

PRESIDENTIAL AIDS ADVISORY PANEL REPORT

A synthesis report of the deliberations by the panel of experts

invited by the President of the Republic of South Africa,

the Honourable Mr Thabo Mbeki

March 2001

Contents

CONTENTS	2
ACKNOWLEDGEMENTS	7
ABBREVIATIONS	8
CHAPTER 1 – SETTING THE SCENE	9
1.1 BACKGROUND	9
1.2 COMPOSITION OF THE PRESIDENTIAL AIDS ADVISORY PANEL	10
1.3 TERMS OF REFERENCE FOR THE PRESIDENTIAL AIDS ADVISORY PANEL	11
1.4 THE REPORT.....	13
CHAPTER 2 - AETIOLOGY AND TRANSMISSION OF AIDS	15
2.1 INTRODUCTION.....	15
2.2 DOES HIV CAUSE AIDS?.....	16
2.2.1 <i>Visualisation and Isolation of the Virus</i>	16
2.2.2 <i>PCR (Polymerase Chain Reaction) and ELISAs</i>	18
2.2.3 <i>Clinical and Laboratory Evidence of Causation</i>	19
2.2.4 <i>Evidence from Animal Models</i>	22
2.2.5 <i>Epidemiological Evidence</i>	22
2.3 ALTERNATIVE HYPOTHESIS ON THE CAUSE OF AIDS.....	23
2.3.1 <i>The Chemical AIDS Hypothesis</i>	23
2.3.2 <i>The Immunotoxicological Hypothesis</i>	24
2.3.3 <i>The Oxidation Hypothesis</i>	24
2.4 THE INVOLVEMENT OF COFACTORS (OR RISK FACTORS) IN AIDS.....	24
2.4.1 <i>Involvement of cofactors in HIV-causes-AIDS Hypothesis</i>	25
2.4.2 <i>Risk factors that are the primary cause of AIDS according to alternative hypotheses/theories</i>	27
2.5 TRANSMISSION OF HIV AND AIDS	28
2.5.1 <i>HIV Transmission as Estimated from ‘AIDS Deaths’</i>	29
2.5.2 <i>Sexual Transmission</i>	30
2.5.3 <i>Mother-to-Child Transmission</i>	32
2.5.4 <i>Blood-borne transmission and Occupational Exposure</i>	33
2.5.5 <i>Epidemiology of Transmission</i>	34
CHAPTER 3 – SURVEILLANCE	37
3.1 WHAT ARE THE QUESTIONS AND ISSUES?	37

3.2	OVERVIEW ON THE NECESSITY FOR SURVEILLANCE.....	37
3.3	SOUTH AFRICAN EPIDEMIC – FACT OR FICTION.....	38
3.3.1	<i>AIDS mortality</i>	39
3.4	EPIDEMIOLOGICAL THEORY OF CAUSAL INFERENCE.....	41
3.5	SOCIO-ECONOMIC RISK FACTORS.....	42
3.6	DIFFERENCES IN THE AFRICAN EPIDEMIC, COMPARED WITH EUROPE AND THE USA.....	43
3.7	THE ROLE OF MATHEMATICAL MODELS IN FORECASTING THE EPIDEMIC.....	44
3.8	SURVEILLANCE RECOMMENDATIONS – WHAT SHOULD BE DONE ABOUT THE SOUTH AFRICAN EPIDEMIC?.....	45
3.8.1	<i>Deliberations of the panel</i>	45
	RECOMMENDATION.....	45
3.8.2	<i>Discussion on mortality data</i>	45
	RECOMMENDATION.....	45
3.8.3	<i>Recommendations from panellists who do not subscribe to the causal linkage between HIV and AIDS</i>	45
3.8.4	<i>Recommendations from panellists who subscribe to HIV as the cause of AIDS</i>	46
3.8.5	<i>General recommendation</i>	48
	CHAPTER 4 - HIV TESTS AND THEIR ACCURACY.....	49
4.1	HIV TESTING.....	49
4.1.1	<i>ELISA test</i>	50
4.1.2	<i>Western Blot</i>	51
4.1.3	<i>PCR test for viral load</i>	52
4.1.4	<i>CD4 count</i>	53
4.2	VIRUS ISOLATION OR CO-CULTURING.....	53
4.3	MORATORIUM ON HIV TESTING.....	53
4.4	RECOMMENDATIONS ON HIV TESTING.....	54
4.4.1	<i>Proposed studies and experiments</i>	54
4.4.2	<i>Recommendation on future HIV testing</i>	55
4.4.3	<i>General recommendations on testing</i>	55
	CHAPTER 5 –THE TREATMENT OF AIDS AND THE USE OF ANTI-RETROVIRAL DRUGS	56
5.1	INTRODUCTION.....	56
5.2	EVIDENCE IN SUPPORT OF THE USE OF ANTI-RETROVIRAL DRUGS.....	56
5.3	EVIDENCE AGAINST THE USE OF ANTI-RETROVIRAL DRUGS.....	57
5.4	RECOMMENDATIONS ON TREATMENT WITH ANTI-RETROVIRAL DRUG.....	59
5.4.1	<i>Recommendations on the use of anti-retroviral drugs from the group opposed to their use</i>	59
5.4.2	<i>Recommendations from the proponents of anti-retroviral drug use</i>	60
	RECOMMENDATIONS:.....	61
	CHAPTER 6: PREVENTIVE AND PROPHYLACTIC MEASURES AGAINST AIDS	63

6.1	PREVENTION OF AIDS FROM THE POINT OF VIEW OF PANELLISTS WHO DO NOT SUPPORT THE CAUSAL LINK BETWEEN HIV AND AIDS	64
6.1.1	<i>Recommendations</i>	64
6.2	PREVENTION OF AIDS FROM THE POINT OF VIEW OF PANELLISTS WHO SUPPORT THE CAUSAL LINK OF HIV TO AIDS	65
6.2.1	<i>General recommendations</i>	66
6.2.2	<i>Recommendations on prevention of HIV/AIDS through sexual transmission</i>	66
6.2.3	<i>Recommendations on prevention of blood-borne transmission of HIV/AIDS</i>	67
6.2.4	<i>Recommendations on prevention of mother-to-child transmission of HIV</i>	67
6.3	PROPHYLAXIS AGAINST OPPORTUNISTIC INFECTIONS	69
6.3.1	<i>Introduction</i>	69
6.3.2	<i>Opportunistic infections</i>	70
CHAPTER 7 – SOCIO--ECONOMIC FACTORS IN THE CONTEXT OF HIV/AIDS		72
7.1	MALNUTRITION AND SANITATION.....	72
7.2	ORPHANS	73
7.3	ETHICS AND HUMAN RIGHTS	73
7.3.1	<i>Ethics</i>	73
7.3.2	<i>Human rights</i>	73
7.4	SEXUAL BEHAVIOUR	74
7.4.1	<i>Rape</i>	74
7.4.2	<i>Stigmatisation</i>	74
7.4.3	<i>Promiscuity</i>	75
7.4.4	<i>Condom use</i>	75
7.4.5	<i>Issues of economics</i>	76
7.5	VACCINE DEVELOPMENT	76
7.6	SUMMARY AND RECOMMENDATIONS.....	76
CHAPTER 8: RECOMMENDATIONS.....		78
8.1	INTRODUCTION.....	78
8.2	RECOMMENDATIONS ON SURVEILLANCE – WHAT SHOULD BE DONE ABOUT THE SOUTH AFRICAN EPIDEMIC? ..	78
8.2.1	<i>Deliberations of the panel</i>	78
	RECOMMENDATION	78
8.2.2	<i>Discussions on mortality data</i>	78
	RECOMMENDATION	78
8.2.3	<i>Recommendations from panellists who do not subscribe to the causal linkage between HIV and AIDS</i>	79
8.2.4	RECOMMENDATIONS FROM PANELLISTS WHO SUBSCRIBE TO HIV AS THE CAUSE OF AIDS.....	79
8.2.5	<i>General recommendation</i>	81
8.3	RECOMMENDATIONS ON HIV TESTING.....	81

8.3.1	<i>Proposed studies and experiments</i>	81
8.3.2	<i>Recommendation on future HIV testing</i>	82
8.3.3	<i>General recommendations on testing</i>	82
8.4	RECOMMENDATIONS ON TREATMENT OF AIDS WITH ANTI-RETROVIRAL DRUG	82
8.4.1	<i>Recommendations on the use of anti-retroviral drugs for the treatment of AIDS from the panellists opposed the causal link between HIV and AIDS</i>	82
8.4.2	<i>Recommendations on the treatment of AIDS from the proponents of anti-retroviral drug use</i>	83
8.5	RECOMMENDATIONS ON PREVENTION OF AIDS.....	86
8.5.1	<i>Recommendations on prevention of AIDS from the point of view of panellists who do not support the causal link between HIV and AIDS</i>	86
8.5.2	<i>Recommendations on prevention of AIDS from the point of view of panellists who support the causal link of HIV to AIDS</i>	87
8.6	RECOMMENDATIONS ON SOCIO-ECONOMIC FACTORS THAT IMPACT ON AIDS.....	91
CHAPTER 9: PROPOSED RESEARCH PROJECTS AND STUDIES		92
9.1	GENERAL RECOMMENDATIONS ON RESEARCH	92
9.2	PROPOSAL 1: QUALITY ASSESSMENT OF HIV TESTING: ESTABLISHING A BASELINE AND VALIDATING HIV ELISA TESTING IN SOUTH AFRICA.....	92
9.2.1	<i>Rationale</i>	92
9.2.2	<i>Establishing a Baseline: Quality Assessment of HIV Testing of five independent sites in South Africa</i>	93
9.3	PROPOSAL 2: DETERMINATION OF THE ROBUSTNESS OF THE CURRENT HIV ELISA TESTS THAT ARE BEING USED IN SOUTH AFRICA.	94
9.3.1	<i>Purpose of experiment</i>	94
9.3.2	<i>Methodology</i>	94
9.4	PROPOSAL 3: MOLECULAR BEACONS	95
9.5	PROPOSAL 4: DO MOST PEOPLE WITH HIV INFECTION SHOW SIGNS OF AIDS WITHIN FIVE (5) TO TEN (10) YEARS?	95
9.6	PROPOSAL 5: PREADSORPTION AND VIRUS ISOLATION EXPERIMENTS - THE NEED FOR A GOLD STANDARD IN THE DIAGNOSIS OF HIV INFECTION.	95
9.6.1	<i>Importance of the Proposed HIV Experiments</i>	96
9.6.2	<i>Principles of the Proposed Experiments</i>	98
9.7	PROPOSAL 6: QUESTIONABLE AFRICAN AIDS /HIV STATISTICS - EPIDEMIOLOGY.....	100
9.8	PROPOSAL 7: PROPOSED INVESTIGATION OF THE DIAGNOSIS OF HIV/AIDS.....	100
9.8.1	<i>Current procedure</i>	100
9.8.2	<i>Investigation of reliability of serological tests for HIV</i>	101
9.8.3	<i>Extensions</i>	102
9.8.4	<i>Interpretation of findings</i>	102

9.9	PROPOSAL 8: STUDY TO FIND OUT THE REAL MEANING OF HIV TESTS	103
9.10	PROPOSAL 9: TO TEST THE RELIABILITY OF ONE OF THE MAIN LABORATORY METHODS CURRENTLY USED TO QUANTIFY HIV IN THE BLOOD OF SEROPOSITIVE INDIVIDUALS - USING THE ELECTRON MICROSCOPE.	104
9.10.1	AIM OF THE EXPERIMENTS.	104
9.10.2	MATERIALS AND METHODS.....	104
9.10.3	TECHNICAL ASSISTANCE NEEDED:	105
9.11	PROPOSAL 10: TO DETERMINE WHICH IS MORE HARMFUL - HIV OR ANTI HIV DRUGS?.....	106
CHAPTER 10: CONCLUSION		107
APPENDIX 1		109
	INTERNET DISCUSSION OF THE PRESIDENTIAL AIDS REVIEW PANEL.....	109
APPENDIX 2		118
	DATA ON ADULT MORTALITY PRESENTED BY DR MW MAKGOBA AT THE SECOND MEETING.....	118
APPENDIX 3		126
	STATS SA RESPONSE TO THE MEDICAL RESEARCH COUNCIL'S INTERPRETATION OF DEATHS	126
APPENDIX 4		133
	STATS SA REJOINDER TO THE MRC'S RESPONSE.....	134

Acknowledgements

The letter from President Thabo Mbeki inviting eminent persons to participate in the Presidential Advisory Panel on AIDS referred to the World Health Organisation report on the 'Global situation of the HIV/AIDS pandemic, end 1999' to describe the gravity of the situation that South Africa and the rest of the world were confronted with. The panel was constituted as part of the government's decision to respond to the AIDS catastrophe in an urgent and comprehensive manner, using all means at its disposal.

The invitations went out to eminent scientists and persons from all continents of the world who were expected to bring into the debates all points of view on the issues of HIV and AIDS. The responses to the invitations were instantaneous and reflected the overwhelming desire and determination to assist the South African government as it confronted the challenge posed by AIDS. Within a short period of two weeks, thirty-two (32) of these eminent persons assembled in Pretoria for the first meeting of the panel which took place on 6-7 May 2000. The second meeting of the panel took place in Johannesburg on 3-4 July 2000 and was attended by thirty (30) of the original invitees. Several invitees who could not attend either of the two meetings made their contributions to the debate through the Internet medium that was provided.

The panel was further enhanced by fifteen (15) members, mainly South African, who were invited by the Secretariat that supported and facilitated the work of the panel. The response of these invitees was just as overwhelmingly positive as that of the Presidential invitees.

The government and the people of South Africa are deeply indebted to these persons who responded without hesitation and in a selfless manner when the clarion call went out. Their generous contributions will undoubtedly prove pivotal as the world grapples with the challenge described in the WHO report referred to in the Presidents letter of invitation.

The debate of the complexity that was envisaged could not progress smoothly without expert facilitation. Such facilitation was ably provided by Professor Stephen Owen, Professor Ephraim Mokgokong and Dr Stephen Chandiwana. Their collective performance was a study in patient facilitation as they navigated the panel through complex and at times heated discussions.

Great debt is also owed to members of the Secretariat who were ably assisted by officials from the Departments of Health and of Arts, Culture, Science and Technology. Special words of appreciation also go out to the team that produced the first draft of the report as well as the final editors of the report.

Individual names of the many people involved in the working of the panel have not been included because the list would be just too long. The government and the people of South Africa are deeply indebted to you all.

Abbreviations

ADD	AIDS-defining disease
AIDS	Acquired immune deficiency syndrome
AZT	Azidothymidine
CDC	Centers for Disease Control and Prevention
CTL	Cytotoxic T-lymphocytes
CMV	Cytomegalovirus
DNA	Deoxyribonucleic acid
EM	Electron micrograph
HBV	Hepatitis B Virus
HHSV-VI	Human herpes simplex virus 6
HHV	Human Herpes Virus
HIV	Human Immunodeficiency Virus
HTLV-II	Human T-cell Leukaemia Virus 2
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NIV	National Institute of Virology
OD	Optical Density
PCR	Polymerase chain reaction
PEP	Post exposure prophylaxis
RCT	Randomised Controlled Trial
RNA	Ribonucleic acid
SADHS	The South African Demographic and Health Survey
SAIMR	South African Institute of Medical Research
SIV	Simian Immunodeficiency Virus
STD	Sexually transmitted disease
STI	Sexually transmitted infections
US(A)	United States (of America)
WHO	World Health Organisation

CHAPTER 1 – SETTING THE SCENE

1.1 Background

The South African government is currently confronted with the challenge of responding to the growing AIDS (Acquired Immune Deficiency Syndrome) epidemic. The government's response has been characterised in the main by a prevention strategy, supported by a multi-sectoral programme involving partnerships between government departments, civil society, NGOs (non-government organisations) as well as other sectors like the women's sector, faith-based organisations, the youth, traditional healers and traditional leaders.

The nature of the AIDS epidemic in South Africa, and sub-Saharan Africa in general, has been a growing cause for concern and recent developments in several areas of the response have created a need to evaluate some of the interventions. It is also an established fact that the determinants of the epidemic and some of the factors that continue to fuel it lie outside the health sector. The strategies adopted by the South African government for an effective response to this challenge have incorporated this reality.

Early in 2000, the South African government posed pertinent questions on several key issues relating to this epidemic. Among these were questions relating to the accuracy of the tests currently used to make the diagnosis of human immunodeficiency virus (HIV) infection; the impact of poverty and malnutrition on the ability of people to respond to this infection; and the relationship between HIV infection and many other infections which are common in Africa such as Tuberculosis (TB), malaria, hepatitis as well as other parasitic infections.

Discussions among officials of the South African National Department of Health (NDOH), local and international experts in the fields of AIDS and HIV yielded a variety of differing and consensual views on some of the matters. Opinions on some of the pertinent issues were so diverse that it seemed important to interrogate these in an open debate. The South African government became aware of divergent views on the existence, detection and actions of the 'primary' aetiological agent for AIDS, the human immunodeficiency virus (HIV). Theories were being advanced to explain causes of AIDS other than HIV infection. Views were also expressed which doubt the accuracy of the data upon which the extent of the disease in South Africa, as well as globally, is being assessed. In fact, some of these views questioned the authenticity of the claim that an AIDS epidemic exists at all in South Africa.

In order to gain a full knowledge of AIDS, a decision was taken to invite an international panel of experts to South Africa and provide a platform for them to deliberate on the issues pertaining to the subject. The report of such deliberations will be used to inform and advise the government as to the most appropriate course of action to follow in dealing with AIDS. This decision was endorsed by the Cabinet of the South African government in April 2000. A world-wide search took place to identify eminent specialists in the fields of AIDS and HIV, ranging in scope from basic scientists, physicians, historians, economists, public health professionals as well as policy makers. It was also decided that persons living with AIDS, as well as lay persons would be invited to serve on the panel.

1.2 Composition of the Presidential AIDS Advisory Panel

Both local and international scientists were invited to form part of the Presidential AIDS Advisory Panel. They were:

Invited by the President and were present at both meetings

Professor Salim S Abdool-Karim	Dr Clifford Lane
Dr Stefano M Bertozzi	Dr Marsha Lillie-Blanton
Dr Harvey Bialy	Dr Malegapuru W Makgoba
Dr Awa Marie Coll-Seck	Professor Sam Mhlongo
Dr Etienne de Harven	Professor Ephraim Mokgokong
Dr Ann Duerr	Professor Stephen Owen
Professor Peter Duesberg	Dr Jorge Perez
Dr Christian Fiala	Dr David Rasnick
Dr Helene Gayle	Mr David Scondras
Dr Roberto A Giraldo	Dr Joseph Sonnabend
Dr ET Katabira	Dr Zena Stein
Dr Claus Koehnlein	Dr Gordon Stewart
Dr Manu VL Kothari	

Invited by the President and present only at the first meeting

Dr W Chalamira-Nkhoma	Dr Mark D Smith
Dr Andrew Herxheimer	Dr Stefano Vella
Proffesor Luc Montagnier	Dr Jose M Zuniga
Dr Walter Prozesky	

Invited by the President and present only at the second meeting

Dr Stephen Chandiwana	Professor Eleni Papadopoulos-Eleopoulos
Professor Roy Mugwera	Prof Heinz Spranger
Dr Valender Turner	

Invited by the President but could not attend

Professor Francoise Barre-Sinoussi

Dr Robert Gallo

Dr Kaptue

Dr Souleymane M'Boup

Professor Fred Mhalu

Dr Kary Mullis

Professor Valerie Mizrahi

Professor Pierre Mpele

Dr Paranjape

Dr Praphan Phanuphak

Professor Robert Root-Bernstein

Present at the second meeting only - invited by the Secretariat

Professor Jerry Coovadia

Professor Charles Geshekter

Dr Glenda Gray

Dr Anthony Mbewu

Professor James McIntyre

Dr Lynn Morris

Dr Dan Ncayiyana

Dr Philip Onyebujoh

Dr Priscilla Reddy

Professor Barry Schoub

Professor Allan Smith

Dr Jimmy Volmink

Professor Allan Whiteside

Dr Carolyn Williamson

Mr Winston Zulu

Those who were not able to attend the first meeting in Pretoria, as well as other invited scientists, could, however, participate in the Internet discussion forum that ran between the first and the second panel meetings.

1.3 Terms of reference for the Presidential AIDS Advisory Panel

The terms of reference set for the panel before the first meeting in May 2000 were:

1. The following questions needed to be addressed in dealing with this issue of the evidence of viral aetiology of AIDS and related concerns about pathogenesis and diagnosis:
 - a) What causes the immune deficiency that leads to death from AIDS?
 - b) What is the most efficacious response to this cause or causes?

- c) Why is HIV/AIDS in sub-Saharan Africa heterosexually transmitted while in the western world it is said to be largely homosexually transmitted?
2. What is the role of therapeutic interventions in the context of developing countries? This should cover therapeutic interventions in the following contexts:
- In patients with AIDS
 - In HIV-positive patients
 - In the prevention of mother-to-child transmission
 - In the prevention of HIV transmission following occupational injury
 - In preventing HIV transmission following rape
3. Prevention of HIV/AIDS
- a) The discussions above should be underpinned by considerations of the social and economic context, especially poverty and other prevalent co-existing diseases and the infrastructural realities of developing countries.

The international panel met on two occasions in Pretoria (6-7 May 2000) and in Johannesburg (3-4 July 2000). In opening the first meeting of the panel on 6 May 2000, President Thabo Mbeki quoted from a World Health Organisation (WHO) report on "Global situation of the HIV/AIDS pandemic, end 1999". The report stated that of the 5.6 million people, who were [newly] infected with the HIV in 1999, 3.8 million lived in Sub-Saharan Africa. During the same year [1999] it was estimated that 2.2 million people in Sub-Saharan Africa died of HIV/AIDS, which figure represented 85% of the global total of death due to HIV/AIDS [in 1999]. In addition, the report stated, there were more women than men among the 22.3 million adults and 1.0 million children in sub-Saharan Africa who are estimated to be living with HIV/AIDS.

This report as well as other information at the disposal of the government, President Mbeki stated, pointed to the reality that South Africa and sub-Saharan Africa were confronted by a catastrophe. As governments are not expected to respond to catastrophes by merely doing what is routine, the South African government wanted to respond to this catastrophe in a manner that recognised that we were faced with a catastrophe. This was particularly important in this case as we were talking about the lives of millions and millions of people.

President Mbeki referred to the interventions that were implemented at national government level, as well as at the level of other layers of government, to combat HIV and AIDS which the Minister of Health, Dr Manto Tshabalala-Msimang had earlier informed the panel of. An appropriate response to this catastrophe necessitated that the government be properly informed as to what it was dealing with. It was when he was in the process of informing himself that he realised that the profile of HIV/AIDS in sub-Saharan Africa had changed quite drastically between 1985 and the mid-1990s. Important among

these changes was the HIV/AIDS profile in Southern Africa moving from being confined to a sub-population of male homosexuals in 1985 to being an endemic disease within a short period of seven years.

It was the desire of the South African government to get answers to questions like these that prompted him to establish an Advisory Panel of experts to assist the government in its informed response to the HIV/AIDS catastrophe.

A secured Internet facility was provided to enable the panellists to engage in in-depth deliberations and discussions during the period between the two meetings. The two meetings were characterised by robust debates and exchanges of views which were facilitated by presentations by panellists. The Internet debate set up between the two meetings lacked the robustness and vigour of the two meetings, the primary reason being the unevenness of inputs from panellists. Very few panellists who subscribe to the notion that HIV causes AIDS took advantage of the Internet medium to further the debate.

The lack of participation in the Internet debate by panellists who subscribe to the HIV theory of AIDS was lamented by the Minister of Health when she opened the second meeting of the panel on 3 July 2000. The Minister reminded the panellists that they had been invited because of the expertise and experience that they each brought to the debate. She further informed the panel that the participation rate and the nature of the participation in the Internet debate had indeed influenced the structuring of the second meeting of the panel.

Extensive references to original articles and sources were made, especially during the Internet deliberations (Appendix 1). It should, however, be recorded that at times panellists, without any supporting data or evidence, made broad and sweeping statements.

1.4 The report

The transcripts from audio recordings of the two meetings and the electronic record of the Internet deliberations will undoubtedly provide the South African government with a rich source of information as it confronts the AIDS challenge. It is only these transcripts that will convey the full richness of the deliberations, debates and discussions that took place over a two-month period. However, the audio recordings will only convey the temperament of the two meetings. This report captures the deliberations of the panel. It was written from these transcripts and will undoubtedly lack the completeness that the transcripts themselves can boast of.

For ease of reading and to fully capture the extent of the deliberations from the first meeting, through the intervening Internet discussions and then the second meeting, the report is presented in a format that captures the major identified themes and topics. The report therefore treats the entire exercise as one event and is not structured in such a manner as to distinguish whether input was made during the first or second meeting or during the intervening Internet debate.

It should be noted that it is not the purpose of this report to present a comprehensive compilation of the source materials referenced during the deliberations. A comprehensive compilation of these reference materials will nevertheless be catalogued in a separate document for ease of access.

The Presidential AIDS Advisory Panel was constituted in such a manner as to bring together diverse expertise and experience on the subjects of HIV and AIDS. Each member of the panel was invited in her/his personal capacity as an expert and not as the representative of a particular group or position. Although this wide representation of expertise included panellists who held contrasting viewpoints on some or most issues, it was not the intention of the principal sponsors of the panel to create a platform for confrontation between holders of particular points of view. Therefore, the mandate of the facilitators of the discussions was to ensure as smooth as possible a 'round-table' discussion among a group of experts. The gallant efforts of very able facilitators did not succeed in preventing the panel from polarising into two main camps based on whether HIV is the primary aetiological agent for AIDS.

The report attempts to reflect as objectively as possible the content of the deliberations, contrasting opposing views, highlighting areas of consensus and identifying gaps in knowledge. It was written with no intention to favour, reinforce or disfavour any particular viewpoint or side as any such favouritism would be contrary to the spirit and instruction of the Cabinet of the South African government. The report represents a summary of the deliberations, debates, views, opinions and recommendations and explicitly avoids passing judgement on the validity, or lack thereof, of the arguments made by the panellists individually or collectively. It needs to be emphasised that facilitators and rapporteurs were not judges who were expected to pronounce a verdict on winners and losers.

Finally, the report reflects the recommendations made by the panellist and identifies areas for future research and collaboration. Where consensus was not reached, the recommendations reflect the divergence of views. Considerable care has been taken to employ a language which does not take for granted one set of conclusions.

CHAPTER 2 - AETIOLOGY AND TRANSMISSION OF AIDS

2.1 Introduction

Most of the participants agreed that HIV exists, but not all acknowledged that it causes AIDS. Prof Duesberg reminded the panel that he had studied retroviruses for 30 years; and had elucidated their genetic structure, as well as the complexity of their genome and its three genes. He had also analysed the composite proteins, including the glycoproteins, which are the basis for the HIV test. (Note: p24 used in most diagnostic tests is not a glycoprotein). Intrigued by claims that retrovirus can cause disease in humans, he had started research in this field. In his experience, retroviruses do not kill the cells they invade but are latent passengers in humans and animals. He pointed out that 16 years and 16 billion dollars later, not a single HIV-positive patient had been cured. Two hundred thousand Americans get chain terminators every 6 hours, he said, and they are even given to pregnant women. He added that people with antibodies to HIV should have protection against HIV disease, since vaccines protect by inducing the production of antibodies. However, scientists find only antibodies in HIV-positive patients, rather than the virus itself. Furthermore, the virus replicates rapidly yet tends to cause disease only 10 years after infection, compared with other viruses, which cause disease within 5–10 days.

Dr Giraldo informed the panel that he started studying immune deficiency in 1965. He was convinced that the AIDS epidemic was worse than what the people who assert HIV as its cause believed. The levels of immune deficiency in Africa were increasing and had been increasing since 1974/1975, which preceded the recognition of AIDS by almost ten years. His preoccupation with AIDS arose out of a concern that the assertion that HIV was the cause of AIDS masked the catastrophe of AIDS and prevented politicians and governments from dealing with the real catastrophe and its real causes.

Both Prof Duesberg and Dr Giraldo do not subscribe to the causal link between HIV and AIDS. They do, however, believe that AIDS does exist, caused by factors other than HIV. There were, on the other hand, panellists such as Dr Rasnick who argued very consistently that AIDS does not exist and that AIDS would disappear instantaneously if all HIV testing was outlawed and the use of anti-retroviral drugs was terminated.

Those panellists who do not subscribe to the notion of HIV causing AIDS posed the following questions as key to the deliberations of the panel:

- Does HIV cause AIDS?
- Is AIDS contagious?
- Is AIDS sexually transmitted?
- Do the anti-HIV drugs do more harm than good?

2.2 Does HIV cause AIDS?

Dr Williamson gave a presentation that affirmed that HIV causes AIDS. It is a retrovirus belonging to the lentivirus family of these RNA (*ribonucleic acid*) viruses. Its genome consists of the following genes: gag, pol, env, nef, tat, vpr, vpu, vif. Like other retroviruses, it utilises the enzyme reverse transcriptase to produce DNA (*deoxyribonucleic acid*) within the host cell from the template of viral RNA. This DNA is then inserted into the host cell's genome. She reminded everyone that there are two types of HIV: HIV-1 and HIV-2; but that HIV-2 is much less common and is clustered in various geographical areas of the world such as West Africa. She displayed a phylogenetic tree of the various subtypes of HIV-1 that have been well characterised and sequenced and also showed a slide of an electron micrograph of the virus by Hans Gelderblom (1997). She further alluded to the Simian Immune Deficiency Virus (SIV) that causes AIDS in some monkeys.

There was a body of opinion expressed in the panel that 'purification' of a virus, as well as electron micrographs of the 'pure' virus was essential to answering the question as to whether a particular virus exists or not. According to Drs de Harven and Turner, HIV has never been 'purified' and no electron micrograph of the 'pure' HIV ever published.

2.2.1 Visualisation and Isolation of the Virus

2.2.1.1 Visualisation of HIV

Dr Turner in a presentation to the panel referred to the first description of the human immune deficiency virus by the groups of Montagnier and Gallo (1983). He described how Prof Montagnier 'supposedly purified' the retrovirus by running culture material from AIDS patients through sucrose density gradients. One of the three proteins extracted from this purified material reacted with sera from AIDS patients, and was later 'claimed' to be HIV p24 – a protein that is unique to HIV.

Dr Turner then went on to explain that in virology it is usually considered essential to take an electron micrograph of the gradient-purified material to prove that it contains retroviral particles. All of the 'supposed' electron micrographs of HIV published since the mid-1980s were from cell culture and never from a patient. The first electron micrograph of a gradient-purified HIV from a patient was only published 14 years later in March 1997 in the journal *Virology* by Gelderblom's group at the Koch Institute. Unfortunately, the Gelderblom article did not present immunoreactivity evidence to confirm that what had been visualised was indeed HIV. The second electron micrograph was from the US National Cancer Institute. The latter electron micrograph does not possess particles that are typically retroviral in morphology; nor does it meet the specific morphology of a particular retrovirus. Furthermore, independent data indicate that the proteins labelled p24 and p18 have been found in a variety of uninfected human tissue using monoclonal antibodies to these 'HIV proteins'. Thus if gradient purified infected material consists of the same proteins as uninfected material and does not contain retroviral particles and is not pure, then it is difficult to see how this material can be called 'purified HIV', Dr Turner argued. This series of arguments was supported by several contributions from Dr de Harven who insisted that nobody has ever demonstrated by electron microscopy a single retroviral particle in the blood of a patient supposedly having a very high viral load count.

Furthermore, Dr Turner claimed that Prof Montagnier in a 1997 interview had said that he had not purified his 1983 virus and had been unable to find any particles with morphology typical of retroviruses in his gradient-purified material. Dr Turner concedes that regardless of where the proteins come from, AIDS patients certainly have antibodies that react with these proteins and these reactions correlate with having AIDS or developing AIDS or being at risk for AIDS. In spite of this, there appears to be a need to utilise a 'gold standard'; which would involve relating the antibody test to viral isolation.

Prof Montagnier stated that in 1983 there was so little virus in the supernatant harvested from the first patient's culture that no virus could be visualised in the electron microscope even after pelleting. Moreover, the sucrose gradient used to purify the virus would have altered its morphology. Therefore, the evidence for a retrovirus was only indirect, namely, reverse transcriptase activity; p25 antigen associated with the peak of reverse transcriptase activity at the density of 1.155 – 1.16 in the sucrose gradient; cross reactivity of the p25 antigen with that of equine infectious anaemia virus (another lentivirus); and transmissibility of these characteristics from the initial cell culture to lymphocyte cultures of blood donors showing no antibody against p25. He further stated that it remains very difficult to isolate infectious HIV from peripheral blood lymphocytes of asymptomatic patients since at this stage the virus is almost exclusively located in the hyperplastic lymph nodes. Subsequent work done by his group and many other groups working on the subject makes untenable the contention that HIV does not exist. Dr Morris elucidated further that HI viral material has been visualised on dendritic cells using *in situ* hybridisation techniques.

Dr Morris pointed out that it was still difficult to visualise the virus in peripheral blood in spite of high viral loads. She asserted, however, that visualising the virus is not really necessary since there were other equally acceptable ways of 'seeing' the virus including PCR, p24 antigens and viral culture. She further argued that it would hardly be possible to culture an organism that was not found in peripheral blood in the first place. She also indicated that purifying HIV from blood is really not relevant in terms of validating ELISAs. Thus, while it may be difficult to visualise HIV in peripheral blood, it is extremely easy to see it in lymph nodes that are the major site of viral replication. In the light of the above, she argues that Dr Turner's insistence on withdrawing the ELISA test was inconsistent, especially when he admits that these tests in fact do correlate with AIDS. Dr Giraldo also accepted the epidemiological correlation between AIDS and positive ELISA and Western Blot tests. He stressed, however, that his difficulty lay in the conclusion that positive ELISA and Western Blot tests resulted from patients being infected with HIV.

2.2.1.2. Isolation of HIV

By contrast, Prof Montagnier further stated that HIV could be readily isolated from peripheral blood lymphocytes (after *in vitro* activation) of patients at the full-blown stage of AIDS. This was indeed the case of the virus isolated by his group from patient LAI who had full blown AIDS with Kaposi's Sarcoma. The virus that was isolated from both the blood and the lymph node biopsy of this patient became the prototype for all HIV-1-antibody testing. Dr Williamson pointed out that isolating HIV from peripheral blood is still difficult because of interference by plasma proteins. Dr De Harven was not convinced by the 'difficulty' argument stating that it had been routine for him in his training to isolate other retroviruses from the blood of leukaemic mice.

Dr de Harven pointed out that the retroviral markers that are protein in nature are non-specific because the virus has not been isolated and the proteins being measured could be cellular in origin. Tests reliant

on the detection of p24 are therefore not reliable. According to Dr de Harven, it is of no surprise that tests reliant upon immunoprecipitation of these markers, (i.e. ELISA and Western Blot), are not specific either as over 70 medical conditions unrelated to AIDS frequently test positive. He asserted that epidemiological studies of transmission were therefore based on the scientific fallacy of "virological studies based on viral markers in the absence of viral particles".

Dr Turner insisted that in order to determine the specificity of an antibody test, a viral load test or a viral burden test for HIV infection, it is essential to use a gold standard, which in this case is isolation of HIV from infected individuals. This, he asserted, should not be difficult to establish in South Africa.

2.2.2 PCR (Polymerase Chain Reaction) and ELISAs

As already stated above, some panellists, including Dr de Harven, concurred that there is not one single report in the entire medical literature in which a correlation has been established between high viral load measured by PCR of AIDS patients and the observation of HIV particles by electron microscopy. According to him, the best experts in the field concur that this essential correlation has never been made. Dr de Harven went on to stress that (1) any epidemiological studies based on ELISA or Western Blots would have to be fundamentally re-appraised; and (2) that following up AIDS patients with PCR measurement of viral load is, in his opinion, scientific nonsense.

Furthermore, there were repeated assertions by some panellists that Dr Kary Mullis, who won the Nobel Prize for developing the PCR, has cautioned that the PCR is not an acceptable method for measuring viral load. It was also argued that the PCR is not a test for virus *per se* but could be totally non-specific and therefore not identify HIV. In contrast Dr Williamson argues that one can directly detect the virus by PCR, virus culture and p24 antigen assays. She emphasised that the PCR was an acceptable method of specifically identifying HIV. The evidence for this, according to Dr Williamson, derives from the fact that the PCR test is based on very specific primers that are short stretches of DNA. When designing a PCR test, a data search is performed to ensure that the stretch of DNA identified is absolutely specific for HIV. PCR does not amplify random pieces of DNA - they might be small stretches of DNA, but they are highly specific. In further support of this, Dr Makgoba stated that the data he collected showed that all PCR tests performed locally are concordant with the available serology; and all serological tests are as good as international standards.

Dr Giraldo accused the proponents of the theory that HIV causes AIDS of attaching a lot of value to PCR amplification of fragments of nucleic acids because of their inability to isolate the complete HIV particles even from patients at the height of the disease. Furthermore, PCR is not quantitative because it is not reproducible - repeat amplifications of the same sample delivering different results. Prof Montagnier concurred that the PCR test was not very quantitative. However, Dr Morris presented data showing that virus could be quantitated using PCR and that this quantitation was of prognostic value.

Dr Lane pointed out that the ELISA is a screening test to detect whether someone might be infectious and is not a diagnostic test for HIV. However, a combination of the ELISA with a Western Blot provides a very accurate method of diagnosing HIV infection. Dr Giraldo did not understand how two tests that were individually not diagnostic could be the basis of a diagnosis when combined. Reference was made to the following statements made by the manufacturers of kits used for ELISA, Western Blot and PCR tests:

- “ELISA testing cannot be used to diagnose AIDS, even if the recommended investigation of reactive specimens suggests that antibodies to HIV are present” and “Specimens found to be repeatably reactive by Abbott HIV AB HIV-1/HIV-2(rDNA) EIA must be investigated by additional more specific supplementary tests”¹
- “Do not use this kit as the sole basis of diagnosing HIV-1 infection”²
- “The Amplicor HIV-1 Monitor test is not intended to be used as a screening test for HIV or as a diagnostic test to confirm the presence of HIV infection”³

Furthermore, Dr Fiala cautioned that the reality in most countries other than the USA and in Europe forces them to use only ELISA or rapid tests meaning that their AIDS statistics are only derived from 'diagnostic tests' acknowledged by everyone to be inadequate.

Prof Montagnier explained, that the panel of sera which the ELISAs use for calibration are seroconversion sera, from people who have just started producing HIV antibody. Also, multiple tests are used because the kits are validated against false positive controls.

Dr Duesberg remarked that two million young people are tested each year for HIV antibodies when they are screened for the US Army. One in a thousand tests positive but there has never been any report of any developing AIDS in the 12–15 years that these tests have been performed. These assertions were contested by Dr Gayle who argued that data existed which contradicted what Dr Duesberg was claiming. Dr Duesberg remarked upon a paper describing a subset of AIDS patients who were antibody positive but PCR negative.

2.2.3 Clinical and Laboratory Evidence of Causation

Opinion was divided as to whether HIV causes AIDS.

Dr Williamson presented evidence that HIV is *necessary* and *sufficient* to cause AIDS but that cofactors increase the risk. She asserted that:

- All patients diagnosed as having AIDS have HIV, but someone with HIV does not necessarily have to develop AIDS

¹ Abbott Laboratories, Diagnostic Division, 68-0158/R12; December 1996

² HIV-1 Western Blot Kit, Epitepe, Inc., Organon Teknika Corporation PN201-3039 Revision #8

³ Roche Diagnostic Systems, Inc., Amplicor HIV-1 Monitor Test Kit. US:83088. June 1996)(13-06-83088-001

- Cofactors may increase the rate of transmission of HIV; or the rate of progression to AIDS; but cannot in themselves cause AIDS
- HIV is transmitted sexually
- SIV, a virus closely related to HIV, causes AIDS in monkeys
- HIV levels in blood measured by viral load predict the chances of transmission of HIV; as well as progression, as does the level of CD4 cells and HIV-1 specific cytotoxic T-cells.
- Lowering the amount of HIV in an infected individual reduces the rate of progression to AIDS
- HIV is the pathogen that causes AIDS, and is not an innocent bystander

Dr Morris described how the onset of HIV infection in South Africans is accompanied by HIV-1 specific cellular responses such as cytotoxic T lymphocyte cell responses. In addition one can detect the virus by PCR and p24 antigen assays. Low CD4 counts are extremely rare in people without HIV. A single factor — HIV — predicts whether someone will develop AIDS.

Extensive epidemiological evidence has shown that the detection of a number of AIDS cases in countries is preceded by the detection of HIV antibodies in the population.

There are a large number of reports that have shown that transmission of HIV results in AIDS, and a number of examples where it has been proven, by characterising the virus in both the donor and the recipient, that transmission has occurred. Haemophiliacs who developed AIDS all received HIV-contaminated blood whereas haemophiliacs who did not receive contaminated blood did not develop AIDS. Accidental infections of researchers and healthcare workers have resulted in reduced CD4 counts in these individuals and the subsequent development of AIDS. HIV infected mothers may transmit the virus to their children, and paediatric AIDS is always associated with HIV.

Dr Morris presented evidence to show that HIV is not an innocent bystander but a pathogenic virus that destroys the immune system. This is known both from laboratory data as well as from what happens in an HIV infected person. She posed the following as certainties:

- HIV infects and destroys CD4 T-cells and these are precisely the cells that are depleted in a person with AIDS
- HIV destroys the architecture of the lymph nodes and the result is that follicular dendritic cells are unable to trap the virus, resulting in a spillover of the virus into the blood
- HIV causes cells to fuse and form giant cells, and people that have these syncytia-inducing viruses have a faster progression to AIDS

- In HIV infected persons, cells show what is called apoptosis or programmed cell death, as well as anergy, which means that they are unable to respond to other antigens.
- HIV also stimulates a number of specific immune responses, for example cytotoxic T-lymphocytes (CTL) as well antibodies, and some of these also contribute to the pathogenesis of the disease.

She described a study by Mellors that demonstrated that in those HIV-positive individuals with the highest viral load, 62% of them had developed AIDS after five years. In those that had the lowest viral loads, only 8% had developed AIDS after five years. This viral load stays fairly constant during the long asymptomatic phase of infection, but it can fluctuate. Factors such as immune activation caused by opportunistic infections can increase viral loads. In addition the use of anti-retroviral drug therapies reduces the viral load which subsequently reduces the risk of developing AIDS.

Some individuals are classed as rapid progressors. They develop the disease very quickly and these individuals have very high viral loads that do not decline as they would in most persons – a decline in viral load due to the induction of specific immune responses. Rapid progressors show a precipitous drop in CD4 cell counts and the acquisition of symptoms. However, there are some individuals who have been infected for up to 20 years and show very low viral loads and very stable high CD4 counts. These are called long-term non-progressors.

Prof Montagnier averred that HIV can reduce the number of CD4 cells and destroy the immune system; but only some strains can directly kill the CD4 T-lymphocytes. There are however more indirect ways of killing T-cells and we know that most of the cells that are not infected die of apoptosis.

The opponents of the HIV/AIDS hypothesis described the assertion of AIDS as an infectious, viral and transmittable syndrome as based on a set of beliefs and myths and not on scientific facts. They argued strenuously to refute the HIV/AIDS hypothesis and posted numerous references on the Internet site to support their stance. They advanced various arguments and references that would explain why HIV was either not implicated at all in AIDS or was at best a passenger virus to the disease. These would also explain why it is possible to have HIV-negative AIDS patients. Prof Duesberg explained that the PCR test typically identifies only 1 in a 1 000 or, at most, 1 in 100 cells, as being infected with HIV, and, in some patients, the virus is not found at all. In the case of a true pathogenic infection of a virus (for instance, hepatitis virus), every liver cell would be infected.

Dr Papadopoulos-Eleopoulos claimed that she had at least 15 references where the evidence shows that HIV does not destroy the CD4 cells. In fact, she said, even Dr Anthony Fauci says that the decrease in CD4 cells is only apparent and is due to down-regulation of the CD4 cells and not due to their destruction.

Dr Lane corrected the statement attributed to Dr Fauci who was on record as having said that HIV can down-regulate CD4 expression and that HIV destroys CD4 cells. Dr Lane reported that his laboratory has demonstrated reproducibly that HIV “chews up CD4 T-lymphocytes”. He invited the South African government to send researchers to his laboratory to witness this phenomenon and learn how the experiments are conducted.

Dr Duesberg pointed out that part of Koch's postulate states that the virus should be present in the course of disease in amounts corresponding to a disease. To which statement Dr Morris responded by illustrating that HI viral load correlated with the risk of developing AIDS. Drs Williamson and Gayle also added that a number of cases existed where Koch's postulate was fulfilled.

Dr Duesberg was puzzled why, in the case of the three laboratory workers who contracted HIV disease through treating patients, the cases had not been written up in medical journals, as this would have been an opportunity to fulfil Koch's postulate of causation by a microbe.

He also gave the example of Kaposi's Sarcoma occurring in homosexual young men who were HIV-negative, caused, he claimed, by inhalation of nitrates.

Dr Bialy asserted that the case of Kimberly Bergallis, who was reported to have died after contracting HIV from her dentist, was actually a case of AZT (azidothymidine) poisoning. Dr Bialy asserted that the replicatory behaviour of HIV during the so-called 'latent period' and its sporadic changes in titre during the natural history of the disease were typical of a passenger virus.

2.2.4 Evidence from Animal Models

Dr Williamson then covered evidence from animal models. She explained that one can clone the entire genome of SIV, a virus that is a close relative of HIV, insert this into a plasmid and then inject this into macaques. The macaques then get a viraemia and they develop antibodies against SIV. Subsequently they experience a reduction of CD4 T-lymphocytes and the development of AIDS. This progression of disease mimics what happens in humans. According to Dr Williamson, this is clear evidence that SIV, a virus closely related to HIV, causes AIDS with no cofactors present.

Dr Rasnick proposed treating chimpanzees that had been inoculated a long time ago with blood from AIDS but never developed the disease, with the same anti-retrovirals now given to human patients. He was certain that these chimpanzees would develop AIDS because of the drugs.

2.2.5 Epidemiological Evidence

Prof Abdool-Karim quoted epidemiological evidence that HIV causes AIDS. The South African Demographic and Health Survey (SADHS) shows a reversal in mortality trends in South Africa, and a study from King Edward VIII Hospital in Durban show that the two-year fatality for children infected with HIV is almost 60%. The infant mortality rate has been shown to be more than double in HIV-positive children versus HIV-negative children at Chris Hani Baragwanath Hospital in Soweto. Data collected at the King Edward VIII Hospital shows that case fatality rates over the last four years have increased from 4.5% to 22.6%.

Dr Bialy mentioned the foolish challenge given to Dr Duesberg when he delivered the graduate speech at the Albert Einstein College of Medicine to inject himself with HIV if he were so sure that it did not cause AIDS. He recommended instead a "series of easily undertaken, immediately do-able,

epidemiological studies” to prove or disprove once and for all that HIV causes AIDS. He also pointed out that epidemiological associations could not be used to demonstrate causality.

Despite over 700 000 patients in the USA being treated, there is no example of doctors and researchers having contracted AIDS from exposure to HIV-positive patients, claimed Dr Duesberg. Dr Gayle, who stated that she would be happy to provide information on the fact that there has been transmission to healthcare workers both in the US as well as in other continents refuted this contention.

Dr Stewart observed that in the USA and Europe AIDS was spreading only in very well-defined risk groups who were mainly homosexual men, their female partners who were consorts to bisexual men, and also in some groups of drug addicts. The plain fact was that it was spreading only in well-defined groups where behaviour and lifestyle was a predominant feature. Epidemiological information to date would not support any hypothesis that assumed that there was a single exclusive microbial cause of AIDS. “It is a fact that the passage of time has shown beyond all doubt that in the USA and Europe, AIDS is a disease that is not spreading in the general population by heterosexual transmission of HIV or anything else, although that may be a marker, but it is continuing to occur in the original risk groups.”

2.3 Alternative hypothesis on the cause of AIDS

The panellists who do not subscribe to the notion of HIV causing AIDS presented various alternative theories and hypotheses on the cause of AIDS.

2.3.1 The Chemical AIDS Hypothesis

Dr Duesberg believes that the ‘chemical AIDS hypothesis’, and not HIV, explains all aspects of AIDS in the USA, Europe and Africa. The steady rise in AIDS cases is more in keeping with toxic causes as an infection would be expected to produce a bell-shaped curve with decline due to spontaneous immunity and deaths. Furthermore, infections would be expected to affect people randomly, rather than the selectivity shown by AIDS. Also, viral infections are specific causing only one syndrome and not over 30 AIDS-defining conditions. Dr Morris countered by stating that the steady rise in AIDS cases is not incompatible with HIV as the cause of AIDS because of the long period between infection and the onset of disease. Concerning the selectivity of AIDS, she explained that the sexual transmission of HIV meant that the virus will only be transmitted to sexually active individuals, and will not affect people randomly. Prof Duesberg suggested that the panel perform a study in which 100–200 patients, identified as having AIDS according to the Bangui definition,⁴ have their actual antibody status assessed.

⁴ World Health Organisation. 1986. Acquired immunodeficiency syndrome. WHO/CDC case definition for AIDS. *Weekly Epidemiological Records*. 61:69-76.

Bangui definition: 2 major signs plus one minor sign: in an adult in the absence of exclusion criteria or in a patient with generalised Kaposi's Sarcoma or in a patient with cryptococcal meningitis.

Major signs: (1) weight loss of at least 10% of body weight; (2) diarrhoea for at least one month; (3) fever for at least one month (intermittent or constant).

Several panellists, including Drs Rasnick and Giraldo, supported the Chemaids hypothesis. They explained that it takes 10 years of exposure to toxins (such as recreational drugs, irradiation and AZT and possibly vitamin deficiency) to cause AIDS in the USA and Europe; whereas in Africa poverty, malnutrition and parasitic and tropical diseases were probable triggers of AIDS; which explains why AIDS in Africa is roughly equally distributed between the sexes.

Dr Bialy felt that the chemaids hypothesis alone was not sufficient to explain AIDS in Africa but that factors such as the biological parasitic burden that Africans experience in terms of multiple infections, etc over long periods of time is most definitely a contributor to the chronic immunodeficiencies that Africans experience.

2.3.2 The Immunotoxicological Hypothesis

The proponent of the immunotoxicological model (Dr Giraldo) listed five groups of stressors that can destroy the immune system - chemical stressors, physical stressors, biological stressors, mental stressors and nutritional stressors. The immunosuppression caused by these stressors can lead to AIDS even in people who are HIV-negative. The members of the panel who subscribe to HIV as the cause of AIDS accepted the suppression of the immune system by the stressors listed above. They did, nevertheless, point out that immunosuppression due to HIV is very different from toxin-related immunosuppression.

2.3.3 The Oxidation Hypothesis

Dr Papadopoulos-Eleopoulos suggested that oxidising agents could lead to immunosuppression and cause AIDS.

2.4 The involvement of cofactors (or risk factors) in AIDS

In a paper entitled 'AIDS pathogenesis: Alternative views', Prof Root-Bernstein advances several theories that may elucidate the relationship between HIV infection and what are termed cofactors. The interaction between these may explain the nature of the epidemic in different parts of the world.

The usage of the term 'cofactor' was, however, strongly opposed by some members of the panel, particularly the Perth Group, on the grounds that this term implies the existence of a primary factor and that this primary factor is HIV. They argue that HIV cannot be the primary factor since its existence has not been proven. Proof of the existence of the virus can only be obtained by isolation of the virus,

Minor signs: (1) oropharyngeal candidiasis; (2) pruritic skin rash; (3) herpes zoster; (4) generalised lymphadenopathy; (5) cough for at least one month (without TB); (6) chronic ulcerated herpes simplex; (7) tuberculosis

Exclusion criteria: cancer, severe malnutrition or other recognised causes

which has not yet happened. Instead, these panel members asserted that the elements commonly called 'cofactors' are the primary factors that cause AIDS in the absence of any requisite HIV infection. A more neutral term to accommodate factors involved in AIDS without denoting the primacy of HIV as a cause of the disease was 'risk factors'. Therefore 'cofactor' is used in this chapter only in the context of proponents of HIV as the cause of AIDS.

2.4.1 Involvement of cofactors in HIV-causes-AIDS Hypothesis

The paper by Prof Root-Bernstein articulated three theories on the primary cause of AIDS where cofactors may or may not be required:

2.4.1.1 Theories that link cofactors to the cause of AIDS by HIV

(a) **Theory A: The HIV-only theory**

The implications of HIV-is-both-necessary-and-sufficient theory of AIDS causation are that everyone is at equal risk of HIV infection and AIDS. Everyone exposed to an equal dose of HIV should have an equal chance of chronic infection. Everyone infected with HIV should progress to AIDS at the same rate. The only way to stop the progress of AIDS would be to stop HIV (Weiss 1993; Ho 1996).

Though Prof Montagnier is convinced that HIV plays a central role in the cause of AIDS, he found it difficult to explain, on the basis of the HIV-only-theory, why the AIDS epidemic was restricted to male homosexuals and intravenous drug users in the USA and Europe but has a heterosexual profile in countries of the South. Dr Sonnabend was another proponent of the HIV-causes-AIDS hypothesis who believed that issues of poverty and malnutrition were more important in the development of AIDS than the mainstream scientific establishment was currently acknowledging.

(b) **Theory B: The cofactor-promoted HIV theory**

This theory is based on the premise that, in addition to the fact that HIV is necessary for the development of AIDS, the rate of development of AIDS following HIV infection may be determined by the presence or absence of specific cofactors. These cofactors may be other viral, bacterial or parasitic infections, malnutrition, sexually transmitted diseases, TB or anything else that could have a profound effect on the immune system. It is well established experimentally that HIV infection requires that a potential T-cell host be in an activated or stimulated state and that many of these cofactors can achieve such activation.

(c) **Theory C: The cofactors-required theory**

A second version of the cofactor theory argues that HIV is necessary but not sufficient to cause AIDS. According to this theory, in the absence of cofactors, HIV is neither able to infect people nor to replicate within individuals once infection has occurred. Thus, healthy individuals are

unlikely to become infected with HIV in the first instance; and HIV-infected individuals who can eliminate existing cofactor risks may be able to drive the infection into latency. Like the cofactor-promoted theory, the rate of progression to AIDS will be determined by cofactor presence, but, since cofactors are necessary and not just modulators, the elimination of cofactors should be as effective at stopping AIDS as is the treatment of HIV.

Many cofactors induce the production of cytokines, immune suppression and immune depression independent of HIV. Many of these cofactors induce immune system cells to express the receptors required by HIV for the infection of cells.

2.4.1.2 Cofactors that need to be considered strongly

I. Allergenic cofactors

The interplay between HIV infection and infections such as TB, mycoplasma, Human Herpes Simplex Virus 8 (HHV-8), cytomegalovirus (CMV), Human T-cell Leukaemia Virus II (HTLV-II), hepatitis B, chancroid, and other sexually transmitted diseases is significant due to the concurrent burden imposed on the immune system.

- (a) The relationship between TB and HIV has been of concern to health professionals, especially because HIV infection has increased the number of identified cases of TB. Active tuberculosis infection also increases the rate of progression from HIV infection to AIDS. A proposed mechanism for the increased rate of immune deterioration has been proposed by Placido *et al.* (1997), who showed that viable *M. tuberculosis* increases the rates of apoptosis of alveolar macrophages in AIDS patients. Apoptosis was not increased with HIV alone. The microenvironment in the lungs of TB patients may also be rich in cytokines, which stimulate HIV replication there.
- (b) Hepatitis B has been implicated as a cofactor in two ways. Twu *et al.* (1993) make a case for increased numbers of HIV seroconversions in individuals infected with active hepatitis B virus (HBV) after controlling for sexual behaviour and changes in disease over time. This suggests either that an existing active HBV infection is a cofactor which helps establish HIV infection after exposure, or that HBV is a 'surrogate' for other factors that perform that function. A second form of interaction is seen in increased disease severity in children infected with both HIV and hepatitis (Anitpa *et al.* 1995).
- (c) Another candidate cofactor is a member of the gamma lymphotropic herpes virus family, particularly HHV-8, which fulfils the ideal portrait of an HIV cofactor in Africa. Sero-epidemiological studies indicate a high prevalence of infection with HHV-8 in homosexual men in developed countries and a low prevalence in their general population, whereas in Africa there is a very high prevalence in the adult heterosexual population, particularly in East and Central Africa. HHV-8 strains are sexually transmitted in homosexual men in the West. However, in Africa, infection starts early in childhood and is probably achieved by other means of transmission, possibly because of poor hygiene. HIV and HHV-8 are mutual cofactors; HIV is a cofactor of the Kaposi Sarcoma induced by HHV-8. In Uganda the incidence of Kaposi Sarcoma among males, which was 14.6 per million during the period 1964–1968, increased by

1993 to 300 per million, representing 48.6% of all cancers diagnosed histologically and clinically at the Makerere University Hospital. This difference can be accounted for by the appearance of HIV in the interval between the two periods. The immuno-suppression induced by HIV favours the emergence of Kaposi Sarcoma tumour cells.

In turn, HHV-8 may be a cofactor of HIV transmission and AIDS progression. Monocytes are common targets of HHV-8 and macrophage tropic strains of HIV-1, allowing double infections. Moreover, it has already been shown that both HHV-8 and HIV-1 are present in semen.

The link between HIV and cofactors may explain why the epidemic in Africa is mainly heterosexual. This may be due to the concomitant presence of an epidemic of sexually transmitted disease in Africa as well as practices such as dry sex.

Control of AIDS will require the link between cofactors and HIV to be broken. The nature of the AIDS epidemic becomes a function not alone of prevalence, but rather a complex function of the interaction of HIV with cofactors.

II. Oxidative cofactors

It was reported to the panel that researchers from the USA and Malawi have shown that the deficiency of the anti-oxidant vitamin A is common among pregnant women in Africa, and that the deficiency is strongly associated with increased mother-to-child transmission of HIV.

2.4.2 Risk factors that are the primary cause of AIDS according to alternative hypotheses/theories

According to the alternative hypotheses/theories on the cause of AIDS that were presented in section 2.3 above, the following risk factors, and not HIV, are the primary causes of AIDS. The presence of HIV in AIDS patients can at best be that of a passenger virus that has no role in the cause or development of the disease.

Dr Giraldo made a presentation to outline the following risk factors that cause AIDS:

2.4.2.1 Malnutrition

Malnutrition has been shown to result in:

- Decreased tissue levels of reduced glutathione, one of the most important antioxidants that detoxifies reactive oxygen species and promotes cell growth.
- Loss of weight, which according to some members of the panel may lead to the development of a positive HIV antibody test and not *vice versa*, as the HIV theory demands. In a study of Rwandan

women over a period of 24 months, beginning in 1998, it was reported that nutritional status assessed by loss of body weight "was a significant predictor of eventual HIV seroconversion".

2.4.2.2 Chemical stressors

Industrial chemicals and environmental pollutants are important causes of different abnormalities upon lymphocyte activation, proliferation and differentiation. Heavy metals, pesticides, diesel engine emission and food additives are also capable of this immune-suppression.

2.4.2.3 Physical stressors

Exposure to lasers, electromagnetic fields, infrared light radio frequencies and free radicals have been shown to affect the immune system.

2.4.2.4 Biological stressors

Human semen has been shown to induce chronic stimulation of the immune system with subsequent depression of the immune system. Blood and its components are known to be immuno-suppressive.

2.4.2.5 Mental stressors

Different immunological abnormalities have been found in people under psychological stress. For example, anxiety and depression decrease lymphocyte counts. Bereavement decreases the response of lymphocyte proliferates to mitogen and lowers natural killer cell activity.

In concluding, Dr Giraldo proposed that at a physiological level, AIDS can be explained as a progressive degenerative alteration of different immune cells and immune metabolic reactions, secondary to multiple, repeated and chronic exposures to immunological stressors.

At a molecular level, AIDS is the result of alterations of immuno-competent cells and immune metabolic reactions due to an excess of free radicals, especially oxidising agents. Whilst the proponents of HIV as the cause of AIDS acknowledged that malnutrition and the stressors listed above will weaken immunity and increase vulnerability to HIV, these factors could not, on their own, result in the collapse of the immune system that is witnessed in AIDS patients. Nevertheless, Prof Montagnier requested that identification of the relative weights of these cofactors and/or risk factors on the immune system was vital to build up a rational policy on the prevention and treatment of AIDS.

2.5 Transmission of HIV and AIDS

Several of the panellists accept that HIV is blood-borne, transmitted through both heterosexual and male homosexual sex and vertically transmitted in breast milk from infected mothers to babies. However, as reported above, there were panellists who disputed that AIDS is an infectious and transmittable disease.

The latter panellists noted that HIV does not survive freeze drying yet haemophiliacs get AIDS. This was contested by Dr Williamson who noted that there are a large number of reports that have shown that transmission of HIV results in AIDS and a number of examples where it has been proven, by characterising the virus in both the donor and the recipient, that transmission has occurred. Furthermore, she stated that haemophiliacs who developed AIDS all received HIV contaminated blood whereas haemophiliacs who did not receive contaminated blood did not develop AIDS.

2.5.1 HIV Transmission as Estimated from 'AIDS Deaths'

Some panellists disputed the estimated size of the 'AIDS epidemic' in South Africa.

Prof Duesberg pointed out that the figures for transmission of HIV in Africa as assessed by HIV seroprevalence do not tally with the WHO reported incidence of AIDS deaths over the past 15 years "which showed few AIDS deaths in 1985 rising to 50 000 annually in 1990 for the whole continent, reaching a plateau at 70 000 in 1992. For South Africa AIDS deaths in 1999 were estimated at 8 000." This suggested a rate of conversion from HIV to AIDS in Africa of 0.5% per annum compared to 3.5 to 5% per annum in the USA. He testified as to how mathematical models had consistently overestimated AIDS deaths; and the curious practice of the WHO of talking of cumulative AIDS cases and deaths rather than annual incidence. Even if the 75 000 cases reported annually by WHO for Africa are true AIDS deaths, this still represents only 0.6% of Africa's annual mortality. He asked whether the scale of the epidemic had been determined by South Africans or by external agents.

The estimated mortality figures also did not tally with the growth rates in the population of 2.8% for South Africa and more for the rest of the continent, with Africa adding 150 million to its population in the first decade of the epidemic and 149 million during the second.

Dr Prozesky explained that because in South Africa AIDS is not a notifiable condition, there is a reluctance to record it as a cause of death on the death certificate, possibly resulting in an under-reporting of AIDS deaths. Furthermore, he explained, South Africans, not Americans, had described and quantified the scale of HIV seroprevalence through antenatal clinics. Dr Makgoba agreed with Prof Duesberg and Prof Mhlongo, that a National Register of AIDS deaths is needed.

Dr Fiala said that, "although all the predictions of the so-called AIDS experts of the mid-1980s for North America and Europe were totally wrong, this did not come as a surprise as these predictions were based on wrong data and assumptions". Dr Stewart believes that the predictions were wrong because lifestyle, rather than HIV positivity, determines the course of the epidemic. Dr Fiala noted that the diagnosis of AIDS in Africa is usually a clinical one, made by using the Bangui definition that is non-specific. (Note: Dr Makgoba had reported that South Africa used the US CDC definition of AIDS and not the Bangui definition). The usual infectious diseases in Africa could account for such deaths. He went on to illustrate the issues around the AIDS debate, thus:

- Those suffering from well-known infectious diseases are diagnosed as suffering from AIDS.
- Most scientific information about AIDS comes from Europe and the USA and developing countries are dependent upon it.

- Through the AIDS discussion the industrialised countries have ensured themselves the right to determine the internal affairs of the developing countries such as budget distribution and assessment of health priorities.
- In view of the shortage of resources it is not medically comprehensible why such funds should be spent on the documentation of HIV on the basis of unreliable tests and of AIDS on the basis of unsatisfactory definitions. Ultimately these funds are not then available for other areas.

Prof Mhlongo noted the inaccuracy in death certification in Africa, making estimates of AIDS deaths and therefore transmission difficult. Furthermore, he quoted Prof Coovadia's textbook as attesting to poverty and poor socio-economic conditions as being the main causes of death in Africa. This includes malnutrition causing death from conditions such as *Pneumocystis carinii* pneumonia in neonates; dirty water causing diarrhoeal diseases; and overcrowding facilitating spread of infectious diseases.

Prof Montagnier pointed out that young adults in Africa were dying in great numbers and that Kaposi's Sarcoma had risen from an incidence of 1% of cancers in Africa in 1980 to 40% in Uganda currently.

Dr Coll-Seck attested to the reliability of HIV seroprevalence testing in African countries, that she herself conducts, that indicated increasing transmission in these countries. Methods of surveillance used include special sentinel surveillance in antenatal clinics and anonymous linked special surveys. These are the basis of WHO's figures.

Prof Duesberg asserted that in African studies of patients diagnosed clinically as having AIDS, 50% were later found to be antibody free suggesting the original diagnosis of AIDS was incorrect.

Dr Chalamira-Nkhoma reported that in Malawi the population growth rate from the census had been 3.2% in 1988 but only 1.9% in 1998, accompanied by a 10 to 20 fold increase in diseases such as TB. Other African panellists reported that deaths occurring in husbands followed by wives on a large scale in African villages were indicative of a lethal, STD (sexually transmitted disease) occurring.

Prof Gesheker quoted from two articles written by Morgan *et al.* that were published in *Lancet* in January 1998 and July 1997. As of 1987, there were approximately 1 to 1.5 million Ugandans said to be HIV-positive. However, according to the WHO's weekly epidemiological record of November 1999 the cumulative number of cases of AIDS reported in Uganda is 54,712. The question therefore is "what has happened to the other 946 000 HIV-positive Ugandans who after 10 years, evidently according to the WHO have not progressed to AIDS?"

2.5.2 Sexual Transmission

Dr Morris described a study published just a few months ago by Thomas Quinn showing that the level of virus in the plasma was directly related to the risk of transmitting to an uninfected person. Those individuals with undetectable levels of virus did not transmit to an uninfected partner. All the patients were antibody positive. The transmission data were true for both male to female transmission and female to male.

Prof Papadopoulos-Eleopoulos quoted Dr Robert Gallo as saying in 1984 that 'of 8 different sex acts, seropositivity correlated only with receptive anal intercourse'; and in 1986 that, 'we found no evidence that other forms of sexual activity contributed to the risk'. She also quoted the Multicentre AIDS Cohort Study of 1986 as saying that it is the 'frequency of passive anal intercourse and not the number of partners that is important'.

Others referred to Padian's paper of 1997 in the *American Journal of Epidemiology*⁵ that showed that in a 10 year follow-up prospective study of heterosexual couples of whom only one partner of either sex was positive "no seroconversions occurred among exposed partners", suggesting no transmission via the vaginal route. They also noted Goudsmit's view that for heterosexual HIV transmission anywhere in the world, including Haiti, Africa, and Thailand, 'a homosexual or anal factor seems to be required'. The question was posed that if HIV is transmitted from active to passive partner in the sex act like other STDs, then how does the active partner become positive?

Dr Fiala noted that all the predictions of the scale of heterosexual transmission of HIV in Europe had not materialised, and new HIV infections had peaked in 1984 indicating that effect was not caused by preventive measures being taken. He had a sense of *déjà vu* coming to Africa and seeing all the dire predictions of pandemics, similar to those made in Europe and the USA in the late 1980s. He quoted from the 1997 Durex study of frequency of sexual intercourse that showed that Europe and the USA were world leaders in this regard while South Africa and Thailand lagged behind. Some panellists discounted market research done by Durex as questionable.

Prof Stewart reported that in 1983, when he took up leadership of the AIDS epidemiology work at WHO, "the speculation was that there would be a global pandemic spread by heterosexual sex of HIV. The fact was that with the data then available, or becoming available in the USA especially and also in Europe this was not so."

Dr Vella pointed out that in Italy, unlike other western countries, the initial cases of AIDS were spread by heterosexual contact, and consequently maternal-to-child remain the commonest mode of transmission in Italy.

Prof Abdool-Karim reported that there were data to suggest that the rapidly increasing seroprevalence for HIV in South Africa might be due to factors such as increasing pathogenicity of the several strains of subtype C entering South Africa; to cofactors such as STD; and to social dislocation caused by migrancy.

Prof Mhlongo pointed out that the data presented could be interpreted as suggesting that the HI virus is highly selective in terms of race. The high prevalence of HIV positivity in the black population of South Africa would therefore have to imply that black people were more promiscuous than white people. He went on to point out that there is no evidence to support such a conclusion. On the

⁵ Padian NS, Shiboski SC, Glass SO, Vittinghoff E. 1997. Heterosexual transmission of human immunodeficiency virus (HIV) in northern California: results from a ten-year study. *Am. J. Epidemiol.* 146:350-357.

contrary, African people are very conservative in their sexual habits. The claim on the supposed promiscuity of Africans also contradicts the conclusions of the Durex study that Dr Fiala alluded to.

Dr Gayle presented evidence of sexual behaviour in youth in the USA with “38% of ninth graders already having sexual intercourse, and of twelfth graders 61%”.

Dr Reddy highlighted the poor quality data on the psychosocial determinants of behaviour, on the environmental determinants of behaviour, and on the economic determinants of behaviour. She recommended questions in research be designed to look at and understand behaviour within the cultural context, and the ethnic context.

Dr Stewart revealed that, from his experience as an AIDS epidemiologist, predictions that were correct were those which were based on lifestyle and behavioural parameters. Thus drug addiction, men having sex with men and disadvantaged people, were good predictors of AIDS. But if seroprevalence was used as a guide to predict AIDS, one derived a gross over-estimate.

2.5.3 Mother-to-Child Transmission

For more than a decade, publications have addressed the possibility that HIV can be transmitted through breast-feeding. Several studies in Africa have shown that those HIV-negative infants born to HIV-positive mothers later tested positive when their mothers continued to breast-feed them. This was considered enough proof of the infectivity of breast milk.

Several panellists challenged these studies, questioning the rationale, which is based on an incorrect diagnosis. They argued that the researchers employed definitions in accordance with what is known or believed about HIV causing AIDS. HIV-1 infection was assessed by a positive PCR. HIV transmission was defined by a negative HIV-1 PCR at birth but a positive PCR one month later and was further confirmed by genetic relatedness between viral strains from the mother and from the child and viral strains from the breast milk. It was argued that both antibody and amplification tests for HIV can react positively to more than 70 other different conditions, all related to oxidative processes.

Dr Giraldo suggested that the only objective way to confirm the hypothesis of the transmission of HIV/AIDS through breast milk is by searching not only for HIV but also for all other potential risk factors for testing positively for HIV and immune deficiency in at least four different groups of people:

1. One group of HIV-positive mothers and their infants living in a variety of African conditions
2. One group of HIV-positive mothers and their infants living in a variety of developed conditions
3. One group of HIV-negative mothers and their infants living in a variety of African conditions
4. One group of HIV-negative mothers and their infants living in a variety of developed conditions.

In each group, there have to be a significant number of mothers that breast-fed exclusively, that used formula feed only and that mixed both forms of feeding. A retrospective questionnaire looking at past exposure, both voluntary and involuntary, to immunological stressor agents would need to be administered. Prospectively, all groups should be followed up for several years to establish if seroconversion to HIV-positive or the development of AIDS is secondary to exposure to immunological stressors.

Dr Morris reported that in the setting of mother-to-child transmission the viral load is a very predictive criterion for transmission of the virus to the infant. Women with undetectable viral loads or very low viral loads did not transmit the virus. It followed, therefore that by reducing the viral load in infected pregnant women with anti-retroviral drug therapies, one could prevent the transmission of HIV.

Dr Makgoba described a study based on data collected from the Perinatal Research Unit at the Chris Hani Baragwanath Hospital with a cohort of 504 infants of whom 54 acquired their HIV through mother-to-child transmission. After 18 months, 46 out of those 54 died. He also noted that mother-to-child transmission had been demonstrated by typing of viral nuclear material from mother and infant demonstrating that the same virus had infected both.

Further evidence for this mode of transmission was the fact that when certain anti-retroviral drugs were given to HIV-positive mothers during pregnancy transmission was significantly reduced.

Dr Rasnick quoted a paper by Coovadia *et al.* of follow-up of 133 infants born HIV-negative to HIV-positive mothers. Twenty-one of the cohort were exclusively formula-fed in the subsequent months, 36 were exclusively breast-fed and 76 received mixed feeding. Transmission rates among exclusively formula-fed infants were 24%, among mixed fed 32%, and 39% among breast-fed infants. How was it, he asked that some of the exclusively formula-fed, initially HIV-negative babies could contract the disease?

2.5.4 Blood-borne transmission and Occupational Exposure

In the report-back from the group of panellists who deliberated on prevention strategies, Dr Mossie reported that evidence for blood transmission had been derived from occupational exposure data, which the CDC had accumulated over time. From these data health workers who had been exposed through needle stick injuries involving their HIV-positive patients, had subsequently contracted HIV infection and sero-converted to HIV-positive status.

Studies conducted among drug users also proved that it was only when there was sharing of needles that HIV transmission occurred between them. The success of needle exchange programmes in reducing HIV transmission was also testimony to this fact.

Further evidence for blood-borne transmission has been derived from haemophiliacs who had contracted the virus from transfusion with infected blood products.

Dr Duesberg was, however not convinced by this evidence, expressing surprise that in Africa and also in the West very few doctors and healthcare workers had contracted this infection despite working with

the so-called infected patients daily. He expressed concern that in South Africa, where such a serious epidemic was said to be occurring no data on hospital workers who had contracted HIV from their patients was available.

There was also another point of view expressed that healthcare workers appear to contract HIV but not AIDS. The focus of this argument rests on the contention, raised by Drs Rasnick and Bialy and Prof Duesberg, that despite having over 700 000 patients being treated for advanced HIV disease in the USA, no healthcare worker has been known to contract AIDS from exposure to HIV patients.

This was contradicted by the reported 17 reported cases of seroconversion in healthcare workers following needle-stick injury, with clear documentation of the patients' sexual history included. Dr Bialy pointed out that this was very small incidence compared to that of healthcare workers contracting hepatitis following needle-stick injury. Others then rejoined that it is common knowledge that HIV is less contagious than hepatitis B, but it is still transmissible by blood and infected cells.

Drs Williamson and Gayle provided examples of healthcare workers who subsequently acquired AIDS from HIV transmission from accidental inoculation through contaminated instruments. The variability in the time it takes from HIV infection to AIDS was raised as a discrepancy regarding the transmissibility of AIDS.

The issue of viral latency as distinct from clinical latency as is the case with AIDS was raised. The early literature does not clearly indicate an increase in virus titre with progression of the disease. This was considered the hallmark of a passenger virus. However, a paper written by Fauci in *Science* showed clearly that the viral load was higher with progression of the disease. This notion was contested. Dr Morris presented data showing that the higher the viral load the greater the chance of developing AIDS within five years, the greater the chance of transmitting HIV to a sexual partner and the greater the chance of vertical transmission to babies.

Dr Turner requested clarification on the blood-borne transmission of HIV infection in haemophiliacs as the latter received plasma, which had been freeze-dried and stored prior to transfusion. Scientifically, the virus does not survive extreme conditions such as freezing and in the light of this fact how did freeze dried plasma still infect those who received it a few months after it had been stored. No explanation for this was proffered during the deliberations.

2.5.5 Epidemiology of Transmission

Prof Duesberg described the three classical hallmarks or the characteristics of an infectious epidemic that distinguish it from an epidemic caused by toxins or lack of nutrients.

- Firstly the hallmark of an infectious epidemic, viral or bacterial, is that its increase in incidence is exponential. Incidence then declines within weeks or months as originally described by William Farr. The decline in incidence reflects spontaneous vaccination or immunity of the survivors. As a result microbial and viral infections are actually self limiting and typically seasonal; they degenerate over time producing a bell-shaped curve of incident cases.

- Secondly the epidemiology of a microbial epidemic is typically random with no discrimination of heterosexuals from homosexuals; or men from women.
- Thirdly the microbes that cause microbial or infectious epidemics are highly specific, reflecting the very limited genetic information of the causative viruses or microbes.

In contrast to this pattern, Prof Duesberg claimed, chemicals or toxins like nicotine, alcohol, cocaine or heroin; nuclear radiation; and lack of nutrients such as vitamin and protein deficiencies cause the epidemics. The kinetics or the time course of such epidemics are not specific because they are not self replicating. The dose and the duration of the toxin or the time of the lack of the essential nutrient determine the kinetics. They are not self limiting as there is no immunity against them – they are only limited by the withdrawal of the toxin or by the supplementation of the food with the missing nutrient.

The specificity of a non-infectious chemical or a drug-induced disease depends in part on the nature of the toxin and the nutrient that is lacking - it is typically not very high. An example would be the epidemic caused by smoking in America, or England. Smoking causes lung cancer, emphysema, heart disease, and bronchitis; but is not specific in the way a pneumococcus, influenza, hepatitis virus or a polio virus would be.

Prof Duesberg claimed that the so-called HIV epidemics in Europe and USA correlate exactly with the recreational drug epidemics followed by the 'antiviral drug epidemics'. They started in America after the Vietnam War. Before then there were a couple of thousand heroin and cocaine addicts and there are currently in America 20 million daily users of illicit drugs, eight million of whom use hard drugs including cocaine, heroin, nitrate and amphetamines.

Quoting from WHO data, he showed that "the African AIDS epidemic is not exponential, it is not self-limiting and it is not bell shaped. It is unlike any microbial or viral epidemic that we have learned of so far. The kinetics are compatible with, let us say, a chemical epidemic like lung cancer and smoking or liver cirrhosis and alcohol or recreational drugs and AIDS in the United States or Europe".

The 1990 data from USAID he pointed out suggest that "there were 616 million Africans generating 75 000 AIDS patients, that is a very small percentage indeed. So, epidemiologically, this epidemic is restricted to a minority that appears to have in common malnutrition and poor sanitation. That is reflected by the clinical markers of African AIDS."

"So the epidemic appears to be non-randomly restricted to groups that are defined by malnutrition, poor sanitation and parasitic infection, as originally proposed by Anthony Fauci from the National Institute of Allergy and Infectious Diseases and Maurice Seligman from Paris who published in the *New England Journal of Medicine* in 1984 that African AIDS and AIDS in underdeveloped countries is due to parasites and malnutrition."

According to Prof Duesberg, the Bangui definition is explicitly unspecific. "Likewise, the anonymous AIDS notification forms from the South African Department of Health points out that weight loss over 10%, chronic diarrhoea for over a month, fever for more than a month, persistent cough, generalised periodic dermatitis, recurrent herpes zoster, candidiasis, oral and oesophageal chronic persistent herpes, cryptococcal meningitis and Kaposi's Sarcoma, all of these are AIDS defining diseases. You

could not get less specific than that. Thus the African AIDS epidemic is clinically complex and highly unspecific, unlike any microbial epidemic we have ever seen". Dr Makgoba pointed out that in South Africa the definition used for the diagnosis of AIDS was that of the US Centers for Disease Control and Prevention (CDC) and not the Bangui definition.

So in view of its clinical lack of definition and the lower than expected number of AIDS cases, the following question arises: Is the African epidemic new, like its US/European namesake, or does it comprise old diseases reported under a new name?

Dr Williamson recommended that "we need further studies in South Africa on the virus, to look at the natural history, the rate of disease progression in HIV infected people, is it shorter in Africa, is it shorter in South Africa and why is it shorter. Is this the effect of the cofactors that will result in increasing viral loads or are there other effects that we do not know about that are resulting in shorter disease progression? Although, in fact, there are no data to indicate that there is shorter disease progression in South Africa."

Dr Williamson also mentioned that the other unique feature in South Africa is the fact that we have a predominantly sub-type C epidemic in South Africa. Further basic research is needed on this sub-type to look at the unique properties of HIV sub-type C and see how this is impacting on transmission and pathogenesis.

For recommended research and studies please see Chapter 9.

CHAPTER 3 – SURVEILLANCE

The discussions on surveillance occupied a significant part of the deliberations of the panel with particular emphasis placed on the availability of surveillance data from South Africa and elsewhere and the ability of these data to demonstrate the presence and magnitude of an AIDS epidemic. Several panellists insisted that the unavailability of direct statistical data on how many South Africans have contracted AIDS or have died from AIDS as distinct from the question of how many South Africans were HIV-antibody positive bedevilled any proper discussion on AIDS and its impact on South Africa. These questions were critical given the arguments already advanced in Chapter 2 of this report on the cause of AIDS or whether an HIV antibody positive test could be declared indicative of infection by HIV in the absence of isolation of the virus from seropositive patients. Several panellists argued that the answers to these questions would fundamentally influence the debates as well as any recommendations that could be made on the issue of surveillance.

3.1 What are the questions and issues?

Some key discussion points that were raised with respect to HIV and AIDS surveillance include:

- Whether the AIDS epidemic in South Africa is indeed a reality
- Why the pattern of the epidemic differs so significantly between Africa and Europe/USA
- Whether available data sufficiently demonstrate an AIDS epidemic
- What the standard AIDS-defining criteria are in South Africa
- How reliable serological tests are in assessing HIV
- What elements are necessary to strengthen surveillance in South Africa so as to better plan for the impact of the epidemic

3.2 Overview on the necessity for surveillance

There was widespread agreement that surveillance is a necessary tool for understanding the AIDS epidemic. However, there were two opposing schools of thought on the issue of HIV surveillance. One group subscribed to the argument that HIV surveillance is an exercise in futility as it has not been proved that an individual that is HIV-positive will develop AIDS. Thus a more useful marker is AIDS disease. The opposing school of thought argued for the importance of conducting both HIV and AIDS surveillance. They argued for observed correlation between HIV-positive status and AIDS disease.

Dr Gayle gave an overview of the general principles surrounding current practice in the surveillance of HIV and AIDS as used by agencies such as the CDC, WHO and UNAIDS. She described the history of HIV surveillance in the USA as having started with AIDS case surveillance and case definitions for AIDS

on the basis of a cluster of illnesses and symptoms. At that stage, AIDS had been identified mainly in homosexual men, haemophiliacs and other recipients of blood products, intravenous drug users, their partners and infants.

These profiles contributed to the identification of the main modes of transmission – sexual contacts, blood and blood products, perinatal transmission from pregnant women to their infants and the observation of ‘slim’ disease around Lake Victoria.

It was pointed out that the main components of current HIV and AIDS surveillance include:

1. Serological surveillance, the key components of which include sentinel antenatal testing for HIV prevalence using the ELISA HIV-incidence testing (still new but under development are the serological testing algorithms for recent HIV seroconversion – STARHS), as well as testing among TB patients, patients with sexually transmitted diseases and among high-risk population groups
2. Behavioural surveillance for programme monitoring
3. AIDS and HIV mortality surveillance.

Dr Gayle described the purposes of surveillance as being to estimate the magnitude of the epidemic and assess trends.

There was a debate arising largely from the school of thought that questioned the causal link between HIV and AIDS and around the philosophy underlying the current public health surveillance practice. Other concerns that were debated included whether surveillance tools (such as the serological ELISA test) are sufficiently sensitive and specific to accurately detect true HIV-positive status; whether measuring sexual behaviour, for instance, is informative, since the causal link between HIV and AIDS is still in question, and whether mathematical models are reliable predictors of epidemics.

3.3 South African epidemic – Fact or fiction

There were differences of opinion on whether there is an AIDS epidemic in South Africa. Those from the school of thought that argues that HIV does not cause AIDS also argued the futility of discussing an HIV epidemic, as they do not believe that HIV causes AIDS. There were some in this latter group who even argued that there was insufficient evidence to support the notion of an AIDS epidemic in Africa.

This argument was refuted with HIV-prevalence statistics from the South African Department of Health’s national antenatal survey, showing that HIV prevalence amongst women attending antenatal clinics has increased exponentially from 0.73% in 1990 to 22.4% in 1999. Dr Abdool-Karim, preferring to use his own study data, similarly showed antenatal prevalence statistics from Hlabisa (KwaZulu-Natal), which rose from 4.2% in 1992 to 30% in 1998. He indicated that this increase was characteristic only of the Southern African epidemic. He noted the high prevalence rates among young women aged 20 to 24, by showing the rise in 1992, 1995 and 1998 from 7%, 21% and 39% respectively. Data were also presented from Chris Hani Baragwanath Hospital that showed an increase in the incidence of HIV from 26% in 1997 to 30% in 1999 using the unlinked HIV tests.

HIV indicator diseases such as other sexually transmitted infections (STIs) and TB are seen to be useful markers of the burden of HIV-associated disease. Studies show that STIs make individuals more infective and more susceptible to HIV infections. Data obtained from a community-based randomised trial in Mwanza, Tanzania substantiate this position, demonstrating that improved treatment of STIs lowered HIV incidence by 42%.

3.3.1 AIDS mortality

On the issue of whether there is an AIDS epidemic in South Africa, Dr Rasnick argued that no evidence on AIDS had been presented to demonstrate an AIDS epidemic. He emphasised that the evidence required was “not HIV, not antibodies to HIV but people who have died from AIDS”.

Prof Duesberg contended that scientists and non-scientists alike typically diagnose an infectious epidemic on the grounds of a sudden increase in the morbidity and mortality of a given population. In the case of an epidemic, the general trend is that the numbers of the affected population would decline significantly, and a relatively immune population would emerge and would be resistant to the new epidemic for a considerable length of time.

It was noted that AIDS is not a notifiable condition in South Africa and thus reliable statistics on AIDS do not exist. Other panellists argued that there is an HIV epidemic in South Africa. In support of his argument, Dr Abdool-Karim cited data from the South African Demographic and Health Survey, which suggests that while infant mortality was on the decline in the mid-1990s, an upward trend in infant mortality had been observed in the 1998 survey.

Further supporting data for this argument were presented from a study conducted at King Edward VIII Hospital in KwaZulu-Natal, showing a 60% death rate among children with HIV infection who were followed up over a two-year period. He indicated that the case fatality rates among HIV-positive infants had increased from 4.5% to 22.6% over a four-year period, and that studies at Chris Hani Baragwanath Hospital had shown that HIV-positive infants had a mortality rate that was double that of infants who were HIV-negative.

Dr Makgoba expanded on this theory by presenting data that demonstrated that the infant mortality rate among HIV-negative infants in Soweto was 17 per 1 000 live births, in comparison with 362 per 1 000 live births among HIV-positive infants. (The national infant mortality rate is 42 per 1 000 live births.) He further discussed paediatric mortality research conducted at Johannesburg General Hospital by Cooper, which showed that mortality trends had remained more or less constant between 1991 and 1996. After 1996, the HIV positivity rate had increased to 48% and continued to rise.

Dr Mhlongo pointed out that increased access to healthcare facilities and the easing of travel restrictions from rural to urban areas as a result of the recent changes in the political climate in South Africa were bound to lead to changes in the profile of patients in clinics and hospitals. Free access to healthcare facilities by pregnant women enabled impoverished people to seek medical attention in hospitals that would previously have denied them access.

With respect to adult mortality, Dr Makgoba presented data from the South African Department of Home Affairs that the Medical Research Council had received only a few days prior to the second meeting of the panel. It was for that reason that he could not make the data available to other members of the panel prior to his presentation. The data had been processed by the Medical Research Council and modelled by the Actuarial Society of South Africa (see Appendix 2). Dr Makgoba made the following observations on the basis of the data:

- The groups most affected by AIDS range between the ages of 20 and 40, with a peak in deaths at the age of 30 for women and 35 for men.
- Total deaths per annum in South Africa for this age group increased by 23% between 1997 and 2000.

He further presented data for the period from April 1999 to May 2000, suggesting an almost exponential rise in AIDS deaths over the four quarters.

The Actuarial Society projected deaths using two scenarios: deaths expected in the absence of HIV and those that had actually occurred. The conclusion drawn was that the deviation of mortality trends from expected trends could be accounted for by HIV/AIDS.

Prof Whiteside confirmed Dr Makgoba's observations and added that in a recent census conducted in Malawi, two million people could not be accounted for. Dr Chalamira-Nkhoma from Malawi shared similar observations, suggesting that HIV would have contributed to a decrease in the growth rate from 3.2% to 1.9% in the 1998 census.

Prof Whiteside further argued that similar observations had been made in the Rakai district of Uganda where the population pyramid had hollowed out. He concluded that these deaths could only be attributed to AIDS deaths.

Dr Fiala and other panellists responded to the South African mortality data presented by Dr Makgoba with the argument that they were unable to analyse and adequately comment on the statistics as they had not been presented with the information prior to the verbal presentation (in the second panel discussions) and had therefore not been afforded the opportunity to apply their minds to the data. Dr Bialy's views were that if South Africa had not already determined the epidemic before external influence, the observations made on the epidemic might not be real. He suggested that Dr Duesberg's hypothesis of a chemical causal agent for AIDS be closely examined.

Subsequent to the second meeting of the panel and to the publication of the mortality data by a Sunday newspaper, Statistics South Africa issued a statement cautioning against the propriety of comparing the 1999 mortality data with that from 1990 and suggesting alternative approaches to the problem (see Appendix 3). The 1990 data provided a profile of what the pre-1994 government called Republic of South Africa which did not include the Transkei, Venda, Bophuthatswana and the Ciskei which were supposedly independent states and had a population profile that was overwhelmingly African. Given that Africans in South Africa have a demographically younger population profile than whites and Indians, and the distribution of deaths among Africans is different from that found among whites and Indians, Statistics South Africa concluded that the mortality profile for 1990 would not be that drastically different from that of 1999 if all population groups from all geographical areas were taken into consideration. Furthermore, the causes of death statistics for 1995 for all population groups in all geographical areas show that the largest proportion of causes of death among males was 'unnatural'.

Following other meetings between the Medical Research Council and Statistics South Africa, a further rejoinder was issued (Appendix 4).

3.4 Epidemiological Theory of Causal Inference

The concept of causal inference is critical to epidemiological practice because theory on causal inference in the context of a particular disease sets 'standards' on whether a specific infection could or does result in disease. Various theories and hypotheses on the cause of AIDS are presented in Chapter 2 (sections 2.2–2.4) of this report.

Prof Root-Bernstein explored the theory in a discussion paper on the aetiology of HIV in AIDS. In this aetiological theory he distinguished three hypotheses:

- That HIV is both 'necessary' and 'sufficient' to cause AIDS
- That HIV is sufficient but not necessary to cause AIDS
- That HIV is neither necessary nor sufficient to cause to cause AIDS.

The debate was therefore whether HIV is both necessary and sufficient to cause AIDS. Some panellists argued that it has not been proved that HIV does cause AIDS and that, while HIV can be present in individuals that develop AIDS, it cannot be proved that HIV caused AIDS. Dr Stein argued that in standard epidemiological practice, causes do not need to be 'necessary' and 'sufficient' to cause disease. She quoted from Dr M Sussers' manuscript for a forthcoming encyclopaedia on public health: "HIV is (and can be so regarded) as a cause of AIDS even if everyone who has HIV does not get AIDS".

This is similarly the case with conditions related to syphilis and tuberculosis. She explained that modern-day epidemiologists share a multi-causal perspective that deviates somewhat from Galileo's seventeenth century formulation that causes should be necessary and sufficient, and Koch's subsequent postulates, which served to guide the search for specific organisms as one-to-one causes of given diseases. Thus, in her view, HIV does not need to be necessary and sufficient to cause AIDS.

This view was challenged by Dr Papadopoulos-Eleopoulos, who turned the argument around to support an alternative theory (that AIDS may be caused by another agent e.g. Chemical agent) by concluding that, if a factor can cause disease without necessarily being sufficient, then we can have AIDS without HIV. Scientifically that is the only conclusion that can be drawn. Dr Fiala contributed to this debate a presentation of data published in the *European Journal of Epidemiology*, which demonstrated that of a total of 465 patients with clinical AIDS, 40% were found not to be HIV-positive. Views expressed by panellists in other discussion suggest that this may not necessarily be unusual and could be influenced by the progression of disease state or tests used.

3.5 Socio-economic risk factors

There were two opposing views on the debate around risk factors that are critical for the transmission and spread of AIDS. One school of thought argued that poor economic status was a sufficient risk factor in the acquisition of AIDS. Another argued that low socio-economic status and poverty contributed to circumstances that would increase the risk of acquiring AIDS, but that these factors are not in themselves sufficient in the acquisition and spread of AIDS.

Scientists of the former school, notably Prof Duesberg and Dr Giraldo, argued that poverty is an important risk factor for AIDS.

An opposing view was expressed Dr Bertozzi, who argued that higher HIV and AIDS cases do not necessarily correlate with low socio-economic status. Dr Bertozzi cited Mohanda and Allan, who wrote on the basis of their research in Tanzania, Rwanda, Zimbabwe and Zaire that the initial spread of HIV and the initial cases of AIDS that were identified in the population were not correlated with lower socio-economic status, rather the opposite was true, they were correlated with higher incomes and higher educational achievement. This position was supported by observations made by Dr Mugwera, who demonstrated that the earlier cases of HIV were in men from Rakai district who were involved in trade with Tanzania and whose socio-economic status was relatively higher than those who had not initially contracted HIV.

Discussing paediatric mortality and the work done by Professor Cooper in Johannesburg, Makgoba said that mortality trends had remained more or less constant between 1991 and 1996. After 1996, the HIV positivity rate had increased to 48% and continued to rise. Dr Bialy challenged the paediatric mortality data and asked to know what proportion of those infants had received AZT. The response to this was that the two groups were comparable with respect to socio-economic status and caesarean section rates of 23%, and that the only difference was the presence of HIV by antibody test and PCR. Dr Makgoba challenged the panellists to devise a general predictive model that explains such figures. He was convinced that poverty, malnutrition, TB, malaria, stress and chemical toxins would not explain these data.

Dr Reddy cautioned against interpretation of the mortality data for causality of death without taking socio-economic and political parameters into consideration. She proposed that the data be studied by a trans-disciplinary team which included Social Scientists.

3.6 Differences in the African epidemic, compared with Europe and the USA

Several panellists presented the issues surrounding why and how the South African epidemic differs from the epidemic in Europe and the USA. According to one group, the similarities are that initially AIDS occurred predominantly among homosexuals and haemophiliacs in the USA, Europe and South Africa, and that subsequent heterosexual spread and perinatal transmission were predominantly low among all socio-economic groups in all regions.

One of the differences is that in Africa and South Africa in particular, the epidemic has been explosive, with considerable perinatal transmission, probably through breast-feeding. Survival time appears to be shorter and the spectrum of disease differs due to local infections. Factors that contribute to the differences and the larger epidemic in Africa include poverty and infections, severe manifestations of sexually transmitted disease, higher diversity in HIV clades on account of migration, and the *ccr5* gene being much rarer in Africa, thereby making more rare the possibility of natural immunity to the disease.⁶

A distinguishing feature of the African epidemic has been in the area of transmission dynamics, host biological factors, and behavioural and viral factors. A high level of heterosexual transmission is one important factor. While most scientists who ascribe to the theory that HIV infection leads to AIDS argue that HIV is sexually transmitted, Dr Giraldo, in his submissions on the Internet debate, challenged this position and argued that there was no logical reason why HIV would be transmitted heterosexually in the South and homosexually in the North.

Dr Sonnabend's contribution to the debate on the differences between Africa and countries such as the USA relates to the issue of HIV transmission. Whereas heterosexual transmission of AIDS from women to men is inefficient in the USA, it seems to be efficient in Africa. The explanation provided is that the HIV inoculum in female to male transmission is very small and is transmitted very inefficiently. The situation in Africa, however, is different because of the high incidence of sexually transmitted diseases and other infections.

Dr Abdool-Karim argued that the most important factors include:

- The way the epidemic was introduced
- The South African strain – the phylogenetic tree analysis. While in India, the viruses that have been isolated and sequenced are 'related to one another', the South African isolate shows much more diversity. The close relationship between the Indian strains suggests a single introduction and subsequent spread (clonal epidemic) whereas the high genetic diversity in South Africa is suggestive of multiple introductions. The latter would confirm the importance of migration in fuelling the epidemic.

⁶ *ccr5* gene is known to be protective against HIV infection in the sense that it reduces risk of transmission and infection. If infection has taken place, it reduces the risk of progression of AIDS.

- The fact that sexually transmitted infections are so highly prevalent
- With the migrant labour system, various strains are brought together, causing multiple epidemics in South Africa.

A study comparing 70 couples where one partner was a migrant and 50 couples where both were non-migrants showed that the level of HIV discordance (where one person is positive and the other negative) is 30% in migrant couples and 12% in non-migrant couples.

3.7 The role of mathematical models in forecasting the epidemic

Data obtained through mathematical modelling were presented to support the argument that AIDS deaths are on the increase. This argument was supported by data from the national population register of the Department of Home Affairs (see section 3.3.1). While the CDC documentation and other official statistics including the South African Department of Health apply models to forecast events and the epidemic, information published by WHO, UNAIDS and other agencies were widely criticised by panellists such as Prof Duesberg and Drs Fiala and Giraldo. Prof Abdool-Karim expressed a concern about the use of mathematical models.

In a critique, Prof Root-Bernstein discussed mathematical models of AIDS, saying that they could be used in addition to experimental and clinical studies to investigate and compare theories of AIDS pathogenesis. He categorised them into two groups:

1. Models of the epidemiological behaviour of the epidemic
2. Models of the effect of HIV and cofactors on the immune system. The principal limitation of statistical and mathematical models is that such "models are actually an assortment of assumptions and simplifications that reflect the collective understanding and disposition of investigators concerning the natural history of disease and how it is spread".

It was widely recognised that there are inherent limitations in the use and application of mathematical models. These limitations result from the wide number of assumptions, and sometimes simplifications, that are made. The point of departure seemed to be the extent to which different individuals and groups are prepared use data obtained from models in spite of their limitations. While panellists suggest that using models is unhelpful, and even misleading, others ascribe to the position (evident from their continued use of models) that models have their usefulness in situations where planning data are required and unavailable and that they should continue to be used with caution.

3.8 Surveillance recommendations – what should be done about the South African epidemic?

3.8.1 Deliberations of the panel

The deliberations of the panel were at all times bedevilled by the absence of accurate and reliable data and statistics on the magnitude of the AIDS problem or even HIV prevalence in South Africa. Repeated requests for such data and statistics, particularly by panellists who refuted the causal link between HIV and AIDS, failed to result in the provision of such data by either South African panellists or the officials of the Department of Health.

Recommendation

It is therefore strongly recommended that appropriate measures be taken to establish the necessary infrastructure and provide the necessary expertise and resources to collect the data and develop reliable and up-to-date statistics on the magnitude of AIDS and prevalence of HIV in South Africa. All efforts must be made to ensure AIDS reporting in South Africa is up to the highest standards in the world.

3.8.2 Discussion on mortality data

The discussions around the mortality data presented by Dr Makgoba revealed the necessity for a study to unpack the numbers and gain deeper understanding as to whether the changing mortality profile resulted from AIDS only and/or from factors other than AIDS.

Recommendation

It is recommended that a trans-disciplinary team comprising members from all the relevant branches of science, including social sciences and humanities, other relevant professional spheres and representatives of relevant government departments be constituted to undertake an in-depth study of the mortality trends in South Africa and report on the results of the study to the South African government.

3.8.3 Recommendations from panellists who do not subscribe to the causal linkage between HIV and AIDS

It was recommended that the South African government commit to the following:

- a) Suspend the dissemination of the psychologically destructive and false message that HIV infection is invariably fatal and assist in reducing the 'hysteria' surrounding HIV and AIDS

- b) Suspend all HIV testing until its relevance is proved especially in the African context, given the evidence of false positive results in the tropical setting and the fact that most assumptions and predictions about AIDS in Africa are based on HIV tests
- c) Continue to improve social conditions in South Africa
- d) Continue to decrease poverty
- e) Continue to control infections and sexually transmitted diseases
- f) Continue to increase the nutritional status of the population.

3.8.4 Recommendations from panellists who subscribe to HIV as the cause of AIDS

Dr Gayle and Prof Abdool-Karim, representing panellists who endorse the causal link between HIV and AIDS, reinforced the importance of the following initiatives for the South African government:

- a) Continue strengthening the surveillance of risk factors such as the behaviour of youth
- b) Surveillance of HIV prevalence in antenatal clinics, blood banks and among workers
- c) Conducting incidence surveys
- d) AIDS surveillance at health facilities
- e) Keeping death registers
- f) Standardisation and evaluation of diagnostic criteria and their completeness for reporting purposes
- g) Surveillance of antenatal syphilis
- h) Laboratory reporting
- i) Health facility reporting.

3.8.4.1 Recommendations on surveillance as it pertains to reduction of blood-borne infection

The South African government needed guidance on the following issues:

- (a) The most appropriate policies on screening and quality assurance for blood safety
- (b) The most appropriate policy to reduce or prevent needle-stick injury with specific reference to policies on single use needles
- (c) Policies on the management of occupational HIV exposure, including post-exposure prophylaxis. Research on post-exposure prophylaxis needs to be pursued vigorously.
- (d) Policies on education and implementation of universal precautions
- (e) Most appropriate education and training related to reduction of risk of HIV and transmission in nosocomial settings and related to surgical operations.
- (f) Policies on intravenous drug use

3.8.4.2 Recommendations on surveillance as it pertains to reduction of HIV from Mother to Child

The South African government needed to pay attention to the following issues:

- (a) The most appropriate policy on voluntary HIV testing and counselling of pregnant women
- (b) The best policy for contraception promotion, including targeting HIV-positive women
- (c) The best policy on the use of anti-retroviral drugs to treat HIV-positive pregnant women. There were several research issues that were listed in this regard, including:
 - investigating the extent of Nevirapine resistance when used to prevent transmission of HIV from mother to child
 - the role of early weaning and non-exclusive breastfeeding
 - what other mechanisms can be devised to reduce transmission of HIV from Mother to Child

3.8.4.3 Recommendations on surveillance as it pertains to sexual transmission of HIV

The following issues require attention:

- (a) The most appropriate policy on safe sex education
- (b) How best to promote the use of condoms

- (c) The best policy on the most appropriate and comprehensive treatment of sexually transmitted diseases
- (d) The most appropriate policy on post-exposure prophylaxis for rape
- (e) Regulation of commercial sex work and gender equity issues
- (f) Research into finding an efficacious and effective microbicide and into the development of a vaccine for therapy and prevention needs to be continued vigorously

3.8.5 General recommendation

There was general consensus on the need for the case definition of AIDS to be standardised for clinical practice in South Africa.

CHAPTER 4 - HIV TESTS AND THEIR ACCURACY

4.1 HIV testing

The ELISA, Western Blot and PCR viral load are the most frequently used tests to confirm HIV infections. The ELISA and Western Blot tests detect HIV antibodies in the serum of patients, whereas the PCR Viral Load test is a genetic test that detects small HIV nucleic acid fragments in whole blood. The veracity and reliability of these tests are key to the validity, reliability, quality and accuracy of epidemiological data used by any country. The ELISA test is mainly used to screen for HIV infection in blood donors and for general surveillance, whereas the Western Blot and PCR are generally used as confirmatory tests and in the context of research. All these tests, individually or in combination, are considered by the proponents of the HIV/AIDS theory as important indicators of infection by HIV. The CD4 count is an additional laboratory test used in combination with ELISA to make a diagnosis of AIDS; and with the Viral Load Test to determine the clinical progression of the AIDS disease and the monitoring of the effectiveness of anti-retroviral treatment. The Western Blot test is more expensive and requires a well-developed laboratory infrastructure; it is therefore not affordable for many developing countries. Dr Fiala also informed the panel that the Western Blot test is not accepted in the United Kingdom as a confirmatory test for HIV infection due to its unreliability.

Co-culturing of virus is used to isolate the virus from the blood of infected AIDS patients. This method is generally used as a research tool as it is too expensive and time-consuming to conduct as a routine surveillance and screening method. It also requires highly specialised staff and infrastructure.

According to Dr Lane, a substantial number of research publications indicate the value of HIV testing and making a diagnosis of HIV infection on the basis of the antibody tests. AIDS surveillance was first based on the clinical case definition, and AIDS was initially regarded as just a cluster of diseases. The subsequent discovery of HIV led to the incorporation in the definition of the disease of various clinical and immunological patterns, and, as recently as 1993, the CDC AIDS definition was widened to include a wider spectrum of clinical disease also utilising CD4 counts. Again, Dr Fiala informed the panel that European countries do not include the CD4 count in the definition of AIDS.

However, Dr Gayle pointed out that there is a general lack of standardisation of the definition of AIDS throughout the world. This, she argued, arose because it is possible to diagnose HIV infection by means of non-standardised laboratory tests, as well as by the verification of the presence of clinical symptoms. Since data are compared across countries, there is a need to standardise the definition of AIDS.

A particular concern raised by some members of the panel was that after 15 years of research, there is the lack of a 'gold standard' against which to measure the accuracy and reliability of the data generated from the commonly used methods to diagnose HIV infection.

4.1.1 ELISA test

The ELISA test is the most commonly used test for screening blood from donors. Its specificity and high sensitivity make it widely acceptable since it is able to detect all the possible HIV infections. It has also been found to be useful in surveillance. It is generally accepted that a single test cannot be regarded as proof of HIV infection. However, in order to improve the reliability and validity of ELISA, the CDC testing guidelines state that "a test for HIV antibody is considered positive when a sequence of tests, starting with a repeatedly reactive enzyme immunoassay (EIA) and including an additional, more specific assay, such as a Western Blot, are consistently reactive".⁷ Similarly, the WHO testing guidelines require confirmation of samples that are repeatedly reactive by ELISA using the same blood sample but a different ELISA kit. Both testing regimes call for repeated ELISA testing of a single blood sample rather than ELISA testing of more than one blood sample. However, the UNAIDS–WHO recommendations state: "An additional blood sample should be obtained and tested from all persons newly diagnosed as seropositive on the basis of their first sample. This will help eliminate any possible technical or clerical error".⁸ Major concerns surrounding the ELISA test, however, include its specificity, reliability and reproducibility, as well as the lack of a comparative 'gold standard'.

Dr Giraldo claimed that the HIV ELISA tests are not specific for HIV. He cited the fact that four repeat ELISA tests plus a Western Blot are required for a diagnosis of HIV disease in the USA - an example of how unsure the manufacturers are of its specificity. Furthermore, he elucidated that there is no standard by which to establish the specificity and sensitivity of the ELISA test. He also pointed out that the Roche Amplicor PCR kit specifically states that it must not be used as a screening test for HIV nor to diagnose HIV infection (see section 9.10.3).

Dr Turner pointed out that WHO, in its description of the 34 HIV antibody ELISA tests on the market, uses one antibody test as a gold standard for another. In his opinion mycobacterial and fungal antigens can cross react with HIV ELISAs causing false positives.

Prof Montagnier argued that no test is perfect and, moreover, that the current generation of ELISA tests is much more sensitive and more specific than in 1984. The current ELISA test uses recombinant proteins made from clones and consequently minimises cross-reactivity by other proteins from the plasma. This view was echoed by Dr Makgoba, who repeatedly pointed out that all immunoassays used in South Africa are based on recombinant viral proteins, which are more specific than tests used previously and are similar to those used in other countries. All HIV diagnosis in South Africa is supported by laboratory tests "and HIV screening is always followed by two confirmatory tests. All immunoassays in South Africa are designed, calibrated, optimised and standardised to the level of their discriminating power – which is the power to discriminate between negative and positive cases." According to Makgoba, the tests used in South Africa have high confidence results of 99.9%. In a low risk population with more than 36 000 regular blood donors in South Africa, the results showed that

⁷ MMWR Vol 36(31): 509 – 515, 1987

MMWR Vol 38: S-7, 1989

⁸ *Weekly Epidemiological Record* Vol 72: 81 – 88, 1997

99.9% of the tests produced negative results. Furthermore, comparison of data from three laboratories in South Africa shows a low false positive rate. The rates of false positive diagnoses in over 2000 cases for various South African HIV testing institutions were: 1.6% false positive reports at the National Institute of Virology (NIV), 0.23% at the South African Institute of Medical Research (SAIMR) and about 0.33% at a Stellenbosch laboratory. Dr Magkoba pointed out that the ELISA test has a predictive rate of over 99% in South Africa. Both the predictive rate and the false positive rate of ELISA tests in South Africa compare very well with similar results obtained in the United Kingdom. Screening tests used in South Africa are as good as those used anywhere else in the world. The tests are highly specific, sensitive and reliable.

There were, however, a number of opposing views in the panel about the specificity, reliability and validity of ELISA.

Dr Turner argues that the data used as a basis for the AIDS pandemic in South Africa are generated from the antibody ELISA test, which is fundamentally inaccurate, unreliable and invalid. The antibody ELISA test is based on the reaction between the unique viral protein (the p24 proteins 'supposedly' from HIV) and serum antibodies from a blood sample. Independent data show that p24 proteins, the basis for the ELISA antibody test, have been found to cross react with a wide variety of uninfected human tissue and blood samples from other disease states. For example, antibodies to candidiasis and mycobacterium infections cross react with p24. Furthermore a warning in the manufacturer's inserts suggests that the ELISA should not be used on its own for HIV diagnosis. According to Dr Giraldo, many other disease conditions – such as leprosy, malaria, leishmaniasis and other viral infections – give rise to false positive results in the ELISA test without the concomitant HIV infection. Furthermore, many of the conditions that cause a false positive result in the ELISA test are conditions that are also prevalent in many of the recognised AIDS risk groups. A great deal of scientific data indicate widespread non-specific interactions between what are considered retroviral antigens and unrelated antibodies. A positive HIV ELISA test may also indicate previous antigenic stimulation by other retroviral infection. Another concern is that there is no precedent for the diagnostic utilisation of the ELISA test for other viral diseases. In general, the presence of antibodies specific to a particular disease is a major indicator of potential immune protection by the body, which is not the case with HIV infection, since antibodies to HIV fail to confer any immunoprotection against HIV. The ELISA test may therefore not be a true indicator of infection but an artefact arising from cross reactivity of other naturally occurring viral proteins.

The lack of standardisation of ELISA results, both within the country and across countries, was a source of major concern to some panellists. Results of ELISA tests may be interpreted differently within a single laboratory, between laboratories within one country, and between countries. This may mean that a person that tests positive at one laboratory in South Africa may test negative at a different laboratory in the same country. Moreover, the lack of standardisation across countries could result in an individual's testing positive in one country and negative in another.

4.1.2 Western Blot

The Western Blot is an antibody test, which, according to Dr Makgoba, is one of the tests used to confirm the diagnosis of HIV infection in South Africa. Dr Sonnabend reported that he regularly uses the Western Blot as a confirmatory test for HIV infection in the USA. A positive Western Blot result is

synonymous with HIV infection and the attendant risk of developing AIDS. He was satisfied that there was general agreement on the correlation between Western Blot and AIDS and patients that were suffering from AIDS always reacted positively to the Western Blot test.

However, a number of concerns were raised around the specificity, reliability and reproducibility of the Western Blot test.

Dr Turner believed that the Western Blot should not be used to confirm and validate the results of the ELISA test since the Western Blot and ELISA tests are based on the same antibody reaction mechanism. As with the ELISA test, another concern over the use of the Western Blot test is its non-specific positive reaction to a number of diseases (including tuberculosis, a variety of parasitic infections and other viral infections) in the absence of HIV infection. The antigens used in the Western Blot test may be similar or identical to other human proteins, and hence the results of the Western Blot may thus not provide an indication of HIV infection.

Dr Papadopoulos-Eleopoulos presented a transparency showing the results of a Western Blot test with a number of samples from leprosy, TB and AIDS patients. It appeared that the Western Blot results from the different samples were indistinguishable from one another, showing the Western Blot test to be non-specific and unreliable. All the samples tested positive, even those from leprosy and TB patients. In further deliberations, Dr Mark Smith pointed out that Max Essex had already demonstrated the indeterminate results from Western Blot results in 1994. The above underlines the fact that the Western Blot test cannot be used as a determinate diagnostic tool.

4.1.3 PCR test for viral load

The PCR viral load test is also used as a confirmatory test. It is based on the amplification of tiny HIV viral particles that are supposed to originate from HIV in the blood. This test is virus specific and specifically detects HIV RNA. It is used to determine the level of viral load in the blood. It is mainly used in the tracking of the clinical progression of advanced HIV infection to AIDS disease, the monitoring of the effect of anti-retroviral treatment and the monitoring of mother-to-child transmission. There is a high correlation between clinical disease progression and the viral load. A high viral load is associated with an increased risk of transmission and the clinical progression to AIDS. Also the level of virus in the blood is directly related to the degree of risk of transmission to uninfected individuals. People with undetectable levels of virus in their blood do not transmit to uninfected partners. Mothers with high viral loads had the highest chance of transmitting the virus to their infants.

Arguments against the use of PCR are that this test is characterised by high variability and lack of reproducibility. In addition, the very wide variability may lead to the erroneous interpretation of results, thus compromising the accuracy and validity of the PCR results. Dr Bialy pointed out that the PCR viral load test might not be a legitimate measure of infectious virus. It demonstrates a high level of fluctuation, and the viral load can be increased non-specifically by other viral and bacterial infections (opportunistic infections may also increase viral load). Research results indicate that the viral load test may not always be an indicator for the clinical progression of HIV to AIDS.

Another point of concern that was raised was the fact that the PCR test was developed for the non-C-clade virus, whereas the clade-C virus is the most prevalent in South Africa.

4.1.4 CD4 count

The CD4 count is a determination of the concentration of CD4 T-lymphocytes in the blood. The associated immune deficiency leading to infection by opportunistic infections is ascribed mainly to the depletion of CD4 T-cells. The CD4 count can therefore be regarded as an accurate determination of the robustness and functionality of the immune capability and status to effectively protect the body against general infections. HIV infects and destroys CD4 cells (though some dispute this), rendering the immune system incapable of protecting the body against general infections, hence the resultant immunodeficiency in HIV infection and AIDS. This immunological test is used to monitor the progression of HIV infection to clinical AIDS disease and to monitor the effectiveness of anti-retroviral therapy. The CD4 count can be inversely correlated with the viral load. The higher the viral load, the lower the CD4 count will be. Intermediate progressors (patients who take longer than 10 years to progress from HIV infection to AIDS) consistently maintain the concentration of CD4 within normal range. When the CD4 count drops, it predicts the onset of opportunistic infections. In rapid progressors (those who developed AIDS within 2-4 years after infection), the CD4 drops precipitously, coinciding with the onset of infections and clinical progression to AIDS.

The improvement of the concentration of CD4 during anti-retroviral therapy is used as a surrogate marker for the effectiveness of the treatment.

4.2 Virus isolation or co-culturing

It is standard practice in virology to use virus isolation or co-culturing to confirm the presence of a virus in any sample (a requirement stated by Prof Montagnier's co-workers a decade ago). Two laboratories have been credited with the successful isolation of the virus from AIDS-infected patients. These are the Koch Institute (work published by Hans Gelderblom) and the US National Cancer Institute. In both of these cases, the authors admitted the possibility of contamination from other viruses in the blood. Once the virus has been cultured, it can be visualised by electron microscopy. While the difficulty of visualising HIV in blood culture is generally accepted, it is possible to see the virus in lymph nodes, which is the major site for replication. Dr Morris pointed out that the large amounts of plasma proteins complicate the visualisation, so that, even when the viral load is high, it is difficult to see any virus by electron microscopy. Transmission electron microscopy, as well as *in situ* hybridisation, demonstrating that HIV resides on the surface of follicular dendritic cells, are satisfactory means for the visualisation, she said.

Dr Turner supported a proposal that will enable comparison of the antibody titre with the isolation of the virus. However, HIV isolation is difficult and expensive to undertake.

4.3 Moratorium on HIV testing

Dr Rasnick, supported by Prof Mhlongo, recommended that the South African government should consider terminating HIV testing by blood banks and for general surveillance since the results of all the

tests are unreliable and non-specific and hence give wrong information. He argued further that AIDS would disappear instantaneously if all HIV testing were outlawed. The basic question was whether hundreds of people in South Africa are dying of AIDS or of TB, malaria, *Pneumocystis carinii* pneumonia and parasitic infections. The absence of data indicating the rate of deaths due to AIDS should receive urgent attention.

Prof Mhlongo spoke of the preoccupation with biomedicine in an attempt to be scientific even at the expense of the wider distressing situation of poverty, poor housing, lack of sanitation and a multitude of diseases associated with the deprivation and urban squalor that characterise the reality of the majority of black South Africans. He presented evidence to show that mortality in England and Wales due to tuberculosis declined precipitously from 1838 with hardly any people dying of TB in the United Kingdom by 1960 (McKeown). This occurred despite the fact that TB chemotherapy only started in 1945 and the BCG vaccine was only developed in 1956. This decline in mortality due to TB had nothing to do with medical interventions but was rather a consequence of improved sanitation, improved housing, improved nutrition and improved environmental conditions that occurred in the United Kingdom during the course of the period under review. Prof Mhlongo went on to present evidence that a similar picture was demonstrated in the USA from 1920 to 1991 (Seale and Stephen).

4.4 Recommendations on HIV testing

4.4.1 Proposed studies and experiments

The key issue that came under focus was the reliability of the ELISA testing in terms of delivering time infection data. As a diagnosis of HIV infection has such a profound effect on a person's life and future, it was considered of utmost importance that the tests are unimpeachably reliable. Since all epidemiological predictions concerning HIV/AIDS in South Africa are based on the results of such tests, their absolute reliability was declared to be of utmost importance.

A major recommendation arising from the two meetings was to apply a series of HIV tests of increasing stringency in order to establish the validity, veracity, rigour, reliability and concordance of ELISA, PCR and viral isolation. **Details on some of these experiments are presented in Chapter 9 of this report.**

The experiment will consist of the following series of steps:

- (a) ELISAs as they are currently employed
- (b) The same tests using a pre-absorption protocol to remove cross-reacting antibodies such as those against *Mycobacteria* which some panellists asserted frequently confound ELISA tests
- (c) A variety of nucleic acid based protocols
- (d) The application of the classical gold standard of virus isolation, including electron microscopy

These tests will be performed on cohorts chosen to represent the full spectrum of the South African population.

4.4.2 Recommendation on future HIV testing

The panellists who refuted the causal linkage between HIV and AIDS recommended the suspension of all HIV testing until its relevance is proved, especially in the African context, given the evidence of false results in a tropical setting and the fact that most assumptions and predictions on AIDS in Africa are based on HIV testing.

4.4.3 General recommendations on testing

- (a) The case definition of AIDS to be standardised for clinical practice in South Africa.
- (b) Any positive HIV ELISA result to be repeated with at least two additional blood samples before an HIV diagnosis is confirmed in order to improve the reliability and validity of ELISA.
- (c) Apply a series of HIV tests of increasing stringency in order to establish the validity, veracity, rigour, reliability and concordance of ELISA, PCR and viral isolation.

CHAPTER 5 –THE TREATMENT OF AIDS AND THE USE OF ANTI-RETROVIRAL DRUGS

5.1 Introduction

Issues pertaining to the use of anti-retroviral drugs dominated the debate on the treatment of AIDS. On the one hand, panellists who disputed the causal linkage between HIV and AIDS, the use of an anti-retroviral drug to treat a disease that was not caused by a retrovirus was deemed morally indefensible. On the other hand there were panellists who subscribe to the causal linkage between HIV and AIDS and who argued that sufficient and incontrovertible evidence existed in the scientific literature and from clinical experience which affirmed the value of anti-retroviral drugs in the treatment of HIV/AIDS.

The toxicity of anti-retroviral drugs was not in dispute from any of the panellists. It nevertheless generated two different sets of attitudes based on whether these drugs should be used or not. One group felt strongly that anti-retroviral drugs were toxic to the point of producing disease conditions in otherwise healthy people. Consequently the drugs should under no circumstances be used in the treatment of AIDS. The other group felt there was incontrovertible evidence from well-conducted randomised clinical trials that anti-retroviral drugs were of substantial clinical value when used in correct dosages and under carefully monitored conditions. The latter group presented varying opinions on which drugs to use, and how and when to use them.

5.2 Evidence in support of the use of anti-retroviral drugs

Proponents for the use of anti-retroviral drugs produced evidence that these drugs improve the quality of life of HIV-infected people. There was reference to clinical experience proving this effect.

Some of the panellists quoted examples from clinics in the USA, where previously people died of AIDS-related infections, whereas now no deaths are being recorded and people are living longer since the introduction of anti-retroviral medications.

There was evidence from a number of areas, for example, Prof Montagnier quoted a decline in death rates from 72 patient years lost per 100 patient to 2.92 patient years since 1990 following the use of three anti-retroviral drugs. His slide, however, also showed that patients not receiving any anti-retrovirals had also improved with a current mortality of 50 per 100 patient years, presumably due to the use of supportive therapies such as multivitamins, nutritional supplements and psychological support. It was also notable that improvements in mortality are never quoted as average increase in life expectancy per patient, but rather as cumulative 'patient years saved'; and there are of course no control groups to measure such presumed increases in life expectancy against. Prof Montagnier also referred to hospitals in France that had closed down due to lack of patients. However, he conceded that these drugs are toxic and cannot be used without proper monitoring. Dr Sonnabend confirmed the efficacy of these drugs in his own experience of treating patients at his clinic.

Dr Vella, who explained that new techniques in drug development have led to the development of less toxic drugs, provided further evidence of efficacy. He also argued that the decline in AIDS-related deaths was certainly due to the drugs, because there was no decline in new infections.

Dr Lane highlighted the fact that there cannot be a blanket approach to the administration of these drugs, and that it was necessary to categorise the treatment groups according to the stage that the disease had reached. What may work for one group may, in fact, be toxic to another. With patients in the very early stages of the disease, who show no evidence of significant immunological compromise, giving them anti-retroviral drugs may, in fact, be the wrong thing to do.

Claims were made that there are no hard data to confirm that there are gains in terms of survival with the use of anti-retroviral drug therapy, because many other factors impact on outcome. Such factors include compliance, whether the choice of anti-retroviral drug therapy was correct in the first place, issues around the development of resistance, as well as prior use of anti-retroviral drugs.

In developing countries, where issues of costs are significant, the choice of drugs may be dictated by what is affordable. Strategies in this regard may include negotiating for price reductions, parallel importation, local manufacturing and the use of generics.

5.3 Evidence against the use of anti-retroviral drugs

Panellists opposed to the use of anti-retroviral drugs asserted that the evidence in favour of their use comprised only anecdotal claims of benefits, and no real scientific data. They requested that any recommendation to provide anti-retroviral drugs to South Africans must be accompanied by scientific evidence.

On the contrary, Dr Rasnick presented a case against the use of anti-retroviral drugs based on their toxicity and scientific references that questioned the merits of prescribing these drugs. Statements from published articles by, *inter alia*, Jay Levy,⁹ Phillips and Smith,¹⁰ and Abrams¹¹ were presented which included the following:

- "These drugs can be toxic and can be directly detrimental to a natural immune response to HIV...This effective antiviral immune response is characteristic of long-term survivors who...have not been on any therapy. ...[T]he current antiviral therapies...do not bring about the results achieved by a natural host anti-HIV response. This immune response, observed in long-term survivors, maintains control of HIV replication without the need for antiviral therapy."

⁹ Jay Levy. 1996. *JAMA*. **276**:161-162

Jay Levy. 1998. *Lancet*.I **352**: 982-983

¹⁰ Phillips and Smith. 1997. *NEJM*. **13**: 958-959

¹¹ Abrams.1996. *Synapse*. **4**: 1-5

- "I have a large population of people who have chosen not to take any anti-retrovirals...They've watched all their friends go on the antiviral bandwagon and die, so they chose to remain naïve [to therapy]. More and more, however, are now succumbing to pressure that protease inhibitors are 'it'...We are in the middle of the honeymoon period, and whether or not this is going to be an enduring marriage is unclear to me at this time..."
- "No randomised trials in asymptomatic patients have established that those treated early survive any longer than those for whom treatment is deferred. Extended follow-up of patients in one trial, the Concorde study, has shown a significantly increased risk of death among the patients treated early. The suggestion is that the situation is different for combination therapy. But where is the evidence...?"
- "There is no more hard evidence now of the benefits of early therapy than there was in 1990. We need new randomised trials to determine whether the notion that was probably not true in the era of [AZT] monotherapy – that early therapy prolongs survival as compared with deferred therapy – is now true."

The director of the National Institute of Allergy and Infectious Diseases (NIAID) Dr Anthony Fauci was quoted as saying: "There is an increasing percentage of people in whom, after a period of time, the virus breaks through, people do quite well for six months, eight months or a year, and after a while, in a significant proportion, the virus starts to come back."

It was also highlighted that the label on AZT bottle produced by Sigma reads: "Toxic. Toxic by inhalation, in contact with skin and if swallowed. Target organs, blood, and bone marrow. Wear suitable protective clothing."

Furthermore, it was mentioned that there was considerable evidence to support its toxic effects on other organs. Researchers have documented that persons on protease inhibitors develop abnormal fat accumulations called buffalo humps. As time passes, more and more metabolic and endocrine disturbances are described in such individuals, including hypertrophy of the breasts, increase in blood sugar, cholesterol and triglycerides, pancreatitis and angina. Protease inhibitors can also induce the development of AIDS-defining diseases, such as mycobacterium infections.

It was also argued that the drugs themselves caused AIDS, since they act on cells that are either metabolically active or in constant division. A characteristic feature of immune cells is that they have to divide during the immune response, making them much more vulnerable to the action of these drugs.

The well-documented Concorde study showed that AZT was unable to prevent progression to full-blown AIDS in asymptomatic HIV-positive patients; and that, instead, mortality was increased by 25% in the treatment group, compared to the controls. The possibility that AZT may actually contribute to the pathogenesis of AIDS is real. Dr Koehnlein also cited the Darby study that was published in *Nature* (1995) which showed a sudden ten-fold increase in mortality of HIV-positive haemophiliacs who had been given the then recommended dose of 1500 milligrams of AZT. Other studies were cited which showed that AZT users experienced more rapid depletion of CD4 cells.

The use of AZT for pregnant women has been shown to cause congenital malformations such as cavities in the chest, abnormal indentations at the base of the spine, heart defects, extra digits and many other abnormalities.

Dr Giraldo concluded by stating that enough data exist to demonstrate that it is not rational to treat or prevent AIDS with toxic anti-retroviral drugs. It is contrary to common sense to treat a highly toxic syndrome with even more toxicity.

5.4 Recommendations on treatment with anti-retroviral drug

5.4.1 Recommendations on the use of anti-retroviral drugs from the group opposed to their use

The recommendations on the treatment of AIDS from panellists who refute that HIV has a causal link to AIDS were informed by their observation that the definition of AIDS in western countries was different from that used in Africa. These definitions have changed over time to the point where a person diagnosed with AIDS in Africa would not be considered an AIDS patient in the USA, Europe and Australia. There was also the critical question of whether Africans clinically diagnosed with AIDS were in fact HIV-positive. These considerations led to the following assertions:

- AIDS is not contagious, although many of the opportunistic infections are
- AIDS is not sexually transmitted
- AIDS is not caused by HIV
- The admittedly toxic anti-HIV drugs are killing people
- The drug-induced toxic effects cause AIDS-defining conditions that cannot be distinguished from AIDS

These considerations led to the following recommendations on treatment of AIDS:

1. The South African government should devote the bulk of national and international biomedical and other resources to the eradication of prominent AIDS defining diseases such as malaria, TB and enteric infections and also to the improvement of nutrition and the provision of improved sanitation and clean water.
2. Anti-retroviral drugs and any other immune suppressive drugs should under no circumstances be used to treat AIDS patients or any other patients that are immune-compromised. These drugs inevitably require significant amounts of compensatory medications and are claimed to produce, at best, only short-term benefits in seriously sick patients.

5.4.2 Recommendations from the proponents of anti-retroviral drug use

Given the demonstrated benefits of anti-retroviral drugs in the treatment of HIV/AIDS, the usage of that accumulated knowledge to the benefit of South Africans living with HIV infection was critical. However, given the fact that there is relatively little relevance of the recommendations on the use of anti-retroviral drugs in the USA and Europe for a developing country like South Africa, there is a need for more locally derived evidence based on strategies that are based on locally relevant research. This research will enable the identification of manifestations of HIV infection and of cofactors as well as the definition of local standards for the diagnosis of the conditions and the description of the local epidemiology. There is also a need for South Africa to collaborate with other countries and international organisations that are addressing the issue of how anti-retroviral drugs use is or should be different in a South African type setting. The development of these strategies would need to address the following specific issues:

1. In whom should these drugs be used. Secondary to this question are the following issues:
 - how should these drugs be used
 - at what stage of infection should the drugs be used
 - how should the use of these drugs be affected by the different recipient populations such as adults, children, pregnant women, etc
 - how might the use of these drugs be influenced by the ongoing transmission that is likely in different populations
 - issues related to use in post-exposure prophylaxis, whether in healthcare settings or after rape
2. The choice of the anti-retroviral drug or drugs that might be used, their dosing and the scheduling of the dosing as well as the cost and effectiveness
3. How might the effectiveness of the chosen drugs be affected by concomitant use of traditional medicines?

The issues listed above generated a number of considerations which informed the recommendations that were made on treatment. These considerations are as follows:

- (a) Protocols need to be developed according to what is affordable and sustainable.
- (b) Protocols will also be decided by the resistance profile in the community. This may necessitate expensive tests for resistance, which may not be cost-effective.

- (c) Under the most ideal circumstances, a combination of drugs is best. This combination should comprise two protease inhibitors and a reverse transcriptase.
- (d) Decisions on when to start anti-retroviral treatment may be difficult and must be based on the onset of symptoms. There is a move away from the early introduction of anti-retroviral medication.
- (e) Starting treatment too early increases costs and may also undermine compliance. The development of resistance limits the number of combinations that may be effective.
- (f) There is the possibility that patients may present late when they have opportunistic infections. The recommendation in this regard is to deal effectively with the opportunistic infections before instituting therapy with anti-retroviral drugs.
- (g) Prior to commencing treatment, it is important to undertake a baseline assessment of CD4 and viral load.
- (h) Finally, there seems to be a need to have guidelines on the use of anti-retroviral drugs, which must be updated regularly as new developments emerge.

Recommendations:

1. A constantly evolving set of guidelines needs to be developed for the treatment, care and support of patients with HIV and AIDS. These guidelines need to address patients at all levels of care, including those in institutions and under community-based care, and include the following:
 - Diagnosis, initial evaluation and long-term management
 - Prophylaxis and management of opportunistic infections
 - Psychological support and end-of-life care
 - Anti-retroviral therapy
2. Infrastructure needs to be developed for the purpose of :
 - Provision of medication, monitoring of usage of anti-retroviral drugs and of clinical outcomes, including drug toxicity
 - Education and training of healthcare workers
 - Counselling and support of patients

- Establishment of a panel for the development of guidelines and continuing review of new data, clinical outcomes and uses of medication. This panel should include local experts, health officials and persons with HIV and AIDS.
3. Ongoing programmes for the control of sexually transmitted diseases and tuberculosis should be linked to initiatives outlined above
 4. There remains a series of unanswered questions of relevance to the treatment of HIV and AIDS in South Africa which must be addressed through direct clinical research

The Strategic Plan (2000–2005) developed by the South African government to combat HIV, AIDS and sexually transmitted diseases was considered a good start to addressing some of the recommendations made here.

CHAPTER 6: PREVENTIVE AND PROPHYLACTIC MEASURES AGAINST AIDS

The basic tenets for the prevention of any disease have to be based on a good understanding of the aetiology as well as the natural progression of that disease. Chapter 2 of this report reflected the split of the panel into two factions around the aetiology of AIDS. The diametrically opposing views on the causal link between HIV and AIDS made the deliberations on prevention strategies extremely challenging. This split on aetiology produced the unavoidable consequence that the deliberations on the prevention of AIDS necessarily had to take place in two parallel streams. Some proponents of HIV as the primary cause of AIDS declared their disinterest in discussing preventive strategies with panellists who did not believe that HIV causes AIDS. Similarly, panellists who do not support the causal link between HIV and AIDS argued that prevention strategies based on this assumption were doomed to fail. The report will therefore present two sets of recommendations in order to capture the arguments accurately.

In support of the view that the severe immune deficiency that is currently observed in Africa was due to exposure to toxins and a variety of stressors of a chemical, biological, and sometimes physical nature, Dr Giraldo emphasised that prevention should focus on these stressors and not on an innocent virus. He expressed scepticism about the prevention strategies recommended by the CDC since these had been published even before Prof Montagnier had isolated the virus. Prof Montaigner countered this line of argument by highlighting the fact that these recommendations were based on epidemiological evidence of how transmission occurred. This approach was scientifically acceptable and was the basis for interventions for many other diseases.

Pursuing the argument for a toxicological basis for AIDS, Dr Duesberg argued that despite propaganda generated from the west on what the real cause of AIDS is, there was enough evidence that the epidemic was concentrated on specific groups of people who had in common malnutrition, poor sanitation and constant exposure to environmental toxins.

Dr Giraldo recommended that the first point of entry for prevention was to stop the media-generated hysteria on AIDS. He argued that this hysteria and fear contributed to suppression of the immune system of people who were told that they are HIV-positive on the basis of unreliable tests and were doomed to die. The recommendations, he suggested, should focus on:

- limiting exposure of people to toxins
- improving the physical conditions under which people live
- encouraging the involvement of traditional healers and other forms of healing in the process.

For those whose immune system had been compromised already, it was important to detoxify their bodies using naturally occurring anti-oxidants such as vitamins A, C, E, glutathione and others. The use of immune-boosters to stimulate the immune system was also recommended.

In a passionate presentation, Dr Giraldo submitted that the focus on HIV was distracting leaders in the developing world from focussing on the real causes of AIDS – such as poverty, malnutrition and poor sanitation. He argued that the developed world was forcing African governments to focus on the use of anti-retroviral drugs, which did nothing more than compound the problem. He urged the South African government to resist the violation of its integrity by the international community and to continue its quest for African solutions to this problem.

Dr Bertozzi shared his experiences on his work on the epidemiology of the disease in Africa. He shared his experiences from several countries in Africa, arguing that although there were gaps in the knowledge on the epidemiology of this epidemic, there were clear transmission patterns and groups, and people at risk could be identified even on the basis of such limited knowledge. His experience had convinced him that sub-Saharan Africa is 'on fire' due to this epidemic. The nature of the problem was so urgent that emphasis had to be placed on what could be done now to halt the spread of this epidemic. To Dr Bertozzi South Africa was like “a building that is burning and our first focus needs to be on getting people out of the building and putting out the fire. We will have time over the decades to come to debate the mechanisms of how the fire was started...”

In support of this view, Mr Scondras argued that historically public health had benefited very little from arguments on aetiology but more benefit had been derived from the application of proven therapeutic and prevention techniques *vis-à-vis* any illness. Emphasis should therefore be placed on the wide-scale implementation of effective interventions in a controlled and sustainable manner.

There was consensus that whilst the search for scientific solutions was being pursued, everything should be done to slow the spread of the disease and to mitigate its impact.

6.1 Prevention of AIDS from the point of view of panellists who do not support the causal link between HIV and AIDS

Sections 2.3 and 2.4 of this report captured the submissions on the causes of AIDS from the point of view of those panellists who do not subscribe to the notion that HIV causes AIDS.

6.1.1 Recommendations

The recommendations listed below were proposed as necessary and sufficient to combat all the risk factors that are the real cause of AIDS:

- Improving sanitation and public health measures to decrease water-borne diseases.
- Strengthening health infrastructure.

- Reduction of poverty and improving general nutrition and implementing nutritional education and supplements for the general population.
- Improving screening for and treatment of sexually transmitted diseases.
- Promoting sex education based on the premise that many sexually transmitted diseases and pregnancies could be avoided.
- Implementing public education campaigns to destigmatise AIDS and reduce public hysteria surrounding the disease.
- Investigating the use of immune-boosting medication, such as interferons, growth factors, B-complex vitamins and herbs (such as ginseng, Chinese cucumber, curcumin, aloe vera, garlic and echinacea).
- Encouraging the detoxification of the body through several inexpensive interventions, such as massage therapy, music therapy, yoga, spiritual care, homeopathy, Indian ayurvedic medicine, light therapy and many other methods.
- Treating infections vigorously and timeously.
- Increased support for and promotion of research into the development of drugs against AIDS, its cofactors and risk factors.
- Encouraging the involvement of complementary medical and health practitioners, including indigenous healers, in research and clinical fields.
- Implementing aggressive programmes to empower women and change the power relations between men and women.
- Reducing the vulnerability of communities by improving access to health care.
- Improving literacy.

6.2 Prevention of AIDS from the point of view of panellists who support the causal link of HIV to AIDS

Panellists who support the causal link of HIV to AIDS proposed that preventive strategies be linked more specifically to the different modes of transmission of HIV/AIDS. These panellists did, however, also support some of the more general medical and public health interventions listed in section 6.1.1 above as critical to ensuring a healthy society.

Three specific modes of transmission of HIV/AIDS were identified in Chapter 2 of this report as follows:

- Sexual transmission.
- Blood-borne/occupational transmission.
- Mother-to-child transmission during pregnancy, at the time of delivery and during breastfeeding.

6.2.1 General recommendations

- Other strategies need to be put in place to address the social environment, promote safer sexual practices and provide a supportive environment for people who are infected.
- Establish and support programmes that minimise the spread of disease through the migrant labour system

6.2.2 Recommendations on prevention of HIV/AIDS through sexual transmission

- A stronger emphasis should be placed on sex education.
- Improving public awareness and the use of safer sex practices, including condom use, in order to interrupt the transmission of sexually transmitted diseases.
- Improving blood screening for sexually transmitted diseases and other infectious diseases.
- Improving screening for and treatment of sexually transmitted diseases.
- Campaigns should be mounted to encourage the youth to delay their sexual debut.
- Sexually transmitted infections should be treated comprehensively.
- Regulation of commercial sex work.
- Strategies should be devised and implemented to address gender inequality.
- Reduction in the number of sexual partners.
- There was a need to continue research on finding appropriate microbicides for prevention of sexual transmission.

Dr Fiala suggested that although he did not support the view of the sexual transmission of HIV, the above recommendations did make sense as long as the focus was on a broader approach to healthy sexual habits which encompass prevention of unwanted pregnancy, rather than a single focus on HIV.

6.2.3 Recommendations on prevention of blood-borne transmission of HIV/AIDS

- Improving screening methods for infectious agents in blood.
- Education campaigns for the community in order to identify potentially safe donors.
- Training of medical practitioners on the rational use of blood and blood products.
- Strict adherence to universal precautions by healthcare providers at all times.

6.2.4 Recommendations on prevention of mother-to-child transmission of HIV

Panellists who believe that infants can be infected during pregnancy and delivery and through breast-feeding provided several recommendations on preventing these forms of transmission from mother to infant.

6.2.4.1 General

- Supportive and effective reproductive health services must be provided to all women.

6.2.4.2 Education

- Healthcare providers must inform women about the risks of being infected with HIV. They must educate women that infection occurs through sexual exposure, and that abstinence, mutual monogamy and consistent condom use are the only preventive methods known. (This, according to Dr Fiala, was futile, as 2000 years of such messages from the Catholic Church do not seem to have had much success.)
- Healthcare providers must be trained in proper counselling skills so that they can effectively counsel clients.
- Women must be educated about dual protection, namely use of a condom and, in the event of failure, recourse to emergency contraception.
- All women of child bearing age, and pregnant women in particular, must have access to voluntary counselling and HIV testing. Rapid tests must be used in this context so that women can make decisions about their health and access the care they need during their pregnancy. As far as possible, couple counselling must be encouraged in order to expand access to care to the family and to ensure psychological and emotional support for the woman.

6.2.4.3 Breastfeeding

- Where feasible, HIV-positive mothers should not breastfeed their babies.
- When breast milk is the only option for infant feeding, women should be encouraged to breastfeed exclusively and to wean the baby early.

Dr Stein cautioned that the recommendations on breastfeeding had to be done in such a way that the long-established benefits of breastfeeding for other women are not undermined.

6.2.4.4 The use of anti-retroviral drugs

Evidence of the efficacy of anti-retroviral drugs is obtained from randomised-controlled trials as well as systemic reviews.

(a) Zidovudine (AZT) – Efficacy and toxicity

The efficacy of AZT in preventing vertical transmission of HIV has been sufficiently demonstrated in several randomised-controlled trials. The reduction in the risk of transmission varies from 37% to 67% in the different studies.

No serious side effects in pregnancy were detected in the above studies and in the infants born to these mothers followed up to the age of four years. There is enough evidence to show that the benefits outweigh the risks, and it is recommended that this drug be provided to women in pregnancy where resources are available to do so.

(b) Nevirapine – Efficacy and toxicity

The HIVNET 012 trial, a randomised-controlled trial comparing Nevirapine and AZT, was conducted in Uganda. Nevirapine use resulted in a decrease in vertical transmission of 48% (95% CI 17 to 60%). The regime is easy and cheap to administer.

Concerns have been raised over the development of resistance in women who have been exposed to a single dose of Nevirapine. Further research on the implications of this resistance is necessary.

There are concerns regarding the impact of breast-feeding on the transmission of HIV. Follow-up studies on mother–infant pairs where anti-retroviral drugs have been used show a reversal of efficacy when breast-feeding continues beyond six months. More research in this area is warranted. In the interim, the best feeding advice would be formula feeding for those who can afford it and exclusive breast-feeding with early weaning when women cannot afford to purchase formula.

(c) Combination anti-retroviral use for MTCT prevention

Good evidence has been presented from the PETRA trial. This randomised trial assessed the combination of AZT and Lamivudine (3TC). This regimen resulted in a 48% risk reduction of HIV transmission.

6.2.4.5 Caesarean section in preventing HIV-1 vertical transmission

The role of caesarean section has been tested in a recent randomised-controlled trial (RCT). This demonstrated an 87% reduction in vertical transmission in the group randomised to caesarean section. In a further analysis of this subgroup, which focused on women who had had prior exposure to AZT, the effect of caesarean section became less dramatic.

This intervention however, cannot be recommended as policy in South Africa for several reasons:

- There are staff constraints in terms of obstetrics anaesthesia, availability of blood products and antibiotics.
- The incidence of infectious morbidity may be higher in our population due to a higher rate of genital tract infections.
- In the absence of anti-retroviral drugs, 29 caesarean sections would have to be done to prevent one case of HIV-1 vertical transmission.

6.2.4.6 Vaginal lavage during labour

The evidence from a RCT indicates that vaginal lavage is only of value if the labour is longer than four hours in duration. Reasonable guidelines would include not rupturing membranes in active labour unless there is an obstetric or foetal indication. Invasive monitoring techniques are not recommended. Routine performance of an episiotomy is also contraindicated.

6.3 Prophylaxis against opportunistic infections

6.3.1 Introduction

Dr Sonnabend pointed out that the control of AIDS infections should not be seen in isolation from other morbidity factors that exist in society, but should be considered in the context of broader social conditions. There is a need to improve overall public health measures in order to improve the health of the population in general. The control of endemic diseases such as TB, malaria, helminthic infections and diarrhoeal diseases and the general provision of clean water have a major impact on the reduction of morbidity and on the spread of the AIDS epidemic in the population. Although HIV infection is diagnosed by antibody tests, other very important baseline tests need to be conducted to provide an indication of the presence of other infections, namely, the Skin test for TB, as well as tests for syphilis,

toxoplasmosis and hepatitis A, B and C. For female patients, tests for chlamydia, gonorrhoea and varicella are important.

After a diagnosis of HIV infection, it is necessary to determine the risk for opportunistic infections. Patients with a declining CD4 are more susceptible to opportunistic infections and therefore prophylactic treatment becomes more appropriate with declining CD4 counts. Drugs such as Bactrim (cotrimoxazole) to prevent general bacterial infections and Isoniazid (INH) for tuberculosis are inexpensive and affordable for prophylaxis.

Dr Sonnabend presented a convincing case for prophylactic therapies for the treatment of opportunistic infections rather than treating the so-called surrogate markers.

The most important step is to determine the common causes of mortality in AIDS and determine the most appropriate prophylactic intervention strategy or drugs. For example, if much of the AIDS mortality is due to TB, a prophylactic regimen for tuberculosis, such as INH, will be the most suitable intervention strategy.

Generally, the earlier the treatment is started, the better the chance of preventing and managing opportunistic infections. There are two types of prophylaxis, namely:

1. Primary prophylaxis is the instigation of prophylaxis before a patient has actually contracted any opportunistic infection.
2. Secondary prophylaxis is the treatment given after at least one experience of an opportunistic infection that is usually lifelong.

The most common opportunistic infections are cryptococcal meningitis, TB, bacterial, yeast and parasitic infections, *Pneumocystis carinii*, as well as cervical cancer associated with the human papilloma virus.

6.3.2 Opportunistic infections

A frequent question is how early prophylactic therapy against opportunistic infection should be initiated after HIV infection/diagnosis. Work done in the Ivory Coast suggests that early intervention for opportunistic infections with co-trimoxazole is beneficial and effective. Where facilities exist for conducting a CD4 cell count, an additional guideline is that anyone with a CD4 cell count of less than 500 should be given prophylactic treatment.

INH is the most effective prophylactic drug against TB, but care should be taken to monitor any emergence of resistance against INH. The recommendation for the prophylactic treatment of TB should only be considered, however, where there are facilities for counselling, testing for and excluding active TB infections. Moreover, it is recommended that INH prophylaxis be considered only in countries with a well-established TB control programme, without which INH prophylaxis might lead to further resistance to TB. The recommendation thus needs to be adapted to country specificities.

Bactrim is the most generally used prophylactic drug against many bacterial infections. It is an inexpensive drug that many developing countries can afford.

There is some debate around whether one should institute primary prophylaxis for cryptococcal infections. If it is instigated, the drug of choice is Fluconazole. A concern is the possible development of resistance to the drug, which would reduce its usefulness when needed in the future treatment of the patient.

For cytomegalovirus (CMV) disease, the drug of choice for prophylaxis is Ganciclovir, which is useful for patients with CD4 counts lower than 50. However, this drug is expensive and is beyond the means of many patients.

For prophylactic therapy against mycobacterium avium, the drugs of choice are Perithromycin and Rifobutin.

CHAPTER 7 – Socio-economic factors in the context of HIV/AIDS

Socio-economic factors that enhance the spread of AIDS were not discussed extensively in the two meetings of the Presidential Aids Advisory Panel. They formed part of discussions on other issues and were used as contributing factors or otherwise in defending the various theories. Prof Abdool-Karim made it very clear on several occasions that in South Africa, "it is not enough to educate, it is not enough to inform, it is also necessary to create the social environment to implement health promotion in its broadest context". What is needed is the training of healthcare workers in implementing solutions to the needs.

The socio-economic factors that are related to the spread of HIV/AIDS include:

7.1 Malnutrition and sanitation

The issues of malnutrition and sanitation were discussed at both meetings. These two factors exacerbate the spread of the disease and hamper recovery, not only among HIV-positive patients but also among those with sexually transmitted diseases.

Prof Duesberg claimed that the epidemic is restricted to a minority that appears to have in common malnutrition and poor sanitation. Dr Giraldo agreed that the immune system of the foetus can be destroyed if the mother is severely malnourished. He went on to say that malnutrition and nutritional and vitamin deficiencies are a risk factor for AIDS. He reiterated that transmission of HIV can be prevented by ensuring that mothers in South Africa have good levels of vitamin A. Dr Gray interjected that she had yet to see a report that a vitamin A-deficient HIV-negative mother gave AIDS to her baby.

Endemic diseases such as TB and bacterial diarrhoea plague South Africa, along with many parts of Africa. The need for public health measures that will improve the health of the population in general will also have an impact on the spread of AIDS.

The panellists were divided as to whether breast-feeding transmits HIV or not. Dr Giraldo argued that "there is no objective evidence for the hypothesis that neither HIV nor AIDS can be transmitted from mother-to-child through breast milk" as these beliefs originate from non-controlled surveys. Even those who believe in the transmission of HIV and AIDS through breast milk, such as Dr Coll-Seck, argued that although it is important to inform HIV-positive women that they can infect their children through breastfeeding, the children are likely to die of malnutrition and disease unless there is clean drinking water and a viable alternative to breastfeeding. Dr Stein suggested that one factor that is important in Soweto, for example, is that clean water is universally available, which makes it safer and more practicable to bottle-feed, and there are often funds available in the family to purchase baby feeding formula.

The solutions offered throughout are to adopt a preventative strategy as a policy that will involve commitment from services and also counselling to women and, ideally, also those close to them.

7.2 Orphans

The issue of children, with or without AIDS, that are orphaned when their parents die of AIDS was not discussed in any significant detail at either meeting. Prof Whiteside quoted Dr Makgoba as saying that South Africa faced an increase in mortality among the people it could least afford to lose, the young people in society, and that the country should not lose sight of the equally important issues that many of those who died were leaving behind orphans. Dr Rasnick requested data to support the claim that AIDS deaths have generated orphans.

7.3 Ethics and human rights

7.3.1 Ethics

Panellists who advocated that HIV/AIDS patients should be given drugs to assist them in recovery argued that it was unethical to deny drugs to HIV/AIDS patient, regardless of which laboratory they come from, as long as the drugs are known to be beneficial. The main concern of the panellists opposed to anti-retroviral therapy was the ethics of administering such drugs if they are not properly tested through a controlled study. Prof Duesberg maintained that there are no studies to show that AZT and other anti-retroviral drugs have been tested on animals and have shown that they benefit the animals, or at least have no side effects. Additionally, there is a solid body of published research that implies that these drugs are indeed harmful, and, according to some, it is therefore unethical to administer drugs whose clinical actions in relation to dosage and time of application are poorly known, or not known at all. Prof Montagnier held that such drugs are toxic and should not be administered without appropriate monitoring, while Dr Vella maintained that, due to new techniques, drugs are now less toxic than previously.

The panellists who disputed that AIDS is caused by HIV declared it unethical for any person who reacted positive to HIV test to be told that they suffer from a deadly disease and face certain death unless they received treatment.

7.3.2 Human rights

Within the South African environment, the most important issues related to a non-discriminatory supportive social environment, according to Dr Bertozzi, include issues related to social conditions, the status of women and other marginalised groups in society, inequality, the alleviation of poverty and human rights.

However, while South Africa is undergoing transformation in terms of human rights, the issue of virginity testing is still prominent in our society. This, according to Prof Mhlongo, is unacceptable and an insult to black South African women.

The AIDS epidemic highlights the dynamics of gender-based inequalities, as shown by an already cited survey in KwaZulu-Natal, which demonstrated far higher levels of HIV infection among women than among men in the age groups 20 to 24 and 25 to 29.

7.4 Sexual behaviour

The only data on sexual behaviour came from an international comparison by Durex to evaluate the commercial potential to sell condoms, which was presented by Dr Fiala. The data showed that Americans and Europeans are in the lead when it comes to the number of sexual partners and that South Africans as well as Thailanders are rather average. Americans and Europeans also have the highest frequency of sexual intercourse.

Seroprevalence studies indicate that more homosexual men and fewer of the general population are diagnosed with HIV in developed countries, while the opposite is true for the African population, especially in East and Central Africa.

Dr Giraldo argued that among male homosexuals the main cause of AIDS is drug abuse.

It was argued that the link between HIV and cofactors might explain why the epidemic in Africa is mainly heterosexual. It might relate directly to the high incidence of sexually transmitted disease and practices such as dry sex.

Age at first sexual encounter is an important risk factor in HIV infection. In many countries in sub-Saharan Africa, girls become sexually active at an earlier age than boys. They also tend to have sex with older men. Data have already been cited on the higher HIV-infection rates among girls than among boys aged between 15 and 19. A further risk factor for young women is that studies have shown that in some societies, initiation into sex often involves coercion, increasing the risk of trauma during intercourse and the potential for HIV transmission.

7.4.1 Rape

Most panellists maintained that addressing gender issues and reducing the risk of rape were very important factors in reducing the spread of HIV. However, Dr Duerr made the point that there are very few data on the efficacy of post-exposure prophylaxis in rape victims. Prof Abdool-Karim recommended that, in the case of rape, the panel should advise the administration of a combination of two anti-retroviral drugs, which would mean a very short course of anti-retroviral therapy. He was, however, opposed to recommending a policy of administering the drugs to everybody that was raped.

7.4.2 Stigmatisation

Stigmatisation of HIV sufferers is very common in South African society, as is the case in other African countries, Asia, Europe or the USA. Changing people's attitudes is not easy.

The reduction of stigma and discrimination should be considered seriously with particular attention to young women and people living with HIV and AIDS. There is a need for legal protection for such people and for more openness on this disease. People living with HIV and AIDS, their families, and 'at risk' groups such as sex workers and migrants are often subject to outright social alienation.

Those panellists who dispute that HIV causes AIDS declared stigmatisation and ostracism of HIV-positive persons as particularly unfortunate.

Protection of the right to confidentiality and freedom from inhuman treatment has been proved to encourage and facilitate people seeking voluntary counselling and testing.

7.4.3 Promiscuity

During the first Presidential AIDS Advisory Panel meeting, it was suggested that the initial spread of AIDS originated with promiscuous, homosexual drug users, from Los Angeles, through the United States, into Europe and various other countries. However, the concern was raised that certain other, possibly toxic factors, had not been taken into consideration with regard to the spread of the AIDS disease.

A puzzling bit of information to some of the panellists was the repeated claims that AIDS has wiped out whole villages in Africa in a matter of weeks or months, whereas nothing like that had ever happened in the USA or anywhere else, even among the most sexually promiscuous society that ever existed – i.e. people that frequented homosexual night-clubs and bath houses in San Francisco, New York and Los Angeles in the 1980s.

Since it seems that most of the people infected with HIV in South Africa are black, any sex theory about the transmission of HIV/AIDS would have to postulate that African people are highly promiscuous. Moreover, Dr Fiala had presented figures that showed that Europeans and Americans are much more highly promiscuous than people in South Africa, or in Africa as a whole (see section 2.5.2).

7.4.4 Condom use

According to the macro international DHS surveys, which are used by a whole range of agencies, condom are used between 60% and 80% of the time in the case of first sexual acts in the USA and Europe, compared to only 14% in South Africa. This shows that people are not adapting their behaviour, despite the fact that there is a high level of knowledge in many South African communities about the nature of AIDS and the fact that it is sexually transmitted. However, Dr Fiala cited contradictory data from the Deutsche Latex Forschung that suggested that condom usage in Germany increased only from 2 to 2.3 condoms per year per capita between 1980 and 1995.

Prof Abdool-Karim suggested that it is necessary to create the social environment to implement health promotion in its broadest sense when one is looking at creating condom use as the normative behaviour – to bring about a change in mindset that it is 'cool' to use a condom.

7.4.5 Issues of economics

Reference was made to a World Bank study that claimed that post-exposure prophylaxis is only likely to be cost-effective where the probability of HIV infection in the course of rape is high. Dr Giraldo, however, claimed that pharmaceutical companies would welcome such an idea, as they would commercialise the production of anti-retroviral drugs, syringes, condoms, formula meals and so on. He criticised the World Bank for promoting international loans to get Africa to purchase AZT and other anti-retroviral drugs and condoms as well as do more HIV testing. This, he claimed is bound to increase poverty in Africa and increase the wealth in the west.

Western Blot tests for the confirmation of HIV infection are not used in South Africa not only because they are indeterminate in their results but also because they are expensive and are not practical for developing countries.

Panellists who advocated of anti-retroviral drug therapy maintain that it is cost-effective in preventing hospitalisation, which is the most expensive aspect of caring for HIV-infected individuals. Studies by Neil Soderland have shown that, if the costs of therapy could be reduced to between 10% and 20% of their current costs, it would bring about a cost saving in the country. This would affect only the cost of the healthcare system, and not costs in terms of the impact of AIDS on the economy, or lost education opportunities, training and skills. These are aspects of the broader impact of the epidemic on the country.

Prof Montagnier suggested that adaptation of the treatment could serve to make it more accessible and affordable.

However, Dr Giraldo suggested that the only rational way to stop the spread of the AIDS epidemic in the African continent is by finding solutions to the economic disparities that are rampant.

7.5 Vaccine development

The main criteria for a vaccine for use in South Africa are that it should be suitable for South African conditions and sub-types of virus, as well as affordable for South Africa, its neighbours and the rest of Africa. Dr Prozesky reminded the meeting that with almost every virus-caused disease, real progress in fighting the disease had only been made with the development of a vaccine, often leading to effective eradication.

7.6 Summary and recommendations

As Dr Sonnabend put it: "It is not simply the cost of drugs. We need a whole lot more. We need the capacity to provide for people and to be able to monitor." Starting treatment too early increases the cost of treatment without being appropriately effective.

Dr Coll-Seck very clearly suggested an efficient system for monitoring and evaluating the following recommendations to ensure that they would be helpful, not only to South Africa but also to the countries and continents in the developing world:

1. Improving the social environment.
2. Reviewing laws (both customary and written) and their implementation to protect the safety of people living with HIV and AIDS and their families.
3. Initiating strategies to negotiate for reductions in the price of drugs, local production and generics.
4. Improving public awareness and use of safer sex practices in order to stop the transmission of HIV and sexually transmitted diseases.
5. Improving sanitation and public health measures.

CHAPTER 8: RECOMMENDATIONS

8.1 Introduction

The purpose of this chapter is merely to group together all the recommendations made in the different chapters of this report.

8.2 Recommendations on surveillance – what should be done about the South African epidemic?

8.2.1 Deliberations of the panel

The deliberations of the panel were at all times bedevilled by the absence of accurate and reliable data and statistics on the magnitude of the AIDS problem or even HIV prevalence in South Africa. Repeated requests for such data and statistics, particularly by panellists who refuted the causal link between HIV and AIDS, failed to result in the provision of such data by either South African panellists or the officials of the Department of Health.

Recommendation

It is therefore strongly recommended that appropriate measures be taken to establish the necessary infrastructure and provide the necessary expertise and resources to collect the data and develop reliable and up-to-date statistics on the magnitude of the AIDS problem and the prevalence of HIV in South Africa. All efforts must be made to ensure AIDS reporting in South Africa is up to the highest standards in the world.

8.2.2 Discussions on mortality data

The discussions around the mortality data presented by Dr Makgoba revealed the necessity for a study to unpack the numbers and gain deeper understanding as to whether the changing mortality profile resulted from AIDS only and/or from factors other than AIDS.

Recommendation

It is recommended that a trans-disciplinary team comprising members from all the relevant branches of science, including social sciences and humanities, other relevant professional spheres and representatives of relevant government departments be constituted to undertake an in-depth study of the mortality trends in South Africa and report on the results of the study to the South African government.

8.2.3 Recommendations from panellists who do not subscribe to the causal linkage between HIV and AIDS

It was recommended that the South African government commit to the following:

- a) Suspend the dissemination of the psychologically destructive and false message that HIV infection is invariably fatal and assist in reducing the 'hysteria' around HIV and AIDS.
- b) Suspend all HIV testing until its relevance is proved especially in the African context, given the evidence of false positive results in a tropical setting and the fact that most assumptions and predictions about AIDS in Africa are based on HIV tests.
- c) Continue to improve social conditions in South Africa.
- d) Continue to decrease poverty.
- e) Continue to control infections and sexually transmitted diseases.
- f) Continue to increase the nutritional status of the population.

8.2.4 Recommendations from panellists who subscribe to HIV as the cause of AIDS

Dr Gayle and Prof Abdool-Karim, representing panellists who endorse the causal link between HIV and AIDS, reinforced the importance of the following initiatives for the South African government:

- a) Continue strengthening the surveillance of risk factors such as the behaviour of youth.
- b) Surveillance of HIV prevalence in antenatal clinics, blood banks and among workers.
- c) Conducting incidence surveys.
- d) AIDS surveillance at health facilities.
- e) Keeping death registers.
- f) Standardisation and evaluation of diagnostic criteria and their completeness for reporting purposes.
- g) Surveillance of antenatal syphilis.

- h) Laboratory reporting
- i) Health facility reporting.

8.2.4.1 Recommendations on surveillance as it pertains to reduction of blood-borne infection

The South African government needed guidance on the following issues:

- a) The most appropriate policies on screening and quality assurance for blood safety.
- b) The most appropriate policy to reduce or prevent needle-stick injury with specific reference to policies on single use needles.
- c) Policies on the management of occupational HIV exposure, including post-exposure prophylaxis. Research on post-exposure prophylaxis needs to be pursued vigorously.
- d) Policies on education and implementation of universal precautions.
- e) Most appropriate education and training related to reduction of risk of HIV and transmission in nosocomial settings and related to surgical operations.
- f) Policies on intravenous drug use.

8.2.4.2 Recommendations on surveillance as it pertains to reduction of HIV from Mother to Child

The South African government needed to pay attention to the following issues:

- a) The most appropriate policy on voluntary HIV testing and counselling of pregnant women.
- b) The best policy for contraception promotion, including targeting HIV-positive women.
- c) The best policy on the use of anti-retroviral drugs to treat pregnant women. There were several research issues that were listed in this regard, including:
 - Investigating the extent of Nevirapine resistance when used to prevent transmission of HIV from mother to child.
 - The role of early weaning and non-exclusive breastfeeding.

- What other mechanisms can be devised to reduce transmission of HIV from mother to child.

8.2.4.3 Recommendations on surveillance as it pertains to sexual transmission of HIV

The following issues require attention:

- (g) The most appropriate policy on safe sex education
- (h) How best to promote the use of condoms
- (i) The best policy on the most appropriate and comprehensive treatment of sexually transmitted diseases
- (j) The most appropriate policy on post-exposure prophylaxis for rape
- (k) Regulation of commercial sex work and gender equity issues
- (l) Research into finding an efficacious and effective microbicide and into the development of a vaccine for therapy and prevention needs to be continued vigorously

8.2.5 General recommendation

There was general consensus on the need for the case definition of AIDS to be standardised for clinical practice in South Africa.

8.3 Recommendations on HIV Testing

8.3.1 Proposed studies and experiments

The key issue that came under focus was the reliability of the ELISA testing in terms of delivering time infection data. As a diagnosis of HIV infection has such a profound effect on a person's life and future, it was considered of utmost importance that the tests are unimpeachably reliable. Since all epidemiological predictions concerning HIV/AIDS in South Africa are based on the results of such tests, their absolute reliability was declared to be of utmost importance.

A major recommendation arising from the two meetings was to apply a series of HIV tests of increasing stringency in order to establish the validity, veracity, rigour, reliability and concordance of ELISA, PCR and viral isolation. **Details on some of these experiments are presented in Chapter 9 of this report.**

The experiment will consist of the following series of steps:

- a) ELISAs as they are currently employed.
- b) The same tests using a pre-absorption protocol to remove cross-reacting antibodies such as those against mycobacteria that some panellists asserted frequently confound ELISA tests.
- c) A variety of nucleic acid based protocols.
- d) The application of the classical gold standard of virus isolation, including electron microscopy.

These tests will be performed on cohorts chosen to represent the full spectrum of the South African population.

8.3.2 Recommendation on future HIV testing

The panellists who refuted the causal linkage between HIV and AIDS recommended the suspension of all HIV testing until its relevance is proved, especially in the African context, given the evidence of false results in a tropical setting and the fact that most assumptions and predictions on AIDS in Africa are based on HIV testing.

8.3.3 General recommendations on testing

- a) The case definition of AIDS to be standardised for clinical practice in South Africa.
- b) Any positive HIV ELISA result to be repeated with at least two additional blood samples before an HIV diagnosis is confirmed in order to improve the reliability and validity of ELISA.
- c) Apply a series of HIV tests of increasing stringency in order to establish the validity, veracity, rigour, reliability and concordance of ELISA, PCR and viral isolation.

8.4 Recommendations on treatment of AIDS with anti-retroviral drug

8.4.1 Recommendations on the use of anti-retroviral drugs for the treatment of AIDS from the panellists opposed the causal link between HIV and AIDS

The recommendations on the treatment of AIDS from panellists who refute that HIV has a causal link to AIDS were informed by their observation that the definition of AIDS in western countries was different from that used in Africa. These definitions have changed over time to the point where a person diagnosed with AIDS in Africa would not be considered an AIDS patient in the USA, Europe and

Australia. There was also the critical question of whether Africans clinically diagnosed with AIDS were in fact HIV-positive. These considerations led to the following assertions:

- AIDS is not contagious, although many of the opportunistic infections are.
- AIDS is not sexually transmitted.
- AIDS is not caused by HIV.
- The admittedly toxic anti-HIV drugs are killing people.
- The drug-induced toxic effects cause AIDS-defining conditions that cannot be distinguished from AIDS.

These considerations led to the following recommendations on the treatment of AIDS:

1. The South African government should devote the bulk of national and international biomedical and other resources to the eradication of prominent AIDS-defining diseases such as malaria, TB and enteric infections and also to the improvement of nutrition and the provision of improved sanitation and clean water.
2. Anti-retroviral drugs and any other immune-suppressive drugs should under no circumstances be used to treat AIDS patients or any other patients that are immune-compromised. These drugs inevitably require significant amounts of compensatory medication and are claimed to produce, at best, only short-term benefits in seriously sick patients.

8.4.2 Recommendations on the treatment of AIDS from the proponents of anti-retroviral drug use

Given the demonstrated benefits of anti-retroviral drugs in the treatment of HIV/AIDS, the usage of that accumulated knowledge to the benefit of South Africans living with HIV infection was critical. However, the fact that there is relatively little relevance of the recommendations on the use of anti-retroviral drugs in the USA and Europe for a developing country like South Africa, there is a need for more locally derived evidence based on strategies derived from locally relevant research. This research will enable the identification of manifestations of HIV infection and of cofactors as well as the definition of local standards for the diagnosis of the conditions, the description of the local epidemiology. There is also a need for South Africa to collaborate with other countries and international organisations that are addressing the issue of how anti-retroviral drugs use is or should be different in a South African type setting. The development of these strategies would need to address the following specific issues:

1. By whom should these drugs be used. Secondary to this question are the following issues:
 - How should these drugs be used.

- At what stage of infection should the drugs be used.
 - How should the use of these drugs be affected by the different recipient populations such as adults, children, pregnant women, etc.
 - How might the use of these drugs be influenced by the ongoing transmission that is likely in different populations.
 - Issues related to use in post-exposure prophylaxis, whether in healthcare settings or after rape.
2. The choice of the anti-retroviral drug or drugs that might be used, their dosage and the scheduling of doses, as well as their cost and effectiveness
 3. How might the effectiveness of the chosen drugs be affected by the concomitant use of traditional medicines

The issues listed above generated a number of considerations that informed the recommendations that were made on treatment. These considerations are as follows:

- Protocols need to be developed according to what is affordable and sustainable.
- Protocols will also be decided by the resistance profile in the community. This may necessitate expensive tests for resistance, which may not be cost-effective.
- Under the most ideal circumstances, a combination of drugs is best. This combination should comprise two protease inhibitors and a reverse transcriptase.
- Decisions on when to start anti-retroviral treatment may be difficult and must be based on the onset of symptoms. There is a move away from the early introduction of anti-retroviral medication.
- Starting treatment too early increases costs and may also undermine compliance. The development of resistance limits the number of combinations that may be effective.
- There is the possibility that patients may present late when they have opportunistic infections. The recommendation in this regard is to deal effectively with the opportunistic infections before instituting therapy with anti-retroviral drugs.
- Prior to commencing treatment, it is important to undertake a baseline assessment of CD4 and viral load.

- Finally, there seems to be a need to have guidelines on the use of anti-retroviral drugs, which must be updated regularly as new developments emerge.

These considerations led to the following recommendations:

1. A constantly evolving set of guidelines needs to be developed for the treatment, care and support of patients with HIV and AIDS. These guidelines need to address patients at all levels of care, including those in institutions and under community-based care, and include the following:
 - Diagnosis, initial evaluation and long-term management.
 - Prophylaxis and management of opportunistic infections.
 - Psychological support and end-of-life care.
 - Anti-retroviral therapy
2. Infrastructure needs to be developed for the purpose of:
 - Provision of medication, monitoring of usage of anti-retroviral drugs and of clinical outcomes, including drug toxicity.
 - Education and training of healthcare workers.
 - Counselling and support of patients.
 - Establishment of a panel for the development of guidelines and continuing review of new data, clinical outcomes and uses of medication. This panel should include local experts, health officials and persons with HIV and AIDS.
3. Ongoing programmes for the control of sexually transmitted diseases and tuberculosis should be linked to initiatives outlined above.
4. There remains a series of unanswered questions of relevance to the treatment of HIV and AIDS in South Africa which must be addressed through direct clinical research.
5. The Strategic Plan (2000–2005) developed by the South African government to combat HIV, AIDS and Sexually Transmitted Diseases was considered a good start to addressing some of the recommendations made here.

8.5 Recommendations on prevention of AIDS

8.5.1 Recommendations on prevention of AIDS from the point of view of panellists who do not support the causal link between HIV and AIDS

The recommendations listed below were proposed as necessary and sufficient to combat all the risk factors that are the real cause of AIDS:

1. Improving sanitation and public health measures to decrease water-borne diseases.
2. Strengthening health infrastructure.
3. Reduction of poverty and improving general nutrition and implementing nutritional education and supplements for the general population.
4. Improving screening for and treatment of sexually transmitted diseases.
5. Promoting sex education based on the premise that many sexually transmitted diseases and pregnancies could be avoided.
6. Implementing public education campaigns to destigmatise AIDS and reduce public hysteria surrounding the disease.
7. Investigating the use of immune-boosting medications, such as interferons, growth factors, B-complex vitamins and herbs (such as ginseng, Chinese cucumber, curcumin, aloe vera, garlic and echinacea).
8. Encouraging the detoxification of the body through several inexpensive interventions, such as massage therapy, music therapy, yoga, spiritual care, homeopathy, Indian ayurvedic medicine, light therapy and many other methods.
9. Treating infections vigorously and timeously.
10. Increased support for and promotion of research into the development of drugs against AIDS, its cofactors and risk factors.
11. Encouraging the involvement of complementary medical and health practitioners, including indigenous healers, in research and clinical fields.
12. Implementing aggressive programmes to empower women and change the power relations between men and women.

13. Reducing the vulnerability of communities by improving access to health care.
14. Improving literacy.

8.5.2 Recommendations on prevention of AIDS from the point of view of panellists who support the causal link of HIV to AIDS

Panellists who support the causal link of HIV to AIDS proposed that preventive strategies be linked more specifically to the different modes of transmission of HIV/AIDS. These panellists did, however, also support some of the more general medical and public health interventions listed in section 6.1.1 above as critical to ensuring a healthy society.

Three specific modes of transmission of HIV/AIDS were identified in Chapter 2 of this report as follows;

- Sexual transmission.
- Blood-borne/occupational transmission
- Mother-to-child transmission during pregnancy, at the time of delivery and during breastfeeding.

8.5.2.1 General recommendations

1. Other strategies need to be put in place to address the social environment, promote safer sexual practices and provide a supportive environment for people who are infected.
2. Establish and support programmes that minimise the spread of disease through the migrant labour system.

8.5.2.2 Recommendations on prevention of HIV/AIDS through sexual transmission

1. A stronger emphasis should be placed on sex education.
2. Improving public awareness and the use of safer sex practices, including condoms use, in order to interrupt the transmission of sexually transmitted diseases.
3. Improving blood screening for sexually transmitted diseases and other infectious diseases.
4. Improving screening for and treatment of sexually transmitted diseases.
5. Campaigns should be mounted to encourage the youth to delay their sexual debut.

6. Sexually transmitted infections should be treated comprehensively.
7. Regulation of commercial sex work.
8. Strategies should be devised and implemented to address gender inequality.
9. Reduction in the number of sexual partners.
10. There was a need to continue research on finding appropriate microbicides for prevention of sexual transmission.

Dr Fiala suggested that although he did not support the view of the sexual transmission of HIV, the above recommendations did make sense as long as the focus was on a broader approach to healthy sexual habits which encompass prevention of unwanted pregnancy, rather than a single focus on HIV.

8.5.2.3 Recommendations on prevention of blood-borne transmission of HIV/AIDS

1. Improving screening methods for infectious agents in blood.
2. Education campaigns for the community in order to identify potentially safe donors.
3. Training of medical practitioners on the rational use of blood and blood products.
4. Strict adherence to universal precautions by healthcare providers at all times.

8.5.2.4 Recommendations on prevention of mother-to-child transmission of HIV

Panellists who believe that infants can be infected during pregnancy and delivery and through breast-feeding provided several recommendations on preventing these forms of transmission from mother to infant.

I. General

- Supportive and effective reproductive health services must be provided to all women.

II. Education

- a) Healthcare providers must inform women about the risks of being infected with HIV. They must educate women that infection occurs through sexual exposure, and that abstinence, mutual monogamy and consistent condom use are the only preventive methods known. (This, according to Dr Fiala, was futile, as 2000 years of such messages from the Catholic Church do not seem to have had much success.)

- b) Healthcare providers must be trained in proper counselling skills so that they effectively counsel clients.
- c) Women must be educated about dual protection, namely use of a condom and, in the event of failure, recourse to emergency contraception.
- d) All women of child bearing age, and pregnant women in particular, must have access to voluntary counselling and HIV testing. Rapid tests must be used in this context so that women can make decisions about their health and access the care they need during their pregnancy. As far as possible, couple counselling must be encouraged in order to expand access to care to the family and to ensure psychological and emotional support for the woman.

III. Breastfeeding

- a) Where feasible, HIV-positive mothers should not breastfeed their babies.
- b) When breast milk is the only option for infant feeding, women should be encouraged to breastfeed exclusively and to wean the baby off early.

Dr Stein cautioned that the recommendations on breastfeeding had to be handled in such a way that the long-established benefits of breastfeeding for other women are not undermined.

IV. The use of anti-retroviral drugs

Evidence of the efficacy of anti-retroviral drugs is obtained from randomised-controlled trials as well as systemic reviews.

a) Zidovudine (AZT) - Efficacy and toxicity

The efficacy of AZT in preventing vertical transmission of HIV has been sufficiently demonstrated in several randomised-controlled trials. The reduction in the risk of transmission varies from 37% to 67% in the different studies.

No serious side effects in pregnancy were detected in the above studies and in the infants born to these mothers followed up to the age of four years. There is enough evidence to show that the benefits outweigh the risks, and it is recommended that this drug be provided to women in pregnancy where resources are available to do so.

b) Nevirapine – Efficacy and toxicity

The HIVNET 012 trial, a randomised-controlled trial comparing Nevirapine and AZT, was conducted in Uganda. Nevirapine use resulted in a decrease in vertical transmission of 48% (95% CI 17 to 60%). The regime is easy and cheap to administer.

Concerns have been raised over the development of resistance in women who have been exposed to a single dose of Nevirapine. Further research on the implications of this resistance is necessary.

There are concerns regarding the impact of breastfeeding on the transmission of HIV. Follow-up studies on mother–infant pairs where anti-retroviral drugs have been used show a reversal of efficacy when breastfeeding continues beyond six months. More research in this area is warranted. In the interim, the best feeding advice would be formula feeding for those who can afford it and exclusive breastfeeding with early weaning when women cannot afford to purchase formula.

c) Combination anti-retroviral use for MTCT prevention

Good evidence has been presented from the PETRA trial. This randomised trial assessed the combination of AZT and Lamivudine (3TC). This regimen resulted in a 48% risk reduction of HIV transmission.

V. Caesarean section in preventing HIV-1 vertical transmission

The role of caesarean section has been tested in a recent randomised controlled trial (RCT). This demonstrated an 87% reduction in vertical transmission in the group randomised to caesarean section. In a further analysis of this subgroup, which focused on women who had had prior exposure to AZT, the effect of caesarean section became less dramatic.

This intervention however, cannot be recommended as policy in South Africa for several reasons:

- There are staff constraints in terms of obstetrics anaesthesia, availability of blood products and antibiotics.
- The incidence of infectious morbidity may be higher in our population due to a higher rate of genital tract infections.
- In the absence of anti-retroviral drugs, 29 caesarean sections would have to be done to prevent one case of HIV-1 vertical transmission.

VI. Vaginal lavage during labour

The evidence from an RCT indicates that vaginal lavage is only of value if the labour is longer than four hours in duration. Reasonable guidelines would include not rupturing membranes in active labour unless there is an obstetric or foetal indication. Invasive monitoring techniques are not recommended. Routine performance of an episiotomy is also contraindicated.

8.6 Recommendations on socio-economic factors that impact on AIDS

As Dr Sonnabend put it: "It is not simply the cost of drugs. We need a whole lot more. We need the capacity to provide for people and to be able to monitor." Dr Coll-Seck strongly recommended an efficient system for monitoring and evaluating the following recommendations to ensure that they would be helpful, not only to South Africa but also to the countries and continents in the developing world:

- a) Improving the social environment.
- b) Reviewing laws (both customary and written) and their implementation to protect the safety of people living with HIV and AIDS and their families.
- c) Initiating strategies to negotiate for reductions in the price of drugs, local production and generics.
- d) Improving public awareness and use of safer sex practices in order to stop the transmission of HIV and sexually transmitted diseases.
- e) Improving sanitation and public health measures.

CHAPTER 9: PROPOSED RESEARCH PROJECTS AND STUDIES

9.1 General recommendations on research

1. To undertake a series of immediately doable laboratory, epidemiological and mortality studies on the South African AIDS epidemic to gain better insight into the link between HIV infection and the development of AIDS.
2. Undertake further studies in South Africa on the virus, to look at the natural history; the rate of disease progression in HIV infected people; the effect of the co-factors in viral loads.
3. Design questions in research that would seek to understand behaviour within the cultural and the ethnic context.
4. Research into general anti-AIDS drugs that attack both HIV and the cofactors.

The following research projects and studies were proposed by indicated panelists during the period following the panel meetings.

The proposals that follow (proposals 1,2 and 3) have been put forward by the group that was set up by the Presidential AIDS Advisory panel during their meeting in South Africa in May 2000. The members of the group are Drs H Bialy, P Duesberg, H Gayle and MW Makgoba.

9.2 Proposal 1: Quality assessment of HIV testing: Establishing a Baseline and validating HIV ELISA testing in South Africa.

9.2.1 Rationale

The basic idea in the validation of HIV ELISA Testing in South Africa is to proceed in stages, graded in order of simplicity, and designed so that the results of each stage will determine what, if any, form the next stage will take. This study is based on the fact that:

- A virus named Human Immunodeficiency Virus (HIV) has been isolated
- The validity and quality assessment of HIV testing is critical for accurate estimates, diagnosis, monitoring and surveillance (mostly for epidemiological data) of the HIV/AIDS epidemic

9.2.2 Establishing a Baseline: Quality Assessment of HIV Testing of five independent sites in South Africa

A random and blinded Quality Assessment study of 2500 samples from different sites will be undertaken. The sites are:

- National Institute of Virology
- Blood Transfusion Service
- South African Institute of Medical research
- Department of Virology, University of Stellenbosch

These sites cover the spectrum of high risk and low risk groups as well as high prevalence and low prevalence samples.

The samples will be subjected to time-tested protocols for quality assurance in South Africa and at the Centers for Disease Control in the USA. The correlation between the results in South Africa and the Centers for Disease Control will be analysed to provide the following:

- Assist in establishing such baseline parameters as the level of false positives, sensitivity and specificity
- Confidence in the validity and accuracy of HIV ELISA Testing done in South Africa

These data should also form the basis of subsequent studies as proposed below in the PreadSORption and Virus isolation experiments.

Time table for the study:

- Randomised and coded sample collection was completed in December 2000
- Testing is already in progress and results will be obtained shortly

Costs: The MRC and the CDC will cover the costs of shipping and testing, respectively which will add up to US\$75 000.00.

9.3 Proposal 2: Determination of the robustness of the current HIV ELISA tests that are being used in South Africa.

9.3.1 Purpose of experiment

To determine the robustness of the current HIV ELISA tests that are being used in South Africa when the sera that is being tested has been treated to remove antibodies that are reactive to a series of known antigens that have been previously reported to interfere under certain conditions with HIV ELISA tests that depend on either recombinant proteins, or recombinant proteins and synthetic peptides such as V3.

9.3.2 Methodology

Blood samples from 100 TB patients that have had no prior HIV serology will be obtained by Professor Mhlongo. An additional 100 blood samples from "HIV/AIDS" patients from the most densely affected region in the country will be obtained by Dr Makgoba.

These blood samples will be taken to the major laboratory in South Africa that does HIV ELISA testing, where Drs Makgoba and Roberto Stock (an investigator from the Institute of Biotechnology in Mexico, an expert on immunodiagnostics of all varieties and protein purification and biochemistry), along with South African colleagues of the panel's choosing (scientists, students, technicians) will have prepared a series of ELISA plates that have been coated to contain:

- a. Antigenic preparations from the most common strains of Mycobacteria in South Africa. If such preparations (we require about 500 micrograms of each) are not available, a detailed protocol is available for their preparation.¹²
- b. A BCG preparation (commercially available).
- c. HTLV-I and HTLV-II antigens (also commercially available).
- d. Antigenic preparations from common parasitic infective agents in the parts of SA that are heavily HIV/AIDS infected and from which your samples are drawn.
- e. Antigenic preparations from the most common (non-TB) bacterial and viral infections in these populations. (Sufficient quantities of d and e are available either through WHO/TDR or commercially.)

¹² Escobar-Gutierrez *et al.* 1996. *International Journal of Leprosy*, **64**:417-427

Sera from each of the 200 samples will be added to the ELISA wells of these plates and incubated for two hours, after which the contents of the wells will be transferred to HIV ELISA plates and treated as is normally done. Everything will be done in duplicate.

9.4 Proposal 3: Molecular beacons

South African HIV researchers need to be assisted to gain even greater awareness of the power and usefulness of the beacon technology as a general diagnostic tool, but particularly with reference to Multiple Drug Resistant Tuberculosis. It is not being proposed that the beacon assay be used as any form of gold standard.

The first proposed step is to set up and calibrate the ABI Prism Machine as well as teach South African researchers how to operate the machine and how to synthesise, purify and use molecular beacons. Once this is done, decisions will then be taken as to what degree and how the use of the beacon technology on the samples collected for the Quality Assessment of HIV Testing (as in Proposal 1 above) would be productive.

The proposals that follow were suggested by members of the Presidential AIDS Advisory Panel either during the panel meetings in May and July 2000 or during the Internet debate between the two meetings.

9.5 Proposal 4: Do most people with HIV infection show signs of AIDS within five (5) to ten (10) years?

Proposer: Prof Peter Duesberg

One Thousand and Five Hundred (1500) healthy HIV-positive and 1500 matched healthy HIV-negative men from the South African army and/or mining industry, or some other governmental institution would be required for this study. This experiment will exclude people who suffer poverty, malnutrition, poor sanitation. Since the time of infection of these men is not known, and since they are currently healthy, their times to AIDS would be randomly distributed from a maximum of 5-10 years to a minimum of one day to AIDS. On average they are half way into their HIV to AIDS latent period of 5-10 years, or 750-1500 days (1/2 of 5-10 years) from getting AIDS. Therefore in the HIV positive group there should be 1 or 2 AIDS cases per day, and in the negative group there should be no AIDS cases. We would know much of the answer in a few months and certainly within a year if we had 1500 men in each group. It would take longer if the groups are smaller. The cost would be one conventional HIV test per person, and perhaps a second one if a AIDS disease co occur and a phone call per person or to their supervisor every 2 months to find out how they are.

9.6 Proposal 5: PreadSORption and Virus Isolation Experiments - The need for a Gold Standard in the diagnosis of HIV infection.

The proposal on the preadsorption studies has strong similarities with proposal 2 above, but is included in this document as it appears as a package with the proposed experiments on virus isolation.

9.6.1 Importance of the Proposed HIV Experiments

At present, all the HIV experts admit that:

- Agents other than HIV can cause decrease in T4-cells (Acquired Immune Deficiency, AID).
- The diseases, which are said to indicate AIDS (the syndrome, that is, the "S" in AIDS, can manifest in the absence of HIV infection.

Since the late 1970s, all the HIV experts claim that:

- The main cause of AID is a new agent, HIV.
- AID leads to the appearance of S, the syndrome.
- Any patient who has AIDS and is infected with HIV, the cause of AIDS in that patient is defined to be HIV.

This means that once the existence of HIV is accepted, it is not possible to refute the HIV theory of AIDS by claiming that:

- HIV does not fulfil the Koch postulates.
- HIV does not fulfil the Farr law.
- AIDS is caused by recreational drugs and sex plays no role in the causation of AIDS.
- AIDS is caused by antiretrovirals.
- HIV antibodies neutralise HIV.

Each of the above arguments against the HIV theory can be easily refuted :

- Regarding the Koch postulates, if the existence of HIV is accepted and if the antibody tests are considered to prove HIV infection, then the Koch postulates have been fulfilled.
- There are many examples (TB, malaria, hepatitis B) showing that the Farr law which stimulates that the epidemics of infectious diseases have a "bell-shaped" epidemiological curve does not apply.

- Basic scientific and epidemiological evidence shows that sex, namely high frequencies of passive anal intercourse, plays a role in the acquisition of both a positive antibody test and AIDS.
- Since AIDS was diagnosed five years before antiretrovirals started to be used, the antiretrovirals cannot be considered as an argument against the HIV hypothesis.
- Since 1935 evidence existed which shows that antibodies to infectious agents do not neutralize them. At present, immunologists are trying to find a mechanism that excludes neutralization to explain the effect of vaccines.

The only way to prove or disprove the HIV theory is by experiments. Several experiments have been proposed including the following:

- Test a number of African patients who clinically have AIDS for HIV antibodies and/or perform PCR tests.
- Identify young American military recruits who have been found to be HIV positive 10 years ago and determine how many have progressed to AIDS.
- Study the relationship between retroviral particles in the plasma as determined by electron microscopy (pictures) and the viral load test.

Although these experiments are useful, they never can prove or disprove the HIV theory of AIDS. Regarding the first experiment listed above, finding for example that only 50% of African patients who satisfy the clinical definition of AIDS in Africa have a positive antibody test will show that the African clinical syndrome has a poor positive predicting value for HIV infection and will reduce the number of AIDS cases by 50% but will not disprove the HIV theory. With respect to the second experiment listed above, even if a very small proportion, for example 10%, of military recruits had developed AIDS in ten years, it does not prove that HIV is not the cause of AIDS. There are many infectious diseases in which only a small proportion of infected patients end up with the clinical manifestation. Finally, the third experiment listed above, even if it shows that no correlation exists at all between retroviral-like particles observed in the plasma, it does not prove that HIV is not the cause of AIDS or even that the patients are not infected with HIV.

From the very beginning when the HIV theory was introduced, we wanted to perform pre-adsorption experiments. These experiments like the ones outlined above even if they show that all the antibodies present in AIDS patient's sera can be adsorbed by antigens other than HIV are not going to disprove the HIV theory or that the patients are infected with HIV. However, they will show that it is not possible to claim that a positive antibody test proves HIV infection unless HIV isolation (purification) is used as a gold standard to prove the specificity of this test.

The reasons why we have been proposing, again from the beginning of the HIV era, for the HIV isolation (purification) experiments are:

- The necessity of HIV isolation as a gold standard.

- The absolute necessity of isolation to prove the existence of a unique retrovirus, HIV.
- The lack of such proof.

Claims for HIV isolation (purification) have been made by Montagnier's group in 1983 and by Gallo's group in 1984. However, in 1997 Montagnier acknowledged that his group did not obtain proof for isolation (purification) and in his view neither did Gallo's group. In the same year, some of the best known retrovirologists noted that no one had presented proof for isolation (purification) of a unique retrovirus, HIV.

The isolation experiments, as proposed by us, will prove once for all if HIV has been isolated (purified) and thus if there is such a thing as a human retrovirus, HIV. There are several indications that this has not been achieved so far:

- According to Montagnier, what he called "purified HIV" did not even have particles with the morphology typical of retroviruses.
- In 1997, for the first time, two groups of researchers published pictures showing the results of their efforts to obtain HIV isolation (purification). Both groups accept that their pictures show that most of the material that was supposed to be "purified HIV" in fact are non-retroviral-like particles (cellular microvesicles, "mock virus"). These particles are also present in the pictures of material obtained in the same way as the "purified HIV" from cell cultures which were said not to be infected. Nonetheless, these researchers did claim that although they could not obtain "purified HIV" particles, the material obtained from "infected" cultures did contain some particles which were "HIV". However as we have repeatedly pointed out elsewhere including at the Johannesburg meeting of the Presidential AIDS Advisory Panel :
 - a) The particles did not have even the most basic characteristic of retroviruses, the dimensions. A fact which has not been denied by the principal author of one of the publications.
 - b) If some of the particles in the "purified HIV" material were indeed "HIV" then this material will have at least some proteins which were not present in the "mock virus" which originated from the non-infected cultures.

9.6.2 Principles of the Proposed Experiments

9.6.2.1 Pre-adsorption experiment

1. Serum is taken from patients who have a positive "HIV" ELISA and divided into two parts.
2. One part is used to repeat the "HIV" ELISA and the intensity of the reaction (optical density, OD) is noted.

3. The other part is incubated for at least one hour with non-"HIV" proteins. These non-"HIV" proteins can originate from lymphocytes, semen (sperm), E.coli, M.tuberculosis, or other infectious agents which are relevant to a diagnosis of AIDS.
4. Following incubation with the non-"HIV" proteins, the serum is tested with the "HIV" ELISA and the OD noted.
5. If the OD in 4 is lower than the OD in 2, it will mean that the antibodies present in the patient's original serum react both with "HIV" proteins and non-"HIV" proteins. There are two reasons for this, either:
 - a) The antibodies are "HIV" antibodies but they cross-react with non-"HIV" proteins; or
 - b) The antibodies are non-"HIV" antibodies.

From this, it follows that the antibody test cannot be used to prove "HIV" infection unless "HIV" isolation (purification) is used as a gold standard to prove (a) is the reason and not (b).

9.6.2.2 "HIV" Isolation (purification)

One of the physical characteristics of retroviruses is their density. In sucrose density gradients, they band at the density of 1.16gm/ml. So for this experiment:

1. Bands of sucrose of different densities are layered in a centrifuge tube, the lighter at the top and the heavier at the bottom.
2. Establish cell cultures by taking cells from patients who are said to be "HIV" infected (test cultures) and patients who are said not to be "HIV" infected (control cultures).
3. Take the supernatant, that is, the culture fluid, (specimen) and place it at the top of the centrifuge tube.
4. Spin the centrifuge tube for many hours at very high speed.
5. If the specimen contains retroviral particles, they will aggregate (band) at 1.16gm/ml.
6. Extract the 1.16gm/ml band and examine it with an electron microscope (EM).
7. Compare the EM pictures obtained from the test and control cultures. Particles with the morphology of retroviruses should be present only in the EMs from the test cultures. To claim that the 1.16gm/ml band is pure then the EM should show no other material but retroviral-like particles.

8. If there is no difference in the EMs of the test and control cultures no matter what is seen, then it is not possible to claim that the test cultures are infected with a retrovirus.
9. Extract the proteins from the 1.16 gm/ml band obtained from both test and control cultures and compare them. If no difference exists then there is no proof that the test cultures contain "HIV" regardless what the EMs show.
10. Extract the nucleic acids from the 1.16gm/ml band obtained from both test and control cultures and compare them. If no difference exists then there is no proof that the test cultures contain "HIV" regardless what the EMs show.

9.7 Proposal 6: Questionable African AIDS /HIV Statistics - Epidemiology

Proposers: Prof. Gordon Stewart, Prof. Sam Mhlongo, Dr. Christian Fiala, Prof. Charles Gesheker and Dr. Roberto Giraldo

The proposers will need to spend some 2 - 3 days in Geneva re: UNAIDS data.

9.8 Proposal 7: Proposed investigation of the diagnosis of HIV/AIDS

Proposers: Prof. Gordon Stewart, Dr. Roberto Giraldo, Dr. Harey Bialy and Prof. Sam Mhlongo

Principal Proposer: Prof Gordon T. Stewart

9.8.1 Current procedure

The investigations should be arranged in consultation with Professor Schoub or Dr Gray, and performed in the laboratory or laboratories responsible for routine serological tests for HIV by the ELISA method or Western Blot or both.

For clinical purposes and for surveillance, a diagnosis of AIDS (AIDS/HIV, HIV Disease) is made by the demonstrations of antibodies to antigens of HIV obtained from original LAV-BRU, HTLV3 or similar complex cellular co-cultures. This is usually done by the ELISA method of immunofluorescence with or without "Confirmation" by a chromatographic test for identification of the same reacting antibodies by Western blot.

There is a consensus among expert advisers and health authorities internationally supporting this procedure and indeed denying, as in the Durban Declaration, that there is any reason to doubt the reliability of diagnoses, surveillance or clinical decisions made on this basis. But, irrespectively of the state of health of an individual or community, a positive result by either method supports and in many cases mandates a diagnosis of AIDS. The latest revision of the ICD assumes that all seropositive persons are at risk of AIDS and that the majority will proceed to develop signs, sooner or later.

Although false-positive, false-negative, cross-reactive and indeterminate results frequently occur for various reasons or for no obvious reasons, it is further assumed that a "True" positive result can be identified as a reliable indicator of infection with live HIV and therefore of active disease which will progress to AIDS or AIDS-related conditions (ARC's). This belief prevails despite the fact that direct isolation of HIV as proof of infection is difficult or impracticable, and that other surrogate tests such as the PCR/RNA and lymphocyte counts are not appropriate for routine diagnosis.

Presymptomatic screening of all pregnant females is deemed to be necessary for prevention or treatment of HIV disease in them and in their infants. However, it is known that many results are indeterminate, that false positive and negative results can occur and that many other disorders and physiological changes can give indeterminate or non-specific results. In situations where the incidence of "True" seropositivity is low, the likelihood of false or indeterminate results may be higher. This leads to uncertainties, anxieties, and unnecessary interventions like cessation of breast-feeding or termination of pregnancy. Errors in either direction are frequent and can cause catastrophes in relationships, families and communities, especially in countries where stigmatisation, social exclusion and expulsions occur when positive results are known or suspected

Reliability of sero-diagnosis is therefore the critical element in the identification and management of all forms of HIV/AIDS, and for assessment and prevention of vertical as well as horizontal transmission. To improve quality control in diagnosis and surveillance, it is suggested that the following method and precautions be adopted. This will measure the overlap between HIV/AIDS and other prevalent disorders, give ongoing estimates of sensitivity and specificity of serological results, and provide a data-base for checking projections. Since the object of the exercise, is to check and improve the reliability of diagnosis and prognosis by these tests, which often precede clinical diagnosis or development of disease, especially in pregnant women and infants, the test is regarded as the independent and the outcome as the dependent variable.

9.8.2 Investigation of reliability of serological tests for HIV

Under present procedure, a person who is seropositive to HIV (i.e. whose blood contains antibodies to HIV) is diagnosed as having AIDS or a related condition (ARC, or AIDS-defining Disease (ADD)), or being at risk of it. But it is known that many conditions unrelated to HIV/AIDS can also give positive or indeterminate results for shorter or longer periods. These conditions include tuberculosis and malaria, recent vaccinations, certain tumours, pregnancy and other altered states of health which are commonplace in populations where AIDS is prevalent, especially in Africa. For accurate diagnosis and to enable appropriate advice to be given to patients, contacts and families, it is important to recognise this overlap. For doctors and health authorities, it is essential to know the full implications and extent.

Since seropositivity in itself mandates a diagnosis of AIDS, the overlap has to be ascertained by recording details of any other conditions present at the time in samples of blood sent to designated laboratories from clinics, hospital wards and surveys. Results, whether positive, negative or indeterminate, are then tabulated for comparison with the information held by the senders, each set of data being "Blinded". This produces data sets in which the frequencies of these three grades of results are shown in relation to *clinical diagnosis of presumed AIDS, at risk of AIDS from behaviour or contact, AIDS-defining diseases (ADD's), AIDS or ADDS plus other named diseases or conditions, and other diseases or conditions without AIDS.*

With thousands of samples of blood being routinely tested as at present, this procedure will yield data sets from which the frequency of true positive (AIDS only) results can be measured against those in the other categories. If, for example, 10 out of a hundred samples are true positive but 10 positive results are obtained also from those with other diseases without unequivocal clinical signs of AIDS, a person with a positive result in that sample is as likely to have some other condition, and so on according to the alternates indicated in the text of the full proposal.

Because direct identification of HIV itself is not required and is indeed impracticable at present for routine diagnosis, indirect serological tests are the measures used for decisions about all aspects of HIV/AIDS, and especially for assessing and controlling vertical, perinatal and puerperal transmission. Failure to detect false positive and false negative reactions leads to errors not only in diagnosis, treatment and other interventions, but also to erroneous projections and fear – or alternatively irresponsible disregard – of dangers to persons, families and entire communities. *These dangers apply to underestimates no less than to overestimates of AIDS and also to risks of overlooking other diseases submerged in the over-riding classification of HIV/AIDS.* The present proposal, which should be discussed and implemented co-operatively with existing clinical and laboratory services, is designed to minimise these dangers.

9.8.3 Extensions

This investigation could be extended to Sentinel surveillance and all cases of AIDS (with controls) admitted to hospitals. Samples giving positive and indeterminate results should be, as often as is practicable, subjected to tests for antibodies to other agents, for example: CMV, HSV, VZ, EBV, and to tests for auto-immune and non-specific antibodies, in such conditions as pregnancy, disseminated lupus erythematosus and other auto-immune disorders to see if patterns of cross reactions can be identified. These data might then be used for more critical analysis of the hypothesis that HIV is the essential cause of AIDS.

9.8.4 Interpretation of findings

- a) Measure sensitivity as % of cases detected in one or two tests, and also consistency and reproducibility between the tests.
- b) Assess sero-positivity in relation to general state of health.
- c) Relate B to **ADD's**.
- d) D. and E. will identify conditions associated with non-specific positive results.
- e) F. will indicate the weighting that might be attached to a given result.

This proposal is submitted in outline so that it can be circulated for comment and revision.. It is accepted that further detail will be required for implementation which should be arranged if possible

with the National Institute of Virology, with those responsible for testing and surveillance, and for compilation of registration data in South Africa.

Although Sentinel Surveillance as organised by the WHO requires serodiagnosis by Elisa, using recombinant antigens prepared from co-cultures of HIV, it should be noted that the Bangui definition of AIDS agreed by the WHO and member States in 1987, is regarded as sufficient to warrant a diagnosis of AIDS or AIDS-related conditions without any serological test. National and international data do not normally indicate the proportion or location of diagnoses or projections made on this basis but it is obviously important to include in the programme described above some provision for identifying this proportion.

9.9 Proposal 8: Study to find out the real meaning of HIV Tests

Principal Proposers: Dr Harvey Bialy and Dr Roberto Giraldo

To take blood from four groups of people and run the tests highly diluted, undiluted and at a wide spectrum of dilutions in between.

- a) The first group would be a group of healthy people of many different age groups.
- b) The second group would be a group of people from the AIDS risk groups.
- c) The third group would be a group of people with clinical conditions unrelated to AIDS; and
- d) The fourth group would be a group of patients with full manifestations of AIDS.

All groups would be subjected to both ELISA and Western blot tests. Additionally, all plasma samples will be subjected to the viral load test for HIV.

The result of such experiment could determine whether these tests measurements bear any relationship to an individual's level of exposure to stressor or oxidizing agents. If so, the tests could be salvaged as a measure of individual's level of intoxication.

Bases and references for these experiments can be seen in my postings "Tests for HIV are highly inaccurate" and "Everybody is HIV-positive".

9.10 Proposal 9: To test the reliability of one of the main laboratory methods currently used to quantify HIV in the blood of seropositive individuals - using the Electron Microscope.

Proposer: Prof. Etienne de Harven:

9.10.1 Aim of the experiments.

To test the reliability of one of the main laboratory method currently used to quantify so-called HIV in the blood of sero-positive individuals. More specifically, to use electron microscopy (EM) to verify that the blood plasma of patients identified as having a high "viral load" by PCR does indeed contain retroviral particles, and that, therefore, such samples could be used to isolate and purify HIV, free from cell debris and adventitious material from co-cultures.

9.10.2 Materials and Methods

Using the Roche Diagnostics Corporation "Amplicor HIV-1" monitor test:

Readily access to 5 patients with very high PCR counts. (Group A)

Readily access to 5 patients with undetectable PCR counts. (Group B)

Low speed centrifugation to separate and discard erythrocytes, leukocytes and platelets. Plasma samples (10 ml) diluted 1/1 with cold heparinized Ringer solution. Filtration by aspiration through a Millipore 0.6u membrane. Collecting filtrate #1, and filtering it this time using a Millipore 0.2u membrane. Collecting filtrate #2 and placing it in appropriate Beckman tubes for ultracentrifugation in either a fixed angle or a swinging bucket rotor, using the refrigerated ultracentrifuge to spin the sample under 30.000g for 2 hours. Inspect the tubes for the likely presence of extremely small pellets. Avoiding any risk of resuspending the pellets, cover them with 1.5 % glutaraldehyde in 0.1M cacodylate buffer (pH7) overnight at 0-4°C, rinsed with buffer and post-fixed with 1% osmium tetroxide for 90 min. After rinsing, the pellets will be kept for several hours in 0.5% uranyl acetate at 0-4°C, dehydrated in ethanol and propylene oxide and embedded in Epon. Thin sectioning with diamond knives, staining with uranyl acetate and lead citrate will be followed by examination under the transmission electron microscope at initial magnification ranging between 10.000 and 40.000x.

If the current interpretation of PCR "viral load" result is correct, EM should show plenty of retroviruses in Group A, none in Group B. Otherwise, the existence of a viremia in "high viral load" patients will have to be fundamentally re-appraised.

Samples from the same patients will be used to perform a classical PCR test by the Roche Amplicor HIV-1 routine method, following rigorously the test kit manufacturer's recommendations.

The pellets obtained in the microfuge, with the 5 samples from Group A, will be analyzed by EM using a methodology comparable to the one described above. This could, eventually, confirm the presence of retroviral particles and will certainly permit to evaluate the presence and the amounts of cell debris.

The absence of HIV particles from the discarded supernatant should be verified, simply by submitting it to high speed centrifugation at 30.000xg for 2 hours and subsequent analysis of the resulting pellet, as described above.

Control samples should be prepared by the double Millipore filtration method that is known to eliminate most cell debris and to concentrate retroviruses in an almost pure form. The final viral pellet will be compared to a "microfuge" pellet from the same patients, both pellets being then processed identically for RNA amplification.

9.10.3 Technical assistance needed:

Technical assistants, trained in routine virology, knowledgeable in ultrafiltration and ultracentrifugation methods, and fully trained in routine Roche Amplicor PCR method.

Technical assistant knowing routine transmission EM procedures, with special proficiency in chemical fixation, plastic embedding, and ultrathin sectioning.

Major equipment needed:

Laminar flow hood, Millipore filtration equipment, refrigerated ultracentrifuge, PCR test kit, ultramicrotome fitted with diamond knives, high resolution transmission electron microscope.

Estimated cost:

If trained technical assistance and all the major equipment are available, the cost of running these experiments can be anticipated to be approximately 500 US dollars for each patients. Total cost for 10 patients would run around 5,000 US dollars. If the results of the proposed experiment are clear-cut and unambiguous, the number of 10 patients should suffice to make the point. If they are not, another group of 10 patients should be considered for an extension of the study.

Time required:

If the appropriate patients can be reached without delay, the total time frame of these experiments should probably not exceed a matter of 4 to 8 weeks. My presence would be essential in setting up the sampling procedures and to perform all the EM examinations.

At this time, priority should be given to the identification of ZA labs were this type of work could efficiently be performed, efficiency depending on 3 main factors: 1) a friendly welcome, 2) satisfactorily trained and available assistants, and 3) appropriate equipment. If this would appear difficult, we should then consider doing part of the work either in Europe or in New York.

Finally, it would be of considerable importance for me to be informed of the experimental proposals presented by Dr. Peter Duesberg and by the Perth group, in order to coordinate the entire project in a coherent fashion.

9.11 Proposal 10: To determine which is more harmful - HIV or Anti HIV drugs?

Proposers: Dr. David Rasnick and Dr. Claus Köhlein

Brief Description:

Chimpanzees are known to be susceptible to HIV infection (i.e., develop antibodies to HIV), however, none to date has come down with AIDS. We propose to take 60 chimpanzees divided into three groups of 20 each as follows:

- Group A is the HIV negative controls.
- Group B is infected with HIV but otherwise treated exactly as Group A.
- Group C is treated with HIV and is put on a life-time course of the three drug anti-HIV cocktail known as HAART.

There are two outcomes of the study:

- a) which animals come down with AIDS-defining and other diseases?
- b) which live longer?

CHAPTER 10: CONCLUSION

Chapter 1 of this report set the scene to explain the events that led to the constitution of the Presidential Advisory Panel on AIDS. The Terms of Reference for the panel included very specific questions that the panel had to deliberate on and generate possible answers to. The Presidential Advisory Panel on AIDS was quite deliberately constituted in such a manner as to bring together individuals who were expert and/or had experience in a broad diversity of areas that are relevant to the understanding of the AIDS issue. This diversity of expertise and experience also included diametrically contrasting views on several key questions pertaining to AIDS. The assumption, therefore, was that members of the panel would unpack the merits and de-merits of particular scientific, public policy and health policy viewpoints in a dispassionate manner and generate the best possible collective advice to the South African government. This lofty ideal usually underpins the constitution of advisory panels. A possible alternative of constituting panels according to common belief systems of the members would necessarily generate advice that is biased in favour of those particular belief systems.

It would have been quite clear to the reader of this report that the recommendations to the South African government that emanated from the panel deliberations are presented in the main according to the viewpoints of the panel members on the cause of AIDS. Such a presentation reflected a painful reality of the deliberations. The panel split quite early on in the process on the basis of what the cause of AIDS was. That primary split on aetiology generated consequential splits of views on the treatment and prevention of AIDS. The depth of the cleft on the aetiology of AIDS was such that the commonalities of views on health policy and public policy were by and large swallowed up.

The central basis of the split was, in the opinion of the author of this report, not based on deeply entrenched ideological positions or blind passion. The split was instead based on fundamental disagreement on the interpretation of the scientific and clinical data and evidence on the cause and progression of AIDS. It was also apparent during the deliberations that there were many legitimate scientific questions to which scientific research has not yet generated answers. In the latter case, no amount of debate between adversaries can manufacture an answer. The only way of generating the answers is to carry out proper scientific investigations. An example of such a question is by what specific mechanism does the HIV induce the depletion of CD4 cells?

The implications of this situation for public policy should not be underestimated. On the one hand, it could be argued that since there is no known mechanism by which retroviruses kill host cells and, as some panellists have argued, that the evidence that HIV is a retrovirus belonging to the lentivirus family of RNA viruses is not compelling, it should therefore be concluded that HIV cannot be the primary cause of AIDS. Such a conclusion would lead public policy in a particular direction. On the other

hand, it could equally be argued that we may not yet know the mechanisms by which HIV leads to the depletion of CD4 cells, but there is sufficient evidence to establish a primary causal link between HIV and AIDS. This conclusion would drive public policy in another particular direction.

Results of scientific research and scientific investigations are key drivers of public policy. The Presidential Advisory Panel on AIDS was constituted ostensibly to interrogate available scientific and clinical data and evidence and to make recommendations to inform and advise the South African government as to the most appropriate measures to take in combating AIDS. Such a step was taken in direct recognition of the fact that science does not necessarily have to provide exhaustive, irrefutable and non-controversial evidence before public policy can be developed. More often than not, public policy is developed on the basis of the best possible interpretation and understanding of the data and information available at the time. These policies may be adapted or abandoned as more data, information and evidence are continuously generated by, *inter alia*, scientific research and investigation and experience.

The nature and format of the deliberations of the panel could not allow the in-depth scientific argumentation that is necessary to resolve many of the differences over scientific issues of a fundamental nature. An inevitable consequence of this reality was different sets of recommendations made from the varying perspectives of what is perceived to be the 'real' cause of AIDS.

Appendix 1

Internet discussion of the PRESIDENTIAL AIDS REVIEW PANEL

Threads of discussion

Author	Topic	Date of posting
Christian Fiala • Jorge Perez • Christian Fiala	HIV test	17 May 2000 19 May 2000 21 May 2000
David Rasnick • Jorge Perez • David Rasnick	What's next?	18 May 2000 20 May 2000 21 May 2000
Roberto Giraldo	The Sexual Transmission of AIDS ?	23 May 2000
Moderators • David Rasnick • Roberto Giraldo • Perth Group • David Rasnick • Perth Group • Christian Fiala	Launch of the Internet debate	23 May 2000 24 May 2000
Perth Group • Roberto Giraldo • Harvey Bialy	The oxidative stress theory and HIV/AIDS	24 May 2000 25 May 2000
David Rasnick	Dissidents in the main stream	24 May 2000
Perth Group	Our posting truncated problem with the website Remainder of oxidative stress HIV Transmission (parts III and IV)	25 May 2000
David Rasnick	'Room C' discussion?	25 May 2000
Harvey Bialy	Some questions for Drs Gallo, Montagnier & Makgoba	26 May
Perth Group	Comments on suggested experiments	26 May 2000
Sam Mhlongo	Cofactors: HIV/AIDS Debate	26 May 2000
Peter Duesberg • David Rasnick • Ray Mabope • Roberto Giraldo	Next panel meeting	27 May 2000 30 May 2000 31 May 2000
Roberto Giraldo	The origin of the 'transmission' of AIDS	27 May 2000
David Rasnick • Roberto Giraldo • Perth Group • Ray Mabope	Topics deleted	27 May 2000 28 May 2000 30 May 2000
Robert Giraldo • Harvey Bialy	Tests for HIV are highly inaccurate	28 May 2000
Harvey Bialy	Questions for Drs Gallo, Montagnier & Kakgoba	28 May 2000
Robert Giraldo	Questions for the moderators	29 May 2000
Robert Giraldo	'Cofactors' cause AIDS	29 May 2000
David Rasnick	Defenders of HIV, where are you?	30 May 2000
David Rasnick • Ayanda Ntsaluba	Thanks to moderators	31 May 2000
ML Kothari	Issues for the next HIV meeting	31 May 2000
Harvey Bialy • Christian Fiala	A request of South African epidemiologists	31 May 2000
Moderators • Harvey Bialy • David Rasnick	Moderators perspective	1 June 2000
Harvey Bialy	Protease Inhibitors and magical cures	2 June 2000
Roberto Giraldo	Circumcision and AIDS in Africa	2 June 2000 10 June 2000
David Rasnick • Harvey Bialy • Roberto Giraldo • Harvey Bialy • Roberto Giraldo	Animal models of AIDS	3 June 2000 7 June 2000
David Rasnick	Overwhelming evidence	3 June 2000

Author	Topic	Date of posting
Harvey Bialy	More on protease inhibitors / AIDS docs take note	4 June 2000
David Rasnick	1992 AIDS peaked in USA	4 June 2000
David Rasnick	Decline in AIDS deaths	4 June 2000
Moderators <ul style="list-style-type: none"> • Joseph Sonnabend • Harvey Bialy • David Rasnick • Roberto Giraldo 	Moderators perspective	5 June 2000
Harvey Bialy <ul style="list-style-type: none"> • Gordon Stewart 	The overwhelming evidence is presented here	5 June 2000 6 June 2000
David Rasnick	Break the silence	5 June 2000
David Rasnick	New folks, Welcome!	6 June 2000
ML Kothari <ul style="list-style-type: none"> • Zena stein • David Rasnick 	Dr Rasnick's call to break the silence	6 June 2000 9 June 2000 10 June 2000
Helpdesk <ul style="list-style-type: none"> • David Rasnick • Gordon Stewart • Harvey Bialy • Harvey Bialy • Helpdesk • Roberto Giraldo 	Website problems that are experienced by the panel	6 June 2000
	How do we send graphic files?	14 June 2000
	Website problems that are experienced by the panel	7 June 2000
C Koehnlein <ul style="list-style-type: none"> • Joseph Sonnabend • David Rasnick • Harvey 	Re: J Sonnabend	6 June 2000 7 June 2000 8 June 2000
Robert Giraldo <ul style="list-style-type: none"> • Zena Stein 	Breastfeeding and AIDS in Africa	7 June 2000 9 June 2000
Perth Group <ul style="list-style-type: none"> • Harvey Bialy 	Agenda for proposed July meeting	7 June 2000
David Rasnick <ul style="list-style-type: none"> • Charles Geshekter • Zena Stein 	TB versus AIDS in South Africa	7 June 2000 9 June 2000
David Rasnick	Anti-HIV drugs fail in children	7 June 2000
David Rasnick	Malaria versus AIDS	7 June 2000
Sam Mhlongo <ul style="list-style-type: none"> • C Koehnlein 	Perth-Group versus William Makgoba HIV/AIDS debate	7 June 2000 8 June 2000
Harvey Bialy	AIDS among US ethnic Minorities	8 June 2000
Perth Group <ul style="list-style-type: none"> • Harvey Bialy • David Rasnick 	First comments on revised NIH document	8 June 2000
David Rasnick	Pregnant monkeys exposed to AZT	8 June 2000
David Rasnick	HIV protease inhibitors and diabetes	8 June 2000
Alan Whiteside <ul style="list-style-type: none"> • Roberto Giraldo • Harvey Bialy • David Rasnick • Christian Fiala <ul style="list-style-type: none"> • Harvey Bialy • Charles Geshekter 	Increased mortality	8 June 2000
	Increased mortality due to what?	9 June 2000 11 June 2000
	Increased mortality	12 June 2000
Moderators <ul style="list-style-type: none"> • Joseph Sonnabend • Harvey Bialy • Harvey Bialy • David Rasnick • Harvey Bialy • Harvey Bialy <ul style="list-style-type: none"> • Moderators • Jorge Perez • Peter Duesberg 	Moderators perspective	9 June 2000
	An apology	11 June 2000
	Moderators perspective	9 June 2000
		16 June 2000 19 June 2000 10 June 2000

Author	Topic	Date of posting
<ul style="list-style-type: none"> • Christian Fiala • David Rasnick • Helene Gayle • David Rasnick • Helene Gayle 	Where are the data from SA? Firmly established strategy Moderators perspective Should we worry? Moderators perspective	13 June 2000 14 June 2000 13 June 2000
Sam Mhlongo <ul style="list-style-type: none"> • Gordon Stewart 	Perth Group vs William Makgoba	9 June 2000 11 June 2000
Joseph Sonnabend <ul style="list-style-type: none"> • David Rasnick • Harvey Bialy • Alan Whiteside • Harvey Bialy 	Associated infections, poverty and HIV	9 June 2000
Harvey Bialy <ul style="list-style-type: none"> • Roberto Giraldo • Harvey Bialy 	EUREKA	9 June 2000 10 June 2000
Harvey Bialy	Six questions refried & reposted	9 June 2000
Roberto Giraldo	The causes of AIDS	9 June 2000
Carolyn Williamson <ul style="list-style-type: none"> • David Rasnick <ul style="list-style-type: none"> • Carolyn Williamson • Harvey Bialy • David Rasnick • Harvey Bialy 	The virus	9 June 2000 10 June 2000
Harvey Bialy	The overwhelming evidence against, or 'a rose by any other name'	10 June 2000
Roberto Giraldo	Question to moderators	10 June 2000
David Rasnick	HIV innocent of crime of AIDS	10 June 2000
David Rasnick	Exhibit B for the defense	10 June 2000
David Rasnick <ul style="list-style-type: none"> • Harvey Bialy 	Exhibit C for the defense	
ML Kothari <ul style="list-style-type: none"> • Roberto Giraldo 	Alleged moderation of the debate	10 June 2000 11 June 2000
David Rasnick <ul style="list-style-type: none"> • Harvey Bialy 	Exhibit D for the defense	11 June 2000 13 June 2000
David Rasnick	Witnesses for the defense	11 June 2000
Joseph Sonnabend <ul style="list-style-type: none"> • Joseph Sonnabend <ul style="list-style-type: none"> • Peter Duesberg <ul style="list-style-type: none"> • Joseph Sonnabend • Charles Gesheker • Harvey Bialy • Peter Duesberg <ul style="list-style-type: none"> • Joseph Sonnabend • Harvey Bialy • David Rasnick <ul style="list-style-type: none"> • Joseph Sonnabend <ul style="list-style-type: none"> • David Rasnick <ul style="list-style-type: none"> • J Sonnabend • David Rasnick • J Sonn... • D Rasnick • Harvey Bialy • Harvey Bialy • Joseph Sonnabend 	Heterosexual transmission: Differences in Africa Your first question Heterosexual transmission: Differences in Africa An honourable contribution Progress Prescribed drugs Your 1 st question Progress An honourable contribution	11 June 2000 12 June 2000 13 June 2000 15 June 2000 16 June 2000 12 June 2000 13 June 2000 14 June 2000 13 June 2000 16 June 2000 12 June 2000
Roberto Giraldo	The natural history of AIDS	12 June 2000
Roberto Giraldo <ul style="list-style-type: none"> • Ray Mabo • Charles Gesheker • Helpdesk 	Moderators: Where are you?	12 June 2000 14 June 2000
David Rasnick	Witness for the defense	12 June 2000
Perth Group	Questioning the HIV/AIDS theory	12 June 2000

Author	Topic	Date of posting
<ul style="list-style-type: none"> David Rasnick 	To the majority	
ML Kothari	HIV causes AIDS (!)	12 June 2000
David Rasnick	Textbook on HIV/AIDS	12 June 2000
<ul style="list-style-type: none"> C Koehnlein 		13 June 2000
David Rasnick	Witness for the defense	13 June 2000
<ul style="list-style-type: none"> Etienne de Harven Roberto Giraldo 		14 June 2000
David Rasnick	Witness for the defense	13 June 2000
<ul style="list-style-type: none"> Harvey Bialy 	Collaboratory testimony	
Roberto Giraldo	Anti-retrovirals cause AIDS	14 June 2000
Harvey Bialy	An explanation for why the majority pretends uninterested	14 June 2000
Perth Group	The NIH and Montagnier's virus	14 June 2000
<ul style="list-style-type: none"> Ray Mabope (Robert Root-Bernstein) 		15 June 2000
David Rasnick	Televisе the next meeting	15 June 2000
<ul style="list-style-type: none"> Roberto Giraldo 		
Harvey Bialy	The Orwellina Coovadia	15 June 2000
David Rasnick	Root-Bernstein	15 June 2000
<ul style="list-style-type: none"> Harvey Bialy David Rasnick 	Good point!	16 June 2000
Alan Whiteside	Evidence on increased mortality	15 June 2000
<ul style="list-style-type: none"> Harvey Bialy Roberto Giraldo Alan Whiteside Roberto Giraldo 		16 June 2000
<ul style="list-style-type: none"> Charles Gesheker Harvey Bialy Alan Whiteside 		18 June 2000
	More on increased mortality	25 June 2000
		26 June 2000
Harvey Bialy	Some words from the truly wise, with a comment from the merely inquisitive	15 June 2000
Perth Group	Answering Root-Bernstein	16 June 2000
<ul style="list-style-type: none"> David Rasnick 	Check task team	
Joseph Sonnabend	A physician's perspective	16 June 2000
<ul style="list-style-type: none"> David Rasnick Joseph Sonnabend 	Visit your facility	17 June 2000
<ul style="list-style-type: none"> Peter Duesberg Joseph Sonnabend Harvey Bialy C Koehnlein Perth Group 		18 June 2000
	There you go again	
	A physician's perspective	
Perth Group	NIH and 'HIV' antibodies + experiments	16 June 2000
Roberto Giraldo	An effective treatment of AIDS	17 June 2000
David Rasnick	Witness for the defense	17 June 2000
David Rasnick	Before it's over	17 June 2000
Harvey Bialy	A reply to Prof Makgoba	17 June 2000
<ul style="list-style-type: none"> Harvey Bialy Harvey Bialy 	Correction	
	Addendum	
Harvey Bialy	Witness for the prosecution	17 June 2000
<ul style="list-style-type: none"> C Koehnlein 		18 June 2000
Roberto Giraldo	Everybody is HIV- positive	18 June 2000
<ul style="list-style-type: none"> The moderators Carolyn Williamson 		23 June 2000
		26 June 2000
Harvey Bialy	A general question	18 June 2000
<ul style="list-style-type: none"> Alan Whiteside Harvey Bialy 		19 June 2000
Etienne de Harven	Answering Root-Bernstein	18 June 2000
David Rasnick	Summary dismissal of the charges	18 June 2000
Perth Group	Perth group postings	19 June 2000
Roberto Giraldo	An effective prevention of AIDS	19 June 2000

Author	Topic	Date of posting
Harvey Bialy	A final few words about the 'data in the public domain'	19 June 2000
Stefano Bertozzi <ul style="list-style-type: none"> • David Rasnick • Harvey Bialy • C Koehnlein • Harvey Bialy 	How to be helpful?	19 June 2000 20 June 2000 21 June 2000
Perth Group	NIH and 'HIV' antibodies + experiments	19 June 2000
ML Kothari	Suppressio Veri - Suggestio falsi	19 June 2000
Etienne de Harven	Statement	19 June 2000
Etienne de Harven	Proposal #1	19 June 2000
Etienne de Harven	Proposal #2	19 June 2000
David Rasnick	What does all of this mean for South Africa	20 June 2000
David Rasnick <ul style="list-style-type: none"> • The moderators • Elephant or mouse 	Is there a role for consensus in science?	20 June 2000 23 June 2000
Perth Group	Answer to Bob Root-Bernstein	20 June 2000
Moderators <ul style="list-style-type: none"> • Peter Duesberg • Joseph Sonnabend • David Rasnick • Roberto Giraldo • The moderators 	Some specific questions	20 June 2000 21 June 2000 23 June 2000
ML Kothari <ul style="list-style-type: none"> • Harvey Bialy 	All ART is cytotoxic	20 June 2000
Etienne de Harven <ul style="list-style-type: none"> • Harvey Bialy 	Proposal #3	20 June 2000
Ray Mabope <ul style="list-style-type: none"> • David Rasnick <ul style="list-style-type: none"> • Roberto Giraldo <ul style="list-style-type: none"> • Ray Mabope <ul style="list-style-type: none"> • P Duesberg • Harvey Bialy • Perth Group 	July meeting	20 June 2000 21 June 2000
Perth Group	Questions for the moderators	21 June 2000
Roberto Giraldo	Some possible trials	21 June 2000
Perth Group <ul style="list-style-type: none"> • J Sonnabend 	Comments on Joe Sonnabend's posting Reply	21 June 2000
ML Kothari	Waxing/waning on vaccine/ART	21 June 2000
Peter Duesberg <ul style="list-style-type: none"> • Harvey Bialy 	Panellists engaged in pogrom of non-HIV-AIDS minorities	21 June 2000
Harvey Bialy <ul style="list-style-type: none"> • Harvey Bialy • Harvey Bialy • Harvey Bialy 	A copy of a letter to Helene Gayle and William Makgoba A reply from Prof Makgoba A reply from Dr Gayle Further words from Prof Makgoba	21 June 2000 22 June 2000 23 June 2000
David Rasnick	The Cold War of AIDS	21 June 2000
David Rasnick	Flights to Johannesburg	21 June 2000
Harvey Bialy	A query of Drs Gayle and Bertozzi in light of their signing the Durban declaration	22 June 2000
ML Kothari <ul style="list-style-type: none"> • Lynn Morris <ul style="list-style-type: none"> • Roberto Giraldo • Peter Duesberg <ul style="list-style-type: none"> • The moderators <ul style="list-style-type: none"> • Carolyn Williamson <ul style="list-style-type: none"> • D Rasnick • H Bialy • C Williamson • Lynn Morris • Perth Group 	Bottomline on HIV-AIDS Response to the moderators Moder of AIDS Response to the moderators Bottomline on HIV-AIDS Questions to Dr Morris	22 June 2000 23 June 2000 25 June 2000 23 June 2000

Author	Topic	Date of posting
<ul style="list-style-type: none"> • Etienne de Harven • J Sonnabend <ul style="list-style-type: none"> • David Rasnick <ul style="list-style-type: none"> • J Sonnabend <ul style="list-style-type: none"> • David Rasnick <ul style="list-style-type: none"> • J Sonnabend <ul style="list-style-type: none"> • D Rasnick • Perth Group • Etienne de Harven • Roberto Giraldo	<p>Bottomline on HIV-AIDS</p> <p>How big a benefit?</p> <p>It's your patients I'm asking about</p> <p>We are getting closer</p> <p>Bottomline on HIV-AIDS</p>	<p>22 June 2000</p> <p>23 June 2000</p>
<p>Peter Duesberg</p> <ul style="list-style-type: none"> • Joseph Sonnabend • Peter Duesberg <ul style="list-style-type: none"> • Joseph Sonnabend 	<p>The African AIDS epidemic: New and contagious or old under a new name?</p>	<p>23 June 2000</p> <p>24 June 2000</p>
<p>Perth Group</p>	<p>Response to nature's open letter to President Mbeki</p>	<p>23 June 2000</p>
<p>Perth Group</p>	<p>No evidence that HIV originated from African monkeys</p>	<p>23 June 2000</p>
<p>Andrew Herxheimer</p> <ul style="list-style-type: none"> • Peter Duesberg 	<p>A personal statement and a suggestion</p>	<p>23 June 2000</p> <p>24 June 2000</p>
<p>Harvey Bialy</p>	<p>Finally an answer from William Makgoba from my frequently posted six questions on HIV/AIDS etiology</p>	<p>23 June 2000</p>
<p>Ray Mabope</p> <ul style="list-style-type: none"> • Harvey Bialy • Joseph Sonnabend <ul style="list-style-type: none"> • Ray Mabope 	<p>Input from Prof Makgoba</p> <p>Am I missing something</p> <p>Input from Prof Makgoba</p>	<p>23 June 2000</p> <p>24 June 2000</p> <p>25 June 2000</p>
<p>Ray Mabope</p>	<p>Input from Prof Salim Abdool-Karim</p>	<p>23 June 2000</p>
<p>David Rasnick</p>	<p>Moderators as advocates? De-cloak thyself</p>	<p>23 June 2000</p>
<p>Harvey Bialy</p>	<p>A particularly telling exchange between Perth & Makgoba</p>	<p>24 June 2000</p>
<p>Moderators</p> <ul style="list-style-type: none"> • Harvey Bialy • Peter Duesberg 	<p>Correction</p>	<p>24 June 2000</p>
<p>Ray Mabope (for Prof Salim Abdool-Karim)</p> <ul style="list-style-type: none"> • Peter Duesberg • Ray Mabope (for Prof Salim Abdool-Karim) <ul style="list-style-type: none"> • Roberto Giraldo <ul style="list-style-type: none"> • Ray Mabope • Harvey Bialy <ul style="list-style-type: none"> • Harvey Bialy • David Rasnick 	<p>Similarities and differences in the patters of HIV/AIDS epidemics: South Africa compared to Western Europe and the USA</p> <p>Addendum</p> <p>Prof Salim Abdool-Karim</p>	<p>24 June 2000</p> <p>25 June 2000</p>
<p>Ray Mabope (for Prof Luc Montagnier)</p> <ul style="list-style-type: none"> • Harvey Bialy • David Rasnick <ul style="list-style-type: none"> • Ray Mabope • Peter Duesberg <ul style="list-style-type: none"> • David Rasnick • Ray Mabope 	<p>Facts, figures and propositions about AIDS</p> <p>Prof Luc Montagnier</p> <p>Facts, figures and propositions about AIDS</p> <p>On behalf of Montagnier</p>	<p>24 June 2000</p> <p>25 June 2000</p>
<p>David Rasnick</p> <ul style="list-style-type: none"> • Peter Duesberg • Harvey Bialy <ul style="list-style-type: none"> • David Rasnick 	<p>One more experiment</p>	<p>25 June 2000</p> <p>26 June 2000</p> <p>27 June 2000</p>
<p>Peter Duesberg</p>	<p>Drug holidays? Or why even the HIV/AIDS orthodoxy isn't all bad</p>	<p>25 June 2000</p>
<p>Christian Fiala</p>	<p>Epidemiological evidence against heterosexual transmission of HIV and against prevention-</p>	<p>26 June 2000</p>

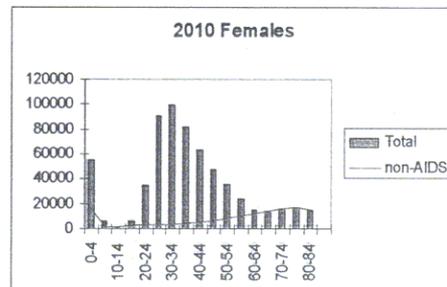
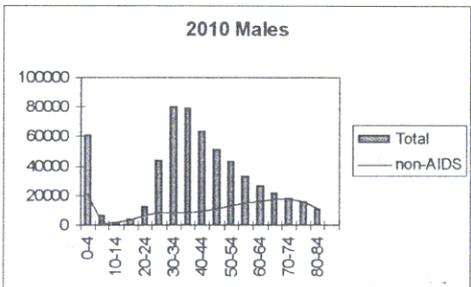
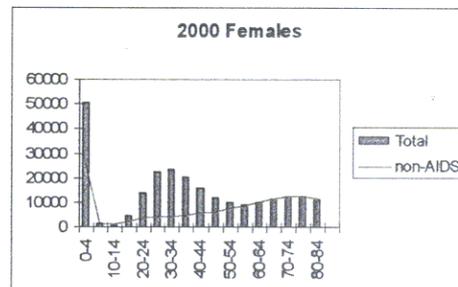
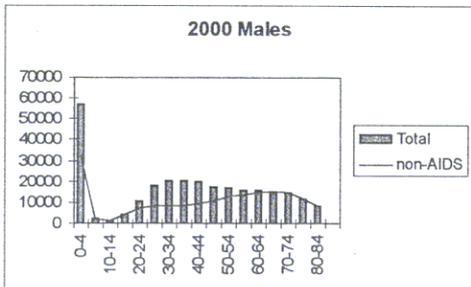
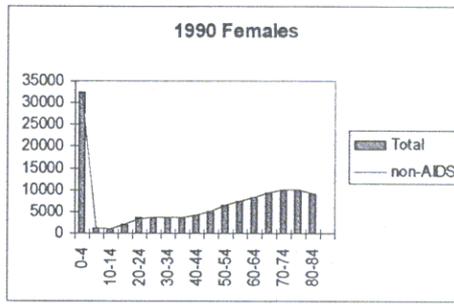
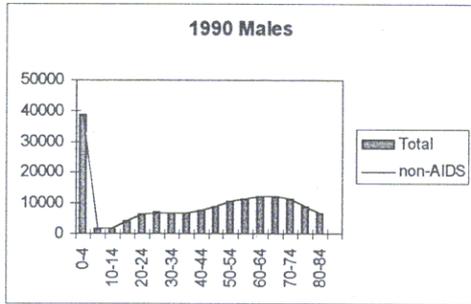
Author	Topic	Date of posting
	campaigns	
Etienne de Harven • Peter Duesberg	Durban Declaration	25 June 2000
Perth Group	Does HIV exist? Reply to Peter Duesberg and the case against.	26 June 2000
Lynn Morris • Peter Duesberg • Perth Group	Former dissidents take HAART	26 June 2000 27 June 2000
Ray Mabope (for Drs AD Mbewu, P Onyebujoh, SP Reddy, S Singh and P Matchaba) • Etienne de Harven	The South African response to HIV/AIDS	26 June 2000 27 June 2000
Lynn Morris • Carolyn Williamson • Alan Whiteside • David Rasnick • Peter Duesberg • Harvey Bialy	Panel meeting and format and topics	26 June 2000 27 June 2000
Perth Group	No proof for simian AIDS	26 June 2000
Etienne de Harven	Durban declaration	26 June 2000
Roberto Giraldo	Is HIV 69 years old?	27 June 2000
Ray Mabope (for Helene Gayle)	Perinatal prevention	27 June 2000
Ray Mabope (for Helene Gayle)	Blood safety	27 June 2000
Ray Mabope (for Helene Gayle) • Carolyn Williamson • Harvey Bialy	Surveillance UNAIDS stats	27 June 2000 28 June 2000
Ray Mabope (for Helene Gayle) • Roberto Giraldo	Prevention of sexual transmission	27 June 2000 28 June 2000
ML Khotari	Principles governing HIV debate	27 June 2000
Ray Mabope (for Helene Gayle)	Post exposure prophylaxis	27 June 2000
David Rasnick	Ray Mabope	27 June 2000
Zena Stein • Etienne de Harven • Harvey Bialy • Peter Duesberg	Preventing HIV in infants	27 June 2000 28 June 2000
Zena Stein	Causal inference	27 June 2000
Lynn Morris • Peter Duesberg • Lynn Morris	Factors affecting transmission and progression	27 June 2000 28 June 2000
Ray Mabope • Etienne de Harven • Ray Mabope	Details of the July meeting	27 June 2000 28 June 2000
Lynn Morris	HIV ELISAs	27 June 2000
Harvey Bialy	The rash of sudden posts	28 June 2000
Christian Fiala	Answer to Prof Salim Abdool-Karim	28 June 2000
Perth Group	SIV and SAIDS	28 June 2000
Alan Whiteside	The agenda	28 June 2000
Ray Mabope (for Prof W Makgoba) • Roberto Giraldo • Peter Duesberg	HIV testing	28 June 2000
Sam Mhlongo	Role of media	28 June 2000
Sam Mhlongo	Virginity tests	28 June 2000
Sam Mhlongo	Pre-determined outcome HIV/AIDS debate	28 June 2000
Sam Mhlongo	The shocking truth about protease inhibitors... a visual 'wake-up-call'	28 June 2000
David Rasnick	CDCs documented deception (and upload of document)	28 June 2000
Sam Mhlongo • Peter Duesberg	The Durban declaration vs the Presidential AIDS Panel	28 June 2000 29 June 2000
Sam Mhlongo	Cofactors: HIV/AIDS debate	28 June 2000

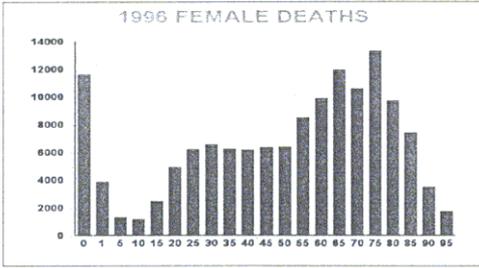
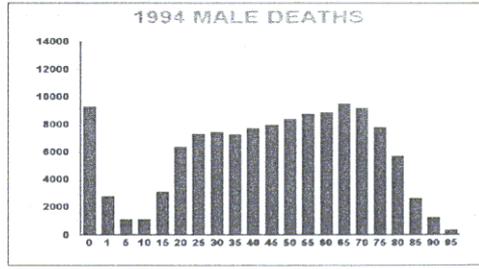
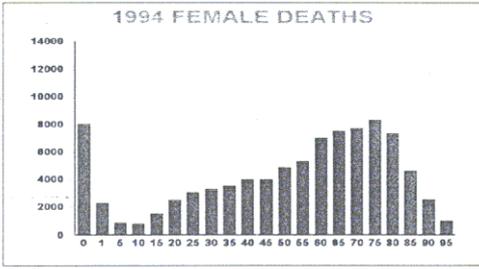
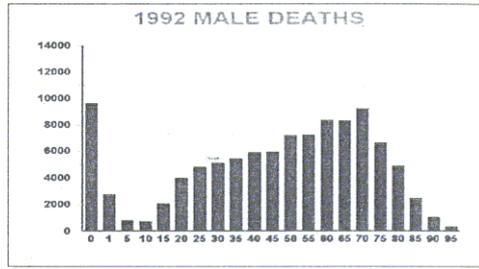
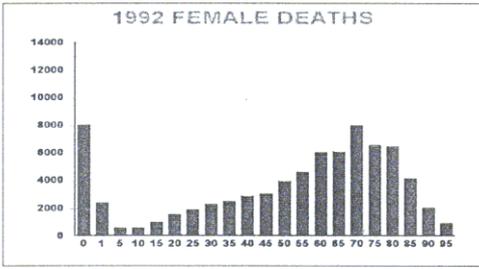
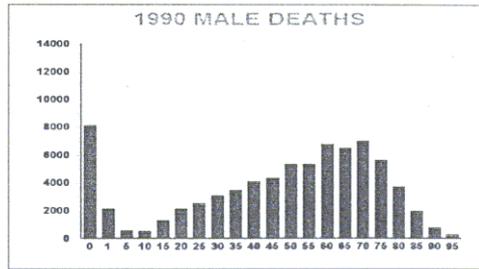
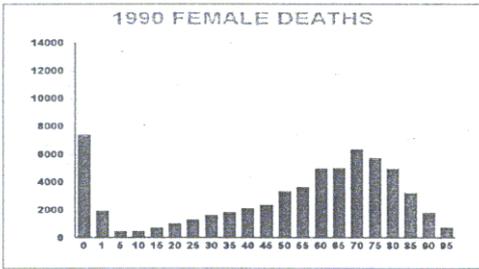
Author	Topic	Date of posting
<ul style="list-style-type: none"> • Peter Duesberg 		29 June 2000
Sam Mhlongo <ul style="list-style-type: none"> • Peter Duesberg 	Jose Zuniga? Private Internet co-owner	28 June 2000
Sam Mhlongo	?? Micrograph of the HIV	28 June 2000
David Rasnick	One more experiment revisited	28 June 2000
Zena Stein	Causal inference	28 June 2000
Zena Stein	Preventing HIV in infants	28 June 2000
Zena Stein	Agenda	28 June 2000
Zena Stein	Preventing mother-to-child transmission	28 June 2000
Zena Stein	Preventing HIV in infants - continuation	28 June 2000
Zena Stein	Causal inference	28 June 2000
<ul style="list-style-type: none"> • Peter Duesberg 		29 June 2000
Zena Stein	Causal inference - continuation	28 June 2000
<ul style="list-style-type: none"> • David Rasnick • Peter Duesberg 	Is this your best evidence?	29 June 2000
Ray Mabope	Nominations of presenters on the topics	29 June 2000
Ray Mabope	Wind down discussions	29 June 2000
<ul style="list-style-type: none"> • Robert Root-Bernstein • Robert Root-Bernstein • Ray Mabope 	Final comments Wind down discussions	30 June 2000
Ray Mabope	Programme for the panel meeting	29 June 2000
Christian Fiala	The future of this forum	9 July 2000
<ul style="list-style-type: none"> • Ray Mabope 		20 July 2000
Anthipi Pouris	Draft AIDS report for comments	31 August 2000
<ul style="list-style-type: none"> • Elliot Small 		12 September 2000

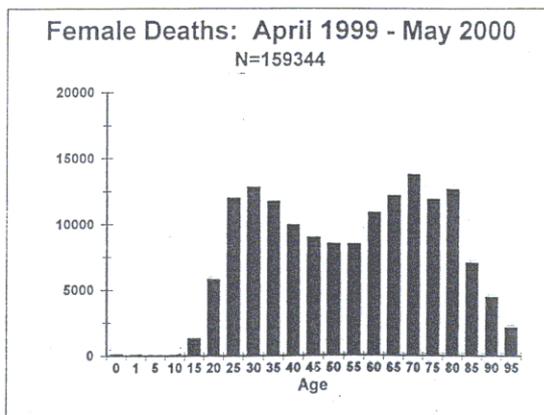
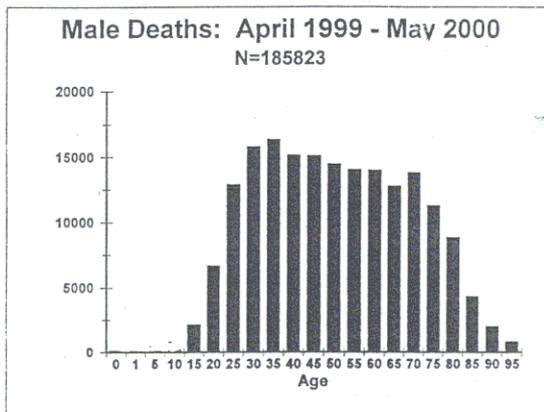
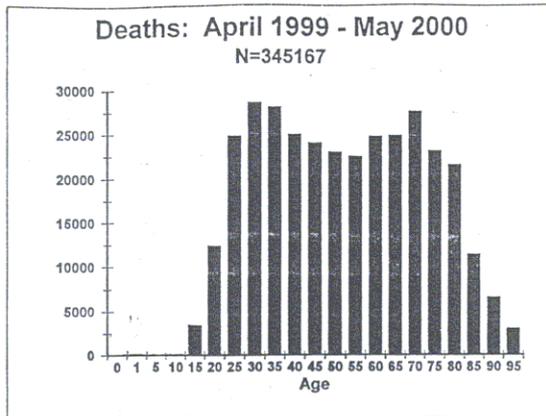
Appendix 2

Data on adult mortality presented by Dr MW Makgoba at the second meeting

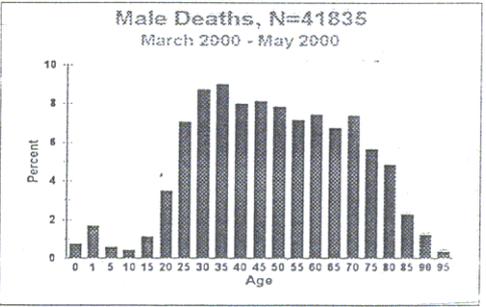
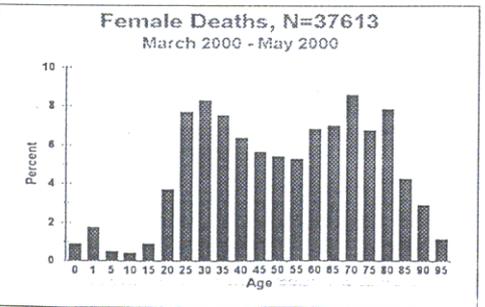
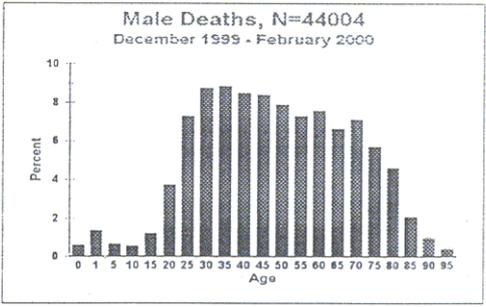
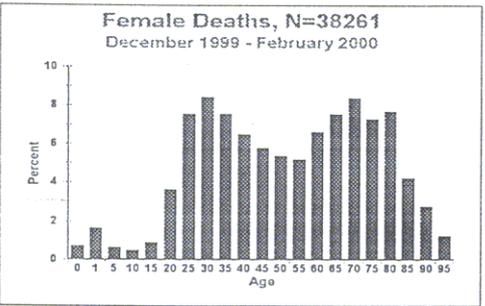
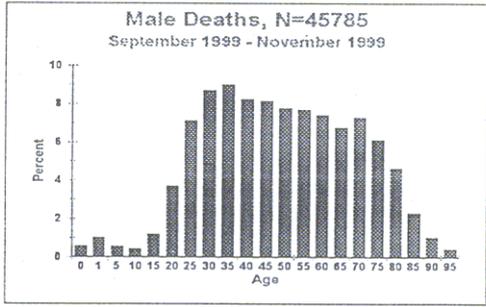
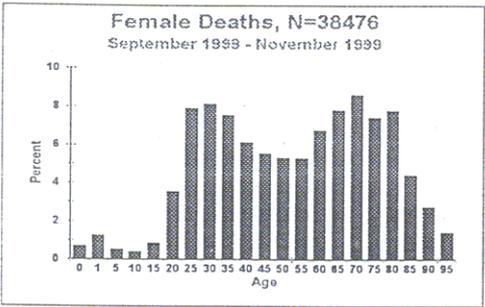
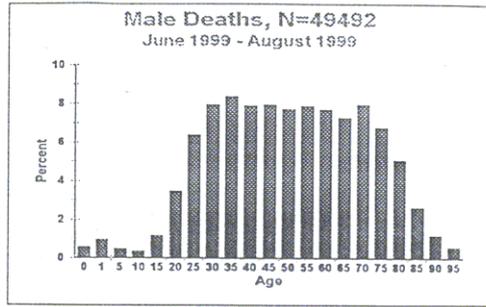
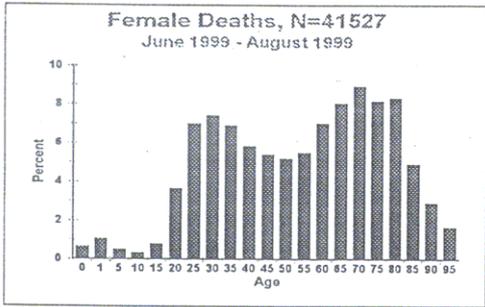
TOTAL AND NON-AIDS DEATHS (SA) AS PREDICTED BY MODEL



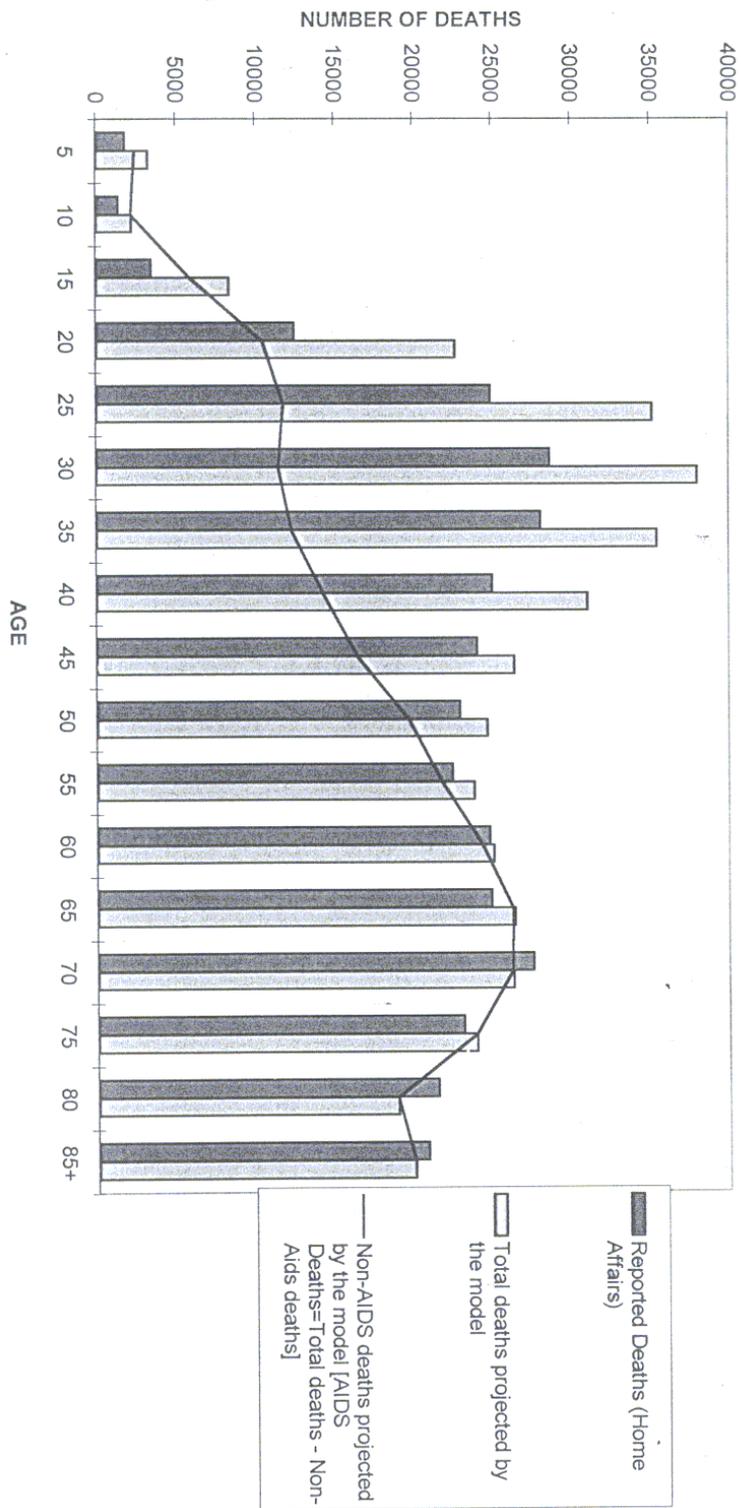




SOURCE: HOME AFFAIRS POPULATION REGISTER AGES 15+



MODEL FIT 1999/2000 DEATHS



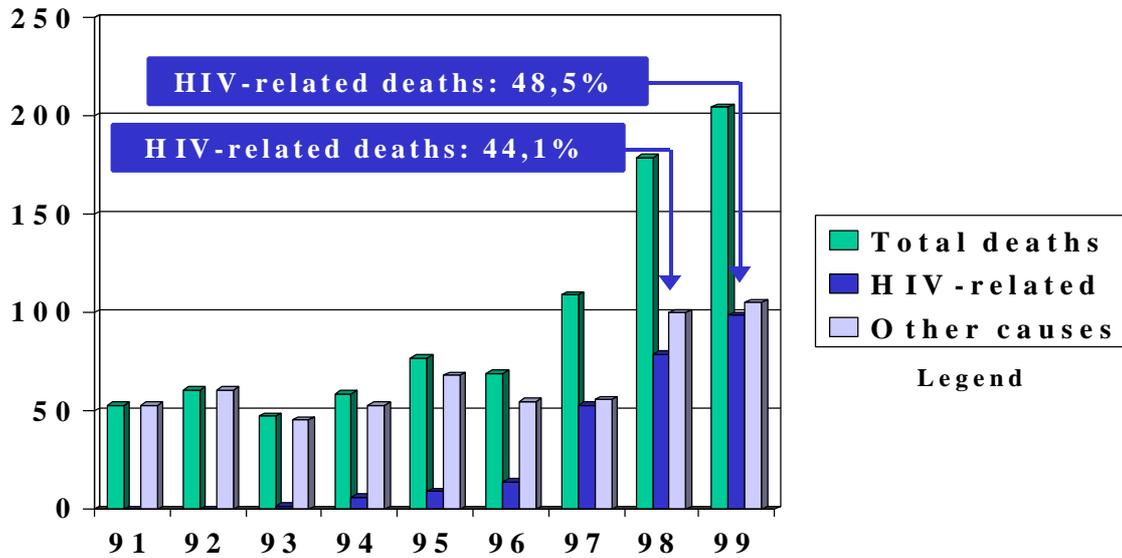
SHIFT IN AGE DISTRIBUTION OF ADULT DEATHS

$$\text{RATIO : } \frac{\sum \text{Deaths (15 - 49 yrs)}}{\sum \text{Deaths (50 + yrs)}}$$

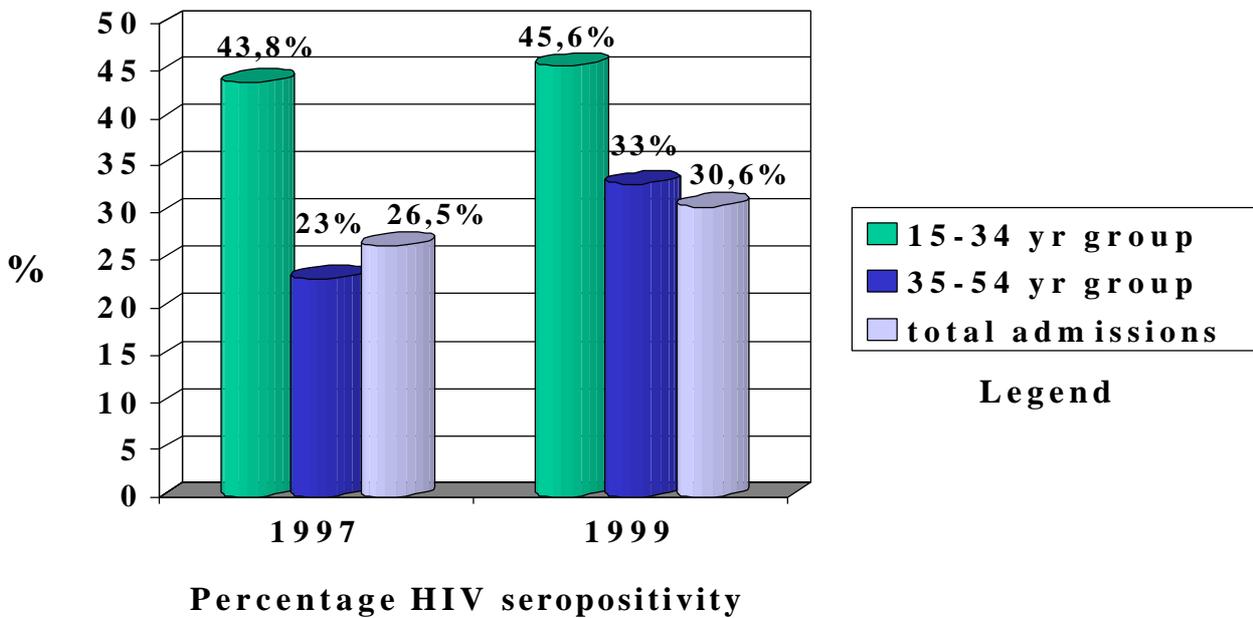
The larger this ratio, the more the distribution is skewed to younger ages

YEAR	MALE	FEMALE
1990	0.48	0.27
1994	0.75	0.39
1997/8	0.78	0.52
1999/00	0.87	0.68

Johannesburg Hospital: mortality trends, paediatric general wards



Anonymous unlinked testing in adult admissions to Medical Wards



Appendix 3

STATS SA response to the Medical Research Council's interpretation of deaths

Stats SA's response to the Medical Research Council's interpretation of deaths

(Officially Approved)

Stats SA

Pretoria, Tuesday 11 July 2000

The analysis of deaths statistics is very important in shedding light on the changing profile of diseases and causes of death. The statistics on overall deaths show the total number, and its age and sex distribution. It is only through the analysis of causes of death that one can attribute the observed level of mortality to certain causes of death. However, even with the availability of causes of death statistics, the problem of not stating the cause of death or mis-stating it, leads to some uncertainty in determining the exact contribution of the different causes of death.

The Medical Research Council (MRC) is reporting to have observed an increase in adult mortality in the younger age groups and is attributing this to HIV/AIDS. It supports this view by comparing 1999 statistics with that of 1990. The 1990 deaths statistics is shown to have the distribution of deaths towards the older ages (pre-AIDS) while the 1999 deaths is shown to have the distribution of deaths towards the younger adult ages. Stats SA has several problems with this interpretation and would like to suggest alternative approaches to the problem. The main points are as follows:

1. The 1990 deaths statistics are not geographically comparable with those of 1999.

The breakup of South Africa into the RSA (former RSA) and the former TBVC states took place over the period from 1976 to 1990. As each TBVC state 'gained independence' it was removed from the South African statistical system. The 1990 statistics were therefore referring to death statistics in which the former TBVC states were excluded, while the 1999 statistics included all these former homeland 'states'.

2. The distribution of deaths among Africans and those of non-Africans is different

In South Africa, Africans are a demographically younger population than whites or Indians or other Asians. As such the distribution of deaths among Africans is different from that found among the other population groups. The distribution of deaths among Africans tends to be more concentrated in the younger ages, and in the young adult ages while the distribution among whites and Indians or other Asians is more concentrated in the older ages. The Figures 1 and 2 attached show the 1990 distribution of deaths among Africans in the former RSA and Figure 3 shows the distribution of deaths among whites, Indians or other Asians and coloureds. Figure 1 shows that among African males in RSA in 1990 there was an appreciable number of deaths in the younger age groups. Among African females however, Figure 2 shows that this pattern is less marked. Among Indians and other Asians and whites, the pattern is reversed with an appreciable number of deaths in the older age groups. The 1999 deaths profile show similar profile as the 1990 one for Africans, albeit toned down a little because of the contribution of the other population groups. Because of the larger number of Africans in the population, they tend to swamp the graph. But large numbers of Africans were excluded from the 1990 illustration of the Medical Research Council. As such, the 1999 profile is not a drastically new profile as portrayed.

3. Causes of death statistics show that the largest proportion (27%) of deaths among males were attributed to unnatural causes.

The causes of death statistics for 1995 for all population groups and all of South Africa show that the largest proportion of causes of death among males was unnatural causes as shown in Figure 5. The breakdown shows that 27% of South African males die of accidents and violent deaths. This profile is therefore not necessarily fully attributable to HIV/AIDS.

4. A skewed distribution of deaths does not directly translate into a skewed distributed of death rates.

The profile of deaths reflects the effect of the age composition. A high number of deaths do not mean a high death rate. Only when the age structure is taken into account can we begin to say that deaths is high in certain age groups. The deaths rates computed for 1996 do not show a remarkably skewed distribution.

[Graphs attached]

Fig 1: Number of deaths among Africans, males, RSA 1990

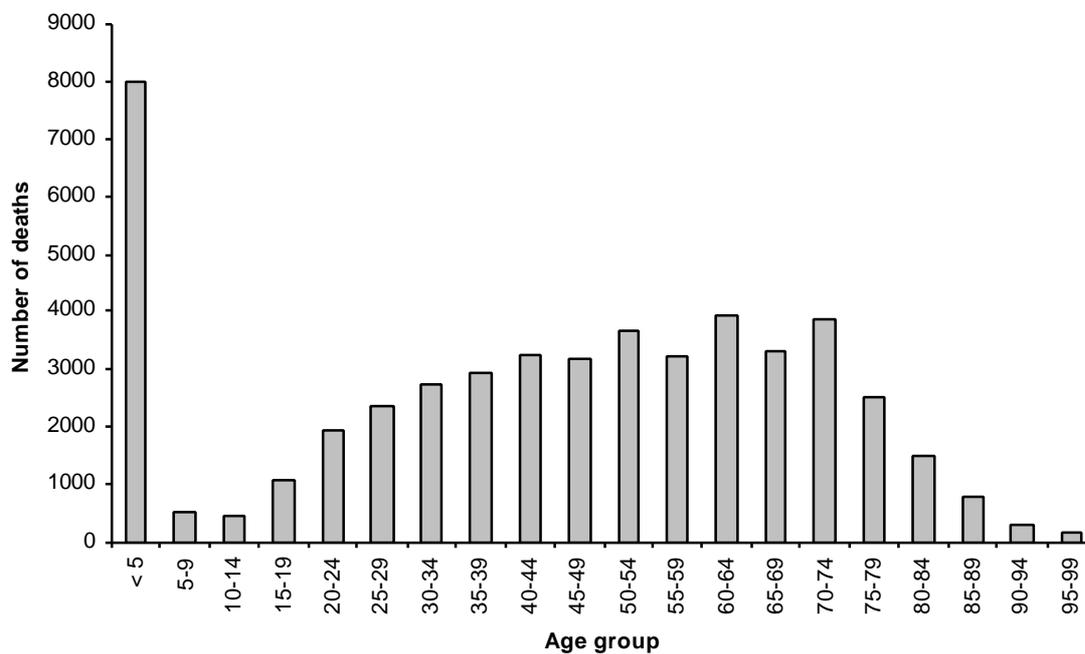


Fig 2: Number of deaths among Africans, females, RSA 1990

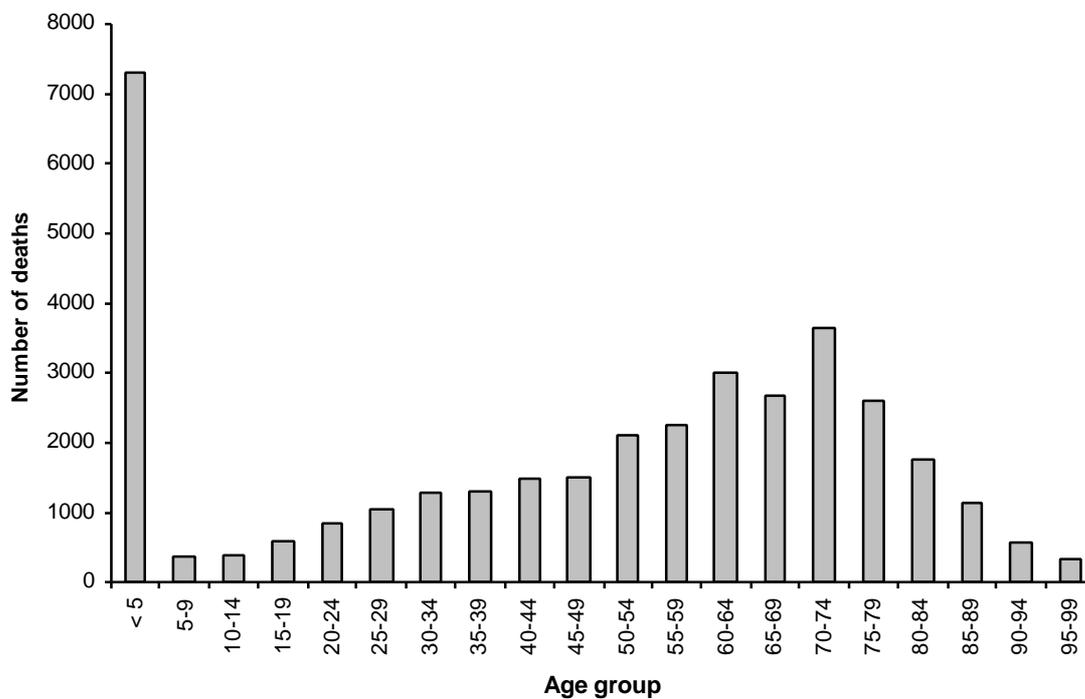


Fig 3: Number of deaths by population groups, RSA 1990

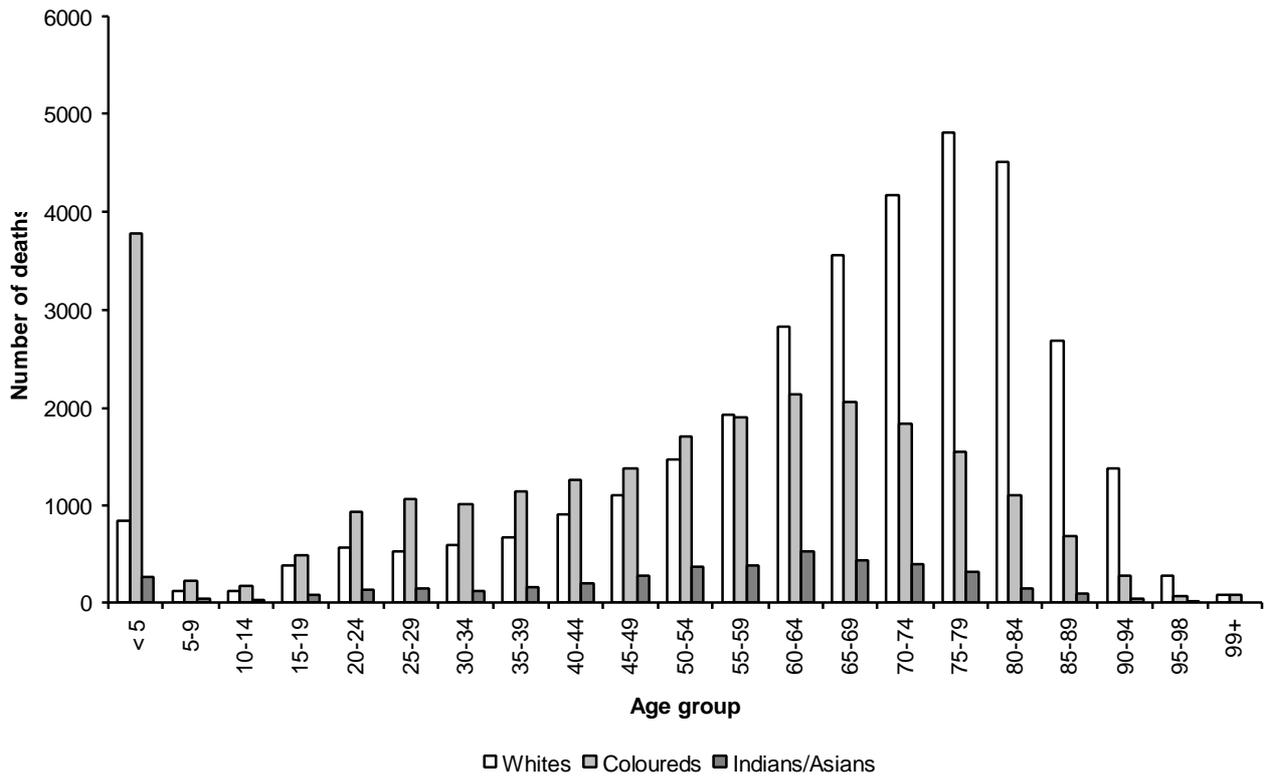


Fig 5: Distribution of total deaths by leading causes of death for males, RSA 1995

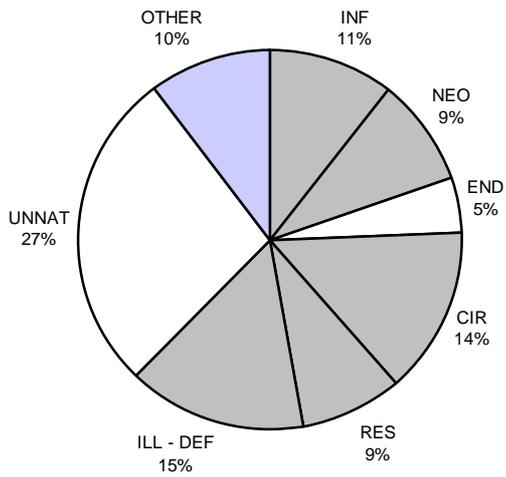
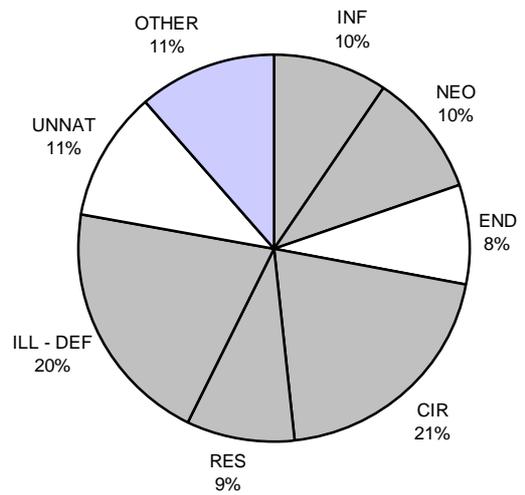


Fig 6: Distribution of total deaths by leading causes of death for females, RSA 1995



Key

Abbreviation

INF

NEO

END

CIR

RES

ILL - DEF

Full name

Infectious and parasitic diseases

Neoplasm

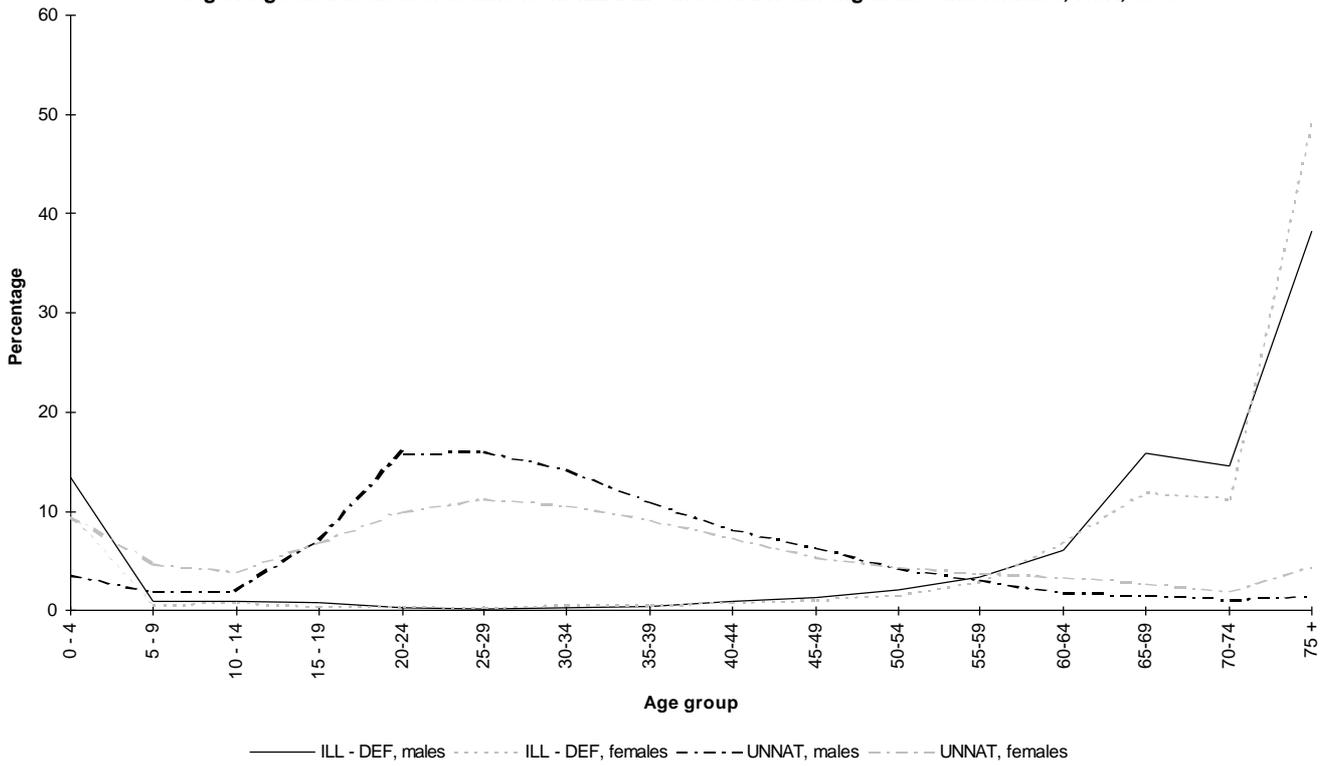
Endocrine, nutritional and metabolic diseases and immunity disorder

Diseases of the circulatory system

Diseases of the respiratory system

Ill-defined causes

Fig 7: Age distribution of deaths from ILL-DEF and UNNAT among males and females, RSA, 1995



UNNAT

Unnatural causes

Abbreviation	Full name
ILL - DEF	Ill-defined causes
UNNAT	Unnatural causes

Appendix 4

STATS SA rejoinder to the MRC's response

Rejoinder to the MRC's response

Stats SA, Pretoria

August 2000

Stats SA has had discussions with the MRC and most of their differences have been resolved. Stats SA would like to make the following clarifications:

1. Stats SA was asked by the Department of Home Affairs to produce a response to the newspaper article that appeared in Sunday Times. This response was not meant for publication, but it was meant as a spring board for further discussion. Stats SA raised issues of concern in this document.
2. Stats SA acknowledges that the MRC is mandated to do health-related research. The MRC was operating within its mandate in engaging in AIDS research and presenting its findings to the Presidential AIDS Review Panel. Stats SA supports the MRC in its research endeavours and dissociates itself from allegations that the MRC sought to discredit the government by presenting its findings to the AIDS Review Panel.
3. In accordance with the Fundamental Principles of Official Statistics, the National Statistical Office is entitled to comment on published statistics. The Sunday Times only gave a small extract of the actual presentation, but this was what Stats SA was asked to comment on as a matter of urgency.
4. Having later seen the more detailed presentation of the MRC, Stats SA agrees that the mortality profile, especially that of females, has changed over the past decade.
5. While it is hard to separate out deaths due to HIV/AIDS from those due to other causes, the mortality profiles portrayed suggest that the deaths in the younger ages could be possibly explained in part by the impact of the AIDS epidemic.
6. Prior to presentation of MRC's findings, there was no clear institutional framework for handling mortality research findings that could be controversial. An interdepartmental task team for mortality statistics has been formed by the Director-Generals of the Department of Health, Home Affairs, Welfare and Population Development, the Acting-Head of Stats SA and the President of the MRC. The Task Team comprises of representatives of all the above mentioned Departments. The Task Team is developing a coherent approach for the rapid processing and analysis of mortality and causes of death statistics. With this Task Team in place, unnecessary controversies will be minimised.