This is the first in a series of Leaflets that seek to explain in lay terms the nature of Pernicious Anaemia.

A simple explanation of a complicated subject. Written by members of the Pernicious Anaemia Society to help anyone with an interest in P.A. understand the condition.

This leaflet is for information only and is not intended as a substitute for professional medical advice. Any symptoms should always be discussed with your doctor.

Your doctor is the best person to advise you of any medical complaint.

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What is Pernicious Anaemia?

Firstly a few words about Blood. Technically blood is a tissue and is made up of two main parts: Blood Plasma and Blood Cells. Plasma is the liquid suspension that the Cells float in. Plasma will also contain vitamins, clotting agents, various dissolved proteins, glucose, hormones and anti-bodies that fight infections. The Blood Cell part of blood is made up of three types of Cells:

Red Blood Cells (RBC’s) also known as Erythrocytes, White Blood Cells (WBC’s) also called Leukocytes and Platelets or Thrombocytes. The body uses Platelets to clot the blood to stop bleeding. The White Blood Cells fight infections while the Red Blood Cells carry oxygen from the lungs to wherever it is needed.

All blood cells are produced in bone marrow. In adults, only specific bones produce blood cells (the sternum, backbone, ribs and pelvis) whilst almost all the bones in the body produce blood cells in children. The process by which the body produces blood is called Haematopoiesis. Red blood cells live for about 120 days and old cells are removed by the liver and spleen. Iron, Folic Acid and Vitamin B12 are all needed to produce healthy RBC’s. Red Blood Cells form the largest part of blood. The percentage of RBC’s in blood is known as the Haematocrit. A normal healthy person will have 600 RBC’s to every one White Blood Cell and 40 Platelets.

The main purpose of Red Blood Cells is to carry oxygen from the lungs to cells throughout the body. Some oxygen is carried in the Plasma but a protein in the Red Blood Cell called Haemoglobin allows a much larger concentration of oxygen to be carried by the RBC. Haemoglobin also makes the plasma more viscous. Red Blood Cells are able to change shape to allow them to carry the oxygen into very narrow capillaries where the exchange of oxygen takes place.

Left: a Red Blood Cell, A Platelet and a White Blood Cell
Right: Healthy Red Blood Cells – note the concave saucer shape on both sides.
Red Blood Cells have an unusual shape as they have a concave middle on each side of the cell. Without B₁₂ the cells become larger and ‘stretch’. When this happens the concave shape is lost. 33% of a Red Blood Cell is Haemoglobin (see a 3D image of this to the right). Each molecule of Haemoglobin contains four iron atoms and it is these iron atoms that give blood its red colour.

As stated above, Red Blood Cells need three essential ingredients to perform their main function – transporting oxygen around the body. These three ingredients are:

1. **Folate**
   Also known as Folic Acid which is a B vitamin – Vitamin B₉. Folate takes its name from the Latin Folium which means leaf so it should come as no surprise that it is found in leafy vegetables and peas and dried beans. Marmite and Vegemite also contain high concentrations of Folate as do most breakfast cereals. Folic Acid is added to bread in several countries.

2. **Iron**
   The second essential ingredient for healthy red blood cells is Iron. This is found in Red Meat, Fish, Poultry, Lentils, Beans, Black-eyed Peas and in Beery Drinks such as Bovril.

3. **Vitamin B₁₂**
   The third essential ingredient needed for healthy red blood cells is Cobalamin or Vitamin B₁₂. This is structurally the most complex vitamin - (C₆₃H₈₈CoN₁₄O₁₄P) and is found naturally in Meat, Fish and Dairy products including Milk, Butter and Eggs. Strict Vegans who eat no animal products are therefore at risk of developing B₁₂ deficiency especially if they only eat washed vegetables (there is some Vitamin B₁₂ in soil).

B₁₂ is extracted from these various food stuffs in a very complex biochemical process that takes place in the stomach. The B₁₂ enters the stomach bound to proteins found in saliva. Gastric Parietal Cells in the stomach release a special protein called Intrinsic Factor when food is being digested. The Intrinsic Factor binds itself to the B₁₂ and this partnership (IF/B₁₂) is then absorbed by the Ileum which is part of the stomach found in the small bowel. The B₁₂ then goes on to play its part in forming healthy RBC’s.
The absorption of B12 is, then, dependent on the Gastric Parietal Cells working correctly to produce the Intrinsic Factor. Without the Intrinsic Factor the B12 cannot be absorbed by the stomach. And so it may come as a surprise to discover that Pernicious Anaemia is not caused by a malfunction of blood but by a faulty digestive process that leads to lack of B12 that results in a problem with Red Blood Cells in the patient’s blood. If the gastric parietal cells do not produce the Intrinsic Factor then the B12 cannot be absorbed and the Red Blood Cells will not be able to do their job properly. This is why some people who have undergone major stomach surgery sometimes develop Pernicious Anaemia.

However, the number of people suffering from Pernicious Anaemia because the parietal cells do not produce Intrinsic Factor is a very small percentage of people who have the condition. This is because most sufferers of Pernicious Anaemia have a correctly functioning digestive system that produces the Intrinsic Factor necessary to bind with the B12 that can then go on to being absorbed into the blood supply.

So where’s the problem? If the person with P.A. is producing the Intrinsic Factor why can the B12 not be absorbed? Because as well as producing the needed Intrinsic Factor, patients with Pernicious Anaemia somehow, and for an unknown reason, also produce something that ‘kills off’ the Intrinsic Factor. People with Pernicious Anaemia produce Intrinsic Factor Antibodies that destroys the Intrinsic Factor that they have produced. This is why one of the tests used to diagnose Pernicious Anaemia is the test for Intrinsic Factor Antibodies – the Intrinsic Factor Antibody Test. If a patient tests positive for the antibodies then he or she is diagnosed as having Pernicious Anaemia.

Deprived of B12 the Red Blood Cells become larger, (measured by doctors as the Mean Corpuscular Value or M.C.V.), and they also become elongated rather than round. As they ‘stretch’ into an elongated shape the concave depression in the middle of the cell flattens out. This concave shape was responsible for carrying the Oxygen molecules and so the larger, elongated cell is able to carry much less Oxygen than a healthy cell. Therefore the body is deprived of adequate supplies of vital Oxygen.
Doctors do not know why some people produce antibodies that kill off the Intrinsic Factor. P.A. is not the only condition where this self-destruction of essential body functions occurs. Doctors classify medical conditions where this self-destruction happens as Auto-Immune Diseases.

There is a tendency for patients of Pernicious Anaemia to also suffer from other autoimmune diseases and research into why this is so is being undertaken by doctors who specialise in Genetics. And while we are on the subject of Genes, there is around a 30% chance of Pernicious Anaemia being inherited from and/or passed on to relatives.

The other auto-immune conditions that many sufferers of Pernicious Anaemia develop include: Tinnitus*, Psoriasis, Rosacea, Autoimmune, Thyroiditis (over or under active thyroid) Coeliac Disease.

*not strictly an auto-immune disease but is so common among members of the PA Society that some doctors believe it to be a symptom of Pernicious Anaemia.
What are the symptoms?

The Symptoms Of Pernicious Anaemia

It is important to realise that the symptoms of Pernicious Anaemia varies from patient to patient. And while some sufferers might well share some common symptoms, they might experience the symptoms to a greater or lesser degree than other patients. There are some people who have been diagnosed and confirmed as having Pernicious Anaemia who experience none of the following symptoms (although these are few in number) and some unfortunate patients who experience most or all of the following and struggle to cope with everyday life because of this. This list of symptoms has been gathered from postings on the forum of the Pernicious Anaemia Society between November 2007 and August 2009. Some patients have reported isolated symptoms but where only one or two people have experienced the symptom it has not been included. The following have been experienced by many patients of Pernicious Anaemia.

Physical Symptoms (Common)

1. Tiredness, Lethargy, Exhaustion, Fatigue, Weariness - The Strange Tiredness

None of the above accurately describes how a person with Pernicious Anaemia feels. The feeling is neither one of the words, nor is it a combination of the words. Together they go some way to explaining how the person feels, but there is no single word that gives an accurate description of the feeling. Feeling tired or exhausted can be a very positive experience as anyone who has played sport can tell you. But this is not a pleasant experience. It is an insidious, creeping, overpowering feeling that seems to sap any strength that you might have. It doesn’t quite leave the sufferer being unable to do normal and everyday tasks but rather makes such tasks (however trivial) a real trial. Sufferers often cope with everyday work and domestic tasks, but most struggle to do so. There is no one word in English that accurately describes the feeling that people with Pernicious Anaemia experience in relation to their tiredness. Perhaps the best description used by one sufferer is “that strange tiredness”.
2. Waking-up Tired
This is very common amongst sufferers. Despite sleeping heavily for over the usual 8 hours the patient is still tired on waking-up. A great many patients report needing at least 10 hours sleep with 12 hours being the norm.

3. Shortage of Breath - The Sighs
This is one of the most misunderstood of all the symptoms. There are some sufferers who begin to breathe heavily when performing any physical activity such as walking up stairs, general household cleaning, lifting and brisk walking, but only very rarely is there any gasping for air. However, it is the need to take deep breaths when not performing any activity that causes the most concern. Sufferers often refer to this need to take in ‘lumps’ of air as ‘The Sighs.’ Often it may seem that the patient is struggling to breathe, but he or she will simply be trying to satisfy the need to take in a deep breath. This can often be accompanied by the need to yawn, sometimes almost continually. One of the strangest aspects of The Sighs is that they don’t occur every day. Patients often talk of good & bad days. On good days the patient might not feel the need to ‘sigh’. On bad days he or she might need to ‘sigh’ for most of the day or for just a short period.

4. Brittle, Easily Damaged Nails
The nails on both hands and feet become brittle and split or break very easily. Not only will the nails be brittle but they may often have ridges running down the length of them. Many patients never have to trim or cut their nails as they break off whenever they become anything other than short.

5. Unaccountable Sudden Diarrhoea
Again this is often experienced but not often talked about. This is often preceded by a spell of constipation.

6. Swollen Tongue - Glossitis
This is often quoted as being one of the most common symptoms of P.A. However, only a small percentage of sufferers of Pernicious Anaemia experienced a swollen, smooth and ‘beefy’ red tongue. Perhaps the figure is as low as 10%. Those who do have a swollen tongue often complain that their tongue bleeds and becomes tender.

7. Feeling Bloated or Full
This is often accompanied by a physical swelling of the stomach. The patient will feel ‘full’.

8. Pale Yellow - Tinged Skin
Again, this is not as common as previously thought and is related to abnormal liver function.

9. Pins & Needles
This can be the first sign of damage to the peripheral nerves.
The pins & needles can be experienced anywhere on the body, but it mainly affects the tips of fingers and feet. Many patients report that these pins & needles disappear completely after they receive their prescribed treatment. Rather strangely in some cases the pins and needles disappear within hours of the first injection of Hydroxocobalamin being administered.

10. Sock and Glove
This refers to a numb sensation in the patient’s fingers and feet – it feels as if you are wearing socks and gloves. Again this can be seen as damage to the peripheral nerves but patients often report that this sensation disappears once treatment is started.

### Physical Symptoms (Less Common)

#### 1. Unusual Gait
This occurs when the central nervous system has been damaged. The central nerves are located in the spinal cord. The degree to which the nerves will have been damaged will determine how awkwardly the patient walks. When both peripheral (feeling of numbness) and central nerves have been damaged the diagnosis is Sub-Acute Combined Degeneration of the Cord Secondary to Pernicious Anaemia.

#### 2. Unsteadiness - **The Shoulder Bumps**
This is linked to the above and, again, the severity of the symptom will depend on how much damage has been done to the central nervous system. Typically the patient will have problems with the following:

- **Showering:** the patient will not be able to stand up unaided with his or her eyes closed.
- **Dressing:** especially when trying to put on underwear or hosiery when standing up.
- **Walking:** because of damage to the balance functions in the brain, the sufferer will compensate for that damage by looking at the ground, or a wall in close proximity.

The ground or wall provides a reference point for the brain to balance the patient. There are other instances where this need for a reference point becomes a problem. Most of these are related to dark rooms, walking during the night and Vertigo. The inability of the patient to
Mental Symptoms (Common)

As well as physical symptoms, sufferers of P.A. also experience changes to their mental ability and personality. These cognitive symptoms are often more difficult to explain and deal with than the physical symptoms. It seems to be the case that these mental challenges are often not recognised or acknowledged by some medical professionals. As with the physical symptoms, the degree and effect of these symptoms will vary between different patients.

1. ‘The Fogs’
This is by far the most common complaint by sufferers of P.A. Patients find it difficult to define exactly what they experience on a ‘foggy’, but there is a general feeling of lack of focus and a lack of clarity in everything they experience. It’s as if the patient is experiencing being in a thick fog, with all of the senses failing to respond as quickly as they usually did. The degree to which this occurs is directly proportional to whether the patient is experiencing a good or bad day.

On a bad day it is possible that the patient will forget the names of even their closest relatives, be unable to recall even the most common proper nouns, repeatedly ask the same question, forget a conversation from even the shortest time before, make mistakes in their work — even the most fundamental mistakes and feel ‘not with it’. The patient will often seek peace and tranquillity in order to give full concentration to the task he or she is dealing with.

The most common way in which the patient can explain what it feels like to be in a fog can be summarised by the following statements: “I just want the world to go away”. “I just want to be left alone”. “I don’t want to be forced into conversation”.

Patients also state that leisure activities such as reading, watching television or going to the cinema can be enjoyed during a ‘fog’, but the next day the chapter of the book that was read, or the outcome of a t.v. programme and the plot of a film will be forgotten. The chapter of the book would have to be re-read and the television programme or film would have to be seen again. ‘Fogs’ can last a few hours, a day, or a few days.

3. Burning feet/legs - Grierson-Gopalan Syndrome
This occurs mainly in middle-age and is usually worse at night. It is directly linked to B12 deficiency and usually disappears once treatment is started. It is known to doctors as Grierson-Gopalan syndrome.
Patients are aware that they are experiencing a ‘fog’ but are unable to do anything about it. It’s simply a case of ‘riding it out’. Most patients wake up either the next day or in a few days time and experience a clarity and focus to their thinking which had been absent during the fog.

2. Irritability / Impatience and Mood Swings.
This is another very common condition amongst sufferers of Pernicious Anaemia and probably has the greatest impact on personal relationships. It was only through the PA Society’s Forum that this characteristic has been clearly identified as being a major consequence of Pernicious Anaemia.

These periods of irritability or impatience or sudden mood swings can manifest themselves at different times and over different periods of time. Some patients are aware that they become irritable and lack patience on a daily basis, usually in the afternoon of a working day when tiredness and problems with concentration results in a change in attitude and mood.

The demands of work, or family or friends, often lead to the patient struggling with tiredness, and lack of concentration and frustration manifests itself in bad humour. Other patients go through a period of calm before experiencing a few ‘bad days’ when the energy needed to meet all kinds of demands is non-existent and exasperation and exhaustion leads to frustration with all aspects of the patient’s life. This can lead to irrational and uncalled for outbursts. It is important to realise that it is not all patients who display such behaviour, and often the patient is able to somehow develop a coping strategy that allows him or her to manage the frustrations being experienced.

For others who are unable to cope with the pressure, the outbursts of irrational reactions to situations and demands can lead to workplace issues as well as problems with his or her domestic life. Having understanding work colleagues and an understanding family who are able to refrain from making any demands on the patient is obviously the best way in which to deal with this issue. This would take the pressure off the patient and lessen the feelings of frustration that culminate in outbursts. Many patients are able to manage this problem by simply not dealing with any demands that are being made of them.
These symptoms have been reported by members of the Pernicious Anaemia Society and are infrequent but not unheard of. It is important that, if you believe you have any of the following symptoms, you make your doctor aware of your experiences.

1. Depression
This can take many forms and it is beyond the scope of this information leaflet to describe this in any detail. Unlike the changes in emotions and the irritability as described on the previous page, depression, in all its manifestations, tends to last much longer than the symptoms previously described. The mental symptoms described in this leaflet are acute — sometimes lasting just a few hours, maybe days — and patients soon learn that it is only a matter of time before he or she will return to a more normal state of mind.

However, if the common mental symptoms described previously in this leaflet seem to be long-term then it could be that you are experiencing a form of depression and you should seek medical help. There are a wide range of medicines and other treatments which can help you to deal with your condition and your doctor will be able to help you in a variety of ways.

2. Inability To Cope At Work
Living with P.A. and working or developing a career is often difficult and many sufferers struggle. However, if you are struggling to cope at work and you risk putting the safety of others at risk, it would be in the interest of everyone to discuss this matter with your immediate supervisor.

In rare circumstances, the inability to cope with the demands of a career has meant that patients have had to make the difficult decision and change careers or even give up working completely. Like so many other aspects of P.A., the impact of the condition on the individual will vary considerably from patient to patient.

3. Pica
This is often experienced but not often talked about. Pica occurs when the patient craves something unusual to eat. Surprisingly popular among sufferers of P.A. is the craving for ice. Other less common but still documented is a craving for eating earth, leaves and garden weeds. Another craving experienced by a few members is for decorator’s filler — such as Polyfilla.

Nobody really understands why these cravings happen but it is thought that it is associated with an instinctive response for the need for Iron which is associated with soil. This doesn’t explain why ice continues to head the table for unusual cravings.
Unfortunately, sufferers of Pernicious Anaemia have a disposition towards other auto immune conditions. Doctors still do not know why this is the case which is why there are various research programmes being undertaken to find out why this is so. The Pernicious Anaemia Society is playing an active part in one such study which is looking for a common gene that would explain why patients of Pernicious Anaemia are prone to developing these other auto immune conditions:

1. **Tinnitus**
The patient will experience ‘ringing’ in the one or both ears. The ‘ringing’ takes many forms and includes high pitched howling or whining or whistling that can last a few seconds or hours.

2. **Psoriasis**
This is where the skin regenerates itself quicker than it needs to which leads to white scaly patches appearing. Psoriasis can be chronic or occur as a ‘flare up’ especially in the spring. Various treatments are available depending on the severity of the condition and include steroid creams and UV Light therapy. The effectiveness of the various treatment regimes varies from patient to patient. Associated with this is the rarer Genital Psoriasis which is fully treatable.

3. **Psoriatic Arthritis**
This is associated with Psoriasis and usually develops about ten years after Psoriasis first appears and causes painful joints and sometimes swelling - especially in the fingers and toes. It is a type of inflammatory arthritis and is treated using anti-inflammatory drugs.

4. **Vitiligo**
This causes irregular pale patches of skin due to loss of pigment. The exact cause is unknown but it is thought to be a combination of auto-immune and genetic conditions. Vitiligo is a chronic condition. Cosmetic make-up, steroid creams and UV light therapy are all used to treat the condition.

5. **Rosacea**
The ‘curse of the Celts’ - it mainly affects people of north European ancestry - manifests itself in redness of the face and neck. Treatment depends on the type of Rosacea encountered but is mainly by antibiotics tablets and antibiotic creams.

6. **Autoimmune Thyroiditis**
This is caused by either an over or under-active thyroid gland. This condition shares many of the symptoms of PA including tiredness and lack of concentration. There are different types of Thyroiditis and each type has its own treatment regime.
7. Rheumatoid Arthritis
Where the body’s auto-immune system attacks the bone joints leading to what can be a severely painful condition that makes moving of certain parts of the body very difficult. There are various treatments used to treat RA including Cortisone therapy.

8. Coeliac Disease
Which is a reaction to Gluten, a type of protein found in wheat, rye, and barley. A few people are also sensitive to oats. It is characterised by chronic diarrhoea which can be a symptom of PA. A Gluten free diet is used to treat the condition.

9. Eczema
Which is a broad umbrella term for a wide variety of skin conditions that range from mild itching to large areas of severe red ‘angry’ skin. Various treatments are available.

As is always the case, your doctor is the best person able to advise and treat any issues that have been addressed in this leaflet and he or she should always be consulted as soon as any symptoms occur.

The Treatment of PA

Serum B12 Tests

There are many issues surrounding the treatment of Pernicious Anaemia. The single most common complaint by members of the society is that most members do not believe that the usual treatment regime used by doctors in the U.K. is adequate. Unfortunately it is all too common for members who ask for a more frequent treatment regime to be offered anti-depressants instead of a harmless vitamin. The reason for this is that the amount of B12 in the patient’s blood will usually be well within the reference range used by doctors to determine whether or not the patient is B12 deficient. So why would
doctors prescribe more frequent injections when the total amount of B12 in the patient’s blood is adequate?

The fact is that there is mounting evidence to support the patients view that more frequent injections are needed including the following:

- In the 1960’s the treatment regime to treat B12 Deficiency in the U.K. was an injection of Hydroxocobalamin every month. That was changed in the 1970’s to every two months and then to every three months in the 1980’s.1

- There are two types of B12 in blood. One is Active B12² and the other is Inactive B12³. The active B12 is the important type to measure because it is responsible for the biological activity taking place. The inactive B12 is not playing any part. If a person has a large percentage of inactive B12 in his or her blood then this would account for the person experiencing the symptoms of PA. Yet when the total B12 is tested there is no differentiation between active and inactive B12. And if the test result shows total B12 in the sample as being over the lower limit the patient is regarded as having ‘normal’ levels. There is a test that has been developed that identifies only active B12 levels in blood and the PA Society is campaigning to get this test made available in the NHS.

### Treatment Regimes

In the U.K. and most other countries, the treatment for Pernicious Anaemia involves replacement therapy using Hydroxocobalamin⁴ which is a form of B12. This is injected (usually by a nurse) into a muscle. However there are other treatment regimes available but research into the effectiveness of these different forms of treating PA is either non-existent or very scant and usually very old.

You are advised to discuss these alternative treatment regimes with your Doctor before attempting to access them as he or she is the best person to advise you.

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1 This was taken from the British National Formulary publications from the past.
2 Holotranscobalamin
3 Holohaptocorrin
4 Other European countries, along with Canada and the U.S.A. use Cyanocobalamin. Cyanocobalamin can be bought over the counter in pharmacies in most countries in mainland Europe.
Cyanocobalamin Tablets. These are available on prescription in the U.K. and from many health food shops. They are used to treat patients who are extremely needle phobic and they do contain cyanide. They are extremely strong tablets and, whilst most of the B12 is not absorbed, some does make its way into a section of the stomach where it is absorbed. The society has adopted a policy that is against the use of these tablets instead of injections.

Sub-Lingual Methylcobalamin Lozenges. Methylcobalamin is a ‘purer’ form of B12 than Hydroxocobalamin. Placing the lozenge under the tongue (sub-lingual) means that the B12 passes into the bloodstream via the membrane situated under the tongue. They are available from health food stores and online stores.

Methylcobalamin Sub-Lingual Spray. These have similar effects as the Sub-Lingual Lozengers.

Methylcobalamin Infusions. These are available in the Private Sector in the U.K. The treatment involves receiving an infusion of B12 directly into the bloodstream. The patient then uses Methylcobalamin to self-inject just under the skin as often as he or she thinks they need it. You should always seek your doctor’s advice before exploring this treatment and you should ensure that the person carrying out the infusion is a fully qualified and insured doctor who is a member of the G.M.C.

Other Leaflets In The Series Include:

- P.A. PAIL 1
- SACDCS P.A. PAIL 2
- Vitamin B12 Deficiency in pregnancy and new born infants PAIL 3
- Juvenile P.A. for parents PAIL 4
- Juvenile P.A. for patients PAIL 5
You can receive further information about Pernicious Anaemia by:

**Visiting our website**

www.pernicious-anaemia-society.org

To access all of the information you will need to join using the online membership form.

There is a lifetime, one-off membership cost of £20. We accept all major Debit and Credit cards.

**Telephoning our Helpline**

Leave a message and our qualified nurse counsellor will telephone you back as soon as she can.

Telephone: 01656 769717

**Join by post**

The Pernicious Anaemia Society  
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Becoming a member means you will receive our regular newsletter ‘Cobalamin News’ that will keep you up to date with developments in the treatment and diagnosis of Pernicious Anaemia. You will also receive:

- Informative welcome pack
- Access to our professionally manned helpline
- Invitations to social events
- Details of local support groups

Telephone: 01656 769717

The information displayed in this leaflet is for information only. It is NOT designed to be a substitute for advice given by your doctor or other medical professionals.

Your Doctor is the best person to advise you.