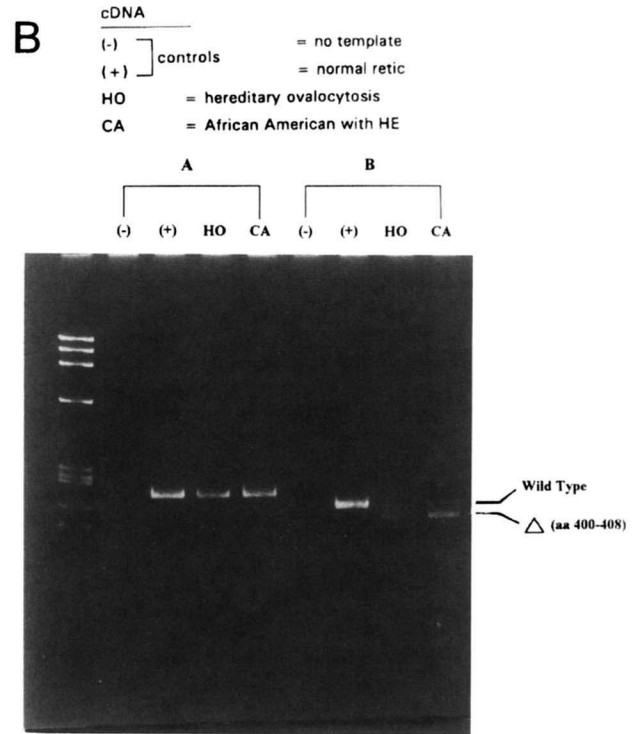
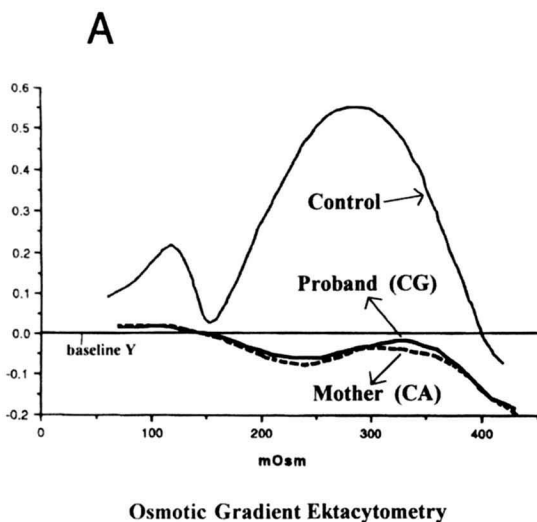


### Southeast Asian Ovalocytosis in an African-American Family

To The Editor:

A form of hereditary elliptocytosis (HE) characterized by extremely rigid erythrocytes and resistance to invasion by malarial parasite is found in high frequency in several Southeast Asian countries, reaching an incidence of 30% in certain ethnic groups.<sup>1-5</sup> The first characterization of rigid properties of these HE erythrocytes was in patients from Malaysia (Melanesian ovalocytosis),<sup>1</sup> but the

same disorder has been described in individuals from Papua New Guinea, the Philippines, and Indonesia and is now given the name Southeast Asian ovalocytosis (SAO).<sup>4,5</sup> The prevalence of SAO in the Indian subcontinent and Africa is unknown, but there is at least one report of SAO in a Mauritian of Indian descent.<sup>6</sup> The molecular defect of SAO erythrocyte is now well known to be the deletion of amino acids 400-408 of band 3, the anion exchange protein, which lie at the interface between the N-terminal cytoplasmic domain and



### RT/PCR analysis of Reticulocyte RNA

Fig 1. (A) Osmotic gradient ektacytometry. Red blood cell deformability was measured in the ektacytometer at various osmolalities as described by Clark et al.<sup>16</sup> (B) RT/PCR analysis of reticulocyte RNA. Total RNA was extracted from whole blood and was amplified with band 3 primers (A) spanning nucleotides 464-723 of the cytoplasmic domain and (B) spanning nucleotides 1104-1334, which contain the deletion characteristic of SAO.

the point at which the polypeptide chain enters the membrane.<sup>6-8</sup> Band 3 also has a common polymorphism, the so-called Memphis-1 variant, in which the point mutation lys56 → glu produces a protein with slower electrophoretic mobility and an abnormal chymotryptic fragment.<sup>9,10</sup> All of the cases of SAO to date have been associated with the Memphis-1 polymorphism. The molecular defect in the case of the Mauritian Indian in Tanner et al<sup>6</sup> was identical to the defect noted in SAO cases from Papua New Guinea.

The polymorphic variant, band 3 Memphis 1, is found in 6% to 7% of random human blood samples and is common in all populations but is present at higher frequency in American Indian and African-American populations.<sup>11,12</sup> Despite this high frequency of Memphis 1 variant, HE with characteristics of SAO has not been described to date in African-Americans. Rather, the HE in African-Americans (and in North Africans) is often associated with an increased membrane fragility and is caused by point mutations involving the dimer-dimer association site in the  $\alpha$ -spectrin molecule.<sup>13</sup>

We now describe an African-American family in which the proband and her mother had the characteristic stomatocytic elliptocytes that were virtually nondeformable as measured by osmotic gradient ektacytometry (Fig 1A). On sodium dodecyl sulfate-polyacrylamide gel electrophoresis, the band 3 protein has a slower mobility than normal and chymotryptic digestion of band 3 protein yielded the two fragments consistent with the presence of the Memphis 1 heterozygosity (data not shown). Anion exchange activity was reduced to 51% of normal in the mother of the proband, which was also consistent with earlier findings with SAO.<sup>14</sup> Reverse transcriptase/polymerase chain reaction (RT/PCR) analysis of reticulocyte mRNA (performed in Dr Mohandas Narla's laboratory) using band 3-specific primers that span the deletion in SAO gave the normal 362-bp band 3 product as well as the smaller 355-bp product containing the 27-bp deletion corresponding to the deletion of 8 amino acids in the peptide chain characteristic of the SAO band 3 protein (Fig 1B). We believe this to be the first example of SAO like HE in Sub-Saharan Africans (to be distinguished from North Africans) and the first such case we have seen among 23 consecutive HE cases in African-Americans we have studied, all of whom had the more common abnormalities involving the  $\alpha$  T1 spectrin variants.

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