Issue 3 December 2016

pathology@viapath

Message from the Editor

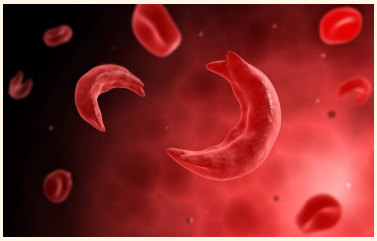
Welcome to the third edition of "pathology@viapath", an update on a selection of interesting projects and work being performed by Viapath's scientists as well as some of the fun events that have taken place.

In this edition, alongside the scientific content, there are some fascinating facts. For example, did you realise that, whilst folic acid is essential during pregnancy to prevent foetal abnormalities, too much folate supplementation may have adverse effects on other members of the population? Or that, whilst there are very few treatment options available for sickle cell disease, Viapath's scientists have been involved with a clinical trial of a new drug? Some of you may be aware that Viapath has a new CEO, but did you know that he competed in the Olympics?

Viapath is involved with many aspects of pathology, so if there are any topics that you would like to be covered in future editions of pathology@viapath, please get in touch!

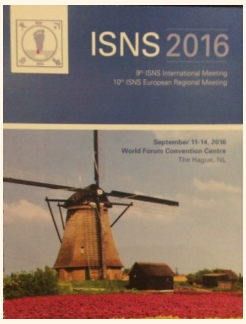
Inside this Issue:

Why the Implementation of a Mandatory Folic Acid Supplementation Should be Opposed in the UK



Assessment of Promising New Drug for Sickle Cell Disease

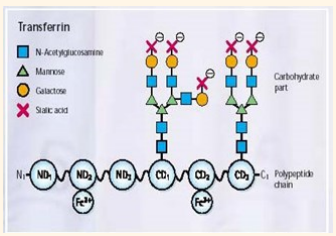
Testing Times to Come? Cancer Research UK's Evaluation of Pathology Capacity Across the UK



Conference Update: International Society of Neonatal Screening

Viapath Celebrates World Quality Day

Guy's Hospital Opens a New Cancer Centre



Carbohydrate Deficient Transferrin: A Marker of Chronic Excessive Alcohol Consumption

Viapath Leadership Update

You can keep up with more news from Viapath as well as sharing this edition of our newsletter on Facebook, Linkedin and Twitter.

Why the Implementation of a Mandatory Folic Acid Supplementation Should be Opposed in the UK

Folic acid is a synthetic compound which is used in supplements and fortified foods. Currently scientists around the world are debating the adverse effects of excessive folic acid use within the general population.

Folate and Folic Acid

Folate (vitamin B9) is essential for numerous metabolic processes including DNA synthesis and regulation of gene expression. Natural folate sources are found in a variety of foods such fruits, vegetables and grains. Deficiency of folate is common, with causes ranging from diet and lifestyle, to pathological and pharmacological processes and leads to macrocytic anaemia, peripheral neuropathy and increases the risk of neural tube defects (NTD) such as spina bifida and anencephaly.

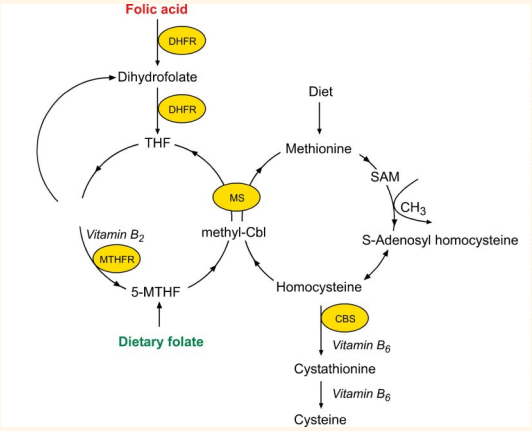


Figure 1: Folate and folic acid metabolism

Folic acid (Figure 1) is metabolised differently to naturally occurring forms of folates. It requires a two-step reduction, via dihydrofolate reductase (DHFR) before it has any coenzyme activity, and this occurs mainly in the liver. This reaction allows folic acid to be used for metabolic processes but most tissues, including the liver, have limited ability to reduce folic acid due to low activity of DHFR. It is also known that the process ofabsorption and biotransformation of folic acid to its active form (5-methyltetrahydrofolate) is saturated at doses in region of 200–400 µg of folic acid. The limitation of this metabolic process results in the inability to metabolise high doses of folic acid, which leads to the appearance of unmetabolised folic acid in the circulation. Since the consumption of folic acid has increased in many countries worldwide, either because of mandatory fortification or voluntary supplementation, concerns have arisen regarding the potential adverse effects unmetabolised folic acid may have.

Folic Acid Supplements

Because of the well-known role of folate in prevention of NTD, numerous countries have implemented strategies to increase folate intake, including mandatory grain fortification. As a result, the intake of folate in these countries is often higher than the recommended dietary allowance for many groups of people. Although folate is believed to be non-toxic, the potential adverse effects of excessive intake of folic acid have not been highlighted well by authorities. In the UK, mandatory folic acid supplementation has not been implemented; however, high-strength folic acid supplements and fortified foods, such as cereals and breakfast spreads, can be found in most food stores. In fact, Viapath's studies have shown that, in patients from the UK, cereals contributed to 26% of their total folate intake.

Despite studies showing positive results in relation to NTD in the USA, and many other countries such as Canada, Chile and Argentina, it has been debated as to whether this intervention should be implemented in Europe. Many countries in Europe do not fortify their grains with folic acid, partially due to earlier reports linking folic acid with cancer

Is there a Link Between Folic Acid and Cancer?

Folic acid intakes have been linked to increased cancer risk. Proposed mechanisms include folic acid enhancing DNA synthesis and replication within cells, while reducing the natural killer cell response to carcinogenic cells. For example observational research carried out in Chile by Hirsh et al. (Eur J Gastroenterol Hepatol, 2009) showed that after folic acid fortification was implemented in this country, there was a 162% increase in colorectal cancer in the 45–64 year group and a 192% in the 65–79 year group, compared with the pre-fortification period.

Conversely, studies which concluded that high levels of folic acid did not increase the risk of colorectal cancer have also been published. A study by Stevens et al. (Gastroenterology, 2011) showed that doses up to 660 µg per day caused no increased risk of colorectal cancer and suggested that doses up to 800 µg and day should not be expected to increase the risk of colorectal cancer.

Folic Acid and Pregnancy

Folic acid is very effective at preventing NTD but recent work from India by Krishnaveni et al. (Diabetologica, 2014) demonstrated that high levels of folic acid during gestation were associated with insulin resistance and greater adiposity in children at 5 years of age which may be contributing to increasing levels of childhood obesity and type 2 diabetes mellitus.

Folic Acid and Vitamin B12

Masking vitamin B12 deficiency with high levels of folic acid needs to be considered when folic acid supplements are taken, as the diagnosis and treatment of vitamin B12 deficiency may be delayed, potentially leading to irreversible neurological damage. Moreover high serum folate concentrations combined with low vitamin B12 status have been associated with an increased risk of cognitive impairment in subjects over 60 years old.

Studies have also shown that having a high folic acid to vitamin B12 ratio during pregnancy increases the risk of baby being small for gestation age (SGA) at birth. Being SGA may lead to increase rates of hypertension, coronary heart disease and type 2 diabetes mellitus in the middle aged.

In addition to above, recent studies on animals suggest that high levels of folic acid supplements may be hepatotoxic particularly for those with lower levels of the methylene tetrahydrofolate reductase (MTHFR) protein.

Folic Acid and Drug Interactions

Unmetabolised folic acid has been shown to interact with antiepileptics, possibly inducing seizures in patients taking drugs such as phenytoin, carbamazepine and phenobarbital. For example, studies looking at the interaction with phenytoin suggest that folic acid acts as a co-factor in phenytoin metabolism, with higher levels of folic acid increasing the efficiency of breakdown by raising the affinity of the metabolising hepatic enzymes.

What is the Future of Mandatory Folic Acid Fortification in the UK?

Folate is a vital component of a human diet, with deficiency causing impairment of many metabolic processes. However, in modern society with greater awareness, availability and access to folic acid, hypertoxicity rather than deficiency may become an issue and the excessive use of folic acid may impact on multiple areas of public health.

No clear consensus regarding the safety of folic acid has yet been reached and gaps in knowledge are still present. The debate about the adverse outcomes and lifetime exposure to folic acid excess continues.

In light of the evidence so far, suggesting additional supplementation with folic acid may be harmful to certain groups of people if their diet is assumed to be adequate in folate and absorption is normal. Countries planning on fortification strategies need to thoroughly assess all of the risks and benefits and the UK should oppose mandatory folic acid supplementation until this has been done.

For more information about the adverse effects of excessive folic acid use, please refer to the recent article:
Patel KR, Sobczyńska-Malefora A. **The adverse effects of an excessive folic acid intake**. Eur J Clin Nutr. 2016 Oct 12. doi: 10.1038/ejcn.2016.194. [Epub ahead of print] Review.PMID:27731331 https://www.ncbi.nlm.nih.gov/pubmed/27731331 or contact Dr Agata Sobczyńska-Malefora at agata.malefora@viapath.co.uk

For more information on folate status testing at Viapath, please refer to Viapath's website:
5-methyltetrahydrofolate (plasma/serum): http://www.viapath.co.uk/our-tests/5-methyltetrahydrofolate-plasma-serum
5-methyltetrahydrofolate (whole blood): http://www.viapath.co.uk/our-tests/5-methyltetrahydrofolate-whole-blood
Folate (serum): http://www.viapath.co.uk/our-tests/folate-serum
Folate (whole blood/red cells): http://www.viapath.co.uk/our-tests/folate-whole-bloodred-cells
Homocysteine: http://www.viapath.co.uk/our-tests/homocysteine

Other Publications Relating to Folic Acid/Folate from the Nutristasis Unit

1. Sobczyńska-Malefora A, Cutler J, Rahman Y. Elevated homocysteine with pseudo-homozygosity for MTHFR677T as predisposing factors for transient ischemic attacks: a case report. Metab Brain Dis. 2016 Oct;31(5):1205-8. doi: 10.1007/s11011-016-9875-1.PMID:27431289

2. Sobczyńska-Malefora A, Harrington DJ, Gorska R, Shearer MJ, Lomer MC, Sobczyńska-Malefora A et al. Hyperhomocysteinaemia and B vitamin intakes in patients with a history of cardiovascular disease. One Carbon Metabolism, Vitamins B and Homocysteine Conference; 2015; Nancy, France.

3. Bednarska-Makaruk M, Graban A, Sobczyńska-Malefora A, Harrington DJ, Mitchell M, Voong K, Dai L, Łojkowska W, Bochyńska A, Ryglewicz D, Wiśniewska A, Wehr H. Homocysteine metabolism and the associations of global DNA methylation with selected gene polymorphisms and nutritional factors in patients with dementia. Exp Gerontol. 2016 Aug;81:83-91. Doi 10.1016/j.exger.2016.05.002. Epub 2016 May PMID:27167582

4. Sobczyńska-Malefora A, Harrington DJ. Are vitamin supplements necessary for all? A role for vitamin status assessment. *The Biomedical Scientist*; Jan 2016

5. Sobczyńska-Malefora A, Harrington DJ, Lomer MC, Pettitt C, Hamilton S,Rangarajan S et al. Erythrocyte folate and 5-methyltetrahydrofolate levels decline during 6 months of oral anticoagulation with warfarin. Blood Coagul Fibrinolysis 2009; 20: 297–302.

6. Sobczyńska-Malefora A, Harrington DJ, Voong K, Shearer MJ. Plasma and red cell reference intervals of 5-methyltetrahydrofolate of healthy adults in whom biochemical functional deficiencies of folate and vitamin B 12 had been excluded. Adv Hematol 2014; 2014: 465623.

7. Sobczyńska-Malefora A, Harrington DJ, Rangarajan S, Kovacs J, Shearer MJ, Savidge GF. Hyperhomocysteinemia and B-vitamin Status after Discontinuation of Oral Anticoagulation Therapy in Patients with a History of Venous Thromboembolism. *CCLM,* 2003; 41(11):1493-1497

8. Schmeleva VM, Kapustin SI, Papayan LP, Sobczyńska-Malefora A, Harrington DJ, Savidge GF. Prevalence of hyperhomocysteinemia and the *MTHFR C677T* polymorphism in patients with arterial and venous thrombosis from North Western Russia.*Thrombosis Res* 2003; 111:351-35

Assessment of a Promising New Drug for Sickle Cell Disease

What is Sickle Cell Disease?

Sickle Cell Disease is an inherited disease of haemoglobin and gets its name from the resulting, unusually shaped, red blood cells. The disease is a serious, lifelong condition, associated with anaemia, intermittent episodes of pain and other acute and chronic complications including stroke and renal failure, but there are very few treatment options available.

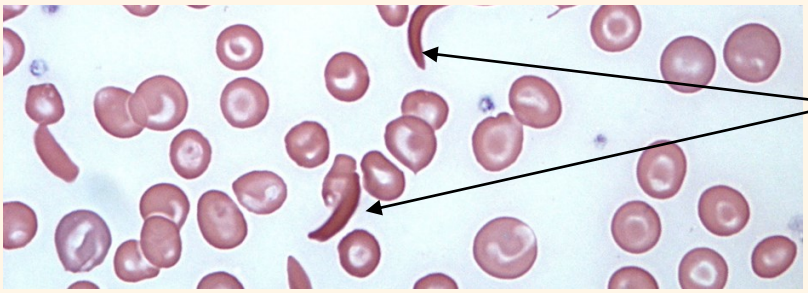


Figure 1: A blood film showing Sickle Cells (as indicated by the arrows)

A New Drug Trialled

Viapath's Special Haematology Team, at Guy's Hospital, have been involved in a randomized, placebo-controlled, double-blind, phase I/II clinical trial with a new treatment drug called GBT440. The results were promising as the drug was well tolerated by the patients who exhibited decreased haemolysis and increased haemoglobin levels with an increased affinity for oxygen shifting the curve towards normal. GBT440 will start a phase 3 clinical trial in 2017.

The results from the initial drug trial were presented at the American Society of Hematology meeting in December see: https://ash.confex.com/ash/2016/webprogram/Paper95146.html.

How was the Efficacy of the Drug Measured?

One of the effects of GBT440 is to increase the oxygen affinity of haemoglobin and so the initial trial used P50, a measurement of the affinity of haemoglobin for oxygen, as an indicator of the efficacy of the drug . This functional assay produces an oxyhaemoglobin dissociation curve, which relates oxygen saturation and partial pressure of oxygen in the blood (PO2), and hence is used to indicate whether the drug has altered the haemoglobin's oxygen affinity. The PO2 at which the haemoglobin is 50% saturated, is known as the P50, the higher/lower the value, the greater the affinity of the haemoglobin for oxygen, and allows an assessment of how readily oxygen is taken up and released to the tissues by the red cells.

P50 Analysis in Patients with Unexplained Erythrocytosis

The P50 analysis for the GBT440 trial was carried out in the Viapath Special Haematology Laboratory at Guy's Hospital, one of the few centres offering this test in the UK. Although the P50 measurement was an important factor in assessing the efficacy of the GBT440 in the phase I/II trial, in clinical practice it is more frequently requested to exclude a high affinity haemoglobin as part of the recommended investigations for patients with unexplained erythrocytosis and guidelines can be accessed at:
http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2005.05535.x/full

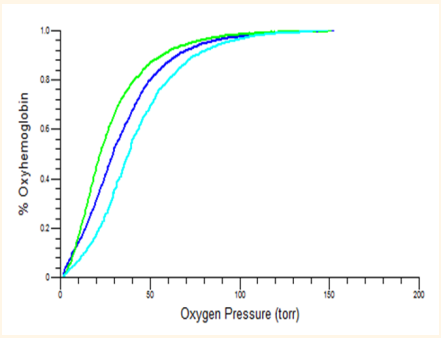


Figure 2: Examples of P50 curves

Key: **Dark blue**: normal curve
Green (shifted left): a high affinity haemoglobin, Hb Yakima
Light blue (shifted right): Sickle Cell Disease.

Please contact the laboratory for any enquiries regarding P50 analysis on:
0207 1883 421

Or via email:

Dr Yvonne Daniel, Consultant Scientist: Yvonne.daniel@viapath.co.uk
Tracey Mare, Senior Biomedical Scientist: Tracey.mare@viapath.co.uk
Daniel Dos Santos Monteriro, Senior Biomedical Scientist: Daniel.monterio@viapath.co.uk
Leanne Kelly, Senior Biomedical Scientist: Leanne.kelly@viapath.co.uk

Testing Times to Come? Cancer Research UK's Evaluation of Pathology Capacity Across the UK

Whilst cancer survival is at its highest ever level, health services are under considerable pressure. Increasing cancer incidence, an ageing population and efforts to improve outcomes means that the demand for cancer diagnostics has never been higher. Cancer Research UK, the world's leading cancer charity, commissioned research to understand the pressures facing pathology services across the UK and to identify solutions to address these issues.

By 2035, 500,000 people could be diagnosed with cancer in the UK each year: ensuring diagnostic services can cope with future patient demand is essential

The evaluation was conducted by 2020 Delivery and involved interviews with 25 different pathology providers, a survey of 11 laboratories and use of centrally collected data. Cancer Research UK gave a special thanks to the Northern Ireland Pathology network and David Wells from Viapath for making considerable time to support the research. The research focussed on the pathology disciplines most relevant to cancer: cellular pathology (which encompassed both histopathology and cytopathology); blood sciences; and molecular pathology.

The comprehensive report outlines the current landscape within these pathology disciplines and comments that, based on the number of pathologists currently in training and the age profile of the current workforce, there is likely to be a severe crisis in pathology capacity within the next five to ten years and immediate action is needed to avert a crisis in pathology capacity and ensure the service is fit for the future.

The report makes the following recommendations:

ENSURE PATHOLOGY SERVICES ARE MAXIMISING EFFICIENCY

RECOMMENDATION 1: NHS England and NHS Improvement should continue to support Sustainability and Transformation Plan Footprints areas (STPs) and Trusts to consolidate pathology services, in order to facilitate testing taking place at the appropriate level.

OPTIMISE THE PATHOLOGY WORKFORCE

RECOMMENDATION 2: Trusts and their pathology departments, supported through guidance from professional bodies and NHS England, should:

1. Ensure biomedical scientists (BMS) are being utilised to cut up specimens where possible, in accordance with 'Principles of Good Practice for Biomedical Scientists Involved in Histopathological Dissection.'
2. Explore the role of clinical scientists to support complex diagnostics and research. Clinical Scientists input should be recognised in their job plans with backfill provided for existing duties.
3. Develop graduated increase in trainee responsibility. The Royal College of Pathologists should update and promote their guidance document.
4. Ensure widespread use of BMS reporting following their completion of the Biomedical Scientist reporting programme.

RECOMMENDATION 3: Health Education England should include either cellular and molecular pathology within their review of the cancer and related workforce, to enable longer-term workforce planning. The Royal College of Pathologists should continue to run programmes aiming to attract more staff to cellular pathology.

RECOMMENDATION 4: In considering the new consultant contract, the Department of Health and NHS England should consider the impact on near-retirement consultants.

FUTURE-PROOF PATHOLOGY

RECOMMENDATION 5: There should be continuous support from the NHS, researchers, funders and professional bodies for the CM-Path initiative and delivery of the four work streams within its strategy. Workforce initiatives should allow pathologists to spend time on research. The recommendations from 'Every Patient a Research Patient' should also be implemented to encourage a more positive research environment in the NHS, including investment in academic pathology training posts and chairs.

RECOMMENDATION 6: Departments and Trusts should invest in infrastructure to support digital pathology and businesses/researchers should look at how to make this worthwhile. Sharing results and on-screen examination of histological slides should both be utilised in the short term to enable more efficient, networked services. Electronic requests should also be used.

RECOMMENDATION 7: Molecular pathology should be more involved with the whole diagnostic process for solid tumours (including how molecular pathology results are reported), in a similar way to blood cancer. This should be facilitated through better IT connectivity and closer working between relevant staff.

IMPROVE UNDERSTANDING OF PATHOLOGY PROVISION

RECOMMENDATION 8: NHS Trusts should invest in technology so departments can comply with requirements to supply pathology data to the Cancer Outcomes and Services Dataset (COSD). The Royal College of Pathologists should pro-actively collect comprehensive workforce information from departments across the UK.

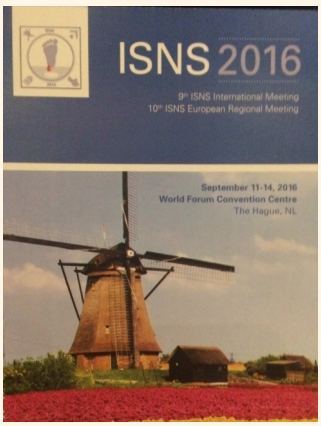
RECOMMENDATION 9: The impact on pathology should be factored into NHS workforce and resourcing plans to ensure that pathologists and clinical scientists are involved in the dialogue.

Conference Update from Viapath's Rosalind Bray and Ian Hutton at The International Society for Neonatal Screening

The UK currently screens for 9 conditions, while some states in the US screen for 50

The International Society for Neonatal Screening (ISNS) aims to advance screening for neonatal and infant disorders, enhancing the quality of testing and medical services through dissemination of information, guidelines and best practices to help to ensure protection of babies from life-quality threatening conditions.

This year the ISNS Conference was held in The Hague, Netherlands, and as usual a huge array of topics were covered including the Wilson and Junger screening criteria (which were first published in 1968), bloodspot quality and worldwide screening programmes.



It was a privilege to hear Wilson and Junger's own children speaking and the first session addressed whether the screening criteria are still fit for purpose in the modern day, particularly with recent advances in genetic screening. Discussion centred on the international differences in evaluation criteria for the inclusion of screening programmes, with the UK currently screening for 9 conditions (including cystic fibrosis and sickle cell anaemia) but some US states screening for 50.

How is Newborn Screening (NBS) Evolving in Developing Countries

Interesting examples of NBS programmes in developing countries included:

A smartphone app that allows for real-time results as opposed to a TAT of 2-3 days

- Screening across the Philippines, which has more than 7000 islands, has seen significant developments over the last twelve years. They currently have 5 screening laboratories with follow-up clinics in 14 regions. Special emphasis was put on ensuring public awareness of the NBS programme, including a National NBS Week with information disseminated via TV adverts, on billboards, online and in newspapers. Although still challenging, especially with the number of home births occurring, coverage has increased significantly over the years with many hospitals achieving special recognition for screening more than 90% of babies in their area.

- A Smartphone Thyroid Stimulating Hormone (TSH) point of care app, currently being trialled in China, enabling the measurement of TSH and provision of a result in real-time (as opposed to a 2-3 day wait). This could be a useful technique for collecting results on patients in remote, rural communities as if there is a problem, it can be managed immediately removing the difficulty of finding the child again.

- The pilot Nepalese screening programme which currently involves flying samples between Nepal and Switzerland. This poses many issues, such as delayed transit, lack of education within Nepal itself and sustainability of the programme. However, it is hoped that the results of the pilot could help persuade the government to fund their own in-house programme in the future.

Why do Tandem Mass Spectrometry (MSMS) Screening Results Vary Between UK Screening Laboratories

Viapath's Dr. Rachel Carling presented a talk on the variability of MSMS screening results between UK screening laboratories. Variability stems from the different methods used by NBS labs, commercial versus home brew kits and different models of MS. Rachel explained the efforts to try and harmonise laboratories, including using a common internal standard, by citing work that was made possible by an award from Viapath's Innovation Fund. Other analytical discussions included the future of automated screening. There was special interest in new devices to collect samples, which can be linked with automated sample preparation. These devices could eliminate bloodspot cards and remove manual punching, potentially reducing punching errors and issues related to bloodspot card quality.

Why Patient Advocacy Groups are Valuable

The final session covered patient advocacy groups and patients' influence on driving forward screening programmes. John Hall showed how parents of phenylketonuria (PKU) children pushed clinicians and laboratory scientists to discover ways to detect and screen for PKU. John highlighted how the persistence of these parents helped to ensure a screening programme for PKU was started.

Advocacy groups continue to be an important part of decision making and with screening programmes continuing to expand across the world, it is important that their voices are heard.

Viapath's Posters on Newborn Screening:

1. Performance Monitoring in Newborn Screening - a Co-ordinated National Approach, Kate John, Jim Bonham, Christine Cavanagh and Rachel Carling (http://www.viapath.co.uk/articles-and-papers/performance-monitoring-in-newborn-screening-a-co-ordinated-national-approach)

2. The Retrospective Audit In Decline Rates In The South East Thames Screening Laboratory, Rosalind Bray, Rachel Carling (http://www.viapath.co.uk/articles-and-papers/a-retrospective-audit-in-decline-rates-in-the-south-east-thames-screening

For further information contact ian.hutton@viapath.co.uk or Rosalind.bray@viapath.co.uk

Figure 1: Ian Hutton presenting his poster on bloodspot stability at ISNS

Figure 2: Rosalind Bray presenting her poster on NBS decline rates at ISNS

Viapath Celebrates World Quality Day

World Quality Day (WQD) takes place every November and was introduced by the United Nations in 1990. The day was designed to increase worldwide awareness of the important contribution that quality makes towards a nation's and an organisation's growth and prosperity. Its aim is for quality leaders within an organisation to spread the importance of quality to non-quality professionals.

Viapath raised over £2,000 for Cancer Research UK

Quality is at the centre of all we do at Viapath and Professor Jonathan Edgeworth, Viapath's Medical Director, has defined quality as 'The right result on the right specimen for the right patient, that is accurate, timely and properly interpreted every time, as part of a positive service experience for patients and customers alike.'

Since 2014, Viapath has been organising team challenges across all its sites, based on a theme set out by the Chartered Quality Institute (CQI). In 2014 the Viapath quality pledge was created as a result of the outcomes of that year's WQD. This pledge was designed to ensure that quality is at the forefront of everything Viapath does.

"We pledge to continually improve our services by listening to our patients, customers and colleagues and taking positive action as the result of each interaction."

Viapath Future Leaders in Innovation (FLiI) are a group of talented and skilled individuals who are being developed to become the scientific and business leaders of the future; they are fast becoming a powerful force for positive change and innovation at Viapath. 2016 saw a change in the theme of challenges set out by Viapath's FLiI team. In previous years the tasks had revolved around sporting challenges including swimming, cycling and running.

Figure 1: Viapath employees taking part in the pool tournament

This year saw our teams use logic, intellect and problem solving skills in a series of challenges comprising of an escape room, a scavenger hunt around London and a pool tournament. Each of these challenges included a sub challenge for the teams to complete with quality at the centre. The day was a huge success, enjoyed by all and supported by the amazing donations from individuals, across all Viapath's sites, and through cake sales to raise over £2,000 (and still increasing) for Cancer Research UK.

You can read more about our commitment to quality on our website and view all the pictures from the day on our Facebook page

Quotes from World Quality Day

'This year's World Quality Day challenge was a little different to previous years, capturing many new volunteers to join our site specific teams, which was fantastic! The day was great fun, with all teams really getting in to the spirit of the challenges. I am thrilled we raised so much money for Cancer Research UK as they were a great support when it came to the fundraising aspect of the day. Bring on World Quality Day 2017!' Louise James, Specialist Biomedical Scientist, Viapath

"This year Viapath's third World Quality Day challenge event involved all six Viapath sites and raised over £2,000 for Cancer Research UK. It was a great way for people on each site to get to know each other and the importance of quality at Viapath as well as having some fun in the process." Dr. Katharine Bates, Senior Clinical Scientist, Viapath

Guy's Hospital Opens a New Cancer Centre

Designed by Patients for Patients

On September 26th, one of Viapath's founding trust hospitals, Guy's Hospital, opened the doors to a new state of the art Cancer Centre. This patient- centred, clinically-led and research driven centre represents a significant leap in the journey to transform cancer treatment, care and research by encompassing the majority of Guy's and St Thomas' cancer treatments and research into a single building.

During the planning and design of the building there was significant staff involvement from medical, nursing and scientific backgrounds as well as patients. This has resulted in a state of the art Cancer Centre that puts patients first. The building is divided into 4 villages; the Welcome Village, Radiotherapy Village, Outpatients Village and the Chemotherapy Village, represented by the needs of patient treatment and management pathway.

How Are Viapath Involved in the Treatment of Patients in the Cancer Centre?

Viapath will be playing a key role in the treatment of patients by providing an on site dedicated phlebotomy and haematology testing service via a mini lab.

As front line staff, Viapath phlebotomists are only too aware of the fact that behind every test there is a patient. The Phlebotomy department provides a service on the Ground Floor of the Welcome Village between the hours of 08.00 and 18.30 Monday to Thursday and till 15.30 on a Friday. In addition to being bled via a direct venous method, Cancer Centre patients are bled from either a peripherally inserted central catheter (PICC) or a central venous catheter (Hickman Line) which is often used for administrating chemotherapy and other medicines.

All Full Blood Count Samples are run within minutes by the Viapath Haematology mini lab, so that the results are available for other clinical staff to see before the patients consultations. The remaining Blood Sciences samples are processed urgently by the laboratories at Guys Hospital so that if the patient needs to have treatment the same day then appropriate decisions can be made.

More recently, Viapath's "Mohs" Service, one of the largest units within the UK, moved into the new Cancer Centre within the dermatological laser surgery unit housed in the Outpatient's Village to support the holistic approach to patient care. The Mohs Service was fully operational by the end of October and the unit looks forward to building the service in the future to reflect a centre of excellence provision for Mohs within the UK

Figure 1: Viapath Phlebotomists at the Cancer Centre

What is Mohs Surgery?

Mohs micrographic surgery is a specialised method for removing certain types of skin cancer and was first developed by Frederic Mohs in the 1930s.

Over the last decade in the UK (between 2002-2004 and 2011-2013) malignant melanoma incidence rates in males and females have increased by 46% (Cancer Research UK). Traditionally, operations for treating skin cancer surgically have involved removal of the area affected by the skin cancer together with an area of healthy unaffected skin, around and below the skin cancer in order to remove the entire cancer.

Mohs micrography surgery is often used for the removal of a type of common skin cancer known as a basal cell carcinoma (BCC) but often recommended for the removal of other types of skin cancer, for example squamous cell carcinoma (SCC) and lentigo maligna melanoma (LMM) as these types frequently arise on the head and neck areas where minimising surgical wounds is important. The Mohs Service is a highly effective method for removing skin cancers and has a cure rate of 99% for primary (new) tumours and 95% for recurrent tumours (British Association of Dermatologists, 2016).

How is Mohs Surgery Performed?

The Viapath laboratory specialises in Mohs and slow Mohs micrographic surgery techniques for the removal of skin cancers. The procedure is a very precise and detailed method which involves the skin cancer being removed a thin layer at a time, with a small margin of healthy skin surrounding it, keeping the wound as small as possible. Each layer of skin is removed and examined under a microscope in horizontal sections until all of the cancer has been fully removed. This method allows the patient and the surgeon to be almost certain that the skin cancer has been removed on that day, rather than waiting the 2 weeks it takes for traditional surgically removed skin cancer results.

Fulfilling the Vision

"The Cancer Centre operational team and Viapath worked in partnership to provide an enhanced blood testing service in the Cancer Centre. Viapath representatives were instrumental in the current design of the service that is now in place. The aim is to bleed all patients within 15 minutes and ensure all FBCs are turned around in 15 minutes so that the results are available to clinicians in clinic. This will improve patient experience through shorter waits and with the FBC results now available in clinic to inform the consultation. Together we will strive to further improve the experience for patients and clinical team." Dr Majid Kazmi; Consultant Haematologist, Guy's and St Thomas' NHS Trust and King's College Hospital

Carbohydrate Deficient Transferrin: A Marker of Chronic Excessive Alcohol Consumption

What is Carbohydrate Deficient Transferrin (CDT)

Transferrin is a 80kDa glycoprotein, synthesised in the liver and is the main iron transporting protein in the blood. The molecule is a single polypeptide with two N linked-side-chains. After its amino acid sequence has been formed, transferrin undergoes further modification by the addition or removal of carbohydrate (sugar) side-chains. This process is under the control of two enzyme systems; one which adds the side-chains (glycosyl transferases) and one which removes them (sialidases). This results in transferrin being exhibited in various isoforms and, based on the sialic acid content, there are up to seven of these, 3-5 of which can appear in the blood of normal subjects.

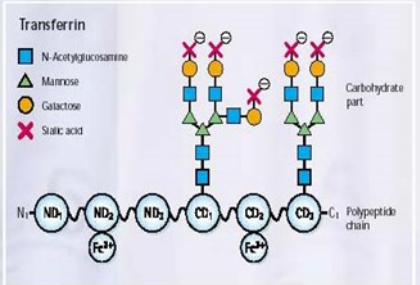


Figure 1: Molecular Structure of Transferrin

Carbohydrate Deficient Transferrin (CDT) is the term used for the group of isoforms of transferrin which are deficient in sialic acid residues, hence the term 'carbohydrate deficient transferrin'. The asialo (without a side-chain), monosialo (1 side-chain) and di-sialo (2 side-chains) isoforms of transferrin are collectively called CDT.

Alcohol appears to have a direct effect on the enzyme systems involved in regulating the transferrin side-chains; it inhibits the enzymes adding the side-chains and stimulates the enzymes removing the side-chains. Thus excessive and repeated alcohol consumption modifies the isoforms' distribution, resulting in an increase of the less sialylated forms, disialo and asialo (CDT). This means that CDT can be used as a marker of excessive alcohol consumption

CDT—A Marker of Chronic Excessive Alcohol Consumption

The most accurate way to use CDT as a biomarker for excessive alcohol consumption is to express its concentration as a percentage of total transferrin, thereby avoiding falsely high or low test results that may be due to very high or low total transferrin concentrations, and this utilisation of %CDT is approved by the US Food and Drug Administration (FDA) as a clinical diagnostic test for the detection of heavy alcohol consumption.

In normal individuals, CDT comprises of less than 1.6% of the total transferrin concentration. However, individuals that misuse alcohol typically have a higher proportion of transferrin as CDT (>2%) but, as the half-life of the protein is 7-28 days (i.e. the time it takes for the protein to be cleared from the circulation), the excess intake of alcohol would need to fall within this time period.

CDT is not a good marker of occasional excessive alcohol intake or binge drinking. However, CDT is a better marker of excessive alcohol misuse than the traditionally used markers of γ-glutamyl transferase (GGT) and mean corpuscular volume (MCV), due to the fact that it is not affected by mild alcohol-related liver disease, fatty liver (due to obesity, diabetes etc), chronic disease or B12/folate deficiencies.

It had been reported that in subjects potentially misusing alcohol CDT has 95% specificity i.e. 19 out of 20 times the increase in CDT level is due to excess alcohol intake.

There are three major genetic variants of transferrin in humans

1. Type C: common form with a prevalence 95- 97 %
2. Type B: extremely rare (only 20 cases so far identified) but causes false low CDT values
3. Type D: rare (less common in Caucasians but more common in Africans) but causes false high CDT values.

Types B, C, D can be separated on the basis of their charge but are indistinguishable antigenetically. Therefore, it is recommended that analytical methods based on charge separation are used in CDT testing, rather than immunoassays, to reduce the interference from type C and D variants.

Method Used to Measure CDT at Viapath

The Capillary Electrophoresis (CE) method (Capillarys 2, Sebai) is used to for CDT testing at Viapath. The CE provides a visual account of all isoforms present in the sample enabling determination of potential interferences such as paraproteins and complement degradation products. This method also enables the identification of the genetic variants of transferrin that may give false positive CDT value.

CDT Service at Viapath

A CDT service has been offered by the Metabolic Section of Viapath's Reference Biochemistry Laboratory for more than 10 years and this service is available to both internal and external users. Presently Viapath is providing this service to the Driving Vehicle Licencing Agency (DVLA) and is used as an important part of the decision-making process for the reissuing of driving licences.

CDT testing is run every day and TAT is two working days. Last year 26,000 tests were performed.

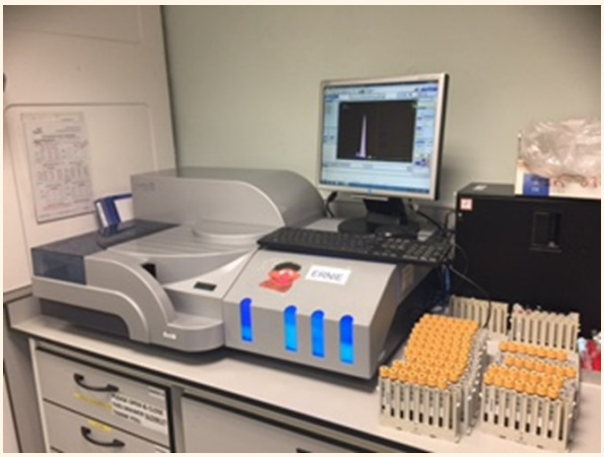


Figure 2: Capillarys 2 (Sebia)

Sample Requirements and Stability

Only serum should be used as EDTA/Heparin anticoagulants may disturb Fe^{3+} in-vitro TF saturation and may give false positives. Also, a blood sample stored unseparated for more than four days may give a false positive result so the sample should be separated within 2 hours of collection and then the serum sample is stable for 1 week if stored at 4C or for a longer period if stored at -20C

Figure 3: Viapath's Metabolic Team

For any Clinical enquires please contact
Dr Hagosa Abraha: h.abraha@nhs.net

For sample requirement or any further enquires contact the Metabolic Laboratory at
020 3299 4128 or visit the Viapath website: http://www.viapath.co.uk/our-tests/carbohydrate-deficient-transferrin-cdt

References:

1. K.Wolff , S.Gross, E.J.Marshall, N.Walsham, N.Durani, F.Keaney and R. Sherwood (2010) The Role of Carbohydrate Deficient transferrin an Alternative to Gamma Glutamyl Trasferase as a marker of Continuous Drinking in High Risk Drivers. Road Safety Research Report, No 104, Department of Transport, London

2. Keating, J., Cheung, C., Peters, T. J., Sherwood, R. A. (1998) Carbohydrate deficient transferrin in the assessment of alcohol misuse: absolute or relative measurements? A comparison of two methods with regard to total transferrin concentration. Clinica Chimica Acta. 27;272(2):159–69

Viapath Leadership Update

We're excited to announce that Viapath has a new Chief Executive Officer. Dougie Dryburgh has been working for Viapath for several years as our Chief Operating Officer and was recently promoted to lead the Company on its growth journey. We're delighted to have someone who knows our pathology business leading our organisation.

Dougie has an interesting career history. Originally serving in the RAF, he joined Viapath from his role as Group Operations Director at NHS Blood and Transplant. Dougie is a keen sportsman and he's an expert at throwing stones down ice rinks - he led the GB Curling Team at the Winter Olympics in 1998. Here's a picture of him in action back in '98!

Viapath is a provider of pathology services, a scientific organisation with a clinical purpose.

Viapath is majority-owned by the NHS

For Customer Service related issues please contact our dedicated team on:

020 7188 9684 or 0203 299 1741
customersupport@viapath.co.uk

Viapath
Francis House
9 King's Head Yard
London
SE1 1NA

viapath
pioneers in pathology

www.viapath.co.uk

You can keep up with more news from Viapath as well as sharing this edition of our newsletter on Facebook, Linkedin and Twitter.