Genetic testing for spinal muscular atrophy

To the Editor: We read with interest the description relating to spinal muscular atrophy (SMA) in the black South African population.[1] The authors have described an interesting local group. We are, however, concerned that this may not be representative of the whole of South Africa.

We would be particularly interested to hear more about the clinical phenotype and epidemiology of this cohort of patients. The authors have, for example, included phenotypic patients with facial weakness in their grouping. This is of significance because the international guidelines (ENMC, 1998) regard these as exclusion criteria for SMA.[2] In our cohort of patients, facial weakness in the SMA molecularly genetically confirmed group is not a feature. Our 4 patients who presented with facial weakness, and were found to be negative for the common SMN (survival motor neuron) gene mutation, were subsequently confirmed to have other pathologies (congenital myopathy or congenital dystrophy).

We are concerned that the authors' findings are not representative of the whole of South Africa and that incorrect genetic advice could therefore be given to families and patients of indigenous African descent. As described in our paper,[3] we found no deviation from the international detection rate for the common SMN gene deletion (95 - 100%), regardless of our patients' ancestry. This paper was published in 2002. Our figures have not altered since then and have now increased to a total of 50 patients assessed clinically and genetically confirmed to have SMA, with 22 being of indigenous African origin. We have had no patients of indigenous African origin referred through the services who complied with the international guidelines for SMA and were negative for the common SMN gene deletion on genetic testing.

This discrepancy in SMA findings between two geographically distinct institutions is of diagnostic import, and we look forward to the published evidence from the authors that their discordant black patients have some other defect, either localised to the SMN gene or impacting on SMN gene expression.

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1. Labrum R, Krause A, Rodda J. Genetic testing for spinal muscular atrophy (SMA) in South Africa. *S Afr Med J* 2006; **96:** 200.
2. 59th ENMC International Workshop: Spinal Muscular Atrophies: recent progress and revised diagnostic criteria. 17-19 April 1998, Soestduinen, The Netherlands. *Neuromuscl Disord* 1999; **9:** 272-278.
3. Wilmshurst JM, Reynolds L, Toorn VR, Leisegang F, Henderson HE. Spinal muscular atrophy in black South Africans: Concordance with the universal SMN1 genotype. *Clin Genet* 2002; **62:** 165-168.

New protocol for HIV screening for life assurance

To the Editor: The insurance industry has used the third-generation ELISA protocol as a screening test for human immunodeficiency virus (HIV) infection over the last number of years. In order to utilise new technology and keep up with developments in the clinical field, the fourth-generation Combi protocol has been developed in consultation with experts and discussion with the National Pathology Group. The third-generation protocol will be used concurrently with the fourth-generation protocol for the next 2 years.

This protocol uses one of the LOASPA approved fourth-generation combination HIV tests (Combi test). The Combi tests for both the HIV antibodies and the virus itself (P24, antigen component), shortening the window period from an average of 16 days to an average of 7 days.

The Medical and Underwriting Standing Committee (MUSC) of the Life Offices' Association of South Africa (LOA) has extensively investigated the results of the new test on local blood samples for the last 18 months. The aim was to ensure that there is not an increase in the false-positive test ratio, as this has serious implications. Two major studies have been done by Ampath and the University of Pretoria to compare the existing ELISA tests to the combination tests. The latter study is ongoing.

As with all underwriting tests, as well as the previous protocol, these tests must be regarded as screening tests and further testing is recommended in the event of a reactive test. Any further tests will be for the client's own cost.

A non-reactive Combi test result is reported as such and no follow-up test is done. A new category of 'low-reactive' results has been defined. Any low-reactive or reactive result will be retested with a third-generation ELISA immuno-assay to retest the antibody component. If this does not confirm the result of the first test, it will be followed with a P24 antigen test to retest the antigen component. Any low-reactive third-generation test will also be followed with a P-2 antigen test. All second and third line follow-up tests will be from a different manufacturer than that of the Combi test (Fig. 1).

Cut-off values for 'reactive' as well as 'low reactive' results for all approved third-generation ELISAs, as well as fourth-generation Combi tests, will be defined from time to time by mutual agreement between the National Pathology Group and the Medical and Underwriting Standing Committee of the LOA.

The LOA is confident that the use of 'low-reactive' values with sequential follow-up tests of both the antigen and antibody components will reduce the possible number of false-reactive results to a minimum.

Further information is available on **http://www.loa.co.za** Chapter 6 HIV Testing Protocol.