Recent advances in the treatment of the thalassaemias

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The thalassaemias are the commonest single gene disorders in man. In the Indian subcontinent and Southeast Asia the thalassaemia disorders of most clinical importance are β thalassaemia and haemoglobin E thalassaemia. Alpha thalassaemia is also very common in parts of Southeast Asia although it seems to be of less importance in India and Sri Lanka.

The β thalassaemias and haemoglobin E thalassaemia are all associated with imbalanced globin chain synthesis due to defective β chain production. It is now known that the abnormality in β chain synthesis reflects many different mutations of the β globin genes and it is quite easy to isolate these genes and discover the particular mutation in individual patients. It is also possible by analysing families in genes to try to predict the severity of the course of thalassaemia in a particular family.

The main forms of treatment of thalassaemia include blood transfusion, iron chelation therapy and the judicious use of splenectomy. Currently, the only adequate form of chelating therapy is desferrioxamine given by a long subcutaneous infusion. Recent work provides clear evidence that if this is done regularly transfusion-dependent thalassaemics grow and develop normally and have a good prognosis. Without adequate iron chelation these patients usually die in the second decade of iron loading, or if transfusion is inadequate, even earlier. A number of promising oral chelating agents are being evaluated but at the moment they are not available for clinical use. Of these, L1 is particularly active although it does produce transient arthritis in a high proportion of children.

Bone marrow transplantation may be curative for a proportion of patients with β thalassaemia although more experience is required in many different centres before the precise figures are known. Much current experimental work is directed at trying to reactivate fetal haemoglobin synthesis as a way of controlling the disease.

Finally, it has to be said that for most countries the most cost-effective way of managing thalassaemia is by prevention. This requires population screening, or screening in the antenatal clinic, followed by genetic counselling. Parents at risk for having a child with serious thalassaemia may decide not to have children or to adopt. If they wish to have their own children they can be offered prenatal detection with termination of pregnancies which carry severely affected thalassaemics. Modern DNA technology allows the detection of thalassaemia in the fetus by about nine weeks of gestation. Approaches like this have caused a remarkable reduction in the birth of new patients with thalassaemia in Sardinia, Italy, Greece, and other countries.

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References

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