Quadratech Diagnostics Ltd

P.O. Box 167
Epsom
Surrey
KT18 7YL

Phone: 020 8786 7811
Fax: 020 8786 7822
E-mail: quadratech@btinternet.com
Web: www.quadratech.co.uk

STOP PRESS

CE marked Stago methods are available for the Coatest classic APC resistance assay and using FV deficient plasma.

Exhibitions in 2009

Quadratech will be at the following exhibitions this year. Make sure to come and visit us on our stand.

September 2009

28th -30th : IBMS Congress, Birmingham

October 2009

7th -9th : BSHT, Newcastle

November 2009

10th: Near Patient/POC INR Testing Meeting, Sheffield

Stand 406

This ends the year for Quadratech as far as scheduled exhibitions and meetings go. We trust you found those you attended both beneficial and enjoyable. We look forward to seeing you all next year when the exhibition season starts all over again.

Focus on Fibrinogen

Fibrinogen is a coagulation factor, otherwise known as Factor I, which is essential for blood clot formation. It was first isolated from horse plasma by Hammarsten in 1876, although the existence of an inactive precursor of fibrin was proposed nearly 20 years earlier.

Fibrinogen is an abundant plasma glycoprotein which is synthesised in the liver. The intact molecule is composed of 3 pairs of disulphide bound polypeptide chains called Aα, Bβ ,and λ. It is a triglobular protein consisting of a central E domain and terminal D domain. Both these domains contain important binding sites for the conversion of fibrinogen to fibrin, for fibrin assembly and cross linking, and for platelet aggregation.

In the event of tissue damage or blood vessel injury fibrinogen is one of the many clotting factors released.

> "FIBRINOGEN IS ESSENTIAL FOR BLOOD CLOT FORMATION"

A rapid cascade system activates the clotting factors in turn, with fibrinogen bringing up the rear. Thrombin cleaves fibrinogen to transform it from soluble monomers to insoluble gel-forming fibrin. Fibrin polymers cross link forming a fibrin clot, which is stabilised by Factor XIIIa.

Low levels of fibrinogen impair the ability to form a stable blood clot, and are seen in a number of conditions. Decreased production of fibrinogen is seen in inherited conditions such as afibrinogenemia or hypofibrinogenemia, also in acquired conditions of liver disease and malnutrition. Over consumption of fibrinogen in conditions such as DIC and abnormal fibrinolysis also lead to low levels.

However, elevated levels are also a concern as they can result in an increased risk of developing blood clots. Elevated levels may be seen with acute infections, cancer, coronary heart disease, myocardial infarction, stroke, inflammatory disorders and trauma.

Both Hyphen Biomed and Affinity Biologicals have a range of fibrinogen products to facilitate the monitoring of fibrinogen levels. They include complete EIA kits, deficient plasmas, control plasmas, polyclonal antibodies and matched pair antibody sets.

Please contact Quadratech for further details about these and other products.

Q News & Views

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Quadratech Diagnostics Ltd

Special points of interest:

- *Drinking can be good for you!!!*
- *Crush syndrome - the importance of early diagnosis*
- *Reaffirming the importance of rapid tests*
- *A modern twist on APC resistance detection*
- *Focus on Fibrinogen*

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Quadratech news

Since our last newsletter in April the news has been full of all sorts of scandalous doings by those in positions who should know better. But this has been overshadowed by the worldwide focus on swine flu. The good news is, at time of writing, the cases of swine flu in the UK are dropping. However, with the usual flu season fast approaching there is likely to be a significant rise again. The decision whether to test for swine flu seems mixed. However, the Scottish government recently returned to laboratory testing to detect new cases of swine flu over concerns about the effectiveness of clinical diagnosis alone. This re-focus on the importance of laboratory testing seems a wise precaution but puts increased pressure on already overworked labs. With the flu season looming the US CDC has warned us all not to be blinkered by swine flu. Labs should not just focus on H1N1 testing but continue with broad flu virus screening as usual.

With this advice ringing in our ears, Quadratech trust you and your loved ones have not been adversely affected by swine flu and hope you keep well as we enter the traditional flu season.

As expected, the last few months have been busy with exhibitions near and far. The latest of which was the ISTH in Boston, USA, where we joined Hyphen Biomed on their stand. For the meeting Hyphen produced a number of posters about their haemostasis products and showcased their newest assays. Please see Hyphen News on page 3 for more details.

Hyphen at the ISTH

The next exhibition in our calendar is the IBMS Congress. This is being held in Birmingham between the 28th and 30th of September 2009. Tickets for the exhibition are free, if you have not got yours yet we have pdf versions we can email you - let us know if you want one (page 4 for contact details). We hope to see you there on stand 406.

Your health!

Recent health news has included a male midwife telling mothers that a drug free birth is the way to go, then we hear swearing helps increase your tolerance to pain - are these two related I wonder? But the best news is that a few drinks help to reduce the risk of dementia.

It has been found that if you are already a moderate drinker (8-14 drinks per week) and have no existing memory problems you are 37% less likely to be at risk from dementia.

From animal studies it would appear that low amounts of alcohol helps stimulate the brain chemical acetylcholine, which is important for memory.

A drink a day keeps dementia at bay!

So, in the spirit of all things healthy Quadratech would like to invite you to our stand (406) at IBMS and enter our wine draw, also join us at happy hour in a bid to keep dementia at bay.

Myoglobinuria and crush syndrome

Crush syndrome occurs due to prolonged crush injury to a large mass of skeletal muscle. This leads to severe systemic ischaemia and permeability of the cell membrane resulting in leakage of potentially toxic cell contents, including myoglobin. During entrapment the released cell contents are largely restricted to the damaged site but when pressure is removed from the crushed limb the contents enter the circulation and can result in the death of the victim. Death is mainly due to renal failure with myoglobinuria as a contributing factor. Crush syndrome, or Bywater's syndrome, was first described by Bywater in the British Medical Journal in 1941 after the London Blitz. These days crush injury is seen in victims of natural disasters, building collapses, industrial accidents such as those occurring in mining, as well as road traffic accidents.

RTAs: a major cause of crush injury

Myoglobin is an intracellular haem protein, found in skeletal and cardiac muscle, where it acts as an oxygen reservoir. Its presence outside the muscle cells indicates muscle cell damage has occurred. Once released myoglobin is very rapidly cleared from the bloodstream via the kidneys and eliminated in urine (myoglobinuria). In high concentrations e.g. crush injury, myoglobin can cause acute renal failure by precipitation in the renal tubules and by conversion to products toxic to the tubules. If untreated death may follow. Therefore, rapid diagnosis and treatment is essential following suspected prolonged crush injury.

A rapid immunochromatographic urine myoglobin assay for use in cases of suspected crush injury is available. Please contact Quadratech for further details (see page 4 for contact details)

Procurement after PASA

Back in May 2009 the Department of Health (DH) published the new Commercial Operating Model for the NHS and DH. The main aim of the model is to 'improve support and increase commercial capability throughout the NHS'. The key elements of the model include the establishment of:

- the Procurement, Investment and Commercial Division (PICD) in the DH to replace the Commercial Directorate and Private Finance Unit. The aim of the PICD is to strengthen commercial and procurement support for the DH and bring together functions that are currently dispersed across the DH.
- regional Commercial Support Units (CSU's). CSU's will provide support for providers and commissioners to help them improve their skills and to secure better value for money for goods and services. Local procurement hubs will be expected to align themselves with these new regional CSU's.
- a new National Procurement Council
- a Cooperation and Competition Panel

"PASA WILL BE CLOSED AND ITS FUNCTIONS TRANSFERRED"

In addition the NHS Purchasing and Supply Agency (PASA) will be closed and its functions transferred.

The implementation of the Commercial Operating Model will ultimately result in a radical reform of the UK medical technology sector, but has been welcomed by Association of British Healthcare Industries (ABHI). However, as with all new NHS reforms, only time will tell if this new model has been a success.

Rapid tests - a new focus?

Most labs run or have run rapid tests in the past. Often, due to their ease of use, rapid tests are performed by supervised MLA's, leaving the more involved procedures to experienced, qualified staff. However, due to increasing workloads and the greater availability of automated assays, testing procedures are changing. Even PCR, which used to be too sensitive to contamination, expensive and involved for use in routine hospital laboratories, is now being introduced for routine infectious disease testing. However, rapid tests still have an important role.

Whilst PCR is great for batch testing and running non urgent samples it is not ideal for late arriving samples or out of hours testing. This is where rapid tests come into their own as they allow quick and easy result generation enabling labs to offer an efficient 24/7 infection control service. Sample turnaround time and patient management is improved.

Rapid tests have an important role to play

Rapid tests can also be a back up clarification test where a mixed result picture is obtained by the usual lab methods e.g. EBV screening.

So do not forget about rapid tests, they really can make a difference.

APC resistance—the new kit on the block

APC-Resistance was first identified in 1993 by Prof. Bjorn Dahlback of Malmö University, Sweden. He found 2 families, prone to thrombosis, who showed no prolongation of clotting time when APC was added to their plasma. No other abnormalities were found. As a result of these findings Dr Steffen Rosen developed the classic APTT based assay to generate clot times in the presence and absence of Activated Protein C. Ratios >2.0 indicated a normal result , anything <2.0 suggested a heterozygote or homozygote result. However, individual users should establish their own normal cut-off level for every batch of reagent.

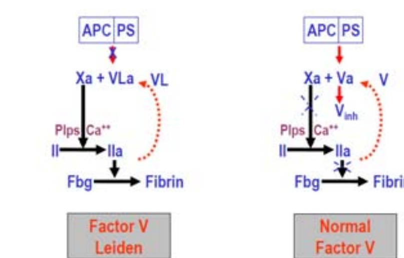
Further studies quickly showed that Factor V (FV) was involved in APC-resistance and work from the USA and Leiden University (The Netherlands) found that a mutation of FV caused a 'disturbance' to the kinetics of the inhibitory action of Activated Protein C, slowing the rate of FVa inactivation. This discovery led to the adaptation of the classic APC-R assay. Using FV deficient plasma to pre dilute the patients plasma meant APC-Resistance due to a genetic fault in the patients FV could be detected. The downside being that it could miss acquired non FV APC-resistance e.g. in pregnancy.

At least 90% of those showing APC resistance have a point mutation in the FV gene, around point 506.

Therefore the mutation is known as FV:Q^{506}, or more commonly FV Leiden (FV-L). Due to the mutation frequency the modified APCR kits are predominantly detecting FV-L, although they will also detect the other FV mutations.

Over the years other alternative assays have been developed to measure APC-Resistance e.g. utilising venom activated endogenous Protein C, where an APTT assay is run with or without the venom.

All these assays require two tests per patient to be run to generate a ratio, which can then be normalised if required. In addition, the modified versions require the use of FV deficient plasma to pre-dilute the patients sample. Often samples need special handling to reduce the risk of interfering substances. These steps are time consuming and costly. Also, abnormal results are often referred for confirmation by PCR - which increases both the costs and turnaround time further.



APC-Resistance and FV mutation

However, the latest assay to be developed does not use a ratios or FV deficient plasma, nor is PCR confirmation required to identify the genotype. This newest assay is the Hemoclot Quantitative FV-Leiden (QV-L) from Hyphen Biomed. It is an automatable clotting method which quantitatively measures FV-L concentration in citrated plasma, by its resistance to the action of Activated Protein C (APC). A clotting time is obtained which is inversely proportional to the FV-L concentration. The FV-L (expressed as a percentage) is determined from a calibration curve generated from pooled heterozygote plasma and a normal plasma pool.

Hyphen are specialised at manufacturing very stable and pure factors, which are then used in their relevant kits. This means there is no reliance on endogenous factors or factor deficient plasmas. In addition, the use of a calibration curve in their Hemoclot QV-L assay removes the need to define a normalised cut-off level and eliminates batch to batch variation.

Hyphens own studies and customer evaluations have shown a clear differentiation between the normal, heterozygote and homozygote groups. Subsequent PCR analysis has confirmed the genotyping.
For further details about the Hemoclot Quanti FV-L assay please contact Quadratech (see page 4 for contact details)

Hyphen news

Hyphen unveiled their new catalogue at the recent ISTH meeting. The new look format is divided into four clearly definable sections. The newest area is the 'Animal Models' section which includes details of cross reactivities for the various Zymutest EIA kits and details on kits suitable for use with rat studies.

Hyphens newest products include the smaller version Zymutest HIT assays; the Biophen DTI assay (a chromogenic assay for the measurement of direct thrombin inhibitors); the Liaphen ATIII latex antigen assay; Argatroban calibrator and control sets and many more.

In addition to the catalogue Hyphen produced posters for the ISTH meeting. One focused on their assays which offer detection of true anti-thrombin activity of direct thrombin inhibitors in plasma. They have both a clotting based and chromogenic assay both of which are automatable, with no matrix effect and exhibit a linear dose response curve at both low and high concentrations.

The other poster highlights the risk of pseudo HIT associated with antibodies to protamine sulphate. They showed that there are atypical cases which can produce similar clinical complications to those of typical HIT. Whilst the mechanisms are slightly different, they always develop in the presence of heparin.

For copies of these posters please contact us (details on page 4).