MEDIESE GENETIKA IN SUID-AFRIKA ... LESSE UIT DIE VERLEDE, UITDAGINGS VIR DIE TOEKOMS
MEDICAL GENETICS IN SOUTH AFRICA ... PAST LESSONS, FUTURE CHALLENGES

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Prof Arnold Christianson received his medical training at the Godfrey Huggins School of Medicine, Harare, Zimbabwe, where he qualified MBChB(Birm) in 1974. After his internship year at Harare Hospital and a year as a senior house officer in Obstetrics and Gynaecology and Paediatrics at Mpilo Hospital, Bulawayo, he spent a further year working in rural hospitals in Zimbabwe.

In 1978 he attended the University of Edinburgh’s postgraduate course in Medicine prior to becoming a senior house officer in Paediatrics at Groote Schuur Hospital, Cape Town in the latter half of that year. His formal training in Paediatrics at the Red Cross Children’s War Memorial Hospital commenced in 1979 and he obtained the MRCP(UK) in 1980. He completed his registrarship in Paediatrics with a year as a senior registrar in Paediatric Neurology, before becoming a lecturer in Paediatrics at the University of Cape Town in 1983. During that year, working as a neonatologist at the New Somerset Hospital, his interest in dysmorphology was initiated.

In 1984 he left academia for private practice in paediatrics in Durban. During his six and a half years in private practice, he maintained his interests in neurodevelopmental paediatrics and dysmorphology, and on returning to academic medicine as senior lecturer in Paediatrics at the University of the Witwatersrand, he was able to continue working in these fields.

Over the past seven years, Professor Christianson’s major interests have been in the field of clinical and community genetics. Much of his research has been directed at the concept of developing an appropriate genetic/disability health service based on primary health care, which would provide for the needs of the underserved sector of South Africa’s population. His other interests include fetal medicine and congenital anomalies. He transferred to the Department of Human Genetics and Developmental Biology in 1992 as senior lecturer, as the department offered him the opportunity of developing his interests in these fields of endeavour, and he was elevated to the Chair of the department on 1 March, 1997.

Prof Christianson is married with two children. His wife, Marylyn, a senior lecturer in Law at UNISA, shares his academic interest in childhood disability. His extramural activities include reading, hiking and fly-fishing, when time permits.

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PAST LESSONS, FUTURE CHALLENGES

The process undertaken in the preparation of this my inaugural lecture, in which I will present to you my vision of Medical Genetics in South Africa, with particular reference to its past, present and future relevance, has, I have found, been one of deep introspection. Being afforded the honour of addressing you on this matter, in itself prefaces the reality that for me to have reached this juncture in my career, I have travelled a road - my own personal history, albeit short, but nonetheless intrinsic, to this lecture. In essence, a career of 29 years in Medicine, including my years as a medical student, are concentrated into the next hour. In contemplating the main influences that have led me to this moment, and to which the theme of this lecture is dedicated, I wish to turn to the first dictum of the Hippocratic Oath: "To hold my teacher in this art equal to my own parents."

My parents were my first teachers and from them sprang my love of books and learning - for this and so much more I am forever grateful. And to my teachers, who were and are the parents of my career, is due the credit for so much of what is to follow.

Three of my early teachers I have come to realise had an incalculable influence in my formative years as a medical student and young doctor - an influence that in a recurring pattern during my career has guided my thoughts and actions and with each cycle this influence has increased.

Prof R H Philpott was an obstetrician who, despite the limited resources of the teaching hospital in Harare, Zimbabwe, undertook clinical research that led to the development of the partogram, the basis of an active method for the management of labour. I have subsequently seen it used in such diverse places as the labour wards of teaching hospitals in London and small bushveld clinics, and it remains in use to the present day. Prof Michael Gelfand, author of "The Sick African", among other things introduced me to the socio-cultural aspects of medicine. It is only now, as I counsel the parents of African children with a disability, and continually strive to ensure that this counselling is relevant to them, that I realise the extent of his influence, inculcated in student field trips to meet traditional healers, rural health care workers and patients in their home setting. And finally there was Prof J E P Thomas, the complete physician and arguably the best teacher of medicine I have encountered, who epitomised for me the role of the physician/healer in patient care, a role centred on the word "care."

In 1997, we live in an era in which Genetics, the science of biological variation, is pre-eminent. Human Genetics, the science of biological variation in the human, which is dictated by the structure and function of our genes, is the subject of the greatest and most expensive scientific endeavour people have ever undertaken - the Human Genome Project. Its purpose is to delineate the genetic Map of Man and in doing so clone the 80 000 - 100 000 genes that regulate the development and functioning of our bodies from conception to death. Medical genetics, that is genetics related to health and disease, has obviously derived significant benefits from the Human Genome Project and all that preceded it. Due to its association with disease, it is inextricably linked with clinical genetics, the science and practice, or art, of diagnosis, management and prevention of genetic disorders. For medical genetics as a discipline to succeed in any given country, it is implicit that a system capable of coping with the public's needs and demands for "genetic care" is a prerequisite. Herein, as I will attempt to elucidate, lies the conundrum currently facing medical genetics in South Africa.

The relation of genetics to humankind dates back to ancient Greece and possibly beyond. The disastrous consequences of the intermarriage between Oedipus and his mother in the fifth century BC are woefully told in Sophocles's Oedipus the King. However, it was not until the beginning of this century that Human and then Medical Genetics became a subject for systematic research. Then again, for the first half of the century this study was mired in the morass of eugenics and social Darwinism which led ultimately to the "murderous science" of Nazi Germany. From this holocaust arose the science of Medical Genetics practised today, that is based on the principles maintaining that people have the right to full and non-directive counselling and the choice of accepting or rejecting this counselling and genetic screening.

In South Africa the man to whom much of the credit for the origins of Human and Medical Genetics is due, is Prof Philip V Tobias. Although renowned for his work in palaeo-anthropology, Prof Tobias commenced his scientific career in 1945 in the field of cytogenetics. He described this in his Valedictory Address in 1990 in the following words: "Chromosomes formed the object of enquiry in my Science and Honours projects and in my Master's and PhD researches. What had started as a mild flirtation developed inexorably into an infatuation with the chromosomes." This infatuation, recorded in his own inimitable style in such early papers as Early Adventures with Chromosomes in South Africa, and his inaugural address,
Embryos, Fossils, Genes and Anatomy, had far-reaching consequences. Being simultaneously qualified as a medical practitioner and scientist, enabled Prof Tobias to give genetic counselling to patients with hereditary diseases. According to his own recollections this began informally in the early 1950s, but must have been well established by 1953 when he wrote a paper on a family with Osteogenesis Imperfecta or Brittle Bone Disease, thus further distinguishing himself as an early dysmorphologist. In 1956, after training with the American geneticist, James V Neel, Prof Tobias formalised his early work in clinical genetics in the form of a designated “hereditary” clinic, conducted in his department.

It was, however, in the field of the teaching of medical genetics that I believe Prof Tobias was most prophetic. He initiated courses for third-year medical students on the genetics of congenital abnormalities as early as 1947, and in 1962, in his opening address to the first conference on Human and Medical Genetics in South Africa, he states:

"The change in pattern of disease demands a change in the pattern of medical education. And by that, I do not mean simply that, instead of 15 lectures on human genetics spread over six years, there should be 45. Rather, it is necessary for our teachers, both those in the basic medical sciences and those in the clinical sciences, to become more genetics-conscious.

"The increased genetics-consciousness for which I am pleading should be manifest in the dissection-hall and the laboratory, the post-mortem room, the ward and the clinic, and it must inevitably reflect itself in the training of our doctors and dentists. Students, I have found, are extremely sensitive to the attitudes of their teachers; and a genetics-conscious teacher will engender genetics-consciousness in his students. And, alas, the teacher who ignores and despises this development will have the effect of driving out from the minds of many of his students an appreciation of the importance of genetics in human health and disease."

Oh, that these words had been heeded.

There were, of course, others involved in the earlier development of Human and Medical Genetics in South Africa. However, in view of his involvement in cytogenetics, clinical genetics, genetic counselling and most significantly human genetic education, I believe it is appropriate to accord Prof Tobias the title of the Father of Human Genetics in South Africa.

Prof Tobias withdrew from the field after assuming the Chair of Anatomy at the University of the Witwatersrand in 1959. His legacy to the following generation of geneticists was so complete that for the next 30 years the discipline academically grew, prospered and achieved significantly, despite major impediments, including financial constraints, staff shortages and a fragmented and racially discriminating health care system. It fell to one of the sons of this generation, Prof Trevor Jenkins, present incumbent of the Chair of Human Genetics at the University of the Witwatersrand, to document these achievements in a seminal paper published in the Journal of Medical Genetics in 1990. The other major figure and indeed character of this era was Prof Peter Beighton, the first Professor of Medical Genetics in South Africa at the University of Cape Town.

However, it is to Dr Molly Nelson, one of the daughters of this generation, that I wish to refer in greater detail. Dr Nelson started her career as a medical social worker in London, returned to night school to matriculate with subjects that would gain her entry to Medical School at the University of Edinburgh and eventually specialised in Cytogenetics and Clinical Genetics. She joined the Department of Medical Genetics, University of Cape Town, in 1972, where she established nationally and internationally her reputation as a Clinical Geneticist and Dysmorphologist. Dr Nelson, in her own way, encompasses many of the traits exhibited by my three early teachers and it is to her that I owe the birth of my academic and medical genetics career. It has been and remains my privilege to have been taught and mentored by her over the past 14 years. Many of the concepts regarding genetic care in the Third World that I subsequently developed, were tempered by her measured and critical insight, and rigorous standards of practice and care.

There were obviously other members of this generation who were central to the development of medical genetics in that era. Reviewing that process and comparing it to the development of Human and Medical Genetics in the First World as outlined by Prof Victor McKusick in his Presidential Address to the Eighth International Congress of Human Genetics in 1992, it was striking to note the similarity. Indeed, South Africa, despite its political ostracisation, had in the field of human and medical genetics almost exactly paralleled the course of development of First World genetics.

Despite the magnificent achievements in human genetics and the impending commencement of the Human Genome Project, the latter part of the 1980s drew to a close with medical genetics grappling with major dilemmas. These concerns arose because during this period, discussion and contemplation surrounding the Human Genome Project served to concentrate the minds of medical geneticists. The enormity of what the Human Genome
teaching averaged 5.5 hours, and medical students attended genetics clinics in fewer than half the medical schools. Perhaps the most telling comment was that teaching of medical genetics in British medical schools was generally of unknown quality or clinical relevance. This was 28 years after the oracular words of Prof Tobias on teaching medical genetics.

But what about South Africa in this critical period? In both spheres, medical genetics teaching and medical genetics services, South Africa, like its First World contemporaries, was found wanting. In 1989, two medical schools, Cape Town and the Witwatersrand, had Chairs of Medical and Human Genetics respectively, and a third, Stellenbosch, had a medical genetics division in the Department of Obstetrics and Gynaecology. The curriculum content of medical genetics in South African medical schools is an issue currently being addressed. I have recently been given the task by the Southern African Society for Human Genetics, of researching this subject so that appropriate recommendations can be made if necessary. Regarding medical genetics services, the obverse side of the coin described by Prof Jenkins in his paper on Medical Genetics in South Africa, was that despite the significant academic achievements in South African genetics, the gains derived from them were available only to a limited sector of the population.

In 1985, in a country then considered to have 33.6 million people, 75% of whom were black, 4 538 patients were seen at genetics clinics. Only 18% of these patients were black. The majority, 63%, came from the white, middle socio-economic class, and were seen in clinics conducted almost exclusively in major urban centres. This situation had arisen as the clinical genetics services available in the country at that time were largely centred in academic units, and staff and finance were limited. Only eight medically qualified specialists were available to undertake the clinical load and counselling, supported by a limited number of medical scientists and nursing staff trained to offer counselling. This situation was further complicated by the existing racially discriminating, fragmented and poorly co-ordinated State health care system. This system ensured that all the barriers to care, previously described as experienced by the underserved populations in developed countries, were equally or more prevalent in South Africa. Indeed, these circumstances ensured the marginalisation of the black population, especially rural people, from obtaining specialist medical care, including the most basic medical genetics care.

This situation is best illustrated by the recent publication of a series of articles on Down syndrome in the black population of South Africa. Down syndrome is the commonest cause of congenital intellectual disability in the
Western world, and is the most researched genetic condition in medical literature. Up to 1990 it had been the subject of no less than 12,000 papers. In South Africa at that time, its existence in the white population was well recognised; its birth incidence was considered to be the same in other Western countries, namely one in 760 live births; prenatal counselling and diagnostic services were available in the major centres; and a child born with the condition could be diagnosed early and receive First World care.

As a paediatrician in training in Cape Town in the late 1970s, I was taught that Down syndrome was rare among black Africans. This myth persisted into the early 1990s when three separate studies in South Africa documented birth incidences of Down syndrome in African neonates as high as one in 750, and indeed higher, one in 590 and one in 480. The latter figure, one in 480, was for rural African newborns. Fifty per cent or more of these infants were born to mothers of advanced maternal age, and it was notable that the majority of these mothers did not recognise their newborn Down syndrome babies as being different from their other infants. Perhaps of greater significance, neither did the medical or nursing staff. In one study, only 16% of these infants were diagnosed in the postnatal hospital or clinic stay, and more than 50% were only diagnosed when 6 months or older - some as late as 12 years of age. It has been estimated that as many as 75% of these infants will have died, obviously unrecognised, from cardiac disease, infection, malnutrition or a combination of these factors, by the age of two years. Finally, and quite obviously, the First World facilities for the management of these children, and prenatal diagnosis and counselling for their mothers, are simply not available in most parts of the country.

Although the situation described would appear to have only negative connotations for the management and prevention of Down syndrome in South Africa, it was not dissimilar to the situation in Western countries in the pre-cytogenetic era, i.e. pre-1960. However, it did preface the need for the development and application of new approaches for the delivery of medical genetics services for all the people of South Africa.

(Translation: It was in this scenario that the Faculty of Medicine of the University of Pretoria established a Chair of Human Genetics in 1989. However, the Faculty's involvement in matters related to medical genetics, and particularly congenital anomalies, can be traced back to 1966 with the publication of an international multicentre World Health Organisation study. One of the centres involved was the present Pretoria Academic Hospital, then named the Victoria Hospital, and the work was undertaken by one of the Faculty's previous Deans, Prof F C Geldenhuys. This study remained the major study on congenital anomalies in Africa until the more recent publications of two separate papers, one from the Kafalang Akademiese Hospital and the other from the rural Northern Province. The research in the former was meticulously undertaken by Prof S Delport from the Department of Paediatrics, and the publication of both papers involved members of the Department of Human Genetics and Developmental Biology. Indeed, the diagnosis and management of infants and children with congenital anomalies, especially in rural underserved populations was, and remains, one of the major research and service development thrusts of the Department.)

In 1989, Prof P A Venter, a cytogeneticist and newly appointed to the Chair of Medical Sciences at the University of the North, initiated a birth defect screening programme involving him and a specially trained nursing sister at Mankweng Hospital, Sovenga, Northern Province. Although housed in an impressive building, Mankweng Hospital at that time was a typical Third World rural South African hospital serving the surrounding community. It had 400 beds, was staffed by medical officers, had no medical consultants, and most of the routine antenatal, maternity and neonatal care was undertaken by the nursing staff. The initiation of this birth defects screening programme was to have immediate and ultimately far-reaching consequences. It soon became apparent that contrary to "local conventional wisdom", a significant
number of infants with birth defects were being born in the hospital. When preparing the paper which published the results of this study, I also developed the concept of the congenital anomalies iceberg. In essence this formalised the knowledge that the birth defects diagnosable on the first day of life represent approximately 25% of the total diagnosed at age five years. Extrapolating from the figures derived in this and other studies, it was thus estimated that up to 8.5% of children born in the area of this study could have suffered the effects of a serious congenital anomaly by the age of five years. As with the Down syndrome infants, many of these would have gone undetected and died. Two anomalies in particular were prevalent, neural tube defects and Down syndrome. The diagnosis of these and other congenital problems stimulated the demand for a clinic in the hospital for the counselling of parents with affected children and the diagnosis of the more complex conditions that could not be done by Prof Venter, the nursing staff or the doctors in the hospital.

Thus began a genetics outreach clinical service on a three to four monthly basis, initially to Mankweng Hospital, but later spreading to seven rural hospitals in the province. This programme, named “Genetics for Africa”, was a collaborative effort by the University of Pretoria’s Department of Human Genetics and Developmental Biology, the Department of Medical Sciences at the University of the North, the Genetic Services Division at the Department of National Health, and nursing staff in the designated hospitals. Its development was based on the education of nursing staff volunteers in medical genetics, the provision initially of the outreach’s diagnostic and counselling service for the patients whom the nursing staff recognised and referred, and the collection and collation of data regarding the patients of the developing programme. The initial concept behind the programme, to take a genetic service to the communities, serviced by the hospitals involved, flowed in the face of the conventional medical wisdom derived from the First World. Conventional wisdom held that in developing countries a medical genetics service was a luxury, given the high proportion of infant deaths still attributable to malnutrition and infectious diseases. This concept was also prevalent in South African medical circles, where it had gained the status of current dogma. However, it obfuscated the fact that, in developing countries including South Africa, the incidence of congenital anomalies was as high, if not higher than that in developed nations, and the burden of a child with a congenital anomaly is far heavier on families in Third World circumstances. The demands on the fledgling service grew so rapidly that careful consideration had to be given to its future development. From the data being collected, both from neonatal screening programmes undertaken in several of the hospitals and the clinics, it became clear that three conditions, namely neural tube defects, Down syndrome and albinism, comprised more than one-third of the anomalies in patients. If other common conditions were incorporated, including clubfoot, microcephaly, hydrocephaly, haemophilia, Turner syndrome and congenital ichthyosis, then these collectively represented in excess of 50% of the patients being assessed by the nursing staff trained in genetics.

The elucidation of these facts coincided in 1993 with the realisation that with the limited finances, number of clinicians and time available, it was not possible to cope with the demand for genetic care that the programme had stimulated in the community. A decision was therefore made, which at the time was contentious, but in retrospect, I believe, will be recognised as pivotal in the development of medical genetics services in South Africa. All of the above conditions were imminently recognisable and diagnosable by nursing staff, given appropriate training. Furthermore, the medical management involved could either be given in situ, or if necessary referred easily to an appropriate tertiary institution. And finally, we had developed immense confidence in the nursing staff we were privileged to work with on the programme. With respect to these conditions it was therefore decided that their genetic management, including diagnosis, referral, treatment where applicable, and most notably genetic counselling, should be made entirely the responsibility of the nursing staff trained in genetics. This they obviously undertook in collaboration with a hospital medical officer when necessary. In essence we had accepted that it was not possible to undertake an outreach programme to an area and render a clinical service there, but that the objective of the outreach programme had to be to develop a service in the community, capable of managing, to the greatest extent possible, the clinical load.

The objective of the programme therefore changed from service delivery to education and the building of local infrastructure. The lesson learnt in coming to this point was, however, not new. In 1993 we found a framed, faded poem in a rural hospital corridor, the author of which remains anonymous, but in whose footsteps we had unerringly tread and would wish to walk further. His or her words I would recommend to all involved in the development of rural medical services in our country:

Go to the People
Live with them
Learn from them
Love them
Start with what they know
Build on what they have

But with the best teachers
When the work is done
The task accomplished
The People will say:

"We have done this ourselves".

The growth and development of this initiative to develop rural, clinical genetics services was documented in papers, and presentations at succeeding Southern African Society of Human Genetics congresses and other venues from 1993. These included the 17th David W Smith Workshop at Lake Arrowhead, California, in 1996, where I was invited to present a paper on Congenital Anomalies in the Black Population of South Africa: Incidence, Prevalence and Public Health Significance.

The principles of the "Genetics for Africa" Outreach Programme were to be the topic of much local discussion and debate, and were certainly not unanimously accepted. The concept of breaking from First World-based traditions with such services, centred on academic genetics units and with control firmly in the hands of medical geneticists, was anathema to some. Ironically, the First World genetics services were at the same time undergoing a similar developmental process but obviously oriented to their particular circumstances.

The need for such changes in the delivery of medical genetic services was recognised by an increasing number of mainly younger, South African trained geneticists, and similar programmes were being developed in the Western and Eastern Cape by clinicians from the Universities of Cape Town and Stellenbosch, and more recently in the Free State and the North West Province. This latter service has the distinction of being established and managed by a nursing sister trained in genetics. The University of Natal has now also designated a paediatrician who has the responsibility of developing community genetics services in KwaZulu-Natal.

For South Africa, 1994 was a momentous year. In the wake of the installation of the new democratic government came numerous changes, including the significant shift in health care priorities to primary health care, with a strong emphasis on woman, maternal and child health. Perhaps equally as important was the inclusion of the rights of the disabled in the new Constitution of South Africa. Together, these two features of the new South

Africa have given significant impetus to the growing movement in medical genetics in the country to developing a service that would serve all the people of South Africa. In 1995 I was asked by the National Department of Health to develop a protocol for the "Role of Medical Genetics in Primary Health Care for the new National Health Programme". This proposal, developed with the assistance of Prof P A Venter, was accepted by the Commission for Woman, Maternal and Child Health, and has formed the basis for the ongoing development of a Medical Genetics Policy for the Management and Prevention of Birth Defects in South Africa.

This policy development is being undertaken by a Department of National Health Task Force, comprising the identified relevant parties from throughout South Africa, and is being co-ordinated by a young, enthusiastic medical genetics scientist, Dr Busi Madolo. She is the current Deputy Director of Genetics Services in the Maternal, Woman and Child Health secretariat of the Department of National Health. The process to date has been largely funded by the World Health Organisation, and is, I believe, unique in South Africa. It is the first such all-embracing, national, collaborative effort to address the problem of medical genetics services in South Africa. As such it is possible that this is one of the first such movements in the Third World. To the best of my knowledge the only other Third World country to have addressed medical genetics on a national basis, is Cuba. In striving for the goal of developing a medical genetics service appropriate to and inclusive of all South Africa's people, I believe South Africa's third generation of medical geneticists has come of age and established its raison d'être. In undertaking this task, and much is still to be accomplished, we are currently all collaborating to establish the role, principles and standards for medical genetics in public health, for South Africa. Hopefully they will also be applicable to other developing countries. In this I believe we have a significant future responsibility.

During the past seven years while the battle to establish the role of medical genetics in South Africa continued, human and medical genetics in the remainder of the world has developed at a pace exceeding even that which was expected from the impetus of the Human Genome Project. With this the face of medical genetics has altered significantly in a manner once again predicted by Prof Tobias. In 1962 he noted that for two million years humankind had succumbed to "bad germs" and only rarely to their "bad genes". However, with improved health and social services, this picture was set to change with the modern day killers having a significant genetics component. The success to date of the Human Genome Project has largely been in the mapping of single gene disorders but this has opened the way
forward for the investigation of polygenic and multifactorial conditions. Circumstances have conspired to ensure that the Department of Human Genetics and Developmental Biology is and will continue to be involved in this new direction for medical genetics.

Starting in 1990, when she joined the department as a student, Ms Antonel Ockers has been involved in research on Malignant Hyperthermia, a potentially lethal condition predisposed to by autosomal dominant genes, but only precipitated by exposure to volatile anaesthetic gases. This work led to the identification of a novel locus on chromosome 17q involved in the aetiology and pathogenesis of this pharmacogenetic disorder. Much of the research, which ultimately led to her PhD, was undertaken at Johns Hopkins Medical Institutions. This expertise has now been returned to South Africa and the work is continuing in a collaborative effort involving Johns Hopkins Medical Institutions, the Allegheny University of Health Sciences, the University of the Witwatersrand and the Department of Human Genetics and Developmental Biology at the University of Pretoria.

It is now accepted that cancer is a genetic disease at cellular level, which is generally not inherited as a genetic disease in families, but usually arises from somatic, non-heritable mutations. However, susceptibility to cancer can be inherited and in these rare instances cancer is a genetic disease at the level of the family as well as at the level of the cell. Therefore, in these families, predisposing cancer genes can be mapped in the same way as genes for purely genetic diseases.

In 1992, Dr Lizette van Rensburg, the Department's Senior Research Officer who was also instrumental in the establishment of the Department, decided to enter the field of cancer genetics research. She subsequently spent a postdoctoral year of study with Prof Bruce Ponder at the Cancer Research Campaign's Human Cancer Genetics Research Group in Cambridge. Her specific interests include breast-ovarian cancer, hereditary colorectal cancer and retinoblastoma. Dr van Rensburg's endeavours have progressed significantly, and at present her approach to these problems is that of molecular epidemiology. Therein, in a prospective manner, while she searches for gene mutations in the laboratory, carefully designed questionnaires administered to the patients seek the underlying environmental catalysts involved in the genesis of the tumour. Ultimately the concept is to collate statistically the gene mutation results with those of the epidemiological studies to provide specific answers related to designated cancers. A feature of this research is its collaborative nature. Several departments in the Faculty, including Anatomical Pathology, Obstetrics and Gynaecology, Medical Oncology, Paediatrics, Dietetics and Surgery, are associated with the research in this laboratory. Strong external South African liaisons have been cemented with the Universities of the Witwatersrand, Free State and Stellenbosch, and Dr van Rensburg's close association with the Human Cancer Genetics Research Group at Cambridge University has continued since her postdoctoral year. Stemming directly from the research undertaken in this laboratory, and in association with the Department of Obstetrics and Gynaecology, the most recent accomplishment of this unit is the initiation of a Familial Cancer Clinic, arguably the first such endeavour of this type in South Africa and possibly in sub-Saharan Africa.

It is in the nature of the "New Genetics" that the advances, both technological and scientific, are intrinsic to all fields of medicine. The Department of Human Genetics, in collaboration with the Department of Chemical Pathology, is also involved in research on another multifactorial condition, namely neural tube defects, which includes anencephaly and spina bifida. This collaboration arose from the internationally recognised knowledge and expertise of Professors Hayward Vermaak and Job Ubbink in folic acid metabolism. One of the most significant recent developments in the field of the prevention of birth defects, was the documentation in the early 1990s in First World countries, that folic acid supplementation could significantly reduce the occurrence and recurrence of neural tube defects. This, plus the documentation of a high incidence of neural tube defects in the Northern Province, led to a major research effort involving not only the two departments in the Faculty, but also the University of the North, and Prof Margot Van Allen from the University of Vancouver, Canada. The first paper stemming from this work, involving African mothers who had had a baby with a neural tube defect, is currently in preparation with more to follow. The findings of this study indicate that the folic acid levels and metabolism of rural African mothers, both with and without an affected infant, are normal. They differ from those documented in similar First World studies and they question whether the underlying aetiology of neural tube defects in this population is the same as that documented elsewhere in the world, confirming the necessity for prospective research principally directed at problems of South African public health significance and related to local circumstances. Increasingly in such issues, especially in relationship to multifactorial disorders, it is no longer acceptable to follow First World findings and dictates, without ensuring they are applicable to our Third World population, geographic location and environmental circumstances. Perhaps of greater significance, is that this research involves genetic technology for the elucidation of the frequency, of among other things, the thermo-labile polymorphism of the methylene tetrahydrofolate reductase gene. This research is
being undertaken by the Department of Chemical Pathology, underscoring the issue that the "New Genetics" is not the preserve of geneticists, but indeed needs to be taken up by people in all fields of Medicine. The facilitation of this ideal will be one of the responsibilities of the Department of Human Genetics in the future.

Beginning in the early 1950s, human cytogenetics, the study of the chromosomes, was at the forefront of laboratory-based developments in medical genetics. Eventually such significant progress was made that by the 1970s, the role of cytogenetics had evolved to become the backbone of medical genetics laboratory service. Since its inception, the Department of Human Genetics and Developmental Biology has had a Cytogenetic Laboratory functioning in this capacity. However, recently a new development in cytogenetics, fluorescent in situ hybridisation or FISH, has opened exciting new possibilities for both research and service in this field. Because this technology is faster and cheaper than conventional cytogenetics, its potential role in providing a cost-effective diagnostic facility for the underserved sectors of our population is now being considered. The Department has recently been fortunate in appointing a new head of the Cytogenetic Laboratory, Mrs Nisha Singh, who has extensive experience with FISH, especially in its application to haematological cancers. It is therefore envisaged that this technology will shortly be available in the department for service and research, particularly as regards its appropriate application in the development of our Third World services in medical genetics.

Traditionally the scientific laboratory component of South African medical genetics has been of an international standard. Although still young, I believe the Department of Human Genetics' medical scientists and laboratories have lived up to this tradition, and will enter the next century well suited to confront the emerging challenges in medical genetics and indeed medicine.

But it is ironic that it is laboratories such as these which have given medical genetics the reputation of being a high cost, high technology speciality, and have called into question the relevance of medical genetics to the Third World. It is my contention that it is only with the efforts and input of laboratories such as these that not only medical genetics, but indeed medicine in South Africa, will endure and flourish in the next century. Not to maintain, and indeed develop them, would be the equivalent of informing physicians in South Africa in the latter part of the last century that they should not practise medicine according to the principles and practices relating to infection prevention then being developed by Lister, Pasteur and others, as these

were too expensive! Obviously, however, the future efforts of such laboratories should principally be directed at the research and development of techniques and strategies for conditions with public health significance in South Africa.

The use of technology in genetics is not confined to the laboratory. When I was a fifth year medical student in 1973, the first ultrasound diagnosis of a fetal congenital anomaly was documented. Since then prenatal diagnosis of congenital anomalies, mainly by using ultrasound and amniocentesis, has become routine in developed countries and in that sector of South Africa's population which can afford itself of private medicine. For the rest of the population it is only available in some tertiary care institutions, mainly those attached to academic hospitals. Yet it can be envisaged that prenatal ultrasound will become more widely available in the country, and newer techniques in cytogenetics, which are currently being developed in the Department's cytogenetic laboratory, may in the not too distant future make prenatal chromosomal screening in designated circumstances, more affordable and therefore accessible. But what do the women in South Africa now being offered these services know, understand and consider about these techniques? This topic is at present the subject of a collaborative investigation between the Departments of Human Genetics and Developmental Biology and Obstetrics and Gynaecology. It will not surprise anyone that black South African women are significantly less informed and aware of these techniques and their consequences than their white counterparts. However, when the results were viewed from the perspective of education level, regardless of race, the discrepancy in knowledge was found to be as marked between women of high and low education levels as between black and white women.

Reviewing these results has illuminated for me what I believe will be one of the challenges for the future of South African geneticists. Given that a school generation is twelve years, it can be anticipated that the children entering school in 1998 will graduate in 2010 significantly better educated than their peers of today. To an extent far greater than that being experienced today, they will expect of medical genetics the ability to help people with a genetic disadvantage to live and reproduce as normally as possible. This was the stated objective of medical genetics as defined by a World Health Organisation Advisory Group in 1985. At present the efforts described to develop medical genetics services in South Africa are largely directed at enabling people with a genetic disability to live as normally as possible, given the country's circumstances. This emphasis is, I believe, essential at this time in our history and development, and is commensurate
with the dictates of our new Constitution. In time, prenatal diagnostic services will become more extensive and readily available, allowing genetica-
ly disadvantaged people the opportunity to more reproductive choices. But in such choices await ethical dilemmas that will have to be faced in the not too distant future.

The new Choice on the Termination of Pregnancy Act in South Africa is probably one of the most liberal in the world today. The Human Genome Project has ensured that genes for disease and also normal structure and functioning of the body, are cloned. So in the foreseeable future the prena-
tal identification of genes which regulate characteristics such as aggression, weight, height, sexual orientation and intellect, will be possible. The combination of the new Termination of Pregnancy Act, these advances and continually shifting social mores could, unless guarded against, result in what could be termed prenatal eugenics. The slippery slope towards social
engineering, using medical genetics knowledge and technology, is a pitfall constantly present when considering issues related to medical genetics and prevention of genetic diseases. It is and remains the responsibility of medical geneticists to actively guide society in the appropriate use of this know-
ledge and away from the inhuman excesses of the past.

On 28 July, 1997, the first group of first-year medical students commenced the first semester of the new, integrated, problem-oriented curriculum of the Faculty of Medicine. The University of Pretoria’s Medical Faculty is the first in the country to embark on this new approach to medical education. Its initia-
tion has offered the Department of Human Genetics and Developmental Biology the opportunity to integrate medical genetics education into the training of medical students throughout their medical training, at an appro-
riate level and at the respective time. Thus, chromosome and gene structure and function will be taught at the same time as micro-anatomy or histology, and the aetiology and pathogenesis of congenital anomalies will be taught alongside the normal embryological development of the fetus. Similar integration is already being planned in future blocks in the years to come. The medical class of 2002 will be the first to qualify from the Faculty in the mould of "Prof Tobias’s fully genetically conscientised doctors". This develop-
ment will ensure that these and future medical graduates from our Faculty will be appropriately trained to meet the demands and expectations of the matriculation class of 2010 and beyond.

Meneer die Visekanselier en Rektor, meneer die Dekaan, geagte kollegas en gaste, in die voorafgaande rede het ek my visie oor die kernrol van mediese genetika soos van toepassing op die Suid-Afrika van vandag, uit-
gesper. Vir hierdie doel het ek die internasionale ontwikkeling van mediese en mensgenetika met die gelyksoortige ontwikkelingsproses in Suid-Afrika bespreek. Daarna het ek gepoog om die uitdaging wat die huidige geslag mediese genetici met die draai van die eeu in die gesig staan, uit te lig. Hierdie uitdaging bied aan ons die geleentheid om oplossings vir ons eie, unieke Suid-Afrikaanse situasie te ontwikkel. Ek is egter daarvan oortuig dat hierdie oplossings nie slegs van belang vir ons is nie, maar dat die invloed daarvan sal uitkry na ander ontwikkelende lande en ook na die Eerste Wêreld. Hoewel die Departement Mensgenetika en Ontwikkelingsbiologie redelijk jonk en klein is, is ek vol vertroue dat, soos wat ons tans ons plek in die voorhoede van ontwikkeling in mediese genetika ingeneem het, ons ook so die nuwe era sal binnegaan.

(Translation: Mr Vice-Chancellor and Principal, Dean of the Faculty of Medicine, colleagues and friends, I have in the preceding address delineat-ed my vision of the core role of medical genetics as it pertains to medicine in South Africa today. In undertaking this I have related the development of Human and Medical Genetics internationally to that in our own country, both past and present. Thereafter I have attempted to offer some insights into the challenges my generation of medical geneticists is facing in the new millen-
niunm. These challenges offer us the opportunity of evolving solutions for our own unique South African circumstances. However, I believe implicitly that these answers will have consequences, not only for us but also for other underdeveloped countries and the First World. Although the Department of Human Genetics and Developmental Biology is small and our history short, I am confident that, as we have managed to be in the vanguard of develop-
ments in medical genetics this decade, this will continue into the next cen-
tury.)

However, to achieve this, and as a point of reference to illuminate the road ahead for the next generation of medical geneticists, I would like to reiterate the guiding principles my teachers gave me. Firstly, despite the apparent lack of facilities and other impediments, it is possible to undertake research which is primarily relevant to the South African situation, but will simultane-
ously have international significance. South Africa is a land of diversity, not least among its peoples. In the past this has acted as a barrier, but if that diversity is respected, the barrier falls and, in medicine, can become a gate-
way for the development of appropriate systems of medical management. And finally, in medical genetics as in all branches of medicine, no matter whether the work is undertaken as research or service, in the clinic, the ward or the laboratory, its ultimate objective is the care of South Africa’s people.
REFERENCES

1. The Hippocratic Oath


