Bethlem myopathy

What is myopathy?
The term myopathy is derived from the Greek language and means muscle disorder.

What is Bethlem myopathy?
Bethlem myopathy (BM) is a little known muscle disorder, which is named after the Dutch doctor who first described the condition in 1976. Diagnosis and recognition of it has improved over the past few years following work done by a number of researchers around the world on the identification of the protein involved. The protein is called collagen VI. A fault in any of the three genes for collagen VI can give rise to BM.

How does the disease present?
First symptoms of BM can present at any time from birth through to adulthood and are very variable. In childhood these symptoms can be hypotonia (floppiness), muscle weakness, delayed motor milestones (for example when a baby first sits up unaided or learns to walk), talipes (clubfoot), torticollis (stiff neck) and contractures (tightness) in the ankles, hip, knees and elbows. The contractures are often quite variable and can come and go over time.

Adults with BM can have tight tendons at the back of their ankles, as well as tightness of various other joints (elbows, knees, joints in the back) and especially some of the muscles in the hands. Other symptoms such as poor stamina/poor exercise tolerance and difficulties walking upstairs or doing tasks which require lifting the arms above the head are related to the subtle muscle weakness that tends to go with Bethlem myopathy. In addition, the skin of some people with BM can be unusual. Over the outer surfaces of the arms and legs especially it can feel rough or dry to touch and has been described as looking like “plucked chicken skin”. Other patients might find that they scar in an unusual way, either by forming keloids (raised, rather angry looking scars) or thin silvery “cigarette paper scars”.

How is Bethlem myopathy diagnosed?
The diagnosis of BM is usually suspected from the symptoms and examination, paying special attention to the features described above. Because it is a rare disorder not very many doctors have experience of these features and people with Bethlem myopathy may often have had other diagnoses suggested in the past.

It is often necessary to do a blood test and a muscle biopsy to exclude other conditions that can present in a similar fashion. The muscle biopsy is studied through a microscope to check how the muscle is put together and whether there is any evidence of it being damaged. In BM the muscle fibres, instead of being evenly sized, show some variation but no significant damage or scarring. With special stains we can also check for a special protein called laminin beta 1, which can sometimes be reduced. However this only provides additional evidence, as these findings are not entirely specific to BM. At present the diagnosis of BM is usually made by collating the information gathered from history and clinical examination with laboratory findings.

In some cases it is possible to prove the specific diagnosis by demonstrating a fault in one of the genes encoding for collagen VI. This can be done using a skin biopsy or blood sample. At present it is available on a research basis only and results take months to years to come through. However, we are hoping this will change over the coming year.

Is Bethlem inherited?
BM is inherited in what we call an autosomal dominant way. This means that there is a 50% (one in two) chance for the children of a person affected by BM to inherit the faulty gene and be affected by BM themselves. This is independent of how mildly the parent might be affected. Sometimes when people are diagnosed as having BM, neither of their parents seems to be affected. In some cases the fault in the gene may have arisen for the first time in the affected person, which is quite a common situation.

Are there any risks of developing any complications?
The main complications to look out for at the regular check ups in the muscle clinic are contractures (muscle tightness causing restrictions in the range of joint movement) and chest problems. People with BM can be prone to chest infections if their cough is not strong due to weakness of their breathing muscles and in some cases overnight sleep studies may be required to assess breathing. From what we know so far the heart, although a muscle, is usually not affected by BM.
It is important to note that collagen VI mutations cause a more severe condition as well called Ullrich congenital muscular dystrophy (see relevant factsheet).

Does the condition get worse?
For most patients with BM the weakness and contractures are known to get worse over the years, however, this usually only happens very slowly. Whereas some adults remain unaware of any muscle weakness and only have very slight contractures which do not pose them any functional problems others need to make use of practical home aids to work around their muscle weakness and contractures. A proportion of adults over the years might need aids to help movements (for

example, cane, crutches or wheelchair) outside the house and might also experience breathing problems for which they require treatment.

Is there a treatment or cure?
At the moment, there is no cure, nor any specific drug treatment for Bethlem myopathy. However, there are ways, described below, of helping to alleviate the effects of the condition and to prevent complications from occurring.

What help can be offered?
Physiotherapy is one of the main forms of help. A programme of exercises is usually worked out with a physiotherapist at the time of the diagnosis to stretch tight joints and help to maintain suppleness and keep muscles flexible. It is important to keep a close eye on mobility and joints and this can be done in conjunction with the local physiotherapy team as well as through regular check-ups with your consultant or muscle clinic. Occasionally surgery to release the Achilles tendon can help a person with BM to stand and walk more easily. Children and adults with BM are encouraged to remain as active as possible and ensure that they do not become overweight, so that the strain imposed on their muscles is kept to a minimum.

People with BM can have chest problems if their cough is not strong. It is helpful to keep a close eye on things by doing specific breathing tests at regular intervals. Where there may be a problem, flu and pneumovax immunisations are advisable. It also important, that every chest infection is treated promptly with antibiotics.

Constipation, possibly due to the fact that a person is not very active, can be a problem. This can be treated by high fibre diet, drinking plenty of fluids and very occasionally by laxatives.

Your consultant or muscle clinic may be able to give support and information to schools and other professionals where this is needed to be sure a person with BM is getting the help he or she needs. The specialised Muscular Dystrophy Campaign Care Advisors can sometimes help to liaise between the various professionals such as physiotherapists, occupational therapists, social workers and teachers and may also be able to put you in touch with like-minded people in similar positions.

MC02
Published: 03/2008
Author: Prof .K.M.D.Bushby MD FRCP, Professor of Neuromuscular Genetics, University of Newcastle upon Tyne and Dr Anne Lampe, South East of Scotland Clinical Genetic Service, Edinburgh.