

## Common Variable Immunodeficiency (CVID)

**Provided by Dr David Webster – Medical advisor to the Group**

CVID is the most common of the PIDs. The term ‘common variable’ is used by doctors as an ‘umbrella’ for a spectrum of primary antibody deficiencies (PADs) where they do not know the genetic cause and mechanism. At the severe end of the spectrum (i.e. those that need immunoglobulin therapy) CVID is certainly not common, with only about 2000 affected patients in the 55 million UK population. However, milder PAD defects are relatively common, and in one form or another can be as frequent as about 1 in 1000 people. The reason for thinking that CVID has a spectrum of severity is that milder forms are seen in some family members of about 1 in 10 severe CVID patients, suggesting that the same inherited genes play a part in all CVID types. Having said this, specific inherited genetic defects are gradually being discovered in a few CVID patients, and when this happens these patients are given a new diagnosis and lose their CVID identity. Currently most researchers think that the bulk of CVID patients have a complex genetic disorder with defects in more than one gene being involved, probably with an environmental trigger like a viral infection to push the immune system off the track.

Most CVID patients are diagnosed between the ages of 15 to 40 years although it can occur in children or the elderly. The main defect in those with severe CVID is a complete failure to produce antibodies which protect against a variety of bacterial and viral infections, particularly in the lungs. Most patients initially complain of repeated infection in the sinuses, ears and lungs, although bowel infection with diarrhoea is also common. Although pneumonia and septicaemia can be a serious initial event, most patients suffer from bronchitis that keeps recurring despite courses of antibiotics.

In addition to the antibody defect, CVID patients are prone to chronic inflammation in various organs (e.g. spleen, liver, bowel, lymph glands and lungs) that are not apparently caused by bacterial infection. About a third of CVID patients develop such inflammation during their lifetime and often need steroids or other immune suppressive therapy to control this inflammation. Ongoing research at the Royal Free has found evidence that some viruses are involved in this inflammation. It is not yet clear whether this exaggerated inflammatory response is connected to the cause of the underlying antibody defect.

Once diagnosed and treated with regular intravenous or subcutaneous immunoglobulin (antibody) infusions, most CVID patients do well and have a normal lifespan. The key is to make the diagnosis early in the disease and not to wait until infection has caused lasting damage, particularly in the lungs. There have been awareness campaigns by support groups in the UK to alert doctors and potential patients to the diagnosis.

## A Patient's story

Hi, welcome to my story!

For 15 years or so I had suffered repetitive coughs, chest infections and pneumonia, despite an otherwise healthy and fit lifestyle. I had never smoked, had a drink socially and never abused myself with drugs, but I worked some demanding hours and put it down to recurrent infection due to fatigue and stress.

I was never scared of visiting my GP who I trusted and had an excellence relationship with over many years. In fairness I felt he always had the interests of all of my family at heart. I was prescribed antibiotics on many occasions. The most sinister characteristic of my condition was a very painful and debilitating glandular enlargement just under my ears; I took loads of Nurofen to get me through the day.

I eventually insisted that my GP refer me to a general hospital physician, and due to the nature of my business and the likely wait time I took the private route. After numerous tests and conversations I was then referred to a chest consultant; still more tests followed and time moved on. Frankly I was becoming a little frustrated and concerned over several suggestions on diagnosis which later turned out to be way off the mark.

After many months the break through apparently came when my condition was being discussed at The London Chest clinic in a canteen when a student overheard a conversation and suggested COVID! Within a few days I found myself sitting in front of a very impressive and professional pair of gentleman at The Royal Free who talked me through COVID, and the reasons I had been having repetitive infections for so long.

The conversation was a little surreal, especially the bit when they announced 'you won't' get over this', and 'it's the long game'. I have always taken the view that I was impregnable and have a stoic attitude, but have to say this was not what I had expected to hear. However I was encouraged to hear that there was a plan for me to have regular infusions to replace the deficiencies in my immune system and that this was to start right now as my trough level was only 1!

I had a plethora of questions such as - 'how long has this being going on, will I feel better, will this make me susceptible to cancer, is it hereditary, will my children be affected, what's my life expectancy, why did so many doctors miss this' and so on. In fairness my questions were answered satisfactorily and my mind put at rest. Initially, the most significant drawback was the advice about travelling to certain countries that had a high risk of infection: don't go!! Quite a drawback for me as I am a high-miler traveller for the international businesses I own and run. I did have a couple of scares, one of which was during a business trip to India when I lost two stone and looked very poorly. This naturally bought me a bag of tests and investigations but now I am back to normal. On the positive I have never had any adverse effects to infusions and accept the two weekly visits to hospital as a way of life and something for me!! I won't be travelling to South America or India any time soon but do travel to selected safe countries in Europe, Middle East and North America.

Three years down the line I have enjoyed exceptional care and attention at every level. The environment is one of a high level of care with an appropriate use of humour. Although I live in Hertfordshire I feel lucky to have a solution at a great hospital with great people. I just get on with it and have a very busy and happy life supported by the RFH team.