

# **Mortality in X-linked Hypohidrotic Ectodermal Dysplasia**

by

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There have been few studies estimating the risk of death associated with X-linked hypohidrotic ectodermal dysplasia (XHED), because it is difficult to obtain unbiased information. The best data that I know of are still those from my own study published 18 years ago, although there may be more information that I have failed to spot. When I published my report on the clinical features of XHED in 1987, I relied upon the accounts of family histories given to me by those I interviewed, usually the mothers or sisters of the boys who had died. I excluded the males through whom I made contact with each family, because that would have biased the data, but I took account of all other affected males in each family. Some of the boys who died had been born several decades previously, as far back as the 1940's, but there did not seem to be any great change in the risk of death in infancy over the years. Of course, there might have been an improvement since the mid-1980's but I do not have that information - it would require an updated study to find that out.

My conclusion was that twelve out of 43 affected boys died in the first 3 years (28%), with nine of these deaths occurring in the first year (21%). These figures were cautious estimates, excluding the deaths of some infants who may have been affected but where there was some doubt. Incorporating some of these additional deaths would have increased the mortality in early childhood to about one child in three. The risk of mortality was higher for the first affected boy than for subsequent affected boys born to the same parents, indicating perhaps that early recognition of the condition improves the outlook for an affected child. There has been a substantial improvement in the facilities for paediatric intensive care over the past 20 years so I would be hopeful that the mortality rate is now less than it was.

Why do affected boys die? I think there are three main reasons. First, there is the risk of grave overheating in hot weather, in hot buildings including intensive care units and in response to infectious illnesses. Children become less vulnerable to this as they grow older, and as they become able to say when they feel hot. Second, there is an increased risk of infection because the body's physical defences are impaired in XHED - especially by a lack of mucus in the airways and the bowel, making it easier for bacteria to persist in the lungs or to penetrate into the bowel wall. Third, many affected boys suffer with failure to thrive for the first year or two of life - they may have feeding problems, oesophageal reflux and poor weight gain. This will weaken the boy's resistance to infection, until the failure to thrive suddenly resolves for no very apparent reason.

An additional possible factor contributing to the deaths is that there are a very few boys with a similar physical appearance caused by mutations in another X chromosome gene - NEMO. These boys have a severe defect in the immune system in addition to the features of ectodermal dysplasia - but I should emphasise that this is a rare problem, very much less common than XHED.

What can be done about this? Families who know they have XHED should make sure that their young women, who might be carriers, are aware of the condition so that they can tell their midwife and doctors about it when they have a child. Any boy born to a female carrier should be watched carefully until it is clear whether he does, or does not, have the condition - or genetic testing could be arranged at birth if the family's mutation is known. With a child who has the condition, care can be taken not to overheat him in his cot or in excessively warm clothing - and particular care can be taken if he has to be admitted to hospital. If he is being fed by bottle, he can be given his milk cool or slightly warm, not warmed up as for other infants. If he is too hot, he can be cooled by a combination of sponging with tepid water and giving him cool fluids to drink; if he has fever from an infection then he can also have paracetamol by mouth.

There is much that we do not understand about the control of body temperature in XHED, and I hope that we can set up a study to look into this over the next year or so.

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