mpdlife
the newsletter for people with MPDs

mpd-support
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MPD origins: JAK2 may just be middle step

Dr Ruben Mesa of the Mayo Clinic in the US explains research into the mutations that may cause MPDs

Five years ago we made several discoveries crucial to our understanding of myeloproliferative diseases. We discovered three mutations associated with these disorders: the JAK2 V617F mutation and two other mutations called c-MPL and JAK2 exon 12.

In these last five years, what have we found? We've learned that these mutations may well be a middle step in the development of MPDs – they may not be the complete cause.

Research into MPD origins

In 2010 we're conducting ongoing research into myeloproliferative disorders, which includes attempting to identify what exactly causes these diseases. We're looking at whether additional mutations (for instance the recently discovered TET2) or predispositions (such as haplotype 46/1) may play a role in why people develop MPDs.

New drugs for ET and PV

For many years, therapy for essential thrombocythaemia (ET) and polycythaemia vera (PV) has focused on three main forms of treatment. Most people with ET and PV take low-dose aspirin to reduce the risk of clots. People with PV are given phlebotomy to decrease the risk of blood clots and bleeding. We also give cytoreductive drugs (hydroxycarbamide or anagrelide) for high risk disease – these drugs slow down the production of blood cells in the bone marrow.

We're now testing several new drugs, including JAK2 inhibitors such as INCB-018424 and CEP-701. Although we are far from knowing whether the JAK2 inhibitors will be safe and effective treatments for patients with ET and PV, preliminary results are encouraging.

Additionally, trials of pegylated interferon alpha-2a are beginning this year in the US and the UK and on the Continent to determine the best role for this medicine. We have found that this type of interferon can lead to a reduced level of disease (in other words a molecular remission) in both ET and PV.

New therapies for MF

There are many new agents in development for myelofibrosis (MF). Currently we offer two types of treatment which are both imperfect options. On the one hand we have bone marrow transplantation (BMT), which can be curative – but is a very risky procedure. On the other hand,

MPD expert Dr Ruben Mesa

we have medicines that can help reduce anaemia and enlargement of the spleen but do not really change or in any way cure the disease.

New agents being tested include the JAK2 inhibitors (INCB-018424, SB1518, CEP701, TG101348), and HDAC inhibitors (LBH589) which are all having some benefit in terms of reducing the size of the spleen and improving symptoms in patients with myelofibrosis.

We are in an unprecedented era of MPD research. We're looking into the causes of MPDs and their impact on the patients who have these disorders. And finally, we're studying many interesting new agents that will hopefully have an impact on – or even cure – these diseases. ■

Missed diagnosis nearly leads to amputation

Jenny Charles relates how her husband came to be diagnosed with ET after suffering digital ischaemia

My husband Charlie's path to diagnosis began back in May 2005 when he was 46 years old. It began with a seemingly innocuous event, when he caught a splinter in his little toe. He removed it and gave it no more thought.

But a few weeks later after a holiday abroad, Charlie began to feel pain again. His GP referred him to a chiropodist, who diagnosed a corn and attempted to remove it. Although Charlie has a very high pain threshold, he was forced to stop the chiropodist as the pain became too great.

Charlie was then referred to a podiatrist, who was not sure why Charlie had so much pain. We had spent our holiday in a tropical location and we had worn sandals throughout the holiday, so the podiatrist thought that some foreign matter might have become embedded in Charlie's toe. He gave Charlie a local anaesthetic and removed some tissue.

But Charlie continued to experience severe, burning pain and we made several trips to A&E in an attempt to discover what was wrong.

Jenny has supported Charlie throughout his illness

Eventually he was admitted to hospital and his doctors decided to amputate the toe.

Before the operation was to begin, they took a blood sample and were shocked to see the result. Charlie's platelet count was 2600 x 10^9 /L (a normal count would be 150 to 400). The severe pain in his toe was clearly the result of digital ischaemia – a clot in the small arteries which is a common complication of essential thrombocythaemia (ET).

A haematology consultant came to speak with us and told us that he suspected ET and that Charlie was lucky not to have suffered a heart attack, stroke or other clot.

In the end Charlie did not require an amputation. He was given medicine to dissolve the clot and to reduce his platelet count.

Adjusting to ET

Charlie was in hospital for five weeks and was unable to walk for a further five months. The wound in his foot became badly infected, resulting in tissue loss down to the bone.

Once Charlie was formally diagnosed with ET he began taking hydroxycarbamide, initially on a dose of eight capsules per day. It took a year before his counts stablised.

Strangely, Charlie had never previously experienced any symptoms of ET other than some mild shortness of breath. He is extremely fit, and his doctors have

What is digital ischaemia?

Digital ischaemia – a lack of blood supply to the toes or fingers – is a fairly common condition in people with ET and PV. It is sometimes the first indication that a person has an MPD.

Digital ischaemia occurs when blood clots develop in the small arteries of the toes and fingers, blocking blood flow. Sometimes the problem begins when a small piece of arterial plaque breaks off from another place in the body and lodges in an artery in the toes.

In mild cases, people may feel warmth and pain in the fingers or toes. Sometimes the extremities can become discoloured simply due to cold or exposure. The toes and fingers may also develop a bluish discoloration if red blood cells carrying oxygen cannot move past the clot. In severe cases the pain of digital ischaemia can be excruciating, and gangrene (tissue death) can occur.

said that they believe his strong cardiovascular system protected his body – in fact that it may well have saved his life.

Since his diagnosis, Charlie's skin has become thinner and his nails weaker. At times, his sleep patterns are disturbed. He sleeps and wakes in short cycles, becoming sleep deprived, then collapses and sleeps for 14 hours straight. During the first 18 months after his diagnosis, he complained constantly of burning feet and couldn't bear to have so much as a sheet cover his feet. We swapped sides of our bed so he could dangle his foot off the bed – a bit of comedy in an otherwise distressing situation.

After recovery

Charlie works full time, and although he suffers from fatigue, he fights back by increasing the intensity of his exercise programme. He exercises three times a week – this keeps his energy up so that he can continue to lead a busy life.

Charlie now takes three capsules of hydroxycarbamide per day along with low-dose aspirin. He also takes lanzaprol to reduce the toxins caused by the hydroxy, and allopurinol to reduce the risk of gout. Treatment with hydroxycarbamide has severely weakened his immune system and he suffers from frequent chest infections. We avoid friends with bad colds, and we have often cancelled plans due to illness.

Charlie's toe has never healed properly and it can cause him a lot of pain. He says that he can tell when his counts are high by the texture of the hard skin, which feels rubbery.

Charlie has continued to experience pain

Over the last two years Charlie's platelet counts have been creeping up; his consultant suggested increasing his dose of hydroxycarbamide. We asked if we could delay the increase in dose pending another blood test in six weeks and we are awaiting his next test to know the results.

I have recently been unwell myself, and I became very angry – I didn't feel that Charlie was being supportive. On reflection I realised that he is not only used to, but dependent upon me to care for him. He became quite frightened by my becoming unwell. Since talking to others I realise that this is a normal reaction for someone who lives with a serious illness.

Has Charlie's diagnosis changed us? The simple answer is yes. We live life for today and we don't leave things unsaid in case the opportunity to say them is taken away. More than anything we realise that we have to make the most of every opportunity and live each day as if it is our last. ■

Tips for preventing clots

Stay in shape like Charlie and maintain a healthy weight.

Take low-dose aspirin Aspirin is an anti-platelet drug which is very effective at preventing clots.

Stay hydrated Minimise consumption of drinks containing alcohol and drink plenty of water.

Avoid smoking which can sharply increase the risk of developing a clot.

If you think you may be experiencing a clot Take an aspirin or two, then go to A&E. Be sure to tell them you have an MPD. Contact your haematologist; have your doctors speak with him or her.

Exercise helps everyone with an MPD

Oncology nurse Brenda Keenan explains the benefits of exercise, and how to overcome common barriers

When you first learn that you have an MPD, exercise may be the last thing on your mind, but over time it can become one of your highest priorities and favourite activities.

Exercise can help people with an MPD feel better on many levels. Exercising just ten minutes a day can reduce fatigue, stimulate your immune system and nourish your body, mind, heart and spirit.

If you are already an active person you can use your fitness routine to strengthen and support yourself.

If you have never been an active person, consider simply taking a short walk every day, or practise simple deep-breathing exercises as a way to get started on an exercise programme. Try taking four deep breaths four times a day. You can try adding new relaxation exercises to your life such as walking, yoga and tai chi.

Talk with your GP and your haematologist about your plans. They can give you advice about what types of exercise may work best for you. Ask about your blood tests and the implications for physical activity to ensure it is safe to begin a programme, and whether you need to be aware of any limitations. Think about which exercises can help, and which might be too much for you or even cause harm.

Then start out slowly. Exercise for short periods at different times of the day. Build up your strength and endurance little by little. You can do too much too soon, and hurt yourself. Think through your exercise programme plans if you have not been active in the past.

Exercises should not hurt or make you feel really tired. You might feel some soreness, or be a bit weary. You should not feel pain. Physical exercise makes people feel better, more vigorous, and less tired or depressed.

Problem: I'm feeling unwell

What to know It's important to take good care of yourself. Be sensible and kind to yourself. Recognize your limitations.

What you can do If you are in bed or not feeling well, there are gentle exercises you can do without getting out of bed. Try simple range-of-motion exercises, such as wrist rolls, shoulder shrugs, elbow bends, arm lifts, opening and closing of the hands, wriggling toes, and leg lifts.

If you are out of bed, walking around part of the day, but not ready for the gym, there are exercises you can do even in a sturdy chair or bed that help you stretch and strengthen: move your arms, legs, head, and torso while seated, and use weights and exercise bands if you want and your GP and haematologist approve.

If you have had surgery (for instance after a heart attack) it may

Tips for exercising safely

Don't hold your breath while straining when using your muscles. That could cause changes in your blood pressure. Breathe out while your muscles are working, breathe in when they relax. Work only as hard as you can while still breathing easily enough to talk.

Use safety equipment to keep from getting hurt. Use a helmet for cycling and wear the correct shoes for walking or jogging. You can also use a walking stick for balance.

Be sure to drink plenty of water when you are doing activities that make you perspire, unless your physician advises you otherwise. Minimize your intake of dehydrating drinks such as tea, coffee and alcohol and/or drink more water to compensate for their effects.

Always bend from the hips, not from the waist. Keep your knees slightly bent.

Warm up your muscles Do a little easy biking, or walking and light arm-pumping before you stretch.

Listen to your body and your physician, and do what feels right for you.

take time before you can start exercising. Ask your physician before beginning any physical activities.

As you feel better you may want to try out a fitness centre or gym, where you can try new programmes. It is important to let the staff know you have an MPD and of course check with your doctors first.

Problem: My meds give me side effects

What to know If you are receiving medication you may be having unpleasant side effects. It's important to get side effects under control. Don't try to tough it out.

What you can do Ask your GP or haematologist for suggestions or medications that can help you. Ask about alternatives to the medication you are taking. If the suggestions you're given do not provide enough relief, you can seek out complementary therapies that might help.

Be alert Avoid vigorous exercise if your blood counts are low and you are at risk of infection, anaemia and/or bleeding. Your MPD care team will tell you about your platelet, red cell and white cell levels and whether it is safe to exercise.

Problem: I have a heart or lung condition

What to know If you are receiving treatments that affect your lungs or heart, or you are at risk of lung or heart disease, check with your physician before starting any exercise programme.

What you can do Ask for your blood test results and ask whether it is safe to exercise. Report trouble signs to your physician, such as swollen ankles, unexplained weight gain, or shortness of breath while at rest or with a small amount of exertion. You may be at risk of bleeding if you are taking blood thinners. Avoid falls or injury. If you notice swelling, pain, dizziness or blurred vision, call your physician immediately.

Brenda Keenan: Modest exercise can reduce fatigue

Exercise has many benefits for all people with MPDs – especially that it increases your sense of well-being and reduces fatigue as well protecting your cardiovascular system. Try to live life as normally as possible, and exercise! ■

Benefits	Activities to try	Resources	Check with your doctor
More energy	Consider taking a short walk every day	Use your GP and haematologist as a resource in planning your programme	If your blood cell counts are low/high
Strengthened cardiovascular system	Try taking a few deep breaths, four times a day	After surgery, a physiotherapist can help you to get started with a programme	If you experience pain for any reason
Improved mood	Try relaxation programmes such as yoga or tai chi	Check our website for tips on coping with side effects at www.mpd-support.co.uk	If you are taking blood thinners
Greater sense of well-being	Try simple range-of-motion exercises that can be done in a chair or even in bed	Check our YouTube channel for very easy exercises demonstrated by a physiotherapist (link from www.mpd-support.co.uk)	If you feel short of breath

Expert Briefing

My skin is so dry – what can I do?

Q I am taking interferon for my MPD and I find that it makes my skin so dry, red and cracked, even on my face. What can I do to remedy this? – JL

A A little dry skin might not sound like such a big problem, but side effects like these can potentially be very irritating and troublesome.

As a first step, have a talk with your GP and haematologist and ask them to verify that there aren't any other causes for this problem. Thyroid disease can cause dry skin, and thyroid problems may relate directly to interferon. There are also other possible causes of dry skin, such as iron deficiency or a change in the soap or detergent that you use.

And if your skin is itchy rather than just dry, check our website for our top tips on reducing the itchy skin that is so often a problem for people with PV.

Also, remember to stay hydrated by drinking lots of water. Tea and coffee, caffeinated sodas and alcoholic drinks can be dehydrating, so you may need to reduce consumption and/or drink more water. And finally, find a good moisturizer and use it often.

– Dr Claire Harrison ■

What if I need an operation?

Dr Claire Harrison explains what to know before any procedure

You have an MPD that is under good control. You are doing well from day to day – but what if you need an operation? Many people with MPDs feel some concern when facing surgery.

Plan in advance

Whenever possible, it is always wise to do some planning in advance. Begin by telling the doctor or dentist who will be doing your procedure (no matter how trivial) that you have an MPD. You may need to take the role of the expert and educate your doctor or dentist about MPDs. You should also refer your dentist or surgeon to your haematologist for further advice.

Evaluate the risk

There are two main concerns, which may appear contradictory. People with MPDs have a risk of clotting, and they also have a risk of excessive bleeding. These risks are present in all surgeries, but are increased when you have an MPD. Your level of risk depends on several factors, including what sort of procedure you need, so your surgeon and haematologist need to consider both your own history and the particular operation that you need.

Orthopaedic procedures such as hip replacement are well known to have increased thrombosis risk, whereas in dental extractions bleeding is more of a concern. The type of MPD you have also plays a part in determining your level of risk. In a group of MPD patients evaluated for complications after surgery, arterial thrombosis appeared to be more common in patients with ET and venous thrombosis in those with PV.

Decide on treatment

Your doctor or dentist can consider several options. They will first need to evaluate whether your blood is more "sticky" and whether you have you already experienced a clot or tend to bleed more. Next, your doctors will consider which treatment is most suitable for the type of surgery you will undergo. Heparin is often given for hip replacement surgery to prevent clots, while it is not needed for dental surgery.

Your doctor may suggest stopping anti-platelet agents such as aspirin for some time prior to surgery, or modifying or switching warfarin (or similar drugs) to heparin for a time. If you are not currently treated with drugs to control your blood count, your doctors may sometimes recommend a course of treatment to normalise your blood count before an operation.

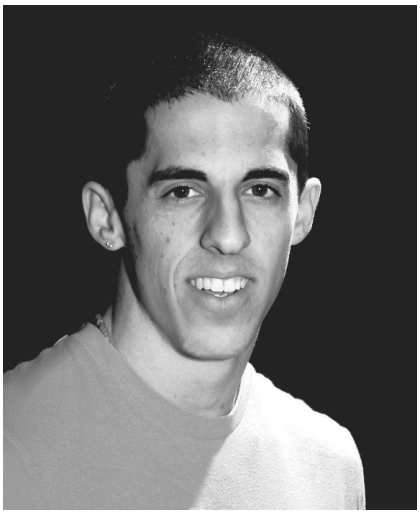
In summary, it is important to tell doctors and dentists you have an MPD. Get them to discuss a planned (or emergency) procedure with your haematologist. The advice you are given will be individually tailored to your particular situation. We wish you good luck with your procedure. ■

From garden parties to the Great Wall of China

Our dynamic and fearless MPD Support fundraisers trek in China, abseil in London and take tea in Essex

Joey Kolirin treks the Great Wall of China

Joey Kolirin (pictured below) explains why he's fundraising for MPD Support: "I lost my father, Haim, to myelofibrosis (MF) in 2008. This year, I am trekking the Great Wall of China in memory of my father who I loved so much. Although I cannot bring him back, I am raising money for MPD Support to benefit people with MF and other myeloproliferative disorders.



My father suffered tremendous mental and physical pain from this devastating illness. He was an avid traveller and always wanted to explore new places.

I strongly believe that we often don't realise from day to day just how lucky we are – that we can live life to the fullest. This trek is an opportunity for me to stay healthy, discover new things about myself and learn about a new culture, all while raising money and trying to aid other people who are in the same situation as my father was." ■

Sponsor Joey at www.justgiving.com/joeykolirin

Chelmsford & District Welsh Society to raise £3,000

Shirley Moody (pictured here) is president of the Chelmsford & District Welsh Society (CDWS), and there are a few perks associated with her position. One such perk is that Shirley can choose which charity the society sponsors for the year 2009/10. Shirley's son-in-law Tim Ellis was diagnosed with essential thrombocythaemia (ET) some 21 years ago, soon after the birth of his first child and Shirley's grandchild. She made a decision in 2009 to raise funds for MPD Support.

The Chelmsford & District Welsh Society has an active membership, and with the members' full support and willing help, it has held a number of fundraising events, including a garden party, a Christmas tea and a concert at Roxwell church in Essex, which raised £1,692 alone. Shirley hopes to raise in the region of £3,000, and as she says, "every little helps". ■

Learn more at http://chelmsfordwelsh.org/Charity

2010 Abseil

MPD Support's hugely popular abseiling event is already fully booked for 2010. Nearly 40 people will strap on climbing gear and abseil down Guy's Hospital Tower in London this June – the highest hospital tower in the world.

While places are full, you can still participate by supporting our abseilers: please visit our website and follow the links from the homepage to make a pledge in support of our abseilers.

You can also organise your own event, or join one of several great fundraisers this summer: cycling fundraiser in the Pyrenees, walks in the UK and more. Email us for the details at info@mpd-support.co.uk ■

From MF and BMT patient to survivor

Richard, profiled in our pages in 2007, relates how he's built a new life

It seems so long since ago since I underwent my bone marrow transplant (BMT) – but a recent six-monthly visit to see my transplant consultant reminded me that it was, unbelievably, four years to the month that I had come in for my BMT.

I have gone from what was at that time a precarious grip on life to having at age 57 what has probably been the best year of my professional career. It took me a full year after my BMT – and coping with some additional health issues culminating in major spinal surgery – to reach a point where I began to feel much stronger.

I expected to be back at work within four to six months of my BMT, so it was a shock to discover that I would eventually need to be off work for 21 months. The next shock came when I did go back to work. I was made redundant, unsurprisingly, because my former colleagues had managed without me for some time. I was faced with a major decision – whether to look for another full-time role and become an employee again. The downsides would be:

- Completing a medical questionnaire for an insurance/ pension policy…I decided no thank you.
- Declaring my immediate past medical situation... hardly likely to help me land that plum job.
- Being made redundant again, something fairly likely given my age…not something I wanted to entertain.

When I began to look for work the credit crunch had not fully hit home, but it was certainly well on its way, bringing severe competition for any jobs.

I mulled over the options, and being a positive sort of person I came to the obvious conclusion: I would set up my own consultancy and become self-employed.

This was a big step for someone who had been employed his entire career. But it meant that I would only be answerable to myself, that my medical history was irrelevant, and that I now had a new challenge, that of launching a new consultancy business.

The first year was very tough. After a promising start, nothing much happened, despite a massive effort in networking to meet other professionals in my field. However, over time I had developed a track record in my area of expertise, and my investment in networking was beginning to pay dividends. A year ago my work suddenly took off – and I have never looked back.

I now have a new and completely different lifestyle running a one-person business. I really enjoy it. My work is much more varied and stimulating than in the past, where I held one job over many years.

I am now back in charge of my life – working hard and playing hard in a way that would never have been possible had I not been forced into making such a monumental decision. I'm a survivor in more ways than one, and I'm happy to be where I am. ■

Our next issue

- Diagnosed with polycythaemia vera at the age of 12
- Get ready for the 2010 Walk for a Cure
- Manage your cholesterol to reduce risks of heart attack and stroke

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