MPN Frequently Asked Questions:

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1. Are myeloproliferative neoplasms a form of cancer?

Myeloproliferative neoplasms (MPNs) are a group of disorders in which the bone marrow cells grow and reproduce abnormally. The abnormal bone marrow stem cells produce excess numbers of one or more types of blood cells (red cells, white cells and/or platelets). The increased numbers of blood cells change the thickness of the blood and increase the risk of thrombosis (clotting) and haemorrhagic (bleeding) complications. MPNs can cause serious health problems unless they are promptly diagnosed, properly treated, and monitored regularly under the care of a haematologist.

MPNs are classified as blood cancers as the cells in the bone marrow grow excessively and do not respond to the normal checks and balances that control blood cell production in healthy people. They result from a change, or mutation, in the DNA (genetic code) of a single bone marrow stem cell, which acquires abnormal growth patterns. This change results in abnormal blood cell development and the overproduction of blood cells.
In MPNs the original mutation is preserved when the affected stem cell divides (proliferates) and produces a group of identical stem cells (a clone) all with the same genetic defect.

MPNs often remain stable for many years and only progress gradually over time. Some people with myeloproliferative neoplasms may develop additional abnormalities, such as acute leukaemia or transformation to ‘secondary’ myelofibrosis.

The three most frequent types of MPNs are:

- Essential thrombocythaemia (ET)
- Polycythaemia vera (PV)
- Primary Myelofibrosis (PMF)
  - PMF, prefibrotic/early stage
  - PMF, overt fibrotic stage

Less common types of MPNs are:

- Myeloproliferative neoplasm, unclassifiable
- Chronic neutrophilic leukaemia
- Chronic eosinophilic leukaemia, not otherwise specified (NOS)

2. Why do I have an MPN?

The exact cause of MPNs remains unknown but it is likely there will be many factors that contribute to the development of this group of bone marrow disorders. They arise from a change, or mutation, in the DNA (genetic code) of a single bone marrow stem cell, which results in abnormal blood cell development and the overproduction of blood cells. Mutations in dividing cells occur all the time and healthy cells have complex mechanisms within them which usually prevent these abnormalities persisting. The longer we live, the more chance we have of acquiring mutations that manage to escape these safeguards which is why MPNs, like most leukaemias and other cancers, become more common as we get older.

Environmental factors have been implicated in the development of MPNs in rare cases (e.g. cluster of PV cases in survivors of the atomic bomb blast in Hiroshima).

Most people with a myeloproliferative neoplasm have no family history of the disease but occasionally a predisposition to develop MPNs can be inherited. Researches in Australia are studying genetic links in MPNs and if two or more members of your family have a MPN please ask your haematologist about the possibility of being involved in this research.
3. What symptoms will I experience?

Although people with MPNs can be highly symptomatic many have no symptoms at the time of diagnosis with the abnormalities in their blood being an incidental finding on a routine blood count. Symptoms in people with MPNs, regardless of their disease subtype, can have a significant impact on both quality of life and life expectancy. The most common symptoms reported in patients with MPNs are fatigue, concentration problems, inactivity, night sweats, itching, abdominal discomfort, bone pain, weight loss and fevers.

(i) Symptoms of Essential Thrombocythaemia (ET)

Many people with ET have no symptoms and their ET is diagnosed when a high platelet count is noted on a blood count performed for some other reason. Other people present with disease-related symptoms or complications.

The most common symptoms that may be present include:

- Thrombosis (clots) (e.g. strokes, heart attacks, deep venous thrombosis)
- Fatigue
- Headache
- Dizziness
- Visual abnormalities
- Leg pain
- Coldness or blueness to fingers or toes
- Burning pain, redness in hands or feet (erythromelalgia)
- Bleeding and bruising

(ii) Symptoms of Polycythaemia Vera (PV)

Many people with PV, like those with ET, may not have any symptoms at the time of diagnosis and their elevated haemoglobin and haematocrit may be found on a routine blood count. Symptoms when present may be due to complications (e.g. thrombosis or bleeding) or disease-related.

The most common symptoms are:

- Facial plethora (redness of the face)
- Fatigue
- Headache
- Dizziness
- Pruritus (itching)
- Blurred vision
- Shortness of breath
Gout
Thrombotic complications (e.g. strokes, heart attacks, DVT)
Bleeding complications
Enlarged spleen which may result in:
    Fullness in the abdomen
    Early satiety (feeling fully rapidly when eating)
    Weight loss

(iii) Symptoms of Primary Myelofibrosis (PMF)

Approximately 20% of people with PMF have no symptoms at the time of diagnosis which is made when they are found to have an abnormal blood count or splenomegaly. The majority of people with PMF have symptoms at the time of diagnosis and these are usually due to:

Pancytopenia (low blood counts) which may result in:
    Tiredness, weakness or shortage of breath as a result of anaemia
    Frequent infections
    Easy bruising or bleeding

Enlarged spleen which may result in:
    Fullness in the abdomen
    Early satiety (feeling fully rapidly when eating)
    Weight loss

Bone pain
Constitutional symptoms
Anorexia
Unexplained weight loss
Night sweats

4. Is there a cure for MPNs?

Allogeneic stem cell transplantation is the only curative option for patients with MPNs and is typically reserved for patients with myelofibrosis (primary or secondary) when their life expectancy is less than 5 years.

5. Can I pass my MPN on to my family?

Myeloproliferative neoplasms are not contagious and you cannot ‘catch’ the disorder by being in contact with someone who has a MPN. Most people with a MPN have no family history of the disease.
6. Will my MPN affect my lifespan?

For many people the diagnosis of a MPN, particularly ET or PV, has minimal or no impact on their lifespan, if the disease is treated effectively. For a small number of people the MPN will have shorten their lifespan as it is associated with a risk of developing acute leukaemia. This complication usually occurs after the MPN has been present for many years.

Myelofibrosis is a more problematic disease and is frequently associated with constitutional symptoms, an enlarged spleen, low blood counts, an increased risk of leukemic transformation and a decreased life expectancy.

7. Do I need a bone marrow biopsy?

Most people with a suspected MPN undergo a bone marrow biopsy to confirm the diagnosis and subtype of the MPN and in some circumstances to provide prognostic information. In some people, such as older people with an elevated haemoglobin and haematocrit and positivity for JAK2, the treating haematologist may decide that a bone marrow biopsy is not required. In all cases the haematologist should discuss their recommendation with the patient.

The 2016 WHO diagnostic criteria for MPNs incorporates the finding on a bone marrow biopsy for all MPN subtypes.

Further information on Bone Marrow Biopsy procedure is available here: http://www.mps.com.au/media/3363941/bone_marrow_patient_dl_4pg_june_2016_final.pdf

8. How will my MPN be treated?

Therapy for your MPN will be determined by your haematologist and their recommendation will take into account your age, comorbidities (other health issues) and the presence of disease-related complications. Treatment aims to reduce burdensome symptoms and the risk of life-threatening complications, and where possible to minimise the risk of progression to acute leukaemia. Cardiovascular risk factors should be aggressively managed for all patients, including smoking cessation. More detailed information on many of the treatment modalities below is available in the “Treatments” Section of this website.

(i) Polycythaemia vera

The management of PV is focused on controlling symptoms and reducing the risk of thrombotic and bleeding complications. The treatment, or combination of treatments, recommended for you by your haematologist will depend on several factors,
including the duration and severity of your disorder, whether you have a history of blood clots, your age and your general health.

Treatment for all patients includes low-dose aspirin and venesections to reduce the risk of vascular and thrombotic events. Aspirin reduces the risk of thrombotic complications by reducing the stickiness of platelets. If you are allergic or intolerant of aspirin an alternate anti-platelet medication is usually recommended.

Venesection (or phlebotomy) is a procedure where blood is removed from your bloodstream. This procedure is commonly used when PV is initially diagnosed because it rapidly reduces the high red cell count and the risk of thrombotic complications. Usually 450 ml of blood is removed from a large vein at the elbow bend by nursing staff at your local hospital. This procedure is repeated frequently until your haematocrit (proportion of blood made up of cells) is reduced to the desired level of <45% in both men and women. The procedure is repeated as required to maintain the haematocrit at the target level.

For many people, particularly younger patients without any complications from their disease, regular venesections (every few months) may be all that is needed to control their disease for many years.

PV patients who are aged >60 years or who have a prior history of thrombosis receive therapy with drugs to slow bone marrow production of blood cells (cytoreductive therapy) in addition to aspirin and venesections. Hydroxycarbamide (hydroxyurea) is standard frontline therapy for PV patients requiring cytoreductive therapy. It is well tolerated with infrequent side-effects which can include low blood counts, macrocytosis (increased red cell size), leg ulcers and rarely drug fever and hepatitis.

Options for second-line therapy include interferon (women during pregnancy), busulfan (usually for older, high-risk patients), melphalan (infrequently used) or JAK inhibitors (not readily available in Australia for PV). If available participation in clinical trials may also be considered.

(ii) Essential thrombocythaemia

The role of aspirin is less clear in low-risk ET patients outside of the presence of microvascular symptoms although most haematologists in Australia recommend its use except in patients with a very high platelet count (>1500 x 10⁹/L) or with a bleeding tendency.

Cytoreductive therapy is used in high-risk ET patients to reduce the occurrence of thrombotic and haemorrhagic events. Frontline cytoreductive treatment may include hydroxycarbamide (hydroxyurea), which has been shown to lower thrombotic complications.
Anagrelide is a viable second-line therapy in ET although it is not currently PBS-funded in Australia. Other second-line options include interferon, busulfan or participation in clinical trials.

(iii) Primary myelofibrosis

The management of patients with myelofibrosis requires evaluation of the risk score using one of the prognostic scores (IPSS, DIPSS or DIPSS-Plus) and the symptom burden of the disease. Low-risk patients are often only observed with regularly monitoring of their blood count and symptom burden.

Patients with symptomatic anaemia may benefit from therapy with androgens (male hormones), low-dose corticosteroids, immunomodulatory agents or erythropoiesis-stimulating agents. Not all of these agents are readily available in Australia.

Cytoreductive treatments including hydroxycarbamide (hydroxyurea), cladribine, melphalan, and busulfan have been shown to be of only modest benefit for splenomegaly but may be used to control high white cell and platelet counts.

Ruxolitinib is approved for patients with myelofibrosis (risk groups: intermediate-1 risk with severe symptoms, intermediate-2 risk or high-risk) and has been shown to reduce splenomegaly, improve symptoms, and prolong survival.

Patients with symptoms due to splenomegaly (enlarged spleen) who have failed ruxolitinib and other pharmacological therapies may occasionally be considered for radiotherapy or splenectomy used to control symptoms.

For some myelofibrosis patients with progressive or advanced disease a stem cell transplant using blood stem cells from a family member or unrelated donor may be considered.

9. Is it safe to have vaccinations when I have an MPN?

Not all vaccinations are recommended for people with MPNs and you need to discuss which vaccinations are safe and appropriate for you with your GP or your haematologist.

(i) Live vaccines: If you have a weakened immune system or low white cell counts you should not have live vaccines and this may affect your choice of holiday
destination. Live vaccinations include BCG, (tuberculosis), MMR, (measles, mumps, rubella), oral typhoid, and yellow fever.

(ii) Inactivated vaccines: These vaccines are not dangerous to patients with MPNs but may be less effective if your immunity is low. These include influenza, pneumococcal, hepatitis A and B, and meningococcal vaccines.

10. Is it safe to travel overseas?

MPNs are a chronic disease and patients are encouraged to live as normal a life as possible despite the disease and for many people this includes travelling or holidaying overseas.

Prior to travel you should:

(i) Consult with your GP and/or haematologist to ensure you are fit for travel and that you have the medications you will require while you are overseas.

(ii) Check if you need any vaccinations prior to travel. Some vaccinations are not suitable for people on certain medications or with particular complications from their MPN.

(iii) Obtain travel insurance and ensure you inform your insurance company of your MPN diagnosis as not declaring the diagnosis of a malignancy may invalidate your insurance. If necessary, you can ask your GP or haematologist to write a letter stating your diagnosis, medications and general health status.

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