MPDlife

The newsletter for people with MPNs
November 2015

Closing the gap: the genetic landscape of MPNs

Professor Claire Harrison writes

Professor Claire Harrison

Since the discovery of the JAK2 mutation, the level of interest and investment in research for myeloproliferative neoplasms (MPNs) has grown significantly. In the latest issue of one of the most prestigious haematology journals aptly titled "BLOOD" two large research groups led by William Vainchenker in France and Robert Kralovics in Vienna, reported the discovery of a number of different new mutations in MPL and JAK2 genes in 5–10% of essential thrombocythaemia (ET) and primary myelofibrosis (PMF) patients, who lacked what are regarded as classical mutations. Such patients lacking classical mutations in JAK2, MPL and calreticulin genes were considered as having a "triple negative" disease, these were effectively new mutations but in "classical genes".

The concept of "triple negative" ET and PMF patients was developed after the discovery of calreticulin (CALR) mutations in 2014. However the term "triple negativity" was, in fact, first employed for patients with breast cancer, who had tumors negative for estrogen or progesterone receptor and HER2 mutations. Over the past few years triple negative breast cancers have subsequently been shown to harbour mutations in several other genes, known as PI3KCA, BRCA1, BRCA2 and PALB2 which are now of increasing importance in clinical management with different sensitivity to different therapies. The findings in these two reports for triple negative ET and PMF patients are similarly important because although at the present time, no new information can be gleaned for clinical practice, they do raise several questions both for future research and clinical practice.

Decades of research

In his 1951 seminal paper Dameshek who first recognized the family of disorders he first called myeloproliferative diseases, now termed MPN wrote "…we find it difficult to draw any clear-cut dividing lines; in fact, so many "transition forms" exist that one may with equal reasonableness call a single condition by at least two different terms." In 2015, a decade from the original descriptions of JAK2V617F, the MPNs are defined by an increasingly intricate genetic landscape. For the haematology world the papers by William Vainchenker and Robert Kralovics are important because they not only reflect Dameshek's observations and increase that "intricacy" but they also illustrate the limitations of some of the tools that are sometimes taken for granted in both clinical practice and research. If the data presented in these two papers is substantiated in further patient cohorts, the proportion of ET and PMF patients still considered as "triple negative" remains high and so their underlying pathogenesis remains to be identified. To read more go to **www.bloodjournal.org**

Website updates

As we go to press we are hoping that by the time this newsletter is being read, our new website will be up and running.

As well as being easier to find your way around, the website will have new sections, with more to be added, a blog and be in line with the advances in new technology, so not only suitable for desktop computers, but also for tablets, smartphone and mobile devices.

Please do have a look and send any feedback, comments or requests for new sections to us at **info@mpnvoice.org.uk**

www.mpnvoice.org.uk

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Activity lifted my spirits

patient story

John's story

John Messenger, a commercial manager talks about how training for a marathon helped him in dealing with the challenges of being diagnosed with essential thrombocythaemia (ET).

John recalls that following a period of about two years suffering extremely painful headaches, distorted vision and visits to osteopaths, neurologists and other specialists, a blood test prior to examination of an old knee injury showed a very high platelet count of around 1,500. A bone marrow biopsy confirmed that the condition was essential thrombocythaemia.

He was immediately put on treatment and over a two and a half year period experienced various side effects and fluctuating test results but thankfully his fantastic consultant persevered and his platelet count finally came under control at a normal level early in 2014.

At around the same time that his platelets reached a normal level a colleague at work told him about the St Albans Half Marathon that takes place in June. John decided that the time was right for a physical challenge and, not having done much exercise at all for more than two years, set about following a training programme to build up for the event. In his twenties, (he is now forty), John says that; 'I once ran a ten mile race and prior to that a few 10k races but a half marathon was a greater distance than I had ever run before. On the 6th June 2014 I completed the half marathon in two hours and seventeen minutes which I was very pleased with given that it was a surprisingly hilly course and a very hot day.

Being back to my more active self lifted my spirits enormously and having completed the half marathon I committed to pursuing further challenges to keep me on the go. When I heard that places were available to run The London Marathon for MPN Voice, I knew that had to be my next goal and I had to take my training seriously. Since early 2014, to train for the half marathon and then the full marathon, I have run something like 650 kilometres, rowed another 120 kilometres and shifted around 80 tonnes worth of dumbbells.

I've noticed one or two other MPN sufferers on the MPN Voice website who have taken on similarly active challenges and I think it is really important to spread the word that being diagnosed with an MPN doesn't necessarily stop you doing all the activities you enjoy. It's also a great opportunity to raise funds for research into these conditions in the hope that one day there will be a cure'.


John running the London Marathon

John adds a word of caution for anyone with an MPN considering taking on an endurance event. 'Just a week or so prior to the London Marathon, my blood results showed that I was seriously anaemic. This was not something I had experienced before but I have since learnt it is not unusual for distance runners to suffer from anaemia. If you have an MPN however, it could take you a long time to recover.

The lack of oxygen getting into my bloodstream as a result of the anaemia made the marathon even harder than I had anticipated from my training runs and it was only when I saw the finish line on the Mall that I truly believed I would finish.

I raised £550 of sponsorship for MPN Voice by running the St Albans Half Marathon and just over £3,000 from the London Marathon which I completed in just over 5 hours. I would like to thank friends and family, the Rubens Palace Hotel and the Museum of the Household Cavalry Museum for their generous support in the fundraising effort and my local running club Ware Joggers who were very friendly, great to train with and full of advice on how to tackle a marathon'.

Editor's note: What a fantastic inspiration! MPN Voice would like to congratulate and thank John for all his focussed training and fundraising achievements on our behalf.

We produce **leaflets for patients** diagnosed with MPNs about the diseases and also the various treatments available. For a copy of any of our leaflets visit the website **www.mpnvoice.org.uk** where you can download copies or order them to be posted out to you free of charge. If your clinic or consultant is not aware of our free leaflets, do let them know that they can order multiple copies too to give to other MPN patients.

Patient forums

MPN Voice is delighted that throughout 2015 we were able to run several regional Patient Forums in regular and new locations. Each was well attended by patients and their families, enabling hundreds of people to be kept up to date on the latest MPN research and treatments for patient care.

- In July at the London Forum we were very excited that we were able to 'live stream' the whole of the forum, enabling registered participants to watch and participate from all parts of the world. A 'first' for MPN Voice. If you haven't already watched it, it's still available on our website, with thanks to Patient Power.
- Thank you to all the consultants and volunteers who help to make these events such an integral part of what MPN Voice is for MPN patients and their families, providing a real community and source of up to date information.
- Our continued thanks too to The Samuel Sebba Charitable Trust who's funding has enabled the increase in running regional forums.
- If you haven't already attended a forum do come along to meet the MPN Voice team in 2016. Dates and locations will be announced on the MPN Voice website, we'd love to meet you.

Fatigue – a key challenge for MPN patients

health update

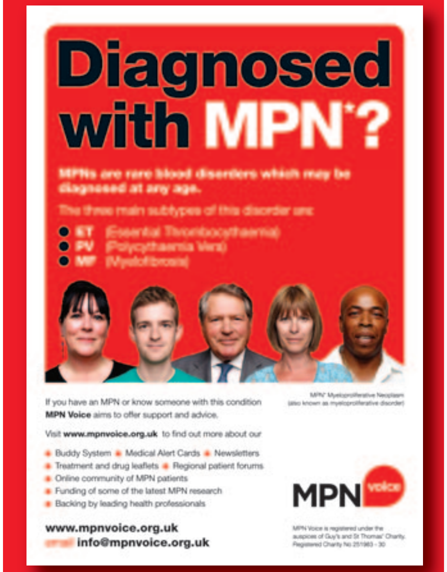
Several research initiatives confirm that fatigue is one of the biggest problems faced by people with myeloproliferative neoplasms (MPNs). In 2005, the Mayo Clinic in the US conducted a survey of over 1000 people with all types of MPNs. Over 80% of those surveyed reported feeling tired, regardless of age or treatment regime.


Professor Ruben Mesa

Professor of Medicine Ruben Mesa, M.D. who conducted this study for the Mayo Clinic, commented that even young patients who don't otherwise exhibit many symptoms of their disorder feel more fatigue than people who don't have an MPN. Mysteriously, the "MPN fatigue effect" doesn't necessarily correlate with blood counts or age, which shows that there is a lot researchers still don't know about the ways MPNs affect our bodies.

The latest research findings from the MPN Fatigue Study are shown on the following page.

Promote MPN Voice


Diagnosed with MPN*?

MPNs are rare blood disorders which may be diagnosed at any age.

The three main subtypes of this disorder are:

- ET (Essential Thrombocythaemia)
- PV (Polycythaemia Vera)
- MF (Myelofibrosis)

MPN* Myeloproliferative Neoplasm (also known as myeloproliferative disorder)

If you have an MPN or know someone with this condition **MPN Voice** aims to offer support and advice.

Visit **www.mpnvoice.org.uk** to find out more about our

- Buddy System
- Medical Alert Cards
- Newsletters
- Treatment and drug leaflets
- Regional patient forums
- Online community of MPN patients
- Funding of some of the latest MPN research
- Backing by leading health professionals

www.mpnvoice.org.uk
email **info@mpnvoice.org.uk**

MPN Voice is registered under the auspices of Guy's and St Thomas' Charity.

Download our poster and ask your clinic or GP surgery to display a copy.

Tips for coping with fatigue

Managing day to day

- Plan your day(s) to include rest and be realistic about what is possible for you to achieve.
- If your fatigue is very debilitating and interfering with your ability to live a normal life ask if you could have a visit from an occupational therapist who could identify ways of helping you to save your energy.
- Look for ways to save energy around the house and ask for help from family members.
- Pace yourself and don't be embarrassed if you need to spread out household tasks over the week or if you can afford a cleaner, this is the time to do it!
- Use labour saving devices such as a wheeled shopping bag/shopping trolley, dishwasher etc.

Keep moving

Research shows that although it may seem counter intuitive, the best thing to combat fatigue is to take some exercise. Always consult your health care team before embarking on any new fitness regime and build up slowly.

Coping with fatigue at work

Whilst some patients cope well and do not need to make any changes, some MPN patients really struggle with work and fatigue and find that they need to give up working because of this or reduce the amount of time at work.

For those MPN patients who do have problems, it will help to talk to the human resources officer and your manager to discuss ways of managing work and your fatigue. Some things that may help at work are:

- Changing your hours and avoiding the rush hour to and from work.
- Working from home for some of the time if possible.
- Asking for help from others when needed.
- Negotiating short breaks to rest if needed.
- If your work involves lifting or physical effort, consider ways to lighten the workload.

Sleep

Whilst fatigue may increase the need for sleep, where possible try to keep a routine for sleeping and aim for quality sleep rather than irregular, disrupted sleep times. Practical pointers include:

- Regular wake up times will help most people's sleep routines.
- Try to maintain an ambient room temperature – avoid extremes of heat or cold.
- Don't sleep for too long – too much sleep can lead to shallow sleep patterns.
- Take some regular exercise where possible, which over a period of time can help in deeper sleep patterns.
- Avoid stimulants and limit your alcohol intake as these may exacerbate any problems with getting a deep sleep; e.g. drinking alcohol will help you to fall asleep quickly but then sleep tends to be interrupted and shallow later in the night.

Talk about it

People with MPNs deal with their illness in different ways but it is important to talk about how fatigue is affecting you, both at home, work and in any areas of your life so that adjustments can be made where necessary.

- Talk to your GP or haematologist and keep a record of when you feel fatigued.
- You may find it helpful to talk to others who have an MPN either through a buddy, email **buddies@mpnvoice.org.uk** or via the online forum HealthUnlocked.

Looking at fatigue from a new perspective

Results from the MPN Fatigue Study

Robyn M. Scherber MD, MPH, Fellow Department of Hematology and Oncology, Oregon Health and Sciences University reports on the latest research on fatigue in MPNs


Robyn M. Scherber

What advancements have brought about the greatest change in the way that MPN patients are managed? Certainly the world of MPN treatments was revolutionized by the discovery of mutations in *JAK2*V617F and *Calreticulin*. Moreover, the development of drugs like JAK2 inhibitors has allowed us to reduce spleen size and improve overall quality of life. However, I propose that rather than a specific discovery, our greatest advancement has been the change in treatment focus from the disease to the individual. Specifically, I am referring to the focus on MPN specific symptoms and their unique effect on the life of each MPN patient. With the development of new treatment options that can significantly alleviate and improve symptom burden, we are now able to tailor therapies to improve quality of life and symptom control. Some of the most recent studies have evaluated sexual difficulties or insomnia, although here we highlight the largest of those recent studies which focused on the evaluation of fatigue.

The MPN Fatigue Study was initiated from the collaborative efforts of MPN patients and patient advocates who hoped that more could be done to improve our understanding of the most common (and often severe) of MPN complaints. Their efforts resulted in the development of a 70-item internet-based survey that was distributed in February to March of 2014. The survey was promoted through the MPN Forum, MPN Net, MPN Research Foundation, and MPN Voice. As a result of this unified team effort, over 1700 international MPN patients responded to the fatigue survey.

Results

The study found that many factors significantly contributed to fatigue, such as use of particular medications, the presence of other medical diseases, or excessive body weight. The presence of additional medical illnesses often worsened fatigue, although fatigue was still severe for patients who did not have other contributing medical illnesses. Patients with worsened fatigue also felt significantly more depressed. These factors demonstrated the importance of a thorough medical evaluation to evaluate contributing causes of fatigue in individuals who have severe fatigue burden.

A second focus of this project was to evaluate the daily practices and habits of patients to alleviate fatigue. The most pertinent result was the correlation between exercise and fatigue severity. Individuals who reported exercising at least once per week reported lower fatigue severity than their non-exercising counterparts. Although it is difficult to say whether this represents a cause or an effect, it is possible that increasing low impact exercise may improve fatigue. A prospective study at the Mayo Clinic in Arizona, United States, is currently underway to see if a daily yoga program can alleviate fatigue.


Gentle exercise may help combat fatigue

The future?

The next few years will likely open many new venues for research and targeted treatment. However, it is our hope that results of the MPN Fatigue Study along with other similar symptom-specific studies will ultimately lead to the greatest improvements in how MPN patients *feel*.

FUNDRAISING

Marilyn Webster, fundraising co-ordinator writes

We would like to thank all our wonderful supporters for their fantastic fundraising during 2015. The MPN Voice Community has held some amazing events, Vintage Fayres, Art Raffles, Fuzzy Bug Sales to name but a few. So many of you have set yourselves personal challenges that have meant hours of pounding the pavement, getting soaked, having paint, mousse and water thrown at you, hundreds of miles in the saddle, not forgetting the gruelling Trek in China through Charity Challenge. Because of all your dedicated efforts, MPN Voice has continued to receive very much appreciated donations from so many of you.

We will be announcing at the Living with MPNs Patients' Day in November how much you have raised this year!

2015 has been amazing! As we continue to support the funding of ground-breaking research let's see if we can make 2016 even better!

Forthcoming events

2016 is already looking to be a very exciting year. Samantha-Jo has decided to do a Charity Challenge Event, participating in the Saigon to Angkor Wat Bike Ride. Andrew will be cycling from London to Paris and so much more! So if you are planning your own event, please contact us at **fundraising@mpnvoice.org.uk** We can send you all the support materials you might need and we will advertise your event to the wider MPN Voice Community in our monthly online fundraising update.

Dates for 2016

- **13 March 2016** Adidas Silverstone Half Marathon
- **24 April 2016** Virgin Money London Marathon
- **30 May 2016** BUPA London 10k
- **June 2016** Abseil Challenge – in Association with Guy's and St Thomas' Charity
- **September 2016** Blood Cancer Awareness Month
- **Various dates in 2016** Skydive

If anyone is interested in taking part in any of the events listed for 2016, please contact us at **fundraising@mpnvoice.org.uk**

Fundraising heroes

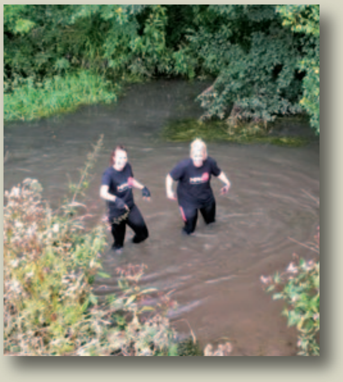
Sheena Hawkin 90 Mile Jurassic Coastal Walk from Seaton to Bournemouth 9th August – raised £4236.00.
Her niece Kate raised £1,000.

Two years ago Sheena was diagnosed with myelofibrosis (MF). Since then, Sheena and her family have valued the support of MPN Voice and have thrown themselves into fundraising so that we can continue to fund groundbreaking research. Sheena's niece Kate organised a very successful Dassett Eventing Fuzzy Bug Fundraiser and Lucy, Sheena's daughter is one of our MPN Voice 2016 Running Team and will be participating in the London BUPA 10k!

Sheena loves walking, so with the support of Barrie and two friends Ken and Dave, Sheena successfully completed the stunning 90 mile Jurassic Coastal Walk.

Kayleigh Spence The Warrior Adrenaline Race on 5th September – Raised £275

Kayleigh aged 21 and her family were heartbroken when her auntie, who is like her best friend, was recently diagnosed with polycythaemia vera (PV). Kayleigh and her family had never heard of this rare blood cancer and decided to show support for her auntie by raising awareness of MPNs and getting as much sponsorship as possible to help fund MPN Voice's research projects. As the start of her journey of fundraising events, Kayleigh took part in the WAR obstacle course race, which featured slides, tunnels, rope climbs, mud and lots of water. Kayleigh's T Shirt will never be the same again!



Regular fundraiser

Andrea Headech is a regular fundraising supporter for MPN Voice and has appeared in previous MPD Life fundraising updates. Recently she took part in a 5K obstacle run and raised a further £480 for us.

Keeping fit and raising funds

Amanda, 33 and a mother of three children was diagnosed with ET in 2010 and is taking interferon. Amanda suffered a TIA (mini stroke) in 2014 and as part of her keep fit campaign and to help awareness and raise funds for research, decided to run the Hull 10k in June with her husband, raising £470.

Laura Blake and Peter Taylor Abseil Challenge London 27th June – Raised £905 and £700 from Peter's employer

Laura and Peter decided to accept our challenge and booked themselves to Abseil 100 feet down the front of the Golden Jubilee Wing of King's College Hospital in London. Or as Laura put it, 'throw ourselves off'! Laura emailed to say; 'Well we did it! Wow! What can I say other than what a fantastic experience! We both got to the bottom and wanted to run back up to the top and do it again. We want to do more abseiling now. It's amazing that we got to experience something great for such a fantastic cause'.

Family fundraising

Ruby's auntie Rachel has essential thrombocythaemia (ET). Determined to show her support, Ruby decided to do a bike ride to raise funds for MPN Voice.

Along with her father Peter, Ruby rode the 25 mile LIDBA bike ride through the Hampshire lanes, starting and finishing at Liphook which took 1 hour and 50 minutes. Ruby and Peter were waved in by family and friends with our MPN Voice balloons and flags and raised £400.

The year in the saddle!

David Brailsford was diagnosed with ET a few years ago and decided he wanted to get fit and needed a target so decided this would be 'The Year in the Saddle'. His cycle challenge covered 1,234 miles and impressively he threw in a bit of swimming and running too! David has raised an amazing £810.

September is Blood Cancer Awareness Month

Inspired by Pamela Simpson's coffee morning last year, the fundraising team launched the 'September is Blood Cancer Awareness Month', to raise funds and awareness of MPNs, at the July London patient forum.

It's been an amazing success and has so far raised over £2,100. All over the country and in Europe, some wonderful cakes and biscuits have been eaten and hundreds of cups of tea and coffee have been poured. Even more wonderful is that we have got the chatter going! So many more people now know about our rare blood cancers.

Pamela Simpson

Don't forget if you've held an event and haven't yet sent in your photos or totals raised, it isn't too late, as we can add you to our Fundraising Heroes Page on the new MPN Voice website. **Thank you for all your amazing support.**

Jo Ward and her wonderful friends had a great time and the raffle went really well too!

MOSAICC

There is little information on the causes of myeloproliferative neoplasms (MPNs). Patients often ask 'Why do I have this disease?' and for the majority there is no obvious reason. Regular readers will recall that in 2013 MPN Voice provided the funding for a pilot study to evaluate the information and technology needed for researching potential causes of the condition.

This research, known as MOSAICC, (**M**yel**O**proliferative neoplasm**S**: **A**n **I**n-depth **C**ase-**C**ontrol) was led by Dr Lesley Anderson, a lecturer in Cancer Prevention at Queen's University Belfast and was an international collaboration of leading medical experts.

International collaborators: Dr Frank De Vocht (left), Dr Lesley Anderson (centre) and Professor Lin Fritschi (right)

Results of the research to date

Because of the lack of information on MPNs, a comprehensive review of published studies was undertaken. This review was then able to report a combined annual incidence rate (i.e. number of new patients diagnosed each year) for polycythaemia vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (MF) of 0.84, 1.03, and 0.47 per 100,000 people, respectively. The research found that there was a lot of variation in the number of patients diagnosed per year in the studies (Titmarsh et al 2014).

Using data from the USA (the Surveillance Epidemiology and End Results-Medicare dataset) the team investigated the role of common community acquired infections in the development of MPNs as well as other myeloid malignancies. It was observed that preceding infections were more commonly associated with acute myeloid leukaemia and myelodysplastic syndrome (including respiratory tract infections and herpes zoster) than chronic myeloid leukaemia and MPNs. Cellulitis was the only infection to have been more commonly diagnosed in MPN patients than population controls (Titmarsh et al, 2014).

The team also assessed symptom burden and quality of life in MPN patients compared with a control group. It found that MPN patients had significantly worse symptom burden. Symptoms in patients with MPN in the UK were similar to those of patients in the USA (Anderson et al, 2015).

Based on the feasibility study, some risk factors that have been previously associated with an increased risk of MPN including smoking were identified. Other factors that may cause MPNs are being investigated but these will require confirmation in a larger study.

Next steps

Funding from MPN Voice has been pivotal, permitting novel research to be conducted with collaboration of experts across the world to optimise methodological approaches for a UK wide study. Applications for further funding to expand the study to 20 UK sites have been submitted with decisions expected by January 2016. The team plan to submit an application to extend the study to Australia in 2016 and to explore study arms in USA.

Other questions raised by the study

The team evaluated methodological approaches in the feasibility study including the number of people who agreed to participate in the research. 66.7% patients with PV, ET or MF, 74% of non-blood relatives/friends and 17% GP controls. Due to the low recruitment rate of GP controls it is planned that the main study will recruit non-blood relatives/friends as the control group. The study also considered the best mechanisms to incentivise participation which will be taken forward to the next study phase.

A key learning point was that due to some patients having difficulty in recalling their lifestyle before diagnosis future studies plan to restrict the UK-wide study to patients diagnosed in the last five years.

If you are interested in the research and have any feedback or suggestions that would be useful for the development of the next phase please contact the lead research co-ordinator Dr Lesley Anderson. **l.anderson@qub.ac.uk**

Time to volunteer?

MPN Voice is a patient led organisation funded by the generous donations of MPN patients, families and supporters for which we are always grateful. We also value any offers of help from volunteers and are always looking for people who could get involved with what we do. Could you run a patient forum, maybe man a stand at an event, proof read our publications, help to research and write articles for our newsletter, to name but a few? Do get in touch at **info@mpnvoice.org.uk**

Visit our **News and Events blog**:
www.mpnvoice.org.uk/news-events
or visit our Facebook and Twitter pages

MPDlife

- Want to be featured in our patient story?
- Do you have tips to share with readers on managing MPNs?

If so, please email the editor at the address below.

Editor Alisia O'Sullivan
Email: editor@mpnvoice.org.uk

Medical Advisor Professor Claire Harrison

Contributors Dr Lesley Anderson, Professor Claire Harrison, Professor Ruben Mesa, Robyn M. Scherber MD, Marilyn Webster

MPN Voice
Contact MPN Voice
care of: Guy's and
St Thomas' Charity
FREEPOST LON 15724
London SE1 9YA
Email: info@mpnvoice.org.uk

We welcome your letters and feedback.
Please send by post or to info@mpnvoice.org.uk

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