Congenital Melanocytic Naevi

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Congenital Melanocytic Naevi
What is a CMN?

A Congenital Melanocytic Naevus (or CMN) is a type of birthmark. It is also a mole.

- **Congenital** = present at birth.
- **Melanocytic** = to do with melanocytes. Melanocytes are cells in everyone’s skin and hair that produce the pigment melanin. This is what gives us our hair and skin colour. The cells in a CMN look most like melanocytes and they produce pigment, so they are called melanocytic.
- **Naevus** = birthmark (the plural is naevi).

Though CMN means birthmark or mole at birth, in fact, not all of them are present at birth. Around 1% of CMN appear after birth, usually in the first year of life. They look exactly the same as the ones present at birth, but are called CMN “tardive”, which means “late”.

How often do CMN occur?

Single small CMN are found in 1% of all newborn babies. Large or very numerous CMN however are rare, occurring in around 1 in 20,000 births. The frequency seems to be similar around the world and amongst different populations.

What does a CMN look like?

Almost every CMN looks different to the next one.

- **Site**: CMN can be on any part of the skin, including palms, soles and scalp, but also sometimes inside the mouth.
- **Colour**: the colour is usually some sort of shade of brown to black, but sometimes they can be more reddish. It is often very mixed inside the CMN, with smaller areas of different colour on a background colour. CMN at birth are often black, or even dark purple/red.
Hairiness: CMN usually have hair growing out of them, although this is often not visible at birth and can remain unnoticeable throughout life. The hair colour can be darker than the child’s head hair, or the same, or very occasionally lighter. If a CMN is on the scalp there is usually more luxuriant hair growth over the lesion and the hair grows faster than on the rest of the scalp. Occasionally, CMN are completely hairless, even ones that occur in the scalp, or can have patchy hair loss or hairs without pigment (like grey hair).

Texture: the texture of large CMN tends to be different from that of normal skin, being softer, looser and more wrinkled. The CMN can be nearly flat or can be very folded or lumpy.

Spontaneous lightening of CMN
In most children the CMN will lighten to some degree in the first few years of life. This is still being studied but it appears to happen more in children with light or red hair and pale skin than in those with darker hair and skin colour. In some children the lightening is very dramatic and in very rare cases the CMN can disappear or stop producing pigment.
Problems with CMN

▼ **Fragility:** many CMN are more fragile than normal skin. They can therefore tear more easily if they are knocked or scraped. However, they do not bleed any more than normal skin, and they tend to heal well with minimal scarring.

▼ **Dryness:** some CMN are drier than the surrounding skin, need to be washed without soap, and moisturised regularly (your doctor can advise you on this). Occasionally, CMN are very itchy which can be due to dryness, or eczema in the CMN, or sometimes for no apparent reason. This itchiness can usually be treated using creams and ointments.

▼ **Underlying decrease in fat:** this is usually only seen with larger CMN. For some reason, the presence of the CMN interferes with the layer of fat that is normally present between the skin and underlying muscle and bone. This can result in the CMN appearing to be depressed below the general skin surface, the limb, buttock or side of the face appearing obviously thinner than normal. The thinner area functions just as normal – for example, a thinner leg will be perfectly strong, as the thinness is only due to less fat and not less muscle.

▼ **Hardness:** very rarely, a CMN may be really quite hard from the beginning, or may become harder over a period of time. This hardness is usually due to fibrosis, a kind of scarring process, the exact cause of which is unknown. This process is generally accompanied by loss of hair and often also by decreasing pigmentation.
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The size and growth of CMN

CMN almost always grow in proportion to the child. In other words, they will usually continue to cover the same area of skin as at birth. (The exceptions to this are “tardive” CMN, as these appear after birth and can therefore appear to grow, or occasionally where part of a CMN is very pale, it can darken up in the first few months and appear to grow). The size that a CMN will end up can therefore be estimated from the size at birth by looking at its size and where it is.

The total number of naevi can increase after birth, although this does not always happen. It is more likely to happen in children with very large and multiple CMN, and new naevi are always relatively small.

CMN classification

CMN are classified according to the size they will be in adulthood (known as “projected adult size”). This is a difficult definition to understand because different parts of the body grow at different rates, but it is used to give doctors a way of comparing different CMN. We no longer define CMN as small/medium/large/giant, but by the size in adulthood of the largest one and the total number of naevi. Usually, but not always, these two measures go together – in other words very large CMN are usually accompanied by lots of other naevi. These other naevi used to be called “satellites”, but now we consider them to be smaller CMN. The classifications we use at the moment are projected adult size of <10cm, 10-20cm, 20-40cm, 40-60cm and >60cm. The total number of other naevi is classified as 0, 1-10, 10-20, 20-50, 50-100, 100-200, 200-400 and >400. Where the numbers are small we tend to count them, but for large numbers we estimate.
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What causes CMN?

For most cases of large and multiple CMN, we have recently discovered the cause - a mutation in a gene called NRAS.

A mutation means that there has been a spelling mistake or other change in a gene and a gene is just one of the instructions in our body. Mutations happen all the time when babies are being formed and during our lifetimes, but many of them are completely unimportant. If, however, a mutation happens in an important gene then it can have a big effect. NRAS is a very important gene, and the mutation in CMN is in a very important place in NRAS. The mutation is not inherited from either of the parents, but happens only to the baby during development. If the mutation happens very early in the baby’s development then it probably results in a very early miscarriage. If it happens a bit later then the baby can survive, but will have CMN and may have the characteristic facial features and/or brain problems.

In the minority of cases where NRAS mutations are not the cause, there will be another gene which is the cause. These are being investigated at the moment.
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We know that the NRAS mutation is not inherited and not passed on. It is therefore extremely rare to have more than one child with a large CMN, and extremely rare for an individual with CMN to pass it on to their children.

However, we have previously found that some families seem to have more CMN than we would expect, and this is probably caused by other genes which are passed down which make it more likely for CMN to occur. One of these genes is the gene responsible for red hair and freckles (known as MC1R), which we have found occurs more commonly in families with CMN than in families without CMN.

**CMN syndrome**

Our recent research has led to the proposal of the term “CMN syndrome.” A syndrome is a collection of findings in one individual that can potentially be explained by the same genetic change. We think the term CMN syndrome is useful to alert healthcare professionals to aspects other than the skin. Apart from the neurological association the new association is as follows:

**Characteristic facial features**

Our research has found that most children with CMN have a similar looking face. This is a normal face, and in fact usually a very attractive face, but it is similar to other children with CMN. This is likely to be caused by the same mutation that causes the skin changes and the brain changes (when there are any).
Complications of CMN

Neurological problems
Problems in the brain or spinal cord are the most common complication seen in children with CMN. The pigment cells of the skin and the brain develop from the same cells in an embryo, and as a result children with CMN can have differences in their brain or spinal cord. The most common problem is pigment-containing cells (a bit like a CMN) in the brain or spinal cord. This is called “neuromelanosis”, or “neurocutaneous melanosis”. Other much rarer problems include benign brain or spinal tumours, too much fluid in the brain, or abnormal brain structure. All of these neurological problems are more common with larger and more numerous CMN, but there is no connection with the site of the CMN. In other words having a CMN overlying the brain or spine does not increase the chance of having neurological problems. Our current recommendations are that any child born with two or more CMN should have a routine MRI scan of the brain and spine, preferably by the age of 6 months. It is not possible to say that MRI abnormalities could never occur in children with only one CMN at birth, but the risk is much less.

The overall chance of finding an abnormality on MRI scan in children with large and multiple CMN is around 25%, but only around half of these children will have any actual problems. If they do have problems these can be fits (convulsions), developmental delay, or problems with their limbs. It is possible to have problems in development even when the scan is normal, but these tend to be milder. The reason for doing the scan is to pick up the rare cases of tumours and extra fluid on the brain that require an operation, and to allow us to monitor development more carefully in children with MRI findings. The pigment cells in the brain or spine cannot currently be treated.

We also recommend that children with CMN more than 20cm projected adult size should be followed up regularly to watch their development, even if they do not have more than one CMN. In addition, any child with any type of CMN who has a problem with development or fits or limbs should have an MRI.
Malignant melanoma

Melanoma is a cancer of melanocytes, the skin cells which produce pigment and which make up CMN. It used to be thought that melanoma was very common in people with CMN, but we now know that it is rare, occurring in around 1-2% of all people with CMN over their lifetime. However, the risk is higher in people with very large and numerous CMN, around 10%, and there is a peak of risk during childhood. When considering these risks, you need to bear in mind that every one of us has a risk of about 40% of developing some kind of malignant tumour at some time in our lives.

Melanoma in children with CMN can occur anywhere, not just within the CMN. It can present as a lump in the CMN, in another area of skin, or in the lymph nodes (which are throughout the body). In about half the cases it occurs within the brain or spine, when it can present with persistent headaches with nausea/vomiting, or visual disturbances, balance problems or fits. Unfortunately, most often it seems to be the case that when malignant melanoma occurs in a person with a CMN, it is aggressive and difficult to treat. Our recommendations are that any rapidly changing area should be reviewed by an experienced doctor, who can decide whether a biopsy is required. Do remember however, that nodules appear in CMN quite frequently, and the great majority are completely harmless. We also recommend that children who develop new neurological problems such as recurrent headaches, visual disturbance, fits, or developmental changes should be seen urgently by a specialist doctor, such as in the Great Ormond St Hospital CMN clinic.

Since finding the NRAS gene mutation, we understand more about why melanoma happens in people with CMN. As lots of the cells in the body carry that gene mutation it makes those cells vulnerable to other mutations, which can then lead to the melanoma. This finding though will also help us to direct treatments for melanoma better.

Sun protection

Children with CMN can and should enjoy a normal life. They should have good sun protection but the same as we would recommend for all children. In particular, it is important that they should not become sun burnt.

▶ As a general rule: sun avoidance, coupled with good clothing protection, are much more important than suncream.

▶ Sun avoidance: children should be kept out of direct sun as much as possible during the hottest hours of the day and in the hottest months of the year, for example, by staying in the shade. The hottest hours of the day are
10am-4pm, and the hottest months of the year are April to October. Outside these times there is usually no need for sun protection in the UK. This does not mean children should not go outside between 10am-4pm in the hot months, it just means they should stay in the shade where possible and wearing appropriate clothing.

▼ **Good clothing protection:** sun hats with a brim that covers ears and the back of the neck as well as the face are ideal, as are longer sleeved tops and longer shorts/skirt.

▼ **Suncream is not a substitute for sun avoidance and good clothing protection.** It should, however, be used as extra protection if the child has to be in direct sun during hot periods for areas that are not protected by clothes. The best sunscreens contain a reflectant barrier such as titanium dioxide; select a high protection factor (SPF), ideally 25 or more, and with high UVA protection (4 or 5 stars, usually on the back of the bottle). Sunscreen needs to be refreshed every 2 hours or so, more often when swimming or sweating.

▼ **Other important points to remember**

▼ UV exposure is much higher when beside water or snow, so special care should be taken when swimming outside or skiing.

▼ The sun is more harmful at higher altitudes.

▼ The sun remains almost as harmful when it is cloudy, so even if the day is cloudy the child should wear appropriate clothing such as a sunhat during the hottest times of the year.

▼ Shade provides less protection when near water or snow or when the weather is cloudy.

▼ The increased risk of skin cancer in children with CMN probably applies to their whole body, not just on their CMN.
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Can CMN be treated with surgery?

We think that the decision to have surgery has to be made on an individual basis, and very much depends if the plastic surgeons think they can improve the appearance, or whether it would not improve. In cases of very large CMN, surgery is often not possible. In other cases the following points should be considered:

1. Many CMN will lighten spontaneously to at least some degree over a period of years. This can be monitored with repeat photographs.

2. Surgery has not been shown to reduce the risk of melanoma in the child.

3. Early surgery has not been shown to be advantageous. We do not do any routine surgery before 1 year of age.

4. The site of the CMN is very important – for example, the child may get more benefit if a CMN on the face is removed, compared to one hidden in the scalp.

5. The size of the CMN is very important - we have found that children with larger CMN were less pleased with the cosmetic result than those with small lesions which could be completely removed.

6. The number of naevi is important, in particular if the child has a tendency to develop lots of new ones as this may reduce the benefit from removing some.

7. Whether you want your child to take part in the decision, in which case it is better to decide later.

8. What is involved in the type of surgery being offered – this will depend on the individual case.
What can we do about hairiness?
Hairiness only needs to be treated if it is causing a problem (eg making an area difficult to clean) or the child or family feel it looks better without hair. An electric shaver is best, and clipping the hair short rather than completely shaving often avoids problems of itchiness with regrowth. Hair removal creams etc should not be used as they can irritate the skin. Shaving does not affect the amount or thickness of hairs that grow. Hair regrowth after shaving is generally slow and the new hairs will have exactly the same appearance and feel as the original ones. Most parents find that they do not need to shave an area more often than once every couple of weeks in order to maintain a satisfactory appearance. Laser hair removal is possible but needs to be done regularly over a relatively long period and needs a general anaesthetic in children under teenage years. Electrolysis is slow and painful and is therefore not suitable for large areas.

Psychological issues
Children who grow up with a prominent CMN or many CMN may well have problems adjusting to the disfigurement that they perceive, particularly during the teenage years. This, however, is a very individual thing, and varies depending on the child’s personality and on the support from family and friends.

It would be ideal if we were able to offer all children at risk some degree of automatic counselling during their childhood. At GOSH we currently have a psychology service available. However, not all families want psychology input, and not all hospitals have this facility. Changing Faces is an example of a support group specialising in all types of disfigurement which has some excellent guidelines and information. Its website is www.changingfaces.org.uk.
Support and Research

Support Group
Caring Matters Now is a registered charity and support group specifically for people with CMN and their families. Their aims are:

▼ To support those affected by CMN
▼ To raise awareness about CMN
▼ To raise funds for the CMN research

Support is provided in many different ways. The group has a dedicated telephone line, a network of trained support contacts, hold family support days and activity weekends, use social media and manage online forums to give the opportunity to chat, share experiences and seek advice. They also have a very informative website

www.caringmattersnow.co.uk.

They use these sources to spread news of the research findings and developments.

Caring Matters Now also coordinates a voluntary fund-raising programme to contribute significantly to the research into CMN at Great Ormond Street Hospital in London.

CMN Research
Dr Kinsler is conducting long-term research into CMN at Great Ormond Street Hospital. If you would like to be involved and are not attending GOSH regularly, please ask your doctor (GP, Dermatologist or Paediatrician) to refer your child for a one-off appointment in order to participate in this research. The aims of this research are to understand what causes CMN, to identify those patients at highest risk of neurological and melanoma complications, and ultimately to design better treatments for CMN.

Disability Living Allowance
Parents of children with extensive CMN or NCM may be eligible for Disability Allowance, but in general this is only for children with neurological problems or melanoma. If you would like further advice, contact your Citizen’s Advice Bureau or the Social Services Department in any hospital your child visits. Alternatively, there is more information at www.gov.uk.
Caring Matters Now Support Group

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