Muscle biopsies

A muscle biopsy is a minor surgical procedure, which involves removing a small piece of muscle for analysis. There are two types of muscle biopsy; open and needle, and these are both usually conducted under a local anaesthetic but may be performed under a general anaesthetic. The muscle sample is sent to a laboratory where it is examined for various abnormalities. Results are usually available in a few weeks.

What is a muscle biopsy?
A muscle biopsy is a surgical procedure in which a small sample of muscle is removed and examined. It is considered to be “minor” surgery, and is usually conducted as a day case, under local or general anaesthetic. A doctor usually requests a muscle biopsy after a physical examination, blood tests, and an EMG (electromyography).

Why have a muscle biopsy?
A muscle biopsy is undertaken to aid diagnosis of a condition and makes it possible to determine whether the condition is muscular or neurological. It can help indicate if a particular gene is involved and help direct molecular analysis towards that particular gene. Neuromuscular conditions often have characteristic patterns which are visible under a microscope and these can help determine the exact condition.

What does it involve?
A muscle biopsy can be taken from a number of different muscles. The most common are the upper arm, shoulder, thigh and calf muscles. It is important that the muscle used is affected in the disorder which is suspected, but that it is not severely wasted. The sample is only a few millimetres in size and with time the area sampled re-grows. A muscle biopsy does not increase any muscle weakness.

There are two different types of muscle biopsy:

Needle Biopsy
This involves inserting a needle, about 5mm in diameter, into the muscle. When the needle is removed a small sample of muscle remains inside the needle and this is taken for analysis. The incision through which the needle is inserted is usually only a few millimetres in length. Once the sample has been taken, the incision is held together with sterile strips and a plaster, and no stitches are required. The scar that remains is very small.

Open Biopsy
This involves making an incision a few centimetres long but the size is kept to a minimum. Once the sample is taken, the incision is closed with stitches. The scar from this technique will be bigger than from the needle biopsy, but it allows a bigger specimen to be collected, which may be necessary in some cases, and makes the need for a second biopsy less likely.

Both types have their advantages and disadvantages, and the preferred method can vary between hospitals.
Are there any risks?
The risks associated with muscle biopsies are very small. With all neuromuscular conditions, care must be taken when using anaesthetics. For all muscle biopsies it is assumed that the patient is at risk for malignant hyperthermia (an adverse reaction) and the precipitating anaesthetic agents are avoided, so the risk is negligible. There is a small risk of muscle damage and infection, but these are very rare. It is not uncommon to have a patch of numbness around the scar which may last for a few weeks.

Is there an alternative?
A muscle biopsy is a standard procedure when testing for most muscle conditions. Molecular genetic testing is available for some conditions and a muscle biopsy may not be necessary, but this applies to only a few disorders. It is common for these conditions to be excluded using a blood sample before a muscle biopsy is performed.

What happens to the sample?
The sample is transported to the laboratory and most of it is frozen. Very thin slices are cut and stained with various dyes and examined under a microscope. Some of the sample is also frozen for biochemical studies. A small portion is placed in a preservative so that it can be examined at very high power in an electron microscope, if required. With the agreement of the patient, any unused portion of the sample is stored so that developments in the field can be applied, even if the faulty gene is identified.

Histology
This involves looking at the overall appearance and structure of the muscle cells. The muscle is stained using various chemicals in order to see different structures. This analysis gives information about the muscle structure and the appearance of characteristics specific to certain conditions.

Histochemistry
This technique also uses chemical stains, but looks at the action of chemicals within the muscle fibres. This includes enzymes, and so is important for the diagnosis of metabolic disorders. In addition histochemistry reveals the characteristics for the two main types of muscle fibres we all have. Changes in the normal pattern are used to identify a particular condition.

Immunohistochemistry
This procedure uses antibodies which bind to a specific protein and can show the presence or absence of important proteins within the muscle. When antibodies are tagged with a marker they can be seen under the microscope and can show if a protein is in the wrong place, or is absent. This is important for several muscular dystrophies such as Duchenne muscular dystrophy, which is caused by the absence of the protein, dystrophin. Antibodies are also used to show changes in several proteins simultaneously using a biochemical technique that separates each protein out on a special type of jelly.

Electron Microscopy
Electron microscopy allows high magnification of each muscle cell, making it easier to see structural abnormalities. This is relevant for conditions such as nemaline myopathy where the diagnosis is based on the presence of rod structures in the muscle. Some abnormal features are only visible with the high magnification provided by electron microscopy.

What are they looking for?

Normal Muscle
Healthy muscle has a characteristic appearance, and is made up of closely packed fibres which are more or less evenly sized (Fig 1). There are two main types of muscle fibre which have different functions. They are called type 1 and type 2. Each fibre has several structures round its edges called nuclei, each of which contains all the genes we inherit from our parents. Blood vessels between the
fibres deliver oxygen and other nutrients, and nerves carry the signal to the muscle fibres for contraction.

Figure 1
Muscle from an individual affected by a muscle condition (Fig 2) looks different from normal muscle. These differences vary between conditions.

Figure 2

Appearance of Fibres
In some conditions, the muscle fibres are smaller or larger than normal. They may be damaged, or the proportion of type 1 to type 2 fibres may be unbalanced. In some cases, only one type of fibre may be affected.

Important Proteins
Muscle fibres are built from a number of different, essential proteins. If some of these proteins are missing, in the wrong place, or there is too much, this may cause problems with the muscle. A number of different antibodies are available to identify many proteins.

Accumulation of Products.
There are many different chemical pathways within muscle tissue which can be affected, resulting in changes in the amounts of key substances. One example of this is glycogen. In normal muscle, this is broken down by a pathway involving several enzymes, but in some conditions, one of these enzymes is missing or abnormal. This results in a build up of glycogen in the muscle. This can be seen under
the microscope with certain histochemical stains and special biochemical studies may be needed to identify the exact problem.

**Structural Changes**
Some conditions are diagnosed by the presence of structural abnormalities within the muscle. For example, muscle from someone affected by central core disease has characteristic core structures which can be shown by the absence of a stain within the muscle fibres. In mitochondrial disorders, structures called mitochondria, which convert food into energy, have a defect in proteins essential for their function. These can sometimes be seen under a microscope, or special biochemical studies may be needed to reveal them.

**Distribution**
It is important to look at the distribution of any abnormalities within the muscle. This can sometimes, but not always, give an indication of the severity of a condition, and the rate of progression.

**How long does it take to get the results?**
This depends on the number of tests that have to be performed. Investigations need to be thorough and carefully conducted to ensure accurate results. For this reason, results can take up to 3-4 weeks. Urgent results can be available more quickly, if necessary.

**What happens after the results are available?**
Once the consultant has received the results of the muscle biopsy, an appointment is arranged to discuss the results and the follow up. This will vary greatly depending on the results of the test, and should be discussed with the clinician.