INCONTINENTIA PIGMENTI

(Bloch-Sulzberger Syndrome)

Ectodermal Dysplasia is not a single disorder, but a group of closely related disorders known as the Ectodermal Dysplasias. More than 170 different syndromes (types) have been identified. The Ectodermal Dysplasias are genetic disorders affecting the development or function of the teeth, hair, nails and sweat glands. Depending on the particular syndrome that an individual has, Ectodermal Dysplasia can also affect the skin, the lens or retina of the eye, parts of the inner ear, the development of fingers and toes, nerves and other parts of the body.

Incontinentia Pigmenti is an ectodermal dysplasia and is a rare genetic disorder mostly affecting girls. Only in very exceptional circumstances does it affect boys.

The condition was named for the way that the pigment accumulates in the skin when it is examined under the microscope. Incontinentia Pigmenti was reported initially in 1906, but the first complete description was written by Bloch and Sulzberger in 1928. "Bloch-Sulzberger Syndrome" is another name commonly used for Incontinentia Pigmenti. Other names are: Bloch-Siemens Incontinentia Pigmenti, Melanoblastosis Cutis Linearis, and the Pigmented Dermatosis, Siemens-Bloch type. All these names describe the same condition which we call Incontinentia Pigmenti. Incontinentia Pigmenti has not been studied in great detail until recently, so the information about it has been both limited and confusing when read historically.

Incontinentia Pigmenti is characterised by abnormalities of the skin, hair, teeth, eyes and nails and may be linked with neurological problems in some cases. If the affected child or adult is troubled by appearance changes, Changing Faces supply useful support materials which are available from www.changingfaces.org.uk.

The Skin

There are typically four stages that occur one after the other, though they may overlap. No specific treatment is needed for the skin changes.

Stage 1 - is the appearance of a blistered skin rash, usually present at birth or soon after birth, normally disappearing by the age of 4 months. This rash may occur anywhere on the body, but is most commonly seen on the limbs and scalp, and rarely on the face. Blistering may recur throughout childhood and into adulthood, but is much less severe than the initial bout of early blistering. During this stage, the blisters should be kept clean and dry. It is common for these blisters to be mistaken for chicken pox, herpes, scabies and impetigo, especially when there is no previous family history of Incontinentia Pigmenti. This can lead to unnecessary treatment until a firm diagnosis of Incontinentia Pigmenti has been made.

Stage 2 - is the verrucous (wart-like) stage. There can be either thick crusts or scabs with healing or areas of increased pigmentation (darkened skin). These skin lesions may be present at birth (implying that the blistered stage took place in the womb), but it often evolves after the first stage. In most cases these clear by six months of age.

Stage 3 - is the hyperpigmented stage in which the skin is darkened in a streaked and swirled pattern that has been likened to marble cake typically on the skin of the trunk and groin. It may be present at birth, but usually begins between 6 and 12 months of life as the blisters heal. The hyperpigmentation may or may not correspond to the areas that were involved in stages I and II. The severity of this stage may range from being barely noticeable to extensive involvement of the skin. These brown streaks remain intense for a few years, fading during adolescence and generally disappearing by the age of 20. This is the stage that gives the condition its name.

Stage 4 - is the atrophic (scarred) stage. These scars are often present before the hyperpigmentation has faded and are seen in adolescents and adults as pale, hairless patches or streaks. These are most easily seen when they are on the calf or on the scalp because hair doesn't grow in the scarred areas. Once most patients reach adulthood (late teens and beyond), the skin changes and these pale patches are usually very subtle and can only be seen when viewed under ultra violet light.

Supporting a normal lifestyle

Other Skin Conditions
Disorders that are somewhat similar to and occasionally confused with Incontinentia Pigmenti include Focal Dermal Hypoplasia, infections (caused by herpes, varicella-zoster virus, staphylococcus, or streptococcus), Epidermolysis Bullosa, linear epidermal nevi, linear and whorled hypermelanosis, congenital Ichthyosiform Erythroderma, and congenital Bullous Mastocytosis. Hypomelanosis of Ito (HI) is also confused with Incontinentia Pigmenti, but HI never has bullous (blisters) or verrucous skin lesions, and the swirled and linear skin is under pigmented compared to the normal surrounding skin.

Temperature Control
One of the main factors of Ectodermal Dysplasia is the lack of temperature control. Children who have Incontinentia Pigmenti also have an inability to sweat due to absent or reduced sweat glands and therefore overheat at any time of year, either from atmospheric temperatures or an impending infection. This can be dangerous particularly to the very young. There can also be problems in the winter months in maintaining adequate body temperature, i.e. they get too cold and have difficulty in warming up. Whether overheating (hyperthermia) or under heating (hypothermia) the child may become tired, lethargic, appear to be in a dream, unable to concentrate or listen, become disruptive or unco-operative. They must be cooled down or warmed up. One sign for some individuals is that their ears go very red whilst the body remains pale when they are overheating. As your child gets older the problem gets easier to deal with, although it will never go away.

Please read our leaflet "Living with Ectodermal Dysplasia" which provides more information on lack of temperature control.

The Teeth
Dental abnormalities are very frequent in people with Incontinentia Pigmenti with over 60% having been reported as affected. Hypodontia, the absence of some teeth, has been seen in 43% of individuals. Other features have also been reported in various combinations such as conical teeth, small teeth and delayed or incomplete tooth eruption. Both primary and permanent teeth may be affected. There have also been some reports of poor mineralization of the teeth. Few individuals have serious dental problems and most can be helped as necessary with orthodontics to align the teeth and prosthodontics to improve their appearance and restore any gaps which are causing concern.

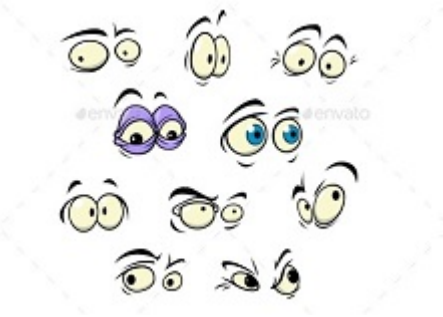
The Nails
Up to 40% of Incontinentia Pigmenti patients may have problems with the nails on their fingers and toes. The nails may be pitted, ridged, thickened (onychogryposis), or completely disrupted. When present, these signs often affect most or all of the nails of the hands and feet and are usually mild and transient, although they can recur. Occasionally, benign growths develop under the nail bed, which can be painful and may be linked to bone deformities at the ends of the fingers.

The Hair
For the most part, individuals do not have substantial problems with their hair. Some girls with Incontinentia Pigmenti have thin hair and a few may have bald patches. Later, about half of individuals with Incontinentia Pigmenti have minor abnormalities of their hair, usually a loss or thinning of hair (alopecia) on the crown of the head. Hair colour is normal, but the hair may be coarse, wiry, and "lustreless".

The Eye – REQUIRED EYE EXAMINATION
More than 90% of Incontinentia Pigmenti patients have normal eyes and normal vision. Some problems, such as short and long sightedness, are no more common in Incontinentia Pigmenti individuals than in the general population without Incontinentia Pigmenti. One third of girls with Incontinentia Pigmenti have a squint.

Supporting a normal lifestyle

The majority of problems result from abnormalities found in the growth of blood vessels in the inside lining of the eye (the retina). The growth of abnormal blood vessels and the associated scarring, bleeding and detachment of the retina can cause loss of vision, but may be treated if recognized sufficiently early.



Our knowledge of the natural history of the retinal changes in Incontinentia Pigmenti is not complete and the duration of screening remains unclear, therefore ophthalmology review should be continued on regular basis throughout childhood.

For this reason, it is **highly recommended** that all females diagnosed with Incontinentia Pigmenti and all female offspring of women with Incontinentia Pigmenti should have an ocular assessment as soon as possible after birth, monthly until 3-4 months, 3 monthly until one year of age, bi-annually until 3 years of age and thereafter annually.

An ocular assessment can be arranged by referral from a GP to the local ophthalmology department.

The Breasts
A small number of women may have some asymmetry in the size and shape of their breasts, extra nipples or possible absence of breast tissue.

The Nervous System
Early studies showed that girls with Incontinentia Pigmenti often had problems with their development, but more recent and more accurate studies have shown this not to be the case. Less than 10% of girls with Incontinentia Pigmenti have developmental or learning problems and only a very small minority of Incontinentia Pigmenti patients suffer from neurological problems. Those who do have problems with development may have fits in the new-born period. Also, neurological signs usually appear quite early in life, therefore an adult with Incontinentia Pigmenti is unlikely suddenly to develop neurological problems. Seizures or other complications should be treated as in any other infant, by a paediatric neurologist familiar with their management, but they do not need special or unusual therapies. In addition, any child with unexplained seizures, developmental retardation, or small head size, should have an imaging study (MRI) to look for abnormal structures or development of the brain.

Causes
Incontinentia Pigmenti is caused by a change in a gene called NEMO. This gene is on the X chromosome. We have a total of 46 chromosomes in each cell of our body. Most of these are the same in both sexes, but females have two X chromosomes and males have an X and a Y chromosome. If a male foetus had an alteration in the NEMO gene, it would almost certainly miscarry. This is why Incontinentia Pigmenti affects females almost exclusively. Females can tolerate having one altered NEMO gene on one X chromosome, since the other, normal gene on the other X chromosome dilutes the effect of the altered gene.

In most cases the altered NEMO gene is passed from mother to daughter. In other cases, the NEMO gene is normal in both parents, but a change occurs in the gene when it is passed in the egg or sperm that made the female.

Genetic testing
Since the recent discovery of the NEMO gene, it has been possible to test the gene. This may be done to confirm the diagnosis. Testing in pregnancy may be offered.

The test is capable of picking up the common mutation found in approximately 80% of new cases of Incontinentia Pigmenti. However, for the remaining 20% of new cases of Incontinentia Pigmenti, diagnosing Incontinentia Pigmenti by DNA testing is more complex but still possible in many cases. This test is also very useful from a family counselling point of view. For

example, a mother of an Incontinentia Pigmenti baby can now be tested to determine whether she herself has Incontinentia Pigmenti, thus gaining information which can be invaluable when planning future pregnancies.

Another benefit of identification of the Incontinentia Pigmenti gene is that we can now distinguish between Incontinentia Pigmenti and other diseases which are often mistaken for Incontinentia Pigmenti. This is particularly useful in the case of boys previously diagnosed with Incontinentia Pigmenti, who may be affected by a completely different disease. We have found that surviving males with Incontinentia Pigmenti have more subtle, less damaging mutations in the NEMO gene, which accounts for their survival.

In the future, identification of the Incontinentia Pigmenti gene should allow development of a prenatal diagnostic test. This would allow expectant mothers to determine whether the child they are carrying has Incontinentia Pigmenti. Ultimately, it may be possible to use in vitro fertilisation/pre-implantation techniques to select healthy embryos prior to implantation.

Treatment

The discovery of the gene that causes Incontinentia Pigmenti will not have a practical impact on Incontinentia Pigmenti patients or their families until the biology of the product of the gene is understood, and this may not be for some time.

Research into therapies and better ways to treat specific symptoms must proceed while geneticists and biochemists strive to uncover the molecular mysteries of NEMO. As some the symptoms of Incontinentia Pigmenti are similar to those experienced in ED, the ED Society documents relating day to day management can be followed.

But there is reason for hope. It may be possible to manipulate other biochemical pathways to compensate for the loss of function of NEMO.

For certain, the discovery of NEMO now allows for a more assured molecular diagnosis in prenatal cases.

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