ABSTRACTS: HIV – GLOBAL AND LOCAL PERSPECTIVES

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SESSION 1
GLOBAL PERSPECTIVES

Chair: Dr D Wilks, Consultant Physician, Western General Hospital, Edinburgh, Scotland

GLOBAL EPIDEMIOLOGY OF HIV AND PREDICTING THE FUTURE SHAPE OF THE EPIDEMIC

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Abstract

After more than two decades of spreading, the devastating impact of HIV can be observed in some populations whereas in others the infection is more limited to particular high-risk groups. However, explaining differences in HIV spread is difficult.

Methods of analysing HIV prevalence data from generalised and concentrated epidemics and predicting the future trends in HIV incidence are reviewed along with factors controlling the potential for continuing and emerging HIV epidemics.[1,2]

In sub-Saharan Africa, where the epidemic has reached a high level, decline in HIV incidence is often being observed. As a new generation of susceptibles is exposed to the risk of infection, infections are further concentrating in marginalised sections of communities.[3] In other regions explosive local epidemics in injecting drug users are often observed but their scope for wider spread is poorly understood.

HIV surveillance and epidemiology has generated some of the best quality data available on disease distributions in developing countries.[4] Nonetheless the complex contact patterns and sensitivity of the system to small changes in parameter values has made prediction difficult. It is important that surveillance is sensitive to emerging HIV epidemics.

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Key words: HIV epidemiology, HIV surveillance, mathematical models.

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NORTH-SOUTH DIVIDE: DEMOGRAPHICS AND ETHICS

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Abstract

Despite spectacular twentieth century scientific and technological progress the world is more inequitable than it was 50 years ago. This is evident both in terms of access to healthcare for individuals, and in relation to the health of whole populations. Disparities in wealth and health within and between nations are widening inexorably and the rapidly expanding global economy has failed to reduce poverty and improve health for all. Billions of people live in degrading poverty with little if any access to healthcare, and disparities have been highlighted by the HIV/AIDS pandemic.

Universal moral and scientific ideals that potentially bind healthcare professionals to a common goal are considered as the basis from which to argue that we have an obligation to provide moral leadership backed by exemplary action to re-shape the future of world health. The challenges are complex and it is argued that an interdisciplinary approach is required.

Bioethics, an interdisciplinary field of activity about actions and relationships, has the ability to contribute to improving health globally if expanded to include the ethics of actions and relationships between institutions and nations.

Making such progress will require new paradigms of thinking to carry forward widely shared foundational values through transformational approaches.

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Key words: Bioethics, global health, globalisation, HIV.

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EFFECTING BEHAVIOURAL CHANGE

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Abstract
In the absence of effective vaccines, the mainstay of HIV prevention is through behaviour change. Interventions aimed at changing behaviour can be directed at individuals or at the broader social environment (structural interventions). The two approaches are not mutually exclusive, in fact it seems likely that individual behaviour change will best be sustained within a community that is broadly supportive of those behaviours. In addition, the broader cultural perspective of the community will greatly influence the feasibility of delivering an intervention within that community and will also affect how the recipients respond to it.

At an individual level interventions seek to change knowledge, skills and attitudes in order to delay sexual debut, reduce partner numbers, increase condom use and promote health-seeking behaviour to ensure timely and appropriate treatment for sexually transmitted infection.

The structural factors associated with HIV risk and prevention have been defined as physical, social, cultural, organisational, community, economic, legal or policy aspects of an environment that impede or facilitate a person's effort to avoid HIV infection. These structural factors can be addressed at various levels.

So much has been written about the difficulties of evaluating complex interventions that a framework for doing so has been established. Effecting behaviour change is difficult, measuring whether or not change has occurred is even more so. Self reporting of socially censured behaviour is notoriously unreliable, so triangulating behavioural data with objective measures of behaviour is desirable.

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Key words: Behaviour change, delay sexual debut, increase condom use, reduce partner numbers, self reporting of socially censured behaviour, structural interventions.

Sponsors: None.

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SESSION 2
CONTRASTING DAILY PRACTICE

Chair: Dr R Fox, Consultant in Infection and Tropical Medicine, Gartnavel General Hospital, Glasgow, Scotland

NATURAL HISTORY OF DISEASE IN AFRICA: THE CONTRAST WITH DEVELOPED WORLD PRACTICE AND THE IMPLICATIONS OF BROADENED ANTIRETROVIRAL TREATMENT ACCESS FOR CLINICAL CARE

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Abstract
HIV dominates clinical practice in most regions of sub-Saharan Africa and places an enormous burden on healthcare services. In-patient HIV prevalence figures vary from 13% in west Africa, 40% in east Africa to 75% in southern Africa. The primary HIV co-infections are tuberculosis, pneumococcal disease community-acquired pneumonia, bacteraemic illness particularly with non-typhi Salmonella, cryptococcal disease and malaria. A large proportion of HIV co-morbidity remains undiagnosed and 'cause of death' reporting is very limited.

Tuberculosis, pneumococcal disease and malaria occur at all stages of HIV-infection but rates of disease increase as CD4 counts fall.[1,2] Non-typhi Salmonella bacteraemia and

cryptococcal disease occur primarily at CD4 counts below 200.[3]

Case fatality from these conditions varies depending on access to care and health seeking behaviour. Prevention of co-infections has been a primary area of interest in recent years in the absence of widely available anti-retroviral therapy (ART). Isoniazid for six months is effective at preventing tuberculosis in smear-positive individuals but has no clear impact on survival.[4] Co-trimoxazole appears to improve survival over a 12-month period by as much as 40%, although the exact mechanism by which this is achieved is unclear. Uptake of these prophylactic approaches has been variable, in part due to uncertainty amongst national health planners as to how study findings can be applied locally.[5]

Although early HIV mortality is higher in Africa than elsewhere, the majority of deaths occur at advanced HIV/AIDS. Median survival times with CD4 counts below 200 are around nine months.[6] Anti-retroviral treatment access is steadily increasing and the benefits in survival are established. In HIV-infected Ugandan adults over the first 12 months of therapy, death rates have fallen to between 6–20% (depending on CD4 count at initiation) of the pre-ART levels.

Questions remain as to what can be achieved with ART. Is it realistic to expect similar improvements in outcome to those in the developed world? Aside from economic and structural problems, therapeutic problems specific to Africa exist. Will immune reconstitution disease (to tuberculosis and cryptococcus in particular) be important? Will effective immune reconstitution take place for malaria and *S. pneumoniae*? Will other chronic health problems (geohelminths, malnutrition) affect ART success? Careful surveillance of ART use in Africa will be essential.

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Key words: Africa, ART, co-infections, HIV, natural history, opportunistic infections, prophylaxis.

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HIV CARE IN MANCHESTER

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SESSION 3
CURRENT SCOTTISH PERSPECTIVES ON HIV

Chair: Dr G Scott, Consultant Physician, NHS Lothian, Scotland

LOCAL EPIDEMIOLOGY: THE CHANGING FACE OF HIV IN SCOTLAND

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Abstract

It is now 20 years since the first case of AIDS was diagnosed in Scotland and since then 1,221 cases of AIDS and 4,023 cases of HIV have been reported, by clinicians and diagnostic laboratories respectively, to the Scottish Centre for Infection and Environmental Health. The response to the epidemic in Scotland has been a remarkable one and, essentially, the four quinquenniums from 1984–2004 each tell a different story. During the first, much was done to identify the extent of the problem and the services required to manage HIV infected persons and prevent HIV infection; HIV testing of blood donors and the heat treatment of factor VIII was implemented to protect transfusion recipients and haemophiliacs, and 'harm reduction' was accepted as a concept so that interventions such as needle and syringe exchange and methadone maintenance therapy could be established to prevent infection being transmitted among injecting drug user populations.

The second quinquennium saw the growth of the voluntary sector, particularly that associated with supporting HIV infected persons many of whom were now on AZT and other therapies. During this period,

harm reduction interventions for injectors developed rapidly and this coincided with a decline in incidence of infection among this population.

The third quinquennium was dominated by the administration of highly active anti-retroviral therapy which completely altered the dynamics of HIV in Scotland; with numbers of new diagnoses remaining steady at around 150 per year and the numbers of deaths due to HIV declining rapidly, the overall prevalence of infection increased year on year. Care of the HIV infected patient moved from the in-patient to the out-patient setting.

The fourth quinquennium saw the continuing success of anti-retroviral therapy but numbers of diagnoses began to increase to around 250–300 per year; this increase was principally due to a rise in the number of diagnoses among persons who had originated from African countries and diagnoses in gay men, among whom HIV testing increased considerably as a result of a drive to make such testing routine for attendees of genito-urinary medicine clinics.

The challenges facing us today are very different from those in the past but are no less demanding. One of the principal challenges will be to provide resources for the ever-increasing numbers of persons who will be living with HIV and those who should be offered an HIV test.

Key words: AZT, epidemic in Scotland, 'harm reduction', highly active anti-retroviral therapy, HIV test, manage HIV infected persons

Sponsors: None.

Declaration: No conflict of interest declared.

THE CHALLENGE OF AN AGEING HIV-POSITIVE POPULATION

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Abstract

Metabolic abnormalities, sometimes accompanied by morphological changes, observed during anti-retroviral therapy strikingly resemble the metabolic syndrome. The metabolic syndrome, or 'syndrome X', is increasingly diagnosed in the setting of ageing populations in general medicine and consists of fat accumulation in the abdomen or viscera accompanied by insulin resistance, hypertension, glucose intolerance and dyslipidaemia.

Dyslipidaemia and insulin resistance commonly precede morphological changes, and individuals who develop metabolic abnormalities do not seem to invariably develop morphological changes. It is presently unclear to what degree, if any, lipid elevations or insulin resistance are predictive of the development of fat loss or fat accumulation. Thus, lipid and insulin sensitivity abnormalities may be considered separately from morphological change.

Some mechanisms by which insulin resistance and dyslipidaemia may arise are reported, and these changes can be reproduced in healthy volunteers receiving anti-retrovirals. Studies in HIV-negative volunteers indicate that insulin resistance can be induced with a single dose of indinavir and multiple doses of Kaletra and that modest shifts in cholesterol and triglycerides are seen with some protease inhibitors in particular ritonavir. Studies using radiolabelled lipid and glucose, and using *in vitro* systems have indicated that some protease inhibitors interfere with glucose uptake receptors (GLUT 4 located on adipocytes and myocytes, and GLUT 2 located on pancreatic islet cells), hepatic output of very-low-density lipoprotein (VLDL) and peripheral lipoprotein lipase activity. Nucleoside analogue drugs have been associated with reduced peripheral lipid trapping and may disrupt metabolism in multiple tissues through mitochondrial mechanisms.

Once established the metabolic syndrome may be a vicious, self perpetuating cycle with few treatment options. Notably, removal of the trigger may not lead to reversal. Lipid accumulation in liver, pancreas, skeletal muscle and visceral sites, due to abnormal peripheral storage, adds to insulin resistance, further worsening peripheral lipid storage. Thus, avoidance of establishing the syndrome may be critical.

The lipid profile that accompanies advancing HIV infection often includes a low high-density lipoprotein (HDL), and elevations in triglycerides. During anti-retroviral therapy elevations in total and low-density lipoprotein (LDL) cholesterol (in particular the high risk LDL particles) occur although HDL may also modestly 'correct' upwards. The resultant lipid profile is a typical high risk profile for future cardiovascular disease. Additionally, insulin resistance has been demonstrated to be a risk factor for cardiovascular disease and diabetes mellitus is considered in NCEP guidelines to be a cardiovascular disease 'risk equivalent'. Thus, the metabolic disturbances that accompany HIV and anti-retroviral therapy are likely to have important consequences for future cardiovascular health. The DADS study has reported that cumulative years on combination anti-retroviral therapy is independently associated with the risk of myocardial infarction in persons with HIV infection. Of note, total cholesterol at entry into DADS was independently associated with the risk of cardiovascular events. These data support the possibility that people with HIV on

therapy may be at greater risk of cardiovascular disease than the general population. Given that durable control of HIV with anti-retrovirals has led to vast improvements and perhaps 'normalisation' of life-expectancy for people with HIV infection, this makes persons with HIV appropriate targets for interventions against modifiable cardiovascular disease risk factors. Guidelines for the management of lipids and cardiovascular risk in HIV have been put forward in several countries and generally indicate that lipid abnormalities should be managed along NCEP guidelines.

Clearly, the best way to limit the need for additional interventions is to endeavour to choose anti-retroviral combinations that durably suppress HIV but also have the lowest risk of triggering metabolic disturbances. In individuals established on therapy, the primary approach to management, wherever possible, is to manipulate an individual therapy to reduce the contribution of their anti-retroviral regimen to the metabolic abnormalities before pursuing intervention with additional agents.

Further reading

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Key words: Anti-retroviral therapy, DADS study, dyslipidaemia, indinavir, insulin resistance, Kaletra, metabolic syndrome, protease inhibitors, ritonavir.

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SESSION 4
PROSPECTS FOR AN HIV VACCINE

Chair: Dr R Brettle, Consultant Physician, Western General Hospital, Edinburgh, Scotland

MARJORIE ROBERTSON LECTURE

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THE ORIGINS AND EVOLUTION OF HIV

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Abstract

Studies of viral evolution use comparisons of viral nucleotide sequences to shed light on the origins of human viruses and the rates and patterns of their diversification.[1] The results can have implications for both therapy and vaccine development. The AIDS viruses, HIV-1 and HIV-2, have their origins among the non-pathogenic simian immunodeficiency viruses (SIVs) infecting numerous species of African primates.[2] HIV-1 groups M, N and O represent three independent transmissions of SIVcpz from chimpanzees, while SIVsmm from sooty mangabeys has been transmitted to humans on numerous occasions to give rise to HIV-2. The vast majority of AIDS cases worldwide are due to strains of HIV-1 group M, the ancestry of which dates back to around 1930.[3] Evolution over the subsequent 70 or so years has resulted in HIV-1 group M strains with envelope protein sequences exhibiting about ten times more diversity than contemporary influenza A or measles virus proteins.[1] Recombination among divergent viral lineages has also added greatly to the complexity of HIV-1 variation, and implies that multiple infections have not been rare. These aspects of the evolutionary pattern of HIV-1 pose severe challenges for vaccine development.

Given the close genetic similarity of humans and chimpanzees, it is particularly interesting to ask why natural SIVcpz infection of chimpanzees does not appear to cause immunodeficiency, and how the virus evolved upon transmission to humans. The origin of the SIV infection in chimpanzees, by acquisition and recombination of viruses from two different monkey species, has recently been elucidated.[4] Generally, there is a need to know much more about the natural reservoir of SIVcpz in chimpanzees.

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Key words: Chimpanzee, evolution, HIV-1, recombination.

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PROSPECTS FOR AN HIV VACCINE

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