

## Van die Redaksie/Editorial

### Cancer balance sheet — bad news and good news

Recently, a very successful booklet was produced by the Anti-Cancer Council of Victoria, Australia, entitled *You've Heard the Bad News: Now Here's the Good News*.<sup>1</sup> It was written to meet 'the irrational and widespread fears of the disease', and to counter 'the traditional anti-cancer language which can make the cancer information bodies seem like ivory towers inaccessible to the public'. The booklet was included in a monthly women's magazine, distributed to medical practitioners, community health centres and other health agencies, and was, moreover, the subject of a 3-hour 'Cancer phone-in' answered by an assembly of 30 cancer experts.

What is the bad news, and what is the good news? How and where do South African populations stand?

First, as regards occurrence, the general news is bad. Critical reviews have noted the disappointingly small progress made in reducing cancer incidence and mortality rates.<sup>2,3</sup> Many incidence rates are still increasing.<sup>4</sup> Mortality rates have scarcely fallen; in the USA in the last three decades the fall has been only 2%.<sup>5</sup> What can be marshalled as good news? Firstly a recent report, which took note of earlier under-reporting of the disease, reached a more hopeful conclusion, i.e. that age-adjusted mortality rates and probable incidence of leading cancers have been declining significantly for decades, with the major exception of respiratory tract cancers.<sup>6</sup> This view could well be valid, for uncertainties in death certification were extremely common in the past,<sup>7</sup> and it is only recently that cancer registries have afforded accurate incidence data. Regarding decreases in individual cancers, the principal good news is that within the last generation rates for gastric cancer, somewhat inexplicably, have almost halved.<sup>8</sup> Substantial falls have also occurred in cervical cancer.<sup>8</sup> Death rates from cancer among children have also declined considerably.<sup>9</sup> Regarding breast cancer (now affecting 1 woman in 10 in the USA<sup>10</sup>), it is noteworthy that a study undertaken in Scotland revealed the incidence in young women to be decreasing *despite* a continuing 'high profile' of known risk factors.<sup>11</sup> Clearly, there are powerful influences at work — inhibiting and promoting — the identities of which are not known. This belief is underlined by the fact that cancer incidence varies widely, not only between equally prosperous countries, but between *adjacent* regions in certain countries.<sup>12</sup> Thus, in Sydney, Australia, a threefold differential in mortality rates from colorectal cancer prevails in neighbouring districts. The existence of presently unmeasured environmental aetiological factors is postulated.<sup>13</sup> Such epidemiological situations cry aloud for elucidation. Then, too, there are segments of populations with particular cultural beliefs and practices that tend to have lower-than-average rates for cancer. These include church

groups, notably Seventh-day Adventists,<sup>14</sup> and vegetarians.<sup>15</sup> Were the reasons for these various contrasting situations resolved, then more would be known about carcinogenesis, and hence there would be greater potential leverage for prevention.

Regarding risk factors, according to the US National Cancer Institute, there are some grounds for considering that diet is a major influencing factor in the causation of about 35% of cancers, smoking in 30%, reproductive and sexual behaviour in 7%, alcohol in 3%, and industrial toxic hazards in 3%.<sup>16</sup> For the public, the only salient factors that lend themselves to change are diet, smoking practice and alcohol consumption. Many believe that with appropriate changes, a third of cancers could be prevented, and a third 'cured' if treated sufficiently early.<sup>17</sup> What is the good and the bad news on the control of these risk factors? Take smoking first — the good news is that in most Western countries smoking frequency in men has fallen, indeed, has almost halved in some populations.<sup>18</sup> The bad news is that although the frequency remains lower in women than in men, the fall in the numbers of women smokers not only has been relatively slight, but today's woman is a heavier smoker than a decade ago;<sup>18</sup> additionally, among schoolgoers, more girls than boys now smoke.<sup>19</sup> As to alcohol consumption, all the news is bad. Alcohol is a risk factor in several cancers, especially of the oesophagus, lung, pancreas and rectum.<sup>20</sup> The level of consumption is still rising, not only in many Western populations, but in all Third-World populations.<sup>21</sup> As one reflection of intake, in a study made in Dundee, Scotland, on women expecting their first child, 53% were smokers, and 90% imbibers of alcohol, before they knew of their pregnancy.<sup>22</sup>

Regarding dietary changes — what is the news? The US National Cancer Institute has urged that many should reduce total food intake, that fat should supply 25-30% instead of the present 40% of energy,<sup>23</sup> and that dietary fibre should be increased from the present 10 g or so to 20 - 30 g daily through increases in the consumption of cereal products, legumes, vegetables and fruit. The bad news is that among prosperous populations there has not been a fall, either in total energy intake or in total fat intake.<sup>24</sup> There has been a major decrease in the intake of saturated fats, and a rise in the intake of unsaturated fats,<sup>25</sup> although their bearing on cancer occurrence is uncertain. Many authorities insist that only a very substantial fall in fat intake, halving it or so, is likely to decrease susceptibility to diet-related cancers.<sup>26</sup> As to dietary fibre intake, in the USA only half the population consumes one serving of fruit and one serving of 'garden' vegetables on any one day.<sup>27</sup> Their intakes of

fibre, for white and black men, have been given as 13 g and 11 g and for white and black women, 10 g and 8 g daily. Clearly, a huge increase in intake would be needed to comply with the recommendations. In the UK, people are not eating more cereals, and also consumption of vegetables, legumes and fruit are stated to be the lowest in Europe.<sup>28</sup>

Is there any message regarding infant nutrition? Breast-feeding for several months can have a twofold effect. It can almost halve the mother's chance of developing breast cancer;<sup>29</sup> and it can lessen the infant's proneness to childhood cancers.<sup>30</sup>

What is happening as regards earlier detection? Here there is good news. In most developing populations, patients now present with less advanced disease, with subsequent increase in survival time. For example, in the 1970s more than half of breast cancer patients had advanced lesions at stages III and IV; nowadays the proportion is as low as 16%.<sup>31</sup> It must be faced, however, that with many cancers — oesophagus, stomach, pancreas, liver — the disease is already far advanced before symptoms become manifest. As to survival, in 1970, for cancer patients generally, only 25% survived for 5 years; at present the proportion is 50%;<sup>4,32</sup> it is 60% for childhood cancers,<sup>32</sup> and 80 - 85% for melanoma and testicular cancer.<sup>4,33</sup> Apart from patients seeking help earlier, benefits have also accrued from screening procedures. In the case of cervical cancer, screening has had excellent results in some contexts, as in Finland with a 50% fall in mortality.<sup>34</sup> But there have been disappointing results elsewhere, for instance in Belgium,<sup>35</sup> the Netherlands<sup>4</sup> and the UK.<sup>36</sup> Regarding benefits from screening for breast cancer, in Utrecht there was a 25% fall in mortality in a 7-year period.<sup>37</sup> However, results in the UK have been disappointing.<sup>38</sup>

As to treatment, the news is good in that advances continue to be made in surgical, radiation and chemotherapy procedures. Of enormous importance, the distressing side-effects of the latter have been greatly lessened.<sup>39</sup>

What are the favourable and unfavourable aspects of the cancer situation in South Africa? For the white population, cancer occurrence and risk factors are much the same as those depicted for overseas populations.<sup>40</sup> Among the black population, as prosperity and educational levels increase, falls may be expected in their two principal cancers — of the oesophagus and the cervix. However, almost inevitably, the cancers of prosperity will rise, as is already occurring with prostate and breast cancers.<sup>40,41</sup> The socio-economically disadvantaged section of the black population naturally wants to eat more, especially more of palatable fat-containing foods. Smoking is increasing among men, but less so among women.<sup>42</sup> Alcohol consumption is certainly rising.<sup>43</sup> The changes described, with some limitations, are also likely to prevail with the Indian and coloured populations. Is there any good news on the horizon? Certainly screening for cervical cancer, the commonest cancer among women in these ethnic groups, could promote a high rate of cure or could greatly lengthen survival time were there willingness for testing and were State financial resources available.<sup>44</sup>

In brief, there is both bad and good news about cancer. None doubt that most malignant diseases are environmentally induced, and hence in measure preventable; yet all the aspects of prevention and amelioration mentioned call for determined efforts, the magnitude of which daunts many.<sup>45</sup> Some sceptics aver that since in several cancers there is a strong genetic element over which we have no control, and since there is much of time and chance in who gets cancer, why enjoin radical changes for doubtful rewards? It is illuminating that in a recent very critical review on cancer and nutrition, in which the association between the two was asserted to be 'very small', the author notwithstanding urged adoption of the diet that has been recommended.<sup>46</sup> Others, more sanguine, argue that since we are not equally susceptible to carcinogenic influences, there might well be quite a large proportion of the population who may have to make relatively little reduction in risk factors to enter a less prone category. Despondency over the slow pace of improvement must be tempered by the realisation that carcinogenesis and endeavours to control the disease are long-term matters.<sup>4,33</sup> Many maintain that control could be hastened were there more determined efforts to advance primary health care<sup>47</sup> and, moreover, greater doctor-to-patient pressure over the combating of smoking<sup>48</sup> and excessive drinking.<sup>49</sup> It must be appreciated, and this is part of the good news, that for cancer prevention the self-same measures, in respect of diet, smoking and alcohol, are precisely the measures also urged to achieve reductions in coronary heart disease and other degenerative diseases.<sup>50,51</sup> An additional aspect of hope is that falls in cancer occurrence could supervene for no obvious reason, as has taken place with gastric cancer, as well as with other diseases — coronary heart disease, stroke, appendicitis and dental caries. In other words, the present highly adverse cancer statistics are not immutable.

In its most elemental form the message for change could be epitomised as: stop smoking, eat less, eat more plant foods, and exercise more. But facing this, the bad news remains, that cancer is an extremely formidable disease; the good news is that people of determination can lessen the likelihood of their eventually getting cancer, and that patients can, with intention, lengthen their survival time.

#### A. R. P. Walker

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## A molecular service for Huntington disease in southern Africa

Huntington disease (HD) is an inherited neurodegenerative disorder with onset usually in middle age. Until recently, there was no way of identifying the presymptomatic gene carrier.<sup>1</sup> The discovery of the first genetic marker for HD in 1983 and, more recently, newer markers closer to the HD gene, have facilitated possible presymptomatic testing and antenatal diagnosis.<sup>2-4</sup>

Predictive testing for HD has to date been designed as a First-World service. However, in southern Africa the situation is more complex and the practical implementation of such a service is considerably different from that in Western Europe and North America. Previously designed protocols do not apply to southern Africa, since cultural differences and social attitudes have a direct influence on the development of this type of service. Careful examination of cross-cultural ethics is therefore critical before such a service could be implemented here.

Since 1986 the possibility of using genetic markers in the prediction of HD has been investigated by the Department of Human Genetics at the University of Cape Town, which has also been involved in national and international discussions on the issues relating to predictive testing for HD. Professional and community resources are essential to deal with the final impact of predictive testing. Safe, cost-effective services need to

be established to meet the demand of such tests. Clearly defined strategies have to be developed to care for otherwise healthy persons in whom presymptomatic diagnosis has been confirmed years before the onset of the condition.

Before such tests can be offered as a diagnostic service in southern Africa several problems need to be resolved. These include: (i) the ethics of possibly predicting an extremely debilitating and eventually lethal condition for which there is very little treatment, much stigmatisation and, as yet, no cure; in addition, for successful linkage analysis to be performed, extended family participation is necessary with its associated problems of confidentiality; (ii) the handling of psychological and social problems that will arise following predictive testing; (iii) the technical limitations of using linkage analysis; and (iv) the considerable expense involved (medical personnel, technical expertise and backup services).

The Huntington Disease Association of South Africa (HDASA) was founded in 1986 and continues to gain strength as a support group. It has been invaluable in assisting with the dissemination of accurate information about HD to its members. The association also helped with the distribution of questionnaires in a recent survey.

In June 1986 a DNA banking service for HD in southern Africa was established at the Department of

Human Genetics, University of Cape Town. DNA has since been isolated from blood specimens obtained from 317 individuals. These include 67 HD patients from 37 separate kindreds, 203 'at risk' people and 47 unaffected spouses.

In HD it is crucial for later family linkage studies that DNA be obtained from terminally ill patients, since the molecular information derived is irretrievable after the death of these affected individuals.

Since DNA samples can be stored indefinitely, the banking service's primary aim is to establish the necessary laboratory procedures and to isolate DNA from all available HD family members.

The application of new probes is of prime importance for improving the accuracy and usefulness of linkage analysis. The service has started investigating certain families using the original G8 probe, and uses new probes as they become available.

Confidentiality is a major issue and it is emphasised to affected families that this service is still in its research phase and that no information will be disseminated. They are guaranteed that personal information will be kept in the strictest confidence.

The technical and logistic problems that complicate the maintenance of a molecular service for HD in southern Africa include:

1. The use of linked markers does not identify the actual HD gene but follows the segregation of DNA variants allowing determination, in some informative kindreds, of who is likely to have, or not have, inherited the gene. For a given marker to be informative, the different haplotypes must be easily discernible in order to identify the variant allele associated with the disease in an HD family. The usefulness of any marker (or probe) for linkage analysis is dependent on the frequency of the different alleles (polymorphisms) in the population group in question. Polymorphic frequencies for each marker locus should therefore be established in each ethnic group in southern Africa.

2. A further major limitation of the use of linkage analysis in predictive testing is the paucity of living affected family members available for study.<sup>5</sup> On analysis of the structure of the HD families in the Cape Town area, 25% appeared to be suitable for prediction using linkage analysis.

3. Southern Africa is a large area with diverse languages and cultures and the logistics of counselling 'at-risk' individuals and the collection of blood specimens from family members poses enormous problems.

Before widespread implementation of predictive testing is considered, the possibility of heterogeneity at the HD locus must be excluded in the various ethnic groups.

For this reason black HD patients from the Lebowa area in the north-eastern Transvaal were investigated in a collaborative study between the Departments of Neurology and Haematology, Medical University of Southern Africa and GaRankuwa Hospital, and the Department of Human Genetics at the University of Cape Town.<sup>6</sup> An assessment was made of the patients' needs and also their attitudes to HD.

Blood was collected for DNA isolation and storage and liaison was established with local social workers. The affected black patients may represent a unique form

of HD, since the gene in southern African whites is known to have originated in north-western Europe and, in general, few genes have reached the black population from these European sources.

A questionnaire survey is at present under way to assess the understanding and attitudes of HD 'at-risk' individuals to predictive testing and antenatal diagnosis in order to provide adequate psychosocial support systems. The questionnaire was submitted to and approved by the Ethics Committee of the University of Cape Town Medical School. It was based on similar surveys in various other countries but adapted to the local situation, and the results will greatly influence the method of implementing predictive testing for HD in southern Africa.

At the first meeting of the Human Genetics Society of Southern Africa in 1987 it was proposed that the Department of Human Genetics at the University of Cape Town be responsible for the preparation for linkage studies of HD in southern Africa. It was agreed that all centres would send DNA specimens to Cape Town for banking and molecular work-up. However, each centre, in turn, would be responsible for the counselling and management of patients in their own areas. The University of Cape Town Molecular Biology Laboratory would thus act as a co-ordinating centre for HD and provide education and data on recent developments, thereby avoiding expensive duplication of services.

The laboratory has received and studied specimens from affected persons and families throughout southern Africa. In addition, a special clinic has now been established at Groote Schuur Hospital, Cape Town, for counselling 'at-risk' individuals. Close liaison is maintained between the laboratory and medical staff, departmental nursing sisters and State Health Genetics Services. The co-operation of all concerned at both local and national levels ensures that the service runs smoothly.

In general it would appear that the attitude of black patients to fatal disorders is very different from conventional First-World responses. Recently, in the context of a discussion on AIDS, Dr M. V. Gumede from the KwaMashu Polyclinic is quoted as saying that: 'Death holds no terror in the black community.' AIDS is grouped among *izishawa* in Zulu, understood in the West as 'Acts of God'.<sup>7</sup> The same attitude probably applies to HD. It was noted during the field trip to Lebowa that there was very little concern about the hereditary aspects of the disorder. While patients and siblings understood that the disease was 'in the family' it was seen as 'an act of God' and accepted as such.

The successful formulation of predictive testing and auxiliary services for HD extends well beyond this one disease. As molecular diagnosis becomes feasible, the implementation of a prediction service for HD could be used as a model for numerous other late-onset genetic neurodegenerative disorders, such as the cerebellar ataxias and familial Alzheimer disease.

The size of the area, the complexity of the sociopolitical situation and the organisation of the medical health services provides a real challenge in devising an acceptable and reliable predictive testing service for HD in southern Africa.

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## Opinie/Opinion

### You are only as old as you feel

Beauty is said to be in the eye of the beholder. In much the same way, provided one is not incapacitated by physical or mental impairment, or both, one's functional age is more or less as one personally perceives it to be, within the very broad boundaries of inevitable functional decline as a result of chronological ageing.

The secret of successful ageing is in retaining or developing a sense of meaning and having something worth while to look forward to or for which to get up in the mornings. There is of course an enormous element of luck, which depends to a large extent upon the right choice of parents and the cards dealt one by life, but within this fatalistically determined prognosis there is enormous scope for individual input. In other words, a skilful poker player certainly still has some scope for making the best of an indifferent hand even if it comes down in the end to putting on a cool act.

In a study<sup>1</sup> to determine the attributes of the typical patient likely to benefit from a referral to our geriatric unit, 100 patients were examined by means of a questionnaire and physical examination that covered the main features of their total psychosociobiological make-up. One hundred age-matched controls were randomly selected from the same sources and subjected to the same examinations.<sup>2</sup> Whereas about four-fifths of the referred patients had impaired or lost independence because of a combination of two or more problems of a physical, psychological or social nature, almost exactly the same proportion of the controls had retained their ability to maintain an independent existence in the community, sometimes despite a combination of quite severe physical ailments. In addition to their good fortune in having retained a reasonable degree of cognitive normality, they displayed varying combinations of the following five characteristics:

1. Timely preparation for residential and financial security in their old age.
2. A healthy lifestyle, often predating the onset of old age by many years.
3. Sensible compliance with the correct medical management of existing health problems.

4. The timely development of satisfying interests, hobbies or alternative occupations.

5. The development of adequate support systems in relation to family, friends and the community which often went hand-in-hand with strong spiritual support and commitment.

All these are potentially within the grasp of most people and yet how few stand back in middle age and, having coolly assessed their own strengths and weaknesses, consciously set about putting right those things which will impair independence in later life and developing those attributes and strengths that will improve their chances for an independent old age. It has been estimated by one major banking organisation that fewer than 4% of South Africans will achieve complete financial independence in retirement. A high rate of inflation is of course one sure way to fulfil this dismal prophecy. Our fiscal authorities should have a long hard look at the root causes of this galloping inflation that daily makes shopping more nightmarish, and at ways to put more savings rands into the pockets of the elderly so that they may be independent of the state pension. The best way this can currently be done is to introduce a compulsory contributory pension scheme that is transferrable from job to job.

People should do all in their power to maintain an adequate social network of friends and family as they grow older. One scenario is that of the elderly man who left his first family years before for a younger woman, who then leaves him as he becomes older and less physically attractive to her. He is often homesick for the original family, who have, however, totally rejected him for what he did to their mother and he is now without a meaningful social support system when he most needs it. And then there is the thoroughly crabby and dysphoric old lady similarly bereft of social support because she has antagonised all her family and former friends. Finally, places like Sea Point are full of lonely old people whose independence is fading and who have sons and daughters who have been scattered by the brain drain to all points of the compass from Toronto to Timaru.