

Cascade

Issue Number: 1

January 2008

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Welcome to this, the first edition of **Cascade**, the professional information newsletter for the Centre for Haemostasis and Thrombosis.

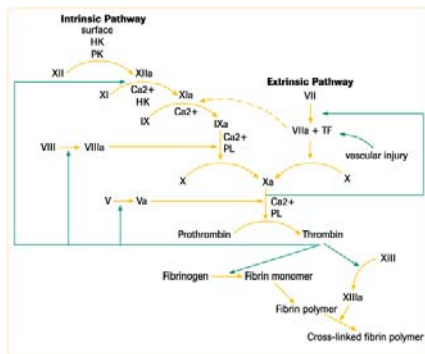
Cascade will be a quarterly publication each one will focus on at least one area of Haemostasis or Thrombosis, and will introduce you to members of the team working from the Guy's and St. Thomas' laboratories.

We hope that **Cascade** will become a useful update for you in the field of Coagulation.

First A Little History

One man more than any other was responsible for turning blood clotting into a scientific subject. This man was Professor Robert Gwyn Macfarlane 26.06.1907 – 26.03.1987, he was born in Worthing in Sussex his father was for many years Solicitor of the High Court in Bombay.

Working as a Haematologist, Macfarlane produced his theory of a clotting cascade in 1964 shortly before Earle Davie released his waterfall theory



The Cascade revolutionised the outlook for sufferers from Haemophilia and other bleeding disorders and created a school of coagulationists extending all over the World.

Personalised Warfarin Therapy

The one drug fits all principle is no longer the concept that pharmacologists are working with. There has been recognition of inter-individual differences in drug response which is an essential step towards optimizing therapy. Over the past decades, much evidence has emerged indicating that a substantial portion of variability in drug response is genetically determined, with age, nutrition, health status, environmental exposure, and concurrent therapy playing important contributory roles.

The cytochrome P450 monooxygenase system of enzymes is responsible for a major portion of drug metabolism in humans. This is true of warfarin therapy where the main metabolizing enzymes for warfarin are members of the cytochrome P450 family. The S-isomer of warfarin is specifically metabolized by cytochrome P450, subfamily polypeptide 9 protein CYP2C9.

Polymorphisms in the CYP2C9 gene are associated with a 2 to 3-fold increased risk of bleeding during warfarin induction but not long term therapy, and so can form part of your initial dosing algorithm. Vitamin K epoxide reductase (VKORC1) is involved in the regeneration of reduced vitamin K which is an essential co-factor for gamma-glutamyl carboxylase which activates the coagulation factors prothrombin, VII, IX and X by carboxylating glutamic acid residues.

Warfarin exerts its pharmacological effect by inhibiting the activity of vitamin-K epoxide reductase. Genetic polymorphisms in this gene can affect the warfarin dosing requirement by up to 25%

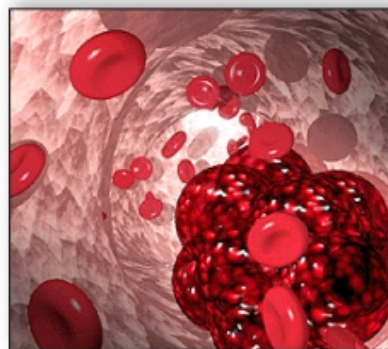
Further information can be gathered for those patients that are hard to stabilise on warfarin therapy, despite repeated dosing changes. In such cases we can test for pathogenic mutations in the VKORC1 gene.

All we need for any of these tests is just an EDTA sample of blood. This will provide you with so much more information so that your patients can be treated according to their individual need and in the long run will reduce costs by avoiding unnecessary testing and reducing the amount of the drug being used.



Jacky Cutler and the team from the Molecular Genetics Laboratory

Training and Development



The Centre for Haemostasis and Thrombosis will be holding a 2 day course entitled "Current Practice in Thrombosis"

The lecture programme will be presented by leading experts from the Centre and external speakers from around the United Kingdom.

The course is aimed at specialist registrars, medical trainees, including both clinical and scientific and

CPD points will be awarded for attendance through the Royal College of Pathologists (RCPath) and the Institute of Biomedical Science (IBMS).

For more information please visit our website (www.c4ht.com) or contact Jackie Smith (jackie.smith@gstt.nhs.uk) or call +44 (0) 20 7188 2781

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Vitamin Analysis

Our Nutristasis Unit has an interest in Vitamin K which is essential for blood coagulation. In the late 1920s, Danish Scientist Henrik Dam investigated the role of cholesterol by feeding chickens a cholesterol-depleted diet. After several weeks, the animals developed hemorrhages and started bleeding. These defects could not be restored by adding purified cholesterol to the diet. It appeared that - together with the cholesterol - a second compound had been extracted from the food, and this compound was called the coagulation vitamin. The new vitamin received the letter K because the initial discoveries were reported in a German journal, in which it was designated as Koagulationsvitamin.

In addition to Vitamin K we can test for other fat soluble vitamins such as A and E. If you have any queries about vitamin K testing or any other fat soluble vitamin please contact Dr Dominic Harrington (Principal Clinical Scientist) Nutristasis Unit on +44 (0) 20 7188 6815



Dr Dominic Harrington and the team from the Nutristasis Unit

The Centre for Haemostasis and Thrombosis

A vital part of the service provided by Guy's and St Thomas' NHS Foundation Trust is the Centre for Haemostasis and Thrombosis, based at St. Thomas' Hospital in Lambeth Palace Road, London.

A UKHCDO approved Comprehensive Care Centre, it provides a holistic approach to treatment of patients suffering from Haemophilia, many bleeding disorders and Thrombotic conditions.

Led by the acting clinical lead Dr Savita Rangarajan, the centre medical team consists of consultant haematologists and specialist registrars who are dedicated to Haemostasis and Thrombosis.

The medical team are supported by specialist nursing staff, who work with patients both in the Centre and out in the community providing support and education to patients who suffer from the various condition we treat.

On site physiotherapy services are utilised to provide further support to patients with Haemophilia and related bleeding disorders. Our physiotherapy team work closely with medical staff to support patient treatment and devise rehabilitation programmes to get our patients moving again and help to prevent further bleeding episodes.

Home delivery of products is also an essential service provided for approved patient groups. Our Blood Products Team co-ordinate and monitor products sent to patients who suffer from condition treated through the Centre.

This service has been advanced through the introduction of an online management system where patient's record any bleeding episodes and update their treatment regime. This information is transmitted in real-time to the Centre for updating in the patient records. This system has recently been nominated for an NHS Innovation Award for ideas which have benefited patient therapy and treatment.

The Centre is supported by dedicated laboratories which are CPA accredited. The laboratories are able to provide an extensive range of diagnostic tests from routine coagulation screening, through to factor assays, thrombophilia screens, platelet function analysis, genetic testing and screening, vitamin K and other associated metabolic pathways.

Contact Us

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End Point

A teacher stands in front of his class to explain the circulation of blood in the body.

"Now you all know that if I stood on my head the blood would all rush to it. Why is it that when I stand upright the blood does not all rush down to my feet?"

One youngster replied

"Because yer feet have already got something in em!"

Laboratory contact details

If you have any queries regarding testing in the laboratories of the Centre, any in depth information not covered in this edition, or would like to arrange testing of your patient samples please do not hesitate to contact one of our dedicated team members.

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Editorial contact

If you have any comments about **Cascade** or have any suggestion about relevant areas of interest you would like to see covered please contact the editorial team:

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