50(9-10): 575–580.
25. Tsuneyama H, Isa K, Watanabe-Okochi N, et al. An unusual variant glycophorin expressing protease-resistant M antigen encoded by the GYPB-E(2-4)-B hybrid gene. *Vox Sang* 2020; 115(7): 579–585.
26. Schenkel-Brunner H. MNS System. In: Schenkel-Brunner H, eds. Human Blood Groups. *Springer, Vienna*; 2000: 304-63.
27. Hassan SN, Kannan TP, Mohamad S, et al. Molecular detection of glycophorins A and B variant phenotypes and their clinical relevance. *Transfus Med Rev* 2019; 33(2): 118–124.
28. ISBT 002. MNS Blood Group Alleles [Internet]. *International Society of Blood Transfusion* 2023; V5.7. Available from: https://www.isbtweb.org/resource/002mnsalleles.html
29. Hassan SN, Kannan TP, Mohamad S, et al. Molecular detection of glycophorins A and B variant phenotypes and their clinical relevance. *Transfus Med Rev* 2019 Apr. Figure 1, General overview of hybrid glycophorins A and B: 120.
30. Heathcote D, Carroll T, Wang JJ, et al. Immunohematology: novel antibody screening cells, MUT+Mur kodecytes, created by attaching peptides onto red blood cells. *Transfusion* 2009; 50(3): 635–641.

Copyright: © 2024 The author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

sthemE
by Stago
Manager

eSolutions
are in our blood.

Boost your Stago analysers

With our new
Data Manager

Minimise
Turn Around Time

Maximise
Quality Management

- Result auto- validation
- TAT alerts
- Patented expert rules
- Method validation
- Full Quality Control management

Conception : L2R.fr ©2024 Diagnostica Stago - All Rights Reserved - Non-contractual photos - 01/2024
This document contains information on products which is targeted to a wide range of audiences and could contain product details or information otherwise not accessible or valid in your country.

Learn more at sthemo.stago.com

sthemE is trademark of the Stago Group. The rights to the trademarks and logos used in this document belong to the Stago Group. These trademarks may not be used without the permission of the Stago Group.

Diagnostica Stago
Always read the label and instructions for use – follow the instructions for use

Stago
Diagnostics is in our blood.

REVIEW ARTICLE

A review of ten years of *Leptospira* serology and PCR testing

Tégan A. Hall, Andrew W. Soepnel and Michael Addidle

ABSTRACT

Objective: To evaluate the use of diagnostic *Leptospira* laboratory testing within the Midlands region of New Zealand and identify the most sensitive testing strategy.

Method: *Leptospira* serology and polymerase chain reaction (PCR) testing performed within the Pathlab remit in 2013-2022 were reviewed by comparing methodologies and request origins to identify trends over time and evaluate the relative performance of serology and PCR testing.

Results: 81% of the cases tested by both serology and PCR that were confirmed infections were detected by either blood PCR, urine PCR, or serology alone. No significant difference was observed between the detection rates of blood PCR and urine PCR. Serology was the most frequently requested methodology, though PCR testing quadrupled in 2017 and uptake has continued to increase since then, becoming the favoured methodology amongst hospital-based requestors in 2022. Appropriately timed paired serological testing was rarely performed.

Conclusions: No single methodology can be relied on to consistently detect leptospirosis infections. Follow-up serology was under-utilised. A combination of PCR and serology testing was the most effective testing strategy.

Key words: Leptospirosis, ELISA, microscopic agglutination test (MAT), serology, PCR.

NZ J Med Lab Sci 2024; 78(1): 25:30

INTRODUCTION

Leptospirosis is an illness caused by infection with pathogenic spirochaetes of the *Leptospira* genus and is a notifiable disease in New Zealand, which has an annual incidence of approximately 2 per 100,000 population (1). Transmission is typically zoonotic, occurring through contact with infected farm animals or rats, or through contact with water or soil contaminated with the urine of infected animals. Risk of exposure is therefore highest for rural occupations and meat workers (2).

After a mean incubation period of ten days, leptospirosis causes a biphasic illness with a range of presentations. During the acute phase, leptospires are present throughout the blood and tissues, commonly causing flu-like symptoms such as headache, fever, myalgia and conjunctival suffusion. In the 10% of cases that are severe, Weil's disease (jaundice, renal failure, haemoptysis, and dyspnoea), meningitis, or respiratory failure can develop. After three to nine days, the acute phase may cede to a brief asymptomatic period before the immune phase begins. The immune phase is characterised by a rise in anti-*Leptospira* IgM antibodies and clearance of leptospires from the blood and tissues, except kidney tubules, resulting in prolonged intermittent shedding in the urine. This phase can present similarly to the acute-phase symptoms, which may progress to multiple organ failure (3,4). When clinical suspicion for leptospirosis is high, treatment with antibiotics is initiated immediately, as treatment is most effective when commenced within five days of illness (4).

The non-specific and variable manifestations of leptospirosis make the infection difficult to identify by clinical presentation alone. The presentation may be similar to other conditions such as viral hepatitis, influenza, toxoplasmosis and septicaemia; other rural infections, such as rickettsiosis; or tropical diseases in the case of returned travellers (3,4). This makes laboratory findings essential to confirming the diagnosis. Leptospirosis tests available in New Zealand include serology and polymerase chain reaction (PCR). Two types of serological tests are used for leptospirosis diagnosis in New Zealand: *Leptospira* IgM by enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CLIA), and the microscopic agglutination test (MAT). The IgM assays qualitatively detect the presence of anti-*Leptospira* IgM antibodies and are commonly employed as a screening test with the MAT used as a confirmatory assay. *Leptospira* IgM assays can be performed on automated platforms with a short turn-around-time. However, a positive *Leptospira* IgM result is not confirmatory for leptospirosis as it may represent a recent infection, a cross-reaction, or a past infection, since anti-*Leptospira* antibodies can remain detectable for months to years post-infection (3,5). MAT is regarded as the gold standard serological test for leptospirosis (2,3), though it also has drawbacks. The method involves the use of a panel of live *Leptospira* serovars. Antibodies of both IgG and IgM isotypes from patient serum bind to the causative serovar in the panel, resulting in agglutination and therefore identification of the infecting serovar (6). A minimum of 50% agglutination at a titre ≥ 400 in a single serum sample, or a minimum four-fold rise between acute and convalescent sera titres is considered serological confirmation of leptospirosis in New Zealand (2). The two diagnostic laboratories where *Leptospira* MAT is available in New Zealand use the same panel of eight serovars known to cause infection in New Zealand and Australia. As there are over 250 pathogenic *Leptospira* serovars worldwide, leptospirosis acquired overseas may give false negative results if the infecting serovar is not present in the MAT panel (2,6). The restriction of MAT to only two laboratories nationwide is a result of its complex and labour-intensive nature. The need to maintain live *Leptospira* cultures presents both a technical difficulty and a biosafety hazard. The test cannot be standardised and must be maintained as an in-house assay and has an interpretation that may be subject to reader variation (6,7).

The sensitivity of serological tests for leptospirosis varies with the stage of infection. Testing should therefore be carried out on temporally paired sera. Both *Leptospira* IgM and MAT have low sensitivity during the acute phase of infection, when the humoral immune response is yet to appear. Sensitivity becomes optimal during the immune phase (8). In practice, this means that a convalescent sample of an infected patient, which is recommended to be taken three weeks after the onset of symptoms (4), compared to the acute sample taken at the first presentation, should show either seroconversion or a rise in MAT titre (7,9), providing a retrospective diagnosis. In some cases, early antibiotic therapy can interfere with the antibody response, and repeat testing beyond the paired sera may be necessary (4,7).

In contrast to serology, PCR can provide a more rapid "real-time" laboratory diagnosis of leptospirosis using blood or urine samples, and in cases of meningitis, cerebrospinal fluid (CSF) (4). PCR on blood samples can detect leptospirosis during the first week of symptomatic illness, before antibodies are detectable by serological methods (10,11). However, leptospiraemia is efficiently cleared during the immune phase, resulting in blood PCR becoming unreliable from the second week of illness (11). Urine is the recommended PCR sample-type during the immune phase. However, as leptospires are shed intermittently from the kidneys during infection, a negative urine PCR result does not exclude leptospirosis and should be repeated in cases with high clinical suspicion of leptospirosis (2,4). A single positive PCR result is sufficient for confirmation of leptospirosis (2).

Testing for leptospirosis is inconsistent throughout New Zealand, as test accessibility, which is dependent on location, dictates how

a patient is tested, as opposed to official guidance. *Leptospira* IgM is performed by three diagnostic laboratories using different test kits and platforms. All positive and equivocal *Leptospira* IgM samples are sent to the same reference laboratory for MAT. Patients who have *Leptospira* serology performed outside the areas covered by these laboratories are only tested by MAT, not IgM ELISA or CLIA, and only when both acute and convalescent serum samples have been submitted (with exceptions). PCR testing is also available at three laboratories, and acceptance criteria for testing varies from none to provision of specific clinical details and sample timing (unpublished survey of New Zealand's medical laboratories, November 2021). Guidance for laboratory testing is also inconsistent. The Ministry of Health recommends that patients be tested by both MAT and PCR (2). This conflicts with advice from Best Practice Advocacy Centre New Zealand (bpac^{nz}) to perform paired serology and only add PCR when illness is severe or if it is necessary to confirm an occupationally acquired infection (4).

This study undertook a retrospective review of *Leptospira* serology and PCR results over a ten-year period from patients in the Pathlab remit, to evaluate the utilisation and value of the different test methods available for diagnosing leptospirosis in the Midlands region. The aim was to identify which testing strategies have been most effective in detecting leptospirosis.

METHODS

Ethics

Ethical approval was not required as per the Health and Disability Ethics Committees' (NZ) screening questionnaire.

Data Collection

Leptospira serology and PCR results were retrieved from the Pathlab results repository accompanied by patient National Health Index (NHI), requestor location, sample identifier, and collection date, to cover 2013–2022, inclusive. The retrieval captured requests from community-based requestors throughout the Midlands region of New Zealand, excluding Tairāwhiti and Taranaki, in addition to four public hospitals located in Tauranga, Whakatāne, Rotorua, and Taupō. Requests collected at Waikato, Thames, Tokoroa, Te Kuiti, and Taumarunui Hospitals do not fall under the Pathlab testing remit and were not included in the data.

Serology consisted of IgM ELISA (PanBio) performed at Pathlab Waikato, and MAT performed by ESR Wallaceville on samples equivocal or positive by IgM ELISA. PCR was performed at Waikato Hospital Laboratory, initially almost exclusively on blood samples, with urine officially validated as a sample-type in 2017.

Result Interpretation

IgM ELISA results were reported qualitatively as either negative, equivocal, or positive, as per manufacturer cut-offs. MAT results were reported quantitatively as a titre, as well as qualitative interpretation. Interpretations included "negative" (titre < 50), "exposed" (titre 50–200, where only one sample was collected, or the titres from paired sera remained within this range without a four-fold rise), and "confirmed" (single titre ≥ 400, or four-fold increase in titre between acute and convalescent sera). PCR results were reported qualitatively as "not detected" or "detected". Any case with a confirmed MAT result and/or PCR detected was regarded as confirmed positive for leptospirosis, as per the Ministry of Health New Zealand's laboratory criteria for diagnosis (2).

Data Analysis

Serology and PCR test numbers, and PCR sample-types used, were compared for hospital- and community-based requestors over time. The relative performance of serology and PCR tests was analysed by applying an inclusion criterion of both serology and PCR results being available for each case of suspected leptospirosis. Test results grouped for each case were required to pertain to the same episode of illness. Where multiple requests were made for the same test during the same episode of illness and the result changed between requests, the convalescent or confirmatory results were deemed to be most useful and used for the purposes of data analysis.

Using the data that met the inclusion criterion, the negative predictive value (NPV) of *Leptospira* IgM ELISA was calculated as the number of cases where IgM and PCR were negative (IgM true-negative) divided by the total number of cases where IgM was negative. The positive predictive value (PPV) of *Leptospira* IgM ELISA was calculated as the number of cases where IgM was positive and supported by a confirmed MAT or detection by PCR (IgM true-positive) divided by the total number of cases where IgM was positive. Equivocal IgM results were excluded from these calculations as they defer to the MAT result.

Results preceding 2017 were removed to give an overview of how clinicians requested *Leptospira*-specific tests when serology, blood PCR, and urine PCR were all available as options, and to review the outcomes of the different testing strategies. A further inclusion criterion of both blood and urine PCR results being available was applied to compare the relative performance of sample-types using McNemar's test (12). Finally, a subset of requests from 2022 was analysed to gauge the frequency at which serology is followed up with convalescent sample testing.

Table 1. Summary of results for all cases that had both *Leptospira* serology and PCR tests performed.

		Serology					
		IgM N	IgM Eq, MAT N	IgM Eq, MAT Ex	IgM P, MAT N	IgM P, MAT Ex	IgM P, MAT CONF
PCR	Bl & Ur ND	86	0	1	8	4	**5**
	Bl ND, Ur NT	56	1	1	2	1	**3**
	Bl NT, Ur ND	36	1	0	0	1	**5**
	Bl & Ur DET	**1**	0	0	0	0	**1**
	Bl DET, Ur ND	**4**	0	0	0	**1**	0
	Bl DET, Ur NT	**3**	**1**	0	0	0	**1**
	Bl ND, Ur DET	**9**	0	0	0	0	**5**
	Bl NT, Ur DET	**2**	**1**	0	0	**1**	0

N = negative; Eq = equivocal; Ex = exposed; P = positive; CONF = confirmed; Bl = blood; Ur = urine; ND = not detected; NT = not tested; DET = detected. Numbers in **bold** are cases meeting the laboratory criteria for confirmation of leptospirosis.

Table 2. Testing modalities requested for suspected cases of leptospirosis in 2017-2022.

	Ser & PCR	Ser only	Bl & Ur PCR only	Bl PCR only	Ur PCR only
Total cases	207	1,353	151	49	32
Unconfirmed cases	173	1,308	136	49	31
Confirmed cases (%)	34 (16%)	45 (3%)	15 (10%)	0 (0%)	1 (3%)

Ser = serology; Bl = blood; Ur = urine

Table 3. PCR results for each sample-type belonging to cases who had serology and both PCR sample-types tested.

		Blood		Total
		Detected	Not Detected	
Urine	Detected	2	14	16
	Not detected	5	104	109
Total		7	118	125

RESULTS

The data collected for the study period included 3,703 *Leptospira* IgM and 843 PCR tests from 3,344 patients. As CSF PCR was performed on only three patients, data on CSF was excluded from this review.

The results of serology and PCR testing are summarised in Table 1 using only the cases that met the inclusion criterion of having both serology and PCR results (241 cases). 43 cases (18%) met the laboratory case-definition for confirmed leptospirosis. Of those 43 cases, 23 (53%) met the laboratory case-definition for leptospirosis due to PCR testing only. 35 (81%) confirmed cases were detected by only one of the three possible confirmatory tests: Blood PCR alone was responsible for 9 (21%) confirmed cases, urine PCR for 13 (30%), and MAT for 13 (30%). IgM ELISA had a NPV of 90% compared to PCR, and a PPV of 58% compared to MAT and PCR.

The number of cases tested by each available combination of testing methodologies during the years 2017-2022 and the proportion that returned confirmatory results is summarised in Table 2.

The 125 cases with both blood and urine PCR results are summarised in Table 3, from which McNemar's test two-tail p-value was calculated to be 0.06. Using a significance threshold of 0.05, this provides insufficient evidence for a difference in the proportion of detected results between blood and urine PCR sample-types.

DISCUSSION

In the community setting, *Leptospira* IgM testing decreased throughout the study period (Figure 1). Uptake of PCR in the community during this period never reached sufficient volume to explain, by way of replacement, the continual and marked decline in IgM testing illustrated in Figure 1. Conversely, serology requests originating from hospitals remained steady throughout, even as PCR was adopted, with PCR eventually becoming the more frequently used methodology for this requestor group in 2022 (Figure 2). A survey to investigate the cause of these trends is out of scope for the current study, but we suggest that the availability of *Leptospira* PCR, a test performed at Waikato Hospital Laboratory, was better known to hospital-based requestors, and GPs may have been unaware that they had access to PCR testing.

As illustrated in Figures 2-4, an increase in the number of *Leptospira* PCR requests and confirmed cases was seen in 2017. This year's quadrupling in total PCR requests coincided with the year urine became a validated PCR sample-type at Waikato Hospital, though the increased requests were for both sample types (Figure 4). 2017 also saw a peak in the national notification rate of leptospirosis at 3 cases per 100,000 compared to 1.8 cases per 100,000 the previous year. Additionally, in this peak year, Waikato had the highest notification rate for leptospirosis, nationwide, at 13.2 cases per 100,000 (13). Beyond the new availability of urine as a PCR sample-type raising awareness of *Leptospira* testing, reasons for the 2017 spike in test numbers and confirmations are unclear.

Since the upsurge in 2017, it can be seen in Figure 2 that the proportion of *Leptospira* test requests that were for PCR increased with a concurrent upwards trend in the number of confirmed cases. The two spikes in confirmed cases in 2017 and 2021 (Figures 2 and 3) are matched by spikes in community PCR testing (Figure 4), and a relatively small spike in community IgM testing for 2021 only but are not reflected in the proportion of non-negative IgM results, which is steady in 2017 and at a trough in 2021 (Figure 5). This indicates that PCR detected cases that were missed or not tested by IgM ELISA during these spikes in testing.

We have reported a low PPV of 58% for IgM ELISA, which does not correlate with the performance reported by other studies (8,9,14). This could be attributed to calculating the PPV based on the corresponding MAT and/or PCR result for each positive IgM ELISA. Research has suggested that the non-serovar-specific IgM detected by ELISA can be detected earlier than the serovar-specific antibodies detected by MAT (6,15). Therefore, the non-confirmed MAT results, taken from a population that has been demonstrated not to test serology routinely with paired sera (Figure 6), may have falsely lowered the IgM ELISA's PPV. Eugene et al. calculated a PPV of 80% for IgM ELISA by using Bayesian latent class modelling to account for the unreliability of MAT in the acute phase (9), which supports the notion that the performance of IgM ELISA may be better than our data suggests.

Analysis of the relative performances of the differing methodologies showed serological testing alone to be responsible for confirming leptospirosis in 30% of cases where both serology and PCR had been performed. This is consistent with Earl et al.'s finding that 36% of the leptospirosis-positive patients enrolled in their study did not have their illness confirmed by PCR (5). In our data review, when both serology and PCR were tested, a greater proportion of the confirmed cases (53%, 23/43) were detected by PCR only. It is not surprising that only 17% (2/12) of the cases that tested positive for blood PCR were also confirmed by serology compared to the 32% (6/19) of urine cases that were also confirmed by serology. This is because the acute leptospiraemic phase is the only window when blood PCR can detect an infection, and this window precedes the antibody response. Cases that are confirmed by blood PCR in the acute phase do not require follow-up serology unless it is deemed necessary to identify the infecting serovar for Public Health purposes. Leptospires are cleared from the blood and intermittently shed in the urine at the time when the antibody response becomes detectable (4), thereby explaining the higher incidence of urine PCR and serology co-confirmations. While urine PCR was responsible for confirming more cases than blood PCR, a comparison of the two sample-types by McNemar's test did not indicate that one detected leptospirosis significantly more than the other. This, in addition to the fact that 81% (35/43) of confirmed cases were detected by only one of the three possible confirmatory tests, indicates that the combined use of serology, blood PCR, and urine PCR is the most sensitive strategy for detecting leptospirosis in suspected cases. This is evident in Table 2, where combined serology and PCR testing gave the highest proportion of cases detected. Earl et al.'s study came to the same conclusion that blood and urine PCR and serology should all be employed for leptospirosis laboratory investigations (5). Additionally, a review by Budihal and Perwez of various laboratory tests for leptospirosis concluded that PCR and IgM ELISA used together is the most effective way to achieve an early diagnosis of leptospirosis (16).

We recommend that New Zealand incorporate this multi-modal approach into the development of a national standardised testing strategy for leptospirosis that optimises case detection, by way of judicious test selection, in an equitable fashion. In order to implement this, further work is required, such as evaluating the worth of the additional expense incurred by increased testing by

a cost-benefit analysis.

While this review has shown that testing by both serology and PCR has been the most sensitive approach for detecting leptospirosis, the sensitivity of either methodology can be undermined by inappropriate sample collection or sample-type. Blood PCR is not indicated after the first week of illness, but appropriate sample timing could not be assessed for our data as date of symptom onset was not available. The timing of serum collection is also important. Earl et al. reported that 84% of patients with suspected leptospirosis presented to their general practitioner during the acute phase of the illness (5). At this time, the antibody response is usually undetectable and a negative *Leptospira* IgM result is to be expected, which should be followed up with a convalescent sample. The importance of testing convalescent samples was demonstrated by Bajani et al., who calculated the sensitivity of IgM ELISA to be 49% in acute sera and 75% in convalescent sera, with MAT also being 49% in acute sera but rising to 94% in convalescent sera (8).

Our analysis of serology testing from 2022 (Figure 6) suggests that sample timing is not performed optimally. That year, no follow-up serology was collected for 87% of cases where serology was performed, and leptospirosis was not confirmed by initial serology or PCR (Figure 6). More than half of the 5.9% that did had the follow-up serum collected earlier than recommended. This is despite each initial negative *Leptospira* IgM result being reported with a comment recommending repeat serology in 3-4 weeks. This rate is comparable to that seen by Waikato Hospital Laboratory, where in 2013, only 16% of *Leptospira* serology requests were followed up with a convalescent sample (17). Earl et al. found that, even with prompting from their medical centre, 32% (15/47) of patients in their study did not return for follow-up serology, and the researchers estimated that up to 31% (4/13) of patients who did not return could have had leptospirosis which was not detected by acute-phase tests (5). It is not always necessary to test follow-up serology, such as when the diagnosis of a different illness is made; also, patients may move between different laboratory remits, resulting in their acute and convalescent samples being tested by different laboratories, giving the false appearance of follow-up serology not being performed. However, these factors are unlikely to fully explain the relative frequency of 2.7% for appropriately paired IgM ELISA samples reported here. In light of this suboptimal use of *Leptospira* IgM ELISA, investigation into its value compared to other methods used outside New Zealand, such as point of care testing, may be of interest.

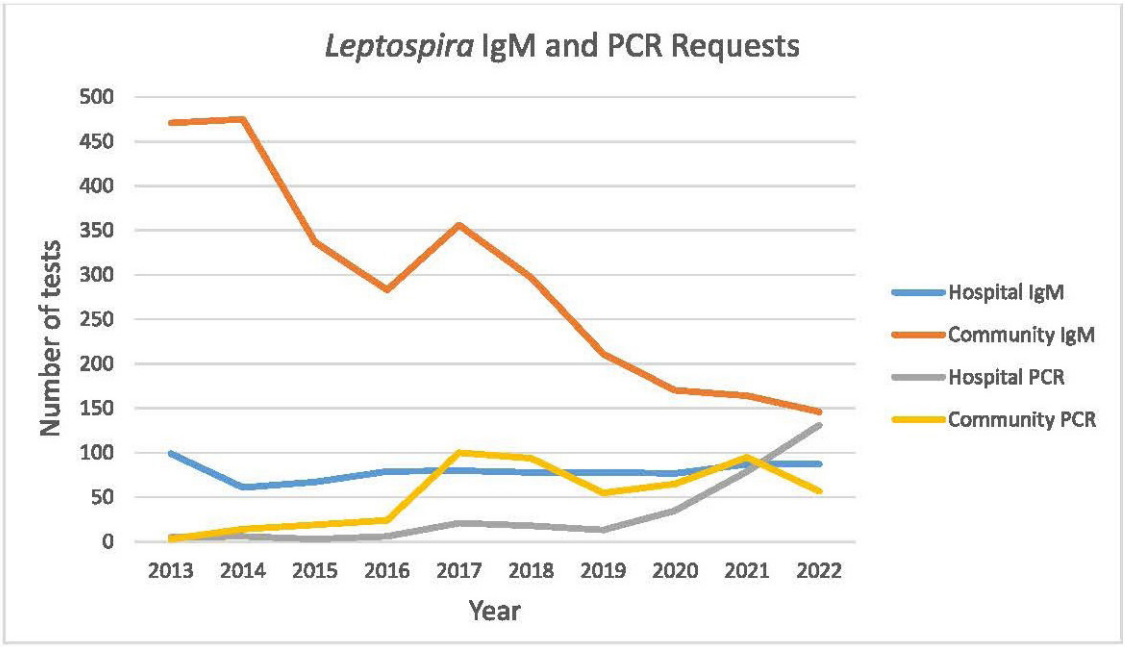


Figure 1. Uptake of Leptospira IgM and PCR testing by community- and hospital-based requestors over time.

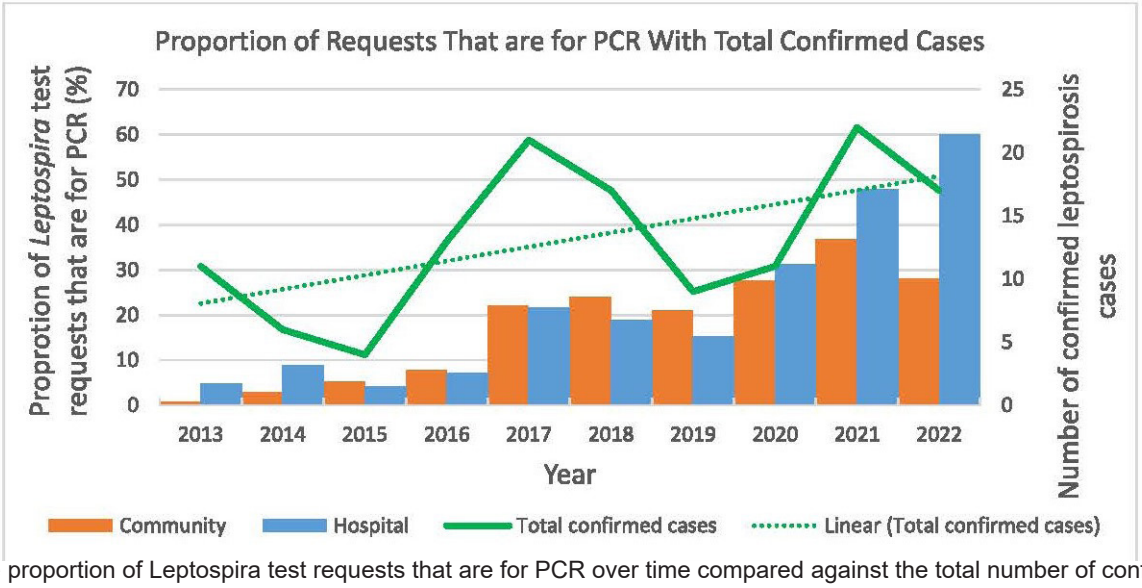


Figure 2. The proportion of Leptospira test requests that are for PCR over time compared against the total number of confirmed leptospirosis cases in the data set, with the linear relationship between the total annual number of confirmed cases and time demonstrated (r = 0.56 by Pearson Correlation).

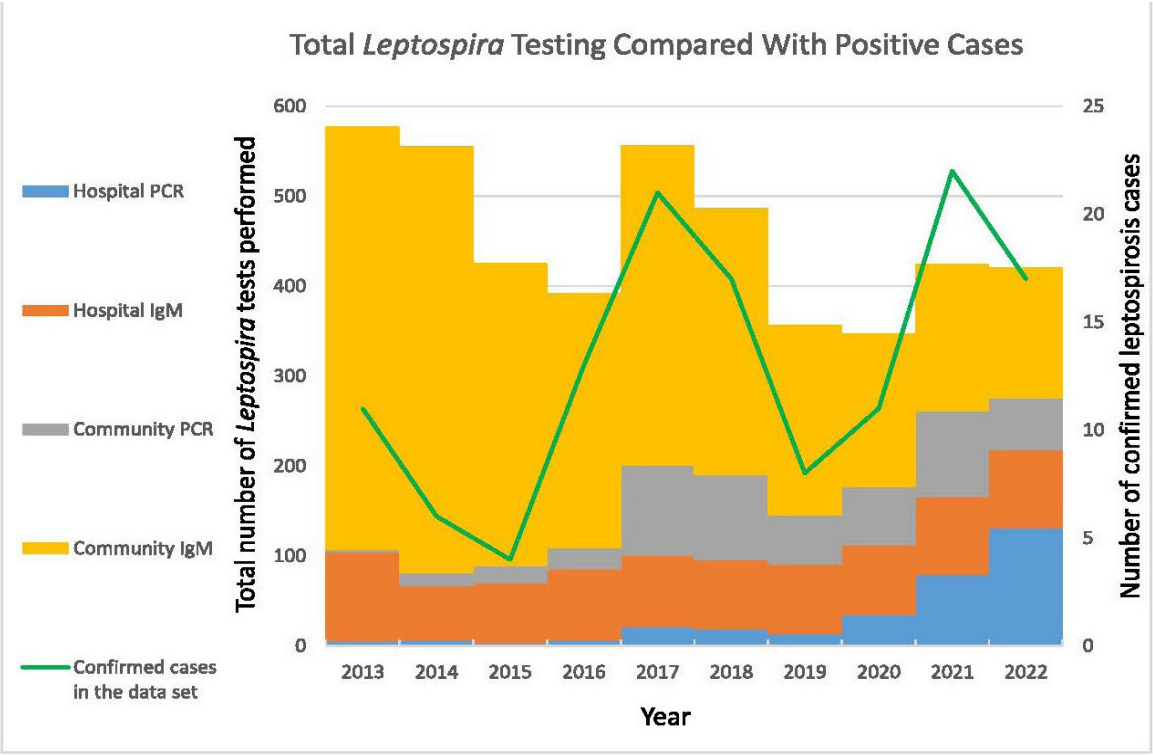


Figure 3. Overall test numbers grouped by requestor and test type over time, with our data set's confirmed case numbers overlaid.

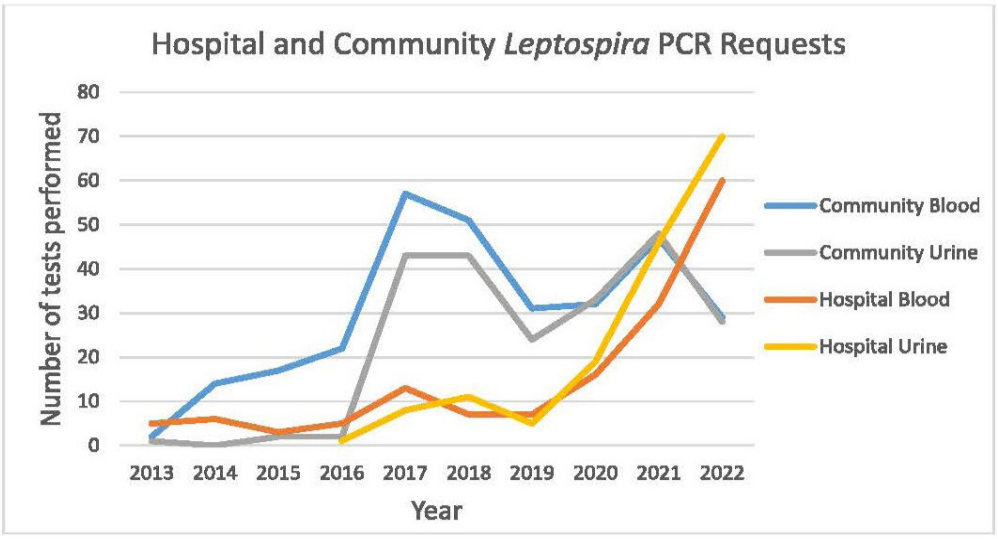


Figure 4. Number of blood and urine Leptospira PCR tests per year, originating from community- and hospital-based requestors.

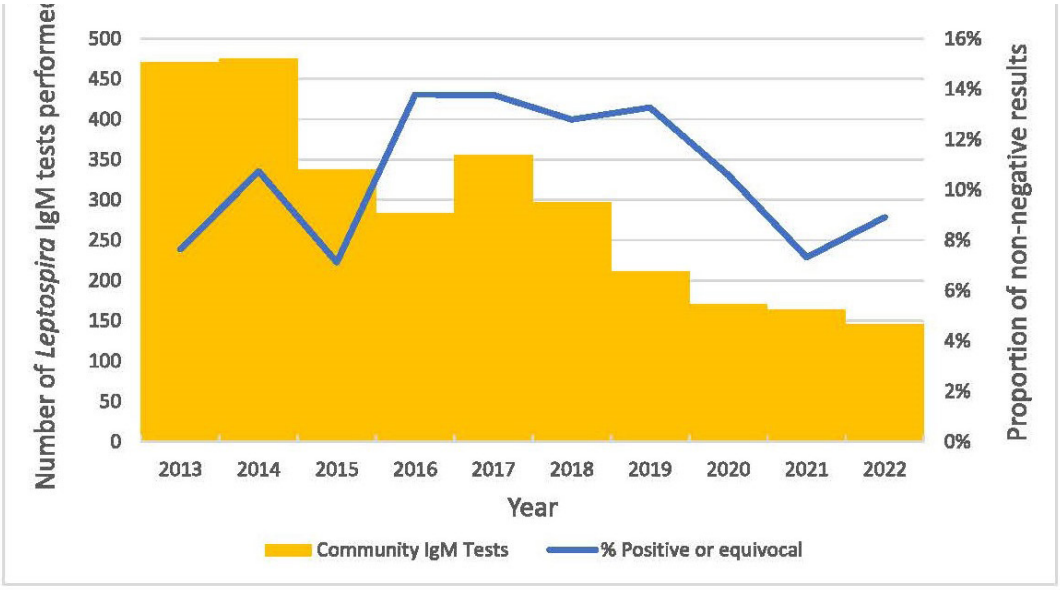


Figure 5. The total number of community-based Leptospira IgM tests over time, with the proportion of those that gave a non-negative (equivocal or positive) result overlaid.

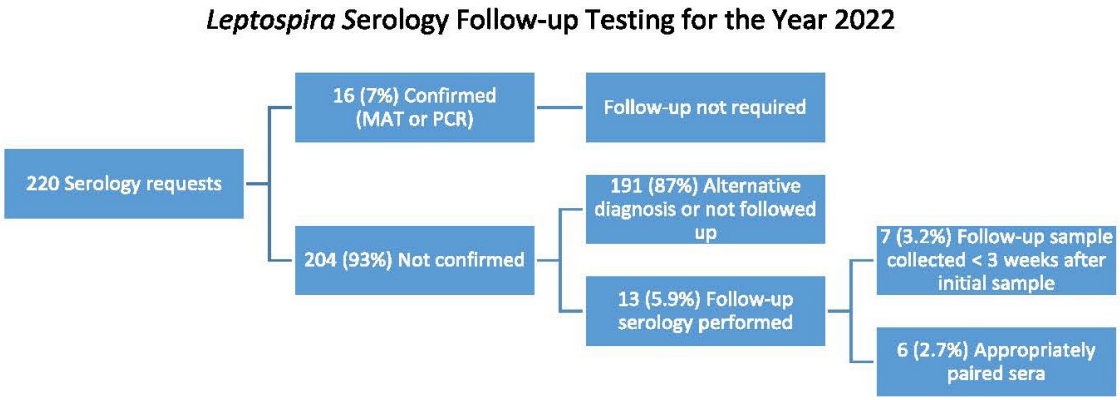


Figure 6: Leptospira serology requests for the year 2022, and the cases followed-up within appropriate and inappropriate timeframes.

Limitations

As leptospirosis is a biphasic illness, studies into *Leptospira*-specific tests often differentiate acute and convalescent results. Such differentiation was not possible here as this information is not a pre-requisite for testing and is seldom provided to the laboratory. Where the identification of follow-up testing was necessary, a presumptive status was assigned primarily by correlating sample collection dates in addition to manual case-by-case review of clinical details provided to the laboratory. The lack of information provided on sample timing relative to symptom onset also precluded any analysis into the appropriateness of blood PCR sample timing.

CONCLUSION

Laboratory diagnosis of leptospirosis in New Zealand remains both challenging and geographically heterogeneous. Our data indicated that follow-up serology is under-utilised. A combination of PCR and serology has been shown to be the most effective testing strategy, as no one test modality captures all clinical cases.

ACKNOWLEDGEMENTS

Warren Wright (Pathlab IT Department) for performing the data extraction.

AUTHOR INFORMATION

Tégan A. Hall, BA, BMLSc, Scientist[1]
Andrew W. Soepnel, BMLSc, MSc, Head of Department, Immunology[1]
Michael Addidle, MBChB, MRCP, FRCPath, DTM&H, Clinical Microbiologist[2, 3]

[1] Pathlab Waikato, Hamilton, New Zealand
[2] ESR, Wallaceville Science Centre, Upper Hutt, New Zealand
[3] Pathlab Waikato, Tauranga, New Zealand

Corresponding author: Tégan Hall, Pathlab Waikato, **email:** tegan.hall@pathlab.co.nz

REFERENCES

1. Nisa S, Wilkinson D, Angelin-Bonnet O, et al. Diverse epidemiology of *Leptospira* serovars notified in New Zealand, 1999-2017. *Pathogens* 2020; 9(10): 841.
2. Te Whatu Ora. Leptospirosis: part of the communicable disease control manual [internet] Wellington (NZ). *Te Whatu Ora* 2014 [updated 2017 Dec; cited 2023 Jun 2]. Available from: www.health.govt.nz/our-work/diseases-and-conditions/communicable-disease-control-manual/leptospirosis.
3. World Health Organization. Leptospirosis: Fact sheet [Internet]. *New Delhi (India) World Health Organization Regional Office for South-East Asia* 2009 Jan 1 [cited 2023 Jun 2] Available from: https://www.who.int/publications/i/item/B4221
4. Best Practice Advocacy Centre (bpac). Rural infection series: leptospirosis [Internet] Dunedin (NZ) *bpac*^{nz} 2013 Nov [cited 2023 Jun 2]. Available from: https://bpac.org.nz/BT/2013/November/rural-infections.aspx
5. Earl E, Fang F, Janes R, et al. An evaluation of diagnostic tests in a case series of suspected leptospirosis patients seen in primary care. *NZ Med J* 2021; 134(1539): 33-43.
6. Musso D, La Scola B. Laboratory diagnosis of leptospirosis: A challenge. *J Microbiol Immunol Infect* 2013; 46(4): 245-252.
7. World Health Organization. Human leptospirosis: guidance for diagnosis, surveillance and control. *World Health Organization,* Geneva, 2003.
8. Bajani MD, Ashford DA, Bragg SL et al. Evaluation of four commercially available rapid serologic tests for diagnosis of leptospirosis. *J Clin Microbiol* 2003; 41(2): 803-809.
9. Eugene EJ, Handunnetti SM, Wickramasinghe SA et al. Evaluation of two immunodiagnostic tests for early rapid diagnosis of leptospirosis in Sri Lanka: a preliminary study. *BMC Infect Dis* 2015; 15: 319.
10. Merien F, Portnoi D, Bourhy P, et al. A rapid and quantitative method for the detection of *Leptospira* species in human leptospirosis. *FEMS Microbiol Lett* 2005; 249(1): 139-147.
11. Agampodi SB, Matthias MA, Moreno AC, Vinetz JM. Utility of quantitative polymerase chain reaction in leptospirosis diagnosis: association of level of leptospiremia and clinical manifestations in Sri Lanka. *Clin Infect Dis* 2012; 54(9): 1249-1255.
12. Lowry, R. Clinical research calculators [internet]. Poughkeepsie (NY): VassarStats; [date unknown] [cited 2023 Jun 25]. Available from: http://vassarstats.net/
13. Health Intelligence Team, Health and Environment Group. Notifiable diseases in New Zealand Annual Report 2017. Overview of notifiable diseases [internet]. *Institute of Environmental Science and Research* 2019 March 27 [cited 2023 June 2] Available from: https://www.esr.cri.nz/our-research/nga-kete/infectious-disease-intelligence/notifiable-diseases/
14. Mullan S, Harivadanbhai Panwala T. Polymerase chain reaction: an important tool for early diagnosis of leptospirosis cases. *J Clin Diagn Res* 2016; 10(12): DC08-DC11.
15. Niloofa R, Fernando N, de Silva NL, et al. Diagnosis of leptospirosis: comparison between microscopic agglutination test, IgM-ELISA and IgM rapid immunochromatography test. *PLoS One* 2015; 10(6): e0129236.
16. Veerappa Budihal S, Perwez K. Leptospirosis diagnosis: competency of various laboratory tests. *J Clin Diagn Res* 2014; 8(1): 199-202.
17. Mansell C, Benschop J. Leptospirosis is an important multi-species zoonotic disease in New Zealand. *NZ Med J* 2014; 127(1388): 5-8.

Copyright: © 2024 The author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

ORIGINAL ARTICLE

Can the use of triglyceride to glucose and triglyceride to high density lipoprotein ratios indicate metabolic syndrome in the spinal cord injured male?

Lynnette M Jones and Michael Legge

ABSTRACT

Aim: To determine whether the use of triglyceride to glucose (TyG:G) and triglyceride to high density lipoprotein (TyG:HDL) indices can indicate the onset of metabolic syndrome in spinal cord injured (SCI) males.

Methods: Fasting plasma from 20, age, BMI, and physical parameters matched controls and 20 spinal cord injured males was analysed for triglycerides, glucose and insulin. In addition to the analyte values HOMA-IR was calculated for both groups. **Results**: Significant differences were identified between spinal cord injured complete and incomplete injuries for the TyG:G (p=0.042) and TyG:HDL (p=0.037) when compared with matched controls. Complete spinal cord injured were significantly different for TyG:G (p=0.039) and TyG:HDL (p=0.001). Those with incomplete lesions were not significantly different from the matched controls TyG:G (p=0.871) and TyG:HDL (p=0353).

Conclusion: Those with complete spinal cord injuries demonstrated outcomes consistent with metabolic syndrome, whereas those with incomplete spinal cord injuries did not differ from the able-bodied controls. It is concluded that the level of de-innervation has a significant role in the onset of metabolic syndrome in the spinal cord injured.

Keywords: spinal cord injured (SCI)

NZ J Med Lab Sci 2024; 78(1): 31:33

INTRODUCTION

Spinal cord injury (SCI) resulting in paralysis causes significant change in body composition below the lesion. The resultant loss of motor function leads to significant skeletal muscle wasting and a fat mass increase at both above and below the lesion (1,2). This significant change in body composition initiates major metabolic changes (3) that has been strongly associated with the development of cardiovascular disease (4). In addition, the development of glucose intolerance, hyperinsulinaemia, insulin resistance and dyslipidaemia are all contributing factors associated with the metabolic syndrome, which is frequently identified in SCI (3,5).

Our previous research using biochemical parameters and factor analysis in SCI identified a strong association with markers of metabolic syndrome (6). Subsequently, we identified using fatty acid analysis that desaturase and elongase activity was significantly different in SCI when compared with matched able-bodied controls (7), confirming a disruption of lipid metabolism. More recently we reported significantly elevated fasting plasma free fatty acids and glycerol in the SCI when compared to the matched controls (8).

In this current work we have investigated the use of the triglyceride: glucose index (TyG:G ratio) in SCI as a potential inexpensive surrogate marker for insulin resistance (9). In addition, we compare the TyG:G ratio to other potential biochemical markers of cardiovascular disease – the triglyceride to HDL ratio (TyG:HDL) and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) (10,11,12).

MATERIAL AND METHODS

Participants and outcomes

The present study was undertaken using plasma from SCI and control individuals from our previous study (7). All data relating to biophysical information, spinal injury classification, dual energy x-ray absorptiometry (DEXA) results and physical activity have been previously published (6). In brief, there were 20 participants in each group (SCI and controls) who were male and matched for age, height, weight, BMI and physical activity. There were no significant differences between all these parameters and between the groups (7). Ethical approval was obtained from both the Regional Health Funding Authority and the Canterbury Ethics Committee.

Biochemical data

Triglyceride (TyG) levels were determined enzymatically, while high density lipoproteins (HDL) were determined using the direct assay method. Both analytes were determined using the Aeroset system (Abbott Laboratories Diagnostics Division, Illinois, USA). Glucose was analysed using the Ultimate 5 glucose kit (Roche Diagnostics Corporation, Indianapolis, USA). And insulin was analysed by radioimmunoassay using the Coat-A-Count assay (Diagnostic Products, Los Angeles, USA). Analysis was undertaken on a Cobas Mira Plus auto-analyser (Roche Diagnostics Corporation, Indianapolis, USA).

Statistical analysis

All data were normally distributed and variances for the groups were the same. The TyG index was log transformed. The tests were two-sided independent t-tests. While able bodied and spinal injured men were similar in height, weight and age, they were independent groups. The t-tests were used primarily as an exploratory procedure to ascertain statistical differences between the controls and the SCI with complete and incomplete spinal injury, and a one-way ANOVA was performed to compare the TyG:G ratio, HOMA-IR and TyG:HDL ratio between the groups. All statistical analyses were undertaken using Statistical Packages for Social Sciences (SPSSv25), (IBM Statistics, Armonk, USA).

RESULTS

The initial exploratory between group t-test revealed a significant difference in the TyG:G ratio between the SCI men with complete lesions and those with incomplete lesions, p=0.042 and for the TyG:HDL ratio p=0.037. Significant differences were also found for comparisons between men with complete lesions and their matched controls, TyG:G p=0.039 and TG:HDL, p=0.001. Results for men with incomplete lesions and controls were not significant for either TyG:G or the TyG:HDL indices, p=0.871 and p=0.325 respectively.

The one-way ANOVA revealed that there was no statistical difference between the groups for TyG:G and HOMA-IR ($F(2,7)=2.858$, p=0.07 and $F(2,37)=0.087$, p=0.92 respectively. However, the TG:HDL ratio was significant ($F(2,37)=7.163$, p=0.02. Post hoc tests for multiple comparisons found significant differences between SCI with complete lesions and incomplete spinal lesions (p=0.037, 95% CI=0.056,2.10) and between complete spinal lesions and controls (p=0.02, 95% CI=4.496, 2.319). There was no statistically significant difference for TyG:HDL between the SCI with incomplete injuries and controls (p=0.614)

DISCUSSION

The purpose of this study was to investigate whether routine biochemical indices could identify at risk SCI for diabetes and cardiovascular disease, namely the use of triglycerides, glucose and HDL. The TyG:G ratio has been previously shown to correlate with insulin resistance (13,14) and with cardiovascular disease (9) in able bodied populations. Similarly, the TyG:HDL ratio has been found to be a suitable marker to identify insulin resistance in the able-bodied population (11.12). Given that SCI are at higher risk for developing both type 2 diabetes and cardiovascular disease (4,15) it was considered that there was a potential to use these indices to identify SCI at risk using routine relatively inexpensive biochemistry tests. More sophisticated non-invasive testing such as ultrasound for local arterial stiffness can provide diagnostic information, however this and related techniques required access to ultrasound and an experienced operator.

The results from this limited small study have identified an interesting relationship between complete and incomplete SCI. Briefly, complete SCI is considered to be where nerve damage is sufficiently severe that nerve impulses cannot be transmitted, whereas incomplete SCI does not have total nerve damage. However, the relationship between nerve damage and function in the incomplete SCI may depend on the level of the spinal cord injury (16). The result from the current investigation clearly indicates an outcome which could be related to the level of nerve damage i.e. completes vs incomplete. There were significant differences for TyG:G and TyG:HDL ratios between the complete and the incomplete SCI. Additionally, TG:HDL ratios from the complete SCI were also significantly different from the matched controls, whereas the incomplete SCI showed no significant difference with controls. We consider that this may well reflect the retention of some muscle innervation in the incomplete SCI thereby providing sufficient metabolic signalling to retain some muscle metabolic activity. Whether this would ultimately be sufficient to prevent metabolic syndrome is outside of the scope of this current work. However, we have previously identified significant changes in individual free fatty acids which are associated with insulin resistance and metabolic syndrome in all SCI (7). Additionally, we have demonstrated significant elevation in total free fatty acids and glycerol in both SCI groups compared to controls (7). This would indicate an overall shift from normal skeletal muscle metabolism below the injury to fat deposition and lipolysis. Although the BMI between the controls and SCI groups has been shown to be not significant, there was a 47% increase in the fat mass and a 16% decrease in lean tissue mass below the lesion (15). This was consistent with subsequent investigations identifying that while the BMI remained within normal limits, the SCI group demonstrated metabolic variables consistent with metabolic syndrome (6). This indicates an overall shift from normal skeletal muscle metabolism below the injury to fat deposition and lipolysis. Although we did not identify a significant difference in the TyG:G index, and no significant difference with HOMA-IR, we consider that the sample size may well be a limitation of this work rather than the overall predictive value of the ratio.

Skeletal muscle is a major body organ involved in both glucose and fatty acid metabolism (17) and a loss of this metabolic activity will ultimately give rise to disruption of the interaction of energy substrates i.e. the loss of the ability to metabolise glucose. Typically, with the loss of the ability to metabolise glucose, insulin resistance will develop and is a precursor to metabolic syndrome and diabetes (18,19). While we accept the limitations of this study, it is clear that the transformation from lean tissue mass to fat mass below the lesion following denervation disrupts the normal metabolic function of skeletal muscle. The possibility of using simple biomarker ratios may help in the early detection of insulin resistance and metabolic syndrome in SCI individuals.

AUTHOR INFORMATION

Michael Legge. BSc, MRSB, FIBMS, FNZIMLS, FFSc (RCPA), PhD, Associate Professor[2]
Lynnette M Jones. BSc, BPhEd (Hons), PhD, Hon Associate Professor[1]

[1]The School of Physical Education, University of Otago, Dunedin, New Zealand
[2] Department of Biochemistry, University of Otago, Dunedin, New Zealand

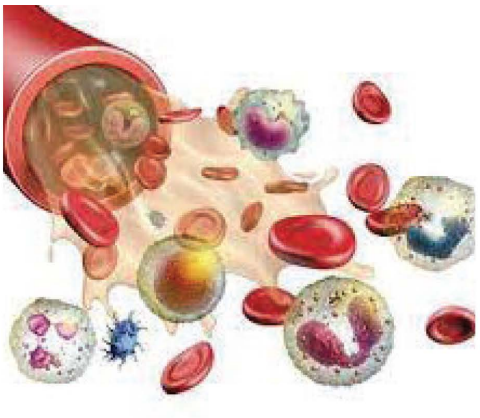
Correspondence: Michael Legge, University of Otago, Dunedin New Zealand
email: michael.legge@otago.ac.nz

REFERENCES

1. Gorgey AS, Dulbow DR, Duobow JD et al, Effects of spinal cord injury on body composition and metabolic profile, part I. *J Spinal Cord Med* 2014; 37(6): 693-702.
2. Spungen AM, Adkins RH, Steward CA et al. Factors influencing body composition on persons with spinal cord injury: a cross sectional study. *J Appl Physiol* 2003; 95(6): 2398-2407.
3. Jones LM, Legge M. Factor analysis of the metabolic syndrome in spinal cord injured men. *Metabolism* 2004; 53(10): 1327-1377.
4. Nightingale TE, Walhin J-P, Thompson D, Bilzon JLT. Biomarkers of cardiovascular health are associated with body composition characteristics but not physical activity or persons with spinal cord injury. *J Spinal Cord Med* 2017; 42(3): 326-337.
5. Moller DE, Kaufman KD. Metabolic syndrome: a clinical and metabolic perspective. *Ann Rev Med* 2005; 56: 45-62.
6. Jones LM, Legge M. Plasma fatty acids as markers for desaturase and elongase activities in spinal cord-injured males. *J Spinal Cord Med* 2019; 42(2): 163-170. doi:10/1080/10790268.2017.1405154.
7. Jones LM, Legge M. Fasting plasma fatty acids and glycerol in spinal cord-injured males. *NZ J Med Lab Sci* 2019; 73(2): 46-48.
8. Hong S, Han K, Park C-Y. The triglyceride glucose index is a simple and low-cost marker associated with atherosclerotic cardiovascular disease: a population based study. *BMC Med* 2020; 18(1): 361. doi.org/10.186/s12916-020-01824-2.
9. Wallace TM, Levy J, Matthew DR. Use and abuse of HOMA modelling. *Diabetes Care* 2004; 27(6): 1487-1495.
10. Kim-Dorner S-J, Deuster PA, Zeno SC. et al. Should triglycerides and the triglyceride to high density lipoprotein cholesterol ratio be used as a surrogate for insulin resistance? *Metabolism* 2010; 59(2): 299-304.
11. Gianni C, Santoro N, Caprio S. et al. The triglyceride-to-cholesterol ratio. *Diabetes Care* 2011; 34(8): 1869-1874.
12. Jeong S, Ho Lee J, Ren M. et al. The verification of the of the reliability of the triglyceride-glucose index and its availability as an advanced tool. *Metabolomics* 2021; 17(11): 97. doi.org/10.1007s11306-0221-01837-9.
13. Zhang Y, Ren L, Ren M. et al. Correlation between the triglyceride-glucose index and high risk of cardiovascular disease: A cohort study of 102,061 subjects from Tiajin, China. *Risk Manag and Healthc Policy* 2021; 14: 2803-2810.
14. Bauman WA, Spungen AM. Carbohydrate and lipid metabolism in chronic spinal cord injury. *J Spinal Cord Med* 2001; 24: 266-277.
15. Jones LM, Goulding A, Gerrard DF. DEXA: a practical and accurate tool to demonstrate total and regional bone loss, lean tissue and fat mass in paraplegia. *Spinal Cord* 1998; 36(9): 637-640.
16. Roberts TT, Leonard GR, Cepela, DJ. Classifications in brief: American spinal cord injury association (ASIA) impairment scale. *Clin Orthop Relat Res* 2017; 475(5): 1499-1504.
17. Glancy B, Balaban, RS. Energy metabolism design of the

striated muscle. *Physiol Rev* 2021; 101(4): 1561-1607.
18. Eckel RH, Grundy SM, Zimmet PZ. Metabolic syndrome. *Lancet* 2005; 365(9468): 1415-1428.
19. Samson,SL, Garber AJ. Metabolic syndrome. *Endocrinol Metab* Clin N Am 2014; 43(1): 1-23. doi.org/10.1016/j.ecl.2013.09.009

Copyright: © 2024 The author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.



Join NZIMLS
at the

NZIMLS
THE NEW ZEALAND INSTITUTE OF MEDICAL LABORATORY SCIENCE (INC)

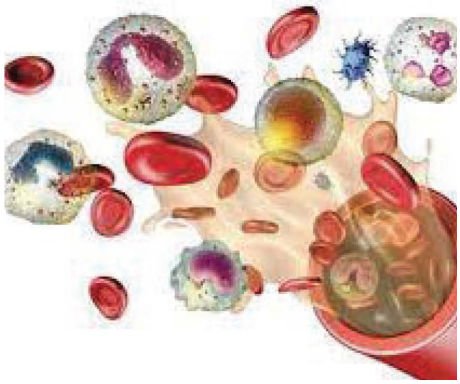
Haematology Special Interest Group Meeting
for
Thalassaemia/Haemoglobinopathy
to raise awareness and upskill

Saturday 16 March 2024

Victoria University Seminar Room, (CS801) Level 8, Clinical Services Block, Wellington Hospital

Programme will commence at 9:00am

Contact Alan Neal
Alan.Neal@pathlab.co.nz



SCIENTIFIC LETTER

Implementation of laser warning markings for equipment and instruments in the International Standard ISO 15189:2022 accredited medical laboratory in New Zealand

Dennis Mok, Naira Eloyan, Rana Nabulsi, Sharfuddin Chowdhury, María del Rocío González Guerrero, Winsome Lee and Donna Marie Gillespie

Equipment and instruments that incorporate laser products to support diagnostic capacity are widely used in the medical laboratory (1,2). The medical laboratory must implement relevant risk control measures to manage safety-related behaviours and warn of hazards (Subclause 5.6 of ISO 15189:2022). This paper was conceived during our communication with medical laboratories in the Asia-Pacific region relating to laser warning markings. The exact requirements seemed to receive scant attention from laboratory personnel. To make matters worse, it seemed the markings were often invisible during routine operation. In addition, it appeared that the markings were often supplemented with Food and Drug Administration (United States) markings provided by the manufacturers.

The main objective of this paper is to enhance the medical laboratory's awareness of requirements relating to the provision of relevant risk control measures through warning markings for Class 1 to Class 4 laser products (Clause 4.3 of AS/NZS IEC 60825.1:2014). Selected organisations were identified to provide relevant information to support communication of hazard information to laboratory personnel: the Food and Drug Administration (United States), the International Electrotechnical Commission (IEC), the International Organization for Standardization (ISO), Standards Australia, and Standards New Zealand.

Definitions

The following definitions should be noted by the medical laboratory:

Good Practice - defined by the ISO as a 'process or method that has been shown to work well, succeeds in achieving its objective(s), is acknowledged and therefore can be recommended as an approach' (Subclause 3.1.2.7 of ISO 22163:2023).

Hazard - defined by the ISO as a 'potential source of harm' (Subclause 3.13 of ISO 15190:2020).

Marking - defined by the ISO and the IEC as 'symbols, pictograms, warning, logos, or inscriptions on the consumer product, label, or packaging to identify its type, which can also include short textual messages' (Subclause 3.12 of ISO/IEC Guide 14:2018).

Contemporary challenges

The risk control measures relating to hazard information communication should include conveying relevant information by displaying relevant warning markings to inform laboratory personnel about laser hazards to minimise undesirable consequences, and such warning markings must be positioned so they are visible to the intended laboratory personnel within a reasonable observation distance (3,4). Implementation of these two abovementioned measures should be in alignment with the medical laboratory good professional practice commitment [Subclause 5.5 a) of ISO 15189:2022].

Laser product warning markings

The medical laboratory is to ensure that appropriate warning markings are displayed according to the laser class (Subclause 9.5.1 of ISO 15190:2020). The markings must be durable, permanently affixed and legible (Clause 7.1 of AS/NZS IEC 60825.1:2014), so that laboratory personnel can recognise a specific source of potential harm, understand the consequences, take appropriate actions and make informed decisions. The appropriate warning markings should be the ones stated in Figure 1 a) (Section 7 of AS/NZS IEC 60825.1:2014); however, the wording of warning labels is recommended, but not mandatory. It is important to note that some Class 1 laser products are classified as exempt laser products, so application of warning markings is not required. The warning markings in Figure 1 b) are from the Food and Drug Administration (United States) that sometimes co-exist with the ones in Figure 1 a) although they do not meet the warning marking requirements in New Zealand.

With the exception of Class 1 and Class 1M, the markings must consist of a laser beam hazard sign (see Sign 448, Table B3 of NZS/AS 1319:1994) with an explanatory label (Section 7 of AS/NZS IEC 60825.1:2014) that includes the name and publication date of the standard to which the laser product was classified or accompanied by a separate explanatory label in close proximity on the product (Clause 7.9 of AS/NZS IEC 60825.1:2014), or an alternative label with an explanatory label.

Figure 1: see supplementary material at https://mix.nzimls.org.nz/journals-recent.html

Placement of warning markings

The medical laboratory is to ensure appropriate warning markings are clearly visible during operation or maintenance (Clause 7.1 of AS/NZS IEC 60825.1:2014); however, providing reasonable visibility only during maintenance of equipment and instruments may reduce the warning effectiveness because it is likely that the warning will be out of view in most circumstances. The medical laboratory should investigate whether such placement could hinder continual awareness communication of the hazard to laboratory personnel during routine operations. The medical laboratory should have the warning markings clearly visible during operations as well as maintenance to ensure the warning to laboratory personnel effectively promotes continual situational awareness. The medical laboratory must, to the extent that is reasonably practicable, make provisions to ensure relevant risk control measures for laser usage are identified unambiguously, implemented effectively, and displayed explicitly for hazard communication to laboratory personnel.

ACKNOWLEDGMENTS

The authors would like to thank: Hideo Sakamoto, PhD, Department Chair and Professor, Department of Medical Technology, Faculty of Health Sciences, Kobe Tokiwa University, Kobe, Japan; Sharita Meharry, BAppSc MMLS (Hons), Senior Lecturer in Biomedicine and Medical Diagnostics, School of Science, Faculty of Health and Environmental Sciences, Auckland University of Technology, Auckland, New Zealand; and Simona Adochiei, BMediaComm LLB LLM, Marketing and Communications Coordinator, Sonic HealthPlus, Brisbane, Australia, for reading the manuscript and suggesting improvements.

AUTHOR INFORMATION

Dennis Mok, Chartered MCIPD CSci MIBMS CMgr FCMI CQP FCQI FIMLS FNZIMLS CPHR, L&D Consultant[1]

Naira Eloyan, BSc MSc CQP MCQI, Head of Quality Control Laboratory[2]

Rana Nabulsi, BSc MSc GEMBA PhD FACHE CPHQ, Consultant[3]

Sharfuddin Chowdhury, MBBS MMed PhD FCS(SA) FACS,

Director of Trauma Center[4]
María del Rocío González Guerrero, MD, Consultant Anaesthetist[5]
Winsome Lee, BA (Hons) MA MSc, Forensic Anthropologist[6]
Donna Marie Gillespie, BS MBA DBA MT(ASCP)SM, Adjunct Professor[7]

[1]Medical Management Consulting, Birkdale, Queensland, Australia
[2]Scientific Center of Drug and Medical Technology Expertise, Yerevan, Armenia
[3] Dubai Health Authority, Dubai, United Arab Emirates
[4]King Saud Medical City, Riyadh, Saudi Arabia
[5] Rio Tinto Hospital, Huelva, Spain
[6]The Chinese University of Hong Kong, Hong Kong
[7]Community Christian College, Redlands, California, United States

Correspondence: Sharfuddin Chowdhury, King Saud Medical City, Saudi Arabia.
email: s.chowdhury@ksmc.med.sa

REFERENCES

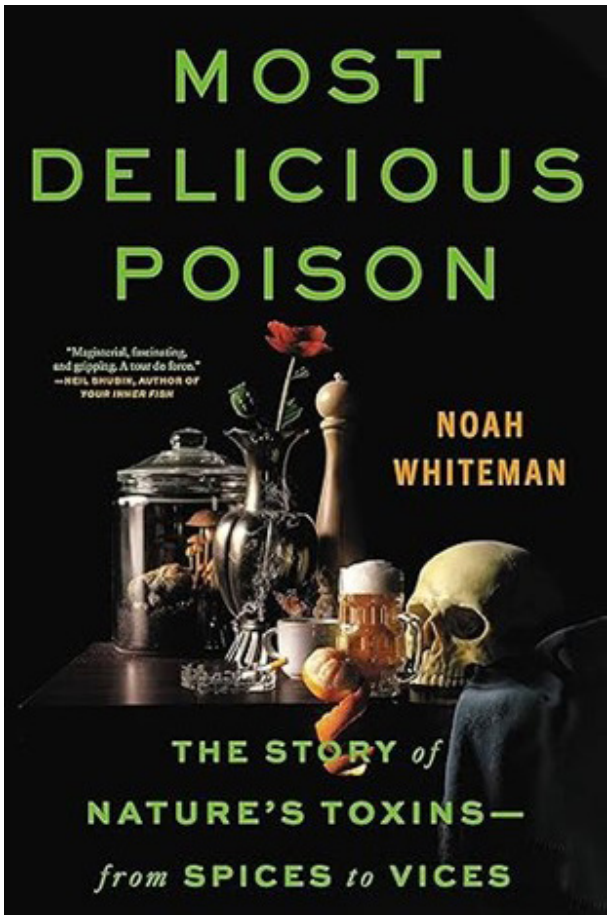
1. Sveinbjornsson B, Gizurarson S. Waves (microwaves, radiowaves, and light) In: Handbook for laboratory safety. Elsevier, Amsterdam 2022: 39-40.
2. Bruno TJ, Svoronos PD. Laser hazards in the laboratory. In: Rumble JR Jr, Bruno TJ, Doa MJ, eds. CRC handbook of chemistry and physics: a ready reference book of chemical and physical data. 104th edn., CRC Press, Boca Raton 2023; 15891590.
3. Mayhorn CB, Wogalter MS, Laughery KR. Analysis and design of warnings in the workplace. In: Wilson JR, Sharples S, eds. Evaluation of human work. 4th edn. CRC Press, Boca Raton 2015; 331358.
4. Wogalter MS, Mayhorn CB, Laughery KR Sr. Warnings and hazard communications. In: Salvendy G, Karwowski W, eds. Handbook of human factors and ergonomics. 5th edn. Wiley, Hoboken 2021; 644667.

Copyright: © 2024 The author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

BOOK REVIEW

Most Delicious Poisons: the story of nature's toxins from spices to vices

Author: Noah Whiteman, Little, Brown Spark, 2023
ISBN: 9780316386579



The author, Noah Whiteman is an evolutionary biologist at the University of California, Berkley. He is Professor of Integrative Biology and Molecular and Cellular Biology, with links to entomology and computational biology at other tertiary institutions. In the book he explores the evolution of poisons and toxins in plants from potential biological defence mechanisms to the use by humans as spices, flavourings, recreational and commercial use and as poisons. The author draws on indigenous knowledge (both historical and current) on the use of plant poisons and toxins to modern day applications in both culinary, medical use and abuse. The book is well structured taking the reader through thirteen chapters based primarily on the chemical nature of the poisons and toxins. This approach lends itself for the author to cover poisons and toxins from many plant species based on their effects. Integrated into this, is the knowledge of their effects on humans and, where known, the pathways and receptors which interacts with the respective poisons and toxins. The author cleverly takes the reader through his own personal journey since childhood learning about plants from his father to developing international recognition as an expert on plant poisons and toxins. The book is well written and structured, and the writing style is easy to read and provides information for both the 'interested' and the 'expert'.

Reviewed by Michael Legge, PhD

Presenters wanted!

Have ever wanted to present at your Professional Body's Annual Scientific Meeting?
Well, now's your chance!
Register your interest, including your speciality to the Conference Convenor,
vanessa.buchan@cdhb.health.nz

Briefing for the Incoming Minister and Associate Ministers

Hon. Dr Shane Reti, Minister of Health
Shane.Reti@parliament.govt.nz

Hon. David Seymour, Associate Minister of Health
David.Seymour@parliament.govt.nz

Hon. Matt Doocey, Associate Minister of Health
Matt.Doocey@parliament.govt.nz

New Zealand Institute of Medical Laboratory Science (Inc.) (NZIMLS)

November 2023

President's Statement

National pathology laboratory services are rapidly approaching a crisis level post COVID. The service is fragmented, has an aging workforce and retention of skilled scientists and technicians is becoming problematic. These dynamics have been highlighted by Health Workforce New Zealand with strategies presented to remedy the situation, however this is a multifactorial problem that requires a broad range of solutions. The current position is that an essential diagnostic pathology health service lacks coordination, any career structure for both scientists and technicians, as well as uncertainty regarding employment as the health reforms are transitioning. Continued education, training and competency are frequently overlooked by the employers in the desire to increase productivity, this will only have serious consequences in the future.

Adding to this serious and complex situation is that the two Universities who provide the specialist graduate workforce (Medical Laboratory Scientists) with Bachelor of Medical Laboratory Science (BMLSc) degree are underfunded for the BMLSc degree programme. Both Universities produce approximately 80 graduate Scientists per year.

The training, education, and qualification Qualified Medical Laboratory Technician (QMLT) provided by the professional body (NZIMLS) is not sustainable in its current format, which will have significant consequences for the sustainability of the profession. The NZIMLS graduates approximately 140 Technicians and Phlebotomists per year. The potential decrease in the specialist workforce will ultimately lead to the reduction or loss of an already fragmented diagnostic pathology service resulting in a loss of diagnostic capabilities and have a significant impact on disease diagnosis and treatment.

The New Zealand Institute of Medical Laboratory Science (Inc.) considers that if the current trend continues there will be a significant risk for both specialist training of the pathology workforce and pathology services in New Zealand.

1. Mission Statement

"*The New Zealand Institute of Medical Laboratory Science (Inc.) (NZIMLS) is the organisation that oversees the professional affairs of diagnostic medical laboratory science in New Zealand. The New Zealand Institute of Medical Laboratory Science (Inc.) (NZIMLS) is the professional organisation that represents those engaged in the profession and practise of Medical Laboratory Science in New Zealand."*

"It has an ongoing commitment to promote professional excellence through communication, education and a code of ethics to achieve the best laboratory service for the benefit of the patient."

There are approximately 3,800 medical laboratory scientists and technicians practising in New Zealand. Examples of similar professional groups within New Zealand include the Medical Sciences Council of New Zealand (MSCNZ) and the New Zealand Nurses Organisation (NZNO). The NZIMLS also has direct collaborative interface with the Australian Institute of Medical Scientists (AIMS) and the United Kingdom Institute of Biomedical Science (IBMS) plus international collaboration with the International Federation of Biomedical Laboratory Science (IFBLS).

2. The Objectives of the NZIMLS:

2.1 To establish and promote standards appropriate to the profession of Medical Laboratory Science.

2.2 To improve the standards, status, education and training of members of the profession.

2.3 To promote, conduct and organise conferences and seminars as may be required for the membership for the further education and professional development of all categories of the membership.

2.4 To promote, conduct and organize Competency and Professional Development (CPD) programmes as may be required by the membership for the management and compliance of Annual Practicing Certificates (APC) according to the Medical Sciences Council of New Zealand (MSCNZ).

2.5 To confer appropriate categories of membership on those entitled to receive them.

2.6 To encourage the publication of material relating to or associated with Medical Laboratory Science and Pathology.

2.7 To design, organise and conduct professional examinations to individuals entering the profession with no formal laboratory background. These examinations are accredited by the MSCNZ and provide graduates with a registerable qualification, QMLT.

2.8 To promote, conduct and organise professional examinations as may be required by the membership (Fellowship of the New Institute of Medical Laboratory Science).

2.9 To provide advice and representation on matters pertaining to Medical Laboratory Science and Pathology. To award prizes, certificates, medallions or other recognition to members who by way of examination, peer nomination or public honour have excelled and/or achieved in the practice of Medical Laboratory Science.

2.10 To liaise with and advise the two Universities providing the Bachelor of Medical Laboratory Science (BMLSc) degree.

2.11 To facilitate and promote the development of post-graduate courses for the membership relating to diagnostic pathology and medical laboratory science. Specifically, the introduction of the Clinical Scientist, a relatively new post tertiary qualification provided by the Royal College of Pathologists (RCPA) through the Faculty of Science, which was developed to help manage the shortfall of specialist pathologists.

2.12 To act in the best interests of the profession and to undertake or conduct the affairs of the profession considered necessary or beneficial to the Institute or its members.

3. NZIMLS Council Members.

3.1 The current NZIMLS Council is made up of the following members who are elected by the membership at the Annual General meeting on a two-yearly basis:

- President – **Tony Barnett** (Awanui, Nelson)
- Vice President – **Sujata Hemmady** (LabPlus, Te Whatu Ora, Auckland)
- Secretary/Treasurer – **Ajesh Joseph** (Te Whatu Ora, Waikato)
- Region 1 (Auckland region) Representative – **Melanie Adriaansen** (Te Whatu Ora, Waitematā)
- Region 2 (Greater Waikato region) Representative – **Hollie Beall** (Te Whatu Ora, Waikato)
- Region 3 (Greater Wellington region) Representative – **Lynne Morgan** (Te Whatu Ora Te Matau a Maui)
- Region 4 (Canterbury/Tasman) Representative – **Gavin Atkinson** (New Zealand Blood Service, Christchurch)
- Region 5 (Otago/Southland) Representative – **Sue Melvin** (Awanui, Clyde)
- Technician representative - **Emma Potton** (Communio NZ Ltd, Dunedin)

The NZIMLS office staff, including the Executive Officer, are employees or contractors for services of the NZIMLS.

- Executive Officer – **Sharon Tozer** (NZIMLS Office, Christchurch)
- Competency and Professional Development (CPD) – **Jillian Broadbent** (Christchurch)
- Office Administrator (Part time) **Sarah Maginness** (Christchurch)
- Journal Editor – **Lisa Cambridge** (Dunedin)
- Academic Advisor – **Associate Professor Mike Legge** (University of Otago, Chair, Faculty of Science, Royal College of Pathologists of Australasia)

3.2 The NZIMLS Council has four meetings a year, each held over two days (excluding virtual meetings as and when necessary).

3.3 The NZIMLS organises a National Annual Scientific Meeting (ASM), as well as regional South and North Island seminars each year.

3.4 Currently, there are nine affiliated medical laboratory discipline groups namely Special Interest Groups (SIG's) that have annual meetings.

3.5 All the financials and risks relating to these meetings go through the NZIMLS accounts, that are independently audited each year.

3.6 The NZIMLS also owns and supports the New Zealand Journal of Medical Laboratory Science which publishes refereed scientific articles three times a year and is freely available to all financial members.

4. Medical Sciences Council (MSCNZ) and the NZIMLS

4.1 The Medical Sciences Council of New Zealand (MSCNZ) Is one of eighteen New Zealand regulatory health authorities appointed by the Minister of Health under the Health Practitioners Competence Assurance Act 2003 (the Act).

4.2 The primary responsibility of the MSCNZ is to protect the health and safety of the New Zealand public accessing medical laboratory scientific services. This is achieved by ensuring that all practitioners hold the appropriate prerequisite qualifications and are competent to practise while fulfilling the continuing education requirements stipulated by the Act.

4.3 All scientists and technicians working in diagnostic pathology laboratories in New Zealand must be registered with the MSCNZ and hold a current Annual Practising Certificate (APC) issued by the MSC.

4.4 The NZIMLS provides the framework for educational and professional development opportunities for scientists and technicians to fulfil the requirements necessary to obtain an APC.

4.5 The NZIMLS Council is elected by its members and works at an advisory level with the MSCNZ. Both organizations have a role to ensure the promotion of medical laboratory science, ensure professional competency and to be actively involved in ensuring the profession continues to provide the public with a safe, efficient, ethical and competent diagnostic medical laboratory service in New Zealand.

4.6 For candidates training to become Medical Laboratory Technicians and Pre-Analytical Technicians within New Zealand, the NZIMLS provides

discipline-based training curricula, practical assessment documents, an examination and certification. This qualifies the candidate for registration with the MSCNZ.

4.7 As an independent professional organization, the NZIMLS also provides the MSCNZ accredited CPD programme that is utilized by the majority of medical laboratory scientists and a significant number of medical laboratory technicians. Belonging to a fully accredited CPD program is a requirement in New Zealand to fulfil the requirements of holding an Annual Practising Certificate (APC).

NZIMLS Concerns

4.8. The NZIMLS has grave concerns relating to the MSCNZ initiating a New Zealand based examination to allow Technicians with a BSc (subject unspecified) to complete an on-line multichoice examination to become registered scientists. This places the MSCNZ as both a registration body and operating as provider for gaining registration, which is inappropriate as a regulatory body and undermines the academic and educational requirements of practising Medical Laboratory Scientists.

5. Medical Laboratory Science within New Zealand

5.1 The New Zealand workforce comprises of Medical Laboratory Scientists, Medical Laboratory Technicians and Pre-analytical Technicians. Most are graduates of the New Zealand BMLSc courses at our Universities or graduates of the NZIMLS Technician examinations but there is also a significant proportion of internationally trained Scientists and Technicians working in New Zealand.

5.2 Within the diagnostic laboratories in New Zealand, Specialist Pathologists (where available) and senior managers provide the oversight.

5.3 All diagnostic Pathology Laboratories operating in New Zealand are accredited with International Accreditation New Zealand (IANZ) and are audited against the ISO 15189 Standard.

5.4 Throughout New Zealand there are both private diagnostic laboratory providers and Te Whatu Ora owned laboratory providers. The main private providers in New Zealand are Awanui (previously Known as Asia Pacific Health Group), Sonic and Pathology Associates.

6. Ministerial Responsibility for Medical Laboratory Science in New Zealand

6.1 The NZIMLS strongly believes pathology services are part of the critical health services framework and must be maintained by ensuring a sustainable training program for our Scientists through the New Zealand University system. Additionally, our Technicians have the opportunity to train through an appropriate fit for purpose programme. Laboratories use technology to ensure efficient and cost-effective diagnostic services that meets international best practice to serve all New Zealanders. It is essential that Pathology is not treated as a commodity that can be continually slashed and downsized, in return of a profit to shareholders.

A thorough overview of policy and planning for New Zealand Pathology Services is required to ensure a sustainable high-quality service to patients and stability to those essential staff working in this profession.

6.2 The NZIMLS are confident the new government will take into consideration the environmental footprint of medical laboratory testing and pathology services in general. Currently in New Zealand some samples travel considerable distances due to the geographical location of the contracted private laboratory, delays associated with this can be detrimental to specimen quality and lead to inaccurate patient results. In addition, increasing specimen transfers from rural and regional laboratories removes the capacity for these communities and rural providers to provide timely care. The NZIMLS would expect that the efficiency of the testing footprint be taken into consideration with future diagnostic laboratory developments.

6.3 The NZIMLS has raised concerns about employer-based recertification programmes (CPD) with the previous Minister of Health. Although approved by the responsible authority (MSCNZ) an employer recertification programme is a direct conflict of interest and does not provide an independent quality assessment for a CPD programme.

There was agreement that while there are professional and education bodies providing approved recertification (CPD) programs then there is no need for employer-based recertification programs. The NZIMLS expects continued Ministerial support on this aspect of recertification.

6.4 The NZIMLS needs to see resolution of the issue of access for New Zealand medical laboratory workers to ongoing training and educational activities and in particular, opportunities to discuss current and future diagnostic approaches with our peers. This requires 'ring-fencing' of appropriate funds for continuing education, qualifications, and career progression.

6.5 The NZIMLS requires a clear training pathway be created for the training of Clinical Scientists and that a career structure is developed for this role within Pathology Services in New Zealand to help overcome the international shortfall of specialist pathologists. This would be consistent with international trends in Pathology and a similar training programme has been operating in the UK for approximately 40 years and is highly successful.

6.6 Currently, the NZIMLS has a voice within a variety of professional pathology organisations that have active involvement in working groups aligned with the Ministry of Health. It is our desire to continue this collaboration with any organisation that significantly influences diagnostic medical laboratory testing and/or health workforce planning. This includes the expectation that the NZIMLS should have a voice within the structure of the Health New Zealand entity to ensure the future sustainability of the New Zealand diagnostic pathology laboratory service.

Tony Barnett
President
New Zealand Institute of Medical Laboratory Science.

IN MEMORIUM

Paul McLeod – Medical Laboratory Scientist, NZIMLS President

August 1947 - 30 June 2022, Life member from 1999

Many of our current members will be too young or have not been working in the Medical Laboratory Science industry in New Zealand to remember one of our past NZIMLS Presidents, Paul McLeod, but it is time we pay tribute and remember this leader within our profession.

Paul grew up in Nelson and fell into the laboratory profession by mistake, he attended a job interview to work in the hospital accounts department but whilst doing so was asked if he would be interested in a job in the laboratory. Paul thought that seemed an interesting option and so took the job as a laboratory trainee. Paul went through the training process of the day, COP in Laboratory Science (Certificate of Proficiency) and found his passion in Microbiology.

Paul was part of a team of young scientists back in the early 1970s who worked in the very old part of Nelson Hospital. The Laboratory ws poorly equipped, and the accommodation was sub-standard to say the least, however this was not unusual for the laboratories of that era. Paul and the rest of the team made the most of the situation and became a very tight knit hard-working group that were well respected throughout the hospital. Much of this may also be down to Paul's engaging and positive personality. The laboratory team was renowned for their involvement in the Hospital Reviews with Paul leading the charge – writing lyrics for songs to be sung and choreographing the dance moves and play to be presented. Paul's wife, Diane, was never far away either, making costumes and providing support. Paul will always be remembered for his enthusiasm on the guitar, his bold singing voice, and his infectious laugh.

In the Microbiology lab, Paul followed the standard doctrine of the time, with no Pathologist oversight it was a case of using textbooks and colleagues from around the country to develop the methods and procedures to handle specimens that came into the laboratory. Paul also became involved in a research project to identify the production of gentamicin antibodies in rabbits at Nelson Hospital for which he won a prize and travelled to an Australian conference to present his finding.

Paul also had the reputation of being a great department manager and boss, he was always fair, respected his staff, encouraged them to exceed their own perceived limits and gave them responsibility and autonomy to grow in their career.

Paul's naturally outgoing and positive personality along with his leadership qualities made him an obvious choice to represent the region on the NZIMLS Council. Paul was on Council when Fran van Til was hired. He was on Council when it was decided they would no longer be involved in the employment contract negotiations and this responsibility would move to the Unions.

Paul also worked on the formation and introduction of the BMLSc degree at Otago University, the development of the CPD programme and many other positive initiatives for the profession. Paul worked his way through many of the roles on Council, culminating in his Presidency and offering 38 years' service to the profession.

Paul was much more than a Medical Laboratory Scientist, he was a devoted family man, and with his wife Diane, raised three children, Anna, Rebecca and Chris and their families were so proud of their father's achievements, but he too was so proud of them. Paul was a keen follower of local, national, and international news and would often offer comment on the news of the day. He was a keen follower of sports, an accomplished boatie and fisherman and loved spending time in the Marlborough Sounds. He was proud of his Scottish heritage but not at the expense of Nelson or New Zealand. He loved his music, and he loved people, Paul would volunteer at a local rest home driving a minivan of residents to the local shops or taking them to appointments.

Having said all of that, for many of us who had the pleasure of knowing and working with Paul, either in the laboratory or on the NZIMLS Council or in some other capacity, Paul will always remain in our hearts and be remembered as a friend.

Contributed by: *Tony Barnett, NZIMLS President*

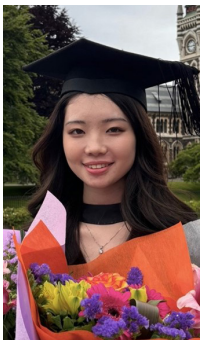
Interview with the recipients of the NZIMLS top student award, 2023

Top Student Awards are offered annually by the NZIMLS for student academic achievement during the third year of the BMLSc degree or in more recent times during the fourth year. The award is made to students at the University of Otago and AUT in New Zealand who offer the BMLSc qualification and is provided in support of the recipient's final clinical training year in the BMLSc programme. The $2,000.00 prize is typically paid to the University who then present it to the winner on behalf of the NZIMLS.

In November, AUT recognised fourth year students; Lillian Birkett and Alejandra Walker as joint top students and Rei Miyamoto was awarded top Otago University student. Coincidentally, Rei also features in this issue as a published author with her review article entitled; 'The MNS Blood Group System'.

Alejandra Walker

Lillian Birkett



Rei Miyamoto

Firstly, congratulations to you all on winning the top BMLSc student awards! What a fantastic accolade to start your careers in medical laboratory science. Thank you for sharing your experiences with us.

1. ***Can you tell us a little about yourself?***

   Alejandra: I am originally from Colombia but moved to New Zealand at a young age. During my high school years, I developed a keen interest in sciences and was attracted to the idea of pursuing a career in medical science. With that goal in mind, I completed a degree in Biomedical Sciences. However, this was just the beginning of my journey, as I later discovered my passion lay in Medical Laboratory Science. I am grateful for the opportunities I've had to learn and grow, and I'm excited to see where my career takes me next.

   Lillian: My name is Lillian Birkett and I am originally from Sunshine Coast Australia but have been living in New Zealand since the age of five. I lived in a very rural region of Whangarei and eventually moved to Auckland for university. I really enjoyed the nature and country lifestyle that Whangarei had to offer and often spent my time outside in the ocean or in the beautiful bush.

   Rei: I have always had a passion for health sciences since high school. I am fascinated by the pathology of different diseases, mechanisms of microbes and the immune system, and the anatomy and the physiology of the human body. I always knew that I wanted to somehow contribute to the healthcare system, so I knew medical laboratory science was for me when I discovered it.

2. ***What interested you about the BMLSc degree?***

   Alejandra: One of the things that attracted me to this programme was its versatility. I liked that the programme allows you to explore the different medical laboratory science disciplines before choosing a specific pathway. This approach lets you customise your academic journey based on your interests. Additionally, the programme's emphasis on practical work captured my attention. I think that the chance to apply theoretical knowledge not only reinforces learning but also prepares students for the demands of the field.

   Lillian: I have always been fascinated by biology and the relationship that diseases impact such a perfectly designed system. Further, how we can determine the presence/absence of such diseases through testing. This made the BMLSc degree very enticing. The blend of these two interests, the comprehensive and specialized curriculum alongside the strong focus of diagnostic procedures, laboratory techniques and sample analysis made this degree really stand out from the rest. Moreover, AUT's BMLSc degree design of covering multiple areas of specialization from haematology, microbiology, clinical chemistry and more created a holistic understanding of multiple laboratory practices which was another key reason why this degree appealed so much to me.

   Rei: I didn't know about BMLSc until I came to university, but I knew that it was what I wanted to study when I saw the course programmes. It consisted of both theory and realistic practical work in a large range of pathology disciplines. I enjoy lab work so I thought it would be fascinating to learn and work in a medical laboratory while I contribute to the healthcare system.

3. ***Was there a defining moment where you thought; 'yes that's what I want to do'? Can you tell us about it?***

   Alejandra: Upon completing my biomedical sciences degree and working in the field for a year, I realised I wanted to play a more active role in the healthcare industry. That's when I came across the BMLSc program and was immediately captivated by the idea of combining my passion for microbiology with the opportunity to positively impact people's health and well-being.

   Lillian: Since the age of ten, my aspiration was to embark on a career as a marine biologist with a noble mission of safeguarding marine life, particularly the turtles. However, it was during my high school years that a transformative encounter with my physical education teacher redirected my path toward becoming a medical laboratory scientist. Interestingly, he, too, had initially aspired to be a marine biologist before transitioning to teaching. His profound insights into the field, coupled with his encouragement to dream beyond my initial aspirations, prompted me to re-evaluate my interests. Despite hailing from a rural school where ambitious career choices were viewed as unconventional, my desire to delve into the realms of science, especially human biology and pathology, intensified. Researching alternatives, I stumbled upon the Bachelor of Medical Laboratory Science (BMLSc) degree the summer before commencing university. As I delved into the intricacies of the program, I was captivated by its unique blend of biological sciences, human health, and critical analysis—elements that resonated deeply with my passions. From that moment, I was resolute in my decision to pursue the BMLSc degree, recognizing it as the perfect amalgamation of my interests and aspirations. This journey, sparked by an early fascination with marine biology and nurtured by the guidance of my teacher, has evolved into a profound commitment to the intricate realms of medical laboratory science.

   Rei: When I found myself enjoying the studying and the practicals, despite the large workload, I knew I wanted to

pursue my career in this field. This passion was reinforced during my placement experiences when I saw that every day is different and there are more learning opportunities even after university.

4. ***What did the programme entail? Was there a speciality or a particular placement that really grabbed you?***

Alejandra: The BMLSc programme offers a great blend of theoretical learning and practical experience across diverse fields of medical laboratory science. There were a few subjects that piqued my interest, but I ultimately decided to specialise in medical microbiology and transfusion science. The fascinating world of bacteria and fungi captivated me, and during my placement, I found the work to be like an exciting puzzle that I couldn't get enough of. As for transfusion science, understanding the different blood groups and their characteristics was intriguing. I particularly enjoyed working on antenatal cases during my placement. The joy of helping pregnant women and ensuring the safety of their neonates was an unparalleled experience.

Lillian: The educational journey I undertook comprised three years of rigorous study at the university, coupled with a transformative one-year placement. The initial two years were dedicated to foundational coursework, delving into general knowledge and exploration of various specialization options. The culmination occurred in the third year when I had the privilege of selecting two specialized papers, immersing myself in a profound exploration of both immunology and clinical chemistry. Thankfully, my placement unfolded at Labplus, where I delved into the realms of clinical chemistry and immunology. Clinical chemistry captivated me with its comprehensive coverage of diverse organ systems and their intricate connections to prevalent diseases. What truly resonated with me was the fascinating interplay between theoretical knowledge acquired in lectures and its practical application to real-life case studies. This experiential bridge between theory and application heightened my academic experience and brought forth a profound enjoyment in the process. In the realm of immunology, my fascination soared as I delved into the intricate mechanisms governing the body's defence and response mechanisms against diseases. The immune system, a marvel of complexity, unveiled itself as a breathtakingly beautiful system. Exploring its intricacies left me awe-inspired by the multifaceted layers of defence and the dynamic reactions orchestrated to maintain the body's equilibrium in the face of pathogenic challenges. In essence, my educational expedition not only encompassed the acquisition of knowledge but also provided a rich tapestry of experiences. The specialized focus on clinical chemistry and immunology during my placements not only deepened my understanding of these disciplines but also fuelled my passion for their intricacies. The hands-on application of theoretical concepts and the profound revelations encountered during these studies have left an indelible mark on my academic journey, fostering an enduring appreciation for the complexities inherent in the field.

Rei: The programme starts off with every discipline so that students can get to know each specialisation before deciding which ones suit them best. The lectures, tutorials, and labs are very fun but can be tough to balance all of the workload. I think it is a great opportunity to learn organisation and time management skills which will come in handy in high-demand labs in the future. I also enjoyed learning each discipline from different angles such as studying the theory, experiencing hands-on practical work, solving problems and case studies, and discussing amongst my classmates and lecturers.

5. ***Top Student, what does this prize mean for you?***

Alejandra: Being recognised as a top student is a great honour that fills me with pride. This achievement validates all the hard work and dedication I have put into my studies and motivates me to continue striving for excellence in both my future academic and professional pursuits.

Lillian: This award holds profound significance for me as it symbolizes the culmination of relentless dedication to enriching my educational journey and absorbing knowledge at every opportunity. Beyond its monetary value, this prize represents an opportunity to joyously acknowledge and express gratitude to my family and friends, unwavering pillars of support throughout my academic pursuits. Their encouragement and support have been integral to my success in attaining the high level of achievement I've reached. This degree is not only a personal triumph but also a collective achievement shared with my loved ones. Their unwavering love and support have played an indispensable role in my academic journey, shaping it into the success it is today. I firmly believe that without their steadfast encouragement, I would not have achieved the position I currently hold. This award is, in essence, a celebration of the collaborative effort and shared triumph that defines my educational accomplishment.

Rei: It feels great for my hard work to be acknowledged! I was surprised when I first got this prize, but it made me feel more motivated to keep learning and growing.

6. ***Was there a person/s who inspired you during this journey?***

Alejandra: Absolutely! Throughout my journey, I've been fortunate to come across remarkable individuals who have inspired me and shaped me in many ways. I was lucky to have professors who were not only knowledgeable in their fields but also genuinely passionate about their work, and they ignited my curiosity. Moreover, my fellow students have also played a crucial role in my journey by creating a positive learning environment with mutual support during challenging times. Lastly, my family has been a great source of inspiration, and their unwavering support and words of encouragement kept me grounded and focused on my goals.

Lillian: I have been fortunate to be surrounded by a diverse tapestry of inspirational figures who have profoundly shaped my outlook on life. The indelible lessons instilled by my parents, emphasizing the unwavering commitment to invest 100% effort into every endeavour, have been the cornerstone of my journey. Their guidance has been the steady compass navigating me through the labyrinth of challenges. In addition to the familial wisdom, my twin sister stands as a beacon of inspiration, effortlessly excelling in every facet of her existence. Her remarkable academic achievements during her university tenure have served as a catalyst, igniting within me the ambition to not only match but surpass her accomplishments. Witnessing her prowess has been a testament to the boundless potential that resides within myself. Among the constellation of influences, my partner, Douglas, has been an unwavering source of encouragement. His steadfast belief in my capabilities has always been a constant reminder that I possess the power to achieve anything my mind sets out to conquer. His motivational words have been the driving force behind my pursuit of excellence, instilling in me the confidence to embrace challenges as opportunities for growth. Together, these inspirational figures have woven a narrative of determination, resilience, and the pursuit of excellence in

my life. Their collective impact has propelled me to strive for greatness, armed with the conviction that I am capable of transcending boundaries and achieving the extraordinary.

Rei: Throughout my studies, I have met many intelligent lecturers, researchers, and scientists. When I saw them immersing themselves in their job, it inspired me to focus on things I enjoy learning. Lecturers are passionate about the topics they are teaching, researchers are always curious and aiming high, and scientists are fulfilling their goal to provide a safe healthcare service. BMLSc provides students with opportunities to meet with these aspiring people which helps us find our path.

7. ***What's next for you in your career?***

Alejandra: My immediate goal as a recent graduate is to secure a position in the microbiology or transfusion science field. I am eager to apply all the knowledge and skills I've acquired throughout my academic journey to real-world scenarios while working towards obtaining my full registration. In the future, I would like to pursue further study.

Lillian: Even before officially graduating, I secured a position as a medical laboratory scientist specializing in clinical chemistry at Labplus, specifically in the special techniques department. This presents a remarkable opportunity to contribute to the same institution where I completed my placement, providing me with invaluable insights into the intricacies of the department and its specialisation. Looking ahead, my immediate focus is on accumulating more experience and honing my skills as a medical laboratory scientist. The goal is to immerse myself in the dynamic field, continually learning and growing in a hands-on capacity. In the long term, I envision a return to Australia, my home country, where my roots lie, and my entire family resides. However, for now, my primary objective is to amass valuable experience, forge professional connections, and lay the foundation for my future endeavours.

Rei: I am working in the Transfusion Science Blood Bank at Christchurch Hospital. It is very exciting to be working in a dynamic field with continuous challenges that allows for both personal and professional growth. My goal is to get fully registered, contribute my skills, and become a scientist who can inspire future scientists. I am also interested in further studies in relevant fields in a few years' time. In university, I enjoyed writing review articles and participating in research projects so I want to continue this passion for knowledge expansion in my career.

8. ***What do you enjoy about the job? And what has your experience in the laboratory taught you?***

Alejandra: As a medical laboratory scientist, I will have the important role of testing patient samples and ensuring the results are interpreted accurately. The information you provide is crucial in guiding clinicians to make informed decisions about the appropriate treatment plan for patients. I believe this work is rewarding, as it gives you a sense of purpose and impact, knowing that what you do can make a real difference in someone's life. Throughout my clinical placements, I had the opportunity to work with a diverse group of people, each with unique backgrounds and experiences. This exposure was invaluable, as it taught me the importance of teamwork and how to appreciate the different perspectives that each person brings to the table.

Lillian: Working as a medical lab scientist fascinates me because it involves the use of analytical methods which directly affect patient care. I enjoy conducting detailed scientific analyses that help diagnose, treat, and prevent diseases. The precise and detail-oriented nature of the laboratory environment aligns with my passion for accuracy and scientific exploration as described above. My experience in the lab has been a valuable learning journey, though a short experience so far as new graduate. Performing different tests and experiments has improved my analytical skills and has allowed me to engage my critical thinking skills.
In summary, working as a medical lab scientist has not only increased my scientific knowledge but has also given me a deep appreciation for the crucial role laboratories play in healthcare. It has taught me the importance of precision, adaptability, and collaboration in delivering results that directly impact patient outcomes, making each day in the laboratory rewarding and intellectually stimulating.

Rei: In general, working in a medical laboratory is very fulfilling and stimulating. It gives us a strong sense of purpose because of the challenges, problem solving, and the large influence we have on the patients. Even in the short time frame of my past laboratory experiences, I have seen many advancements in technology and laboratory tests. Every day and every sample is unique in the medical labs and these changes give us valuable learning experiences. Another quality of medical labs is the people. Not only the laboratory team but the clients, pathologists, and clinicians are all involved in providing the best patient care. Collaborating as a team to work towards the same goal is so special and important.

9. ***The profession has been prominent in New Zealand media since the Covid-19 pandemic and more recently relating to the strikes and protests over MLS/ MLT pay and conditions. What has been your experience or thoughts on this so far?***
How do you think this has impacted both the profession, your career and you personally?

Alejandra: The pandemic has significantly strained our healthcare system, creating an increasing demand for qualified laboratory professionals. As a result, it is encouraging to see individuals in this field working towards improving the working conditions for MLS and MLT. I believe that these efforts will not only attract more people to these critical careers but will also help ensure that existing professionals stay in the field, leading to a more stable workforce that can provide better quality services. Moreover, the pandemic has reinforced my views on how essential this job is and how much positive impact we can have on the community

Lillian: I find myself standing somewhat apart from the prevailing narrative surrounding the impact of COVID-19 on my academic journey. While many of my peers in the degree grappled with the challenges of remote learning, I discovered a sense of empowerment amid the chaos. My inherently dedicated and hardworking nature propelled me to thrive in the online learning environment, relishing the autonomy it afforded me to delve deeply into my studies within a conducive setting. The asynchronous nature of online lectures became a boon, allowing me to meticulously review and absorb the course content at my own pace, a luxury I found conducive to my learning style. Nonetheless, I empathize with those who faced difficulties navigating this shift in educational paradigms. Entering the professional realm during the pandemic has been an enlightening but somewhat uncharted experience for me. While I may not be well-versed in how the pandemic has shaped my chosen profession, I can envision the challenges faced by medical laboratory professionals, navigating the intricacies of their

roles amidst lockdowns and heightened health concerns. The commitment and resilience required to carry out crucial work during such tumultuous times undoubtedly speak volumes about the dedication inherent in the field. Regarding the strikes and pay conditions, my novice status in this career realm leaves me somewhat uninformed about the intricacies of these issues. However, based on my observations during placements and in my current job, I've witnessed medical laboratory scientists tirelessly labouring to deliver quality results for patients. This unwavering commitment to excellence merits not only recognition but also fair compensation reflective of the dedication and hard work invested in ensuring the well-being of those we serve. As I delve deeper into this profession, I am eager to gain a more comprehensive understanding of the challenges and nuances that shape its landscape while advocating for the just recognition and compensation that my colleagues rightfully deserve.

Rei: I think the Covid-19 pandemic has affected medical laboratory science in many ways. It has greatly increased the workload, pressure, and expectations in some labs. On top of the general difficulties that many people faced during the pandemic, scientists were entrusted with more responsibilities in the labs. On a positive note, it has helped this profession be more recognised and appreciated. It would have been impossible without the hard work of scientists all around New Zealand. The strikes have highlighted the need for better compensation and working conditions to acknowledge these diligent scientists. I think this is crucial for protecting their motivation and maintaining the positive influence that medical laboratories have in the healthcare system. Personally, the pandemic has taught me the importance of adaptability and continuous professional development. Although half of my university years have been affected by the pandemic, I think it was a valuable learning experience.

10. ***Do you have any advice for our up-and-coming medical laboratory scientists?***

Alejandra: My advice is to pursue what interests you within the field, stay curious, and never stop learning. Take advantage of every opportunity that comes your way, even if it means stepping outside your comfort zone. Lastly, remember to persevere and work hard, and you will achieve great things.

Lillian: My advice for any up-coming medical laboratory scientists would be to really apply yourself to your studies as you get out of the degree as much as you put in. I really put myself 110% into my degree and I have come out of this degree with so much knowledge and experiences that have really benefited me in placement and the current job I have as a medical laboratory scientist. By truly applying yourself to the degree it also means a greater chance to get into the specializations you are wanting and setting yourself up for a very fulfilling career.

Rei: Experiment with different topics and specialisations and focus on what you are passionate about. Stay curious and enjoy learning while taking care of your well-being. Medical laboratory science is crucial to the healthcare system so being dedicated and positive will make a significant impact on patient outcomes and healthcare advancement.

Thank you, Alejandra, Lillian and Rei, your experiences are truly inspiring and aspirational. On behalf of the NZIMLS and its members we wish you all the best in your careers. I have no doubt that we will be hearing more from you all in the future.

Lisa Cambridge
Editor

2024 NZIMLS CALENDAR

Dates may be subject to change

Date		Event	Contact
March	16	Haematology SIG Meeting, Wellington	Alan.Neal@pathlab.co.nz
	23	South Island Seminar, Nelson	Tony.Barnett@awanuilabs.co.nz
April	20	Closing date for QMLT applications	admin@nzimls.org.nz
May	03-05	NICE Weekend, Christchurch	Raewyn.Cameron@pathlab.co.nz
	15	Material for the July Journal must be with the Editor	editor@nzimls.org.nz
June	22	Biochemistry SIG Meeting, Hamilton	PingTat.Luk@waitematadhb.govt.nz
August	15	Annual Reports and Balance Sheet to be with the Membership	sharon@nzimls.org.nz
	28-30	NZIMLS Annual Scientific Meeting , Te Pae, Christchurch	sharon@nzimls.org.nz
August	29	NZIMLS Annual General Meeting, Te Pae, Christchurch	sharon@nzimls.org.nz
September	15	Material for the November Journal must be with the Editor	editor@nzimls.org.ng
October	05	QMLT Examinations	sharon@nzimls.org.nz
	TBC	Anatomical Pathology SIG, Hamilton	TanyaF@adhb.govt.nz

The Pacific Way
March 2024
PACIFIC PATHOLOGY TRAINING CENTRE

Warm Pacific greetings to you all from the PPTC

A belated happy new year to you all from the PPTC. The PPTC welcomes everybody to 2024 and is thrilled to kick start the year with its programmes.

UPDATE

Centre Based Course- Transfusion Medicine

The PPTC continues with its work towards advancing the development of diagnostic pathology knowledge and practice throughout the Pacific. Five students from the Pacific attended our last centre-based course for 2023. The course was held for 4 weeks at our centre here in Wellington from the 6th of November to the 1st of December. The five students from the Pacific that successfully attended the course are:

1. Pisisami Kalamelu- Tuvalu, Princess Margaret Hospital Laboratory
2. Vaohingano Sika- Tonga, Vaiola Hospital Laboratory
3. Shivangini Devi- Fiji Islands, Labasa Hospital Laboratory
4. Erekana Teingoa- Kiribati, Tungaru Central Hospital Laboratory
5. Janine Kolidani- Solomon Islands, National Referral Hospital Laboratory

The students underwent a comprehensive 4-week training programme in Transfusion Medicine, and all gained a certificate of achievement. The students also had the opportunity to experience laboratories around Wellington. The PPTC would like to thank the New Zealand Blood Service for their fantastic contribution to the course, as well as The Norman Kirk Memorial Trust and Red Cross for their continuous generosity in sponsoring students from the Pacific to attend our courses.

This year the PPTC aims to deliver 4 courses in the disciplines of, Quality Management, Biochemistry, Haematology and Transfusion Medicine

Figure 1. 2023 Transfusion Medicine course students with PPTC CEO and course convener Telesia Apikotoa

Figure 2. Students at the New Zealand Blood Service - Palmerston North

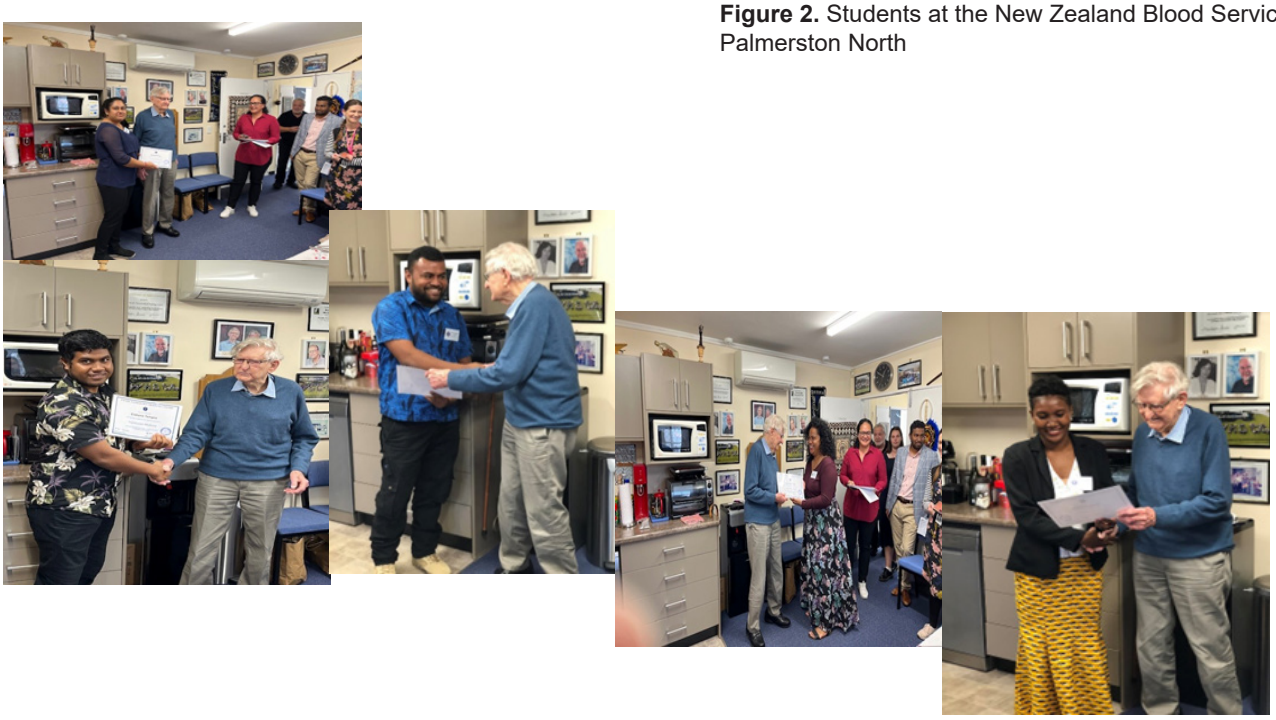


Figure 3. Students receiving their Certificates at the end of the course from PPTC co-founder- Dr. Ron Mackenzie

End of the Year Audits

Towards the end of 2023, the PPTC audited eight countries in its laboratory accreditation alignment programme against the ISO 15189 Medical laboratories standard. The eight countries included:

1. Fiji
2. Samoa
3. Tonga
4. Vanuatu
5. Solomon Islands
6. Kiribati
7. Cook Islands
8. Papua New Guinea

Whilst none of these laboratories in the Pacific are accredited, the laboratories maintain a great level of resilience to deliver quality services. Unlike New Zealand laboratories, laboratories in the Pacific face a number of factors that hinder their pathway to accreditation. Factors include, procurement, laboratory personnel, equipment breakdowns, reagent shortage, etc. This is why the PPTC maintains a strong relationship with Pacific labs and aids them in their journey towards accreditation. Although it is not an easy one, it is the ultimate goal.

Support to the Pacific

The PPTC provides ongoing support to the Pacific the through the following ways:

- In country teaching and training
- Equipment support
- Online Zoom training

In-Country Teaching and Training

Last year the PPTC completed a total of 43 visits to Pacific Island laboratories. Through in-country support, the PPTC consultants are able to work together with staff on the bench to aid in improving processes, procedures and the overall quality of results coming out of these laboratories. The dedicated staff at the PPTC are passionate about the Pacific and aim to develop close relationships with the laboratories so they know that they are never alone in times of need.

Equipment Support

The PPTC provided essential laboratory equipment to Pacific labs in 2023. Laboratory equipment provided to these labs are procured by the PPTC and are delivered to the islands. Equipment purchased includes - Hematek staining machines for Samoa, Fiji and Vanuatu, a FX40 Blood Culture analyser and a chemical safety cabinet for the Cook Islands, a microscope for Fiji and a biosafety cabinet for Samoa. The PPTC also facilitated the shipment of donated Phlebotomy chairs to the Pacific. This year the PPTC anticipates providing further equipment support to Pacific labs.

Online Zoom Training

Through online means of communication, the PPTC provides and organises support to the Pacific laboratories. This is via discipline-specific online lectures, technical support, consultation, and organising support with equipment manufacturers for any troubleshooting requirements. Laboratories continue to engage with the PPTC to maintain their service and the PPTC is always ready to offer support.

Can you help?

If any New Zealand medical laboratories have items of diagnostic instrumentation that have been recently upgraded or continue to be stored in the laboratory but are actually surplus to requirements, the PPTC would be most grateful if such items could be donated through its Centre to Pacific Island laboratories where there is an exceptional need. Pacific laboratories have very restricted budgets and often cannot afford to replace troublesome instrumentation that continues to breakdown, and which is often discontinued because it is so outdated.

The PPTC would also welcome teaching resources in terms of wall charts, Haematology case studies (stained blood films), projector slides, textbooks and journals (within 10 yrs. of publication) etc., for teaching purposes in the Pacific, if you no longer have a use for them. Any contribution is so valuable to us.

Please contact:

Phil Wakem
Chief Executive Officer
Pacific Pathology Training Centre
Wellington, New Zealand
E-mail: pptc@pptc.org.nz or phil@pptc.org.nz

RECENT REVIEWS

The NZIMLS cannot provide direct access to the reviews below due to copyright restrictions, but open access reviews will be indicated. Abstracts are always available on-line and journals may be available via hospital libraries. If there is access to University libraries, then the journals should be available on-line.

Any comments on this addition to the Journal can be sent to: editor@nzimls.org.nz.

1. Reid M, Agbassi YJP, Arinaminpargy N et al. Scientific advances and the end of tuberculosis: a report from the *Lancet* Commission on Tuberculosis. *Lancet* 2023; 402(10411): 1473-1489. /doi/10.1016/SO140-6736(23)01379-X.
2. Sacks DB, Arnold MA, Bakris GL *et al.* Guidelines and recommendations for the laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem* 2023; 69: 808-868.
3. Vynck M, Chen Y, Gleerup D et al. Digital PCR partition classification. *Clin Chem* 2023; 69: 976-990.
4. Skinner MK. Epigenetic biomarkers for disease susceptibility and preventative medicine. *Cell Metab* 2023; S1550-4131(23)00447-3. doi/10.1016/j.cmet.2023.11.105.
5. Shepherd NA. Macroscopic pathology and all that: a personal view. *J Clin Pathol* 2023; doi.org/10.1136/jcp-2023-209106.
6. Najafi S, Asemani Y, Majidpoor J et al. Tumour educated platelets. Clin Chim Acta 2023; doi.org/10.1016/j.cca.2023.117690.
7. Wang Y, Duval AJ, Adli M, Matei D. Biology-driven therapy advances in high-grade serous ovarian cancer. *J Clin Invest* 2024; 134(1):e174013. doi/10.1172/JCI17403. [OPEN ACCESS]
8. Boddupally K, Thuraka ER. Artificial intelligence for prenatal chromosome analysis 2023.*Clin Chim Acta* 2024; 552: 117669. doi.org/10.1016.j.cca.2023.117669.

Rob Siebers Journal Prize

The NZIMLS Council has approved an annual Journal prize to the value of NZ$1,500 for the best peer-reviewed article published by NZIMLS members in the Journal during the calendar year. The article can be a review article, original article, case study, research letter or technical communication. Excluded are Fellowship dissertations.

Many studies are presented at the Annual Scientific Meeting, SIG meetings, and the North and South Island Seminars, yet are rarely submitted to the Journal for wider dissemination to the profession. Consider submitting your presentation to the Journal. If accepted, you are in consideration for the Rob Siebers Journal Prize and will also earn you valuable CPD points.

Please contact the Editor or any Editorial Board Member for advice and help. Contact details are on the NZIMLS web site (www.nzimls.org.nz) as are instructions to authors.

All articles published during the calendar year (March, June and November issues) will be considered. The Editor, Deputy Editors and the President of the NZIMLS, who themselves are ineligible, will judge all eligible articles in December. Their decision will be final and no correspondence will be entered into.

The winners of the Rob Siebers Journal prize for 2023 are Julie Creighton and Bethany Mills, for their article Comparison of the BD Max™ vaginal panel, against standard methods, for the detection of common vaginitis conditions. Published in *NZ J Med Lab Sci 2023; 77(3): 124-127*

Citations to articles from the *New Zealand Journal of Medical Laboratory Science* by international biomedical journals in 2023

Since the *New Zealand Journal of Medical Laboratory Science* (Journal) became open access, citations to the Journal's articles by other journal articles have increased. For the interest of the Journal's authors this yearly column charts citations to the Journal's articles by documenting which Journal's articles have been cited in 2023 and by whom and in which journal. Thirty-nine (39) of the Journal's articles were cited in 2023 (Scopus™ database), four articles twice, and two article three times. Total number of citations to date to Journal articles are in parentheses.

Mozafari J, Fahimi MA, Mohammadi K, et al. The diagnostic accuracy of serum and urinary S100B protein in children and adolescents with mild traumatic brain injury. *New Zealand Journal of Medical Laboratory Science* 2019; 73(3): 88-91. [Total citations: 4].

Cited by: Liu Y, Wang C, Pi Z, et al. Research on the Potential Biomarkers of Mild Traumatic Brain Injury: a Systematic Review and Bibliometric Analysis. *Molecular Neurobiology* 2023; 60(8): 4442–4449.

Cited by: Harris G, Stickland CA, Lim M, Goldberg Oppenheimer P. Raman Spectroscopy Spectral Fingerprints of Biomarkers of Traumatic Brain Injury. *Cell* 2023; 12(22): 2589.

Cited by: Malhotra AK, Ide K, Salaheen, et al. Acute Fluid Biomarkers for Diagnosis and Prognosis in Children with Mild Traumatic Brain Injury: A Systematic Review. *Molecular diagnosis and Therapy* 2023; doi: 10.1007/s40291-023-00685-8.

Hassanejad-Bibalan M, Sadeghi M, Hemmati H, et al. A two-year study of microbiological characteristics of intravascular catheter-related bloodstream infections at Razi hospital, Iran. *New Zealand Journal of Medical Laboratory Science* 2021; 75(3): 202-205. [Total citations: 5].

Cited by: Asadi S, Nayeri-Fasaei B, Zahraei-Salehi T, et al. Antibacterial and anti-biofilm properties of carvacrol alone and in combination with cefixime against Escherichia coli. *BMC Microbiology* 2023; 23(1): 55.

Cited by: Ghasemi J, Shokri D, Ghasemi SM. Emergence of extensively drug-resistant and colistin-resistant Klebsiella pneumoniae isolated from hospitalized patients in Isfahan, Iran. *Reviews and Research in Medical Microbiology* 2023; 34(2): 89–93.

Cited by: Chiari A, Ghasemi SM, Shokri D. Investigating the Antagonistic Effect of Indigenous Probiotics on Carbapenem-Resistant Pseudomonas aeruginosa Strains. *Biomed Research International* 2023; 6645657.

Denholm A, Smith MP, Patterson DM. Accurate diagnosis of high-affinity vWF-platelet disorders: A case study of pseudo von Willebrand disease. *New Zealand Journal of Medical Laboratory Science* 2008; 62(1): 7-9. [Total citations: 3].

Cited by: Malinowski AK, Abdul-Kadir R. Planning Pregnancy and Birth in Women with Inherited Bleeding Disorders. *Seminars in Thrombosis and Hemostasis* 2023; 49(4): 371–381.

Cited by: Al Arashi W, Romano LGR, Leebeek FWG, et al. Desmopressin to prevent and treat bleeding in pregnant women with an inherited bleeding disorder: a systematic literature review. *Journal of Thrombosis and Haemostasis* 2024 22(1):126-139.

Omoregie R, Erebor JO, Ahonkhai I, et al. Observed changes in the prevalence of uropathogens in Benin City, Nigeria. *New Zealand Journal of Medical Laboratory Science* 2008; 62(2): 29-31. [Total citations: 32].

Cited by: Akinduti PA, George OW, Ohore HU, et al. Evaluation of Efflux-Mediated Resistance and Biofilm formation in Virulent Pseudomonas aeruginosa Associated with Healthcare Infections. *Antibiotics* 2023; 12(3): 626.

Cited by: Safdar S, Shamim S, Khan M, et al. Probing Antibacterial and Anticancer Potential of Selenicereus undatus, Pistacia vera L. and Olea europaea L. against Uropathogens, MCF-7 and A2780 Cancer Cells. *Molecules* 2023; 28(24): 8148.

Cited by: Lawrence GA, Frater TG. Change management in healthcare: Managing paradigmatic change in the Australian national cervical screening programme. *New Zealand Journal of Medical Laboratory Science* 2017; 71(2): 31-39. [Total citations: 2].

Cited by: Bavor C, Brotherton JM, Smith MA, et al. The early impacts of primary HPV cervical screening implementation in Australia on the pathology sector: a qualitative study. *BMC Health Services Research* 2023; 23(1), 1073.

Cited by: Samanta AK, Varaprasad G, Gurumurthy A, Antony J. Implementing Lean Six Sigma in a multispecialty hospital through a change management approach. *TQM Journal* 2023; https://doi.org/10.1108/TQM-02-2023-0043.

Cited by: Mok D. ISO 15189:2012 implementation checklists for conformity assessment by accreditation bodies: A comparative analysis. *New Zealand Journal of Medical Laboratory Science* 2017; 71(3): 84-99. [Total citations: 7].

Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Internal Auditing Risk Analysis for Medical Laboratories Seeking Accreditation through the Hong Kong Laboratory Accreditation Scheme (HOKLAS). *Acta Medica Philippina* 2023;

https://actamedicaphilippina.upm.edu.ph/index.php/acta/article/view/6196.

Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Ndem BN, Akwiwu EC, Akpan PA, et al. Timely accessing of antenatal care and prevalence of vitamin b12 and folate deficiencies among pregnant women in a Nigerian population. *New Zealand Journal of Medical Laboratory Science 2021*; 75(1): 12-15. [Total citations: 2].

Cited by: Akpan PA, Akwiwu EC, Njar VE, Odibu BE. Leucocyte Counts and Derivatives as Inflammatory Indicators in Active Tuberculosis. *Tropical Journal of Natural Product Research* 2023; 7(5): 3038–3041.

Podmore R, Schousboe M. Evaluation of a new Legionella longbeachae urine antigen test in patients diagnosed with pneumonia. *New Zealand Journal of Medical Laboratory Science* 2020; 74(3): 220-221. [Total citations: 1].

Cited by: Graham FF, Harte D, Zhang J, et al. Increased Incidence of Legionellosis after Improved Diagnostic Methods, New Zealand, 2000–2020. *Emerging Infectious Diseases* 2023; 29(6): 1173–1182.

Adriaansen M, Williams S, van den Boom J. Evaluation of two transcutaneous bilirubin devices for the assessment of neonatal jaundice in a diverse New Zealand population. *New Zealand Journal of Medical Laboratory Science* 2020; 74(1): 11-16. [Total citations: 1].

Cited by: Okwundu CI, Olowoyeye A, Uthman OA, et al. Transcutaneous bilirubinometry versus total serum bilirubin measurement for newborns. *Cochrane Database of Systematic Reviews* 2023; 2023(5): CD012660.

Adriaansen MJ, Perry HE. Validation of column agglutination technology for blood group alloantibody titration. *New Zealand Journal of Medical Laboratory Science* 2013; 67(3): 92-96. [Total citations: 4].

Cited by: Loschmann TM, Garrett NKG, Perry HE. Comparison of tube and column agglutination technique for the quantification of blood group antibody anti-D by titration. *New Zealand Journal*

of Medical Laboratory Science 2023; 77(1): 24-27.

Adriaansen MJ, Perry WNC, Perry HE, Steel RC. Binary male-female laboratory reference ranges do not reflect reality for transgender individuals on sex-hormone therapy. *New Zealand Journal of Medical Laboratory Science* 2017; 71(3): 101-105. [Total citations: 4].

Cited by: Appleton NS. Hormonal contraception: From demographic histories to pleasurable futures?
[Book Chapter]. *A Companion to the Anthropology of Reproductive Medicine and Technology* 2023; pp. 332-348.

Hajinabi Y, Khamene EA, Forouzesh F, et al. The genes expression of NF-kB inflammation pathway in treated celiac disease patients. *New Zealand Journal of Medical Laboratory Science* 2022; 76(2): 55-59. [Total citations: 2].

Cited by: Abdelrahman AH, Ibrahim AA, Eid CM, et al. A pilot study on promoter methylation of MTHFR, MALT1 and MAP3K7 genes in pediatric celiac disease. *Human Gene* 2023; 36: 201180.

Olaogun JG, Akanbi GO, Atiba AS, et al. The predictive value of preoperative serum bilirubin and white blood cell count in simple and complicated acute appendicitis. *New Zealand Journal of Medical Laboratory Science* 2020; 74(3): 185-188. [Total citations: 1].

Cited by: Sikander B, Rosenberg J, Fonnes S. Individual biomarkers in the blood are not yet applicable in diagnosing complicated appendicitis: A scoping review. *American Journal of Emergency Medicine* 2023; 67: 100–107.

Hassanejad-Bibalan M, Sadeghi M, Hemmati H, et al. A two-year study of microbiological characteristics of intravascular catheter-related bloodstream infections at Razi hospital, Iran. *New Zealand Journal of Medical Laboratory Science* 2021; 75(3): 202-205. [Total citations: 5].

Cited by: Ghasemi J, Shokri D, Ghasemi SM. Emergence of extensively drug-resistant and colistin-resistant Klebsiella pneumoniae isolated from hospitalized patients in Isfahan, Iran. *Reviews and Research in Medical Microbiology* 2023; 34(2): 89–93.

Leaver CC. CC. Method evaluation for methylmalonic acid: Use for assessing vitamin B_{12} deficiency. *New Zealand Journal of Medical Laboratory Science* 2004; 58(2): 27-39. [Total citations: 3].

Cited by: Nemati R, McEntyre C, Yeo J, et al. Water soluble vitamins: Mechanism and metabolism. A narrative review. *New Zealand Journal of Medical Laboratory Science* 2023; 77(1): 11-18.

Nemati R, McEntyre CJ, Li BV, et al. Fat-soluble vitamins: Mechanisms and metabolism. A narrative review. *New Zealand Journal of Medical Laboratory Science* 2022; 76(1): 3-8. [Total citations: 1].

Cited by*:* Nemati R, McEntyre C, Yeo J, et al. Water soluble vitamins: Mechanism and metabolism. A narrative review. *New Zealand Journal of Medical Laboratory Science* 2023; 77(1): 11-18.

Siebers R. Gender trends in authorship of articles in the New Zealand journal of medical laboratory science: 1995-2019. *New Zealand Journal of Medical Laboratory Science* 2020; 74(2): 126-128. [Total citations: 1].

Cited by*:* Siebers R. Are articles authored by women under-cited compared to articles authored by men? *New Zealand Journal of Medical Laboratory Science* 2023; 77(1): 38.

Osazuwa F, Okoije R, Akinbo FO, et al. Genetic diversity of norovirus among children under 5 years in the South-South region of Nigeria. *New Zealand Journal of Medical Laboratory Science* 2020; 74(1): 39-43. [Total citations: 3].

Cited by: Arowolo KO, Ayolabi CI, Ohore HU, et al. Genetic Diversity of Norovirus in Children with Acute Gastroenteritis in Southwest Nigeria, 2015–2017. *Viruses* 2023; 15(3): 644.

Lowrey I. Review of Point of Care Testing (POCT) and the evaluation of whole blood for potassium and glucose on the Roche Reflotron®. *New Zealand Journal of Medical Laboratory Science* 2005; 59(2): 22-32. [Total citations: 3].

Cited by: Calvo-López A, Arasa-Puig E, Alonso-ChamarroJ, Puyol M. Serum/plasma potassium monitoring using potentiometric point-of-care microanalyzers with improved ion selective electrodes. *Talanta* 2023; 253: 124100.

Udo N, Bassey LE, Akpan UO, et al. Differences in micronutrient levels between urban and rural children in Cross River State, Nigeria. *New Zealand Journal of Medical Laboratory Science* 2020; 74(2): 129-134. [Total citations:1].

Cited by; Wrottesley SV, Mates E, Brennan E, et al. Nutritional status of school-age children and adolescents in low- and middle-income countries across seven global regions: a synthesis of scoping reviews. *Public Health Nutrition* 2023; 26(1): 63–95.

Taylor T. The Pae Ora Healthy Futures Bill and health reforms. *New Zealand Journal of Medical Laboratory Science* 2022; 76(2): 96. [Total citations: 1].

Cited by: Shaw S, Atkins D, Hoskyn K, et al. Enabling action: Re-envisaging education of health professionals in Aotearoa New Zealand. *Policy Futures in Education* 2023.

Siebers R. Accuracy of references in the New Zealand Journal of Medical Laboratory Sciences. *New Zealand Journal of Medical Laboratory Science* 1999; 53(2): 46-48. [Total citations: 12].

Cited by: Logan SW, Hussong- Christian U, Case L, Noregaard S. Reference accuracy of primary studies published in peer-reviewed scholarly journals: A scoping review. *Journal of Librarianship and Information Science* 2023; https://doi.org/10.1177/09610006231177715.

Mok D, Nabulsi R, Chowdhury S. Identification of ISO 22870:2016 conformance requirements for medical laboratory internal auditing. *New Zealand Journal of Medical Laboratory Science* 2017; 71(2): 41-54. [Total citations: 4].

Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Internal Auditing Risk Analysis for Medical Laboratories Seeking Accreditation through the Hong Kong Laboratory Accreditation Scheme (HOKLAS). *Acta Medica Philippina* 2023;
https://actamedicaphilippina.upm.edu.ph/index.php/acta/article/view/6196.

Mok D, Chowdhury S. The strategic management stage of ISO 15189:2012 management system standard: An implementation update. *New Zealand Journal of Medical Laboratory Science* 2019; 73(3): 103-107. [Total citations:5].

Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Mok D, Ang E. ISO 15189:2012 implementation: An update of related international standards and guidance documents for medical laboratory quality management. *New Zealand Journal of Medical Laboratory Science* 2016; 70(2): 42-66. [Total citations: 12].

Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Mok, Chowdhury S. Identification of ISO 22870:2016 conformance

requirements for medical laboratory internal auditing. *New Zealand Journal of Medical Laboratory Science* 2017; 71(20; 41-54. [Total citations: 4].
Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Mok D, Chowdhury S. The process control, design and planning stage of ISO 15189:2012 management system standard: An implementation update. *New Zealand Journal of Medical Laboratory Science* 2020; 74(2): 103-105. [Total citations: 3].
Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Mok D, Eloyan N, Chowdhury S. The process evaluation and improvement stage of ISO 15189:2012 management system standard: An implementation update. *New Zealand Journal of Medical Laboratory Science* 2020; 74(3): 1-4. [Total citations: 2].
Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Mok D, Nabulsi N, Chowdhury S. Management review input checklist for iso 15189:2012 internal auditing: An optimisation guide for medical laboratories . *New Zealand Journal of Medical Laboratory Science* 2020; 74(1): Supplementary material. [Total citations: 2].
Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Mok D, Nabulsi N, Chowdhury S. Management review input checklist for iso 15189:2012 internal auditing: An optimisation guide for medical laboratories. *New Zealand Journal of Medical Laboratory Science* 2020; 74(1): Supplementary material. [Total citations: 2].
Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Mok D, Nabulsi N, Chowdhury S. Conformity evaluation checklists of API 20 E for ISO 15189:2012 internal auditing: An optimisation tool for medical laboratories. *New Zealand Journal of Medical Laboratory Science* 2018; 72(3): 90-95. [Total citations: 2].
Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Mok D, Chowdhury S, Nabulsi N, et al.. Implementation of Class II biological safety cabinet good maintenance practice: Protective countermeasures against SARS-CoV-2 for ISO 15189:2012 accredited medical laboratories. *New Zealand Journal of Medical Laboratory Science* 2021; 75(1). [Total citations 1].
Cited by: Dayrit GB, Mok D, Nabulsi R, et al. Conformity Evaluation of Afinion 2 Analyzer Maintainability: Compliance Practicality for Philippine National Standard PNS ISO 15189:2013 Accreditation. *Acta Medica Phillippina* 2023; 57(11): 72-91.

Siebers R. How accurate is data in abstracts of research articles? New *Zealand Journal of Medical Laboratory Science* 2000; 54(1): 22-23. [Total citations: 9].
Cited by: Handel KW, Ofri R, Sebbag L. Accuracy of data in abstracts of veterinary ophthalmology research articles published in peer-reviewed journals. *Veterinary Ophthalmology* 2013: 393-397.

Akwiwu EC, Edem MS, Akpotuzor JO, et al. Glycaemic control and associated platelet indices among apparently healthy caregivers in Southern Nigeria. *New Zealand Journal of Medical Laboratory Science* 2020; 74(2): 87-90. [Total citations: 3].
Cited by: Akwiwu EC, Edem MS, Okpokam DC, et al. Prediabetes and Endothelial Involvement among Apparently Healthy Persons. *Tropical Journal of Natural Product Research* 2023; 7(2): 2468–2471.

Edem SS, Akwiwu EC, Akpotuzor JO. Endothelial cell markers in diabetes and prevalence of uncontrolled type 2 diabetes mellitus in Southern Nigeria. *New Zealand Journal of Medical Laboratory Science* 2022; 76(1): 15-17. [Total citations: 1].
Cited by: Akwiwu EC, Edem MS, Okpokam DC, et al. Prediabetes and Endothelial Involvement among Apparently Healthy Persons. *Tropical Journal of Natural Product Research* 2023; 7(2): 2468–2471.

Oladeinde BH, Ooregie R, Osakue EO, Onifade AA. Evaluation of laboratory request forms for incomplete data at a rural tertiary hospital in Nigeria. *New Zealand Journal of Medical Laboratory Science* 2012; 66(2): 39-41. [Total citations: 10].
Cited by: Degfe C, Mohammed O. Magnitude of extra-analytical errors and associated factors in medical laboratories in thirteen Public Hospitals in Addis Ababa, Ethiopia. *SAGE Open Medicine* 2023: 11: 20503121221148062.

Jones LM, Legge M. Biochemical markers of bone activity in active and sedentary spinal cord injured men. *New Zealand Journal of Medical Laboratory Science* 2009; 63(2): 40-43. [Total citations: 4].
Cited by: Ponzano M, Wiest M, Coleman A, et al. The use of alkaline phosphatase as a bone turnover marker after spinal cord injury: A scoping review of human and animal studies. *Journal of Spinal Cord Medicine* 2023; 46(2): 167–180.

Sami H, Singh A, Ahmed S, Shahid M. Emergence of linezolid resistance in Enterococci: Prevalent genotypes and resistance pattern in vancomycin-resistant Enterococci in a North-Indian tertiary care hospital. *New Zealand Journal of Medical Laboratory Science* 2020; 74(1): 27-30. [Total citations: 1].
Cited by: Smout E, Palasinamy N, Valappil SP. Prevalence of vancomycin-resistant Enterococci in India between 2000 and 2022: a systematic review and meta-analysis. *Antimicrobial Resistance and Infection Control* 2023; 12(1): 79.

Austin PM, McCarthy SM, Faiva-Thompson HT. Diffuse fine speckled (DFS70) antibody in ANA testing: Identification and proposed management in a New Zealand tertiary hospital setting. *New Zealand Journal of Medical Laboratory Science* 2017; 71(3): 113-119. [Total citations: 2].
Cited by: Wahab AA, Jauhary EJ, Ding CH. The recognition of anti-nuclear antibody's dense fine speckled pattern and the detection of anti-DFS70 antibodies in the laboratory practice: Its prevalence and clinical significance. *Malaysian Journal of Pathology* 2023; 45(2): 157-173.

Alizadeh V, Hashemi SJ, Rafat Z, et al. Isolation of candida species on human mucosal surfaces. *New Zealand Journal of Medical Laboratory Science* 2021; 75(1): 33-37. [Total citations: 1].
Cited by: Cyprowski M, Lawniczek-Walczyk A, Stobnicka-Kupiec A, et al. Assessment of exposure to fungi in archives and libraries based on analyses of filter and nasal samples: preliminary investigation *Aerobiologia* 2023; 9: 415-428.

Holloway R. Sideroblastic anaemia secondary to chronic alcoholism: A case study and review. *New Zealand Journal of Medical Laboratory Science* 2007; 61(3): 69-70. [Total citations: 1].
Cited by: Marginean CM, Pirscoveanu D, Popescu M, et al.

Diagnostic Approach and Pathophysiological Mechanisms of Anemia in Chronic Liver Disease - An Overview. *Gastroenterology Insights* 2023; 14(3): 327-341.

Abu-Lubad MA, Helaly GF, Aqel AA, et al. Putative virulence factors of candida species colonising asymptomatic pregnant Jordanian women. *New Zealand Journal of Medical Laboratory Science* 2021; 75(1): 51-56. [Total citations: 3].

Cited by: Puello M, Young G, Suárez P. Actividad de fosfolipasas y proteasas en aislamientos de especies de Candida colonizadoras y causantes de vulvovaginitis en mujeres gestantes |Phospholipase and proteinase activities of isolates of colonizing Candida spp. causing vulvovaginitis in pregnant women]. *Biomedica* 2023; 43: 89-96.

Alqershi KA, Kadhim AM, Al-Muaala AMN. Clinical evaluation of a newly developed point-of-care haemoglobinometer. Comparison with colorimetric and cell counter haemoglobin determination methods. *New Zealand Journal of Medical Laboratory Science* 2020; 74(1): 31-34. [Total citations: 3].

Cited by: Appiah O, Tandoh MA, Puotege PS, Edusei AK. The Effect of a Turkey Berry (Solanum torvum)-Fortified Biscuit on the Hemoglobin Level and Cognitive Performance of Adolescent Females in the Ahafo Region of Ghana: A Pilot Study. *International Journal of Food Science* 2023; 1388782.

AUTHOR INFORMATION

Rob Siebers, PGCertPH, FNZIMLS, FRSB HonFNZAP
Associate Professor[1] and Emeritus Editor[2]

[1]Wellington School of Medicine & Health Sciences, University of Otago, Wellington
[2] New Zealand Journal of Medical Laboratory Science, NZIMLS

Correspondence: Rob Siebers
email: rob.siebers@otago.ac.nz

This year, we were proud to have combined once again NZIMLS Biochemistry Special Interest Group Meeting with the AACB Roman Lecture. This opportunity enabled us to bring together experts and key industrial figures from across the field to delve into the latest advancements and research being undertaken within the speciality of Clinical Biochemistry. The event was full of informative presentations which invoked some interesting questions and discussions. The highlight of the meeting was the Roman Lecture presented by international speaker Professor Sverre Sandberg, director of the Norwegian Quality Improvement Laboratory Examinations (Noklus), who shed light on the significant role medical laboratories play in enhancing medical decisions and ultimately improving patient outcomes. Interestingly, this became a bit of a theme for the rest of the meeting.

AACB Roman Lecture, Professor Sverre Sandberg: *Aspects of how Laboratorians can Contribute to Better Medical Decisions and Improve Patient Outcomes*
Drawing on extensive experience, and from an international perspective Professor Sandberg addressed the pivotal role of medical laboratories in the healthcare system. He specifically discussed quality aspects of Biochemistry, including internal quality control assessments and external quality assurance schemes. The final part of the presentation concentrated on point of care (POC) equipment and the importance of laboratory involvement. This included emphasis on how critical the laboratory input is in the decisions of which POC equipment to use and the tests to be offered, and most importantly how the continued laboratory oversight of the equipment improves the quality of point of care testing.

Dr Andrew Reynolds (Otago University): *Wholegrains for Health*
This thought-provoking presentation explored the impact of a wholegrain diet on patients' post-myocardial infarction (MI). Dr Reynolds' research provided compelling evidence supporting the notion that dietary interventions, specifically the incorporation of wholegrains, can significantly benefit cardiovascular health in the aftermath of an MI. The question was asked whether providing free healthy groceries to cardiac patients in recovery less expensive for the health system than the cost of re-hospitalisation after a second event. The presentation prompted thorough discussions on the practical implications of dietary recommendations in post-MI care.

Cat Roynayne (Otago University): *Through the Lipid Glass – is everything as it seems?*
Cardiovascular risk assessment (CVRA) took centre stage in another engaging session exploring the significance of lipid blood tests and their ability to predict cardiovascular events. Historic patient data from the Otago region was shared showing interesting trends in lipid markers over the last 30 years. The implications of these trends were examined, and explanations of the reasons for these trends were explored. Attendees gained valuable insights into the evolving landscape of cardiovascular risk assessment and how laboratory data can be used to increase our understanding of the relationship between lipid profiles and the overall assessment of cardiovascular risk.

Dr Colin Simon Shelly (Otago University): *Novel Breast Cancer Markers*
One of the key sessions of the meeting focused on the latest developments in breast cancer research. Dr Shelly is founder of Leukaemia Therapeutics LCC, in Boston, Massachusetts and he was in New Zealand to collaborate with Otago University researching a novel breast cancer marker using CD43. The presentation centred on cutting-edge molecular research that identified CD43 as a novel biomarker for predicting the progression of breast cancer, paving the way for more personalized and effective therapeutic interventions. The audience expressed keen interest in the potential impact of these advancements on the clinical management of breast cancer patients.

Professor Peter McIntyre (Otago University): *Immunogenicity of MMR Vaccines*
Professor McIntyre is leading a study in the immunogenicity of the MMR (measles, mumps, rubella) vaccine and the potential effects of different modes of administration of these vaccines. The presentation described recent research findings related to vaccine responses, shedding light on the intricacies of immune reactions to these vaccines. Along with his Assistant Research Fellow, Melanie Millier they explained the study in detail, which involved administrating vaccines via different modes to university students who had shown low antibody levels when tested as part of their Health Sciences screening blood tests. Discussions created from this presentation revolved around the importance of promoting vaccinations and how the different modes of administration may improve immunogenicity whilst also helping to address vaccine hesitancy.

Christian (Awanui Labs): *HbA1c Test Methods*
The meeting also addressed the technical aspects of diagnostic testing, with a dedicated session on HbA1c test methods. Christian summarised the theory and the nuances of different testing techniques and their impact on the accuracy of glycaemic monitoring in patients with diabetes. This session facilitated a deeper understanding of the strengths and limitations of various HbA1c testing methodologies and why they are suitable in each different clinical setting.

Sian Horan (Awanui Labs): *Renal Calculi Analysis by FTIR Spectroscopy*
The meeting concluded with a comprehensive examination of renal calculi, commonly referred to as kidney stones. The presentation explained in detail the principle of Fourier Transform Infrared Spectroscopy and how this technique is used to identify organic compounds within kidney stones.

In summary, the Biochemistry Special Interest Group meeting proved to be a dynamic and intellectually stimulating event, bringing together experts and enthusiasts to explore the multifaceted speciality of Clinical Biochemistry. The international speaker's presentation on the role of medical laboratories in improving patient outcomes set the tone for an insightful gathering. The diverse range of topics covered, from breast cancer research to cardiovascular health and renal calculi, reflected the breadth and depth of ongoing advancements in biochemistry. The meeting provided a platform for fruitful discussions and knowledge exchange, fostering a collaborative spirit among professionals committed to advancing the field for the betterment of patient care.

ACKNOWLEDGEMENTS

I would like to thank Roger Barton and Christian, who on behalf of the AACB were pivotal in the organisation of the day and helped create a fantastic programme. I would also like to extend thanks for their generous support to our sponsors; Bio Rad Pty, Roche Diagnostics, and Abacus Dx. I would like to express sincere appreciation to all the participants whose presentations enriched the meeting and stimulated discussions on numerous compelling topics. Lastly, a special thank you to everyone who dedicated their time to travel to Dunedin and attend this gathering, contributing significantly to the success of the day.

Report by: Sian Horan, Head of Department, Biochemistry, Awanui Labs, Dunedin.

Anatomical Pathology Special Interest Group Meeting

21 October 2023, Nelson

The APSIG this year was held in sunny Nelson at the Rutherford Hotel where we had an amazing turn out with some really interesting talks. We were lucky enough to have a range of technical staff speak as well as pathologists and doctors. Ranging from immunohistochemistry to case studies and cultural considerations. Everyone was kept on their toes or their bottoms with some movement during the day as well as when the final quiz took place, testing the knowledge that we learnt over the course of the day. There might have been a slight incentive to win, a cheeky chocolate bar. Old friendships were renewed, and new friends were made over muffins, pastries, tea, coffee and a delicious lunch. It was a great opportunity for us to all meet and discuss ideas, opportunities and put faces to names that we see so frequently over the phone and email.

Kirsty Sewell presented to us an amazing talk about entering the world of theatre and how we could build relations with nurses and doctors. Her case study presentation was mesmerizing with some incredible images. Kirsty was awarded best presentation of the day for keeping us all on the edge of our seats and the drive to cross those theatre doors and build some relationships.

Michelle Cheale and Xin Xin were awarded the runner up presentation and unfortunately had to leave to catch a plane before prize giving. They presented to us a prostate biopsy trial. We were so curious to see how they progressed through the journey from patient to pathologist with the chip. Thank you for sharing this with us and good luck for future trials.

Congratulations to Kirsty, Michelle and Xin Xin and to all our other speakers on the day. Thank you to everyone who took time out of their day to present and to everyone who came to the SIG. It was truly a fantastic day with everyone getting involved and this would not have been possible without the NZIMLS and my team here in Nelson. Looking forward to seeing everyone again next year for another enlightening day!

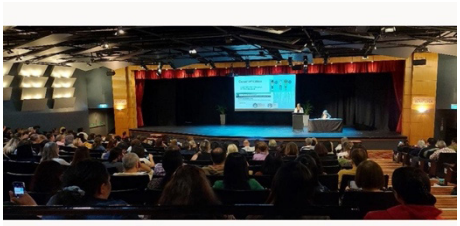
Report by: Paige Chase, Head of Department Histology, Awanui Laboratories, Nelson

Preanalytical Special Interest Group Meeting

11 November 2023, Auckland

Pre- Analytical Services Special Interest Group (PASSIG) had a successful and productive year 2023. The four meetings held throughout the year with 12 to 15 members from different labs attending each time provided a platform for discussing various issues related to Pre-analytical services in New Zealand Laboratories. Congratulations to Ailsa Bunker (Manager, Specimen Services, Middlemore Hospital Laboratory) PASSIG member for being the convenor of South Pacific Congress 2023 and receiving the Life Membership of NZIMLS. The Pre-Analytical session at SPC had great presentations adding to the group's achievements.

The seminar at Waipuna Conference Centre in Auckland also had an impressive turnout with 246 registrations. The 13 presentations from different disciplines showcased the diversity of topics discussed.



PASSIG Seminar 2023

Special congratulations to Eunice De Castro from Te Whatu Ora, Waikato, for winning the best presentation award, and to Jordon Haig from Awanui Labs (Labtests, Auckland) for winning the second-best presentation award. It's always rewarding to see members recognized for their contributions.

As Annette Bissett, the previous convenor of PASSIG and Phlebotomy coordinator from North Shore Hospital, retiring this year after more than 30 years of dedicated service to Pre Analytical Services, the group extends their best wishes for a good and healthy retired life to her. Also, congratulations to all PASSIG members who sat and passed their exams this year.

Lastly, a big thank you goes out to all members of NZIMLS for their kind and continued support throughout the year. Here's to another successful year ahead!

Reported by: Ajesh Joseph (Convenor), NZIMLS Secretary/ Treasurer

Microbiology Special Interest Group Meeting

4 November 2023, Palmerston North Conference & Event Centre

The MSIG was held at the Palmerston North Conference and Event Centre on 4th November 2023. We had approximately 75 attendees and 10 extremely good talks were presented.

Heather Davies from ESR (Environmental Science and Research) kicked off the event with the title of IRIS hibernated to bloom another day". This covered respiratory disease statistics affected by the Covid outbreaks in New Zealand.

ESR provided two other speakers throughout the day, Jenny Szeto with "Colistin Resistant" a recount of an observed phenomenon of well skipping in microtiter plate dilutions. And Audrey Tiong gave Fiona Lee's presentation Clinical Listeriosis- an informative talk on sporadic vs outbreaks of Listeriosis in New Zealand, as unfortunately Fiona was unable to attend.

Lan En, a scientist from Medlab Central Palmerston North was unable to attend due to illness but the SIG was lucky enough to have Lan record the talk over the slide presentation. "Microbiology meets machines" was a "hot" topic regarding AI (Artificial Intelligence) and its role in the microbiology laboratory.

Awanui Labs Dunedin were then represented by Jenna Paterson's talk "Vaginal gram stains. Out with the old and in with the new?" Jenna has recently graduated from Otago University and gave a remarkably interesting and thorough talk about recent technologies to supersede gram staining vaginal swabs. Jenna was a first-time speaker who commanded her audience with her research knowledge and was well equipped to answer questions on the topic.

After a delicious morning tea our guest speaker of the day "Dr Cynric Temple-Camp" a pathologist from Medlab Central gave a scintillating talk on "The perfect murder." This was very well received by an attentive audience, and everyone now has a good understanding of what is needed to achieve a murder and not be arrested for it. The Waikato VRE outbreak was the next topic presented by Sean Munroe. A comprehensive talk on discovering an outbreak and then the measures needed to control it.

Lunch was a sumptuous affair and then Jan Deroles-Main reported on the *Salmonella typhi* outbreak in the Gisborne region." Foggy Fever" was well received and even more so when transmission was human to human not from a food source!
Sabiha Kaur, a technician from Medlab Central, took out the Best Presentation Prize with her talk "The Mysterious case of our night shift discovery" An extremely thorough case study of *Mycobacterium marinum*. Sahiba was a first-time presenter so a big congratulations for taking out the top pr ize.Rebecca Lucas-Roxburgh HOD of Molecular Medlab Central won runner up with her comprehensive account of "Development of an Extraction free qPCR for the detection of Group A Streptococcus in throat swabs." A topic of interest especially since costs were covered as well.

The attendees were all happy to be able to have face-to-face meetings again and the venue facilities and delicious food were well received as well as all the informative talks for the day.

Thank you to all the presenters and Sean Guilfoyle, who stepped in as IT helper at the last minute due to Lan being unwell.

Reported by: Tina Lusher, Technical Director, Microbiology Department, Medlab Central, Palmerston North

Molecular Diagnostics Special Interest Group Meeting

20 October 2023, Auckland

The Molecular Diagnostics (MolD) SIG held in Auckland at the Auckland Domain Lodge was a very successful event! Success being measured by the fact that almost all the delegates who registered were in attendance, the presentations were all excellent, and the food and coffee was plentiful! This was the first in-person MolD SIG to be held since Covid, which is a success to be celebrated in itself.

The day started with a presentation by Dr Max Bloomfield (Awanui Labs, Wellington) via Zoom. Despite some hesitation that it would work, the talk via Zoom was a very positive experience and a wonderful option if being in person is not a possibility. Dr Bloomfield spoke on using real-time low-cost genomic surveillance to identify and control hospital outbreaks (recently published Bloomfield et al, Pathology 2023). Next up was Dr Gary McAuliffe (LabPLUS, Auckland) whose presentation entitled, "Molecular automation – time to think like a robot", made us all think about reducing TAT for infectious disease diagnostics. Jason Copedo (Grafton Clinical Genomics, Auckland) rounded up the first lot of talks with his very thorough overview of NGS and precision medicine.

After morning tea, we had the benefit of hearing from Dr Sandra Fitzgerald (University of Auckland), who presented her PhD work on the translational of liquid biopsies from research to the clinic. Dr Fitzgerald won the Best Presentation Prize, which was a unanimous decision by our wonderful judges. Thereafter, we heard from Dr Mareike Erdmann (LabPLUS), Tom Manning (Labtests) and Dr Clinton Turner (Auckland Hospital). The scope of topics varied from WGS of *Mycobacterium tuberculosis*, to non-invasive prenatal screening and the evolution of brain tumour diagnosis (respectively).

Lunch was delicious affair with a wide variety of options from our caterers; Mahuhu. After lunch, we "navigated our way through genomes, one case at a time" (Polona Le Quesne Stabej/ Jasmine Chew - University of Auckland/LabPLUS), learned all about Lynch Syndrome, specifically an MSH6 case (Sabine Grey - Canterbury Health Laboratories), and heard about an extraction free qPCR for Group A strep in throat swabs (Dr Rebecca Lucas-Roxburgh – Medlab Central). Sabine Grey won our Runner Up Best Presentation Prize for a very well-presented talk.

The final stretch of the day included a case study presented by Yeshmira Moodley (IGENZ) entitled "What the TERT? A telomerase reverse transcriptase case study". Luke Williamson (LabPLUS) ended off with his talk on the validation of a targeted NGS pipeline for gene panel diagnostic testing.

As with all SIG days, a lot of time and effort was put in by a team of people. I would like to especially thank my colleagues at IGENZ as well as Roberto Mazzaschi from LabPLUS for their invaluable input and assistance. I would also like to thank the presenters who put up their hands to give a talk, without which, a SIG would not happen.

Report by: Bronwyn Neumann (Convenor), Team Leader, Molecular Testing, IGENZ DNA Diagnostics, Auckland.

Contributed by Michael Legge

The final step in Bilirubin metabolism

Although bilirubin metabolism is understood, the final step to the conversion to urobilinogen has remained essentially unknown. Bilirubin is an intermediate of the haem degradation pathway and has long been considered to be a well understood series of metabolic steps, however the final step for the conversion from bilirubin to the yellow urobilinogen has remained an unknown metabolic step for over 125 years. Bilirubin glucuronide is excreted into the gut where it is either reabsorbed or excreted. By excreting bilirubin (and its conjugates) as urobilinogen or stercobilinogen the cycle of bilirubin metabolism is completed. In a recent publication (1) a collaborative research investigation in the USA has finally identified the mechanism for the conversion into urobilinogen. Using a combination of biochemical analysis and comparative genomics the authors mapped out the relationship between gut micro bacteria and the conversion of bilirubin to urobilinogen. The authors identified that anaerobic bacteria such as the Firmicutes species all contained an enzyme, bilirubin reductase which can reduce bilirubin and its conjugates to urobilinogen. Additional support for this work by the authors comes from their analysis of newborn bilirubin metabolism which increases urobilinogen production as their gut matures and from patient with inflammatory bowel disease who also have a decreased Firmicutes species gut flora and a diminished synthesis of urobilinogen.

How significant is Barbie®?

The advent of the Barbie® film created a wide-ranging discussion on the role of Barbie® dolls and their influence on girls and young women. In a recent publication from the USA (2), the author has analysed the role of medical and scientific career dolls on influencing career decisions and their accuracy in representing the relevant health related professions. A total of 97 Barbie® dolls across six health professional groups were compared with 65 non-Barbie® dolls across the same health professional groups (medicine, scientist, science educator, nurse, dentist, and paramedic). Overall, the Barbie® brand largely treated children (66%) with only 4% as working with adults. Of the 12 dolls representing scientists none met the criteria for personal protective clothing. The comparison dolls also had similar shortcomings. The author emphasizes the dangers of having loose hair in laboratory settings which all dolls seemed to have. While women are continuing to gain stronger footholds in health care, particularly medicine, dentistry and nursing as well as significant academic achievements the author considers that a more accurate representation of the health-related professions. In addition, the author recommended a more ethnically diverse range of dolls in the health professions.

Effects of mergers and acquisitions in Pathology

A publication from the USA surveyed 732 pathology laboratories subject to mergers and acquisitions (3). In addition, the authors surveyed 819 pathology laboratories that were not subject to mergers and acquisitions. Both surveys considered qualifications, geographic location, age, and gender. Although this publication was based in the USA, there is relevance to pathology in New Zealand, in the present climate. Evidence suggests that despite the perceived corporate benefits there are a range of issues relating to this type of restructuring. The overall result indicated a higher statistically significant levels of personnel burnout amongst staff who were subject to mergers and acquisitions and considered that the lack of leadership contributed to the high levels of staff burnout. They also identified an overall lack of social relationships in those undergoing mergers and acquisitions. The authors concluded that the major contributors to burnout compared to the non-merger and acquisition laboratories was the lack of social interactions and communications as well as a satisfactory policy by the administration to reduce staff burnout.

Diagnostic testing leading to harm

Diagnostic errors can be associated with laboratory testing, however there is a lack of a suitable and relevant measure for evaluation. Where traditionally laboratory testing was only used to test for organ and system dysfunction, now laboratory testing is used for a wide range of diagnostic applications such as; cancer diagnosis and monitoring, molecular analysis, monitoring a patient's response to treatment etc. This increases the medical practitioner's dependence on diagnostic laboratory testing and may in some cases reduce the examination skills. In addition, 40 risk factors have been identified for diagnostic errors associated with send out diagnostic testing. In the current publication (4), the authors identified three major areas contributing to diagnostic testing leading to patient harm. A requirement to have processes to identify patient harm (e.g. ordering an inappropriate test, not ordering the appropriate test and the appropriate test result is misapplied). Second, the appropriate test is ordered but a delay occurs in the testing/reporting process, and third the result of the appropriate test is inaccurate. The authors conclude that there needs to be stronger links between pathology laboratories and clinicians, and the importance of communication between both parties to reduce diagnostic errors. They also considered that a system should be in place to track to track any diagnostic errors.

How chondrocytes survive hypoxia

It is accepted that the availability of oxygen to cells in the body is essential for survival. This is achieved by a sophisticated vascular system and haemoglobin in the red blood cells. The cartlidge system is however avascular and has been believed to rely on diffusion of oxygen to the avascular tissues and on glycolysis to provide the necessary energy requirements. This is controlled by hypoxia inducing factor which if inhibited results in cell death in chondrocytes and immediate tissues. A recent publication from China (5) has provided new and novel evidence relating to chondrocyte oxygen metabolism. The authors identified that haemoglobin is synthesized by chondrocytes under the influence of several transcription factors. The haemoglobin is synthesized as membrane less condensates which form cytoplasmic bodies capable of supplying oxygen to the avascular tissues that have a left shift compared to red cell haemoglobin thereby allowing binding and storing oxygen in low oxygen environments. When synthesis of the haemoglobin condensates was blocked in culture, the chondrocytes died. The authors conclude that this discovery may have implications for diseases such as rheumatoid arthritis and that other non-red cell sites of haemoglobin synthesis are likely.

REFERENCES

1. Hall B, Levy S, Default-Thompson K et al. BilR is a gut microbial enzyme that reduces bilirubin to urobilinogen. *Nat Microbiol* 2024; 9: 173-184.
2. Klamer K. Analysis of Barbie medical and scientific career dolls: descriptive quantitative study. *BMJ* 2023; doi:10.1136/bmj-2023-077276.
3. Chiou PZ, Herring TP, Oh J, Medina E. Health impacts in pathology workforce during mergers and acquisitions (M&A). *J Clin Pathol* 2023; 383: e077276. doi: 10.1136/jcp-2023-209124.
4. Epner PL, Gans JE, Graber ML. When diagnostic testing leads to harm: a new outcomes-based approach for laboratory medicine. *BMJ Qual Saf* 2013; 22 Suppl2 (Suppl2): ii6-ii10. doi:10.1136/bmjqs02012-001621.
5. Zhang F, Zhang B, Wang Y et al. An extra-erythrocyte role of haemoglobin body in chondrocyte hypoxia adaption. *Nature* 2023; 622(7984): 834-841.

MARCH 2024 QUESTIONNAIRE

1. Blood group antigens are inherited markers found on surfaces, including red blood cell membranes. What clinical effects do their corresponding antibodies have?

2. What does the International Society of Blood Transfusion (ISBT) define as a blood group system? And how do these systems arise?

3. What are the major antigens of the MNS blood group system? How many antigens in the MNS blood group have been identified by the ISBT?

4. What rare MNS hybrid variant is present in East African populations? What does this variant confer protection against and how?

5. What causes Leptospirosis? How is it typically transmitted? What makes leptospirosis infection difficult to identify through clinical presentation alone? And what other conditions are similar in their presentation?

6. What are the drawbacks of using the gold standard serological test, microscopic agglutination test (MAT) in New Zealand?

7. PCR can provide a more rapid “real-time laboratory diagnosis of leptospirosis using blood and urine samples, when are blood samples used and why? When is a urine sample recommended? And when can these samples be unreliable?

8. What significant changes in body composition does spinal cord injury (SCI) paralysis cause? What significant metabolic changes are considered contributing factors associated with the metabolic syndrome seen in SCI?

9. What is the difference between complete and incomplete SCI? What differences were significant between complete and incomplete SCI in the presented study?

10. What should be considered in the placement of warning markings for equipment and instruments that incorporate laser products?

NOVEMBER 2023 QUESTIONNAIRE ANSWERS

1. How is Shiga toxin-producing *Escherichia coli* (STEC) O157:H7 transmitted?
   Transmitted via the faecal-oral route by ingestion of contaminated food and water as well as from person to person.

2. Why is *E.coli* O157:H7 a considerable health concern? And what are the characteristics of infection?
   Because of the severity of infection, it causes. This is due to characteristics such as low infective dose, ability to express different virulence factors, long survival time in the environment, unusual acid tolerance, difficulty in treatment, and an apparent special but inexplicable association with ruminants that are used as food sources.

3. What was the percent prevalence of *E.coli* O157:H7 in this study and in what age group?
   Prevalence of E.coli O157:H7 in this study was 4.67% and prevalence of E. coli was significant within the age group 11-20 years.

4. What is Familial Mediterranean Fever (FMF)? How is it characterised? And what genetic trait causes the disorder?
   Familial Mediterranean Fever (FMF) is a chronic systemic autoinflammatory disorder, characterized by recurrent attacks of fever, headache, and inflammation of serous membranes.
   It is an inherited autosomal recessive trait associated with a missense mutation in the MEFV gene located on the short arm of chromosome 16. The mutation leads to a loss of pyrin function and results in uncontrolled inflammation.

5. What role does Chemerin play in the early stages of inflammation?
   In the early stages of inflammation, Chemerin acts as a pro-inflammatory molecule, attracting and activating immune cells to the site of inflammation. This helps to fight off infection and heal tissue damage.

6. Chemerin levels in FMF patients in this study were significantly elevated compared to controls. How would this support therapeutic treatment for FMF patients?
   Chemerin that acts as a pro-inflammatory adipokine could be considered as a biomarker reflecting the chronic proinflammatory status in the FMF patients and may facilitate the development of Chemerin as a new therapeutic modality in the treatment of FMF.

7. What is Insulin Resistance (IR)? and in what diseases does it play a significant role?
   Insulin resistance is a condition of glucose homeostasis characterized by a diminished sensitivity of the liver, adipose tissue, muscles and other body tissues to the hormone insulin. It has a significant role in the onset and progression of cardiovascular disease and diabetes mellitus.

8. What is the gold standard technique for measuring Insulin Resistance? What prevents the use of this technique and what substitute is frequently used?
   The hyper insulinemic euglycemic clamp is the gold standard technique for measuring IR however it is complex and has a high cost, preventing its daily use in clinical practice. The homeostasis model assessment for insulin resistance (HOMA-IR) index is frequently used to gauge insulin resistance in adults.

9. In the diagnosis of vaginitis, what laboratory analysis of vaginal swab is performed? What are the problems with this standard method?
   Gram stain testing and culture. Gram stain interpretation can be subjective, even with an experienced operator. The correct distinction of bacterial morphocyctes? Not correct word is difficult by microscopy, gel lubricant residue can result in poor staining, insufficient material and time consuming.

10. The laboratory needs to alert the clinician to the possibility of Bacterial Vaginosis (BV) due to the association of what serious outcomes? What is only revealed by molecular diagnosis and how can this strengthen the potential for improved diagnosis?
    BV association of with serious outcomes such as preterm birth, spontaneous abortion, or acquisition of sexually transmitted diseases.
    Molecular analysis reveals complex vaginal flora dynamics. Importantly, many of the microorganisms involved may not be culturable, easily distinguished or even seen in a Gram stain, so the molecular testing provides improved diagnoses.

Index to Volume 77, 2023

AUTHOR INDEX

PUBLISH IN THE NEW ZEALAND JOURNAL OF MEDICAL LABORATORY SCIENCE!

The NZJMLS is a peer-reviewed publication containing articles on Medical Laboratory Science and related topics. The Journal is the official publication of the New Zealand Institute of Medical Laboratory Science and is circulated to members of the Institute and libraries in New Zealand. The Journal is open access and does not charge publishing fees or charge its readers or institutions for access, and is available to international readers. Users have the rights to "read, download, copy, distribute, print, search, or link to the full texts of these articles" The current circulation of the Journal is about 3,500 and is published three times per year. It has been published continuously since 1946.

Submission of articles for publication is not restricted to members of the Institute. Articles from all major disciplines of medical laboratory science as well as articles of interest to the profession will be considered. The Journal invites submissions under the following categories:

- Original articles
- Review articles
- Research letters
- Case studies
- Book reviews

NZIMLS
THE NEW ZEALAND INSTITUTE OF MEDICAL LABORATORY SCIENCE (INC)

Scan the QR code for author instructions

sharon@nzimls.org.nz

021 229 5454
03 313 4761

www.nzimls.org.nz

PO Box 505,
Rangiora 7440
New Zealand

https://mix.nzimls.org.nz/journals-recent.html