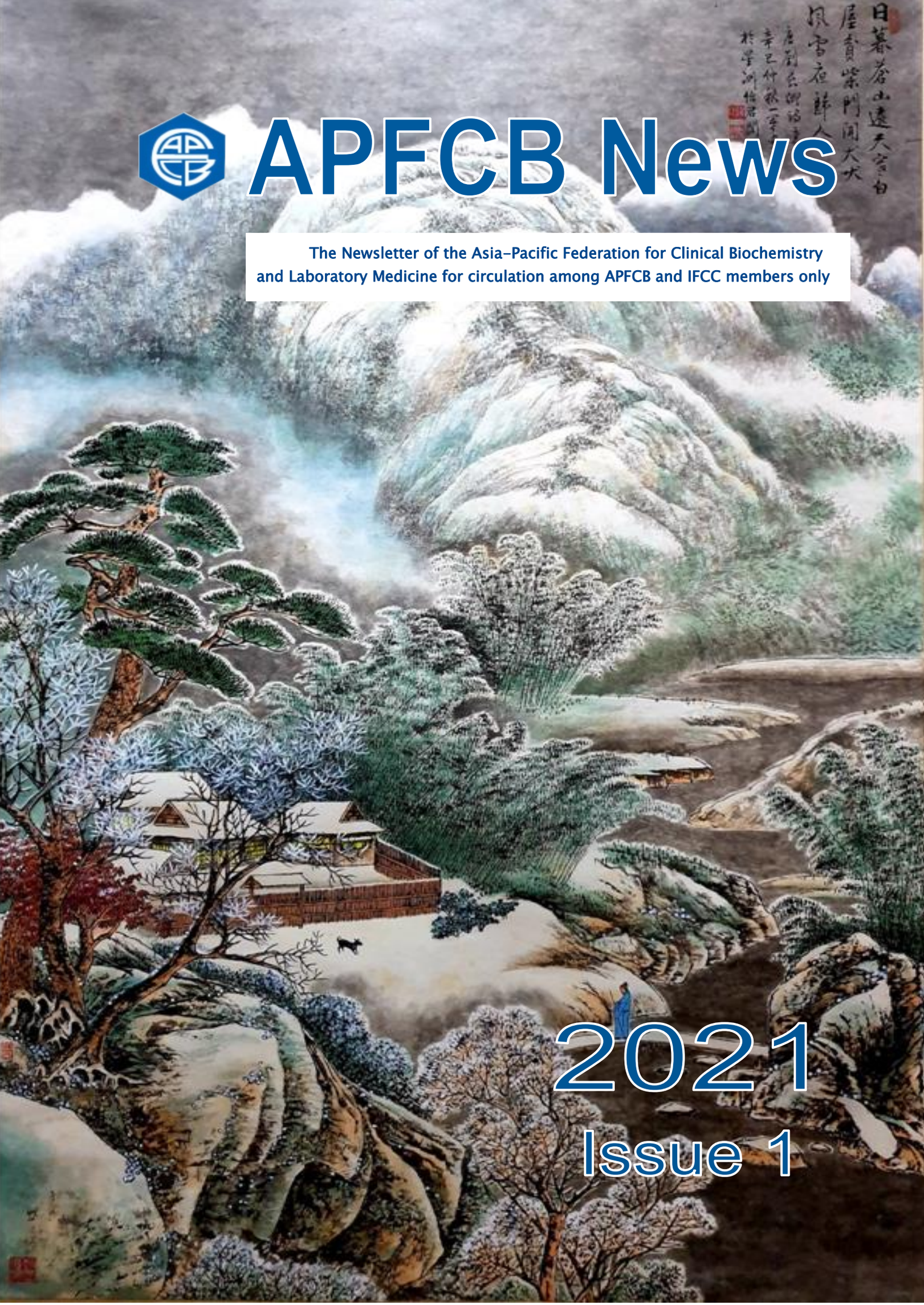

APFCB News

The Newsletter of the Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine for circulation among APFCB and IFCC members only

2021

Issue 1

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The APFCB News welcomes suitable contributions for publication. These should be sent electronically to the Chief Editor. Statements of opinions are those of the contributors and are not to be construed as official statements, evaluations or endorsements by the APFCB or its official bodies.

Contact email: afpcbofficial@apfcb.org

Cover page: "Returning Home on the Evening of a Heavy Snowfall"
Contributed by Dr. Tan It Koon
Founding and Past President APFCB

Address

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Contents

From the desk of Chief Editor

Dear friends and colleagues,

A new year is here. I take this opportunity to extend my warmest greetings to all of you.
2020 has been an unprecedented year. In the past one year, the Covid-19 pandemic has affected almost every aspect of our lives - and till today we are still not free from its far-reaching ramifications. While it was definitely a difficult year, we should also remember the strength with which we responded. In the face of challenges and uncertainties, medical laboratory people have worked hard and played an import role in ensuring the health of people and populations.

Although the Covid-19 pandemic has brought much hardship, it has also brought an opportunity for global togetherness through the application of video conferencing apps. The APFCB community too has embraced this new means of communication as reported in the various activities carried out in the region. In the first publication of the APFCB News 2021, I am pleased to share with you the reports on the various activities of the APFCB committees as well as those of its member societies. In addition, a report on the activities of the IFCC is also included in the newsletter. In our efforts to spread as much relevant information as possible, a new section called “Industry Voice” has been introduced in this issue. We hope that readers will find these technical and educational articles useful. I am especially pleased that this issue carries a feature story on the amazing life’s journey of Dr. Tan It Koon. His is an aspiring story. Dr. Tan It Koon has not only made significant contributions in laboratory medicine but has also contributed significantly to the arts. He paintings has been exhibited in many exhibitions and have been published in art books featuring distinguished Chinese artists. In this issue, we get to know a little more about the artist whose paintings have been on the front covers of the APFCB News for more than a decade. My sincere thank you to Dr. Tan It Koon for not only contributing his beautiful painting for the front cover but also for his continuing support and especially for sharing his life story with us, Also a big thank you to Mr Joseph Lopez for his contribution to this article.

I hope that you will enjoy reading this issue.

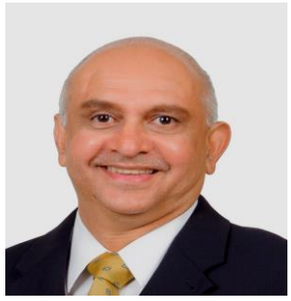
I take this opportunity to thank all those who have contributed to this issue. I wish to also to thank the Editorial Board members and the C-CP members for all their help in getting this issue out in a timely manner. I would like to encourage member societies and corporate member to continue contributing to the APFCB News so that information and news in the region can be shared with the medical laboratory community. The C-CP is very committed in this effort and will continue to make further improvements to future issues of the APFCB News. This is a year full of hope. Vaccines and new treatments offer us new hope against the current pandemic. May 2021 will be a much better year for everyone.

Best wishes,
Dr. Raja Elina

Raja Elina

Chief Editor, APFCB News

Message from APFCB President



Dear APFCB family,

Greetings and best wishes for 2021!

Thank you for taking the time to browse our first offering of the APFCB Newsletter for 2021.

Needless to say, 2020 has been a totally unusual and challenging year. The Covid-19 pandemic overwhelmed and turned our lives towards an entirely new trajectory. As healthcare workers, we were called upon to assist in the fight and there have been many positive aspects of laboratory medicine which has emerged as a result of this pandemic.

The laboratory contribution to the fight against Covid-19 has been significant. Our clinical colleagues have recognized our contributions and many now regard laboratory medicine as an integral and essential component of health delivery. As laboratory professionals, we should take advantage of this new found recognition and ensure that we integrate and not work in silos, and work to further promote the value of laboratory medicine to our clinical colleagues.

Beyond the initial PCR-based antigen testing for the virus, we now face challenges with the application of newer testing modalities for antigen and antibody testing. We will be challenged by providing laboratory verification for vaccination status, Covid variants and the use of newer unfamiliar matrices like saliva and many more challenges. The available vaccines will hopefully signal the beginning of the end of this terrible scourge, but one thing is clear – this will not be a quick end and we have to brace ourselves for a longer battle.

I believe many of us yearn to return to the times where could travel – for conferences and for holiday. Let's hope it will not be too long before this will again be a realistic way of life. I would like to announce that the APFCB has taken our first positive step towards organizing a physical conference and I would like to announce an important upcoming event. Together with the IFCC and the Korean Society of Clinical Chemistry (KSCC), I am delighted to write that we are planning for a joint IFCC WorldLab – 16TH APFCB Congress, in Seoul Korea from 26-30 June 2022. Discussions are recent and ongoing, so do look out for upcoming announcements. I hope that we will all be able to meet up once again in Seoul next year, for a good time of meaningful scientific update, networking and catch-up as a family.

Finally, as I conclude, please join me in acknowledging the work of Dr. Raja Elina and her editorial team as they continue to produce the APFCB Newsletters. I know you will enjoy reading this issue.

My best wishes, always.

SK Sethi

Assoc Prof. Sunil Sethi
President, APFCB

Renaissance Man: Clinical Biochemist, Administrator, Congress and Events Organiser, Artist, Calligrapher and Musician

Dr. Tan It Koon

This article is prepared at the invitation of the Editorial Board with input from Dr. Tan It Koon and Joseph Lopez, Past President of the APFCB

The Renaissance period **was the golden age of European history**. Generally described as taking place from the 14th century to the 17th century, the Renaissance promoted the rediscovery of classical philosophy, literature and art. Some of the greatest thinkers, authors, statesmen, scientists and artists in human history thrived during this era. **The Renaissance Man, also called Universal Man**, or ***Uomo Universale*** in ***Italian***, was an ideal that evolved from that time. It stemmed from the belief expressed by one of its most accomplished representatives, Leon Battista Alberti (1404–72), that "a man can do all things if he will." This philosophy embodied the basic tenets of Renaissance humanism which considered man the centre of the universe with limitless capacities for development. It led to the notion that men should try to embrace all knowledge and develop their own capabilities in multiple spheres of endeavour as fully as possible. Thus, the gifted men of the Renaissance period sought to cultivate skills in all areas of humanities, the sciences, physical development and the arts. The ideal is perhaps most famously expressed in Leonardo da Vinci (1452–1519), whose gifts were manifest in the fields of art, science, music, invention and writing.

One person who could rightly be accorded this moniker of **Renaissance Man** is Dr. Tan It Koon, the founding President of the Singapore Association of Clinical Biochemists (SACB) and the APFCB. Dr. Tan is known to many of us in this region as a pioneering clinical biochemist but during his lifetime he has also received acclaim as an artist, a calligrapher and a concert pianist.

Dr. Tan graduated from the University of Singapore (now known as the National University of Singapore) with a First Class BSc Honours. He spent his entire professional life at the Department of Pathology of the Ministry of Health which was located at the Singapore General Hospital. He completed his PhD in Biochemistry in 1966 while working in the department and was immediately awarded a Commonwealth Fellowship for post-doctorate studies at the Royal Postgraduate School of Medicine in London, as well as hospitals of the Universities of Edinburgh and Birmingham.

Upon his return to Singapore in 1970, he was appointed Head of Clinical Biochemistry Division, to manage and develop the services provided by the laboratories, as well as to conduct training, education and research. Subsequently, he received a WHO Fellowship for attachment at the Mayo Clinic and university hospitals in Washington, Philadelphia, and Connecticut in America as well as in Toronto, Canada. He was successful in gaining several professional qualifications in clinical biochemistry, namely the MCB (Mastership in Clinical Biochemistry) in UK, the Fellowship of the UK Royal College of Pathology (FRCPath) and the Fellowship of the American Academy of Clinical Biochemistry (FACB). He was requested by the Singapore University to conduct lectures and courses for Clinical Biochemistry as well as to serve as examiner for MSc, PhD and MD thesis for the Science and Medical Faculties. In early 1991, he was requested by the Government to set up a national reference laboratory for the investigation and diagnosis of inherited metabolic disorders.

Measurements for amino acids using amino acids analysers, organic acids using Gas Chromatography and Mass Spectrometry, mucopolysaccharides using High Resolution Electrophoreses, blood and tissue enzymes were introduced and close links with centres for study and treatment of inherited metabolic disease were established. The results of a 13-year study were shared in congresses and published in journals. Consequently, newborn screening and diagnostic testing for inherited metabolic diseases becomes a routine service.

Dr. Tan was one of the pioneer clinical biochemists in our region, just as the field was emerging as a profession in its own right. This led him to initiate the formation of the Singapore Association of Clinical Biochemists (SACB) and served as its President for some 20 years. Together with some colleagues from Australia and Japan he was a founder and the first President of the APFCB. Together, these colleagues, pioneered the series of Asian-Pacific Congresses of Clinical Biochemistry, now known as the APFCB Congress. Dr. Tan organized the first two congresses (1979, 1982) in Singapore and continued to be actively involved with the subsequent ones in Indonesia, Hong Kong, Japan, and Thailand. He served as plenary, symposium speaker or session chairman in many national, regional, international congresses and meetings.

He was the first Asian to be elected to the IFCC Executive Board. As a WHO Consultant and Member of its various Expert Committees, he conducted educational training courses for clinical laboratory staff in the Asian Pacific region. He was the longest serving member of the Asian-Pacific Scientific Advisory Board of Beckon Dickinson and for over 10 years, where he was engaged with the publication of BD Analyte Notes and educational courses on pre-analytical problems and issues and non-analytical errors which are not detected by the usual quality assurance programs designed to detect analytical problems.

He contributed more than 150 articles to local and international peer- reviewed journals and served on the editorial board of several international journals and books on clinical biochemistry. Dr. Tan initiated the publication of the APFCB News in 1983 and served as its chief editor and publisher until his retirement. Since 1983, his paintings have appeared on the front cover page and interior of APFCB News, always accompanied with a description.

Over the last 10 years, many of his paintings with related articles have appeared in the prestigious journal Clinical Chemistry that is published by the American Association for Clinical Chemistry jointly with the Oxford University Press and has a world-wide readership. Dr. Tan's talent in both art and music became manifest in early childhood. Despite his strong interests in art and music, his family and friends discouraged him from becoming a full-time artist or pianist, as these professions were considered less desirable in terms of stability and earning capacity. They said that art and music should only be regarded as spare-time interest and life-long hobby. Therefore, even though he was awarded a full scholarship to study music at the Royal Academy of Music in London he chose to enter the University of Singapore for tertiary education, after obtaining good results in the university qualifying examination.

His musical studies commenced under Singapore's most well-known music teachers just before entering primary school. He was also fortunate to be taught by Singapore's first generation artists who were recipients of the prestigious National Cultural Medallion Awards, throughout his secondary school and thereafter. Dr. Tan gave his first public piano recital at the Victoria Memorial Hall in 1957 and won top prizes for piano performance in 1959 and 3 more times in early 1960s in National Piano Competitions and was the winner of the Yamaha Singapore-Malaysia Music Composition Competition in mid-1970.

His winning work was a composition for choir and piano, which was performed by the National Theatre Choir with his piano accompaniment. Throughout his pre-university and university days, he often performed with vocalists and players of string and wind instruments for their final-grade and diploma examinations and concerts, as well as performed with another pianist, choirs and orchestras.

At high school art exhibitions his paintings won top awards. He was invited to participate in the annual National Day art exhibitions organised by the Ministry of Culture from 1970. Due to his outstanding achievements in the arts, he was requested by Cabinet Ministers to become Member of Parliament or take on additional appointment of top management for the National Theatre Trust, to promote cultural development and the performing arts.

He chose the latter and was also simultaneously appointed Board Member of the Cultural Foundation, Steering Committee Member for the organisation of the annual month-long Festival of Arts at which many local and international performances of music, drama, dance and operas were staged, and Science Council, for more than 10 years. He was requested by the Deputy Prime Minister Dr. KS Goh to write a position paper on the value of Biotechnology in Singapore and to organise an international Symposium on Biotechnology, with speakers known for their excellence in the field. These resulted in the establishment of the first Institute for Molecular and Cellular Biology (IMCB). Dr. Tan was active in community work. For several years, he served as the Chairman of the Singapore Professional Centre (which comprises 26 professional societies in its Membership) and organised seminars, conventions, exhibitions, and community projects on matters of concern and interest to the well-being of the country that often require multi-disciplinary professional participation, such as high-rise and high-density living, mass rapid transit system for public transportation, automation and computerisation to improve productivity, community health survey for common diseases, and career guidance for schools.

His outstanding services, contributions and accomplishments were recognized by the Government of Singapore. He was given two National Day Awards, namely, the Award for Excellence in Public Administration, and the Award for Distinguished Contributions to Cultural Promotion and Community Development. His distinguished contributions to the overall management, research and development, data processing, quality assurance, full computerisation of all areas of laboratory operations by 1974 (first in the Ministry of Health and probably in the Civil Service) and educational activities in Laboratory Medicine also won him international awards as well. He was the recipient of the inaugural APFCB Award for Distinguished Service and Contributions to the Federation and Clinical Biochemistry. Coming from a multi-cultural country, it is perhaps no surprise that Dr. Tan is conversant with several languages. Besides English, he is proficient in spoken and written Chinese language. He also speaks Chinese dialects of Guangdong, Fujian, and Chaozhou, and Malay. He studied German at the university, conducted by the Goethe Institute of Germany. Even while he was busy working full-time, involvement with music, painting and calligraphy never ceased. He has continued to practise and perform on the piano. In the last few years, he was invited to perform in several public concerts and private musical soirees. He has also continued to paint and practise calligraphy, often until late into the night. Consequently, he has accumulated quite a large volume of art works. Since the early 1990s, his art works have been exhibited at home and abroad every year. He served as the President of the Southeast Asian Art Association and chairman of the art exhibition organizing committee for a number of years. In the last ten years, he was adviser for promotion of cultural heritage and art in the Ngee Ann Corporation and Chaozhou Clan Association. He has been an adjudicator for annual nationwide calligraphy competition for schools and tertiary institutions. In the last 4 years, Dr. Tan's profile and artworks have been published in China, in four high quality hardcover art books featuring distinguished ethnic Chinese artists.

The modern day Renaissance Man is a rare and exceptional being. We are fortunate to have such a person in our region in the form of Dr. Tan It Koon.

BIBLIOGRAPHY

The following is a list of art books published in the last few years in China (2016 – 2020), which feature Dr. Tan's brief biography and paintings in a chapter each in:

(1) **"One Hundred Years of Classic Artworks (1915 – 2016)".** Heilongjiang Fine Arts Publishing House, First edition in December 2016 (Price: 985 yuan)

(2) **"Varied Styles of Chinese Distinguished Contemporary Artists".** China Federation of Literature and Art Publishing House (Beijing), February 2018, First edition (Price: 288 yuan)

(3) **"Classics of the Time – Outstanding Ethnic Chinese Artists who are Moving Forward with the World".** China Federation of Literature and Art Publishing House (Beijing), First edition in December 2018 (Price: 480 yuan)

(4) **"Moving with the Times" (A Collection of Art Works by Contemporary Artists with Real Capability).** Tianjin People's Fine Arts Publishing House, First edition in September 2020 (Price: 270 yuan)

Two Chinese websites that carry Dr. Tan's biography and paintings:
http://hainan.ifeng.com/a/20190125/7187544_0.shtml
http://ln.sina.com.cn/fs/economy/2019-01-25/detail-ihrfqzka0876928.shtml
http://hn.ifeng.com/c/84exQ6ASosi

A list of some of Dr. Tan's published artworks with associated articles which can be readily accessed on the internet is provided below:
https://academic.oup.com/clinchem/article/57/5/788/5620985
https://academic.oup.com/clinchem/article/58/3/654/5620625
https://academic.oup.com/clinchem/article/58/9/1381/5620853
https://academic.oup.com/clinchem/article/59/10/1541/5622100
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https://academic.oup.com/clinchem/article/62/12/1684/5612064
https://academic.oup.com/clinchem/article/58/3/654/5620625
https://academic.oup.com/clinchem/article/63/7/1311/5612620
https://academic.oup.com/clinchem/article/60/3/568/5621813
https://academic.oup.com/clinchem/article/62/7/1044/5611920
https://academic.oup.com/clinchem/article-abstract/66/8/1122/5880111
https://academic.oup.com/clinchem/article/65/5/712/5608049
https://academic.oup.com/clinchem/article/63/12/1917/5612762
https://academic.oup.com/clinchem/article-abstract/66/5/747/5827404?redirectedFrom=fulltext
https://academic.oup.com/clinchem/article/61/10/1313/561158
https://academic.oup.com/clinchem/article/65/10/1341/5608302
https://academic.oup.com/clinchem/article/64/5/877/5608822
https://academic.oup.com/clinchem/article/67/3/571/6154916?rss=1

A unique set of postage stamps has just been produced in February 2021, jointly by China and Japan in the form of a commemorative album, featuring a number of Dr. Tan's artworks. This is a project to commemorate and celebrate the 42nd Anniversary of Sino-Japan Peace, Cultural and Art Exchange Agreement to promote cultural and artistic exchange and sharing.

Dr. Tan It Koon - A Piano Recital: https://youtu.be/-EHXRovfZCY

"牛"年来临了!

祝大家牛年幸福安康，快乐平安，步步高升，鸿圖大展。!并与大家分享我一幅大中堂彩墨画与书法合璧作品:《黃牛与吹着短笛的牧童》。此画的灵感来至宋朝诗人黄庭坚的《牧童诗》。这是一首四行七言诗:

"骑牛远远过前村，短笛横吹隔陇闻。多少长安名利客，机关用尽不如君。"

现代的译文:

牧童骑着牛远远地经过山村，他吹着短笛，声音随风飘到田陇远处都能听到。长安城

(中国当时的国家首都)内那些追名逐利的人啊，用尽心机也不如牧童这样清闲自在，无忧无虑。

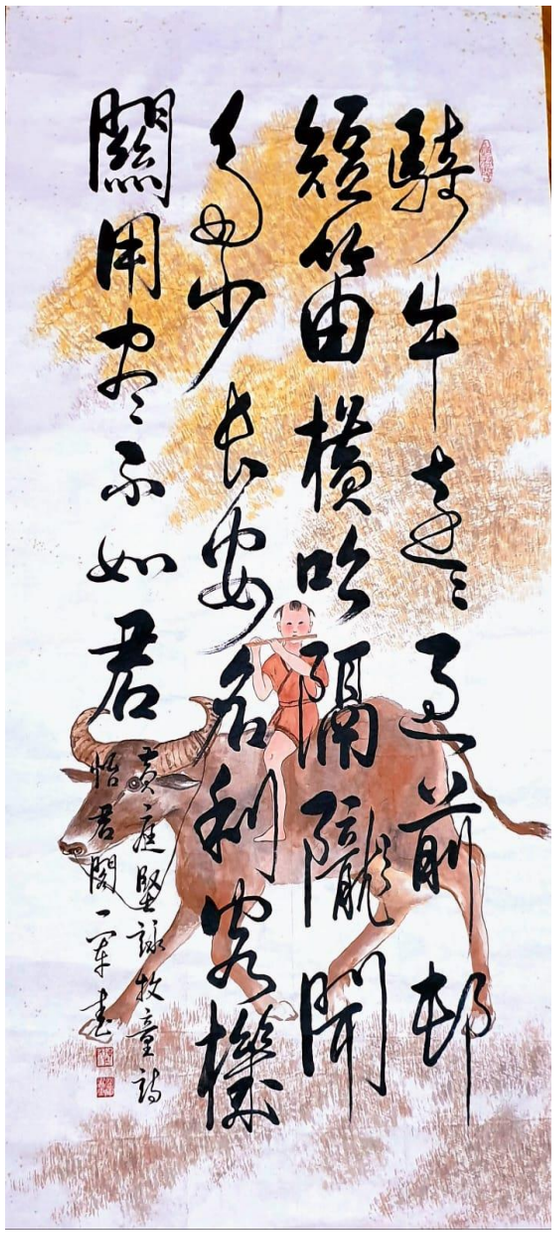
作品里的书法是以"行书"字体书写的。

The Lunar New Year, "Year of the Ox" has arrived! It has a most unusual and auspicious date. You can read the numbers in the date forward and backwards and they are the same! **12.02.2021! This is known as a Palindrome date.**

I would like to wish everyone:

A Happy, Healthy, Peaceful, Fruitful and Prosperous Year of the Ox!

I am glad to share with you my large ink-color Chinese brush painting combined with calligraphy entitled: ***"An Ox with a Young Cowherd Playing the Piccolo*** ". The inspiration for this painting comes from ancient Chinese Song Dynasty poet Huang Tingjian's "Poem of A Young Cowherd". This is a poem of four sentences, each with seven words:



"A young cowherd riding on an ox passes a distant village. Sound of his piccolo-playing can be heard drifting across the farm fields. Many fame and wealth-seeking people in the capital city of Changan spend too much time and effort in plotting schemes to bring them fame and fortune. How can they be compared with the cowherd who is so carefree and void of worry and stress?

The poem in my artwork was written in the Running Script.

With Best Wishes
Dr. Tan It Koon

IFCC Activities: Latest Developments & Future Ahead

Khosrow Adeli, IFCC President (with assistance of Mary Kathryn Bohn and Shannon Steele)

Reflecting on 2020, the IFCC had a very productive year (despite the pandemic!), making significant strides towards development of new programs with potential positive impact on healthcare delivery and patient outcomes including aiding in the fight against the COVID-19 pandemic, global lab quality in developing countries, and a very popular IFCC live webinar series in the field of laboratory medicine. To ultimately achieve these goals, the IFCC has established four Taskforces whose work will continue into 2021.

First, in response to the lack of newborn screening programs in developing countries, the IFCC established the *IFCC Taskforce on* ***Global Newborn Screening*** to initiate and support newborn screening programs in such regions worldwide. The Taskforce is currently working towards the initiation of pilot programs in several countries. The initiation of these programs will be of immeasurable value to developing countries to improve the early diagnosis and treatment of various genetic metabolic disorders.

Another key component of the new IFCC strategic plan is to assist clinical laboratories in improving internal and external quality assurance (IQA and EQA). In this regard, the IFCC established the *IFCC Taskforce on* ***Global Lab Quality***. This group has begun to plan the initiation of an international programs to provide free EQA and IQC to developing countries. In addition, this Taskforce will create a global *reference interval consortium* and work towards achieving evidence-based regional and global harmonization of reference intervals.

In addition to the work on newborn screening and global lab quality, the IFCC Taskforce on **Global eLearning/eAcademy** was recently put together to improve free distance learning opportunities to IFCC members globally. In Fall 2020, the IFCC hosted a live monthly *webinar series*. Each webinar garnered an audience of 2500-3500 attendees for a total of over 10,000 participants in the Fall series. Participants joined around the world from 123 countries, demonstrating the truly international nature of the events. Given the success of this program, the IFCC has decided to start a new series in January 2021, covering a wide range of topics.

Finally, in early 2020, a fourth Taskforce known as the *IFCC Taskforce on COVID-19* was established to summarize, critically review, and disseminate the most up-to-date, evidence-based information about the novel coronavirus as well as provide recommendations regarding test implementation. One of their first achievements was the creation of the *IFCC Information Guide on COVID-19*, a webpage with key information and resources for that is updated on a biweekly basis.

Most recently, the Taskforce published *interim guidelines* based on available evidence for publication, providing practical recommendations to laboratories on molecular testing of SARS-CoV-2 infection, serological testing for antibodies against SARS-CoV-2, as well as biochemical and hematological monitoring of COVID-19 patients.

A free webinar based on these guidelines was held for a global audience as part of the Fall 2020 webinar series. Now, the IFCC has planned the ***IFCC Global Conference on COVID-19***, which will take place virtually on February 15-17, 2021. The theme of this conference will be the Critical Role of Clinical Laboratories in the COVID-19 Pandemic, with the goal of bringing together leading experts on a global platform to present the latest advances in COVID-19 diagnostics and therapeutics.

Despite this year's unexpected challenges due to the COVID-19 pandemic, the IFCC has had an immensely successful year, laying the foundation for the 2020-2023 strategic plan. Moving into 2021, the IFCC is eager to continue its mission of "advancing excellence in laboratory medicine for better healthcare worldwide".

APFCB Education and Laboratory Management Committee Report February 2021

Dr. Tony Badrick
Chair, APFCB Education and Laboratory Management Committee

The Education and Laboratory Management Committee (C-ELM) consists of the following: Lia Gardenia Partakusuma (Indonesia); Tze Ping Loh (Singapore); Ronda Greaves (Australia); Elina Raja (Malaysia); July Kumalawati (Indonesia); Endang Hoyaranda (Indonesia); Jozi Habijanic (Roche Corporate); Amit Manjure (Siemens Corporate); Rojeet Shrestha (Japan); Hong-yew Lim (Roche Corporate). The role of the C-ELM is to provide support for member organisations in education. This usually involves the organisation of visiting lecturers, seminars and training activities. However, the impact of the global pandemic of 2020 has restricted many of the activities of the C-ELM, however we have continued with existing projects as well as some new initiatives.

1. APFCB Travelling Lecturer

The APFCB Visiting Lecturer for 2021/22 is Helen Martin from Australia. Whilst there are travel restrictions on this key role, virtual lectures will continue. On the 26thNovember 2020, Helen was a Plenary Lecturer at the MACB meeting and delivered a lecture entitled “Adding value with patient report commenting.”

2. APFCB – Roche – 12th Chemical Pathology Course – Vietnam

This is an ongoing annual event organised by Roche in collaboration with Rhonda Greaves from Australia. In 2020, the virtual event attracted approximately 400 participants and consisted of a mixture of invited and local speakers presenting on routine chemical pathology topics. The course is supported and endorsed by many prestigious local and international medical organizations and associations, such as International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine (APFCB), Australasian Association of Clinical Biochemists (AACB), Vietnamese Association of Clinical Biochemists (VACB), Ho Chi Minh City Association of Clinical Biochemists (HACB), Ho Chi Minh City Association of Medical Laboratory Technologists (HAMLT), Bach Mai Hospital, Cho Ray Hospital and other medical organizations and Associations

3. APFCB Becton Dickinson Pre-Analytical Improvement Project

The collaboration of APFCB with BD to provide our members with a digital guideline for pre-analytical procedures has now been finalised with the first part which contains:

The collaboration of APFCB with BD to provide our members with a digital guideline for pre-analytical procedures has now been finalised with the first part which contains:

Module A1 – Phlebotomist Attributes
Module A2 – Specimen Collection via Venipuncture
Module A3 – Specimen Collection via Vascular Access Devices
Module A4 – Specimen Transportation.
All are in the format of PDF slides, in English.
The next Modules will be Module B1 – Continuous Improvement and B2 – Troubleshooting.

4. APFCB-AACC Workshops

The APFCB has been collaborating with the AACC with their Global Lab Quality Initiative (GLQI) as part of the Asia Pacific Working Group (APWG). It was not possible to run any workshops in 2020, however it is planned to run the next program in Mongolia in August 2021.

5. Symposia

The C-ELM has organised a two-day virtual workshop on Laboratory Testing of COVID-19. As the information of laboratory diagnosis and monitoring of COVID-19 in rapidly evolving with new information arising in daily basis, laboratory professionals need a constant update on the developments. Furthermore, many developing countries are struggling to meet requirement of appropriate testing not only because of lack of resources but also due to lack well-trained laboratory professionals on the molecular assays. To help lab professionals with appropriate guide in COVID-19 testing, APFCB committee for Education and Laboratory Management is glad to present a virtual workshop that contain a series of lectures from experts as a complete guide on Laboratory Testing of COVID-19.

There are two other significant projects which have been put on hold until travel is possible. The APFCB / VACB / Roche Lean Project has been running for five years now and is developing skills with the implementation of Lean laboratories.

The APFCB has also developed a three-year Chemical Pathology Course which was piloted with the assistance of the MACB. We were hopeful of running this course in a new site in 2020 but this was not possible. We hope to offer this course in 2022.

Report of APFCB Communications and Publications Committee(C-CP)

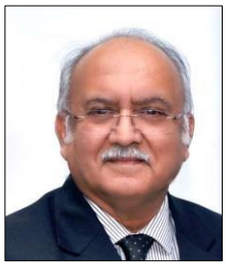
Dr. Raja Elina Raja Aziddin,
Chair, APFCB Communications and Publications Committee

The Communications and Publications Committee (C-CP) is made up of the following members Dr. Purvi Purohit (Web Editor), Dr. Rojeet Shrestha (Media Coordinator), Dr. Pradeep Dabla, Will Greene (Corporate -Roche) and Lim Ai Tin (Corporate -Siemens) The main objective of the APFCB Communications and Publications Committee(C-CP) is to communicate and promote the activities of the APFCB to medical laboratory personnel, clinicians and health care policy makers in the Asia Pacific region and the rest of the world. The C-CP is responsible for the development and promotion of the APFCB website and coordination of the online activities of the APFCB as well as for the online publication of APFCB news. It also provides information and educational material in electronic form to National Societies and Full Members, Corporate and Affiliate Members. In the past one year, the lockdowns, travel restrictions, limited face-to-face interactions brought about by the COVID-19 pandemic has dramatically accelerated the trend towards working remotely and pushed more and more activities online. Realising the need for fact, accurate and reliable information, the C-CP has taken the initiative since April 2020 to upload scientific publications, guidelines, recorded and live webinars on COVID-19 and other topics of interest. The website has also been actively updated with the latest information on webinars, online courses, virtual conferences of the APFCB, its member societies and international professional bodies so as to provide its members access to education and training. In August 2020, we began to actively use social media to communicate and disseminate news and information. APFCB's recent activities, publications, congress and events, nominations and awards, and various eLearning materials produced by the APFCB are now available on the following social media pages:

Facebook Page: https://www.facebook.com/APFCB/
Twitter: https://twitter.com/APFCB_LM
Instagram: https://www.instagram.com/apfcb_lm/
LinkedIn: https://www.linkedin.com/company/apfcb/
YouTube: https://www.youtube.com/channel/UCoiicTsnVX-COjklgZHQ54Q

Recordings of the masterclass webinar series on interpretative commenting as well as other webinars and workshops are now available on the APFCB website - https://www.apfcb.org/webinars.html/ as well as on social media. Despite the pandemic, the C-CP was able to successfully publish two issues of the APFCB News in 2020. In addition to reports on the activities of the APFCB and IFCC, the newsletter included reports from member societies that gave an interesting insight on how countries in the region coped during the pandemic. In line with our effort to provide information and educational material to our readers, we have included technical and scientific articles which we hope are useful. I take this opportunity to thank the EB and Chairs, national societies and corporate members for their continuing support as well as the C-CP members and editorial team for their hard work and commitment.

We look forward to bringing you more news and information in 2021.



Report of APFCB Congress and Conference Committee (C-CC)

Prof Praveen Sharma,
Chair, APFCB Congress and Conference Committee (C-CC)

The Executive Board (EB) of the APFCB appointed Professor Praveen Sharma, the former Chair of Communications and Publications Committee as the new Chair of Congresses and Conferences Committee (C-CC) on February 3rd2020. Later, a full committee was constituted by the EB comprising of three full members: Prof WoeiHorng Fang (Taiwan), Dr. Ronaldo Puno (Philippines) and Dr. Prasenjit Mitra (India) and two corporate members: Will Greene (Roche) and Ai Tin Lim (Siemens).

The mandate of the committee was to streamline the process of granting APFCB auspices to various scientific events like conferences, congresses, events organised by regional society members and corporate member events. With the COVID-19 situation affecting the global scientific community, there was no applications for physical conferences. Rather, there was a surge in the events based on virtual platform. The committee received a number of applications for grant of APFCB auspices. Till October, 2020, the committee members evaluated and recommended five scientific events for the grant of APFCB auspices. These events were:

1. Serological markers in Treatment and Management of COVID-19 (Webinar organised by Snibe).
2. The power of Laboratory Medicine to Achieve Measurable Better Healthcare (Webinar organised by Malaysian Association of Clinical Biochemists (MACB)).
3. Vietnam Chemical Pathology Course (Organised by Roche along with Vietnam Association of Clinical Biochemists, Ho Chi Minh City Association of Clinical Biochemists, Ho Chi Minh City Medical Association, Ho Chi Minh Association of Medical Laboratory Technologists).
4. Clinical Application of Access High Sensitivity Troponin I in the Emergency Department (Webinar organised by Beckman Coulter).
5. Roche Experience Days (RED) 2020 Virtual Event (a virtual event by Roche).
6. Laboratory quality management set of webinars by Seimens Healthineers.
7. ACBI webinar on “Shift in paradigm – Lab Medicine & COVID 19”

The committee is also working on updating the Congresses and Conferences webpage of APFCB to include the details of all the scientific events, which have been granted APFCB auspices.

APFCB Scientific Committee - Report of 2020 Activities

Samuel Vasikaran
Chair APFCB Scientific Committee

The APFCB Scientific Committee currently has the following activities to report for the year 2020.

1. Mass Spectrometry Harmonisation WG

The Mass Spectrometry Harmonisation WG which is Chaired by Dr. Ronda Greaves is undertaking a multicentre study of the influence of internal standard on the analysis of 17-hyDr.oxyprogesterone by LCMSMS, in association with RCPAQAP – AACB and IFCC Emerging Technologies Division Paediatric Hormonics Working Group.

Publication:

Influence of isotopically labeled internal standards on quantification of serum/plasma 17α-hyDr.oxyprogesterone (17OHP) by liquid chromatography mass spectrometry. Loh TP, Ho CS, Hartmann MF, Zakaria R, Lo CWS, van den Berg S, de Rijke YB, Cooke BR, Hoad K, Graham P, Davies SR, Mackay LG, Wudy SA, Greaves RF. Clin Chem Lab Med 2020;58(10):1731-9.

2. APFCB-WASPaLM TF-CKD

APFCB / WASPaLM Task Force on Chronic Kidney Disease which is chaired by Dr. Pavai Sthaneswar is undertaking a survey of testing and reporting practices for CKD related laboratory indices in the region in order to ascertain concordance of reporting practices with current guidelines and industry standards. It is hoped that the results of the survey would help harmonize practice according to current recommendations throughout the region.

3. WG on Diabetes Testing Harmonisation in APFCB Region

The Diabetes Testing Harmonisation WG chaired by Dr. Mithu Banerjee is similarly conducting surveys of diabetes testing and reporting practices in the region. Results of surveys conducted in the Philippines and India have been presented at the PAMET conference in 2018 and the APFCB Congress in 2019 respectively. Surveys have been concluded in Sri Lanka and Singapore and the results are being analysed for publication. It is clear that whilst most laboratories follow recommended practices, there is some lag in laboratory practices in some areas which could benefit from activities to harmonize and update practice. Ideally, this would be locally Dr.iven, led by each national professional body, but APFCB would certainly support these activities going forward.

Publication:

Trends in laboratory testing practice for diabetes mellitus. Banerjee M, Vasikaran S. eJIFCC 2020; 31: (3):231-41.

4. Harmonization of Reference Intervals WG

The Harmonization of Reference Intervals WG chaired by Dr. Tze Ping Loh plans to derive and compare indirect reference intervals from paediatric to geriatric subjects from laboratories within the Asia-Pacific region. To achieve this, they are calling on interested laboratories that are serving primary care (Non-hospital) patients to contribute de-identified laboratory results for derivation of indirect reference intervals study. The output of this study will be returned to the participating laboratories to help inform their practices. It is hoped that the results of this study may contribute towards regionally relevant paediatric to geriatric reference intervals for patient care, as well as provide insights into biological variation within the region.

Submitted for publication in CCLM:
Comparison of nine methods for univariate statistical exclusion of unhealthy subpopulations for indirect biological variation and reference intervals studies. Tan RZ, Markus C, Vasikaran S, Loh TP.

5. WG to Analyse Laboratory Data for Improving Diagnostics

Dr. Mohamed Saleem is chairing a WG to Analyse Laboratory Data for Improving Diagnostics. Results of benchmarking surveys in the region will be used to support healthcare goals for improved disease management. The support of Roche Diagnostics for this activity is acknowledged.

6. Masterclass in Interpretative Commenting on Clinical Chemistry Reports - Webinars

Webinars to discuss and analyse interpretative comments and to educate laboratory professionals on the addition of interpretative commenting are in progress. Five Webinars on various endocrine topics have been concluded with wide participation from the region. Future webinars are planned on a monthly basis. I would like to acknowledge the immense support of Dr. Pearline Teo of Siemens Healthcare Pte Ltd for this activity. The recordings of the webinars and resource materials are available on the APFCB website under the heading of Webinars:
https://www.apfcb.org/webinars.html

I am grateful to my APFCB colleagues and to the corporate sector for their help and support for the activities of the Scientific Committee.

Report on the APFCB Masterclass on Interpretative CommentingWebinar series

The global COVID-19 pandemic and its impact on people movement and face to face meetings led us to organize a series of educational webinars as a collaboration between the Scientific Division and the Communication & Publications Division of APFCB, ably supported by Siemens Healthineers who organised the technical aspects of publicity and registration of participants as well as hosting the Webinars on Microsoft Teams. We are grateful to National Associations for publicising the webinars to their members. Attendance is free, but prior registration is required.

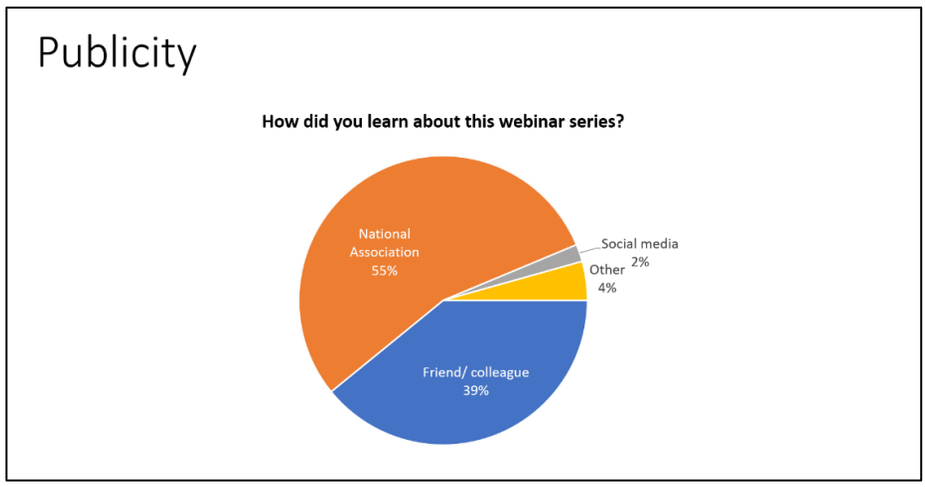
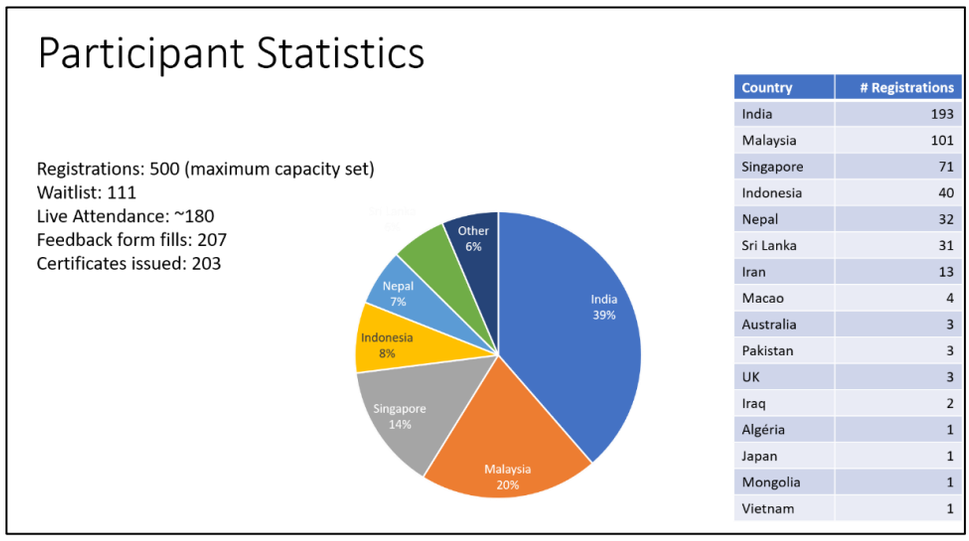


Fig 1: Participants feedback on how they know about the webinar

The webinars have been moderated by Dr. Pearline Teo. The format of the webinars is discussion of a series of case reports for 45 minutes followed by question-and-answer session for about 15 minutes. The first webinar was broadcast in August 2020, followed by monthly webinars since then.



Country	# Registrations
India	193
Malaysia	101
Singapore	71
Indonesia	40
Nepal	32
Sri Lanka	31
Iran	13
Macao	4
Australia	3
Pakistan	3
UK	3
Iraq	2
Algéria	1
Japan	1
Mongolia	1
Vietnam	1

Fig 2: Number of participants according to country of origin

The following topics have been covered:

Topic	Speaker	Date
TFTs (basic)	Dr. Sam Vasikaran	August 2020
TFTs (advanced)	Dr. Sam Vasikaran	September 2020
Endocrine (adrenal)	Dr. Sam Vasikaran	October 2020
Fertility tests	A/Prof Ken Sikaris	December 2020
Calcium and PTH	Dr. Sam Vasikaran	January 2021

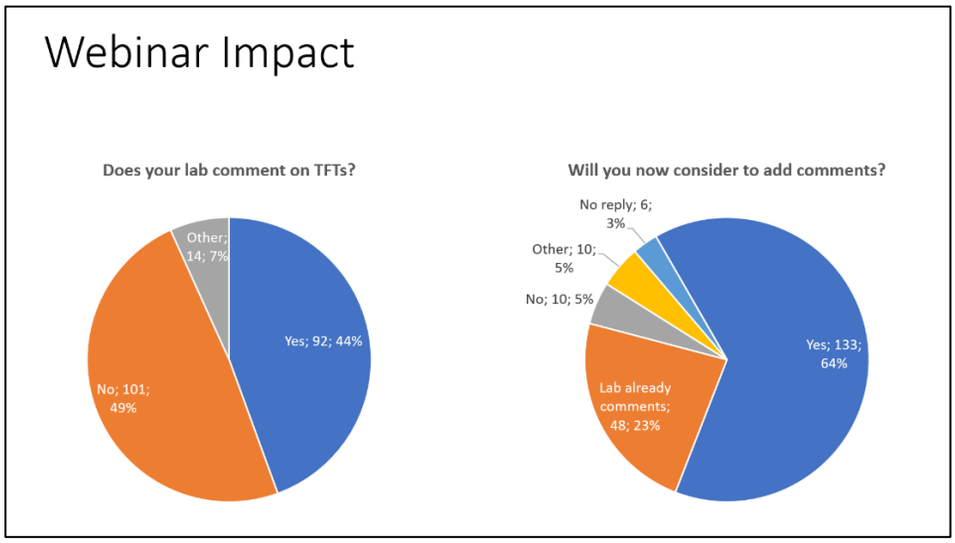


Fig 3: Participants feedback on the impact of the webinar

Participation overall has been increasing over time with some fluctuation in numbers. The question-and-answer sessions have been lively with avid participation by the virtual audience. Feedback from participants has been obtained through online surveys after each session, and has been excellent, and useful ideas for future topics as well as suggestions to enhance the format of the webinar have been received.

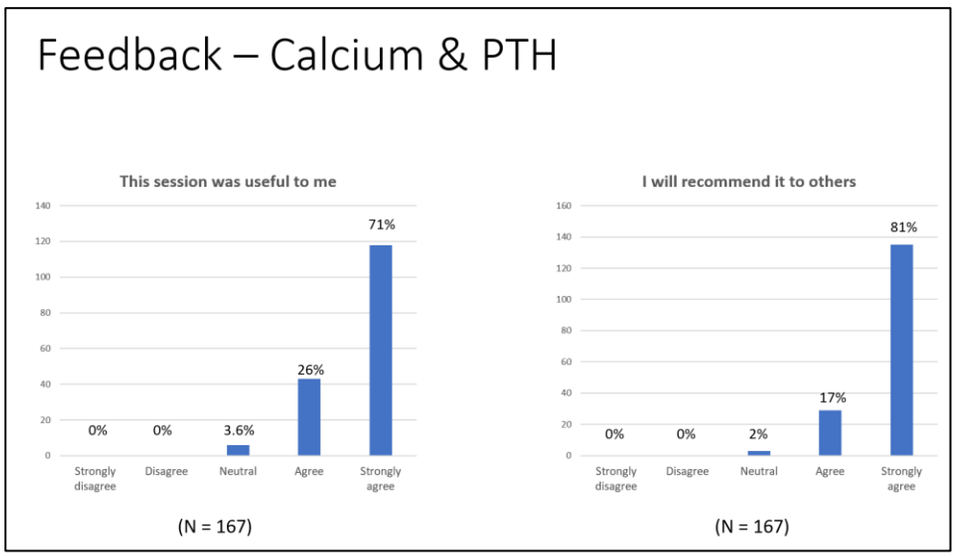


Fig 4: Participants feedback on the Calcium and PTH webinar

Future webinars are planned as follows

Topic	Speaker	Date
Dynamic function testing	Dr. Cherie Chiang	24th February 2021
Lipids	A/Prof Ken Sikaris	24th March 2021
Diabetes	Dr. Moh Sim Wong	28th April 2021

Registration links for future webinars may be found at: http://APFCB.eventbrite.com
Recordings of past webinars are available on the APFCB website at:
https://www.apfcb.org/webinars.html

We would like to thank the participants, speakers and the organisers for the success of these webinars and invite all interested laboratory professionals to consider participating live if possible, in future webinars.

Report by
Dr. Sam Vasikaran, Raja Elina and Pearline Teo

Hong Kong Society of Clinical Chemistry

The Hong Kong Society of Clinical Chemistry (HKSCC) Council for the term 2020 – 2021 was elected at the Annual General Meeting held on 11 January 2020. The 2020 Annual Scientific Meeting (ASM) was also held on the same day and the theme of the ASM was **"Diabetes and Heart Failure Management: New Technologies and Challenges"**. There were two presentations by invited speakers from the Chinese University of Hong Kong: (1) **"Advances in Diabetes Diagnosis and Management"** by Professor Ronald CW MA, Division Head, Endocrinology and Diabetes, Department of Medicine & Therapeutics; and (2) **"NT-proBNP in Heart Failure"** by Professor Alex PW LEE, Director, Echocardiography Laboratory & Director, Laboratory for Cardiac Imaging and 3D Printing. These were followed by four industrial presentations by Abbott Laboratories Limited, Beckman Coulter Hong Kong Limited, Bio-Rad Pacific Limited and Roche Diagnostics (Hong Kong) Limited. The ASM was well attended by 181 HKSCC members and guests. There were also thirteen industrial partners participating in the industrial exhibition.

Group photo of HKSCC Council (term 2020 – 2021)

In view of the COVID-19 outbreak and public gathering restriction, HKSCC has to suspend face-to-face scientific seminars in most of year 2020. With an aim to continue to offer educational activities for members, HKSCC for the first time carried out scientific webinar, which was conducted online via Zoom platform on 24 October 2020. Dr. HAN Siao Cheng Diana, Clinical Lecturer, Department of Chemical Pathology, CUHK, presented on **"Primary Hyperaldosteronism: An Underdiagnosed Cause of Hypertension"**. Dr. CHAN Chun Hei Toby, Resident, Department of Pathology, Queen Elizabeth Hospital and the Hong Kong Children's Hospital, presented on **"Lipids: Basics to Advanced"**. Dr. TONG Hok Fung Edward, Resident, Department of Pathology, Princess Margaret Hospital presented on **"Paraprotein Interference... and how to CATch them"**. The virtual seminar was attended by 80 HKSCC members and guests.

It is sincerely hoped that in year 2021, the COVID-19 pandemic would be under control with launch of vaccines. In the new year, HKSCC Council will continue to try the best to provide educational activities to members via either virtual webinar or if possible physical seminar.

Japan Society of Clinical Chemistry

The 60th Annual Meeting of the Japan Society of Clinical Chemistry

The 60th Annual Meeting of the Japan Society of Clinical Chemistry (JSCC), chaired by Professor Takashi Miida (Juntendo University), was scheduled to be held in Ochanomizu, Tokyo from October 30 to November 1, 2020. Because of the worldwide coronavirus disease pandemic, this meeting was organized online for the first time in the history of the JSCC. Although we could not meet attendees face-to-face as in past meetings, a total of 917 participants joined the web-based conference.
The theme of this year's meeting was "Enjoy Clinical Chemistry!" There was no reduction in the number of academic activities compared to past meetings; these included 3 educational lectures, 14 symposiums/workshops, 13 lunchtime seminars, 2 seminars on diagnostic instruments and reagents, and 1 evening seminar. One of the seminars provided cutting-edge information about newly developed equipment and reagents to test for SARS-CoV-2.

In the Honorary Lecture, Dr. Minoru Tozuka (Professor Emeritus at Tokyo Medical and Dental University) discussed the past, present, and future of clinical chemistry based on his experiences as a laboratory scientist and faculty member.

As Dr. Miida has been studying lipoprotein metabolism, some of the programs, including the chairperson's lecture, were related to this topic. He presented a series of studies on prebeta1-HDL. The JSCC International Symposium has also focused on HDL research. Three Japanese specialists summarized basic and clinical HDL studies, including on LCAT deficiency, CETP deficiency, and the pleiotropic actions of HDL. In the last part of the symposium, Dr. Kasey C. Vickers (Vanderbilt University Medical Center) talked about the mechanisms and impact of lipoprotein small RNAs on inflammation. The joint symposium on inherited dyslipidemia was sponsored by the JSCC and the JAS (Japan Atherosclerosis Society).

A total of 123 papers were presented at this meeting. Eighty-one papers were presented via live streams, and forty-two were presented as e-posters that the attendees could view on an on-demand basis during.

Given the many valuable presentations, attendees, and corporate sponsors, the meeting was a great success. The next meeting, to be held in Fukuoka (November 5-7, 2021), will be chaired by Prof. Kang Dongchon (Kyushu University).

Macao Laboratory Medicine Association (MLMA)

Since the beginning of 2020, the whole world has been affected by the COVID-19 outbreak. Although the prevention and control of the COVID-19 outbreak has been successful in Macau, the limitation of large number of participant-gatherings had affected most of MLMA's activities. Two major activities of MLMA that were held as webinar and an on-line workshop for the year 2020 were as follows:

Local Meeting			
	Name of the Meeting	**Date**	**Topic**
1	Webinar & the 10th General Assembly Meeting of MLMA	2020/10/21	Right Test at the right time to fight against COVID-19
2	Workshop-Advanced In-Service Training for Blood Bank Staff	2020/10/17, 18, 24 (3 days)	Advanced In-Service Training for Blood Bank Staff

Roche Diagnosis Hong Kong hosted a scientific seminar that addressed the high-throughput, reliable and accurate differential diagnosis of COVID-19. The speaker for the seminar was: Mr. Brian Leung, Clinical Marketing Manager of Roche Diagnosis Hong Kong Ltd. Mr. Brian shared the company's vision and experiences on assays including molecular tests for detecting SARS-CoV-2 RNA along with serological tests for detecting antibodies against SAR-CoV-2. Over 100 members and guests attended the lecture.

Webinar & the 10th General Assembly Meeting of MLMA
TOPIC: Right Test at the right time to fight against COVID-19.

Speaker: Mr. Brian Leung, Clinical Marketing Manager, Roche Diagnostic Hong Kong Ltd

After the scientific seminar, the 10th General Assembly was held immediately. Witnessed by the Board of Supervisors and the attending members, the Council report and the financial report were presented and approved.

1. Advanced In-Service Training for Blood Bank Staff

The 2020 On-line Workshop in collaboration with the Taiwan Society of Blood Transfusion (TSBT) was held on 17th, 18th, and 24th October, respectively.

The 2020 On-line Workshop in collaboration with the Taiwan Society of Blood Transfusion (TSBT) was held on 17th, 18th, and 24th October 2020.

The course ran over 3 days with contents based on the TSBT advanced training and focused on advanced theory of transfusion medicine and application of detection methods for blood banking. Some topics covered detailed and up-to-date aspects of blood bank technologies. The on-line workshops gained great success where information was very practical and valuable to our members and guests. Over 60 members attended this event.

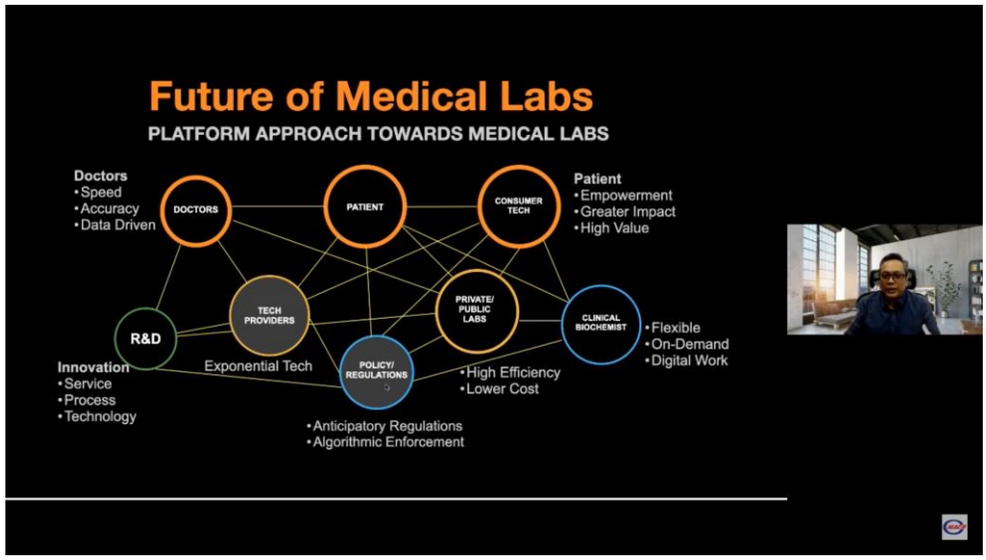
Malaysian Association Of Clinical Biochemists (MACB) 2020

1. MACB Virtual Conference 2020

The Covid-19 pandemic disrupted plans for the 30th MACB Conference 2020 which was scheduled to be held in August 2020. In its place, the MACB held its first virtual conference on 26-28 November 2020. The two- and half-day conference had the theme "Innovative Solutions: The Way Forward in Laboratory Medicine". This theme was chosen as medical laboratories today are faced with many challenges such as rising cost, limited manpower and high public expectation; made worse with the onset of the pandemic. As innovation is a strategic change that creates value, it can provide medical laboratories with the opportunity to overcome current and future challenges.

MACB Virtual Conference 2020

Sixteen lectures on various topics such as Strategies in Overcoming Lab Errors, Guidelines in Diabetic Kidney Disease, Auto-verification of Lab Results, Pandemic Resilient Lab Service, Sars-Cov-2 Serology Testing, High-sensitivity Troponin in POCT, New Technologies, Fatty Liver Disease, PTH, QC Standards- Past and Present, Sigma Metrics in POCT, Remote Assessment in ISO 15189 Accreditation and Licensing of Scientific Personnel in Laboratory Medicine were presented. Lectures were delivered by speakers from Malaysia, Australia, Hong Kong and United States. APFCB Travelling Lecture was presented by Helen Martin on the topic "Adding Value with Patient Report Commenting". Lectures were a mix of pre-recorded and live sessions with live Q & A. An interesting lecture on the topic of *"The Future of Laboratory Medicine: The Impact of Exponential Technologies & Platform Economy"* illustrated how exponential technologies such as artificial intelligence (AI), cloud computing, augmented reality (AR), and virtual reality coupled with cheaper and faster internet availability have transformed organisations to create value, manage their operations and their talent. The lecture described how the future of healthcare is related to key trends namely power of data, flexible organization and the focus on prevention and wellness. It also discussed the risks and possibilities of how trends set by leading platform-based business models can permeate and transform the medical laboratory sector.

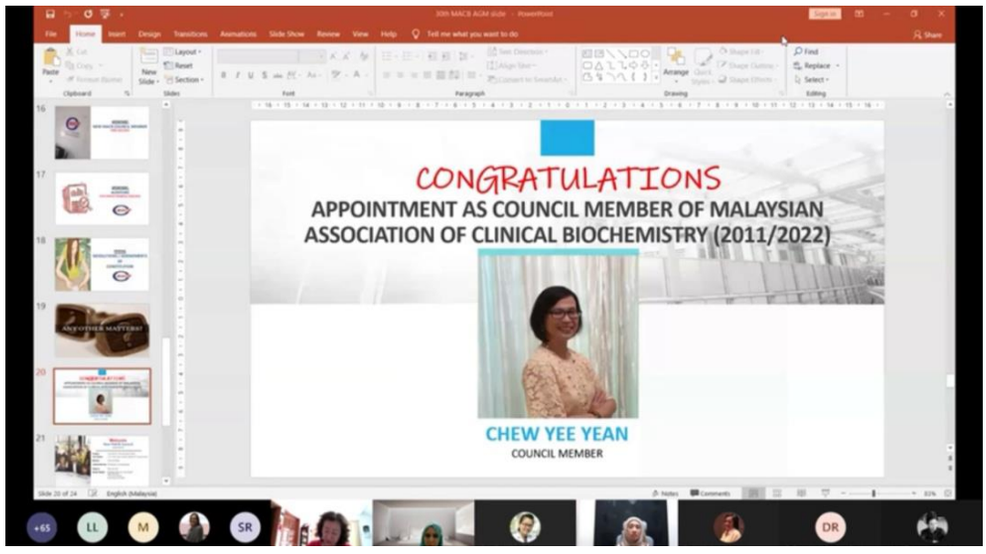


Lecture on "The Future of Laboratory Medicine: The Impact of Exponential Technologies & Platform Economy"

With the generous support from corporate sponsors, this conference was made available to participants free of charge. The conference had 1173 registered participants from 23 countries namely Malaysia, Nepal. India, Sri Lanka, Bangladesh. China, Hong Kong, Singapore, Myanmar, Romania, Iran, South Africa, Kenya, Sudan, Ghana, Pakistan, US, Australia, Indonesia, Saudi Arabia, Qatar, Mongolia and Philippines. The conference received very good reviews from those who attended.

2. MACB Annual General Meeting

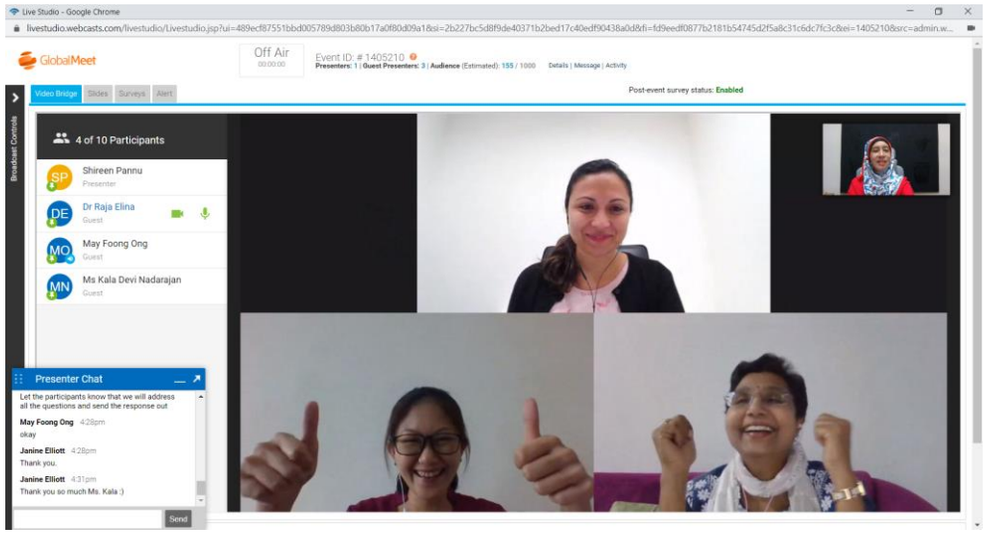
The 30th Annual General Meeting (AGM) of Malaysian Association of Clinical Biochemists (MACB) was held virtually on the 28th November 2020 via Microsoft Team. At the meeting, the newly elected council members were introduced. Dr. Raja Elina Raja Aziddin was re-elected as MACB President. The new council will hold office for the term 2020 -2022.



MACB Annual General Meeting – Appointment of New Council

3. Webinar on Blood Collection Tube Verification: What Your Text-Book Do Not Teach You

This was the third webinar in the Blood Collection Tube Verification Series and was delivered by Miss Kala Devi Nadarajan from Malaysia. In this webinar, Miss Kala shared her hands-on experience in conducting BCT evaluation. Her discussion included what you need to consider when planning and preparing for BCT evaluation, the BCT evaluation protocol itself and the potential challenges and setbacks and how to overcome them.



Webinar on Blood Collection Tube Verification: "What Your Text-Book Do Not Teach You"

A total of 466 people registered for the webinar and 214 viewed the event live. Participants were from Malaysia, Philippines, Indonesia, Singapore, Australia and India. This webinar was supported by BD.

Philippine Council for Quality Assurance in Clinical Laboratories (PCQACL)

The Philippine Council for Quality Assurance in Clinical Laboratories (PCQACL) conducted its very first Virtual 17th Annual Convention with the team "***Growing Laboratory Quality in the Midst of Pandemic***" on Sept 22-24, 2020 through an online platform via Docquity App. This event was well attended and participated by more than 2,000 delegates from different clinical laboratories and medical institutions nationwide.

An array of scientific lectures and panel discussions by renowned and distinguished Speakers were all very informative, timely, and relevant at the time of the pandemic. The convention satisfied participants with respect to the gain in knowledge, learning experience and updates presented.

The 3- day virtual convention started on Sept. 22, 2020 with the Opening Ceremonies, followed by the pre-recorded scientific sessions covering the track on Human Resources Management with the following lecture and panel discussion topics: 1) The role of RITM in Test Validation and Research for COVID19, 2) Panel Discussion 1: Current Issues in SARS-COV-2 Testing & Strategies to increase Surveillance Testing Volume, 3) Safeguarding Mental Health for Laboratory Professionals, and 4) Manpower Management in the Time of COVID- 19 pandemic.

The second day of the convention on Sept. 23, 2020 was loaded with the following lecture and panel discussion topics covering the track on Quality: 1) Maintaining Quality in Adversity: ISO Perspective, 2) Panel Discussion 2: Laboratory Verification of COVID19 Tests: Philippine General Hospital Experience, 3) Panel Discussion 3: Process Improvement for the Post-analytic Phase of Testing: Keeping up with the Demand of the Times, and onward to the third day on Sept. 24, 2020 with the track on Molecular Diagnostics and Updates with the following lecture and panel discussion topics: 1) Panel Discussion 4: Strategies for "Mass Testing": Concept of RT-PCR pooling, 2) Antibody and Antigen Tests for SARS- COV-2: Facts versus Flaws, and 3) Troubleshooting RT-PCR testing for SARS-COV-2. This last day of the convention was highlighted with the culminating activities of the 3-day convention and the Closing Ceremonies.

The PCQACL Continuing Education, Training & Research (CETR) Committee successfully conducted the virtual convention which was made possible via Docquity App online platform. Technical support was provided by our IT Provider (Progressive Productivity Solutions) who assisted on the technical issues, queries and concerns of the participants with the guidance and supervision of the PCQACL Committee on Information, Communication & Technology System (ICTS).

PCQACL17th Annual Convention with the team "Growing Laboratory Quality in the Midst of Pandemic"

As for the other continuing educational activities prior to the Virtual PCQACL 17th Annual Convention, the PCQCL Continuing Education, Training & Research (CETR) Committee has conducted the following Webinars in 2020:

1. **Title: Webinar on Laboratory Empowerment Against Covid-19 (L.E.A.D)**

Date: July 3-21, 2020

Lecture Topics:

A. All about PCR Laboratory
   1. Points to consider in setting up Molecular Laboratory for Covid-19
   2. Good Laboratory Practices when performing Molecular Assays

B. Histopath and Blood Bank
   1. Biorisk Management in the Anatomic Pathology Laboratory amidst Covid-19
   2. Laboratory Preparation for Convalescent Plasma Therapy

Webinar on Laboratory Empowerment Against Covid-19

2. **Title: Webinar on Addressing Current Global Challenges in Healthcare in collaboration with Sysmex Philippines Inc.**
   Date: July 22, 2020

Vietnam Association Clinical Biochemists

Although the control of the SARS.CoV.2 epidemic in Vietnam is very good, the third outbreak of SARS.CoV.2 has returned to our country.

From June 2020 to December 2020, VACB held 2 main events as follows:

In collaboration with the Hanoi Biochemistry Branch Association and Northern provinces, VACB organized the 24th National Scientific Conference and the Congress of Hanoi Biochemistry Branch and Northern provinces on November 26-27 2020 at Muong Thanh Hotel - Nhat Le, Quang Binh province with about 700 delegates nationwide. VACB has published a number of articles in the Vietnam Medical Journal in November 2020, volume 496 with 32 articles covering different fields of clinical biochemistry and focusing on Corona virus disease research. Out of these, 17 articles were chosen and reported at the conference.

BackDr.op of the annual biochemistry conference of VACB. held in Muong Thanh Hotel - Nhat Le, Quang Binh province on November 27-28th, 2020

The scene at VACB Annual Biochemistry Conference, held in Muong Thanh Hotel - Nhat Le, Quang Binhprovinve on November 27-28th, 2020 with about 700 delegates nationwide on the theme "Strengthening the quality management of clinical biochemistry, applying new techniques in diagnostics and treatment ""

The scene at the annual scientific conference of the Ho Chi Minh City Union of Clinical Biochemistry Association (VACB's sub-branch), held at Riverside Palace 3900 Ben Van Don, Ho Chi Minh City on December 4, 2020 with about 300 participants.

In collaboration with the HCMC Clinical Biochemistry Branch Association, VACB organized a Scientific Workshop on December 4, 2020 at Riverside Palace 3900 Ben Van Don, Ho Chi Minh City with about 300 participants. There were 14 reports presented at the conference.

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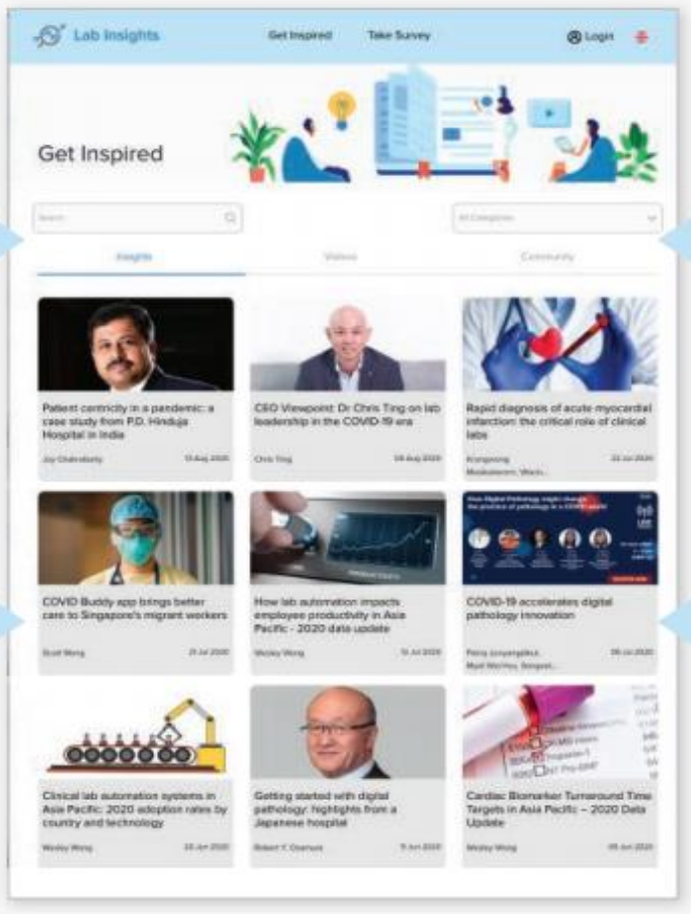

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Targeted MS-based methods show promise in detecting SARS-CoV-2 proteins from various types of biological matrices. We will also discuss solutions for the detection and quantification of SARS-CoV-2 proteins in nasopharyngeal swabs preserved in Universal Transport Medium'

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External Quality Assurance for SARS-CoV-2 - Lessons learnt from the RCPAQAP

The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) has been providing quality assurance programs for more than 30 years covering all disciplines of pathology. Developing External Quality Assurance (EQA) programs requires compliance to ISO/IEC 17043 with careful consideration of a range of issues:

- Sourcing reference material with a suitable range of measurand
- Investigating the choice of methods and units available in the market
- Ensuring homogeneity and stability of the material
- Determining the appropriate analytics to report
- Maintaining an efficient logistics service

In 2020, in rapid response to the COVID-19 pandemic, The RCPAQAP offered one of the world's first SARS-CoV-2 specific EQA programs and by the end of 2020 had developed seven individual SARS-CoV-2 programs covering molecular, point of care, and antigen and antibody testing. In addition, The RCPAQAP also collaborated with the World Health Organisation to provide a SARS-CoV-2 molecular proficiency testing program to over 3000 laboratories world-wide.

The RCPAQAP EQA programs utilise reference materials that mimic the SARS-CoV-2 virus but are non-infectious. This material must be sourced, inactivated, validated, and tested before it can be used. With the rapid development of these programs, ensuring adherence to quality standards was challenging but essential to guarantee the accurate performance of diagnostic SARS-CoV-2 in laboratories.

Several key findings from the RCPAQAPSARS-CoV-2 programs include:

- Many laboratories had multiple kits or analysers in routine use in order to cope with the SARS-CoV-2 testing workload
- The sensitivity of molecular methods for the detection of SARS-CoV-2 was highly variable, however there was significant improvement in 2020, especially in samples with low viral loads
- There was good reproducibility of results for laboratories using the same kit or manufacturer
- IgG SARS-CoV-2 antibody assays showed good concordance across laboratories; however IgM and IgA assays were highly discordant. This was especially evident for antibody point of care devices
- IgA SARS-CoV-2 antibody was detected in samples collected prior to 2019 suggesting poor sensitivity and a limited clinical utility.

For a more detailed overview of the performance of laboratories in the RCPAQAP SARS-CoV-2 EQA programs click here to access our free webinar.

Serum tumour markers and the future of cancer care: China's viewpoint from the clinic and the lab

22 December 2020

Based on interviews with

Ji Wei Liu
Director of Oncology Departmer
Da Lian Medical University China

Wei Cui
Professor and Director,
Department of Laboratory

As the global burden of cancer increases every year, oncology professionals are seeking targeted, precise and sensitive methods to identify tumours and monitor their growth. For over a decade, many have used serum tumour markers (STM) as part of their diagnostic toolkit.

To better understand how STMs are currently used and what the future holds for this approach, Lab Insights spoke to two leading Chinese healthcare professionals: Prof Liu Ji Wei, Director of the Oncology Department at Da Lian Medical University, and Prof Cui Wei, Director of Laboratory Medicine at the Chinese Academy of Medical Science National Cancer Centre.

Today's clinical utility of serum tumour markers

The clinical perspective: Prof Liu Ji Wei

In his clinical practice, Prof Liu uses STMs to evaluate responses to chemotherapy or targeted cancer therapy, monitor recurrence, provide an accurate differential diagnosis, and stage cancers. Since the majority of patients that he sees have stage 4 metastatic or recurrent cancer after surgery, STMs are useful for highly specific and sensitive cancer detection and monitoring. One of the benefits of STMs, according to Prof Liu, is their accessibility, as they are non-invasive. He also notes that they can be highly informative with respect to imaging techniques in some situations.

For example, a Drop in CEA values can indicate that a treatment is working, whereas imaging methods like CT scanning or MRI may overlook tumours that are outside a field of view or too small to detect.

STMs can also provide critical information before targeted therapy or immunotherapy can be initiated. While STMs alone are not the sole or even the key Driver in choosing these approaches, they can be combined with data on tumour mutational burden, microsatellite instability or other indicators to guide treatment selection. Looking ahead, Prof Liu sees the future of such testing involving markers that indicate potential immunotherapy-induced toxicity, which will be critical for ensuring successful treatment outcomes.

The lab perspective: Prof Cui Wei

Prof Cui's clinical laboratory routinely tests serum and plasma samples for over 20 tumour markers commonly seen in cancers, including lung, ovarian and prostate cancer. To provide a comprehensive and accurate perspective on a patient's tumour landscape, her laboratory combines STM tests with molecular, radiological, imaging and histological investigations.

In nonsmall-cell lung cancer (NSCLC), for example, she looks for STMs such as NSE, CYFRA 21-1, ProGRP, CEA and SCC, alongside mutations in key genes like EGFR. In ovarian cancer, HE4 and CA125 testing is done. Since STMs typically require small sample input volumes, they can be advantageous for cancer patients who often need multiple tests.

Additionally, Prof Cui uses STM panel testing to discriminate between tumour subtypes, evaluate cancer risks and monitor disease progression. She also combines STM testing with newer assays such as those for circulating tumour DNA, or with novel molecular tools, to diagnose and monitor therapeutic response, detect residual lesions and target Dr.ug-resistant mutations.

The future of serum tumour markers and cancer care

AI, algorithms and the future of STMs

While the spectrum of uses for STMs is currently limited, many believe that innovations in data science, artificial intelligence and machine learning will expand their clinical utility. Drawing together multivariate datasets, new algorithms and analytic tools allows clinicians to select more specific or suitable treatments based on a patient's STMs.

Machine learning techniques can now distinguish between the early stages of cancer and non-tumourous, controlled growths. Intelligent algorithms can also incorporate imaging, molecular testing, tumour markers and even patient factors such as their medical and family histories. Such integrations may soon be able to pinpoint the most meaningful STMs for clinicians to use at critical decision points in the cancer care pathway.

"A decade ago, Chinese researchers explored the categorisation of lung cancers according to disease stage by combining the detection of 5 lung cancer STMs with big data algorithms," notes Prof Cui. "Now, we can integrate new, intelligent algorithms and multidisciplinary data in sophisticated platforms to better understand patient data."

Prof Cui notes that most labs are only just beginning to implement AI, machine learning and intelligent algorithms in this way. She acknowledges that more research is needed to seamlessly connect algorithms to patient care, but she is optimistic that this process will make STMs more actionable and useful in a wider variety of cancers.

Lab-clinician communication remains essential

Despite these advances, Prof Cui points out that no technology can simultaneously analyse, interpret and clinically explain oncology data. The Chinese Society of Laboratory Medicine understands that the value of STMs is maximised only if genetic screening data are interpreted correctly, and has progressively focused on improving communication between laboratories and doctors.

Prof Cui believes that laboratory clinicians should collaborate with clinicians in patient care, such as by proactively providing data interpretations and treatment suggestions directly to clinicians. When parsing high-STM results, her clinical colleagues may sometimes need to be educated on a test's limitations. For example, some clinicians may not be aware that STMs can manifest even in benign or normal physiological states, such as higher levels of CA125, CEA and AFP in early pregnancy.

As stakeholders come together to establish algorithms and disease models, more regional and global cooperation will be needed to realise the full potential of STMs for cancer care. Such cooperation is starting to take root in China, and will likely Dr.ive progress that has impact far beyond the country's borders

The benefits of patient-based quality control in the clinical lab

22 October 2020

Based on interviews with

Tony BaDr.ick,
CEO, The Royal College of Pathologists of Australasia, Australia

The development of a functional Quality Control (QC) strategy is one of the most important roles of clinical lab managers everywhere. Regular QC helps ensure that test results are accurate and reliable for guiding patient care. But what happens when the QC procedures themselves are subject to error?

This is a key concern of the Working Group on the development of Patient-Based Real-Time Quality Control (PBRTQC) of the Committee on Analytical Quality [1], part of the International Federation of Clinical Chemistry and Laboratory Medicine, which aims to promote international standards and best practices in clinical labs. One of the objectives of the group is to assist laboratories in implementing PBRTQC to complement conventional QC protocols.

With conventional QC, labs typically run synthetic controls, perhaps at the start and end of a shift, or beginning and end of the day. With PBRTQC, labs use virtually every patient result generated throughout the day to identify bias, relying on some patient population parameter such as the mean or median of results across all samples tested to highlight outliers.

This patient-based QC approach has been used for decades in hematology labs because there was no alternative viable Quality Control material for red cell parameters. Now, experts believe it will be adopted for clinical chemistry labs as well. To understand how and why this may happen, the Lab Insights team spoke with Dr. Tony BaDr.ick, CEO of The Royal College of Pathologists of Australasia and one of the leaders behind the PBRTQC push.

What's wrong with conventional QC?

BaDr.ick believes that as labs increase their test throughput, conventional QC approaches become less appealing.

"At one stage we used to run a lot of QC samples, sometimes between every eight or nine patient samples," he says. "Now we're running more and more samples with fewer QC samples between them." This reflects the greater stability of modern analysers, but also creates a problem if bias develops in an assay during the period between QC samples where hunDr.eds of patient samples may be affected. Yet running more QC samples throughout the day could add significant cost to a workflow.

Dr.Tony BaDr.ick, CEO of The Royal College of Pathologists of Australasia, is one of the leaders behind the PBRTQC push.

Another problem is that conventional QC samples are synthetic, may deteriorate during the day, and are handled differently from real patient samples. That makes these QC sample results less comparable to patient samples and non-commutable, raising the possibility that a problem with the analyzer could escape notice until it's too late.

"It's becoming more apparent that conventional QC has problems, and that those problems are significant," BaDr.ick adds.

How does patient-based QC work?

The concept behind PBRTQC is fairly simple: by averaging "normal" samples throughout the day, operators can see immediately if values begin to move outside an expected range, just like conventional QC. "You take something you're measuring routinely, and you use that to try and identify when something has changed with the measurement system," BaDr.ick explains.

Let's look at sodium as an example. With a PBRTQC approach, the lab's software would generate a rolling average for the measured sodium levels from every patient, constantly updating that average as more samples are run. If that rolling average begins to deviate outside the expected range, it would automatically be flagged as a possible quality control issue and the analyzer could be tested and recalibrated if necessary. The reason why the average sodium level of the patient population may change would be if the patient population changes or the measurement system changes, which is bias.

PBRTQC works best for tests run frequently in a lab, so there are enough samples to support the continued generation of rolling averages throughout the day. It is not appropriate for some tests such as tumour markers and other tests that are conducted infrequently or where there are a lot of abnormal results.

PBRTQC also requires a fairly stable patient population, which is not realistic for all labs. A tertiary hospital lab that tests inpatients all morning and outpatients all afternoon, for instance, might have to establish different acceptable range limits based on these two very different patient populations.

For standard community-based testing, though, patient-based QC can be highly effective, says BaDr.ick, noting that LabCorp has been using this technique [2] for years. It's also cost-effective, since there is no need to buy lots of synthetic control samples. Most labs that adopt the approach run a hybrid model, using conventional QC in the morning and evening and patient-based QC throughout the day.

How to get started with patient-based QC

The thought of shifting to a PBRTQC method may sound daunting, but BaDr.ick believes that most labs will be able to implement this approach over time as more and more manufacturers build patient-based QC protocols directly into the analyzers they sell. "In the ideal situation, the analyzer should flag when things go out of control and let the user know when it's time to recalibrate the instrument," he says.

In the meantime, BaDr.ick and his teammates at the Committee on Analytical Quality are doing their best to ensure that the clinical laboratory community has the resources to adopt patient-based QC even before it is built into instruments. They have published several papers and tools on validation, software, simulation and more to help labs get started with best practices. They also recommend setting up some pilot sites and report the results of those efforts in the future.

"It's not an impossible task," BaDr.ick says. "It's a change in mindset as much as anything else."

Resources

Check out these publications to learn more about how to implement patient-based QC:

Implementation of Patient-Based Real-Time Quality Control Critical Reviews in Clinical Laboratory Services, 2020

Patient-Based Real-Time Quality Control: Review and Recommendations Clinical Chemistry, 2019

Recommendations for Laboratory Informatics Specifications Needed for the Application of Patient-Based Real-Time Quality Control Clinica Chimica Acta, 2019

References

[1] Committee on Analytical Quality, International Federation of Clinical Chemistry and Laboratory Medicine

[2] Fleming, K.J., Katayev, A., (2015). Changing the paradigm of laboratory quality control through implementation of real-time test results monitoring: For patients by patients. *Clinical Biochemistry*. 48(7-8), pp.508-513

CDC Standardization-Certification for Total 25-hyDroxyvitamin D and Total Testosterone Assays

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Abstract

Variability in the results of hormone assays such as total 25-hyDroxyvitamin D and total testosterone has the potential to adversely affect proper patient care. Standardization of assays has been proposed as a way to address this problem. Assays that are standardized are designed to provide accurate results, traceable to "true" value-assigned certified reference materials and gold- standard reference methods. Results obtained using standardized methods can be compared across assays, institutions, populations, and with past and future test results, thereby improving diagnosis, treatment, and outcomes of patients.

Vitamin D is a hormone that is vital for healthy bones. Hypovitaminosis D leads to bone defects and has been associated with extra skeletal conditions and diseases. Currently, the concentrations of vitamin D (measured as 25 [OH]D) in the circulation are largely determined using various commercialized automated methods; however, variability in results between methods has made it difficult to assign cut off values for diagnosis and to develop public health guidelines. In 2010, an international collaborative effort, led by the Office of Dietary Supplements (ODS) of the U.S. National Institutes of Health (NIH), in collaboration with the National Institute of Standards and Technology (NIST), the Centers for Disease Control and Prevention (CDC), and Ghent University (Ghent, Belgium), established the CDC Vitamin D Standardization Program (VDSP) to address this problem.

The goals of the VDSP were to improve clinical and public health practice by developing reference methods and materials for standardization and harmonization of vitamin D assays so that results could be compared across manufacturers, laboratories, and time. Additionally, the CDC Vitamin D Standardization-Certification Program (VDSCP) was set up to maintain the quality of vitamin D assays through ongoing quarterly testing challenges of participant laboratories. On a quarterly basis, laboratories achieve certification if they meet CDC requirements of $<$10% imprecision and $\pm$5% mean bias for the preceding four quarters.

Similar to the case for total vitamin D, inconsistencies in total testosterone results between assays have led to the CDC Hormone Standardization Program (CDCHoST) Certified Total Testosterone Procedures.

The goal of the HoST project was to standardize testosterone measurements in order to improve patient care. Standardization of total testosterone measurements in serum is performed by determining whether the bias between CDC's value-assigned reference material and the laboratory values falls within predefined limits. Only then does CDC consider a laboratory standardized. On a quarterly basis, certification is granted if the HoST acceptance criterion of ±6.4% mean bias to the CDC Testosterone Reference Method is met for the most recent four quarters.

What Is Vitamin D?

Vitamin D is a group of steroid hormones that are essential for healthy bones and biological processes. The major forms are vitamin D_3 (cholecalciferol) and vitamin D2 (ergocalciferol), both available in the diet or as supplements (Drepresents the sum of D_3 and D_2). Vitamin D_3 (not vitamin D_2) can be formed in the skin by exposure to UVB sun rays. Both vitamin D_3 and D_2 forms circulate in blood and are hydroxylated in the liver to 25-hyDr.oxycholecalciferol, 25(OH)D3 and 25-hyDroxyergocalciferol, 25(OH) D_2 and further hydroxylated in the kidney to form the biologically active molecules 1,25-dihyDr.oxycholecalciferol D_3, 1,25$(OH)_2$ D_3, (also known as calcitriol) and 1,25-dihyDr.oxyergocalciferol, 1,25(OH)2 D_2. The active 1,25 (OH)2D mediates calcium absorption in the intestine and mineral release from bone (calcium, etc.) and stimulates calcium reabsorption in the kidney.

Although 1,25(OH)2D is the biologically active form, total 25(OH)D is recognized as the best marker of vitamin D nutritional status.[1] This is because 25(OH)D is the most abundant vitamin D metabolite in blood (25[OH]D concentration is approximately 30 ng/mL vs. 1-5 ng/mL for 1,25[OH]2D); is not as tightly regulated as 1,25(OH)2D_3 in response to changes in calcium and parathyroid hormone concentrations; and is dependent on kidney function. In addition, 25(OH) D has a long half-life (around 3 weeks) compared to and 1,25 (OH) 2D (around 8 hours). Combined, these features make 25(OH) D relatively easy to measure. Importantly, oral 25(OH)D supplementation in patients was found to cure bone defects (rickets and osteomalacia) that are attributable to hypovitaminosis D. Currently, along with 25(OH)D, other potential metabolites with biological activity are being considered for standardization as supplemental markers. These markers include 1,25 (OH)2D, 3-epi-25(OH)D, 24,25-dihyDr.oxyvitamin D_3 [24,25(OH)2D3], vitamin D-binding protein (DBP), free/bioavailable 25 (OH) D, and PTH.[2]

Prevalence and causes of vitamin D deficiency

Vitamin D deficiency and insufficiency are a global healthcare problem.[3] Approximately 30% of children and adults worldwide are vitamin D-deficient and 60% insufficient.[3,4] In the United States, 50% of children ages 1-5 and 70% of children ages 6-11 had a 25(OH)D <30 ng/mL.[3,5] The causes of vitamin D deficiency include lack of sufficient exposure to sun, use of sun protection, diet or supplements deficient in vitamin D, obesity, inborn or acquired genetic mutations in vitamin D metabolism, and deficient vitamin D-binding protein. Hypovitaminosis D leads to a variety of bone abnormalities such as osteoporosis, rickets, and osteomalacia.

Vitamin D deficiency has also been associated with several diseases and conditions such as multiple sclerosis, cancer, cardiovascular disease, and aging processes (see Table 1 for list).[6–8] However, definitive evidence is lacking to link vitamin D with extraskeletal beneficial outcomes for cancer and cardiovascular disease.[9]

Table 1. *Vitamin D deficiency is associated with several diseases and conditions.*

Diseases and conditions associated with vitamin D deficiency	
Aging	Inflammatory bowel disease
Allergies	Influenza and respiratory infection
Anxiety	Lupus
Asthma	Macular degeneration
Athletic performance	Muscular sclerosis
Autism	Obesity
Cancer	Oral health
Chronic pain, bone pain	Osteoporosis/osteomalacia/rickets
Cognitive impairment	Overall mortality
Dementia/alzheimer's disease in elderly	Peripheral artery disease
Depression	Rheumatoid arthritis
Heart health (high blood pressure, risk of cardiovascular disease)	Seasonal affective disorder
Incontinence	Tuberculosis
Increased cholesterol	Types 1 and 2 diabetes
Inflammation	

Definition of vitamin D deficiency

Controversy has surrounded the definition of vitamin D deficiency, insufficiency, and sufficiency.[2,3,10] The Endocrine Society's Practice Guidelines on Vitamin D define vitamin D deficiency as "a 25(OH)D <20 ng/mL, insufficiency as 21–29 ng/mL and sufficiency as at least 30 ng/mL for maximum musculoskeletal health. This definition has also been accepted by the National Osteoporosis Foundation, International Osteoporosis Foundation, American Association for Clinical Endocrinologists, and the American Geriatric Society."[3,11] The Institute of Medicine definition is based on minimal requirements for healthy bones and defines risk of vitamin D deficiency as 25(OH)D <30 nmol/L (12 ng/mL), risk of vitamin D inadequacy as 30–49 nmol/L (12–19 ng/mL), sufficiency as 50–125 nmol/L (20–50 ng/mL), and possible increased risk for harm when levels exceed 125 nmol/L (50ng/mL).[1] In children and adults, excess vitamin D (hypervitaminosis D) is defined as concentrations of >250 nmol/L (100 ng/L) and intoxication as >375 nmol/L (150ng/mL).[12–15]

Testing for Vitamin D

Both the Institute of Medicine and Endocrine Society agree that there is no need to screen populations that are not at risk of vitamin D deficiency.[10,11] Testing is recommended to confirm clinical symptoms of rickets in children and osteomalacia in adults, and also for those at risk, such as pregnant women, those with increased skin melanin pigmentation, children and adults who are obese, and those who abstain from direct sun exposure or with fat malabsorption syndromes, kidney disease, other risk factors, or inherited or acquired disorders in vitamin D metabolism.

How Is vitamin D tested?

Vitamin D testing has evolved over the years from methods that involved manual extraction of vitamin D using organic solvents, reconstitution of vitamin D, and measurement using immunoassay techniques[4]. This method had the advantage of producing accurate measurements due to thorough hextraction of vitamin D from vitamin D-binding protein; however, the procedure is slow and labor-intensive.

Liquid chromatography mass spectroscopy (LC-MS/MS) is considered the most accurate method for determining the concentration of 25(OH) D; however, this method is laborious and requires specialized training for laboratory operators.

For higher-volume clinical laboratories, automated chemiluminescent assays have taken the place of the more-manual methods. Automated assays are less labor-intensive, higher-throughput, and meet the higher demand for increased testing; however, assay results from different manufacturers may not be the same (due to different antibodies, assay design, or other causes) and cannot be compared. In addition, automated assay results may be different from LC-MS/MS and manual methods.

Variability in vitamin D assays

The variability between 25(OH) D concentrations as measured by the various 25(OH) D assays and methods may come from several sources. Some assays have differential affinity for 25(OH) D_3 and 25(OH) D_2, which can cause inconsistencies in test results between assays, especially in cases of vitamin D_2 supplementation. Other causes of variability include incomplete extraction of vitamin D from its binding protein (e.g., in pregnant women, who have higher levels), cross-reactivity with the 24,25 $(OH)_2$ D metabolite, and matrixinterferences.[2] Variability in results indicates the need for standardization of 25(OH)D assays.[2,16-21]

Standardization has been defined as a process whereby "all laboratories and assays are brought into alignment with the 'true concentration' based on gold standard reference measurement procedures and certified reference materials. That is, standardized laboratories report the 'true' concentration—in this case, of serum total 25(OH) D—regardless of time, place and assay or measurement system."[2]

CDC Vitamin D Standardization Program

In November 2010, the National Institutes of Health (NIH) Office of Dietary Supplements (ODS) established the vitamin D standardization program (VDSP), an international collaboration between the National Institute of Standards and Technology (NIST), the Centers for Disease Control and Prevention (CDC), and Ghent University (Ghent, Belgium).[16,18,22] The goals of the VDSP were to provide laboratories and manufacturers with reference materials (NIST) and a reference protocol (Ghent University) to standardize the laboratory measurement of vitamin D. The reference methods assign concentrations to reference materials. Reference materials calibrate all 25(OH) D assays and verify calibrations, such that assay results are traceable to a common standard and comparable between assays and laboratories (Figure 1, Table 2). Another VDSP goal was the standardization of 25(OH) D measurement in national health and nutrition surveys (including retrospectively) using reference materials and methods.[18,23,24]

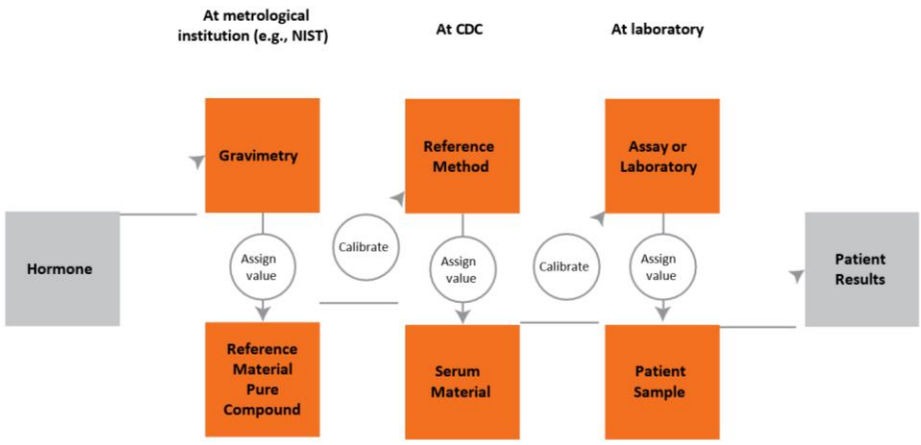

Figure 1. *Schematic of basic activities involved in standardization of assays performed at the National Institute of Standards and Technology (NIST), the Centers for Disease Control and Prevention (CDC), and individual laboratories. Standardization involves traceability to "true" gold-standard reference methods and materials in order to provide accurate results that can be compared between assays and laboratories and overtime.*

Table 2. *Components of the CDC Hormone Standardization Program.*

Reference Method at Reference Laboratory* • For total 25(OH)D (sum of 25[OH] D_2 and 25[OH] D_3) in serum, uses and HPLC-MS/MS. • Separately quantities 25(OH) D2 and 25(OH) D_3 with high level of specificity and is not affected by other vitamin D isomers, such as C3-epi-25(OH) D_3. • Meets stringent analytical performance criteria (maximum allowable bias: ≤1.7%; maximum allowable imprecision:±5%).	Calibrated using "pure compounds", which are primary reference materials (e.g., SRM 2972a for total vitamin D from NIST). Thus, results are traceable to the International System of Units (SI) according to the International Organization for Standardization (ISO) standard for traceability in laboratory medicine. At CDC, primary reference material assigns values to blood samples, which are secondary reference materials using reference method procedures. Secondary reference materials calibrate assays.
Calibration in Laboratory with CDC Value-assigned Secondary Reference Material • For total 25(OH) D, meets stringent analytical performance criteria (maximum allowable mean bias: ±5%; maximum allowable imprecision:<10%). • For total testosterone, meets stringent analytical per formance criterion (maximum allowable mean bias:±6.4%)	VDSCP to monitor total vitamin D assay results over time with CDC-provided reference samples that are value-assigned by the CDC. CDC HoST Certification Project to monitor total testosterone assay results over time using CDC-provided reference samples that are value-assigned by the CDC.
Laboratory Surveys • For total 25(OH)D, meets stringent analytical performance criteria (maximum allowable mean bias: ±5%; maximum allowable imprecision:<10%). • For total testosterone meets stringent analytical performance criterion (maximum allowable mean bias:±6.4%).	Collaboration with College of American Pathologists (CAP) and other proficiency-testing companies.
Training and Education	Instructions for end users of assays Procedures Reference ranges Monitor effectiveness of standardization

**https://www.cdc.gov/labstandards/vdscp_laboratory.html*

CDC Vitamin D Standardization Certification Program

To accompany the VDSP, the CDC established the Vitamin D Standardization-Certification Program (VDSCP) whereby manufacturers and laboratories may participate in an ongoing certification process (Figure 2).[25]

The certification process involves a calibration stage followed by quarterly challenges of 10 samples per quarter, provided by the CDC and value-assigned by the Ghent University RMP. The CDC determines bias, precision, and total error according to Clinical and Laboratory Standards Institute (CLSI) Document EP9-A2. Certification is granted when the mean bias of the 40 Phase 2 samples is ±5% to the CDC and University of Ghent Vitamin D_2 and D_3 Reference Method Procedure, and overall imprecision is <10%. Certification must be renewed quarterly for the most recent four quarters. Several manufacturers of different 25(OH) D methods participate, and some have been certified since the inception of the VDSCP. To date, the Siemens Healthineers ADVIA Centaur® Vitamin D Total Assay has achieved certification for seven consecutive years, the Atellica® IM Vitamin D Total Assay has achieved certification for two consecutive years, and the Dimension® EXL™ Vitamin D Total Assay has achieved certification for three consecutive years.[26]

The international External Quality Assessment (EQA) scheme for vitamin D metabolites (DEQAS) was established in 1989 to monitor variability in 25(OH) D assays.[2,27] In 2013, the NIST Reference Method Procedure value-assigned target values for DEQAS materials, making DEQAS accuracy-based for 25(OH) D. This allowed for unbiased evaluation of assay variation. However, DEQAS results since 2013 still demonstrate considerable sample-to-sample variation within and among different assays and laboratories, underscoring the need for standardization of all assays.[2,22]

Another effort toward helping to reduce inconsistencies among assays was the development of a 24,25$(OH)_2D_3$ Reference Method Procedure by NIST and its use in assigning values to SRMs 972a, 2973, and 2971, supported by the NIH ODS as part of the VDSP effort.[2,27]

Vitamin D Conclusion

The VDSP aligns the results of 25(OH)D assays to gold-standard reference methods developed by Ghent University and certified reference materials provided by NIST, thereby ensuring accurate results that can be compared among assays and institutions. For optimal patient care and outcomes, researchers, clinicians, and sponsors of national surveys should adhere to using the VDSP protocols for 25(OH) D methods and participate in ongoing certification by the CDC VDSCP.

The use of Siemens Healthineers ADVIA Centaur, Atellica IM, and Dimension EXL Vitamin D Total assays that are standardized and CDC-certified should help ensure harmonization and accurate results and diagnoses, resulting in better patient care.

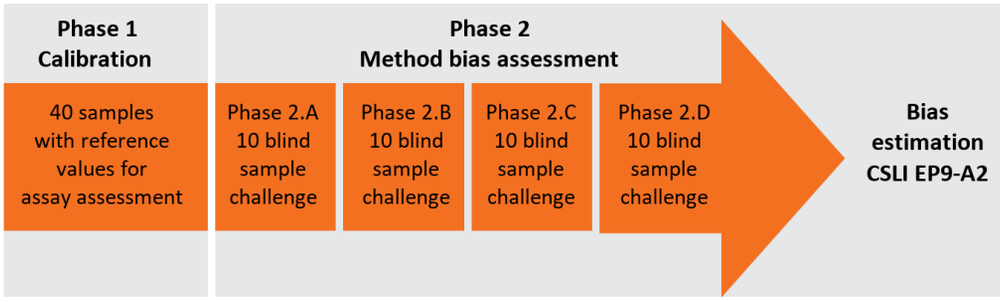

Figure 2. The CDC Vitamin D Standardization-Certification Program (VDSCP) consists of two phases providing 40 value-assigned reference samples for Phase 1 (calibration) and 10 blind sample challenges four times annually (total of 40 blind samples) for Phase 2.[25] The CDC then determines bias according to CLSI Document EP9-A2. Certification is awarded quarterly when results from the most recent four quarters have met the CDC criteria for precision (<10%) and mean bias (±5%).

What Is Testosterone?

Testosterone (4 and rosten 17ß-ol-3-one) is a steroid hormone and the major androgen (male sex hormone) in males, which is produced by Leydig cells in the testes. Testosterone production is controlled by luteinizing hormone, which is released from the anterior pituitary acting directly on Leydig cells. In females, the major sources of testosterone are the ovaries, the adrenal glands, and the peripheral conversion of precursors, specifically the conversion of androstenedione to testosterone. Testosterone levels in women are about 10 times lower than in men.[28]

Abnormal testosterone levels

Disorders involving the male sex hormones (androgens) include primary and secondary hypogonadism, delayed or precocious puberty, and impotenceinmales, and hirsutism (excessive hair) and virilization (masculinization) due to tumors, polycystic ovaries, and adrenogenital syndromes in females.

Testing for Testosterone

Testosterone concentrations in the circulation are measured in the diagnosis and treatment of the disorders listed above (primary and secondary hypogonadism, delayed or precocious puberty, and impotence in males; in females, hirsutism and virilization due to tumors, polycystic ovaries, and adrenogenital syndromes). In recent years, increased demand for total testosterone testing has resulted from promising new therapies for diseases and conditions of testosterone excess or deficiency. Testosterone strongly binds to plasma proteins such as sex hormone-binding globulin (SHBG) (65% of total testosterone) or testosterone-estradiol-binding globulin (TeBG). SHBG transports testosterone throughout the circulation and is a hormone reserve; testosterone bound to SHBG is biologically inactive. Testosterone also binds with low affinity to cortisol-binding globulins (CBG) and albumin. 30-40% of testosterone is bound to albumin, is easily removed, and considered biologically available. Less than 2.5% of total testosterone circulates unbound to plasma proteins (free), also considered biologically active.

Total testosterone assays detect both bound and free testosterone concentrations in the blood. (It should be noted that in women, it is important to measure the amount of biologically available testosterone because SHBG concentrations are affected by avariety of factors, including thyroid and estrogen hormonal changes. High levels of active testosterone can be the cause of hyperandrogenemia in women who have total testosterone levels within the reference range).

How is testosterone tested?

Until the 1970s, extraction and radioimmunoassay (RIA) methods were used to measure testosterone. RIA methods can yield higher accuracy than immunoassays in current use; however, time and cost are major disadvantages for routine use of RIA methods. In the late 1970s, extraction RIA methods were replaced with direct RIAs that did not require extraction or chromatography.

Subsequently, direct immunoanalytical methods with nonradioactive markers were developed for use on analyzers. Direct immunoassays are easy to use and more convenient for routine clinical practice but lack adequate specificity, have higher values than classical RIA, and incompletely extract testosterone from binding proteins, particularly SHBG, which results in less of the total analyte for measurement. This is a problem when measuring very low concentrations, such as in women. Currently in Europe, most laboratories use immunoassays and no extraction; results are obtained quickly, but accuracy is low.[29]

LC–MS/MS was introduced in the 1990s and 2000s and is now considered the gold-standard method. LC–MS/MS demonstrates the highest accuracy at low concentrations and is useful in women. However, this method is often prohibitive due to cost, the need for trained personnel and standardization and validation by each laboratory, and interference by conjugates. LC–MS/MS also has challenges associated with commercial kits whose results are not always more accurate than those of immunoassays.

Variability in testosterone assays

Significant variability in measurements is observed when comparing results from various testosterone assays, particularly at low concentrations, such as found in hypogonadal males, children, and women. Variability relates to measurement inaccuracy and lack of specificity, sensitivity, and precision/repeatability. As in the case of total vitamin D, the clinical and research communities have called for the standardization of testosterone testing.

Standardization of testosterone testing using the CDC reference method and materials has been proposed to adDr.ess variability issues with respect to reference ranges of different groups such as women, men, age, and phase of menstrual cycle.[30] Indeed, a recent publication has demonstrated the feasibility of harmonizing reference ranges in men across assays that generate variable results by calibrating to the CDC reference method and materials.[31]

CDC Standardization of Testosterone Assays

In 2007, the Endocrine Society recommended "accuracy-based testing of testosterone and calibration of all methods traceable to a single high-level reference material."[30,32-34] Standardization of testosterone assays aims to help ensure accurate and comparable results across testing systems (assays), laboratories, and time, thereby improving quality of patient care, clinical research, and epidemiological studies, including the development of evidence-based guidelines. Similar to the VDSP, the HoST for testosterone goals were to develop "true-value" reference materials and reference methods. Reference methods assign values to reference materials. Reference materials calibrate assays and verify calibrations so that different testing facilities and assays can trace their results to a common standard (Figure 1). Using non standardized tests increases the chance of misdiagnosis and wrong treatment and the inconvenience and increased costs caused by retesting.

In 2010, The Endocrine Society and eleven other organizations made the following recommendations toward improving testosterone measurements:[30] First, all users and stakeholders of testosterone assays in the public and private sectors should support the CDC testosterone standardization procedures and demand that manufacturers and laboratories develop accurate and reliable tests worthy of research funding and third-party payer reimbursement. Second, experts should provide total testosterone performance criteria over the full range of values for children, adults, and each sex using standardized methods. Third, reference range values should be determined using standardized methods for children, adults, and each sex. *Fourth, experts should provide guidelines for consistent sample collection and preparation for standardized assays. Fifth, third-party payers and health care organizations should support the use of assays that have been standardized. Sixth, funding bodies and journals should only support and consider for publication research performed with standardized assays demonstrating accuracy. Tests selected for patient care, research, and public health activities should be standardized.*

New testosterone tests should be standardized to the CDC. Seventh, manufacturers and laboratories should continue to develop new methodological approaches for accurate measurement of testosterone; emphasis should be placed on results, not methodology. Standardized testosterone testing should yield comparable test results across methods and time. Currently, similar to the VDSCP, on a quarterly basis, the CDC grants certification to those assays that pass acceptance limits in the CDC HoST Certification Program over the most recent four quarters.

The HoST acceptance criterion is ±6.4% mean bias to the CDC Testosterone Reference Method.[35] To date, the Siemens Healthineers ADVIA Centaur Testosterone II assay has achieved certification for two years, the Dimension Vista Serum Total Testosterone assay has achieved certification for four consecutive years, and the Atellica®IM Test osteroneII has achieved certification for the first year.[26] Between 2012–2013 and 2016, CDC-directed accuracy-based proficiency testing demonstrated that about 15% more participating laboratories had improved analytical accuracy and precision; however, improvements are still needed, especially at lower concentrations.[35,36] A complete and updated list of certified methods are posted on the CDC website.

Testosterone Conclusion

The CDC HoST program for total testosterone assays provides reference methods and materials that help ensure sensitive and reliable detection of accurate total testosterone concentrations. Standardization of total testosterone assays allows a comparison of results across different assays, national surveys, and over time.

Consensus documents prepared by experts recommend that all publications and national surveys use total testosterone assays that are standardized using the CDC HoST Program. Use of the Atellica IM and ADVIA Centaur Testosterone II and Dimension Vista Total Testosterone assays that are standardized and CDC-certified should help ensure harmonization, accurate results and diagnoses, and improved patient care.

References:

1. Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab. 2011;96:53-8.
2. Sempos CT, Heijboer AC, Bikle DD, et al. Vitamin D assays and the definition of hypovitaminosis D: results from the First International Conference on Controversies in Vitamin D. Br J Clin Pharmacol. 2018;84:2194-207.
3. HolickMF. The vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention. Rev EndocrMetabDisord.2017;18:153-65.
4. Daly RM, Gagnon C, Lu ZX, et al. Prevalence of vitamin D deficiency and its determinants in Australian adults aged 25 years and older: a national, population-based study. Clin Endocrinol. (Oxf.) 2012;77:26-35.
5. Kumar J, Muntner P, KaskelFJ, Hailpern SM, Melamed ML. Prevalence and associations of 25-hyDr.oxyvitamin D deficiency in US children: Nhanes 2001-2004. Pediatrics.2009;124:e362-70.
6. Berridge MJ. Vitamin D deficiency accelerates ageing and age-related diseases: a novelhypothesis. J Physiol. 2017;595:6825-36.
7. Alkan A, Koksoy EB. Vitamin D deficiency in cancer patients and predictors for screening (D-Onc Study). CurrProbl Cancer.2019.
8. Oliveira SR, Simao ANC, Alfieri DF, et al. Vitamin D deficiency is associated with disability and disease progression in multiple sclerosis patients independently of oxidative and nitrosative stress. J Neurol Sci.2017;381:213-9.
9. Manson JE, Cook NR, Lee IM, et al. Vitamin D supplements and prevention of cancer and cardiovascular disease. N Engl J Med. 2019; 380:33-44.
10. Rosen CJ, Abrams SA, AloiaJF, et al. IOM committee members respond to Endocrine Society vitamin D guideline.JClinEndocrinolMetab.2012;97:1146-52.
11. HolickMF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of Vitamin D deficiency: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab.2011;96:1911-30.
12. Misra M, Pacaud D, PetrykA, Collett-Solberg PF, Kappy M. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics.2008;122:398-417.
13. Özkan B, Hatun S, BerteketA. Vitamin D intoxication. The Turkish Journal of Pediatrics.2012;54:93-8.
14. Demir K, Doneray H, Kara C, et al. Comparison of treatment regimens in management of severe hypercalcemia due to vitamin D intoxication in chilDr.en. J Clin Res Pediatr Endocrinol. 2019;11:140-8.
15. HolickMF. The role of vitamin D for bone health and fracture prevention. Current Osteoporosis Reports. 2006;4:96-102.

16. Binkley N, SemposCT. Standardizing vitamin D assays: the way forward. J Bone Miner Res. 2014;29:1709-14.
17. SemposCT, Betz JM, Camara JE, et al. General steps to standardize the laboratory measurement of serum total 25-hyDr.oxyvitamin D. J AOAC Int. 2017;100:1230-3.
18. SemposCT, Vesper HW, Phinney KW, ThienpontLM, Coates PM. Vitamin D status as an international issue: national surveys and the problem of standardization. Scand J Clin Lab Invest Suppl.2012;243:32-40.
19. Enko D, FriDr.ich L, Rezanka E, et al. 25-hyDr.oxy- vitamin D status: limitations in comparison and clinical interpretation of serum-levels across different assay methods. Clin Lab.2014;60:1541-50.
20. Koivula MK, Matinlassi N, LaitinenP, RisteliJ. Four automated 25-OH total vitamin D immunoassays and commercial liquid chromatography tandem-mass spectrometry in Finnish population. Clin Lab. 2013;59:397-405.
21. Klapkova E, Cepova J, Pechova M, Dunovska K, Kotaska K, Prusa R. A comparison of four methods (immunochemistry and HPLC) for determination of 25-(OH)-vitamin D in post-menopausal women. Clin Lab.2017;63:385-8.
22. Thienpont LM, Stepman HC, Vesper HW. Standardization of measurementsof25-hyDr.oxyvitamin D3 and D_2. Scand J Clin Lab Invest Suppl. 2012;243:41-9.
23. Durazo-Arvizu RA, Tian L, Brooks SPJ, et al. The vitamin D standardization program (VDSP)manual for retrospective laboratory standardization of serum 25-hydroxyvitamin D data. J AOAC Int. 2017;100:1234-43.
24. Rabenberg M, Scheidt-Nave C, Busch MA, et al. Implications of standardization of serum 25- hydroxyl vitamin D data for the evaluation of vitamin D status in Germany, including a temporal analysis. BMC Public Health.2018;18:845.
25. CDC. http://www.cdc.gov/labstandards/hs_ procedures.html. Accessed 2020 Mar 27.
26. CDC. https://www.cdc.gov/labstandards/hs_certified_participants.html. Accessed 2020 Mar27.
27. Carter GD, Ahmed F, Berry J, et al. External quality assessment of 24,25-dihyDr.oxyvitamin D3 (24,25(OH)2d3) assays. J Steroid Biochem Mol Biol. 2019;187:130-3.
28. Duskova M, Kolatorova L, Starka L. Androgens in women - critical evaluation of the methods for their determination in diagnostics of endocrine disorders. Physiol Res.2018;67:s379-s90.
29. Pugeat M, Plotton I, de la Perriere AB, Raverot G, Dechaud H, RaverotV. Management of endocrine disease hyperandrogenic states in women: pitfalls in laboratory diagnosis. Eur J Endocrinol. 2018;178:R141-r54.
30. Rosner W, Vesper H. Toward excellence in testosterone testing: a consensus statement. J Clin Endocrinol Metab.2010;95:4542-8.
31. Travison TG, Vesper HW, Orwoll E, et al. Harmonized reference ranges for circulating testosterone levels in men of four cohort studies in the United States and Europe.JClinEndocrinolMetab.2017;102:1161-73.
32. Rosner W, Auchus RJ, Azziz R, Sluss PM, Raff H. Position statement: utility, limitations, and pitfalls in measuring testosterone: An Endocrine Society position statement. J Clin Endocrinol Metab. 2007;92:405-13.
33. Vesper HW, Botelho JC. Standardization of testosterone measurements inhumans.JSteroidBiochemMolBiol.2010;121:513-9.
34. Vesper HW, Botelho JC, Wang Y. Challenges and improvements in testosterone and estradiol testing. Asian Journal of AnDr.ology.2014;16:178-84.
35. Cao ZT, Botelho JC, Rej R, Vesper H, Astles JR. Impact of testosterone assay standardization efforts assessed via accuracy-based proficiency testing. Clin Biochem.2019;68:37-43.
36. La'ulu SL, Kalp KJ, Straseski JA. How low can you go? Analytical performance of five automated testosterone immunoassays. Clin Biochem.2018;58:64-71.

Anti-SmAntibodies

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Antibodies to the Sm antigen are highly specific for systemic lupus erythematosus (SLE) and are presentin5to30% of SLE populations (1-3).They are included in the 2019 classification criteria for SLE as SLE-specific antibodies, with atleast the same weight asanti-ds DNA antibodies(4).

In the mid-1960s, a young physician and research fellow at Rockefeller University in New York City, Eng M. Tan, MD, was caring for a young girl with systemic lupus erythematosus (SLE). Using the Ouchterlony agar diffusion method, he and his mentor, Henry Kunkel, MD, demonstrated that the Sera of this young SLE patient showed precipitinb and with soluble issue extracts that could not be accounted for on the basis of the DNA or nucleoprotein content (5). Dr.. Tan had landed on a Discovery that would revolutionize the diagnosis of lupus. Further investigations using the anti bodies to the Sm antigen (named in honor of the patient, Stephanie Smith) would yield not only new diagnostic markers for lupus but also novel research directions and ideas for the field of molecular biology(6).

The Sm antigen belongs to the spliceosome

A spliceosome is a large molecular RNA-protein complex found primarily within the nucleus of eukaryotic cells. Its main role is to remove in trons from transcribed pre-mRNA, through a process call edmRNA splicing. This is acrucial step for the post-transcriptional modification of pre-mRNA to become functional template for ribosomes in protein synthesis (7). The spliceo some is largely composed of five major uridine rich small nuclear ribonucleo proteins (snRNPs, pronounced “snurps”),named U1,U2,U4-6,and U5snRNPs(8,9). Figure1 depicts the structure of U1-snRNP. All snRNPs can be further broken down into 3 main components: small nuclear RNAs, variable proteinsanda common set of core proteins, the Sm proteins. The Smcore proteinis organized asa seven-member ring structure (Smring), contain in geither B,B’or N(28kDa-29.5kDa) plus D1(16 kDa), D2 (16.5 kDa), D3 (18 kDa), E (12 kDa), F (11 kDa), and G (9 kDa)(9-11).

In addition to the core Smring, some proteins are specifically associated with certainsn RNPs.U1- snRNP for example contains three distinct proteins designated70K(68/70kDa),A(32kDa), and C (22 kDa), see figure 1(10).

Anti-snRNP antibodies

The most popular categorizations for antibodies against nRNPs includeanti-Smandanti-U1-snRNP antibodies.

Anti-U1-RNP antibodies are a diagnostic criterion of mixed connective tissue disease (MCTD). The absenceofU1-RNP antibodies essentially rules out this disease (3,13).U1-RNP antibodies are found in up to 32% of patients with SLE, an undifferentiated connective tissue disease, in systemic sclerosis, and in Sjögren’s synDr.ome (3,13).

Anti-Sm antibody is a specific marker for SLE, included in the 2012 SLICC classification criteria as well as in the revised 2019 EULAR/ACR Classification Criteria for SLE(4,12).They appear later than other SLE associated auto antibodies and, on average 1 year before the clinical onset of SLE (11). Sm antibodies have a very high diagnostic specificity (99 %) but a low sensitivity (5-10 %) for SLE in patients of Caucasian descent. The sensitivity is much higher in patients of Asian or Afro-American descent (30 % to over 40 %) (13). Sm antibody has been reported to be associated with disease activity SLE diagnosis, and its alterations could reflect changes of disease activity in patients with new-onset SLE. However, this is not generally agreed as a consensus (14). The data on the association between the antibodies and various manifestations of SLE are inconsistent, but the positive association between Sm antibodies and severe organ manifestations (CNS, kidney), skin vasculitis and mucosal manifestations (discoid lesions, oral ulcers) and ds DNA antibodies is relatively well confirmed (13).

What is the "real" Sm antigen?

The anti-Sm specificity includes auto antibodies that target proteins of the common Sm core, typically B/B'orD.Anti-RNPusuallyreferstoanti-U1-snRNP- specific auto anti bodies that target the U1-snRNP or the U1-specific proteins 70K, A or C. However, there is a significant cross-reactivity between the A, the C and the B/B' proteins, and therefore up to 60% of anti-U1-snRNP sera may react with B/B'.AsU1specific RNPs are more frequently targeted by antibodies that are present in patients with mixed connective tissue disease, Sm Disregarded as the most SLE specific Sm-antigen (11,15).

Methods to detect anti-Sm antibodies

Anti-Sm produces a nuclear speckled pattern on HEp-2 cell nuclei by conventional indirect immune of luorescence (IIF) (10). However, this staining pattern is practically indistinguishable from thatofanti-U1-RNPbythistechnique.Therefore,a confirmatory assay using specific can tigers has to follow to definitively identify this autoantibody (3, 10). Although immunoprecipitation using S35- methionine labeled cell extract is considered the gold standard, the more widely used assay technologies are based on enzyme-linked immunosorbent assays (ELISA), addressable laser bead immunoassays (ALBIA), line immunoassays (LIA), chemiluminescent immunoassay (CLIA) and fluorescent enzyme immunoassay (FEIA)(3).

Along with slight difference sob served between the different technologies, additional discrepancies are related to the use of different antigen sources (3). For solid phase assays, it is of advantage to use recombinant proteins to achieve highest purity and, consequently, a high specificity. While recombinant RNPantigens70K, A and C have been use dinsolidp has eassays for many years, it has never been possible to produce animmunore activere combinant Sm D protein, neither in eukaryotic, norinbacterialcells. In 2005, Mahleretal. Showed, that one particular peptide of SmD3 represents a more sensitive and more reliable sub strate than purified Sm for the detection of a sub class of anti- Sm antibodies (16).

Using immobilized peptides prepared by the SPOT technology, the authors showed that symmetric dimethylation of arginine residues plays an important role in the B-cell epitope recognition of both SmD1 and SmD3 autoantigens. The specificity of antibody binding to SmD3 peptides was higher than that of SmD1 peptides (16).

Harmonization of clinical interpretation of Sm test results

Different assays for Sm and U1-RNP antibodies sometimes give different results, depending on the test conditions and the auto antigens used. This must always be taken into consideration when comparing discrepant results between kits (10). Standardizing the numerical values reported in results obtained by different assays is unrealistic given the differences in methodology. However, harmonizing clinical interpretation of the different Sm and U1-RNP antibody tests might be achievable (to a certain level) by providing test result-specific likelihood ratios (LRs) (17). Current immunoassays for anti-Sm detection typically rely on a single cut off point to divide between positive and negative. However, this approach ignores the clinical value contained in the anti body levels.

Earlier studies on different antibody tests showed that the likelihood of the disease is generally correlated to the antibody level. Test result-specific LRs convey important clinical information in herentin the antibody levels. LR s provide an estimation of the clinical significance of a test result: a positive LR of 10 indicates that the chance to find such results is 10 times higher in SLE patients than in controls. Thus, results that are above the10LR there should are use full to aid in the diagnosis of SLE. However, for the evaluation of the test- and result-specific LRs, a study with a larger group of SLE patients and disease controls is needed.

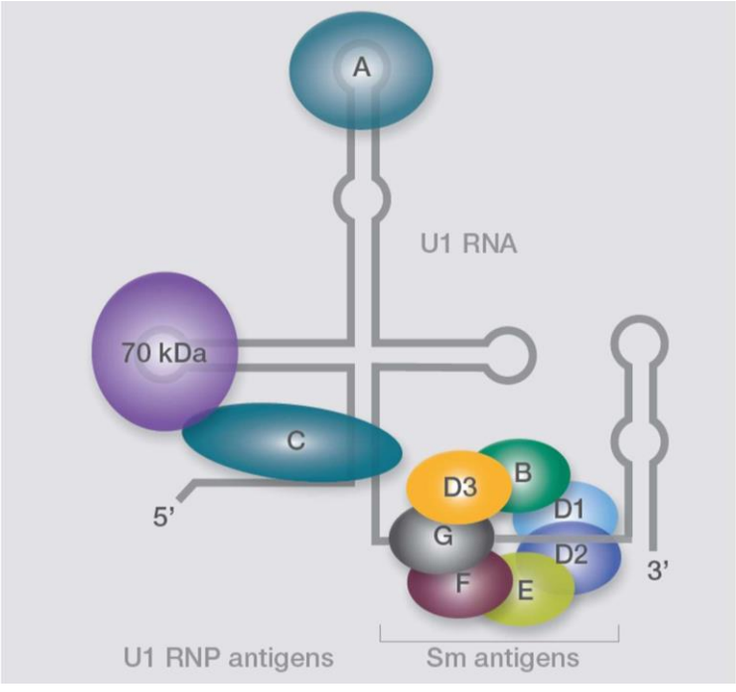

Figure1:U1-sn RNP with uridine-richU1-RNA and associated U1-snRNP-specific proteins70K (also called 68kDa), A and C and the core Sm proteins which are organized in a ring-like structure into which the U1-RNA is inserted(3).

References

1. T an EM. Antinuclear antibodies: diagnostic markers for auto immune diseases and probes for cell biology. Adv Immunol.1989;44: 93-151.
2. CraftJ. Antibodies to snRNPs in systemic lupus ery the matosus. Rheum Dis Clin North Am. 1992;18(2):311-35.
3. LemerleJ, Renaudineau Y. Anti-Sm and Anti-U1-RNPAntibodies: An Update. Lupus: Open Access.2016; 1(´3):1000e104.
4. Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheumatol.2019;71(9):1400-12.
5. TanEM,Kunke lHG. Characteristics of a soluble nuclear antigen precipitating with sera of patients with systemic lupus erythematosus. J Immunol.1966; 96 (3):464-71.
6. Henkel G. He Taught Us to Always Go Deeperhttps://www.the-
7. rheumatologist.org/article/he-taught-us-to-always-go-deeper/6/?singlepage=1.2011.
8. Wikipedia.Spliceosomehttps://en.wikipedia.org/wiki/Spliceosome2020[updated9 November20202020-11-22].
9. WillCL, Luhrmann R. Spliceo some structure and function. Cold Spring Harb Perspect Biol. 2011;3(7).
10. Mattioli M, Reichlin M. Characterization of a soluble nuclear ribonucleo protein antigen reactive with SLE sera. J Immunol.1971;107(5):1281-90.
11. SatohM ,Fritzler MJ, Chan EKL(2021)Anti-his to neend anti-spliceo some antibodies. Chapter 28, In: Systemic Lupus Erythematosus: Basic, Applied and Clinical Aspects, 2nd edition, edited by Tsokos, G.C., Academic Press, p237-47. DOI:10.1016/B978-0-12-814551-7.00028-3
12. Mahler M. Sm peptides in differentiation of autoimmune diseases. Adv Clin Chem. 2011;54:109-28.
13. Petri M, Orbai AM, Alarcon GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum.2012;64(8):2677-86.
14. Conrad K, Schoessler W, Hiepe F, Fritzler MJ. Auto antibodies in Systemic Autoimmune Diseases.3ed. ConradK, Sack U, editors. Lengerich, Berlin, Bremen, Miami, Riga, Viernheim, Wien, Zagreb: Pabst; 2015; 359p.
15. AhnSS, JungSM, YooJ, LeeS-W, SongJJ, ParkY-B. Anti-Smitz antibody is associated with disease activity in patients with new-onset systemic lupus erythematosus. Rheumatol Int. 2019;39: 1937-1944.
16. Van Venrooij WJ, Sillekens PT. Small nuclear RNA associated proteins: auto antigens in connective tissue diseases. Clin Exp Rheumatol.1989;7(6):635-45.
17. Mahler M, Fritzler MJ, Bluthner M. Identification of a SmD3 epitope with a single symmetrical dimethylation of an arginine residues specific target of a sub population of anti-Sm antibodies. Arthritis Res Ther.2005;7(1):R19-29.
18. Bossuyt X, Claessens J, Belmondo T, De Langhe E, West hovens R, Poesen K, et al. Harmonization of clinical interpretation of antinuclear antibody test results by solidp has eassay and by indirect immune of luorescence through like lihood ratios. Autoimmunity Rev.2019;18 (11):102386.

Performance evaluation of the New VITROS XT microslides in VITROS XT 7600 Integrated System

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Introduction:

Laboratory medicine is an essential medical service which plays a pivotal role in diagnosis, treatment, management and prevention of disease by providing patients and/or treating physicians with clinical laboratory information necessary to provide high-quality, safe, effective and appropriate care to patients (Ferraro et al., 2016). In the current era of health care systems, clinical laboratories are challenged with the pressure to deliver accurate and reliable results as fast as possible for early diagnosis and treatment. Hence, in addition to providing quality results, time to deliver results is becoming a key performance indicator of today's clinical laboratories. Multiple studies have shown that the VITROS microslide-based chemistry system could produce consistent, accurate laboratory results with a short turnaround time and fulfill the customers' expectations (Lakshman et al., 2015; Chakravarthy et al., 2017). VITROS microslide technology is based on a multilayer dry chemistry system providing a test environment on a thin piece of film with various layers, viz., spreading layer, masking layer, scavenger layer, reagent layer and registration layer combined on one postage-stamp sized microslide to provide accurate and precise results by taking care of all interfering substances. When body fluids like serum, plasma, urine or other body fluids come into contact with these multilayered microslides, a spectral reaction takes place which can be measured by means of reflectance spectrophotometry. Now VITROS microslide technology, with the goal of setting new standards with enhanced quality and productivity, introduced VITROS XT microslides combining two thin film reagents onto a single slide enabling the clinical laboratory to optimize operations and efficiency without compromising on quality. VITROS XT microslides allow the laboratory to perform two tests that are commonly ordered together, simultaneously in a single test sample. This improves lab productivity and turnaround time in delivering quality test reports.

In addition, VITROS XT micro slides in the VITROS XT 7600 integrated system Digital Chemistry™, powered by a new digital reflectometer which can read the refracted light faster than the current conventional technology. The faster reading, with the digital reading reflectometry with enhanced pixels, improves the throughput. The biggest advantage of digital chemistry is getting away from the troublesome halogen bulb-based technology to an instrument life-long LED-based technology for reflectance measurement. Advanced digital imaging technology gleans more information from the reflected light captured using digital reflectometer as well as the digital image of the end result obtained in each test slide for effective data analysis. All these features lead to increased throughput, enhanced reliability, and improved performance.

The objective of this study was to evaluate the analytical performance of VITROS XT microslides for all the routine parameters as per the standard guidelines. CLSI sets the standards for the validation and/or verification of new assays and/or new analyzers before they are put in use. Successful verification of the assay performance ensure the accuracy, reliability, reproducibility of the assay results generated from the new system and ensure its clinical appropriateness.

Materials and Methods:

The performance evaluation of VITROS XT microslides in VITROS XT 7600 Integrated system was conducted at the Division of Clinical Biochemistry, Department of Laboratory Medicine, Jaypee Hospital, Noida, India. The NABL accredited Department of Laboratory Medicine provides clinical laboratory services to the NABH accredited tertiary care multi-specialty hospital. The VITROS XT 7600 integrated system from Ortho Clinical Diagnostics, USA was installed in the Department of Laboratory Medicine, Jaypee Hospital, in 2019and the Installation Qualification (IQ), Operation Qualification (OQ) and Performance Qualification (PQ) studies were conducted and approved as per the manufacturer's specifications and Department of Laboratory Medicine, Jaypee Hospitals standard operating protocols.

The six pairs of assays, commonly used as a part of comprehensive metabolic panel and frequently requested tests in pairs such as Albumin – Total Protein; Glucose – Calcium; ALT – AST; Total Bilirubin – Alkaline Phosphatase; Triglycerides – Cholesterol; Urea – Creatinine were launched as VITROS XT microslides by Ortho Clinical Diagnostics, USA. The VITROS XT microslides contains two multilayered, analytical elements as mentioned above, coated on a polyester support, separated by a plastic barrier sealed within a single slide frame, for the quantitative measurement of analyte concentration in serum, plasma, urine and other body fluids. A small volume of patient sample is metered onto each chemistry chip and is evenly distributed by the spreading layer to the underlying reagent layers. Based on the concentration of the analytes in the sample, color is formed in the registration layer through various reaction cascades (The Instructions for use manual of XT microslides). The density of the color formed is proportional to the concentration of the analytes present in the sample and is measured by digital reflectance spectrophotometry. With the total volume of about 45.6 ul sample; all the 12 analytes can be performed (Table 3).

Among the six pairs of VITROS XT microslides launched by Ortho Clinical Diagnostics, five pairs of VITROS XT microslides except Glucose – Calcium pair were calibrated in VITROS XT 7600 integrated system using the provided calibrators by following the instructions manufacturer specified in the assay Instruction for use manual and the success of calibration was verified using 2 levels of VITROS Performance Verifier control fluids. All the 10 analytes were also calibrated in the same VITROS XT 7600 system using regular single assay VITROS microslides and the calibration verification was done using VITROS Performance Verifier Level 1 and Level 2 control fluids.

Accuracy and Precision verification:

The analytical performance of each analyte based on VITROS XT microslide assay was verified in terms of both accuracy as well as inter and intra assay precision by using 2 level controls of VITROS Performance Verifier Chemistry controls by following the Westgard Basic Method validation – Replication experiment guidelines (James O Westgard, 2008).

For intra assay precision, each level of VITROS Performance Verifier Chemistry controls were processed 20 times within a run to obtain an estimate of short-term imprecision. From the control values obtained in the intra assay precision, the accuracy verification was performed by calculating the Bias% from the obtained difference between the expected and the obtained value. The obtained bias% value was compared with that of the allowable bias% for each analyte as per the desirable biological variation database specifications (Ricos et al., 2014). For inter assay precision, the VITROS Performance Verifier Chemistry controls were processed for a period of 20 days to obtain an estimate of long-term imprecision. After performing 20 runs for each level of control, the data was analyzed for each level of control and for each analyte, the mean, standard deviation (SD) and co-efficient of variation (CV%) were calculated. For the precision verification, the obtained CV% for both intra run (repeatability) and inter run (within laboratory were compared with the allowable imprecision% for each analyte as well as the total allowable error as per the desirable biological variation database specifications (Ricos et al., 2014). For intra assay, the imprecision shall be below one fourth of allowable error (< 0.25 TEa) and for inter assay, the imprecision shall be below one third of allowable error (< 0.33 TEa) (James O Westgard, 2008).

Analytical measurement range verification:

The analytical measurement range (AMR)or the reportable range of each analyte while using VITROS XT microslide based assay was verified as per CLSI document EP 06-A approved guidelines. The AMR of each analyte was verified by testing five varying concentrations of each analyte, which are known and relative to each other by dilution ratios. The samples with five varying concentrations of each analyte were prepared by selecting calibrator materials having manufacturer assigned analyte concentration level close to the lower limit of AMR of the assay as Level 1 and calibrator materials having manufacturer assigned analyte concentration level close to the upper limit of AMR of the assay as Level 5. The intermittent concentrations, viz., Level 2, Level 3 and Level 4 were prepared by mixing both Level 1 and Level 5 concentrations in the ratio of 3:1, 2:2 and 1:3 respectively as per the CLSI EP 06- A approved guidelines. All the 5 levels of sample mix, covering the AMR of each analyte was tested in duplicate to verify the AMR of each analyte. By using the obtained mean value of each level and the manufacturer assigned or calculated of each level, the XY plot was prepared and analyzed. The assessment criteria for AMR verification was the visual examination of the plots for any potential outlier at each analyte concentration and by linear regression plot and co-efficient of determination (r2).

Method comparison regression verification:

The performance of VITROS XT microslide-based assays were compared with the VITROS microslide (single test microslide) based assays as per the modified guidelines of CLSI EP09-A3 document using a total number of 20 samples covering the analytical measurement range of each analyte. The samples were processed in both VITROS XT microslide reagents and VITROS microslide (single) reagents in VITROS XT 7600 integrated system. The samples were analyzed in the same day and same time one after the other slides to minimize the variation in results due to sample stability. The linear regression analysis between the two assays was carried out to verify the relationship between the two methods.

Turnaround time analysis:

The turnaround time (TAT) for doing sample analysis using VITROS XT microslides was analyzed and compared with the time taken for the analysis using VITROS microslides. A total of 20 samples were programmed in VITROS XT 7600 for all the 10 chemistries and processed. The total time taken to complete all the assays was monitored. All 20 samples were processed for all the 10 chemistries using single VITROS microslides. The TATs in processing 20 samples for 10 chemistries were compared between both systems.

Results:

VITROS XT microslides for all the 10 chemistries were calibrated in VITROS XT 7600 Integrated system and the acceptability of calibration was verified using both VITROS Performance verifier (PV) level 1 and 2 chemistry control fluids as per the manufacturer's recommendations (Performance Verifier Training manual, 2018). The obtained results in both controls were within the range of mean (ROM), mentioned in the PV Assay sheet supplied by the manufacturer. Allowable variation (SD) was defined in the assay sheet. Simultaneously, all the 10 chemistries were also calibrated in VITROS XT 7600 Integrated system using VITROS microslides (single) and the calibration was verified using VITROS PV Level 1 and 2 chemistry control fluids. Both Level 1 and Level 2 controls were within the ROM for all the 10 chemistries of both single and XT microslides. Based on the quality control fluid results, for all the 10 chemistries, calibration was verified successfully for both single and XT in VITROS XT 7600 integrated system.

Accuracy and Precision Verification:

Accuracy, intra and inter assay precision of all the 10 chemistries in VITROS XT 7600 Integrated system using VITROS XT slides were evaluated by following the Westgard Basic Method Validation - Replication experiment guidelines. All the 10 chemistries showed accuracy comparable with the expected value and the obtained Bias% was well within the allowable Bias% (Table 1). The reproducibility of the assay in terms of short-term precision and long-term precision were as performed using VITROS PV Verifier Chemistry controls. The mean, standard deviation and co-efficient of variation (CV%) were calculated for both intra and inter assay precision study done for all the 10 analytes. The obtained CV% results were comparable with the allowable imprecision (I) %%) of desirable specifications (Ricos et al., 2014) except total protein which showed CV% above the allowable imprecision (Table 2).

Table 1: VITROS XT Slides – Accuracy verification study:

Analyte	Control Level	Expected Value	Obtained Value	Bias %	Allowable Bias% (RICOS)
Albumin	Level 1	2.504	2.502	-0.08	1.43
	Level 2	4.56	4.56	0.00	
Total Protein	Level 1	3.72	3.77	1.34	1.36
	Level 2	6.91	6.93	0.29	
Alkaline Phosphatase	Level 1	101	103	1.98	6.72
	Level 2	414	426	3.13	
Total Bilirubin	Level 1	1.64	1.64	0.00	8.95
	Level 2	15.64	15.71	0.45	
ALT	Level 1	20	21	0.83	11.48
	Level 2	165	167	1.26	
AST	Level 1	36	36	0.17	6.54
	Level 2	196	197	0.58	
Creatinine	Level 1	0.93	0.92	-0.22	3.96
	Level 2	5.27	5.33	1.14	
Urea	Level 1	38	40	4.53	5.57
	Level 2	112	117	4.78	
Cholesterol	Level 1	157	160	2.28	4.1
	Level 2	254	258	1.77	
Triglycerides	Level 1	133	133	-0.14	9.57
	Level 2	241	243	0.70	

Table 2: VITROS XT Slides – Intra and Inter assay verification study:

Analyte	Control Level	Intra assay (n=20)		Inter assay (n=20)		Allowable Imprecision (I)% RICOS	Short Term Precision Goal %	Long Term Precision Goal %	Total allowable error (Tea) (RICOS)
		Obtained Mean	Short Term Precision (CV %)	Obtained Mean	Short Term Precision (CV %)				
Albumin (g/dl)	Level 1	2.5	0.97	2.52	1.18	1.6	1.02	1.36	4.07
	Level 2	4.56	0.94	4.6	0.99				
Total Protein	Level 1	3.77	1.23	3.79	1.37	1.38	0.91	1.21	3.63
	Level 2	6.93	1.52	6.99	1.61				
Alkaline Phosphatase (U/L)	Level 1	103	1.5	105	2.15	3.23	3.01	4.01	12.04
	Level 2	427	1.01	434	1.43				
Total Bilirubin (mg/dl)	Level 1	1.64	4.14	1.56	4.65	10.9	6.74	2.96	8.87
	Level 2	15.71	0.97	15.83	1.03				
ALT (U/L)	Level 1	21	1.46	21	1.99	9.7	6.87	8.98	26.94
	Level 2	167	0.94	167	0.78				
AST (U/L)	Level 1	36	0.7	37	0.92	6.15	4.17	5.56	16.69
	Level 2	197	1.25	198	1.5				
Creatinine (mg/dl)	Level 1	0.92	0.73	0.93	1.28	2.98	2.22	2.96	8.87
	Level 2	5.33	5.99	5.4	1.16				
Urea (mg/dl)	Level 1	40	1.65	40	2.17	6.05	3.89	5.18	15.55
	Level 2	117	0.74	117	1.19				
Cholesterol (mg/dl)	Level 1	160	0.91	162	1.34	2.98	2.25	3	9.01
	Level 2	258	0.91	262	1.32				
Triglycerides (mg/dl)	Level 1	133	0.76	134	1.09	9.95	6.5	8.66	25.99
	Level 2	243	0.54	245	1.11				

Analytical Measurement Range Verification:

The analytical measurement ranges of all the 10 chemistries in VITROS XT slides were verified by following the CLSI EP-06A approved guidelines, using 5 different concentrations within the reportable range specified by the manufacturer. Each level was analyzed in duplicate and the mean value was compared to the expected value using linear regression analyses. All the 10 chemistries showed linear recovery as evidenced by the linear regression plot (Fig. 1). The co-efficient of determination (r2) for all the 10 analytes were between 0.99 to 1.0 indicating a perfect recovery through the analytical measurement value.

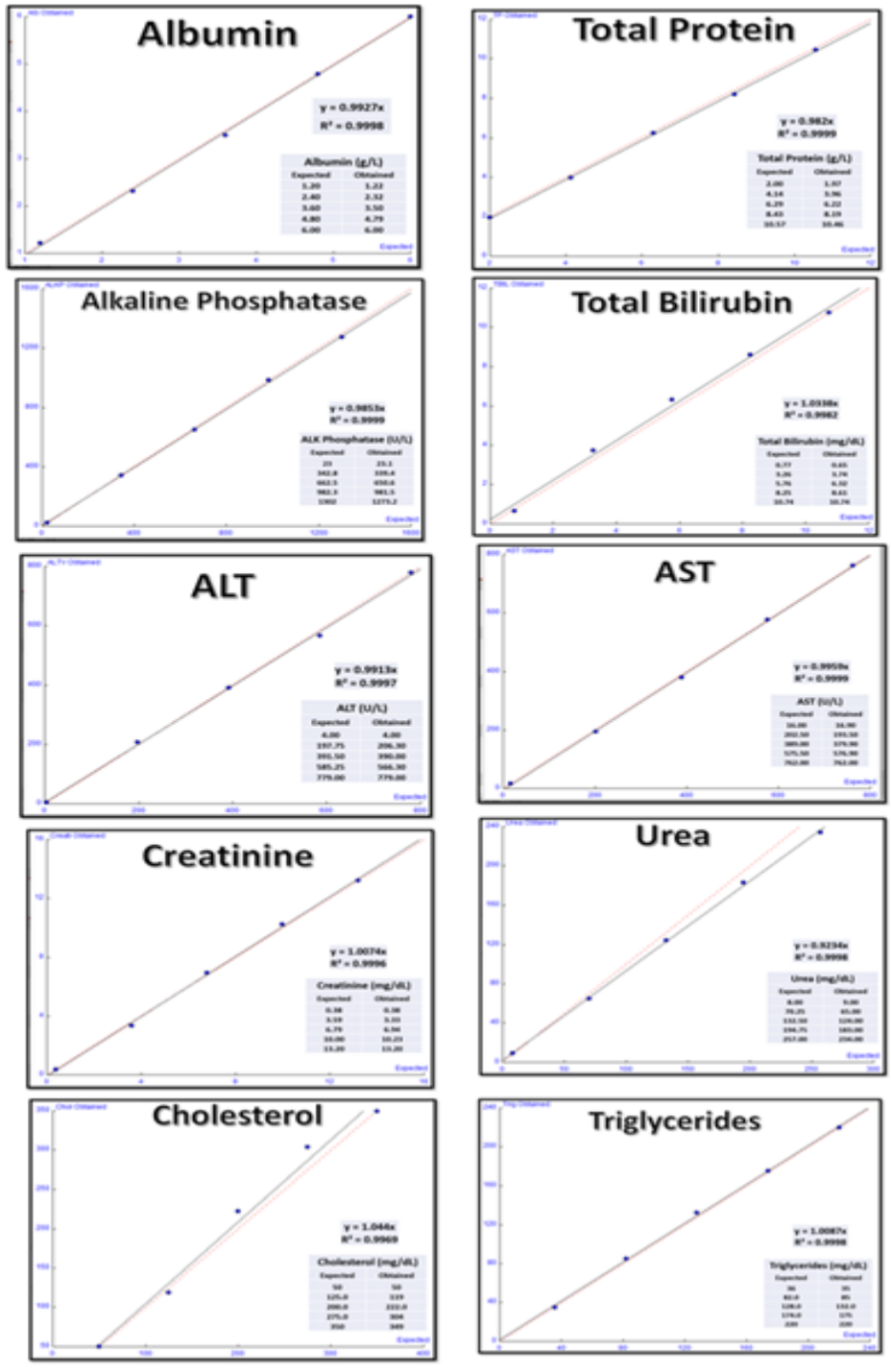


Fig. 1: Analytical Measurement Range Verification of analytes using VITROS XT Slides.

Method Comparison regression verification: The chemistries in the new VITROS XT slides are expected to perform similar to the current VITROS microslides in the patient samples and provide comparable results. To verify this, about 20 samples were performed in parallel in the VITROS XT 7600 system using both VITROS XT slides and VITROS microslides (single) and the results were compared by means of linear regression analysis. All the 10 chemistries in VITROS XT slide formats showed excellent correlation with the VITROS microslides (Fig.: 2) and showed similar comparable results with their corresponding VITROS (single) microslide assays. The slope is close to 1.0 for all the chemistries with range of 0.986 to 1.137 and intercept is close to 0 in the range of -3.6 to +3.4.

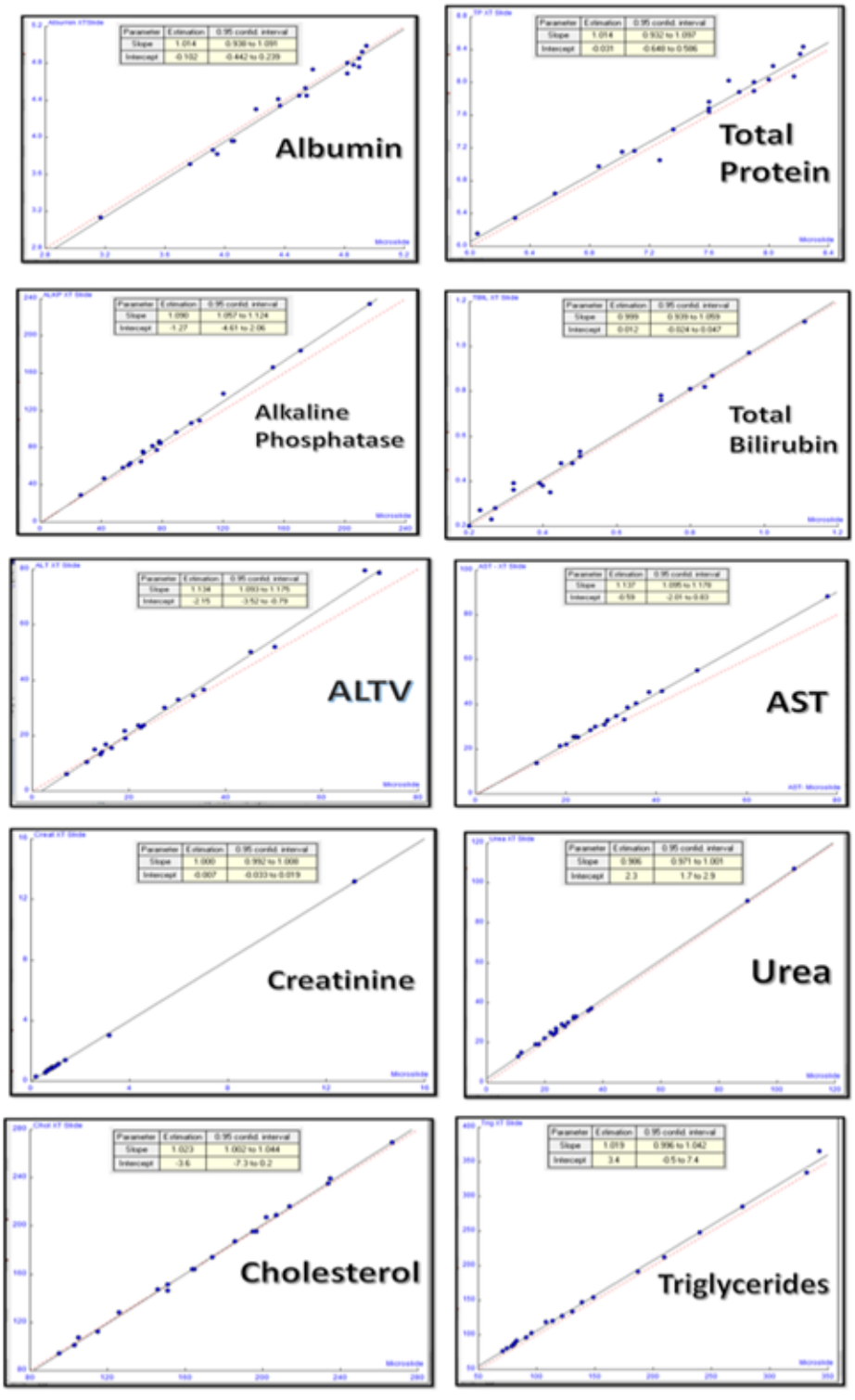


Fig. 2: Method comparison between VITROS microslides and VITROS XT Microslides

Turnaround time analysis: Testing a batch of about 2 samples, using VITROS XT slides vs VITROS microslides (single assay), we have observed around 10% improvement in the turnaround time. The average time taken is 22 min vs 24.5 min. The simulated calculation showed the throughput of the VITROS system in terms of number of tests per hour is improved from approx. 900 tests per hour to 990 tests per hour, with a decrease in the sample volume of approx. 48% (Table 3).

Analyte	Sample Volume (uL)	
	Microslide	XT Slide
Albumin	5.5	4.2
Total Protein	10	4.1
Alkaline Phosphatase	11	5
Total Bilirubin	10	5
ALT	11	3.5
AST	7	3.3
Creatinine	6	3.2
Urea	5.5	4.3
Cholesterol	5.5	3.9
Triglycerides	5.5	2.9
Total	77	39.4
Difference	37.6	48.8%

Table 3: Required sample volume for each assay in both VITROS Microslide VITROS XT Slide

Discussion: VITROS XT slides designed to assay two analytes, which are often requested together, in a single slide are unique by allowing two tests to be run together in a single test element, which is not currently done in any other chemistry system in the clinical chemistry laboratory on an automated analyzer. Only similar formats were observed for urine chemistry using urine strip methods. This study was undertaken to evaluate the performance of VITROS XT slides for 10 routine chemistries in pairs, viz., Albumin and Total protein; ALT and AST; Alkaline phosphatase and Total Bilirubin; Urea and Creatinine; Cholesterol and Triglycerides in the new VITROS XT 7600 integrated system. The study was done for the evaluation of bias (%), intra and inter assay precision, analytical measurement range and sample comparison with the regular VITROS microslides (single assay slides). All the 10 chemistries of VITROS XT slides showed acceptable performance in (%) as well as intra and inter assay verification study, except total protein assay, which showed imprecision slightly above the short-term and long-term precision goal based on one fourth and one third of RICOS. Total allowable error the possible reason is the very narrow specification of RIC OS Total allowable error (TEa) of 3.63% for total protein. Based on the total allowable error specified by other bodies like CLIA (8%); Rilibak (6%) and RCPA (5%) taken from Westgard website, the obtained intra and inter assay precisions are satisfactory. One of the major advantages of the new VITROS XT Slides is the minimized sample volume required for the assay when compared to VITROS single microslides. This feature is very beneficial for the pediatric and geriatric patient population where the collection of sufficient volume of sample is a great constraint. In addition, since two tests can be performed in a single analytical element, the turnaround time can be minimized to a greater extend. DiMagno et al., 2018 showed that with the usage of VITROS XT slides, the simulated throughput running the comprehensive metabolic panel increases from 681 to 976 tests /hr, a 43% throughput increase compared to the VITROS microslides

If only the XT Slides were used in the sample mix, a 100% increase in throughput would be realized. Furthermore, with the XT Slides, the storage requirement of the slides is reduced as cartridge for two chemistries can be accommodated, giving the opportunity to minimize the storage facility by approx. 40 – 50% therefore, economizing on the cold storage facilities and resulting in a reduction in the consumption of electricity. In conclusion, VITROS XT slides showed excellent performance with the exhibition of good correlation of assay results when the samples are processed in both VITROS XT and regular VITROS microslides with added advantages of reduced sample volume, reduced turnaround time, increased throughput and minimized storage space utility.

References:

1. Simona Ferraro, Federica Braga and Mauro Panteghini, Laboratory medicine in the new healthcare environment; Clin Chem Lab Med 2016; 54(4): 523–533.

2. Manchana Lakshman, B.Ravindra Reddy, P. Bhulaxmi, K. Malathi, Mahjabeen Salma and Swati Prakasham, Evaluation of sigma metrics in a Medical Biochemistry lab; IJBR 2015; 6(3):164 – 171.

3. Srinivas Chakravarthy, Satish Ramanathan, Smitha S, Vijayakumar KV, Thirumalai Nallathambi, Micheal S, Phoenix in the lab: The sigma metrics during Chennai's worst disaster: Monitoring and management of the Quality Management System (QMS); IJPLM. 2017;3(1):OA1.

4. James O Westgard, Basic Method Validation – 3rd Edition, Jan 2008, Published by Westgard QC.

5. Ricos C, Alvarez V, Cava F, Garcia-Lario JV, Hernandez A, Jimenez CV, et al. Desirable Biological Variation Database specifications [Internet]. Madison (WI): Westgard QC (US); c2009 [updated 2014]. Available from: https://www.westgard.com/biodatabase1.htm. Cited 22 Nov 2017.

6. James O Westgard (2019), Basic Method Validation – The Replication Experiment – Criteria for acceptable performance. Available from: https://www.westgard.com/lession22.htm.

7. Clinical and Laboratory Standards Institute (CLSI). EP 06 A – Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline, Wayne, PA: CLSI; April 2003.

8. Clinical and Laboratory Standards Institute (CLSI). EP 09 A3 – Measurement Procedure Comparison and Bias Estimation using Patient Samples; Approved Guideline – Third edition, Wayne, PA: CLSI; August 2013.

9. Ortho Clinical Diagnostics Performance Verifiers Training Module, 2018, Part No. J04498; Cat No. 6800325.

10. https://www.westgard.com/clia.htm

11. https://www.westgard.com/rilibak.htm

12. https://www.westgard.com/rcpa-biochemistry.htm

13. DiMagno T, Barbero M, Graby C, Huynh T. Development of the Novel and New Multi-Test VITROS® XT Chemistry Products Slides. 70th AACC Annual Scientific Meeting Abstracts B 488, 2018.

Returning Home on the Evening of a Heavy Snowfall

Dr. Tan It Koon

This painting was inspired by an ancient poem by a Tang Dynasty high-ranking government official, scholar and poet, Liu Changqing or 刘长卿 (709 - 789). It bears the title 《Seeking Shelter and Lodging at Mount Hibiscus on an Evening of Heavy Snowfall》or《逢雪宿芙蓉山主人。

The poem consists of 4 sentences of 5 words each is shown below:

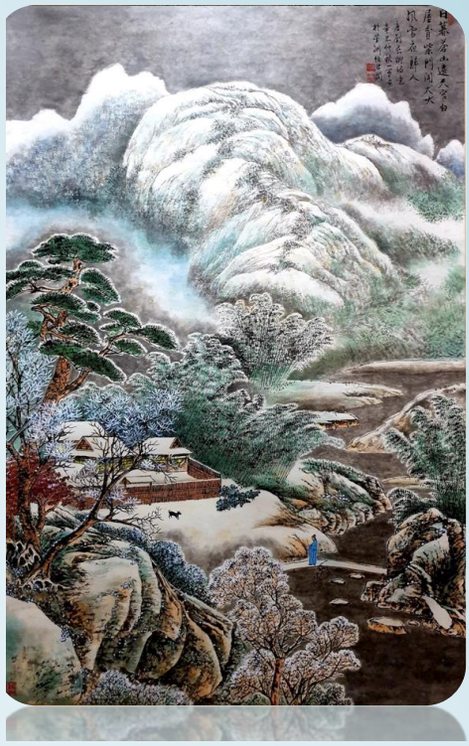
桃红復合宿雨，柳绿更带朝煙，花落家童未掃，莺啼山客猶眠。

"日暮苍山远，天寒白屋贫。

柴门闻犬吠，风雪夜归人"

It may be translated as follows:

"When twilight descends, the mountains appear to recede farther and farther away. As the weather becomes colder, the snow-covered cottages seem more pale and lonely. Suddenly the barking sound of a dog is heard at the wooden gate. It turns out to be someone braving the wind and snow to return home."



The full text of this poem was written in Running Script on the top right-hand corner of the artwork. The painting shows thick layers of snow covering all the mountains, trees, cottages and grounds. The river is also frozen, conveying a strong sense of chilliness. A black dog in front of a wooden gate breaks the silence and barks to welcome its master, who is crossing a bridge over the river in a hurry to return home.