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*Correspondents should present their references in the Vancouver style (see examples in these columns). In particular, the names and initials of all authors must be given unless there are more than six, when only the first three should be given, followed by et al; and the first and last page numbers of articles and chapters should be included.*

## Genetics of diabetes

SIR,—Dr M A K Omar and Professor A C Asmal (4 June, p 1786) report on the prevalence of a positive family history of diabetes in the first degree relatives of both insulin dependent and non-insulin dependent diabetics of African and Indian ethnic groups. The index diabetics were classified as insulin dependent or non-insulin dependent by the current World Health Organisation (WHO) criteria.<sup>1</sup> The authors observed a higher prevalence of family history of diabetes in all diabetics in both ethnic groups than in non-diabetic controls, a result similar to those of most such studies in white and other populations.<sup>2</sup> The data they present on the family history of non-insulin dependent diabetes are compatible with those of studies performed in other populations. The apparently dominant inheritance of non-insulin dependent diabetes in the Indian group might suggest, as the authors comment, a pattern of inheritance similar to that in maturity onset diabetes of the young.<sup>3</sup> The major new finding of this report is the high prevalence of a family history of non-insulin dependent diabetes among the diabetics with insulin dependent diabetes, which was particularly prominent in the Indian group. Dr Omar and Professor Asmal then conclude that there must be genetic heterogeneity of disease among first degree relatives.

We would like to suggest an alternative explanation for these results. This report may give evidence for possible genetic homogeneity to diabetes in the African and Indian populations studied, at least as far as the current WHO classification is concerned. That is, in those populations insulin dependent and non-insulin dependent diabetes may not be

separate disorders but instead may be the range of one disease or even groups of diseases. This is not an altogether surprising concept. Family studies are powerful tools to both split (heterogeneity) and lump (homogeneity) disorders. Thus in white populations family studies have helped separate insulin dependent from non-insulin dependent diabetics.<sup>2</sup> In contrast, family studies also have shown that what may appear to be phenotypically different disorders may really have the same underlying genetic predisposition. For example, many studies have shown gastric and duodenal ulcers to be distinct disorders, but there appears to be a combined phenotype with both gastric and duodenal ulcer that is independent of either individual type of ulcer and may present in relatives with either combined ulcer or solitary gastric ulcer or solitary duodenal ulcer.<sup>4</sup> Another example is familial combined hyperlipidemia, where a given individual in the family may present with either a raised cholesterol concentration, a raised triglyceride concentration, or both, but this appears to be a distinct disorder from either familial hypercholesterolaemia or familial hypertriglyceridaemia.<sup>5</sup>

Thus it is not surprising that there may be aetiological categories of diabetes whose clinical range can encompass both the currently defined insulin dependent and non-insulin dependent diabetes. From the family data presented by Dr Omar and Professor Asmal, it would appear that this may well be occurring in the South African black and Indian populations; in these populations both insulin dependent and non-insulin dependent diabetes may be the range of one (or several) underlying disease process(es). This result is in

sharp contrast to the results obtained in European and North American white populations, and suggests that the form of insulin dependent diabetes found in the African and Indian populations, especially in the Indian, may be different from that seen in white populations. Previous cross sectional studies have suggested on clinical grounds that South African Indian and African diabetics had different types of diabetes, perhaps indicating genetic heterogeneity.<sup>2</sup> Indians in South Africa and elsewhere have a form of diabetes in which vascular complications are frequent and ketoacidosis less common. On the other hand, the African diabetics have a form of diabetes in which ketoacidosis was common and vascular complications rare.

The finding of the increased occurrence of non-insulin dependent diabetes in relatives of patients with insulin dependent diabetes is reminiscent of the finding of Irvine *et al* that there is a subgroup of patients initially identified as having non-insulin dependent diabetes in whom the disease becomes insulin dependent.<sup>6</sup> This is especially true of those who were positive for islet cell antibodies and HLA-B8. It would be of interest to study islet cell antibodies in those index patients with insulin dependent diabetes, and their relatives with non-insulin dependent diabetes. On the other hand, this familial aggregation of both insulin dependent and non-insulin dependent diabetes might indicate totally different diseases in the Africans and Indians, each of which might be different from that seen in white populations. Careful studies of the exact characteristics of diabetes in each of these groups should be undertaken to define those differences, but the report by Dr Omar and Professor Asmal