Incidence of β-Thalassaemia Trait among Cypriots in London

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Summary

The incidence of ß-thalassaemia trait among Cypriots in London is about 14%, and the birth rate of children with thalassaemia major is 0·6%. The high incidence of the ß-thalassaemia gene among Cypriots suggests the desirability of screening Cypriot school-leavers for thalassaemia trait and following up any incidentally discovered cases with family studies and genetic counselling.

Introduction

Thalassaemia major is inherited as a Mendelian recessive. The heterozygous state, ß-thalassaemia trait, is recognizable haematologically though the only symptoms it commonly produces are those of a mild anaemia, especially in children and pregnant women. The main importance of ß-thalassaemia trait is that carriers run the risk of having children with thalassaemia major. In Cyprus, Banton (1951) reported a 20% incidence of thalassaemia trait, which would give a 1% birth rate of infants with thalassaemia major, but Plato *et al.* (1964) reported only a 6-8% incidence of thalassaemia trait, which would give a 0·12% birth rate of infants with thalassaemia major. To clarify the situation in Britain the incidence of ß-thalassaemia trait was investigated among Cypriots in three North London boroughs.

Method

The three boroughs studied were Camden, Islington, and Haringey. The frequency of ß-thalassaemia trait was calculated by setting the birth rate of known cases of thalassaemia major against the total birth rate of Cypriot children for the years 1961-5 inclusive.

The birth rate of cases of thalassaemia major was found by tracing all the cases recorded in the hospitals of the greater London area and from the Registrar General's records of deaths. The place of birth of each child was confirmed from the records of births sent to the medical officer of health in each borough. The rate of diagnosis of thalassaemia major in England was assumed to be 100%.

The birth rate of Cypriot children was calculated from the number of Greek Cypriot surnames appearing in the records of births sent to the medical officer of health, or from the weekly return of births sent to the registrar for each borough. The identification of the names was checked with a Greek priest. Turkish Cypriots cannot be identified by their names, which resemble those of Muslims from other countries. The figures for Greek Cypriot births were corrected upwards by 29% to include Turkish Cypriot births, as although Turkish Cypriots constituted 20% of the original emigrants from Cyprus (Oakley, 1971) they have had 29% of all the children born to Cypriot parents in Britain (Department of Education and Science, 1968).

Twenty-two per cent of this corrected figure was excluded as this is the proportion of Cypriot fathers married to non-Cypriot mothers, and offspring of these marriages, though bearing Cypriot surnames, would not be at risk for thalassaemia major. This is shown in a 10% sample census of Commonwealth immigrants (General Register Office, 1967), confirmed by inspection of the marriage registrar at All Saints Greek Orthodox Church in Camden, and by a special breakdown for Cypriots alone of the figures for intermarriage given in the 1961 10% sample Census (General Register Office, 1965; Oakley, 1971).

Results

The number of children with thalassaemia major born in the three boroughs in 1961-5 inclusive was 25. The total births of children with Greek Cypriot surnames in the three boroughs in the same years was 3,795. When corrected for Turkish Cypriot births and intermarriage with non-Cypriots this becomes 4,160 births of children at risk for thalassaemia major. The thalassaemia major birth rate is 0·6%. This indicates that the carrier rate of ß-thalassaemia trait among Cypriots in London is about 14%—that is, about one in seven of all Cypriots in London are heterozygous for thalassaemia.

Discussion

The estimate of 0·6% for births of thalassaemia major among Cypriots in London is a minimum as we may possibly have failed to trace one or two cases. The figure of 14% for the frequency of ß-thalassaemia trait among Cypriots in London is also a minimum. Other figures obtained by direct screening for thalassaemia trait have been 20% among Cypriot schoolchildren (Banton, 1951), 6-8% among Greek male schoolchildren and adults in three groups of villages in Cyprus (Plato *et al.*, 1964), 18% among Cypriot students in Athens (C. Kattamis, personal communication), and 15% among a group of the National Guard in Cyprus (G. Stamatoyannopoulos, personal communication). In the latter study, the author also calculated a frequency of 13% from births in Cyprus. It may be concluded that thalassaemia trait occurs with the same high frequency among Cypriots in London as it does in Cyprus.

Because of the 14% incidence of ß-thalassaemia trait the risk to all Cypriots of having children with thalassaemia major is considerable, and would probably not be significantly affected by consanguineous marriages. If two carriers of thalassaemia trait marry, 1 in 4 of the children, on average, will suffer from thalassaemia major. If an individual known to carry thalassaemia trait marries at random among the Cypriot population, the risk to him of marrying another carrier is 1 in 7, and the risk to each offspring of the marriage of having thalassaemia major is 1 in 28. If two Cypriots whose carrier status is unknown marry, the risk that they are both carriers of thalassaemia trait is 1 in 49, and the risk to each offspring of having thalassaemia major is 1 in 196.

Because of the seriousness of thalassaemia major these figures suggest the desirability of screening the population at risk for ß-thalassaemia trait. The condition is detectable by increased osmotic resistance of the red cells (Bianco, *et al.*, 1952), by a microcytic normochromic blood picture (Silvestroni

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and Bianco, 1948), and by a raised fraction of Hb A_2 or Hb F or both (Silvestroni *et al.*, 1957). None of these alone is diagnostic for ß-thalassaemia trait, so for effective screening a combination of two or more methods would be necessary (Weatherall, 1965).

A practicable approach would be to test an accessible unmarried cohort of those people with one or both parents born in Cyprus—for instance, school-leavers—initially by a method which errs in picking up other conditions besides ß-thalassaemia trait—for example, indices or fragility. Positive cases could then be examined for raised Hb A_2.

ß-Thalassaemia trait is often an incidental finding in patients examined for other reasons. Because of the high genetic risk that it carries such a finding should always be followed up by haematological investigations of the rest of the family. If the patient is an adult married to another Cypriot the chances are 1 in 7 that the spouse will also be a heterozygote; if the patient is a child the chances are 1 in 7 that both parents will carry the thalassaemia trait. This should be investigated and such couples should be informed of the risk to any further children. Where only one parent carries thalassaemia trait half the offspring will be carriers: these should be detected and the parents clearly informed that their heterozygous offspring have a 1 in 7 chance of marrying another heterozygote if they chose a partner at random from the Cypriot community, but that such risks can be averted by using information derived from blood tests. ß-Thalassaemia trait is most commonly detected in pregnant women, and this presents particular problems. The husband's blood should always be tested. If he also carries ß-thalassaemia trait the infant should be followed up at six months for thalassaemia major or ß-thalassaemia trait. Only then should couples of heterozygotes detected at this time be informed of the 1 in 4 risk of subsequent children having thalassaemia major.

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PRELIMINARY COMMUNICATIONS

Latent Osteomalacia in Epileptic Patients on Anticonvulsants

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Summary

The bone mineral content was measured in 10 epileptic patients on long-term treatment with phenytoin before and during treatment with vitamin D. None of the patients showed biochemical signs of osteomalacia. Initially subnormal values for bone mineral content were found, which increased significantly during treatment. The results suggest the occurrence of latent osteomalacia in a fairly high proportion of epileptic patients on anticonvulsants.

Introduction

Osteomalacia with hypocalcaemia and raised serum alkaline phosphatase levels is found in a high proportion of epileptic patients on long-term treatment with anticonvulsant drugs (Kruse, 1968; Dent *et al.*, 1970; Richens and Rowe, 1970; Hunter *et al.*, 1971). The underlying mechanism seems to be a drug-induced increased breakdown of vitamin D in the liver. With a normal dietary intake of vitamin D this might lead to a relative deficiency of vitamin D (DeLuca, 1969; Kuntzman, 1969; Hahn *et al.*, 1971; Hunter *et al.*, 1971).

These findings raise the question of the incidence of latent osteomalacia in these patients and the best way of diagnosing it. Using a sensitive method, therefore, we have studied the bone mineral content in treated epileptics *without* biochemical signs of osteomalacia. The bone mineral content was measured before and during treatment with vitamin D.

Patients and Methods

Five women and five men aged 21 to 57 years (mean 38 years) consented to the study. They were all fully able to work and attended the epilepsy clinic at Glostrup Hospital at regular intervals. Long-term treatment with phenytoin had been instituted $1\frac{1}{2}$ to 14 years (mean 6·2 years) previously. During this investigation the mean dose was 5·7 mg (range 5·0 to 6·1 mg) per kg body weight, and on this regimen the serum levels (Larsen, 1971) averaged 9·6 mg (range 5 to 17 mg) per litre. None of the patients had hypocalcaemia or raised serum alkaline phosphatase levels.

The bone mineral content was determined by direct photon absorptiometry on both forearms. Cameron *et al.* (1968) showed a direct relation between the absorption of photons from ^{125}I and the bone mineral content. In our modified version of the method (Christiansen and Rødbro, 1972; Jensen *et al.*, 1972) the bone mineral content is expressed in arbitrary units as a mean value of six scans from each forearm. The standard

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