HUMAN IMMUNODEFICIENCY VIRUS: THE EDINBURGH EPIDEMIC

RAYMOND PATRICK BRETTE BSc (Med Sci) MB ChB FRCP

A DISSERTATION SUBMITTED TO THE FACULTY OF MEDICINE IN CANDIDACY FOR THE DEGREE OF DOCTOR OF MEDICINE (MD)

EDINBURGH UNIVERSITY

1994
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Tables</td>
<td>18</td>
</tr>
<tr>
<td>List of Figures</td>
<td>24</td>
</tr>
<tr>
<td>Statement by author</td>
<td>28</td>
</tr>
<tr>
<td>Dedication</td>
<td>28</td>
</tr>
<tr>
<td>Abstract</td>
<td>29</td>
</tr>
<tr>
<td>Research Grants</td>
<td>30</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>33</td>
</tr>
<tr>
<td>Publications</td>
<td>34</td>
</tr>
<tr>
<td>List of Abbreviations</td>
<td>36</td>
</tr>
<tr>
<td>Summary</td>
<td>40</td>
</tr>
<tr>
<td><strong>SECTION I - INTRODUCTION</strong></td>
<td>41</td>
</tr>
<tr>
<td><strong>CHAPTER 1</strong></td>
<td>42</td>
</tr>
<tr>
<td><em>Human Immunodeficiency Virus and The Acquired Immune Deficiency Syndrome</em></td>
<td>42</td>
</tr>
<tr>
<td>Introduction</td>
<td>42</td>
</tr>
<tr>
<td>The Centers for Disease Control Clinical Staging System</td>
<td>44</td>
</tr>
<tr>
<td>Primary HIV Infection</td>
<td>45</td>
</tr>
<tr>
<td>Early Manifestations of HIV Infection</td>
<td>46</td>
</tr>
<tr>
<td>Late Manifestations of HIV Infection</td>
<td>46</td>
</tr>
<tr>
<td>WHO staging system</td>
<td>48</td>
</tr>
</tbody>
</table>
Laboratory Features of HIV Infection 49
  Immunology 49
  Haematology 50
The General Epidemiology of AIDS and HIV 51

Appendix 63
  The surveillance definitions of AIDS 63
  WHO Classification System 67
    WHO Asymptomatic 67
    WHO Symptomatic 67
  WHO - AIDS 68

References for Chapter 1 69

CHAPTER 2 75
Injection Drug Use 75
  Introduction 75
  IDU related infections 80
  Epidemiology of IDU infections 82
  Injection Drug Use and HIV/AIDS 88
  Conclusions 90

Appendix 91

References for Chapter 2 102

CHAPTER 3 115
Clinical features of drug use and drug use related HIV 115
Introduction

Complications of Drug Use - non infection related

Drug effects

Pulmonary oedema

Trauma

Sinusitis

Polyarteritis nodosa

Pulmonary hypertension

Immunology

Endocrinology

Neurological effects

Complications of Drug Use - IDU related infections

Epidemiology and frequency of IDU related infections

Susceptibility of drug users to infections

The effect of HIV on IDU problems

Effect of HIV on Non infective IDU problems

Effect of HIV on IDU related infection problems

Medical problems of HIV infected drug users

Conclusions

References for Chapter 3

CHAPTER 4

Injection Drug Use related HIV Infection in Edinburgh
Method 144
Results 145
Discussion 153
Conclusions 157
References for Chapter 4 158
SECTION II 161
HOSPITAL BASED CLINICAL SERVICES FOR THE HIV/AIDS EPIDEMIC 161
CHAPTER 5 162
Counselling and screening of HIV infected patients 162
  Introduction 162
  The City Hospital Counselling and Screening Clinic 163
    Pre Test Counselling 164
    Post test counselling 164
    Further Management 165
  Results of the first year of the service 165
  Discussion 167
  Conclusions 168
References for Chapter 5 169
CHAPTER 6 170
Hospital Health care for HIV Infection with particular reference to Injecting Drug Users - a review of services outside the UK 170
  Introduction 170
CHAPTER 7

Outpatient medical care of HIV Infection with particular reference to Injecting Drug Users

Introduction 183

Patients and Methods 184

HIV service at the City Hospital 185

Results 188

Initiating and Maintaining Contact 189

Risk behaviour 198

Discussion 201

Problems of health care for drug users 202

Edinburgh model of care for HIV infected drug users 203

Evaluation of the Aim of Initiating and Maintaining Contact 205

The effect of HIV Clinics on other medical services 206

Risk Behaviour 207
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conclusion</td>
<td>207</td>
</tr>
<tr>
<td>References for Chapter 7</td>
<td>209</td>
</tr>
<tr>
<td><strong>CHAPTER 8</strong></td>
<td>210</td>
</tr>
<tr>
<td>Harm Reduction for IDU Related HIV</td>
<td>210</td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
<td>210</td>
</tr>
<tr>
<td>The History of Harm Reduction</td>
<td>212</td>
</tr>
<tr>
<td>Maintenance Methadone Treatment Programmes</td>
<td>212</td>
</tr>
<tr>
<td>Amsterdam</td>
<td>213</td>
</tr>
<tr>
<td>The link between IDU related HIV and equipment availability</td>
<td>213</td>
</tr>
<tr>
<td>Is Harm Reduction effective?</td>
<td>214</td>
</tr>
<tr>
<td>Methadone</td>
<td>215</td>
</tr>
<tr>
<td>Injecting equipment</td>
<td>219</td>
</tr>
<tr>
<td>Outreach education, intervention programmes and cleaning of equipment</td>
<td>222</td>
</tr>
<tr>
<td>Safety of Harm Reduction</td>
<td>225</td>
</tr>
<tr>
<td>Limitations of Harm Reduction</td>
<td>226</td>
</tr>
<tr>
<td>Conclusion</td>
<td>229</td>
</tr>
<tr>
<td>References for Chapter 8</td>
<td>231</td>
</tr>
<tr>
<td><strong>CHAPTER 9</strong></td>
<td>244</td>
</tr>
<tr>
<td>Inpatient Health Care Utilisation for HIV Infection with particular reference to Injecting Drug Users</td>
<td>244</td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
<td>244</td>
</tr>
<tr>
<td>Method</td>
<td>244</td>
</tr>
<tr>
<td>Title</td>
<td>Page</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Results</td>
<td>245</td>
</tr>
<tr>
<td>Admissions</td>
<td>250</td>
</tr>
<tr>
<td>Bed Days</td>
<td>254</td>
</tr>
<tr>
<td>Annual Bed Day Use</td>
<td>262</td>
</tr>
<tr>
<td>First Admissions</td>
<td>266</td>
</tr>
<tr>
<td>Discussion</td>
<td>268</td>
</tr>
<tr>
<td>Clinical Staging: AIDS and Non AIDS</td>
<td>268</td>
</tr>
<tr>
<td>Immunological Staging</td>
<td>270</td>
</tr>
<tr>
<td>Gender</td>
<td>270</td>
</tr>
<tr>
<td>Risk Activity</td>
<td>271</td>
</tr>
<tr>
<td>Conclusion</td>
<td>272</td>
</tr>
</tbody>
</table>

References for Chapter 9  274

CHAPTER 10  277

The health service problems of IDU related health care  277

Introduction  277

Characteristics of IDU which affect the Health Service  277

Health Care Service for IDU  278

Health Care Service for IDU related HIV  278

RIDU Edinburgh  279

Problems of RIDU, Edinburgh  280

Risk of Infection and Isolation requirements  280

Escort duty  280
CHAPTER 14

Analysis of Enrolment, Progression, Survival, Mortality and Baseline Covariates in the Edinburgh City Hospital Cohort

Introduction 354

Methods 354

Patients 354

Laboratory Methods 354

Statistical Methods 355

Results 357

Cohort Summary 357

Follow-up Summary 357

Diagnoses and Mortality 358

Enrolment Pattern 360

Progression from enrolment 362

Survival from diagnoses 368

Zidovudine Therapy 374

Slopes of CD4 Loss 376

Discussion 378

Methodological issues 378

The Edinburgh cohort 379

Progression to AIDS and CD200 379
Survival from AIDS 383
Survival from CD200 386
Non AIDS related Deaths 386
Zidovudine 387
Conclusions 388
References for Chapter 14 389

CHAPTER 15 394

Progression of HIV disease in injection-drug-users: a follow-up of the Edinburgh City Hospital IDU seroconverters 394

Introduction 394

Methods 394

Study Setting and Design 394
Laboratory Methods 398
Statistical Methods 398

Results 399

Cohort Description 399
Progression and Mortality Rates 399
Influence of cofactors on progression 404
Influence of zidovudine on progression 406
Parametric Estimates of AIDS and Mortality Curves 408
Survival 413
CD4 loss 413

Discussion 414
CHAPTER 15

Edinburgh cohort 414
Progression to AIDS and CD200 415
Non AIDS related Deaths 416
Injection Drug Users 416
Women 416
Age 417
Survival from CD200 and AIDS 418
HLA Haplotypes 418
Zidovudine 418
Conclusion 419

References for Chapter 15 420

CHAPTER 16 424

The association of HLA types with rapid and slow progression of HIV disease 424

Introduction 424
Methods 425
Study Setting and Design 425
Laboratory Methods 425
Statistical Methods 425
Results 426
Discussion 432
Conclusion 434

References for Chapter 16 436
CHAPTER 17

Clinical features of HIV in Edinburgh

Introduction 439
Method 439
Results 439
  Pattern of referral 440
  Morbidity 445
  Mortality 469
Discussion 473
  Enrolment 473
  Non AIDS clinical events 474
  Non AIDS mortality 476
  AIDS defining events 477
  AIDS deaths 480
Conclusions 481
Appendix 483
References for Chapter 17 486

CHAPTER 18

Heterosexual Transmission of HIV in Edinburgh

Introduction 491
Patients and Methods 491
  Laboratory Methods 492
Morbidity (Chapter 17) 526
Inpatient medical care (Chapter 9) 527
Mean CD4 count at the time of diagnosis of AIDS. 528
Survival (Chapter 14) 528
Conclusions 529

References for Chapter 19 532

CHAPTER 20 533

Summary 533

Injection Drug Use 533
Injection Drug Use related HIV 533
IDU related HIV in Edinburgh 534
Clinical services for IDU related HIV 535
Alternate site testing 535
Models of care for IDU related HIV 535
Harm reduction 537
Inpatient resource utilisation 537
HIV services for prisoners 538
Problems for the health care service 539
Initial use of anti-retroviral agents in IDU related HIV 539
Natural History of HIV with particular reference to IDU related HIV 540
Classification of HIV disease 540
Progression of HIV disease 541
Clinical features of HIV with particular reference to IDU related HIV 542

Outcome measures or quality of care for HIV/AIDS 543

Heterosexual Transmission of HIV 544

Postscript 545
List of Tables

Table 1.1: Classification of effects of HIV infection 44
Table 1.2: WHO/CDC classification system for HIV 48
Table 2.1: IDU Related HIV Seroprevalence -British Isles 91
Table 2.2: IDU Related HIV Seroprevalence -Europe 93
Table 2.3: IDU Related HIV Seroprevalence -American Continent 99
Table 2.4: IDU Related HIV Seroprevalence -Oceania 101
Table 3.1: Comparison of Drug, IDU and HIV related problems 116
Table 3.2: Medical (non infection) problems of Drug Use 119
Table 3.3: IDU related infections 128
Table 4.1: Frequency and HIV infection of individuals by year of entry to injection drug use in Edinburgh 146
Table 4.2: Relationship between year of entry to IDU and HIV infection 148
Table 4.3: Relationship between needle sharing and HIV infection 148
Table 4.4: Relationship between Hepatitis B markers and HIV infection 148
Table 4.5: Injection Drug Use related illness: hospital Discharges for Lothian 1976-86 149
Table 4.6: Relationship between needle sharing and HIV infection 151
Table 4.7: The location of needle sharing in drug users returning to Edinburgh 152
Table 5.1: City Hospital Counselling Clinic results: October 1985 - September 1986 166
Table 7.1: Appointments made and missed appointments (DNA) for 2 months of each year, 1985-1989 189
Table 7.2: Monthly HIV appointments and missed appointments (DNA), November 1985-May 1987

Table 7.3: Total appointments made and missed appointments (DNA) for each 6 month period from 1986-1987

Table 7.4: Number of new patients referred to the RIDU by half year 1985-1989

Table 7.5: HIV appointments by half year during 1989 and 1990

Table 7.6: Frequency tabulation of missed appointments during 1989-90

Table 7.7: Summary of missed appointments during 1989-90

Table 7.8: Cross tabulation of the number of patients attending during 1989 and 1990 categorised by the number of missed appointments

Table 7.9: Annual number of patients lost to follow up by year

Table 7.10: Drug users attending the City Hospital assessed as injecting more than 50% of the visits during the year or at least once during the year

Table 7.11: Drug users attending the City Hospital assessed as using opiates more than 50% of the visits during the year and at least once during the year

Table 8.1: IDU related HIV and the use of methadone

Table 9.1 Transmission category and gender of all out patients, number admitted and mean age at admission

Table 9.2: Total number of admissions, number of people attending the clinic and mean number of admissions per patient for AIDS and Non-AIDS admissions and CD4 count of greater or less than 200 cells/cumm

Table 9.3: Average length of stay for AIDS or Non-AIDS Admissions and for those with a CD4 Count of less than or greater 200 cells/cumm, by year of admission

Table 9.4: Average length of stay by clinical (AIDS and Non-AIDS) and immunological staging (< or >CD200) for transmission category and gender
Table 9.5: Average annual bed days per living patient for clinical (AIDS or Non-AIDS) or immunological staging (< or > CD200) by transmission category and gender

Table 9.6 Clinical and immunological status on first admission for transmission category and gender

Table 12.1: Patient demographic details and medication

Table 12.2: Zidovudine pharmacokinetic parameters

Table 12.3: GAZT pharmacokinetic parameters

Table 12.4: Summary of pharmacokinetic parameters for zidovudine

Table 12.5: Summary of pharmacokinetic parameters for glucuronide of zidovudine (GAZT)

Table 12.6: Wilcoxon comparison of samples by pairs for zidovudine pharmacokinetic parameters

Table 12.7: Wilcoxon comparison of samples by pairs for GAZT pharmacokinetic parameters

Table 12.8: CDC status of patients commenced on zidovudine

Table 12.9: CDC Category and risk factor of patients who developed side effect zidovudine

Table 12.10: Transfusion requirements of patients becoming anaemic on zidovudine according to CDC category and risk factor

Table 12.11: Defaults from HIV medical clinic according to drug use

Table 12.12: Recruitment into clinical trials June 1989-October 1992

Table 12.13: Length of trial treatment and number of missed appointments

Table 13.1: WHO interim proposal for staging of HIV infection

Table 13.2: CDC/WHO classification of HIV infection
Table 13.3: Modified AIDS case definitions: reportable cases from the Edinburgh City Hospital Cohort 341

Table 13.4: Modified AIDS case definitions: reportable cases in drug users from the Edinburgh City Hospital Cohort 342

Table 13.5: Cross-tabulation of when the proposed new AIDS definitions were met by 288 patients enrolled in 1988 or later 343

Table 13.6: Lifetables from CD200 (x1) to death, CD200 (x2) to death and AIDS (1987) to death 344

Table 13.7: Selected lifetables for injecting drug users and other patients 346

Table 14.1: Clinical endpoints for cohort 359

Table 14.2: Regression of root of enrolment CD4 count on cofactors 361

Table 14.3: Progression and mortality rates from enrolment for whole cohort and IDUs only 365

Table 14.4: Cofactor effects on progression from enrolment to CDC stage IV, AIDS and death 367

Table 14.5: Survival from AIDS, CDC stage IV and CD200 371

Table 14.6: Cofactor effects on survival from CD200, CDC stage IV and AIDS 373

Table 14.7: Use of zidovudine 1987 - 1992 375

Table 14.8: Regression of slope of root CD4 decay on cofactors 377

Table 15.1: Progression and mortality rates for Edinburgh City Hospital IDU seroconverters 401

Table 15.2: Covariate effects on mortality and progression to AIDS, CDC stage IV, AIDS and CD200 405

Table 15.3: Effect of zidovudine on mortality and progression to AIDS and CDC stage IV 407
Table 15.4: Survival from AIDS, CDC stage IV and CD200

Table 16.1: Numbers typed positive for various antigens

Table 16.2: Results of a proportional hazards analysis of the effect of A1-B8-DR3 on progression to clinical endpoints

Table 16.3: Rates of CD4 loss in 164 patients: 41 patients per quarter

Table 17.1: Risk activity of the Edinburgh City Hospital cohort analysed by year of first attendance

Table 17.2: Clinical features (modified WHO code, Non-AIDS) at first visit by year

Table 17.3: Clinical features (modified WHO code, AIDS) at first visit by year of presentation

Table 17.4: Clinical features (modified WHO code, Non-AIDS) at first visit by risk activity

Table 17.5: Clinical features (modified WHO code, AIDS) at first visit by risk activity

Table 17.5a: Clinical features (modified WHO code, AIDS) at first visit by risk activity excluding AIDS events prior to first visit at the City Hospital

Table 17.6: Clinical features (modified WHO code AIDS and Non-AIDS) at first visit by gender

Table 17.7: Cumulative number of clinical events (modified WHO codes, Non AIDS) by risk activity

Table 17.8: Rate of common clinical conditions (Non AIDS) by risk activity

Table 17.9: Cumulative number of clinical events (modified WHO codes, Non-AIDS) by gender with and without homo/bisexuals

Table 17.10: Clinical features of patients with an index diagnosis of AIDS by risk activity

Table 17.11: AIDS incidence/100 person years for risk groups
Table 17.12: Cumulative number of clinical events for AIDS (modified WHO codes) by risk activity 463

Table 17.13: Cumulative number of clinical events (AIDS) expressed as rates/100 person years of follow up (modified WHO codes) by risk activity 465

Table 17.14: Cumulative number of clinical events (modified WHO codes, AIDS) by gender with and without homo/bisexuals 469

Table 17.15: Mortality rates/100 person years by AIDS classification for risk groups 470

Table 17.16: Mortality rates by AIDS classification for Non homo/bisexual patients by gender 471

Table 17.17: Mortality rates by AIDS classification for all patients by gender 471

Table 17.18: Modified WHO classification system in use at RIDU, City Hospital, Edinburgh 483

Table 18.1: Cross-sectional analysis of transmission cofactors 497

Table 18.2: Univariate analysis of longitudinal data: 50 simulations 499

Table 18.3: Model based on duration of HIV infection: multifactorial analysis of longitudinal data with 50 simulations 501

Table 18.4: Model based on immunological decline: multifactorial analysis of longitudinal data with 50 simulations 503
List of Figures

Figure 1.1: AIDS cases by Region reported to the World Health Organisation 52
Figure 1.2: Cumulative cases of AIDS reported to the World Health Organisation 53
Figure 1.3: AIDS reports for the United Kingdom 55
Figure 1.4: HIV reports for the United Kingdom 56
Figure 1.5: AIDS reports for Scotland by risk activity 57
Figure 1.6: AIDS reports for Scotland by region 58
Figure 1.7: HIV reports for Scotland by risk activity 59
Figure 1.8: HIV reports for Scotland by region 60
Figure 1.9: AIDS reports for Scotland by risk activity 1986-92 61
Figure 2.1: Survey of accident and emergency consultations associated with drug use in Edinburgh during 1984 75
Figure 2.2: Survey of admissions associated with drug use in Switzerland 76
Figure 2.3: A survey of admissions to a specialised medical inpatient unit of a New York Hospital devoted to drug addiction 77
Figure 2.4: A post mortem survey of narcotic drug users in New York from 1950-1961 78
Figure 2.5: A post mortem survey of narcotic drug users in New York from 1950-1961 84
Figure 2.6: Survey of admissions associated with drug use in Switzerland 85
Figure 2.7: A survey of admissions to a specialised medical inpatient unit of a New York Hospital devoted to drug addiction 86
Figure 2.8: Survey of accident and emergency consultations associated with drug use in Edinburgh during 1984 87
Figure 4.1: Reported first year of IDU in Edinburgh

Figure 4.2: Injection Drug Use related illness: hospital discharges for Lothian 1976-86

Figure 7.1: Drug users attending the City Hospital assessed as injecting more than 50% of the visits during the year

Figure 7.2: Drug users attending the City Hospital assessed as injecting at least once during the year

Figure 9.1: Transmission category or risk activity of City Hospital Cohort

Figure 9.2: Gender of City Hospital Cohort

Figure 9.3: Mean number of admissions per patient by clinical staging (AIDS and Non-AIDS)

Figure 9.4: Mean number of admissions per patient by immunological staging (CD4 counts of greater or less than 200 cells/cumm)

Figure 9.5: Average length of stay (ALOS) by clinical staging (AIDS and Non-AIDS) and year of admission

Figure 9.6: Average length of stay (ALOS) by immunological staging (CD4 count of less than or greater 200 cells/cumm) and year of admission

Figure 9.7: Average length of stay for AIDS and Non AIDS by transmission category and gender

Figure 9.8: Average length of stay by CD200 status, transmission category and gender

Figure 9.9: Average annual bed days per living patient for AIDS or Non-AIDS by transmission category and gender

Figure 9.10: Average annual bed days per living patient for immunological staging (< or > CD200) by transmission category and gender

Figure 12.1: Mean Zidovudine Plasma Concentration Profile

Figure 12.2: Mean GAZT plasma concentration profile
Figure 12.3: Scatter Plot of Zidovudine Pharmacokinetic Parameters 314

Figure 12.4: Scatter plot of GAZT pharmacokinetic parameters 316

Figure 14.1: Kaplan Meier Plot of Progression to AIDS, CDC stage IV and CD200 363

Figure 14.2: Kaplan Meier Plot of Survival from AIDS, CDC stage IV and CD200 369

Figure 15.2: Risk activity of the 309 seroconverters 397

Figure 15.3: Kaplan Meier plot of progression rate to AIDS and death in Edinburgh City Hospital IDU seroconverters 402

Figure 15.4: Survival functions to AIDS: Estimated and fitted Weibull 409

Figure 15.5: Survival functions to Death: Estimated and fitted Weibull 411

Figure 17.2: Gender of the Edinburgh City Hospital cohort 443

Figure 17.3: Risk activity of the Edinburgh City Hospital cohort between 1984 and 1993 444

Figure 17.4: Clinical features (WHO stage) of patients at first visit to City Hospital 446

Figure 17.5: Rate of some common clinical conditions (Non AIDS) by risk activity 455

Figure 17.6: Clinical features of patients with an index diagnosis of AIDS 459

Figure 17.7: AIDS incidence by risk activity and gender 460

Figure 17.8: Cumulative frequency of clinical events (modified WHO codes) for patients with AIDS by risk activity 464

Figure 17.9: Cumulative morbidity or number of clinical events (AIDS) expressed as rates/100 person years of follow up by modified WHO codes 466
Figure 17.10: Cumulative morbidity or number of clinical events (AIDS) expressed as rates/100 person years of follow up by risk activity 467

Figure 17.11: Cumulative morbidity or number of clinical events (all WHO AIDS events) expressed as rates/100 person years of follow up by risk activity and modified WHO codes 468

Figure 17.12: Mortality rates by risk activity and clinical stage 472
Statement by author

This thesis has been composed by myself and contains work written by myself in collaboration with my research staff and colleagues. The thesis describes services that I initiated and organised, together with research work that I directed, data that I arranged to be collected as well as original observations concerning HIV documented by myself during the early years of the HIV epidemic in Edinburgh. The services were initiated with NHS funds that I together with others in the Lothian obtained from the Scottish Office for the care of HIV patients.

Raymond Patrick Brettle BSc, MB ChB, FRCP(Ed).

Edinburgh , 29th December 1993

Dedication

This thesis is dedicated to my wife Helene and my children; Patricia, Christina, Laura and David as well as to the many patients for whom I have cared over the years and whose lives are described here in an all too brief and scientific account.
Abstract

The Acquired Immunodeficiency Syndrome (AIDS), caused by infection with Human Immunodeficiency Virus (HIV), was only described in 1981 yet there are now over 600,000 confirmed cases world-wide. In the USA where the illness was first described 2/3 of the AIDS cases have been in homo/bisexuals and 1/3 have been injection drug users. In the UK as a whole by mid 1993 over 8000 cases of AIDS had been reported, over 70% in homosexuals and only 6% as a consequence of injection drug use (IDU).

For a variety of socio-economic reasons an epidemic of IDU involving heroin occurred during the early 1980's in Edinburgh: one third were female, most were young, unemployed and living on large council estates. At the peak of this IDU epidemic, HIV arrived and rapidly spread through this community. By July 1989 over 1000 individuals or 0.1% of the population of Lothian (750,000) had been recognised to have been infected with HIV, the majority via IDU. This is of the same order as the worst affected region in England (North West Thames). The majority of these individuals however live in the City of Edinburgh with a population of only around 300,000 (1981 census). Consequently a realistic prevalence for this population is actually 0.3% or 3 times the worst affected English region. Thus this new area of medicine has considerable relevance for future medicine in Edinburgh and Scotland.

The thesis describes the disease, the epidemiology of Injection Drug Use and IDU related HIV and the early epidemic in Edinburgh. It also describes the clinical services that were developed at the City Hospital in Edinburgh and the problems that this new service encountered. The provision of health care for this difficult patient population facilitated a variety of research projects. The thesis describes some of the results of these projects particularly those concerned with natural history, clinical presentation and use of anti-retroviral therapy in IDU related HIV. Lastly the factors found to affect the transmission of HIV to the heterosexual partners of the patients are presented together with their relevance for other populations.
Research Grants

The research work was initiated and supervised by myself with the aid of the following research grants:

1. A study to determine the extent of HTLV-III infection amongst self-referred individuals in Edinburgh. Scottish Home and Health Department grant K/OPR/2/2/C726. 1985

2. A prospective clinical study of cognitive and neuro-physiological abnormalities in heterosexuals infected with HIV. A three year project grant from the Medical Research Council. SPG8702433. 1987-90.


4. Analysis of City Screening Clinic attendance's. One year grant from AVERT. 1988-89.

5. The risk of heterosexual transmission of human immunodeficiency virus (HIV). A three year project grant from the Medical Research Council. SPG 8705550. 1987-90.


7. The risk of heterosexual transmission of human immunodeficiency virus (HIV). A Supplementary Grant for one year and one month from the Medical Research Council awarded in August, 1989. SPG 8705550. 1988-90


10. A Prospective Study of Clinical, Immunological and Virological Parameters of Infants and Children Born to HIV antibody Positive Mothers. A three year study from the charity Aids Virus Education Research Trust (AVERT). 1987-90.

11. The Pharmacokinetics of Zidovudine in Injection Drug Use. A one year grant from the Lothian Health Board. HQ 884 398. 1990-91.


16. HIV testing of Serum Samples Stored in the Lothian Regional Virus Laboratory for the Years 1982 - 1988. A one year grant from the Medical Research Council to examine the serum store in Edinburgh. SPG 9006436. 1990-91.


18. The Natural History of Drug Misuse related HIV infections with reference to potential cofactors. A three year grant from the Medical Research
Council to study the natural history of HIV in Edinburgh drug users. 

SPG9116497. 1992-95.


20. A collaborative multi-centre study of the progression of HIV infection in women in the UK. A three year grant from the Medical Research Council. SPG9116072 1992-95. Grant holders Dr R Keenlyside, Dr A Phillips, Dr S Barton, Dr R P Brettle.


I would like to acknowledge the invaluable help provided by members of my staff over the years in regard to both clinical and research work; particularly Drs Kate Bissett, Francis Cowan, Peter Flegg, Michael Jones, Linda MacCallum, Lorna Willocks, Susan Mchardy, James Bingham, and Gwyneth Jones. The research nursing Sisters; Susan Davidson, Rhona Wyld, Rosena Wightman, Anne Chiswick and the rest of the research staff, Mr Vince Egan, Miss Barbara Hamilton, Mr Angus Foreman, Mrs Sarah Pocock and as well as all the rest of the staff of the Regional Infectious Disease Unit, City Hospital, Edinburgh. I would also like to thank my secretary and Personal Assistant Miss Pauline Douglas.

I acknowledge the generous financial support of the WHO/Council of Europe, the Winston Churchill Memorial Trust, the Abbott Research Travel Fund and the Lothian Health Board without which my travel fellowship would not have been possible. During the fellowship I was able to visit Amsterdam and a number of centres in the USA notably the Montefiore Medical Centre, Beth Israel Hospital, St Lukes-Roosevelt Hospital, Memorial Sloan Kettering Cancer Hospital, Beth Abraham Hospice and Bailey House residential facility in New York as well as the University of California San Francisco Medical Centre, San Francisco General Hospital and San Francisco Department of Health. The fellowship would certainly not have been possible without the generous time and support given by my consultant colleagues Drs James Gray, Philip Welsby and Clifford Leen, Dr Michael Jones who undertook my duties whilst I was away, my referees and the many individuals who gave of their time at the centres I visited. There are unfortunately too many individuals to all mention by name but I would like to especially thank Professor M Adler, Dr B McClelland and Dr A Pinching in the UK for supporting my fellowship as well as Dr A Moss, Dr G Friedland, Dr R Elion, Professor E Drucker and Dr R Coutinho whom I visited.

I also acknowledge the invaluable help of my many co-authors on various research papers and my fellow research grant holders, Dr Alison Richardson, Dr Clifford Leen, Dr Roy Robertson, Dr Sheila Gore, Dr Graham Bird, Dr John Emslie, Dr Sheila Burns and Dr Peng Lee Yap. Statistical analysis was undertaken by Dr Sheila Gore (Chapter 6 and 12), Dr Alison Richardson (Chapters 8), Dr Alex McNeil (Chapters 13, 14, 15) and Dr Katherine Fielding (Chapter 18). Assays for zidovudine and metabolites (Chapter 12) were kindly undertaken by the Wellcome Foundation Ltd, Beckenham, Kent.
Publications

Much of the data contained in this thesis has already been published or is about to be published. Below is a complete list of those papers accepted for publication.


<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACMD</td>
<td>Advisory Council on the Misuse of Drugs</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>ALOS</td>
<td>Average Length of Stay</td>
</tr>
<tr>
<td>AMJ</td>
<td>Dr Ann M Johnson</td>
</tr>
<tr>
<td>ARC</td>
<td>AIDS Related Complex</td>
</tr>
<tr>
<td>ARV</td>
<td>Aids Related Virus, the name used in San Francisco for the virus now known as HIV</td>
</tr>
<tr>
<td>AUC</td>
<td>Area Under the Curve</td>
</tr>
<tr>
<td>AZT</td>
<td>Zidovudine (Retrovir), a nucleoside analogue and anti-HIV compound</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control, Atlanta</td>
</tr>
<tr>
<td>CDPS</td>
<td>Community Drugs Project Service, Edinburgh. A psychiatric service for drug users set up in 1988 to work with drug users via general practitioners.</td>
</tr>
<tr>
<td>CD200</td>
<td>The CD200 diagnosis was defined as the first of two consecutive CD4 counts below 200 or an AIDS diagnosis, whichever was earlier.</td>
</tr>
<tr>
<td>CD4</td>
<td>A specific receptor molecule on a T lymphocyte helper cell, called CD4 after the monoclonal antibodies that specifically recognised the receptor molecule</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CLSL</td>
<td>Clifford Leen</td>
</tr>
<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>cumm</td>
<td>cubic millimetre or millilitre</td>
</tr>
<tr>
<td>DDI</td>
<td>Dideoxydidanosine, nucleoside analogue and anti-HIV compound</td>
</tr>
<tr>
<td>DF118</td>
<td>Dihydrocodeine</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>DSS</td>
<td>Department of Social Security</td>
</tr>
<tr>
<td>DTF</td>
<td>a form of liquid methadone</td>
</tr>
</tbody>
</table>
ELISA  Enzyme linked immunosorbent assay  
FDA  Federal Drug Administration  
GAZT  3'-azido- 3'-deoxy-5'-beta-D-glucopyranosylthymidine or the glucoronide metabolite of zidovudine  
GG&GD  Public Health and Environment Department of Amsterdam Municipal Medical Health Care Service  
GUM  Genito Urinary Medicine  
HBV  Hepatitis B virus  
Het  Infected with HIV via heterosexual intercourse  
HIV  Human Immunodeficiency Virus  
HLA  Human Leucocyte Antigen  
HSV  Herpes Simplex Virus  
HMP  Her Majesty's Prison  
Ho/bi  Homosexual or bisexual  
HTLV III  Human T lymphotropic Virus III, the name used by Dr Gallo in Washington USA to describe the virus now known as HIV  
ID  Infectious Diseases  
IDU  Injection Drug Use  
IDUs  Injection Drug Users  
IgA  Immunoglobulin type A  
IgG  Immunoglobulin type G  
IgM  Immunoglobulin type M  
Inserm  French Medical Research Council  
IP  Inpatient  
ITP  Immune thrombocytopenia  
ITU  Intensive Therapy Unit
LAV  Lymphadenopathy Virus, the name used by Dr Montagnier in France to describe the virus now known as HIV
kg   kilogramme
KS   Kaposi's sarcoma
MA   Missed appointment
MCV  Mean Corpuscular Volume
mg   milligrammes
ug   microgrammes
ml   millilitre
MMTP Methadone maintenance treatment programmes
MRIHS Montefiore Rikers Island Health Service
MRC  Medical Research Council
NIDA National Institute on Drug Abuse, Washington, USA
NOA number of admissions
NS   Not significant
OP   Out patient
OIs  Opportunistic infections
PAIS Patient Assessment Information System
PCP  Pneumocystis Carinii Pneumonia
PGL  Persistent Generalised Lymphadenopathy
PML  Progressive Multi Focal Leucoencephalopathy
RNA  Ribonucleic acid
RIDU Regional Infectious Disease Unit, City Hospital, Edinburgh
ROI  Risk of Infection
RPB Raymond Patrick Brettle
RR   Relative Risk
RW  Sister Rhona Wyld and Sister Roseana Wightman
RVL  Regional Virus Laboratory
SAS  A commercial statistical software package
SCODA Standing Committee on Drug Abuse
SD  Standard deviation
SE  Standard error
SFGH  San Francisco General Hospital
SJD  Sister Susan Davidson
SPSS/PC A commercial statistical package for social sciences
UK  United Kingdom
UTI  Urinary Tract Infection
URTI  Upper Respiratory Tract Infection
US  United States of America
USA  United States of America
TB  Tuberculosis
T cell  A lymphocyte associated with cell mediated immunity
T4 cell  A helper lymphocyte, also known as a CD4 lymphocyte
Tran  Infected with HIV via blood products
WHO  World Health Organisation
WTE  Whole time equivalent
Summary

This thesis contains an initial introductory section describing the condition of HIV and AIDS, injection drug use and injection drug use related HIV particularly the epidemic that affected Edinburgh.

The second section describes services developed at the RIDU, City Hospital, Edinburgh in response to the problem of IDU related HIV, compares them with services developed at other centres in the USA and Holland, evaluates their ability to attract and retain patients, introduces the concept of harm reduction and the ability of the services to reduce high risk behaviour.

The third section aims to describe the research work undertaken as a result of establishing the services at the RIDU in Edinburgh particularly the early use of zidovudine, the natural history of IDU related HIV. It also reviews the clinical problems of IDU before describing the clinical problems of IDU related HIV as seen in Edinburgh. Lastly it details the factors noted to be influential in the heterosexual transmission of HIV.
SECTION I - INTRODUCTION
CHAPTER 1

Human Immunodeficiency Virus and The Acquired Immune Deficiency Syndrome

Introduction

The original description of AIDS or the Acquired Immune Deficiency Syndrome appeared in 1981. It described 26 patients with Kaposi’s sarcoma (a skin tumour which until then had only been seen in elderly men, in African races, and in those with considerable iatrogenic immunosuppression) and 5 men with oral thrush and pneumocystis pneumonia which again, was usually associated with iatrogenic immunosuppression. The connection between the two groups was that the men were all young male homosexuals with a mean age of 32 years. The first 9 cases of AIDS amongst injection drug users were diagnosed retrospectively to have occurred in 1980 and 4 of these were also homosexuals. The first case of transfusion associated AIDS occurred in a young child who had a platelet transfusion. Between 1978 and 1983 in the United States the risk of acquiring AIDS via blood transfusion was estimated at 0.6 cases of AIDS per one hundred thousand adults transfused and 2.8 cases of AIDS per one hundred thousand children transfused. The risk was increased by a factor of 32 for adults given more than 10 units of blood and by a factor of 27 for children given more than 10 units of blood. The risk with whole blood, packed cells, platelets or frozen plasma and the mean incubation period from transfusion to the development of AIDS was 21 months for children and 31 months for adults. The risk of acquiring HIV from an infected blood product appeared to be about 66% and infection was more likely the closer the donor was to developing AIDS. This does rather suggest that infectivity in donors rises as they develop symptoms. Other "high risk groups" were also soon recognised including haemophiliacs, the heterosexual partners of patients with AIDS and children.

At any one time, approximately 50% of the cumulative number of AIDS cases have died. The current mortality depends upon the index condition at presentation; for instance those presenting with an opportunistic infection (OI) have a current case mortality rate of over 50% whereas those with Kaposi’s sarcoma have a case mortality rate of only 33%. Those patients presenting with both an OI and Kaposi’s sarcoma have a current case mortality rate of 63%. The survival time also varies with the type of presentation in AIDS, the medium survival time for those patients with Kaposi’s sarcoma in the absence of OIs varies between 20 and 30 months.
whereas the median survival time for patients with OIs varies between 4 and 11 months.20,21

The causative virus involved in AIDS was first isolated in 1983 by Dr. Luc Montagnier and it was propagated in a cell line by Dr. Robert Gallo in 1984.22,23 A variety of names were used for the virus initially, including LAV, ARV and HTLV-III but these have all now been replaced by HIV.24 HIV is a retrovirus i.e. an RNA virus which utilises an enzyme known as DNA polymerase or reverse transcriptase to produce a DNA provirus that is able to insert itself into the host DNA. It contains 3 major genes, gag, pol and env.25

The gag gene codes for the core or shell proteins that enclose the RNA. These proteins are also known as p24, p18 and p15. The pol gene codes for at least 3 enzymes, protease, reverse transcriptase, and an endonuclease. The env gene codes for the outer spike glycoproteins and transmembrane glycoproteins. These are also known as gp120 and gp41. Before leaving a host cell a newly assembled virus takes with it part of the host cell membrane into which the gp120 and gp41 viral proteins have been inserted.

HIV preferentially infects lymphocytes that function as T helper cells. These cells are distinguished by the presence of a specific receptor molecule known as CD4 after the monoclonal antibodies that specifically recognise the molecule. The gp120 viral protein appears to bind specifically to the CD4 receptor molecule before penetrating into the cell. In addition to helper lymphocytes this receptor molecule may be found on 10 - 20% of monocytes or macrophages, Langerhans cells in the dermis and microglial cells in the central nervous system.25

The various viral proteins produced by HIV infection stimulate an immune response although in many individuals this immune response does not neutralise or protect against the virus. The major antibody response is against the env gene products or outer glycoproteins notably gp120. Antibodies against gp120 appear about 6 weeks after infection and persist until the terminal stages of AIDS. Soon after this antibodies against the gag or core proteins, notably p24, appear. High levels of anti p24 may be protective since low levels predispose to the development of AIDS.25 The commercial assays available for screening purposes detect gp120 antibodies and are usually based on a competitive or anti-globulin enzyme linked immunosorbent assay (ELISA). Commercial assays are now available to detect anti p24 antibody as
well as antigen. The appearance of HIV p24 antigen in the circulation together with the loss of anti p24 antibody is thought to be predictive of progression to AIDS.\(^{25-28}\)

**The Centers for Disease Control Clinical Staging System**

The Centers for Disease Control (CDC) in Atlanta introduced a definition to help collate accurate information about the condition. This definition of AIDS initially only required the clinical diagnosis of conditions that were moderately predictive of cellular immunodeficiency without an underlying cause. The definition was revised in 1987 to take into account serological evidence of HIV infection and is set out in full in the appendix to this chapter.\(^{24}\)

It was soon recognised that in addition to AIDS there were a number of other conditions related to HIV infection. The exact inter-relationship and natural history of HIV is as yet not known but in an attempt to ease the problem of definition, the CDC developed a classification system which is descriptive and does not attempt to define any inter-connections.\(^{29}\) It essentially details four mutually exclusive categories or groups of HIV infection as shown in Table 1.1.

**Table 1.1: Classification of effects of HIV infection**

<table>
<thead>
<tr>
<th>CDC Stage</th>
<th>Clinical Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>acute infection with seroconversion</td>
</tr>
<tr>
<td>II</td>
<td>asymptomatic infection</td>
</tr>
<tr>
<td>III</td>
<td>persistent generalised lymphadenopathy</td>
</tr>
<tr>
<td>IV</td>
<td>Symptomatic HIV disease</td>
</tr>
<tr>
<td>IV A</td>
<td>constitutional symptoms and disease</td>
</tr>
<tr>
<td>IV B</td>
<td>neurological disease</td>
</tr>
<tr>
<td>IV C</td>
<td>immunodeficiency</td>
</tr>
<tr>
<td>IV C1</td>
<td>1982 CDC definition of AIDS</td>
</tr>
<tr>
<td>IV C2</td>
<td>infections out with AIDS definition</td>
</tr>
<tr>
<td>IV D</td>
<td>tumours in CDC definition of AIDS</td>
</tr>
<tr>
<td>IV E</td>
<td>Other e.g. Hodgkins, carcinoma, lymphoid interstitial pneumonia, symptomatic thrombocytopenia</td>
</tr>
</tbody>
</table>

This classification system for HIV is not meant to suggest that every individual has to progress through all stages but it is hierarchical i.e. having reached a particular stage the patients do not revert to earlier stages if the signs or symptoms settle. CDC stage IV is however further divided into 5 subsections which are not exclusive and
patients in this group may be included in one or more of the sub groups. The conditions detailed in stage IV contain all those conditions currently used for the definition of AIDS as well as others that indicate clinically significant HIV infection. A similar staging system was also developed for children but this will not be described in detail.

Primary HIV Infection

**CDC stage I** describes those individuals that undergo a self limiting illness whilst seroconverting for HIV. Primary infection with HIV may be associated with acute clinical manifestations for example a "glandular fever" like illness or less commonly an acute neurological illness for instance meningo-encephalitis or peripheral neuropathy 30-40.

Patients with the glandular fever like illness complain of sore throat, non specific "flu" like symptoms and gastrointestinal disturbances. An erythematous macular rash is present in around 50% of patients. It is initially prominent in the trunk and later involves the extremities. Other skin manifestations include urticaria, loss of hair, and desquamation of palms and soles 30-32,36,41. Generalised lymphadenopathy is a feature in around 75% of patients and in some patients may be associated with splenomegaly and tender hepatomegaly 30,41,42.

Patients may present with symptoms of acute aseptic meningitis such as headache, fever, photophobia and neck stiffness. Cerebrospinal fluid findings are typical of viral infection 30,31. HIV has been isolated from the cerebrospinal fluid in certain cases, and also from peripheral blood 39. The clinical features of HIV encephalopathy during primary infection consist of mood changes, confusion, convulsion and incontinence. Abnormalities on neurological examination include altered conscious level, extensor plantar responses, sensorimotor peripheral neuropathy including facial palsy 38,40. Other neurological manifestations have been reported; myelopathy, Guillain-Barré syndrome, and radiculopathy 43-45.

The incubation period, defined as the time from exposure to clinical symptoms of acute HIV infection has been variable ranging from a few days to up to a few months 30,40. It is felt that the incubation period may be longer in sexually transmitted HIV infection because of a smaller dose of inoculum and the non parenteral route of transmission 31,46. However, incubation periods of up to 6 months have been documented via the parenteral route 47,48.
Seroconversion is defined as the time from infection to the detection of specific antibodies and has occurred from 8 days to 10 weeks after the onset of acute illness. IgM antibodies are first detected by immunofluorescence and an IgG immunofluorescent antibody test has been found to be more sensitive than either ELISA or Western Blotting in detecting primary HIV infection. The characteristic pattern of specific antibody responses to the various viral proteins have been described.

Severe immunodepression may occur during acute HIV infection. Oesophageal candidiasis has been reported in a number of patients during acute HIV infection, and other OIs e.g. tuberculous meningitis have also been reported 8 weeks after acute HIV infection.

**Early Manifestations of HIV Infection**

**CDC stage II** describes those individuals who are essentially well or asymptomatic but have antibodies for HIV. They may be further subdivided after laboratory investigations into those with immunological abnormalities and those without, however this has no prognostic value since at present the natural history of CDC stage II is incompletely understood.

**CDC stage III** describes those individual with enlarged lymph nodes (greater than 1 cm) at two or more non adjacent sites for longer than three months in the absence of any other illness to explain the findings. This condition is also known as Persistent Generalised Lymphadenopathy (PGL). Commonly the enlarged nodes are found down the front and or back of the neck, under the jaw or in the axillae and may not be noticed by the patient. Massive enlargement can occasionally occur. Unusual sites for lymph node enlargement do occur for instance at the elbow, behind the knee, down the front of the thigh, down the side of the chest wall, in the abdominal wall, or behind the nipples. This lymph node enlargement may be accompanied by other troublesome symptoms such as tiredness, lethargy, excessive sweating, aches and pains in muscles or joints.

**Late Manifestations of HIV Infection**

**CDC stage IV** is divided into five further sub- sections labelled A to E and this stage has to be regarded as being more serious although some individuals may be relatively well. AIDS Related Complex or ARC is a term which is commonly used, has a number of definitions but is anyway covered by CDC stage IV.
Stage IV A describes those individuals complaining of the vague constitutional symptoms of stage III but with the addition of more serious problems such as unexplained diarrhoea, fever (greater than 38°C) for longer than 1 month or unexplained weight loss of more than 10% body weight.

Stage IV B consists of neurological problems associated with HIV other than those occurring during CDC stage I. Examples are neuropathy and myelopathy. Disabling cognitive and or motor dysfunction interfering with occupation or the activities of daily living can also occur. Patients or relatives may notice loss of memory and loss of skills such as mental arithmetic or decision making. Relatives may notice changes in personality which early on seem like eccentricities. Frank mental illness, dementia or loss of consciousness if no other pathogens are found in the setting of HIV infection is called HIV encephalopathy and is one criterion for the diagnosis of full blown AIDS.

Stage IV C describes a number of infections which occur as a result of immunodeficiency secondary to HIV infection and is divided into two sub groups IV C1 and IV C2.

- **CDC stage IV C1** includes individuals suffering from one or more of 12 infections which formed the basis of the original CDC definition of AIDS.

- **Stage IV C2** contains those infections which are commonly associated with serious HIV infection but are not in the original description of AIDS. Examples of infections in stage IV C2 are recurrent and invasive salmonella, extensive herpes zoster or shingles, recurrent oral thrush or candidiasis, a condition almost unique to HIV called oral hairy leucoplakia and recurrent severe bacterial sepsis in adults.

CDC stage IV D groups together all those cancers specifically associated with HIV infection and as with CDC stage IV C1 some of these conditions also fulfil the CDC definition of AIDS. Examples are the skin tumour Kaposi's sarcoma and cancers of the lymph nodes such as non-Hodgkins lymphoma or primary lymphoma of the brain.

CDC stage IV E is designed to cover those conditions not yet described or those not yet understood such as chronic lymphoid interstitial pneumonitis, myopathy and symptomatic thrombocytopenia.
WHO staging system

Until recently the CDC classification was the only viable clinical classification system used to stage HIV. It is likely that with the increasing use of CD4 counts a new WHO/CDC classification system will be utilised in its place.\(^5\)\(^6\)\(^7\)

It essentially consists of three broad clinical stages, well or asymptomatic, HIV related diseases and AIDS combined with three stages of immunodeficiency as measured by either CD4 counts (\(\geq 500\) cell/cumm, 200-500 and \(\leq 200\)) or lymphocyte counts (Table 1.2). When combined in a three way table there are thus 9 possible stages. In the USA everyone with a CD4 count below 200 is to be classified as AIDS although this seems unlikely to happen in Europe for the present.\(^5\)\(^7\) The CDC also proposed that three new clinical problems be added to the 1987 definition of AIDS.\(^5\)\(^7\) These are

- cervical cancer
- two episodes of bacterial pneumonia in a 12 month period
- pulmonary tuberculosis.

These new clinical definitions of AIDS may be added to the UK definition in the near future.

**Table 1.2: WHO/CDC classification system for HIV**

<table>
<thead>
<tr>
<th>Laboratory Classification</th>
<th>Clinical Category*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute CD4 count or Total lymphocyte count (TLC)</td>
<td>A</td>
</tr>
<tr>
<td>(\geq 500) cell/cumm</td>
<td>(\geq 2000) cell/cumm</td>
</tr>
<tr>
<td>(\leq 200) cell/cumm</td>
<td>(\leq 1000) cell/cumm</td>
</tr>
</tbody>
</table>

*Definitions of Clinical Groups for Table 1.2

**Clinical category A:** (Asymptomatic disease) Acute infection with HIV; persistent generalised lymphadenopathy; asymptomatic. Conditions in Groups B and C must be absent.

**Clinical category B:** (Symptomatic disease) Any symptomatic conditions not included in Category C. Examples are bacterial infections, candidiasis (oral or vulvovaginal) for \(>1\) month, cervical dysplasia or carcinoma, constitutional symptoms, oral hairy leukoplakia. Two distinct episodes of herpes zoster or involving more than one
Clinical category C: Any condition which meets the 1987 CDC/WHO case definition for AIDS.

Laboratory Features of HIV Infection

Immunology

AIDS is characterised by a marked depletion of CD4 lymphocytes in the peripheral blood. Exactly how this depletion takes place is as yet unclear but a number of possible mechanisms have been suggested including, a direct cytopathic effect of HIV, syncytia or giant cell formation with subsequent cell death and a form of autoimmunity against lymphocytes using either cytotoxic T cells or other anti lymphocytic factors.

The major effect of HIV infection appears to be damage to cell mediated immune mechanism resulting in characteristic susceptibility to opportunistic infections. This susceptibility is usually to intracellular organisms such as latent viruses, fungi or protozoa. Such organisms require the presence of an intact cell mediated immune system which relies on T lymphocytes and macrophages. The clinical course of the illness is associated with a marked depletion of peripheral blood CD4 lymphocytes which play a key role in initiating and promoting immune responses including the initiation of a de novo humoral response. Most adults with HIV infection seem to have reasonable B cell memory although recurrent bacterial infections can occur in HIV infection. This humoral defect is worst in children where B cell memory is limited and the patient may be rendered effectively hypogammaglobulinaemic. The humoral defect also limits the usefulness of serology in the diagnosis of many disorders, for instance latent viruses may exhibit persistent and stable levels of antibodies and other organisms produce little in the way of an antibody response.

The marked loss of T cell immunity results in a susceptibility to reactivation of latent or controlled infections such as CMV, Toxoplasmosis or Tuberculosis (TB) or to attack by relatively non pathogenic organisms which may be endogenous or common in the patient's environment. Examples of this type of infection are Pneumocystis carinii pneumonia (PCP), candidiasis or atypical mycobacteria.

The loss of T cell function also results in only limited macrophage activity. Infection in these patients often produces little in the way of an inflammatory response and
consequently little in the way of clinical signs. A number of immunological abnormalities have been described including:

- leucopenia and lymphopenia.
- loss of T4 lymphocytes from the peripheral blood.
- hypergammaglobulinaemia.
- skin anergy.
- decreased in vitro lymphocyte proliferation, cytotoxic T cell response and antibody production to new antigens.
- elevated levels of immune complexes, interferon and β-2-microglobulin.

**Haematology**

The haematological abnormalities associated with HIV infection vary with the clinical state of the patient but are commoner as HIV infection progresses. For instance 12% of AIDS/AIDS Related Complex (ARC) patients were leucopenic, 20% were neutropenic, 75% were lymphopenic and 93% were anaemic. The reasons for these abnormalities are multifactorial and involve the effects of HIV infection, drug effects, chronic infection and the effects of opportunistic infections. In a series of patients who underwent bone marrow examination a number of abnormalities were noted including:

- reticuloendothelial iron blockade.
- dyserythropoiesis and megaloblastic change.
- erythroid hypoplasia.
- excess histiocytes and viral associated haemophagocytosis.

Despite the peripheral lymphopenia, bone marrow lymphopenia is uncommon perhaps because T cells predominate in the peripheral blood whereas B cells predominate in the bone marrow. Immune thrombocytopaenia (ITP) is usually associated with children and middle aged women. An ITP syndrome was noted early on to be an AIDS related condition in homosexuals, injection drug users, and haemophiliacs. In patients with AIDS about 30% have a depressed platelet count and it often falls further with treatment for PCP. The platelet count is generally depressed in HIV infection and ITP has been noted to occur in HIV infection before the advent of AIDS. In other studies about 5-10% of PGL
patients have mildly depressed platelet counts\textsuperscript{65}. The commonest symptoms are excessive bruising, epistaxis, menorrhagia, gingival and rectal bleeding. Major life threatening haemorrhage is rare. Platelet associated immunoglobulin has been demonstrated in the majority of patients studied\textsuperscript{65}.

**The General Epidemiology of AIDS and HIV**

Transmission of HIV in the USA and Europe basically involves homo/bisexuals and injection drug users whereas in Africa it is essentially a heterosexually transmitted disease\textsuperscript{66}. In the rest of the world transmission of HIV is mainly as a sexually transmitted disease from individuals travelling to these areas from areas of high seroprevalence or occurs because of the importation of infected blood products from areas of high seroprevalence. These patterns of spread have been designated type I, II and III respectively by the WHO\textsuperscript{67}. More recently the importance of bisexuals in the spread of infection to non drug using heterosexual women has been demonstrated in South America\textsuperscript{68}.

By end of 1992, 611,589 cases of AIDS had been notified world wide; 242,146 from the United States alone and 313083 from the whole of the Americas, 209805 from Africa, 81,091 from Europe with 6510 from the United Kingdom, 4846 from the Western Pacific, 1539 from the Eastern Mediterranean and 1225 from South East Asia (Figure 1.1 and 1.2)\textsuperscript{69}. It must be remembered that the cases from Africa are a gross underestimate of the size of the problem for a variety of reasons but mostly as a consequence of a lack of the necessary infrastructure for reporting cases.
Figure 1.1: AIDS cases by Region reported to the World Health Organisation
Figure 1.2: Cumulative cases of AIDS reported to the World Health Organisation
There appears to be little variation between the risk groups with regard to presentation. In the USA, figures are available on the 30,632 cases of AIDS notified to the Centers for Disease Control by the 9 February 1987. These show that conditions such as Kaposi's Sarcoma (KS) are unusual in the absence of homo/bisexuality. In drug users, KS, cytomegalovirus and chronic cryptosporidiosis are all significantly less common than for all other risk groups notified with AIDS; while *Pneumocystis carinii* pneumonia (PCP), TB, oesophageal candidiasis and extra-pulmonary cryptococcosis are more common. The effect of risk group on presentation in Edinburgh will be discussed in Chapter 17.

The distribution of cases was characteristic of a blood borne or blood associated virus since transmission occurred via blood contact, via sexual intercourse and perinatally. Consequently, the patients likely to be affected are:

- homosexuals/bisexuals.
- injection drug users.
- the recipients of blood products either coagulation products or blood itself, especially prior to 1985 when testing became available in the United Kingdom and the United States.
- the children of infected females.
- heterosexual contacts of infected patients.

In the United States 70% of the AIDS cases are associated with homosexual intercourse, 24% with drug use and/or homosexual intercourse, 2% with heterosexual intercourse, 2% with receiving blood transfusions, and 1% with haemophilia. In Europe however, injection drug use is even commoner than in the USA and accounts for 34.5% of the reported AIDS cases. Some 87% of these IDU related cases have been reported by just three countries i.e. France, Italy and Spain. There is a small but an increasing number of paediatric cases, the majority of which are associated with HIV infection in the mother.

In the United Kingdom by 30 September 1993, 74% of the AIDS cases had been associated with homo/bisexual intercourse, 11% with heterosexual intercourse, 4% with injection drug use and 6% with blood products (figure 1.3). The number of HIV reports by risk activity also show a predominance of homo/bisexual transmission (fig. 1.4).
AIDS reports for the UK
Number of cases (8115)

Figure 1.3: AIDS reports for the United Kingdom

30 September 1993
HIV reports for the UK
Total number of cases (20590) by risk activity

Figure 1.4: HIV reports for the United Kingdom

30 September 1993
Only 438 or 5.4% of the UK AIDS cases had come from Scotland but 142 of these were drug users\textsuperscript{72}. By comparison to the UK as a whole, in Scotland, IDU currently accounts for 32% of the AIDS reports and some 50% originate from Lothian (fig 1.5 and 1.6)\textsuperscript{73,74}. In the UK as a whole, whilst IDU represented only 12% of reports of those infected with HIV this contrasted markedly with the position in Scotland where 48% of those infected with HIV have implicated IDU and 51% of those reports had come from Lothian (fig 1.7 and 1.8)\textsuperscript{72,73}. The dramatic change of risk activity distribution over time is shown in figure 1.9.
AIDS reports for Scotland
Number of cases (418) by risk activity

Figure 1.5: AIDS reports for Scotland by risk activity
AIDS reports for Scotland
Total number of cases (285) by region

- Glasgow: 27.4%
- Tayside: 12.3%
- Lothian: 10.5%
- Others: 49.8%

December 1991

Figure 1.6: AIDS reports for Scotland by region
HIV reports for Scotland
Number of cases (2025) by risk activity

Figure 1.7: HIV reports for Scotland by risk activity

30 September 1993
HIV reports for Scotland
Total number of cases (2025) by region

Glasgow: 26.9%
Others: 6.7%
Tayside: 15.5%
Lothian: 50.9%

Figure 1.8: HIV reports for Scotland by region
30 September 1993
AIDS reports for Scotland
Annual reports by risk activity 1986-1992

Figure 1.9: AIDS reports for Scotland by risk activity 1986-92
Appendix

The surveillance definitions of AIDS

The Centers for Disease Control, Atlanta produced a revised definition of AIDS in 1987 which is as follows.

I. Without laboratory evidence of HIV infection.

If laboratory tests for HIV are not available then provided the following conditions (under I A) are not present a diagnosis of AIDS can be made provided the disease is diagnosed definitively (under I B).

I A. Causes of immunodeficiency that disqualify diseases as indicators of AIDS in the absence of evidence of HIV infection.

1. High dose or long term systemic corticosteroid therapy or other immunosuppressive/cytotoxic therapy for < or = 3 months before the onset of the indicator disease.

2. Any of the following disease diagnosed for < or = 3 months after the diagnosis of the indicator disease: Hodgkin's disease, non-Hodgkins lymphoma (other than primary brain lymphoma), lymphocytic leukaemia, multiple myeloma, any other cancer of the lymphoreticular or histiocytic tissue, or angioimmunoblastic lymphadenopathy.

3. A genetic (congenital) immunodeficiency syndrome or an acquired immunodeficiency syndrome atypical of HIV infection, such as one involving hypogammaglobulinaemia.

I B. Indicator disease diagnosed definitively:

1. Candidiasis of the oesophagus, trachea, bronchi, or lungs.

2. Cryptococcosis, extra pulmonary.

3. Cryptosporidiosis with diarrhoea for > 1 month.

4. Cytomegalovirus disease of an organ other than the liver, spleen, or lymph nodes in a patient > or = 1 month of age.
5. Herpes simplex virus infection causing a mucocutaneous ulcer that persists for >
   1 month; or bronchitis, pneumonitis, or oesophagitis for any duration affecting a
   patient > or = 1 month of age.

6. Kaposi's sarcoma affecting a patient < or = 60 years of age.

7. Lymphoma of the brain (primary) affecting a patient < or = 60 years of age.

8. Lymphoid interstitial pneumonia and or pulmonary lymphoid hyperplasia
   (LIP/PLH) complex affecting a child less than or equal to 12 years of age.

9. Mycobacterium avium complex or M. kansasii disease, disseminated (at a site
   other than or in addition to lungs, skin, or cervical or hilar lymph nodes).


12. Toxoplasmosis of the brain affecting a patient > or = 1 month of age.

II. With laboratory evidence of HIV infection.

Regardless of the presence of other causes of immunodeficiency outlined above (under I A),
in the presence of laboratory evidence of HIV infection, any disease listed above (under I B)
or below (under II A or II B) indicates a diagnosis of AIDS.

II A. The following conditions, diagnosed definitively;

1. bacterial infections, multiple or recurrent (any combination of at least two
   within a 2-year period), of the following types affecting a child <13 years of
   age: septicaemia, pneumonia, meningitis, bone or joint infection, or abscess of
   an internal organ or body cavity (excluding otitis media or superficial skin or
   mucosal abscesses), caused by Haemophilus, Streptococcus (including
   pneumococcus), or other pyogenic bacteria.

2. coccidioidomycosis, disseminated (at a site other than or in addition to lungs of
   cervical of hilar lymph nodes).

3. HIV encephalopathy (also called "HIV dementia", "AIDS dementia", or "sub
   acute encephalitis due to HIV").
4. histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes).
5. isosporiasis with diarrhoea persisting >1 month.
6. Kaposi's sarcoma at any age.
7. lymphoma of the brain (primary) at any age.
8. other non-Hodgkin's lymphoma of B-cell or unknown immunological phenotype and the following histological types:
9. small non cleaved lymphoma (either Burkitt or non-Burkitt type).
10. immunoblastic sarcoma (equivalent to any of the following, although not necessarily all in combination: immunoblastic lymphoma, large-cell lymphoma, diffuse histiocytic lymphoma, diffuse undifferentiated lymphoma, or high grade lymphoma).
11. Note: Lymphomas are not included here if they are of T-cell immunological phenotype or their histological type is not described or is described as "lymphocytic", "lymphoblastic", "small cleaved", or "plasmacytoid lymphocytic".
12. any mycobacterial disease caused by mycobacteria other than M. tuberculosis, disseminated (at a site other than or in addition to lungs, skin or cervical or hilar lymph nodes.
13. disease caused by M. tuberculosis, extra pulmonary (involving at least one site outside the lungs, regardless of whether there is concurrent pulmonary involvement.
14. Salmonella (non typhoid) septicaemia, recurrent.
15. HIV wasting syndrome (emaciation, "slim disease").

II B. The following conditions, diagnosed presumptively:
1. Candidiasis of the oesophagus.
2. Cytomegalovirus retinitis with loss of vision.

4. Lymphoid interstitial pneumonia and or pulmonary lymphoid hyperplasia (LIP/PLH) affecting a child < or = 13 years of age.

5. Mycobacterial disease (acid-fast bacilli with species not identified by culture), disseminated (involving at least one site other than or in addition to lungs, skin, or cervical or hilar lymph nodes).

6. Pneumocystis carinii pneumonia.

7. Toxoplasmosis of the brain affecting a patient > or = to 1 month of age.

III. With laboratory evidence against HIV infection.

With laboratory test results negative for HIV infection, a diagnosis of AIDS for surveillance purposes is ruled out unless:

A. All the other causes of immunodeficiency listed above are excluded and

B. The patient has had either:

1. Pneumocystis carinii pneumonia diagnosed by a definitive method or

2. any of the other disease indicative of AIDS listed above diagnosed by a definitive method and

   a CD4 count of less than or equal to 400 cells/cumm.
WHO Classification System

WHO Asymptomatic

WHO Stage 1

This includes the acute retroviral syndrome of initial infection, the asymptomatic and those with persistent generalised lymphadenopathy.

WHO Symptomatic

This has been divided into two areas;

WHO Stage 2

- Weight loss < 10% of body weight
- Mucocutaneous manifestations such as seborrhoeic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis.
- Herpes zoster
- Recurrent upper respiratory tract infections such as bacterial sinusitis.

WHO Stage 3

- Weight loss > 10% of body weight
- Unexplained chronic diarrhoea > 1 month.
- Unexplained prolonged fever (intermittent or constant > 1 month).
- Candidiasis, oral.
- Candidiasis, vulvovaginal for > 1 month
- Oral hairy leukoplakia.
- Pulmonary tuberculosis.
- Severe bacterial infections such as pneumonia or pyomyositis.
- Bed ridden for < 50% of the day during the last month.
WHO - AIDS

WHO stage 4

- Bed ridden for > 50% of the day during the last month.
- Candidiasis of the oesophagus, trachea, bronchi or lungs.
- Cryptococcus, extrapulmonary
- Cryptosporidiosis with diarrhoea for > 1 month.
- Cytomegalovirus disease of an organ other than the liver, spleen or lymph nodes.
- Herpes simplex infection, mucocutaneous for > 1 month or visceral for any duration.
- HIV dementia (encephalopathy).
- Isosporiasis with diarrhoea for > 1 month.
- Kaposi's sarcoma
- Lymphoma
- Mycobacterium tuberculosis - extrapulmonary
- Mycobacteriosis- atypical and disseminated.
- Mycosis - disseminated histoplasmosis or coccidioidomycosis.
- Pneumocystis carinii pneumonia.
- Progressive multifocal leukoencephalopathy.
- Salmonella septicaemia (non-typhoidal)
- Toxoplasmosis of the brain.
- Wasting syndrome due to HIV.
References for Chapter 1


CHAPTER 2
Injection Drug Use

Introduction

The medical complications of drug use are many and varied and include, the excessive effects of drugs themselves, the withdrawal effects from drugs, and a number of associated medical conditions. It is difficult to quantify the workload for the health service but one survey from Dundee revealed that heroin drug users had twice the general practice consultation rate of matched controls (7/yr. versus 3.25/yr.)¹. In Glasgow 0.6% of all consultations at an accident and emergency facility were by injection drug users and two thirds of these consultations were deemed medical or surgical and one third "psychiatric" suggesting that the addiction problems were in a minority². A second Scottish survey of accident and emergency referrals revealed that 60% were related to the effects of drugs (37% related to an excess of drugs or overdoses and 23% related to withdrawal from drugs), 21% to infections, 8% to trauma and 10% to other medical conditions (fig 2.1)³. As far as hospital treatment is concerned, in Basel, Switzerland 0.8% of all admissions to a University Hospital over a 7 year period involved narcotic drug users, 31% as a consequence of infection (fig 2.2)⁴. By comparison in 1973 a survey of 200 consecutive admissions over a 5 month period to a specialised medical inpatient unit of a New York Hospital devoted to drug addiction revealed that 58% were related to infection, 5% as a consequence of drug overdose and 22% for a variety of other medical conditions (fig 2.3)⁵. A different spectrum of medical problems in drug users is revealed by a post mortem survey of 1561 narcotic drug users in New York from 1950 to 1961 in which of the deaths 49% were as a consequence of drug excess but 19% as a consequence of various infections and the rest as a consequence of miscellaneous disorders (fig 2.4)⁶.

Thus whilst the medical problems of drug users reported by the medical profession vary with the exact location there is no doubt that they account for a significant number of medical consultations and that infection related to injection drug use forms a significant part of the clinical spectrum of disease associated with drug use.
INJECTION DRUG USE
Medical Problems

- Drugs: 60.7%
- Infection: 21.5%
- Trauma: 8.4%
- Other: 9.3%

McGowan 1984

Figure 2.1: Survey of accident and emergency consultations associated with drug use in Edinburgh during 1984
Figure 2.2: Survey of admissions associated with drug use in Switzerland

Sheidegger & Zimmerli 1989
Figure 2.3: A survey of admissions to a specialised medical inpatient unit of a New York Hospital devoted to drug addiction
INJECTION DRUG USE
Narcotic Deaths

Figure 2.4: A post mortem survey of narcotic drug users in New York from 1950-1961

Halpern & Rho 1966
IDU related infections

Drug use associated infections usually occur in association with injection drug use (IDU) although the use of animal excreta as fertiliser in the cultivation of marijuana and the subsequent outbreaks of Salmonella gastro-enteritis is a notable exception. IDU related infections occur as a consequence of the use of non sterile equipment (needles, syringes, spoons, cups etc.) and solutions which allow micro organisms to overcome the normal defence mechanisms by direct entry into subcutaneous tissues, muscle or the blood stream. Once the normal defence mechanisms have been overcome, organisms, whether pathogenic, opportunistic or commensal may then produce either local or systemic infections.

It is often assumed that IDU is a relatively modern problem but this is certainly not the case. The injection of morphine under the skin by the "hypodermic method" was described by Dr Lafargue of St Emilion in the 1830's and consisted of a lancet dipped into a solution of morphine inserted beneath the skin. The use of the hollow hypodermic needle and syringe to introduce a solution of morphine appeared in the 1840's. The first reports of an infection associated with injection drug use were of tetanus and appeared as early as 1867. Its occurrence has largely been related to the practice of subcutaneous injections (or skin popping) of morphine or adulterated heroin usually in the region of the abdomen and or thighs. Initially it was relatively rare and Doane commented that over an 8 year period he had seen only 3 cases out of 4000 cases of drug addiction. However by the late 1950's drug addiction accounted for the majority of cases of tetanus in New York and was the cause of between 5-8% of deaths in drug users. The rise in incidence was probably accounted for by a resurgence of subcutaneous drug use as a consequence of a lack of venous access from prolonged drug use. The use of quinine as an adulterant in street heroin was also considered important since this drug itself could produce skin abscesses suitable for the growth of Clostridium tetani. It is possible that the widespread use of immunisation with tetanus toxoid in childhood has been a successful harm reduction measure for IDU since in recent surveys tetanus is now a rare IDU associated infection.

The intravenous administration of drugs including opium dates from the seventeenth century although it was not initially popular. Intravenous drug use was described in detail from Egypt in 1929 and the problem was even described in an article by Beatrix Bellingham in the Illustrated London News of February 1st 1930. This article not only described the problem of drug addiction in Egypt but also noted that
3.6% of 217 Egyptian heroin drug users rounded up in police raids were injection drug users suffering from septic sores and abscesses. The practice was then reported in the medical literature from a number of cities in the United States in the early 1930's.

IDU together with the sharing of injection equipment and paraphernalia between users facilitates the spread of a number of blood borne organisms notably viruses. Two practices seem to favour this spread; firstly washing the drug out of the syringe into the blood stream by repeatedly drawing back and injecting the users own blood. This results in heavy contamination of the equipment with blood which can then be passed onto the next user. Secondly the practice of washing the equipment in a communal glass or bowl of water which rapidly becomes contaminated with blood.

The first blood borne organism associated with equipment sharing was in fact malaria. An example of inadvertent early harm reduction for IDU may have been the practice of using quinine as a diluent for street heroin. This became common in New York during the 1930's such that the problem of artificially transmitted malaria was not seen in New York after 1943.

The association of IDU (subcutaneous and intravenous) with Hepatitis B virus (then known as homologous serum hepatitis) was first described in 1950. One report described the spread of hepatitis through a tight knit group of long term users after one particular individual joined the group. Multiple attacks of hepatitis initially attributed to chronic forms of hepatitis were described in drug users in 1960 and it is now known of course that one form of Non A non B hepatitis, Hepatitis C, is also commonly associated with IDU.

The sudden and sporadic appearance of injection related infections in IDU communities has been previously described; for instance the appearance of various types of malaria into Washington drug users in that area suddenly appeared in drug users in 1943 and until 1946 was of the falciparum type but in 1947 cases of quartan malaria began to be detected. The high prevalence of delta agent, another blood borne virus, in drug users from Italy, Copenhagen, Basel, Dublin and Edinburgh is a further example of the international spread of blood borne viruses by injection drug users.
Epidemiology of IDU infections

How common are IDU related infections? This is difficult to determine since few doctors systematically record drug use as an associated factor for infections and it also depends on the number of drug users in any one particular location. A survey of the deaths in 1561 narcotic drug users in New York from 1950 to 1961 revealed that 19% were as a consequence of various infections. Between 1943 and 1947 infection was concerned with 80% of 139 heroin addicts admitted to one Washington hospital. This had risen from 6% during the years 1938 to 1942 and was attributed by the authors to a lack of antisepsis, use of a community needle and in 95% of the cases occurred in Blacks. This epidemic of drug use and infection has many similarities to the events that occurred in Edinburgh in the mid 1980's.

The post mortem survey of narcotic drug users in New York from 1950 to 1961 revealed that 19% of the deaths were as a consequence of various infections; 44% from tetanus, 35% from pyogenic infections or endocarditis, 11% from tuberculosis, 10% from viral hepatitis (fig 2.5).

In Basel, Switzerland 0.8% of all admissions to a University Hospital over a 7 year period involved narcotic drug users. Of 404 drug use related admissions, 31% were as a consequence of infection (20% of these infections were as a consequence of viral hepatitis), 28% were related to drug intoxication, 5% to drug withdrawals and 15% to other medical conditions (fig 2.5). A pre-HIV series from the USA of 200 consecutive admissions over a 5 month period to the medical inpatient unit of a hospital devoted to drug addiction also revealed that 58% were related to infection, 31% because of acute viral hepatitis and 28% as a consequence of other infections. The other infections identified consisted of endocarditis (3.5%), bacteraemia without an obvious source (11%), chest infections (29%) and skin infections (43.5%) (fig 2.6).

Thus it appears that IDU related medical problems account for between 0.5-1% of all hospital medical admissions and that IDU related infections account for between 20-60% of these admissions i.e. 0.1-0.6% of all hospital admissions.

In Edinburgh during 1983/84 there were an estimated 2000 injection drug users and 80 of these attended the accident and emergency department during a 4 month period. This survey of accident and emergency consultations by drug users reveals that 21% of the consultations were as a consequence of some form of infection. The majority, some 73%, were described as local infections, 17% as
hepatitis and only 10% as a consequence of systemic infection (fig 2.7). Thus this data would suggest an incidence of clinical IDU infection of around 2.5% of the drug using population, 20% of which was viral hepatitis and less than one percent as a consequence of serious infection.

During 1984 there were 100 admissions to Lothian hospitals for infections such as hepatitis, endocarditis, pneumonia and skin infections out of a population of 2000 suggesting an incidence of around 5% for IDU infections\textsuperscript{39,40}. Eighty one percent of these infections were bacterial and 15% were serious (pneumonia or endocarditis). Thus the annual incidence of clinical IDU related infection for a drug using population is probably somewhere between 2.5-5%, around 20% of these infections being viral hepatitis. The annual incidence for serious life threatening infections from this data is some where between 0.25-0.75% which is of the same order as the accident and emergency department survey. If 10-15% of IDU related infections are serious life threatening systemic infections and 0.1-0.6% of all hospital admissions are due to IDU related infections one can conclude that the upper limit of hospital admissions related to serious IDU related infections would be 0.1%.

What are the risks however from the drug users point of view? A general practice survey in Edinburgh revealed that 50% of drug users had suffered some form of infection during their IDU career\textsuperscript{41}. The majority of the IDU infection problems at that time were hepatitis B (76%) with 14% suffering skin infections and only 10% having a history of endocarditis. Thus in this particular population the lifetime chance of a serious systemic infections such as endocarditis for a group was around 5%. This compares with an 80-90% lifetime chance of infection with blood borne viral infections such as Hepatitis B. What is surprising from these figures is perhaps how small is the chance of a serious systemic infection such as endocarditis considering that Edinburgh users were injecting 3-4 times per day. It perhaps demonstrates how effective the host defence system is, particularly against bacteria, for most of the time.
Figure 2.5: A post mortem survey of narcotic drug users in New York from 1950-1961

Halpern & Rho 1966
INJECTION DRUG USE

Infection admissions

- Viral Hepatitis: 20.3%
- Lower Respiratory: 24.0%
- GI: 2.3%
- Bacteraemia: 3.2%
- Skin: 6.0%
- HIV: 13.8%
- Other: 15.7%
- Genital: 14.7%

Sheidegger & Zimmerli 1989

Figure 2.6: Survey of admissions associated with drug use in Switzerland
Figure 2.7: A survey of admissions to a specialised medical inpatient unit of a New York Hospital devoted to drug addiction
INJECTION DRUG USE
Medical Problems

Figure 2.8: Survey of accident and emergency consultations associated with drug use in Edinburgh during 1984
Injection Drug Use and HIV/AIDS

The first nine cases of AIDS amongst injection drug users were diagnosed retrospectively in 1980 and four of these were also homosexuals. The number of cases associated with IDU in the USA increased from 29 in 1981, to 148 in 1982, 324 in 1983, 4500 in 1986 and 26,321 by May 1989 accounting for at least 17% of AIDS cases in the USA. In Europe in 1984 IDU related AIDS accounted for only 2% of cases but this had risen to 26.8% by 1989 and it had been noted that in Europe IDU related AIDS was the fastest growing risk group.

IDU related HIV and AIDS epidemics are noted for their geographical clustering. For instance some 75% of IDU related AIDS in the USA has occurred in the New York City metropolitan area and in Europe 70% of the cases have been reported from Italy, Spain and France. As yet exact explanations for this clustering are not forthcoming although there are suggestions that it is linked to the intense sharing of equipment in localised areas together with mobility of a small number of users.

IDU related HIV was first noted from retrospective analysis of sera to have begun in New York in 1978, in Italy in 1979, in Germany in 1982, in Edinburgh, Dublin and Sweden in 1983, and in Copenhagen in 1984. The extent of HIV seropositivity in drug users is by and large related to the time of introduction of HIV into the community. For instance by 1984 in New York and 1985 in Edinburgh, HIV seroprevalence of drug users had passed 50%. The extent and variability of IDU related HIV seroprevalence is demonstrated in the appendix to this chapter.

In these differing communities the spread of IDU related HIV seems to follow two broad patterns, a slow gradual spread and a rapid explosive spread. The reasons for the different pattern is probably differing relationships between drug users. In some areas, drug users remain in tight knit communities often along racial lines. There may be little mixing between such different groups other than the purchase of drugs. As such, spread is rapid within groups but not between groups. In other situations possibly where there is only one racial group there is more dynamic interchange between users and spread is very rapid.

The scattered pockets of IDU related HIV around Europe may be explained by the movement of small numbers of very mobile users between areas of varying drug availability. In Italy relatively high seroprevalence amongst drug users around US Air Force bases has been suggested as one means of entry of the virus into Italy.
and thus Europe. This pattern of the sudden appearance of pockets of HIV amongst drug users may well be set to continue into developing countries with the reports of HIV seroprevalence amongst drug users of 44% in Bangkok, 22%-48% in Argentina and 54% in North India. The latter report from North India is reminiscent of the events in Edinburgh during 1983-85. The seroprevalence for HIV in North India was reported as being 0% of 2322 samples tested in September 1989 but 54% of 1412 drug users tested between October 1989 and June 1990.

The HIV epidemic in South East Asia has the potential for an enormous future AIDS epidemic in that area in about 7-10 years. The current focus of concern in South East Asia is without doubt Thailand where an explosive HIV epidemic began in 1987 such that by the end of 1990 there had been 76 cases of AIDS out of a total identified HIV population of 25,342, 50% of whom acquired the infection via IDU (personal communication Mr John K Roberts, Wellcome Thailand Ltd, Bangkok, Thailand and Dr Surapol Suwanagool, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand). By the end of June 1991, 123 cases of AIDS had been reported although the estimated numbers of HIV infected were between 200-400,000 individuals. Probably as a consequence of the mobility of drug users and the heterosexual contact's of prostitutes which has been reported elsewhere in the world, HIV is already spreading to neighbouring countries such as South West China where 29.6% of over 400 drug users were HIV seropositive (personal communication Professor Y Zeng, Institute of Virology, Chinese Academy of Prevention, presented at 1st International Conference on AIDS and Reproduction, December 1990, Genoa, Italy) and to Malaysia which by December 1990 had 19 cases of AIDS and over 750 cases of HIV infection, some 76% acquired via IDU (personal communication Professor Rokiah Ismail, Faculty of Medicine, University of Malaya, Kuala Lumpur).

The risk factors associated with HIV infection amongst drug users have not been well elucidated. The link with the frequency of equipment sharing is, however, now well established and in the USA there is also a link with injecting in "shooting galleries". More recently HIV has been cultured from needles and syringes collected from a shooting gallery in Miami, Florida confirming the infection risk. Less well recognised is the importance of the type of drug used. For instance, users inject cocaine intravenously often mixed with heroin and do so far more frequently than when they inject heroin alone. Recently a definite link
between HIV seropositivity and the use of intravenous cocaine has been reported\textsuperscript{66-74}.

Lastly, it is difficult to separate out the importance of the spread of HIV between drug users by sexual intercourse. However an estimate can be made by comparing the seroprevalence of injecting drug users and their non drug using sexual partners. For instance in one Italian study the seroprevalence of double drug using couples was 45\% compared to only 8\% in non drug using sexual partners\textsuperscript{75}. In Edinburgh whilst the seroprevalence of injecting drug users was around 50\% that in non using partners was only 15\%\textsuperscript{76}. These studies suggest that needle sharing is between three to five times as efficient at spreading HIV as heterosexual intercourse.

**Conclusions**

IDU is a small but important cause of medical problems and the problem of IDU related infections continues although the particular organisms involved have varied over time. The use of unsterile equipment increases susceptibility to bacterial and fungal infections which is even further increased in the setting of HIV. The particular organisms involved tend to vary with injection practices. The sharing of injection equipment has resulted in a number of problems over the years notably malaria, various forms of hepatitis and latterly HIV.

IDU related HIV was first reported from New York in 1980 and seems to spread via two broad patterns i.e. slow and gradual or rapid and explosive. Pockets of IDU related HIV are found in Northern Europe as a result of the mobility of drug users. This mobility of drug users is also the likely explanation for the similar explosive outbreak of IDU related HIV that has recently appeared in South East Asia.
Appendix

Table 2.1: IDU Related HIV Seroprevalence -British Isles

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>%HIV</th>
<th>Sample Size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scotland</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edinburgh</td>
<td>1982</td>
<td>0.0</td>
<td>182</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>14.0</td>
<td>124</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>42.0</td>
<td>205</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>38.0</td>
<td>106</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>51.0</td>
<td>164</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>52.0</td>
<td>191</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>56.0</td>
<td>164</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>64.0</td>
<td>203</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>1992</td>
<td>35.2</td>
<td>378</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>1992</td>
<td>20.3</td>
<td>227</td>
<td>141</td>
</tr>
<tr>
<td>Dundee</td>
<td>1986</td>
<td>39.0</td>
<td>251</td>
<td>82</td>
</tr>
<tr>
<td>Glasgow</td>
<td>1986</td>
<td>4.5</td>
<td>600</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>2.0</td>
<td>507</td>
<td>144</td>
</tr>
<tr>
<td>Location</td>
<td>Year</td>
<td>%HIV</td>
<td>Sample Size</td>
<td>Reference</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------</td>
<td>------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td><strong>England and Wales</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E&amp;W</td>
<td>1983</td>
<td>1.5</td>
<td>269</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>2.5</td>
<td>203</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>6.4</td>
<td>236</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>10.0</td>
<td>239</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1986/87</td>
<td>2.1</td>
<td>2712</td>
<td>87</td>
</tr>
<tr>
<td>Manchester</td>
<td>1986</td>
<td>0.0</td>
<td>100</td>
<td>82</td>
</tr>
<tr>
<td>Liverpool</td>
<td>1986</td>
<td>0.0</td>
<td>200</td>
<td>82</td>
</tr>
<tr>
<td>Southport</td>
<td>1986</td>
<td>0.0</td>
<td>36</td>
<td>82</td>
</tr>
<tr>
<td>South London</td>
<td>1985</td>
<td>6.4</td>
<td>236</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>0.6</td>
<td>146</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>6.0</td>
<td>293</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>4.0</td>
<td>313</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>5.0</td>
<td>216</td>
<td>84</td>
</tr>
<tr>
<td>London (overall)</td>
<td>1990</td>
<td>12.8</td>
<td>491</td>
<td>142</td>
</tr>
<tr>
<td>London (never in treatment)</td>
<td>1990</td>
<td>20.6</td>
<td>131</td>
<td>142</td>
</tr>
<tr>
<td>London (current and previous treatment)</td>
<td>1990</td>
<td>10.2</td>
<td>354</td>
<td>142</td>
</tr>
<tr>
<td><strong>Ireland</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dublin (healthy)</td>
<td>1985</td>
<td>27.0</td>
<td>451</td>
<td>51</td>
</tr>
<tr>
<td>Dublin (ill)</td>
<td>1985</td>
<td>37.0</td>
<td>152</td>
<td>51</td>
</tr>
<tr>
<td>Dublin (neonates)</td>
<td>1985</td>
<td>55.0</td>
<td>11</td>
<td>51</td>
</tr>
</tbody>
</table>
Table 2.2: IDU Related HIV Seroprevalence -Europe

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>% HIV</th>
<th>Sample Size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milan</td>
<td>1979</td>
<td>7.0</td>
<td>716</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1980</td>
<td>6.0</td>
<td>716</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1981</td>
<td>8.0</td>
<td>716</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1982</td>
<td>22.0</td>
<td>716</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1982</td>
<td>24.0</td>
<td>67</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>35.0</td>
<td>716</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>21.0</td>
<td>78</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>45.0</td>
<td>716</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>60.0</td>
<td>716</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>53.0</td>
<td>62</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>69.3</td>
<td></td>
<td>89</td>
</tr>
<tr>
<td>Bari</td>
<td>1980</td>
<td>6.0</td>
<td>68</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>1981</td>
<td>10.0</td>
<td>58</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>1982</td>
<td>15.0</td>
<td>47</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>31.0</td>
<td>49</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>53.0</td>
<td>34)</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>76.0</td>
<td>59</td>
<td>90</td>
</tr>
<tr>
<td>Pordenone/ Udine</td>
<td>1985</td>
<td>27.0</td>
<td>315</td>
<td>75</td>
</tr>
<tr>
<td>Pordenone</td>
<td>1985/86</td>
<td>90.0</td>
<td>63</td>
<td>55</td>
</tr>
<tr>
<td>Udine</td>
<td>1985/86</td>
<td>10.0</td>
<td>134</td>
<td>55</td>
</tr>
<tr>
<td>Rome</td>
<td>1985</td>
<td>28.0</td>
<td>207</td>
<td>91</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>52.0</td>
<td>220</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>33.0</td>
<td>120</td>
<td>93</td>
</tr>
<tr>
<td>Location</td>
<td>Year</td>
<td>% HIV</td>
<td>Sample Size</td>
<td>Reference</td>
</tr>
<tr>
<td>--------------</td>
<td>------</td>
<td>-------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Italy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Padua</td>
<td>1985</td>
<td>43.0</td>
<td>460</td>
<td>94</td>
</tr>
<tr>
<td>Naples</td>
<td>1986</td>
<td>14.0</td>
<td>164</td>
<td>93</td>
</tr>
<tr>
<td>Sicily</td>
<td>1987</td>
<td>68.4</td>
<td>684</td>
<td>95</td>
</tr>
<tr>
<td>Palermo</td>
<td>1980</td>
<td>5.0</td>
<td>20</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>40.0</td>
<td>40</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>62.5</td>
<td>341</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>60.9</td>
<td>271</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>49.4</td>
<td>245</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>44.0</td>
<td>250</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>1989</td>
<td>41.0</td>
<td>234</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>38.5</td>
<td>226</td>
<td>145</td>
</tr>
<tr>
<td>Spain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valencia</td>
<td>1983</td>
<td>11.0</td>
<td>58</td>
<td>96</td>
</tr>
<tr>
<td>North Spain</td>
<td>1983</td>
<td>35.0</td>
<td>478</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>71.0</td>
<td>478</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>40.0</td>
<td>174</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>48.0</td>
<td>75</td>
<td>96</td>
</tr>
<tr>
<td>Bilbao</td>
<td>1984/85</td>
<td>50.0</td>
<td>479</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>41.9</td>
<td>313</td>
<td>64</td>
</tr>
<tr>
<td>Catalonia</td>
<td>1985/88</td>
<td>40.7</td>
<td>55</td>
<td>98</td>
</tr>
<tr>
<td>Barcelona</td>
<td>1985/88</td>
<td>70.0</td>
<td>473</td>
<td>99</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paris</td>
<td>1984</td>
<td>75.0</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>64.0</td>
<td>113</td>
<td>61</td>
</tr>
<tr>
<td>Location</td>
<td>Year</td>
<td>% HIV</td>
<td>Sample Size</td>
<td>Reference</td>
</tr>
<tr>
<td>-------------------</td>
<td>--------</td>
<td>-------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tours</td>
<td>1982/83</td>
<td>0.0</td>
<td>52</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>15.0</td>
<td>40</td>
<td>101</td>
</tr>
<tr>
<td>Tours</td>
<td>1985</td>
<td>17.0</td>
<td>125</td>
<td>101</td>
</tr>
<tr>
<td>Toulouse</td>
<td>1985</td>
<td>51.0</td>
<td>402</td>
<td>102</td>
</tr>
<tr>
<td><strong>Holland</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amsterdam</td>
<td>1983</td>
<td>3.4</td>
<td>145</td>
<td>103</td>
</tr>
<tr>
<td>prostitutes</td>
<td>1983</td>
<td>23.0</td>
<td>52</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>33.3</td>
<td>52</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>28.3</td>
<td>52</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>27.8</td>
<td>560</td>
<td>104</td>
</tr>
<tr>
<td><strong>Austria</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tyrol</td>
<td>1985</td>
<td>44.0</td>
<td>34</td>
<td>105</td>
</tr>
<tr>
<td>Vienna</td>
<td>1985</td>
<td>8.5</td>
<td>82</td>
<td>106</td>
</tr>
<tr>
<td>Vienna</td>
<td>1986</td>
<td>14.4</td>
<td>159</td>
<td>106</td>
</tr>
<tr>
<td>Prisoners</td>
<td>1986</td>
<td>17.0</td>
<td>71</td>
<td>63</td>
</tr>
<tr>
<td>Methadone treatment</td>
<td>1988</td>
<td>44.0</td>
<td>136</td>
<td>107</td>
</tr>
<tr>
<td><strong>Switzerland</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geneva</td>
<td>1981</td>
<td>7.0</td>
<td>131</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>52.0</td>
<td>131</td>
<td>108</td>
</tr>
<tr>
<td>Bern</td>
<td>1979/81</td>
<td>0.0</td>
<td>93</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td>1982</td>
<td>16.0</td>
<td>79</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>16.0</td>
<td>49</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>42.0</td>
<td>38</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>32.0</td>
<td>37</td>
<td>86</td>
</tr>
<tr>
<td>Location</td>
<td>Year</td>
<td>% HIV</td>
<td>Sample Size</td>
<td>Reference</td>
</tr>
<tr>
<td>-------------------</td>
<td>------</td>
<td>-------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td><strong>Switzerland</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bern/Basel/Geneva</td>
<td>1983</td>
<td>36.0</td>
<td>103</td>
<td>109</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>53.0</td>
<td>55</td>
<td>109</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>36.0</td>
<td>103</td>
<td>110</td>
</tr>
<tr>
<td>Lausanne</td>
<td>1987</td>
<td>47.3</td>
<td>63</td>
<td>111</td>
</tr>
<tr>
<td><strong>Sweden</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>3.0</td>
<td>67</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>1984/86</td>
<td>16.0</td>
<td>32</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>57.0</td>
<td>60</td>
<td>52</td>
</tr>
<tr>
<td><strong>Denmark</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>autopsies</td>
<td>1988</td>
<td>6.0</td>
<td>83</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>1989</td>
<td>11.0</td>
<td>86</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>14.0</td>
<td>90</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>1991</td>
<td>14.0</td>
<td>130</td>
<td>146</td>
</tr>
<tr>
<td><strong>Greece</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>prisoners</td>
<td>1987</td>
<td>2.1</td>
<td>288</td>
<td>112</td>
</tr>
<tr>
<td>voluntary screening</td>
<td>1987</td>
<td>2.8</td>
<td>434</td>
<td>113</td>
</tr>
<tr>
<td><strong>West Germany</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Berlin</td>
<td>1985</td>
<td>30.0</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>49.0</td>
<td></td>
<td>114</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>30.0</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>30.0</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1989</td>
<td>30.0</td>
<td>114</td>
<td></td>
</tr>
</tbody>
</table>
Table 2.2 continued: IDU Related HIV Seroprevalence -Europe

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>% HIV</th>
<th>Sample Size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>West Germany</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Berlin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>49.0</td>
<td></td>
<td>114</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>38.0</td>
<td></td>
<td>115</td>
</tr>
<tr>
<td>detoxification</td>
<td>1988</td>
<td>13.0</td>
<td>362</td>
<td>115</td>
</tr>
<tr>
<td>prisoners</td>
<td>1988</td>
<td>12.0</td>
<td>362</td>
<td>115</td>
</tr>
<tr>
<td>Hamburg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>autopsy</td>
<td>1985</td>
<td>0.0</td>
<td>362</td>
<td>115</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>23.0</td>
<td>362</td>
<td>115</td>
</tr>
<tr>
<td>Hamburg</td>
<td>1987</td>
<td>16.0</td>
<td>362</td>
<td>115</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>13.0</td>
<td>362</td>
<td>115</td>
</tr>
<tr>
<td><strong>Portugal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Portuguese</td>
<td>1988</td>
<td>8.0</td>
<td>24</td>
<td>116</td>
</tr>
<tr>
<td>foreigners</td>
<td>1988</td>
<td>67.0</td>
<td>86</td>
<td>116</td>
</tr>
<tr>
<td><strong>Yugoslavia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Belgrade</td>
<td>1983</td>
<td>10.0</td>
<td>40</td>
<td>117</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>42.0</td>
<td>19</td>
<td>117</td>
</tr>
<tr>
<td></td>
<td>1986/88</td>
<td>44.0</td>
<td>625</td>
<td>118</td>
</tr>
<tr>
<td>Zagreb</td>
<td>1985</td>
<td>5.0</td>
<td>140</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>5.9</td>
<td>393</td>
<td>119</td>
</tr>
<tr>
<td><strong>Czecho-slovakia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>0.0</td>
<td>228</td>
<td>120</td>
</tr>
</tbody>
</table>
Table 2.2 continued: IDU Related HIV Seroprevalence -Europe

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>% HIV</th>
<th>Sample Size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poland</td>
<td>1986</td>
<td>0.0</td>
<td></td>
<td>121</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>0.0</td>
<td></td>
<td>121</td>
</tr>
<tr>
<td>North East</td>
<td>1988</td>
<td>0.0</td>
<td>30</td>
<td>121</td>
</tr>
<tr>
<td>Warsaw</td>
<td>1988</td>
<td>2.9</td>
<td>718</td>
<td>122</td>
</tr>
<tr>
<td></td>
<td>1989</td>
<td>8.0</td>
<td>718</td>
<td>122</td>
</tr>
<tr>
<td>Israel</td>
<td>1988-89</td>
<td>2.3</td>
<td>300</td>
<td>143</td>
</tr>
</tbody>
</table>
Table 2.3: IDU Related HIV Seroprevalence - American Continent

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>% HIV</th>
<th>Sample Size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Canada</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manitoba</td>
<td>1988</td>
<td>2.1</td>
<td>627</td>
<td>123</td>
</tr>
<tr>
<td>Montreal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hospitalised</td>
<td>1985/88</td>
<td>4.4</td>
<td>294</td>
<td>123</td>
</tr>
<tr>
<td>detoxification unit</td>
<td>1985</td>
<td>7.1</td>
<td></td>
<td>123</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>3.0</td>
<td></td>
<td>124</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>2.0</td>
<td></td>
<td>124</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>6.6</td>
<td></td>
<td>124</td>
</tr>
<tr>
<td><strong>United States</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>San Francisco</td>
<td>1985</td>
<td>10.0</td>
<td>281</td>
<td>60</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>1987</td>
<td>3.4</td>
<td>205</td>
<td>125</td>
</tr>
<tr>
<td>Denver</td>
<td>1985</td>
<td>2.0</td>
<td>76</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>5.0</td>
<td>262</td>
<td>82</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>1981/83</td>
<td>30.0</td>
<td>283</td>
<td>126</td>
</tr>
<tr>
<td>Maimi</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in treatment</td>
<td>1988</td>
<td>12.0</td>
<td></td>
<td>127</td>
</tr>
<tr>
<td>street users</td>
<td>1988</td>
<td>33.0</td>
<td>500</td>
<td>127</td>
</tr>
<tr>
<td>Chicago</td>
<td>1984/85</td>
<td>11.0</td>
<td>35</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>1986/87</td>
<td>33.0</td>
<td>200</td>
<td>128</td>
</tr>
<tr>
<td>Baltimore</td>
<td>1988</td>
<td>24.7</td>
<td>441</td>
<td>129</td>
</tr>
<tr>
<td>Detroit</td>
<td>1985/86</td>
<td>12.5</td>
<td>96</td>
<td>130</td>
</tr>
<tr>
<td></td>
<td>1987/88</td>
<td>15.7</td>
<td>70</td>
<td>130</td>
</tr>
<tr>
<td></td>
<td>1988/89</td>
<td>15.5</td>
<td>71</td>
<td>130</td>
</tr>
</tbody>
</table>
Table 2.3 continued: IDU Related HIV Seroprevalence - American Continent

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>% HIV</th>
<th>Sample Size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minneapolis</td>
<td>1987</td>
<td>1.3</td>
<td>231</td>
<td>131</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>1.5</td>
<td>325</td>
<td>131</td>
</tr>
<tr>
<td>New York</td>
<td>1978</td>
<td>9.0</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>1979</td>
<td>30.0</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>1980</td>
<td>40.0</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>1982</td>
<td>50.0</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>drug treatment</td>
<td>1983/84</td>
<td>33.0</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>Hospitalised non-opportunistic infection</td>
<td>1983/84</td>
<td>70.0</td>
<td>132</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>35.0</td>
<td>103</td>
<td>133</td>
</tr>
<tr>
<td>drug detoxification</td>
<td>1984</td>
<td>58.0</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>50.0</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Bronx, New York</td>
<td>1985</td>
<td>32.0</td>
<td>445</td>
<td>134</td>
</tr>
<tr>
<td>Methadone</td>
<td>1987</td>
<td>59.5</td>
<td>222</td>
<td>125</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>19.4</td>
<td>31</td>
<td>130</td>
</tr>
<tr>
<td>San Antonio</td>
<td>1987</td>
<td>1.3</td>
<td>149</td>
<td>125</td>
</tr>
<tr>
<td>South America</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buenos Aires</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>drug detoxification</td>
<td>1987</td>
<td>22.0</td>
<td>268</td>
<td>57</td>
</tr>
<tr>
<td>hepatitis</td>
<td>1987</td>
<td>48.0</td>
<td>97</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>63.9</td>
<td>36</td>
<td>135</td>
</tr>
<tr>
<td></td>
<td>1988</td>
<td>60.3</td>
<td>338</td>
<td>136</td>
</tr>
</tbody>
</table>
### Table 2.4: IDU Related HIV Seroprevalence - Oceania

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>% HIV</th>
<th>Sample Size</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>1986</td>
<td>0.8</td>
<td>1905</td>
<td>137</td>
</tr>
<tr>
<td>Thailand</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bangkok</td>
<td>1985</td>
<td>0.0</td>
<td>99</td>
<td>138</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>0.0</td>
<td>75</td>
<td>138</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>1.0</td>
<td>3180</td>
<td>138</td>
</tr>
<tr>
<td></td>
<td>3/88</td>
<td>16.0</td>
<td>1649</td>
<td>138</td>
</tr>
<tr>
<td></td>
<td>9/88</td>
<td>43.0</td>
<td>1811</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>6/90</td>
<td>44.0</td>
<td>878</td>
<td>138</td>
</tr>
<tr>
<td></td>
<td>4/89</td>
<td>45.0</td>
<td>1020</td>
<td>138</td>
</tr>
<tr>
<td>India</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North India</td>
<td>9/89</td>
<td>0</td>
<td>2322</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>10/89-6/90</td>
<td>54.2</td>
<td>1412</td>
<td>32</td>
</tr>
</tbody>
</table>
References for Chapter 2


41. Robertson JR & Bucknall AB. Heroin users in a Scottish City - Edinburgh Drug Addiction Study 1986. West Granton Medical Group, 1 Muirhouse Avenue, Edinburgh, EH4 4PL.


45. Communicable Diseases (Scotland) Unit. AIDS Surveillance in Europe: Update to 30th June 1987 (Part 2). Communicable Diseases (Scotland) Unit, Answer 1987; 87/47: 1.


CHAPTER 3
Clinical features of drug use and drug use related HIV

Introduction

The extent of the injection drug use (IDU) related HIV epidemic in Edinburgh requires consideration of the clinical features of IDU as well as those of HIV since each may mimic the other. As an example, lymphadenopathy is associated with both HIV and with the injecting of foreign materials. The fatigue, lethargy and excessive sweating which are an early feature of HIV can all, also be caused by mild withdrawal from opiates. Diarrhoea, a common presentation of early symptomatic HIV (CDC stage IV A) is unfortunately a common problem with opiate withdrawal. A history of diarrhoea for longer than 1 month may be elicited via direct questioning and suggest a possible diagnosis of CDC stage IV A. Such a history would also require a search for specific pathogens such as cryptosporidium which are seen in AIDS. However early morning diarrhoea is common for those on methadone and is simply a symptom of early opiate withdrawal. Weight loss and sweating are both key symptoms of constitutional disease (CDC stage IV A) as well as mycobacterial infections, yet both are associated with heavy opiate use or the use of stimulants (amphetamines or cocaine).

Epileptic fits in patients with HIV requires consideration of cerebral toxoplasmosis but the intermittent use of benzodiazepines can also cause seizures. The regular monitoring of CD4 counts and toxoplasma serology helps to identify those patients at risk of toxoplasmosis and consequently reduces the number of CT scans required. The excessive use of cannabis and benzodiazepines interferes with memory and other cognitive functions in a similar manner to HIV although in the former dramatic improvement occurs with reduction or cessation of drugs. Thus early dementia which might be detected in other risk groups by psychometric testing is extremely difficult to diagnose in current drug users especially since reducing drugs will also help the dementing patient to improve function in the activities of daily living. Syncopal attacks in AIDS are often associated with an autonomic neuropathy or a failing adrenal cortex. This problem however is associated with the use or misuse of antidepressant tricyclic drugs such as amitriptyline. Lastly shortness of breath and a persistent cough are common early symptoms of PCP but can occur with endocarditis, bacterial pneumonia, excessive smoking, recurrent bronchitis and obstructive airways disease.
The medical conditions associated with IDU include asymptomatic abnormalities of pulmonary function tests, life threatening infections, or immunological problems such as polyarteritis nodosa. The advent of IDU related HIV has not only widened the spectrum of disease seen in drug users but has also increased the frequency of some existing conditions. As a consequence the differential diagnosis in a patient with IDU related HIV is extensive. Further examples are detailed in Table 3.1. Because of the difficulties with interpreting the history and the extensive differential diagnosis if there is evidence of current drug use, a short period of admission is often the only way to clarify the situation.

Table 3.1: Comparison of Drug, IDU and HIV related problems

<table>
<thead>
<tr>
<th>Symptom Complex</th>
<th>Drug related problems</th>
<th>HIV related problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent sinusitis</td>
<td>&quot;Snorting&quot; of drugs</td>
<td>Susceptibility to recurrent bacterial infection</td>
</tr>
<tr>
<td>Reduced transfer factor for carbon monoxide</td>
<td>Tale granuloma secondary to emboli, cocaine</td>
<td>PCP</td>
</tr>
<tr>
<td>Respiratory Syndrome (cough, dyspnoea etc.)</td>
<td>Chronic bronchitis secondary to tobacco and marijuana</td>
<td>Increased susceptibility to bacterial infections</td>
</tr>
<tr>
<td></td>
<td>Emphysema (tobacco)</td>
<td>HIV related emphysema</td>
</tr>
<tr>
<td></td>
<td>Inhalation or aspiration pneumonia</td>
<td>PCP, TB, Other OI's, Bacterial Pneumonia, KS etc.</td>
</tr>
<tr>
<td></td>
<td>Acute bronchitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Endocarditis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&quot;Heroin asthma&quot; or pulmonary oedema</td>
<td></td>
</tr>
<tr>
<td>Polyarteritis nodosa related pneumonitis</td>
<td>Tale granuloma secondary to emboli</td>
<td>HIV related pulmonary hypertension</td>
</tr>
</tbody>
</table>

| Pulmonary Hypertension (dyspnoea, hypoxaemia, restrictive lung disease) | |

116
Table 3.1 continued: Comparison of Drug, IDU and HIV related problems

<table>
<thead>
<tr>
<th>Symptom Complex</th>
<th>Drug related problems</th>
<th>HIV related problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>Endocarditis, septicaemia etc.</td>
<td>CDC stage IV A, PCP and OI's such as MAI,</td>
</tr>
<tr>
<td></td>
<td>&quot;Bad fix&quot; or endotoxaemia</td>
<td></td>
</tr>
<tr>
<td>Night sweats</td>
<td>Opiate withdrawals</td>
<td>CDC Stage III, IV A, or early OI</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Heavy addiction, poor diet and use of stimulants such as cocaine or amphetamines</td>
<td>CDC stage IV A, TB or other OI</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Opiate withdrawals</td>
<td>CDC stage IV A or enteric pathogen</td>
</tr>
<tr>
<td>Sore mouth</td>
<td></td>
<td>Thrush OHL etc.</td>
</tr>
<tr>
<td>Sores around mouth /nose</td>
<td>poor diet, snorting or sniffing glue or cocaine</td>
<td>HSV</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Intra-abdominal pathology obscured by opiates e.g. appendicitis, cholecystitis pancreatitis etc.</td>
<td>MAI, cryptosporidium, CMV, lymphoma, KS etc.</td>
</tr>
<tr>
<td>Abnormal liver function tests</td>
<td>Acute hepatitis type A, B, C, D</td>
<td>Recurrence of B, C or D hepatitis, drug reactions e.g. anti TB drugs and MAI</td>
</tr>
<tr>
<td></td>
<td>Paracetamol overdose</td>
<td></td>
</tr>
</tbody>
</table>
Table 3.1 continued: Comparison of Drug, IDU and HIV related problems

<table>
<thead>
<tr>
<th>Symptom Complex</th>
<th>Drug related problems</th>
<th>HIV related problems</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurological</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of vision</td>
<td>Endocarditis, opthalmitis (candidaemia)</td>
<td>CMV/VZV/HSV retinitis, toxoplosmosis, etc.</td>
</tr>
<tr>
<td>Toxic confusional state</td>
<td>Drug use or infection</td>
<td>Bacterial infections, OI's, HIV encephalopathy</td>
</tr>
<tr>
<td>Epileptic seizures</td>
<td>Withdrawals from benzodiazepines or barbiturates,</td>
<td>Toxoplasmosis</td>
</tr>
<tr>
<td>Peripheral nerve paralysis</td>
<td>IDU related traumatic nerve damage</td>
<td>Seroconversion illness of HIV, CDC stage IV B</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>Endocarditis</td>
<td>Toxoplasmosis, cerebral haemorrhage secondary to HIV related thrombocytopaenia</td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purpura</td>
<td>IDU, endocarditis</td>
<td>HIV related thrombocytopaenia</td>
</tr>
<tr>
<td>Itching and scratching</td>
<td>Opiates and stimulant use</td>
<td>Seborrhoeic dermatitis, scabies, HIV related papular urticaria</td>
</tr>
<tr>
<td>Recurrent abscesses</td>
<td>IDU</td>
<td>Susceptibility to bacterial infections, bacillariy angiomatosis, lymphoma.</td>
</tr>
<tr>
<td><strong>Cardiology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart murmurs</td>
<td>Endocarditis</td>
<td>HIV</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>Alcohol</td>
<td>HIV related pulmonary hypertension</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>Talc granuloma's</td>
<td></td>
</tr>
</tbody>
</table>

**Complications of Drug Use - non infection related**

The medical complications of IDU which are not related to infection are summarised in Table 3.2.
<table>
<thead>
<tr>
<th>Problem</th>
<th>Medical complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug effects</strong></td>
<td></td>
</tr>
<tr>
<td>Excess Opiate</td>
<td>Narcosis, coma, small pupils, respiratory depression, aspiration pneumonia, and rhabdomyolysis secondary to pressure</td>
</tr>
<tr>
<td>Opiate withdrawal</td>
<td>Simulates a mild &quot;URTI&quot; (sweating, coryza, lacrimation), pupillary dilation, insomnia, nausea, vomiting, diarrhoea, lethargy, muscle weakness, myalgia, muscle twitching, tachycardia and hypertension</td>
</tr>
<tr>
<td>Excess cocaine</td>
<td>Apprehension, dizziness, syncope, blurred vision, dysphoric states, paranoia, confusion and aggressive behaviour</td>
</tr>
<tr>
<td>Excess amphetamine</td>
<td>Seizures, coma, hyperthermia, respiratory depression, apnoea, sudden death, spontaneous rhabdomyolysis</td>
</tr>
<tr>
<td>Stimulant withdrawal</td>
<td>Headaches, anorexia, nausea, tremors, dilated pupils, tachycardia and hypertension</td>
</tr>
<tr>
<td><strong>Trauma</strong></td>
<td></td>
</tr>
<tr>
<td>Frequent injecting</td>
<td>Sleepiness, lethargy, increased appetite, food binging, depression or even suicide</td>
</tr>
<tr>
<td>Misplaced injections</td>
<td>Track marks and skin scars</td>
</tr>
<tr>
<td></td>
<td>Lack of veins and thrombophlebitis</td>
</tr>
<tr>
<td></td>
<td>Deep venous thrombosis</td>
</tr>
<tr>
<td></td>
<td>Persistent peripheral oedema, venous stasis and ulcers secondary to chronic venous obstruction</td>
</tr>
<tr>
<td></td>
<td>Arterial damage and insufficiency with secondary tissue damage, muscle compartment syndrome and traumatic rhabdomyolysis</td>
</tr>
<tr>
<td></td>
<td>False aneurysms and pulmonary emboli</td>
</tr>
<tr>
<td></td>
<td>Traumatic neuropathy</td>
</tr>
<tr>
<td>Problem</td>
<td>Medical complications</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Pulmonary</strong></td>
<td></td>
</tr>
<tr>
<td>Inhaled cocaine and excessive use of Valsalva</td>
<td>Spontaneous pneumomediastinum/pneumothorax</td>
</tr>
<tr>
<td></td>
<td>Spontaneous pneumopericardium</td>
</tr>
<tr>
<td>Excess sedatives or stimulants</td>
<td>Respiratory depression, coma and pneumonia</td>
</tr>
<tr>
<td>Opiate withdrawals</td>
<td>Simulates a mild &quot;URTI&quot;</td>
</tr>
<tr>
<td>Stimulant use e.g. cocaine</td>
<td>Tachynoea</td>
</tr>
<tr>
<td>Opiates or cocaine</td>
<td>Pulmonary oedema</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Polyarteritis nodosa</td>
</tr>
<tr>
<td>Foreign body emboli (particles injected intravenously) e.g. talc granuloma's</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td></td>
<td>Abnormal pulmonary function e.g. reduced DCO</td>
</tr>
<tr>
<td></td>
<td>Restrictive defect due to interstitial lung disease</td>
</tr>
<tr>
<td>Smoking of tobacco, heroin, marijuana</td>
<td>Abnormal pulmonary function e.g. reduced DCO</td>
</tr>
<tr>
<td></td>
<td>COAD</td>
</tr>
<tr>
<td>&quot;Snorting&quot; stimulants</td>
<td>Chronic rhinitis, rhinorrhoea, anosmia, atrophy of the mucosal membranes, ulceration and perforation of the nasal septum</td>
</tr>
<tr>
<td>&quot;Snorting&quot; opiates</td>
<td>Recurrent sinusitis</td>
</tr>
</tbody>
</table>
### Table 3.2 continued: Medical (non infection) problems of Drug Use

<table>
<thead>
<tr>
<th>Problem</th>
<th>Medical complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiology</strong></td>
<td></td>
</tr>
<tr>
<td>Cocaine</td>
<td>Cardiac arrhythmia's such as sinus tachycardia, ventricular tachycardia and fibrillation as well as asystole</td>
</tr>
</tbody>
</table>
| Adulterants of illicit drugs e.g. quinine | Myocardial infarction  
Severe hypertension  
Cardiac arrhythmia's and death |
| **Endocrinology** |                                                                                       |
| Opiate use      | Increase prolactin levels and gynecomastia  
Amenorrhoea (may be secondary to weight loss) |
| Cannabis        | Oligospermia, impotence and gynecomastia                                                |
| **Neurology**   |                                                                                       |
| Stimulants      | Psychosis  
Depression  
Cerebral infarcts and haemorrhages(cerebrovascular accidents) |
| Depressants such as benzodiazepines or barbiturates | Brain damage |
| **Immunology**  |                                                                                       |
| IDU             | Enlarged lymph nodes  
Elevated serum IgM  
False positive syphilis serology |

As with IDU itself, measuring the frequency of the medical complications of IDU is difficult and may well be underestimated, because the drug use is often not declared on contact with the health service. A pre HIV survey of admissions in the 1970’s to a specialised medical inpatient unit of a New York Hospital devoted to drug addiction revealed that although nearly 60% were due to infection, 21% were for general medical conditions; diabetes 7.5%, pulmonary disease 6%, cardiovascular disease
4%, and gastro-intestinal disease 3.5%\textsuperscript{1}. The pulmonary problems noted were pulmonary fibrosis (obstructive or restrictive), carcinoma of the lung, chronic bronchitis, pleural effusion, pulmonary emboli, and bronchial asthma. Heavy cigarette smoking was regarded as a probable cause of many of the problems although the injection of inert material was also thought to be a contributing cause of the pulmonary fibrosis. The cardiovascular problems included congestive heart failure, cardiomyopathy and viral pericarditis. The gastro-intestinal disorders included, ulcers, gastritis, small bowel dysfunction and cirrhosis\textsuperscript{1}.

A survey of narcotic related deaths in New York in the 1950's which found that nearly 50% of the deaths were related to drug excess, also noted that 20% were due to infections, 18% to medical conditions (including 7% because of respiratory problems other than pulmonary oedema and drug overdose)\textsuperscript{2}. A few of the lungs studied contained microscopic granulomas of the foreign body type which were thought to have occurred because of a reaction to injected foreign particulate matter which adulterates "street heroin". Particles of cotton fibres used to filter drugs before injection were also been seen within these granulomas\textsuperscript{2}.

**Drug effects**

Prior to the advent of HIV, drug use itself had a relatively low mortality with alternating periods of abstinence and drug use. Probably the commonest complication of opiate use is either an excessive dose with subsequent narcosis or coma and respiratory failure or withdrawal effects. It had been estimated that opiate overdoses killed around 1% of drug users each year but this was before the description of HIV\textsuperscript{3-7}. The clinical features of excessive doses of opiates include coma of varying severity, small pupils and depressed respiration. This state may or may not be associated with a respiratory infection. There is an absence of focal neurology, poor peripheral circulation and possibly a fever whilst investigations may reveal a reduced oxygen tension and possibly hypercapnia. Early withdrawal from opiates simulates a mild upper respiratory tract infection with sweating, coryza, lacrimation and even a slight fever. In a known drug user, sweating, involuntary sniffing and pupillary dilation are helpful physical signs of early withdrawal from opiates. Later the patient may suffer insomnia, nausea, vomiting, diarrhoea, lethargy, muscle weakness, myalgia, muscle twitching, tachycardia and hypertension.

The excessive use of stimulants such as cocaine produces apprehension, dizziness, syncope, blurred vision, dysphoric states, paranoia, confusion and aggressive
behaviour\textsuperscript{8}. Seizures, coma, hyperthermia, respiratory depression, apnoea and sudden death have also been reported\textsuperscript{8}. Cardiovascular problems can occur after apparently small doses notably cardiac arrhythmias such as sinus tachycardia, ventricular tachycardia and fibrillation as well as asystole. Myocardial infarction, even in teenagers, severe hypertension and cerebrovascular accidents have all been noted\textsuperscript{8}. Withdrawal from stimulants such as cocaine, produces sweating, irritability, hypersomnia, depression or even psychosis. Excess amphetamines produce headaches, anorexia, nausea, tremors, dilated pupils, tachycardia and hypertension. Withdrawals from amphetamines result in sleepiness, lethargy, increased appetite, food binging, depression or even suicide.

Inhaling or smoking cocaine has also been associated with a decreased diffusing capacity for carbon monoxide\textsuperscript{8}. The commonest abnormality of pulmonary function in injection drug users is a reduction of the carbon monoxide transfer factor which occurred as the sole abnormality in 38\% of one series (in 42\% the reduction was to less than 75\% of the predicted value). Obstructive lung disease (asthma or chronic bronchitis) was observed in 6\% and a restrictive defect due to interstitial lung disease in 7\%. Radiological evidence of pulmonary hypertension was not observed in any patient. The authors concluded that alterations of pulmonary function due to foreign body emboli were common but that significant respiratory symptoms were unusual. Unfortunately follow up was not attempted and whether there are long term pulmonary problems of injection drug use has yet to be determined\textsuperscript{9}.

Regular smoking of marijuana (3-4 cigarettes per day) is associated with the same frequency of symptoms of acute and chronic bronchitis as well as the same type and extent of epithelial damage in the central airways as the regular smoking of 20 tobacco cigarettes per day\textsuperscript{10}. The different methods of smoking marijuana compared to tobacco cigarettes results in a greater quantity of smoke particulate and noxious gases being delivered to and deposited in the lungs during the smoking of marijuana and this probably explains the greater propensity for lung damage associated with marijuana. In one study smoking marijuana was associated with a five fold increment in the blood carboxyhaemoglobin, a three fold increase in the amount of tar inhaled and a one third increase in the amount of inhaled tar retained in the respiratory tract\textsuperscript{10}.
Pulmonary oedema

Heroin related pulmonary oedema is a rare complication of heroin use if one considers the fact that most users inject 3-4 times each day\textsuperscript{11,12}. It was reported in association with morphine by Osler as early as 1880 which was 18 years before heroin was first manufactured\textsuperscript{13}. The majority of reports however have incriminated recreational injections of heroin which may result in sudden unexpected death often with the needle and syringe still in situ\textsuperscript{6,14,15}. In one series this problem accounted for 48% of all deaths in narcotic drug users in New York\textsuperscript{6}. Estimates of 1 death per 150,000 injections have been made which is less than for penicillin anaphylaxis\textsuperscript{15}.

Since opiate related pulmonary oedema was originally associated with sudden death in those injecting recreational opiates a number of theories were suggested including bacterial or endotoxin contamination\textsuperscript{12}. However it has also been described with sterile medical injections of opiates as well as with orally administered opiates. Two cases of methadone associated pulmonary oedema were reported in 1972 in individuals without previous drug use and unassociated with injection drug use\textsuperscript{16}. It would therefore appear to be some form of idiosyncratic reaction, possibly as a result of activation of histamine releasing cells\textsuperscript{16,17}. Investigations have revealed that the pulmonary wedge pressure is normal and the resulting oedema fluid is rich in protein supporting the hypothesis that it occurs because of altered capillary permeability and should therefore be considered as a form of adult respiratory distress syndrome or ARDS\textsuperscript{16,17}.

Trauma

A common complication of IDU is traumatic damage to tissues and organs secondary to injections although it's frequency is difficult to determine; much of it is subclinical, it depends on a number of factors which are difficult to quantify; local drug practices, the skill of the injector and the susceptibility of the individual, since the frequency of thrombophlebitis varies with individuals.

The commonest trauma associated with IDU is the physical damage from frequent injecting also known as tracking or track marks - the hallmark of IDU\textsuperscript{2,3,15}. This cutaneous stigmata of IDU may also be associated with pigmentation of the skin or even scarring around superficial blood vessels\textsuperscript{2,3,15}. There are often also scars of superficial abscesses which are more common with subcutaneous injections (skin popping) of drugs than with intravenous drug use\textsuperscript{2,3,15}. The associated abscesses
may be extensive and infected with micro-organisms or a purely chemical reaction to the substances injected\textsuperscript{2,3,15}.

Individuals who lose superficial venous access may turn to injecting the deep limb or neck veins with more consequent increased risks of damage to adjacent tissues. For instance the use of the femoral veins, a technique often learnt from the physician who cannot obtain blood for investigations, may result in damage to the femoral nerve with a subsequent pressure neuropathy or arterial damage and anoxic damage to distal tissues. The physical signs of a femoral neuropathy include muscle wasting, pain and sensory loss in the limb. False aneurysms of the femoral artery may complicate intra-arterial injections and these false aneurysms may become infected and produce life threatening haemorrhage\textsuperscript{18}. The inadvertent injection of drugs into the arterial circulation may result in vascular spasm with loss of distal tissue due to anoxia. This may be complicated by infections (gas gangrene or tetanus), muscle swelling (compartment syndrome) and rhabdomyolysis which may lead onto renal failure. Such complications often require surgery in the form of decompression of muscle compartments or amputation depending on the severity\textsuperscript{19}.

Excessive tissue damage has been associated with the injection of one particular drug, temazepam, in its varying oral formulations\textsuperscript{20}. Its injection intravenously was originally made easy by the fact that it was marketed in a liquid form contained within a capsule. The drug alone is capable of producing considerable tissue damage especially to vascular endothelium either if it extravasates from vessels or is injected intra-arterially. In an attempt to reduce this practice the manufacturers introduced a solid gel formulation. However attempts to inject this formulation have continued by heating the capsules usually with hot water which temporarily rendered the gel into a liquid form. The present formulation whilst harder to inject seems to cause more damage possibly because the macrogols used to increase the viscosity are also capable of damaging vascular endothelium. This practice seems to have the ability to cause massive venous thrombosis leading to oedema and venous gangrene\textsuperscript{20}.

Other possible traumatic complications of IDU depend on the site of injection but may include air embolus or blindness. Lastly a pyrogenic reaction or bad fix may occur depending upon the substances injected and their endotoxin content.

Lung damage in the form of spontaneous pneumomediastinum and pneumopericardium have been associated with inhaling or smoking free base cocaine. This method of drug use is associated with deep, forced and prolonged
inspiratory efforts together with a Valsalva manoeuvre which produces a sudden rise in intra-alveolar pressure and subsequent alveolar rupture8.

Sinusitis

The use of the nasal mucosa, also known as "snorting", to absorb drugs is associated with a number of medical problems. The frequency of these upper airway problems is unknown amongst "snorters" but is probably fairly common. The use of amphetamine or cocaine has been associated with chronic rhinitis, rhinorrhea, anosmia, atrophy of the mucosal membranes, ulceration and perforation of the septum presumably as a consequence of intense vasoconstriction and necrosis of tissue8,15. Snorting as a cause of upper airway symptoms is well worth considering in injection drug users with limited access to injecting equipment but not drugs e.g. inmates of prisons.

Polyarteritis nodosa

In 1970, 14 injection drug users were described with a necrotizing angiitis indistinguishable from polyarteritis nodosa. At that time it was thought to be an idiosyncratic reaction to the use of amphetamines21. However it is possible that this was in fact an example of polyarteritis nodosa complicating chronic Hepatitis B surface antigen carriage which was described around that time22-24. Pneumonitis and pulmonary oedema are possible pulmonary presentations of this condition.

Pulmonary hypertension

Post-mortem studies have revealed foreign body emboli, thrombosis and granulomas in pulmonary arterioles6,25,26. In 1950 a pattern suggestive of pulmonary fibrosis was noted on the X ray of a middle aged white male morphine addict who eventually died of congestive right heart failure26. The post-mortem demonstrated numerous foreign body emboli in and around the pulmonary arterioles. Many of the pulmonary arterioles contained thrombi in various states of organisation and canalisation. The right ventricle was hypertrophied and dilated.

A number of particular foreign bodies have been associated with these granulomas including cotton fibre and talc. The majority of granulomas are apparently asymptomatic or sub-clinical in life but there have been reports of pulmonary hypertension in drug users. In 1964 Wendt et al reported pulmonary hypertension secondary to arteritis and thrombosis of small pulmonary arteries, arterioles and
capillaries. These changes were associated with granulomatous reactions secondary to crystals induced by the injection of various drugs. Whilst this report may also be an example of polyarteritis nodosa secondary to hepatitis B the clinical features were not typical and subsequently similar pathological features were found after injecting rabbits with drugs containing talc. It thus appears that tablets containing talc are able to induce this reaction when injected intravenously.

Evidence that granulomas may have some clinical effect comes from a case report of a 32 year old drug user who presented with a one day history of low grade fever, dyspnoea and dizziness. The chest X-ray showed diffuse bilateral miliary infiltrates. It appeared that these symptoms recurred each time he injected intravenously a mixture of drugs containing talc. Investigations failed to reveal any pathogens but a transbronchial biopsy revealed talc granuloma.

**Immunology**

Autopsy reports of long term injection drug users prior to the introduction of HIV reported hyperplasia of the reticuloendothelial system; enlarged lymph nodes particularly in the porta hepatitis and persistence of the thymus. Elevated serum IgM levels and false positive syphilis serology were also noted.

**Endocrinology**

The use of cannabis has been associated with reduced testosterone, oligospermia, impotence and gynaecomastia. The mechanisms may be via increase prolactin levels or via increased peripheral conversion of testosterone to oestrogen. Opiates also suppress the secretion of leutenising hormone and enhance the release of prolactin although at present they have not alone been reported to be associated with gynaecomastia. The author has however seen cases which in all probability were related to oral methadone. Drug use during pregnancy has been associated with decreased foetal growth and or an increased foetal death rate.

Sexual dysfunction has been associated with cocaine use. Whilst at low doses cocaine delays ejaculation, prolongs an erection and heightened sensory awareness long term users may have difficulty maintaining an erection or ejaculating.
Neurological effects

A persistent psychopathology has been described amongst long term drug users; 55% of stimulant users developed psychotic reactions like schizophrenia and 57% of depressant users developed a severe depressive illness although no long term opiate users had any measurable psychopathological effects. Opiate use itself was not associated with any direct toxic effect on the brain whilst nearly one third of sedative users had evidence of brain damage. A variety of psychiatric problems have been reported in users of cocaine including paranoid psychosis and severe depression although it is difficult to establish causality. Psychiatric illness may also be the presenting feature of cocaine abuse.

Complications of Drug Use - IDU related infections

The significant IDU related infections are summarised in Table 3.3

Table 3.3: IDU related infections

<table>
<thead>
<tr>
<th>Infection related problems associated with unsterile technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas gangrene</td>
</tr>
<tr>
<td>Tetanus</td>
</tr>
<tr>
<td>Abscesses and soft tissue infections</td>
</tr>
<tr>
<td>Endocarditis</td>
</tr>
<tr>
<td>Ophthalmitis</td>
</tr>
<tr>
<td>Candidaemia</td>
</tr>
<tr>
<td>Bacteraemia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infection related problems associated with the sharing of equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
</tr>
<tr>
<td>Hepatitis B/C/D</td>
</tr>
<tr>
<td>HIV</td>
</tr>
<tr>
<td>HTLV-I/II</td>
</tr>
</tbody>
</table>

Epidemiology and frequency of IDU related infections

The detailed history, epidemiology and frequency of IDU related infections was described in detail in Chapter 2 although a brief summary of the frequency of infections is provided here for the sake of continuity. Prior to the advent of HIV, 19% of narcotic related deaths were as a consequence of various infections. The infection related deaths were mainly bacterial sepsis such as endocarditis (34.5%), tetanus (44%) as well as viral hepatitis (10%). In 1973 58% of drug related admissions to a New York hospital were related to infection. At that time acute
viral hepatitis (30.5%) was the single largest reason for admission and other infections noted (27.5% of the admissions) were endocarditis (3.5%), bacteraemia without a source (11%), chest infections (29%) and skin infections (43.5%). With the advent of HIV, 31% of admissions in Basel, Switzerland were infection related; 24% were due to lower respiratory tract infections, 20% were as a consequence of viral hepatitis, 6% were soft tissue infections and 3% were secondary to bacteraemia including endocarditis.  

In Edinburgh during 1983/84 the incidence of clinical IDU related infection requiring medical attention was 3.5% (20% of which was viral hepatitis and less than one percent as a consequence of serious infection). During 1984 there were 100 IDU related admissions to Lothian hospitals for soft tissue infections, hepatitis, endocarditis and pneumonia out of a population of 2000 drug users; an incidence of 5% for IDU infections that required admission (see Chapter 4). Between 1977 and 1986 there were 252 IDU related admissions for infections to Edinburgh hospitals; 15% were for hepatitis B, 9% for pneumonia, 5% for endocarditis and 71% for subcutaneous infections.

Specific infections

The commonest organisms found in IDU associated endocarditis are coagulase positive staphylococci (50-86%), enterococci and or gram negative bacilli and candida. In the case of bacterial pneumonia the predominant organism isolated tends to be pneumococci in between 30-50% of cases, followed by Haemophilus influenzae (2-10%), Staphylococcus aureus (2-5%) or Klebsiella species. Candida infection is a rare but well recognised complication of intravenous heroin use and disseminated candidiasis has been reported among intravenous heroin users world-wide in small epidemics. This syndrome caused by Candida albicans is characterised by cutaneous, ocular, osteoarticular, and pleuropulmonary involvement alone or in combination. At least 160 cases have been described in the literature many of which have indicated the epidemic nature of this condition, the largest occurring in association with Iranian or brown heroin. In disseminated candidiasis, all patients describe sudden onset fever, shivers, myalgia, headaches and profuse sweating shortly after the intravenous injection of heroin. The fever usually lasts between one to three days, and is followed by cutaneous signs in more than 90% of cases. These are numerous painful nodules
0.5 to 1 cm in diameter occasionally surrounded by some erythema and usually located in the scalp and hairy parts of the body. Untreated they gradually resolve within four weeks generally leaving an area of alopecia. Sometimes, the nodule can discharge thick yellow pus. Painful pustules are also present in some patients; they are 2 - 3 mm in diameter on an inflamed base from which the candida can be easily identified. These can be found disseminated over the body and may appear like streptococcal or staphylococcal folliculitis. Patients often have high titres of anti-\textit{Candida albicans} antibodies but \textit{Candida albicans} is readily isolated from the skin lesions\textsuperscript{40}. Pleuropulmonary involvement was recorded in 8% of cases in one study but \textit{Candida albicans} was always isolated in conjunction with other pathogens such as Staphylococcus or other saprophytes for instance \textit{Torulopsis glabrata}\textsuperscript{42}.

The first blood borne infection identified in association with IDU was malaria, although the blood borne viruses are now, more likely to be identified in association with IDU\textsuperscript{45-48}. The association of IDU (subcutaneous or intravenous) with Hepatitis B virus (also known as homologous serum hepatitis) was described between 1950 and 1960\textsuperscript{49-54}. One report described the spread of hepatitis through a tight knit group of long term users after one particular individual joined the group\textsuperscript{53}. Multiple attacks of hepatitis initially attributed to chronic forms of hepatitis were described in drug users in 1960 and it is now known of course that one form of Non A non B hepatitis, Hepatitis C is also commonly associated with IDU\textsuperscript{55,56}. The levels of Hepatitis B and C in drug users are usually higher than those reported for HIV; up to 65% of a group of drug users may be positive for the core antibodies of hepatitis B and possibly 80% of injection drug users have antibodies for Hepatitis C\textsuperscript{58-62}. A high prevalence of delta agent, another blood borne virus, has also been reported in drug users from Italy, Copenhagen, Basel, Dublin and Edinburgh\textsuperscript{63,64}.

Two retroviruses, HTLV-I/II have been shown to be endemic in some population groups of North America, the Caribbean southern Japan and the northern parts of South America. There is no agreement at present on the effect of this infection on human health other than to suggest an association with adult T-cell leukeamia-lymphoma and tropical spastic paraparesis/myelopathy\textsuperscript{65}. In the USA the prevalence of HTLV-I is reported to be 0.025% among asymptomatic blood donors although the prevalence is higher amongst IDUs and patients in STD clinics\textsuperscript{65}. As with HIV, the highest seroprevalence is found among blacks and Hispanics\textsuperscript{65}. In Europe most individuals with HTLV-I are migrants from endemic areas\textsuperscript{65} and the seroprevalence in blood donors was reported to be of 0.011% in France and 0.00036% in London\textsuperscript{66}.
The virus is spread in a similar way to HIV except that vertical transmission can occur via maternal HTLV-I infected T cells in breast milk65. As far as sexual transmission is concerned, male to female, male to male and rarely female to male have been described. Parenteral infection via blood transfusions and IDU related infections as a consequence of sharing contaminated equipment have been described67-69. Whilst the transmission routes are similar to HIV HTLV-I seems less infectious since HTLV-I cannot be transmitted by cell free body fluids65. Reports of infection in drug users have come from the USA and Italy although without as yet a particular associated clinical syndrome or a clear idea on an effect of mortality65.

**Susceptibility of drug users to infections**

The underlying explanation for an increased susceptibility of drug users to infection is not well understood. Obviously IDU itself by breaching the defences of the skin increases susceptibility to infection. Unsterile IDU exposes the individual to recurrent episodes of bacterial infection. Opiates, however administered are known to reduce or depress the cough reflex which increases the susceptibility of the individual to aspiration pneumonia. In addition opiates also impair the immune system. Morphine given to mice reduced the numbers of neutrophils and macrophages as well as their efficiency in phagocytosing and killing *Candida albicans*. Morphine treated mice succumbed more rapidly to *Klebsiella pneumoniae* peritonitis and a depressed lymphoproliferative response to mitogens was noted in the presence of opiates70,71. Morphine treated mice also develop marked atrophy of the spleen, thymus, lymph nodes and bone marrow as well as a reduced lymphocyte helper/suppressor ratio within 24 hours. The effects were maximal at three days but took 20 days to reverse completely72.

**The effect of HIV on IDU problems**

*Effect of HIV on Non infective IDU problems*

There have been reports of pulmonary hypertension associated with HIV and although some have been drug users it has also been noted amongst non drug using homosexuals. Six patients with AIDS, 4 homosexuals and 3 drug users developed moderate or severe pulmonary hypertension associated with right ventricular hypertrophy and cardiac failure. The authors estimated an incidence of pulmonary hypertension of 0.5%73. The patients presented with dyspnoea on exertion, hypoxaemia, restrictive lung disease, reduced transfer factor for carbon monoxide
and pulmonary hypertension. The most distinguishing feature was right ventricular hypertrophy in the electrocardiogram. The diagnosis was often obscured by the fact that the features developed during an episode of an opportunist infection although the symptoms and signs did not settle with treatment. Histology revealed that in 2 patients in addition to PCP medial hypertrophy of the small pulmonary arteries and arterioles, endarteritis obliterans, intimal fibrosis of the pulmonary veins, lymphohistiocytic infiltration of the interstitium associated with interstitial fibrosis, thickened alveolar septa, and honeycombing was present.

In a prospective evaluation of patients with HIV, 8% had pulmonary hypertension with elevated right ventricular systolic pressures as demonstrated by Doppler echocardiography. This amounted to an incidence of 0.5% in a cohort of 1200 HIV infected patients. In the latter series the problem occurred in both early or late HIV and did not seem related to the level of immune deficiency. Five of the six patients were drug users but post-mortem in two did not reveal evidence of foreign body embolisation suggesting it is distinct from the problem reported previously in drug users. In addition there were no signs of inflammatory vessel changes and the pathology like the others in the literature consists of plexiform lesions typical of primary pulmonary hypertension.

In Edinburgh where over 70% of the HIV patients are IDU related, 7 (4%) had isolated right ventricular dilation. Follow up scans revealed that 4 of the patients reverted to normal after treatment of their chest infections although the abnormality persisted in 3 (1.7%) patients. One had definitive pulmonary hypertension demonstrated by Doppler echocardiography suggesting an incidence of pulmonary hypertension of at least 0.6%.

Emphysema like pulmonary disease in association with HIV has also been reported. Four patients presented with dyspnoea (none were drug users), none had prior lung infections and the chest X rays did not show infiltrates. They were all late stage in that the mean CD4 count was 100 cells/cumm. No organisms were detected by bronchio-alveolar lavage and the pulmonary function tests suggested emphysema with air trapping, hyperinflation and markedly reduced diffusion capacity. Only minimal airflow obstruction was present. Three of the patients had high resolution computed tomographic scans of the chest which revealed emphysema like bullous changes.
Effect of HIV on IDU related infection problems

Amongst drug users, data collected on narcotic related deaths revealed that AIDS cases greatly under represented serious IDU related HIV disease. In New York there was a rapid increase in both AIDS and non AIDS narcotic related deaths between 1978-86 such that for every AIDS related death in a drug user, there was one other as a consequence of conditions such as tuberculosis, endocarditis and bacterial pneumonia. Similar data have also been reported from Europe but there had been no increase in the non infective causes of death. IDU related bacterial infections are very likely to become more common since susceptibility to ordinary bacterial infections is increased by HIV infection. As an example in New York the rate of pulmonary tuberculosis was 4% amongst HIV positive as opposed to 0% in HIV negative drug users. The 36% increase in reported cases of TB between 1984 and 1986 in the USA has been largely ascribed to infection amongst HIV positive drug users.

IDU related HIV patients in the USA also have a higher incidence of bacterial infections such as pneumonia; 12% with a mortality of 2.2% compared to 3% with a mortality of 0% in HIV negative drug users. The annual incidence of pneumonia was nearly 10% for HIV seropositive drug users compared to under 2% for a population of mainly homosexual males with AIDS. The rising mortality from pneumonia in young adults in New York City is primarily as a consequence of IDU related HIV and other cities in the USA are showing similar trends. The morbidity and mortality of bacterial endocarditis in HIV seropositive individuals has been reported to be greater than for seronegative individuals; a mortality of 24% compared to 4%. The poorer outcome was related to more frequent embolisation, a greater diversity of organisms, more prolonged fever, persistent bacteraemia and greater immunological dysfunction. It was not related to recognised opportunistic infections. Another study however showed no increase in mortality and no unusual organisms. The mortality was not surprisingly higher for those with greater immunological dysfunction.

The combined effect of progressive immunodeficiency and attempts at harm reduction has had an influence on the predominant medical problems of drug users. A survey of methadone maintenance patients from the Bronx, New York from 1986-87 revealed that infection now accounted for 62% of the admissions but infection that
might be related to injecting such as endocarditis or skin cellulitis only accounted for 17% of admissions.

Estimates of the effect of HIV on IDU admissions from Edinburgh, where the epidemic of IDU peaked in 1983-84\(^4\),\(^5\) (and Chapter 4) and HIV in drug users did not occur before 1983\(^6\) (and Chapter 4) also reveal increased susceptibility for bacterial pneumonia. The annual admission rate for pneumonia during 1986 for individuals aged 15-44 was 0.6/1000; in drug users aged 15-44 the rate rose from 1.4/1000 between 1983-85 to 12/1000 by 1985-89, an 8 fold increase by 5 years after patients were infected with HIV\(^7\). The commonest single identifiable reason for an HIV admission in Edinburgh was because of a respiratory tract infection (29% of the admissions)\(^7\). Unlike other UK centres only 27% of these respiratory admissions were for PCP whilst 54% were for a bacterial chest infection\(^6\). Despite the fact that 51.5% of the patients were regarded as being asymptomatic as far as their HIV was concerned the respiratory tract infections were serious; 50% had radiological pneumonia, 43% were hypoxic, 28% were hypercapnic and the average length of stay was 10 days reflecting the complicating factor of susceptibility to infection and drug use. Interestingly *Haemophilus influenzae* rather than *Streptococcus pneumoniae* was the commonest organism isolated from these bacterial chest infections.

The reasons for the increased susceptibility to bacterial infections amongst HIV patients are not entirely clear. Although unsterile IDU exposes an individual to episodes of bacterial infection the susceptibility is not specific for drug users since bacteraemia is also increased in HIV positive individuals in Africa\(^8\). In San Francisco where IDU related HIV is unusual the increase of pneumococcal bacteraemia in all HIV individuals has been shown to be 100 times that of the general population\(^9\). In drug users and Africa it might be argued that access to medical services is an additional contributory factor. However antibody production is impaired in HIV infected patients, and low levels of IgG\(_2\) have been associated with bacterial infection\(^9\),\(^8\). Additional susceptibility factors for drug users may be that opiates themselves depress the cough reflex as well as the immune system\(^70\)-\(^72\),\(^10\).

Interestingly despite the absence of a definitive symptom complex associated with the retroviruses HTLV-I/II, drug users infected with both HIV-1 and HTLV-I/II were three times more likely to die of AIDS during the follow up period in Florida\(^10\). However the infection again could not be associated with any particular clinical
syndrome and the association could simply represent those patients who had been infected the longest with HIV-1.

Medical problems of HIV infected drug users

As far as the clinical problems specific for HIV itself, there appears to be little variation between the risk activities with regard to presentation. In the USA, figures available to the Centers for Disease Control show that conditions such as KS are unusual in the absence of homo/bisexuality. In drug users, KS, cytomegalovirus and chronic cryptosporidiosis are all significantly less common than for all other risk groups notified with AIDS; while PCP, tuberculosis, oesophageal candidiasis and extra-pulmonary cryptococcosis are more common. The clinical problems of IDU related HIV in Edinburgh will be discussed in more detail in Chapter 17.

Conclusions

There are a number of important medical problems, both non infective and infective in nature, associated with drug use. The advent of HIV requires practitioners to have not only knowledge of these latter medical conditions but also both the infection and non infection related HIV related medical conditions associated with IDU since they may mimic each other. A variety of micro-organisms are associated with the non sterile nature of IDU whilst a number of blood borne viruses, including retroviruses such as HIV, are easily transmitted to individuals involved in the sharing of injection equipment. Prior to the advent of HIV the mortality rate in drug users was of the order of 1% per annum.

As far as the clinical problems specific for HIV itself, there appears to be little variation between the risk activities with regard to presentation. In the USA conditions such as KS appear to be unusual in the absence of homo/bisexuality. In drug users PCP, tuberculosis, and oesophageal candidiasis seem to be more common. HIV has now been reported to cause some of the non infective problems previously seen in IDUs particularly pulmonary hypertension, cardiomyopathy and emphysema. In addition the literature suggests that a number of conditions which occur commonly in drug users such as tuberculosis, pneumonia and endocarditis are affected by the presence of HIV in the host. The underlying mechanism behind the increased susceptibility to, and mortality of, bacterial infections is not as yet clear.
References for Chapter 3


5. Robertson JR & Bucknall AB. Heroin users in a Scottish City - Edinburgh Drug Addiction Study 1986. West Granton Medical Group, 1 Muirhouse Avenue, Edinburgh, EH4 4PL.


42. Mellinger M, De Beauchamp O, Gallien C, Ingold R, & Taboada MJ. Epidemiological and clinical approach to the study of candidiasis caused by


45. Biggam AG. Malignant Malaria associated with the administration of heroin intravenously. Transactions of the Royal Society of Tropical Hygiene and Hygiene 1929; 23: 147-153.


81. Chaisson RE, Schechter GF, Theuer CP, Rutherford GW, Echenberg DF, Hopewell PC. Tuberculosis in patients with the acquired immunodeficiency


CHAPTER 4

Injection Drug Use related HIV Infection in Edinburgh

Unlike the USA, by 1989 82% of the patients with AIDS notified in the United Kingdom had involved homosexuality or bisexuality alone and only 2% of such reports had implicated IDU alone as a high risk activity. Only 3.8% of the AIDS cases had come from Scotland and only 11 of these were drug users. In the UK as a whole IDU represented only 16% of reports of those infected with HIV and this contrasted markedly with the position in Scotland in which 54% of those infected with HIV had implicated IDU and nearly 60% of those reports had come from Edinburgh.

The first indications that Edinburgh had a particular HIV problem came with the finding that 15/34 or 44% of a group of haemophiliacs had acquired HIV antibody between 1983 and 1984 after being treated solely with locally produced Factor VIII. In 1985 and 1986 surveys found that between 38% and 52% of Edinburgh and 40% of Dundee drug users had been infected with HIV. By comparison only 4.5% of drug users in Glasgow and 10% in England and Wales were infected with HIV. Whilst fewer IDU related HIV infections have occurred in England and Wales all areas have now reported cases. A follow up study on a cohort of drug users revealed that the known HIV seropositivity rate had risen to a maximum of 64% by 1988.

The initial United Kingdom drug problem in the 1960's was centred around relatively affluent individuals in London with smaller numbers in other cities. In the late 1970's and early 1980's, coincident with the arrival of relatively cheap brown heroin from Iran and then Pakistan, a different user appeared - unemployed individuals from large council estates. An epidemic of IDU occurred in Edinburgh starting around 1980 and peaking in 1983-84 and see results below). There is supportive evidence of this epidemic of IDU from a variety of sources and unfortunately HIV was introduced into this community at the peak of the IDU epidemic and see results below). This chapter details what was discovered about the Edinburgh epidemic of IDU and HIV via interviews with drug users attending a counselling and screening clinic as well as via other sources of information concerning morbidity and mortality.

**Method**

A voluntary self referral clinic was established in the Edinburgh Regional Infectious Diseases Unit (RIDU) to provide open access counselling and HIV antibody testing.
The Clinic started on October 16th, 1985 to coincide with the commencement of testing of all blood donations by the National Blood Transfusion Service. As part of the pre test counselling assessment a series of questions were asked concerning injection drug use such as year of first injection, frequency of current injection drug use etc. The responses to these questions were analysed for drug users attending the clinic up to the end of 1987. Where possible, assuming the individual agreed to undergo an HIV test, the results were cross tabulated with the HIV test result. Initial testing of specimens was by competitive or anti-globulin enzyme linked immunosorbent assay (ELISA). All reactive sera were considered positive if confirmed by methodologically distinct assays. The Information Service Division of the Common Services Agency were asked to provide data on admissions to Lothian Hospitals with first or second diagnosis of medical conditions such as pneumonia, endocarditis etc. and or drug misuse.

Results

A total of 368 injection drug users provided a year of first injection drug use and these results together with their HIV result are shown in table 4.1 and figure 4.1. The numbers starting IDU each year were not constant ($\chi^2 = 368.6, p < 0.000$) with a peak occurring in 1983, thereafter the numbers decline sharply. An analysis of the relationship between the year of starting IDU and HIV infection revealed that this was also not constant ($\chi^2 = 279.5, p < 0.000$). The relationship between year of starting IDU and HIV infection was further analysed and the results are shown in table 4.2. An HIV positive drug user was more often associated with starting IDU before or during 1983 than in subsequent years ($\chi^2 = 8.3, p < 0.05$). There was a significant association between the frequency of needle sharing and HIV infection ($\chi^2 = 4.24, p < 0.05$, table 3.3). In addition there was also a significant association between markers of past or present infection with another blood borne virus, Hepatitis B virus and HIV infection ($\chi^2 = 4.81, p < 0.05$ table 4.4).
Table 4.1: Frequency and HIV infection of individuals by year of entry to injection drug use in Edinburgh as reported to Counselling Clinic

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of injection drug users</th>
<th>No. HIV +ve drug users</th>
<th>% HIV +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965/66</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1967</td>
<td>6</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>1968</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1969</td>
<td>5</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>1970</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>1971</td>
<td>6</td>
<td>2</td>
<td>33</td>
</tr>
<tr>
<td>1972</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1973</td>
<td>5</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>1974</td>
<td>6</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>1975</td>
<td>10</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>1976</td>
<td>9</td>
<td>7</td>
<td>78</td>
</tr>
<tr>
<td>1977</td>
<td>13</td>
<td>9</td>
<td>69</td>
</tr>
<tr>
<td>1978</td>
<td>21</td>
<td>11</td>
<td>52</td>
</tr>
<tr>
<td>1979</td>
<td>25</td>
<td>16</td>
<td>64</td>
</tr>
<tr>
<td>1980</td>
<td>33</td>
<td>20</td>
<td>61</td>
</tr>
<tr>
<td>1981</td>
<td>43</td>
<td>25</td>
<td>58</td>
</tr>
<tr>
<td>1982</td>
<td>46</td>
<td>23</td>
<td>50</td>
</tr>
<tr>
<td>1983</td>
<td>59</td>
<td>35</td>
<td>59</td>
</tr>
<tr>
<td>1984</td>
<td>34</td>
<td>12</td>
<td>35</td>
</tr>
<tr>
<td>1985</td>
<td>22</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>1986/87</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>368</td>
<td>175</td>
<td>48</td>
</tr>
</tbody>
</table>

$X^2(22) = 368.6$  
P < 0.000
Figure 4.1: Reported first year of IDU in Edinburgh

Reported first year of IDU in Edinburgh
Evidence for an epidemic of injecting drug use involving heroin combined with

<table>
<thead>
<tr>
<th>HCV Markers</th>
<th>HIV Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>HB+</td>
<td>HIV+</td>
</tr>
<tr>
<td>HB-</td>
<td>HIV-</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
</tr>
<tr>
<td>43</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Frequency of Needle Sharing</th>
<th>HIV Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly or Greater</td>
<td>HIV+</td>
</tr>
<tr>
<td>Monthly or Less</td>
<td>HIV-</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
</tr>
<tr>
<td>49</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>HIV Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>HIV+</td>
</tr>
<tr>
<td>1983</td>
<td>HIV-</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
</tr>
<tr>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>HIV Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1984</td>
<td>HIV+</td>
</tr>
<tr>
<td>1985</td>
<td>HIV-</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
</tr>
<tr>
<td>21</td>
<td></td>
</tr>
</tbody>
</table>
Table 4.5: Injection Drug Use related illness: hospital discharges for Lothian 1976-86

<table>
<thead>
<tr>
<th>Year</th>
<th>Endocarditis</th>
<th>Pneumonia</th>
<th>Skin Infections</th>
<th>Hepatitis B</th>
<th>Opiate Overdoses</th>
<th>Total(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1977</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>1978</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>1979</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>1980</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>36</td>
<td>46(7)</td>
</tr>
<tr>
<td>1981</td>
<td>0</td>
<td>4</td>
<td>13</td>
<td>2</td>
<td>55</td>
<td>74(11)</td>
</tr>
<tr>
<td>1982</td>
<td>2</td>
<td>0</td>
<td>23</td>
<td>3</td>
<td>53</td>
<td>81(12)</td>
</tr>
<tr>
<td>1983</td>
<td>1</td>
<td>4</td>
<td>46</td>
<td>9</td>
<td>53</td>
<td>113(16)</td>
</tr>
<tr>
<td>1984</td>
<td>7</td>
<td>8</td>
<td>66</td>
<td>19</td>
<td>83</td>
<td>183(26)</td>
</tr>
<tr>
<td>1985</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>1</td>
<td>93</td>
<td>104(15)</td>
</tr>
<tr>
<td>1986</td>
<td>1</td>
<td>0</td>
<td>9</td>
<td>3</td>
<td>69</td>
<td>82(12)</td>
</tr>
<tr>
<td>Total(%)</td>
<td>13(2)</td>
<td>22(3)</td>
<td>178(26)</td>
<td>39(5)</td>
<td>442(64)</td>
<td>694(100)</td>
</tr>
</tbody>
</table>

Supplied by Information and Statistic Division of Common Services Agency (Scotland)
Figure 4.2: Injection Drug Use related illness: hospital discharges for Lothian 1976-86
### Table 4.5: Injection Drug Use related illness: hospital discharges for Lothian 1976-86

<table>
<thead>
<tr>
<th>Year</th>
<th>Endocarditis</th>
<th>Pneumonia</th>
<th>Skin Infections</th>
<th>Hepatitis B</th>
<th>Opiate Overdoses</th>
<th>Total(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1977</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>1978</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>1979</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>1980</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>36</td>
<td>46(7)</td>
</tr>
<tr>
<td>1981</td>
<td>0</td>
<td>4</td>
<td>13</td>
<td>2</td>
<td>55</td>
<td>74(11)</td>
</tr>
<tr>
<td>1982</td>
<td>2</td>
<td>0</td>
<td>23</td>
<td>3</td>
<td>53</td>
<td>81(12)</td>
</tr>
<tr>
<td>1983</td>
<td>1</td>
<td>4</td>
<td>46</td>
<td>9</td>
<td>53</td>
<td>113(16)</td>
</tr>
<tr>
<td>1984</td>
<td>7</td>
<td>8</td>
<td>66</td>
<td>19</td>
<td>83</td>
<td>183(26)</td>
</tr>
<tr>
<td>1985</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>1</td>
<td>93</td>
<td>104(15)</td>
</tr>
<tr>
<td>1986</td>
<td>1</td>
<td>0</td>
<td>9</td>
<td>3</td>
<td>69</td>
<td>82(12)</td>
</tr>
</tbody>
</table>

| Total(%) | 13(2) | 22(3) | 178(26) | 39(5) | 442(64) | 694(100) |

Supplied by Information and Statistic Division of Common Services Agency (Scotland)
Figure 4.2: Injection Drug Use related illness: hospital discharges for Lothian 1976-86
The distribution of HIV infected individuals around Edinburgh was not uniform and was concentrated in and around particular areas of Edinburgh. These areas were centred on 4 areas with considerable multiple deprivation, namely Muirhouse (EH4 and EH12), Leith (EH6), Craigmillar (EH 15,16,17) and Wester Hailes (EH11 and 14). In 157 attendees of the City Hospital Counselling and Screening Clinic in whom post codes were available there was a statistically significant increase in the number of HIV infected in those areas \( (\chi^2(1)= 7.67, p<0.01) \). These particular areas were also known from other work to have been heavily affected by the IDU epidemic^15.

Table 4.6: Relationship between post code sector and HIV infection

<table>
<thead>
<tr>
<th>HIV status</th>
<th>Edinburgh Post Code</th>
<th>Remainder</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV +</td>
<td>(4,12,6,3,5, 7,16,15,17)</td>
<td>32</td>
<td>5</td>
</tr>
<tr>
<td>HIV -</td>
<td>97</td>
<td>23</td>
<td>120</td>
</tr>
<tr>
<td>Total</td>
<td>129</td>
<td>28</td>
<td>157</td>
</tr>
</tbody>
</table>

\( \chi^2=7.67, p<0.01 \)

Despite the fact that the majority of individuals involved in drug use in Edinburgh were born in the area, interviews revealed that many had travelled to other areas and had shared injecting equipment in those areas. The extent of this mobility is largely unknown but an idea of its extent is revealed in Table 4.7 which documents the range of movement for 122 drug users interviewed after their return to Edinburgh. The number failing to return to Edinburgh is not known.
Table 4.7: The location of needle sharing in drug users returning to Edinburgh (individuals shared in more than one location)

<table>
<thead>
<tr>
<th>Location of sharing of IDU equipment</th>
<th>Number of individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scotland</td>
<td></td>
</tr>
<tr>
<td>Glasgow</td>
<td>33</td>
</tr>
<tr>
<td>Aberdeen</td>
<td>7</td>
</tr>
<tr>
<td>Dundee</td>
<td>7</td>
</tr>
<tr>
<td>Fife</td>
<td>5</td>
</tr>
<tr>
<td>Wick</td>
<td>2</td>
</tr>
<tr>
<td>Inverness</td>
<td>2</td>
</tr>
<tr>
<td>Falkirk</td>
<td>1</td>
</tr>
<tr>
<td>Stirling</td>
<td>1</td>
</tr>
<tr>
<td>Elgin</td>
<td>1</td>
</tr>
<tr>
<td>Perth</td>
<td>1</td>
</tr>
<tr>
<td>Kilmarnock</td>
<td>1</td>
</tr>
<tr>
<td>England</td>
<td></td>
</tr>
<tr>
<td>London</td>
<td>56</td>
</tr>
<tr>
<td>Oxford</td>
<td>3</td>
</tr>
<tr>
<td>Newcastle</td>
<td>3</td>
</tr>
<tr>
<td>Brighton</td>
<td>2</td>
</tr>
<tr>
<td>Cambridge</td>
<td>2</td>
</tr>
<tr>
<td>Northampton</td>
<td>2</td>
</tr>
<tr>
<td>Liverpool</td>
<td>2</td>
</tr>
<tr>
<td>Stonehenge</td>
<td>2</td>
</tr>
<tr>
<td>Hull</td>
<td>1</td>
</tr>
<tr>
<td>Sheffield</td>
<td>1</td>
</tr>
<tr>
<td>Leeds</td>
<td>1</td>
</tr>
<tr>
<td>Manchester</td>
<td>1</td>
</tr>
<tr>
<td>Nottingham</td>
<td>1</td>
</tr>
<tr>
<td>Derby</td>
<td>1</td>
</tr>
<tr>
<td>Wolverhampton</td>
<td>1</td>
</tr>
<tr>
<td>Birmingham</td>
<td>1</td>
</tr>
<tr>
<td>Bristol</td>
<td>1</td>
</tr>
<tr>
<td>Southampton</td>
<td>1</td>
</tr>
<tr>
<td>Plymouth</td>
<td>1</td>
</tr>
<tr>
<td>Tunbridge Wells</td>
<td>1</td>
</tr>
<tr>
<td>Gt Yarmouth</td>
<td>1</td>
</tr>
<tr>
<td>Unspecified</td>
<td>3</td>
</tr>
<tr>
<td>Prison</td>
<td>4</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td></td>
</tr>
<tr>
<td>Belfast</td>
<td>1</td>
</tr>
<tr>
<td>Europe</td>
<td></td>
</tr>
<tr>
<td>Holland</td>
<td>10</td>
</tr>
<tr>
<td>France</td>
<td>1</td>
</tr>
<tr>
<td>Italy</td>
<td>3</td>
</tr>
<tr>
<td>Spain</td>
<td>1</td>
</tr>
</tbody>
</table>

152
Table 4.7 continued: The location of needle sharing in drug users returning to Edinburgh (individuals shared in more than one location)

<table>
<thead>
<tr>
<th>Location of sharing of IDU equipment</th>
<th>Number of individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elsewhere</td>
<td>3</td>
</tr>
<tr>
<td>USA</td>
<td>1</td>
</tr>
<tr>
<td>India</td>
<td>1</td>
</tr>
<tr>
<td>Turkey</td>
<td>1</td>
</tr>
<tr>
<td>South Africa</td>
<td>1</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>1</td>
</tr>
</tbody>
</table>

It is likely that this mobility of a sub group of drug users was the origin of the epidemic of HIV in Edinburgh. Four individuals reported sharing injecting equipment in Edinburgh as well as Southern Europe where it is now known that the HIV epidemic began 2-3 years earlier (see Chapter 2). One particular individual arrived back in Edinburgh from Spain in early 1983 and developed an episode of clinical hepatitis B. When referred to the clinic in 1987 by his general practitioner because of HIV it was determined from stored specimens taken by his general practitioner, that he had seroconverted for HIV between December 1982 and January 1983. This is to date the earliest known positive specimen from an injection drug users in Edinburgh. This individual remained in Edinburgh for a further 6 months during 1983 and many individuals with whom he shared equipment were shown to have seroconverted around August 1983. Thus the source of the Edinburgh HIV epidemic was probable the heroin and HIV epidemic which affected Southern Europe from around 1979.

Discussion

An epidemic of IDU occurred in Edinburgh, starting in the late 1970's and peaking in 1983-84. The evidence for this epidemic comes from a variety of sources. Self reported data from individuals asked about when they first started IDU at the City Hospital Counselling Clinic, revealed that the year of starting IDU was not evenly spread over the years. More individuals began IDU in the late 1970's and early 1980's. What is perhaps of interest is the fact that the epidemic peaked well before any medical sources were aware of the problem. The reasons for the decline in individuals initiating IDU after 1985 are largely unknown. The response of the police to the epidemic may have influenced the epidemic or IDU may have exhibited the phenomena of saturation in that only a certain number of young individuals may
be attracted at any one time into the activity. For whatever cause the number of new individuals entering IDU fell steeply after 1985.

The other evidence for the existence of an IDU epidemic comes from an analysis of drug use related medical conditions in Lothian Hospitals over the same time period. Drug related problems such as opiate overdoses, drug related soft tissue infections, pneumonia and endocarditis all showed similar explosive increases. In addition reports of IDU related clinical hepatitis B, a blood borne virus infection with similar transmission characteristics to HIV were also increased with a peak occurring in 1985.

The epidemic of IDU was also documented in a variety of non medical statistics. For instance from Home Office and Police Statistics it can be seen that the number of notified addicts both new, old and those receiving treatment peaked in 1984/85\textsuperscript{15}. In addition a similar epidemic of drug offences, drug related arrests and convictions all occurred in Lothian. Whilst most of these figures relate to the Lothians and the Borders areas 75% consistently relate to the Lothian area. Interestingly 69% of these offences were found to occur within the same postal district as that of the accused suggesting that the activity was very much a local community event. The seizure of drugs also showed a dramatic rise over this period\textsuperscript{15}.

In 1985 drug users were generally unemployed, around 25 years of age, started their drug use around the age of 17-20 and at least one third were female\textsuperscript{16,19,21}. They were concentrated in 4 areas of multiply deprived areas of Edinburgh (Muirhouse, Leith, Craigmillar and Wester Hailes) These individuals often had no tradition of heroin use and knew little about how to avoid some of the complications. They were using at least once daily if not more often and in most cases preferred to administer the drugs by injection\textsuperscript{15}. Comparisons of self reported habits between Edinburgh and Glasgow or Edinburgh and London reveal considerably more sharing of needles and syringes in Edinburgh\textsuperscript{17,21}. For instance, the sharing of equipment occurred 46 times per month in Edinburgh compared to only 15 times per month in Glasgow. In addition sharing occurred with twice as many individuals, 14 versus 7 per month\textsuperscript{17}. Of 78 Edinburgh injection drug users 42% shared daily and 63% weekly by comparison to only 14 or 31% of 45 South London injection drug users who admitted to sharing within the last 3 months\textsuperscript{21}.

Historically, drug users report that needles and syringes were in short supply in Edinburgh from around 1981/82 to 1985 when a surgical supplies shop ceased
trading and pharmacists were generally unwilling to supply users. Users also report that equipment was commonly removed from them by the police during searches and then destroyed. Possession of equipment contaminated with heroin may be used as evidence of illicit use and users might then give evidence against a supplier. This resulted in suppliers forcing users to use drugs on site so that on leaving the premises they were free of any incriminating evidence. Unfortunately, because of the limited supply of equipment considerable sharing occurred with possibly only one or two sets of equipment for all the pushers' clients which could number 20-40. There were also large gatherings of users, anything from five to 20, in the style of American 'shooting galleries' where one set of equipment was passed around the group.

The reason Edinburgh was so important in the Scottish heroin epidemic is in part related to the geography of Scotland. Heroin tended to be smuggled in to the UK from Europe via the East coast and Edinburgh, unlike Glasgow, has a radial communication network to the rest of Scotland which eased the distribution of the product around Scotland. With this background it is perhaps not entirely surprising, therefore, that when in 1983 HIV was introduced into Edinburgh it spread rapidly as a consequence of the habit of equipment sharing. Those involved in IDU in 1985 were around 25 years of age and were injecting drugs at least daily if not more often. Commencing IDU in the years 1983 or before was associated with an increased risk of HIV infection as was more frequent injecting drugs, younger age, infection with other blood borne viruses and living in particular areas of Edinburgh. The origins of the IDU related epidemic of HIV in Edinburgh have been traced to the unexpected mobility of a small number of injection drug users who travelled to Southern Europe to access greater quantities of heroin. The variety of locations where Edinburgh drug users shared equipment and then returned to Edinburgh effectively demonstrates the method by which blood borne viruses such as Hepatitis B delta virus, Hepatitis C and HIV are spread geographically via IDU.

By 1989 over 1700 HIV infected individuals had been identified in Scotland and over 1000 in Edinburgh. Estimates of the size of the drug abuse community in Edinburgh are poor but it is thought that there are probably at least 2-2,500. The 3 series of investigations from Edinburgh on HIV infection in injection drug users suggested a level of 50% infection in those individuals injecting drugs in the early to mid 1980's. These two pieces of information when combined suggest that there were at least 1,000 individuals infected by IDU in Edinburgh.
By July 1989 over 1000 or 0.133% of the population of Lothian (750,000) had been found to be infected with HIV the majority by injection drug use\(^3\). The worst affected area in England (North West Thames) has a known rate of HIV infection of 0.089%\(^3\). The majority of infected individuals in Edinburgh live in the City with a population of only around 300,000 (1981 census). Thus the realistic prevalence for the City of Edinburgh is 0.3% or 3.74 times the worst affected English region. Some 77% of the infected individuals in Edinburgh are in the 15 to 35 age group (120,000 in the 1981 census) and therefore a more realistic prevalence rate for HIV is 1 in every 150 (0.64%) of the 15-35 population. Edinburgh may therefore have the worst density of HIV in the UK or at the very least as bad as the region most affected in England Wales (North West Thames).

Could there be even more infected individuals from IDU in Edinburgh? At the peak of the IDU epidemic it was estimated by Standing Committee on Drug Abuse (SCODA) that the prevalence of opiate injecting drug use was 6 per 1000 or 0.6% of individuals aged 15-35\(^5\). Reports from 1985/86 suggest that between 50-65% of injection drug users were infected with HIV and this would therefore suggest that a minimum of 360-480 individuals or 0.3-0.4% of adults aged 15-35 in Edinburgh are now infected with HIV. In fact to date 490 individuals infected with HIV via IDU have been identified in Edinburgh\(^3\). Thus the calculated and observed numbers of HIV infected patients are very similar and confirm the serious nature of the problem for Edinburgh. The data also suggests that there is not as yet a large undetected population of HIV infected individuals.

Whilst the overall prevalence rate of opiate drug use was 6 per 1000 of the population aged 15-35 it was 8.4 per 1000 for males and 3.6 per 1000 for females. Within these estimates there were however considerable variations. For instance the prevalence of problem opiate drug use for males was 36 per 1000 of the 15-35 population in Leith, 29 in Muirhouse and 20 for Craigmillar\(^1\). Similarly the female prevalence of problem opiate drug use was 22 per 1000 for the population aged 15-35 in Leith, 11 for Muirhouse and 9 per 1000 for Pilton\(^1\). Utilising the various opiate drug taking estimates the HIV seroprevalence may obviously vary from 0.3% to as much as 1.8-2.3% for males in Leith. The general practice in Muirhouse has documented the fact that 1 in 10 males between the ages of 15-35 are infected\(^3\). By comparison in the Bronx the HIV seroprevalence of women attending for termination was 2% and 4.6% for patients attending hospitals in general\(^2\).
Conclusions

For a variety of reasons an epidemic of IDU began in Edinburgh in the late 1970's and peaked again for unknown reasons between 1983-85. A clinically unrecognised epidemic of HIV began abruptly in Edinburgh in 1983 and rapidly spread through drug using cohorts. It is likely that this epidemic originated in Southern Europe and came to Edinburgh as a consequence of the unexpected mobility of a small number of injection drug users. The transmission of HIV via IDU was associated with more frequent equipment sharing and evidence of an other blood borne viruses namely hepatitis B.

This dramatic and rapidly spreading epidemic of HIV was the first of its type to be described in the world and unfortunately despite the relatively small number of drug users in Edinburgh it resulted in a large number of individuals infected with HIV. Per head of population the density of HIV infection in the 15-44 age group was certainly as great as any where else in the UK. Unlike other areas such as the USA the epidemic was detected within 2 years of its onset when the majority of infected individuals were asymptomatic and as a consequence there was the opportunity to develop specific services for HIV before the onset of HIV related ill health or AIDS.
References for Chapter 4


31. Personnal communication Dr Gill, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London, NW9 5EQ.

32. Personal Communication, Robertson JR, West Granton Medical Group, 1 Muirhouse Avenue, Edinburgh, EH4

SECTION II

HOSPITAL BASED CLINICAL SERVICES FOR THE HIV/AIDS EPIDEMIC

As a consequence of the knowledge of the HIV epidemic a number of new services were developed at the RIDU, City Hospital and the following chapters describe these services together with an assessment of their effect. Prior to the advent of HIV, drug use was considered as a psychiatric problem and there was no medical service dedicated to managing the medical problems of drug users on a long term basis.

The aims of the service were to initiate and maintain contact and the success or failure of the service should be judged against these aims. Society has two basic methods of coping with the problem of HIV. One method is to identify and control the spread of HIV by coercion. The alternative approach is to provide positive incentives for patients with HIV to enter the health care system and this was the approach adopted in Edinburgh. Whilst many may consider the services as lavish they need to be judged against the objective of attracting individuals into the health care system.

For the asymptomatic patient with HIV their own problems take priority over those of society; those who are homeless or addicted are not likely to worry about their physical health or the dangers of viral transmission. Consequently medical care for HIV particularly IDU related HIV, requires a multi-disciplinary approach. Demonstrating a practical approach to the patient's problems of drug use, housing, low income etc. is a necessary method of working with the patient until he or she can begin to concentrate on the problem of HIV.

The aim of the service was however not only to care for the individual but also to care for society i.e. by understanding and reducing transmission of HIV. Helping individuals to realise that they are infected with HIV is important if health education is to alter their behaviour. This need to be in contact with as many HIV positives as possible in the hope of gradually altering their behaviour, was an important underlying theme in the service developed at the City Hospital. Consequently some assessment of behaviour change is an important part of the results of the service.
CHAPTER 5

Counselling and screening of HIV infected patients

Introduction

The most immediate consequence of the HIV epidemic for society as a whole was the threat to the confidence of society in blood transfusions. The Government's response when antibody testing became available in early 1985 was to introduce mandatory screening of all donated blood in October 1985. In Edinburgh the HIV positivity rate amongst voluntary blood donors was 1/13074 and this compared with 1/41598 in the West of Scotland and 1/50000 for the UK as a whole\(^1\). The screening of blood donations could only be successful if it was combined with a programme of "donor deferment" to direct individuals in high risk groups away from the Blood Transfusion Service since such individuals could be infectious before developing detectable HIV antibody\(^2\). It was, therefore, necessary to provide voluntary confidential screening and counselling at alternative testing centres to prevent the Blood Transfusion Services being used as a diagnostic facility.

Since the majority of individuals infected with HIV in Edinburgh were current or past injection drug users it was important that an alternate test site be both experienced in handling drug users as well as acceptable to those drug users. A decision was therefore made to establish an alternate test site at the City Hospital with 6 months of funding from the Chief Scientist's Office. Thereafter funding was provided by the Lothian Health Board.

Experienced counselling is important to avoid the fear and ignorance surrounding HIV. Headlines such as "Dying mum's baby has AIDS" are a direct result of bad counselling and inexperience on the part of the legal and medical professions. In the extreme, poor or ineffective counselling may result in suicide whilst at the very least it results in the patient losing contact with services. This removes the chance for the service to influence and educate about high risk behaviour. Counselling also provides the opportunity for those not infected with HIV to be educated about reducing high risk behaviour. Consequently pre and post test counselling are important in establishing a relationship between individuals (whether infected or not) and the health service which may eventually be used for health education or harm reduction (see Chapter 8). Poor pre-test counselling or non voluntary testing might eventually also lead to legal claims as a result of difficulty in obtaining life assurance or a mortgage.
The City Hospital Counselling and Screening Clinic

A voluntary self-referral clinic was established in the Edinburgh Regional Infectious Diseases Unit to provide open access counselling and HIV antibody testing. The Clinic started on October 16th, 1985 to coincide with the commencement of testing of all blood donations by the National Blood Transfusion Service.

Apart from self-referrals, patients were also referred by social workers, drug self-help groups, General Practitioners and other hospitals. The HIV antibodies were detected by a competitive ELISA system and confirmed by a conventional ELISA system. Doubtful positives were confirmed by immunofluorescence or Western blotting.

The clinic was supervised by a consultant in Infectious Diseases (RPB) and continues to be held in the Out Patient Department of the RIDU, Edinburgh. It initially operated for a four hour session, five times per week and each session was staffed by a Medical Officer, Nurse Counsellor and a receptionist/secretary. Whilst the initial cost of staffing was only one part time medical officer and one part time nurse/counsellor the sessions were shared by three medical officers and two nurses. The clinic had its own telephone line with an answering machine which informed out of hours callers of clinic hours. Most patients were offered an appointment within 1-2 days of calling. The clinic presented a relatively non-medical image since it did not set out to conduct a full clinical examination and assessment. Because of the expectation that a majority of the patients would be injection drug users it was necessary initially to have a medical officer present at all times because phlebotomy might be difficult.

From the outset, the aim of the clinic was to offer a confidential service and to this end all records were kept within the clinic and there was no other record of attendance unless they took up the offer of medical screening. The aim was always to persuade patients of the advantages of informing their general practitioner of their HIV antibody status. Initially the clinic was often left with results not knowing whether or not to inform other doctors. It then became necessary to obtain written consent to inform general practitioners of the HIV results. The results were otherwise only given out in person at a clinic attendance. Contact tracing was not undertaken but the patients were encouraged to bring their sexual or needle sharing partners to the clinic. When the clinic opened there was no literature specifically for injection drug users and a range of leaflets was produced to provide the clients with written advice.
Pre Test Counselling

Each patient was allocated at least 30 minutes for their initial appointment although in practice strict adherence to such a timetable did not occur. The patients received a simple sheet which explained the advantages and disadvantages of HIV antibody testing and this was discussed at the counselling session. The main objectives of the pre test counselling were general education regarding HIV including modes of transmission, risk activities and risk reduction. Individual specific risk activities were assessed and advice provided. In view of the high default rate and the almost invariable lack of comprehension following a positive result as much information as possible was provided at the first visit.

As a consequence of the prolonged incubation period for seroconversion the policy was to offer repeat testing for up to one year after an individual's last risk activity and during that time the client was advised to assume seropositivity in terms of risk reduction measures. Contraceptive advice and supplies were also available. The implications of the test were then explored and if the patient decided to proceed, blood was taken for HIV antibody and hepatitis B marker tests. A further appointment was given for one week later when a confirmed result would be available. No other specific screening was undertaken, for instance to exclude sexually transmitted diseases, however, if the medical officer considered it necessary referrals were arranged to genito-urinary medicine, dermatology, psychiatry etc.

One important function of the clinic was to act as a point of contact for providing advice and information to Health Care Workers, Social Workers, Occupational nurses and foster mothers, as well as worried individuals whether or not they were in identified high risk groups. The clinic staff were, therefore, an important resource for the dissemination of information to many individuals other than those directly concerned with this infection.

Post test counselling

At the return visit patients with a negative antibody test were given advice which depended upon their suspected exposure time and risk factors. If there had been a high risk activity within the past twelve months, the patient was advised to re attend the clinic for further testing in six to twelve months time.
Patients with a positive test were counselled in relation to relevant risk reduction with the initial emphasis on reducing progression of the disease in the individual and spread of the virus in the community. Depending upon the circumstances this would include advice on safe sex, safe drug use, advice with regard to sexual and needle sharing partners, advice with regard to diet and physical activity as well as reassurance about lack of transmission to non sexual or non needle sharing partners. It also would encompass for men and women the risks of pregnancy.

Further Management

Patients with a positive HIV antibody result were offered further counselling appointments as well as an appointment for a medical examination. With one third of the affected patients being female it was one important aim to offer medical services for both mother and child at one clinic in an attempt to overcome the problems of a haphazard and chaotic lifestyle. One session initially was devoted to the follow up of those children identified as at risk of HIV infection and utilised the services of a nurse counsellor from the Screening Clinic, a Consultant in Community Child Health, an Infectious Diseases physician and a liaison Health Visitor to help co-ordinate follow up. The mothers were encouraged to attend routine baby clinics but the clinic co-ordinated their immunisations and medical care.

The dental health of drug users is generally poor and their attendance at dentists is as irregular as all other medical services. In Edinburgh there was already a mechanism for dealing with patients with Hepatitis B and with the help of the Lothian Area Dental Service treatment was also offered for these patients.

Results of the first year of the service

A total of 441 new patients had been counselled at 980 clinic attendance's by the 30th September 1986 and there were 402 (41%) non attendance's. Three hundred and forty five (78%) of the patients were from the City of Edinburgh, 55 (12.5%) were from the rest of the Lothian Region, 27 (6%) were from the rest of Scotland, 3 (0.5%) were from England and 11 (3%) gave no address.

A total of 30 (6.8%) individuals declined HIV testing after pre test counselling and not surprisingly those with the least risk were more likely to refuse testing (Table 5.1).
Table 5.1: City Hospital Counselling Clinic results: October 1985 - September 1986

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Number attending (% of total)</th>
<th>Number HIV+ (% of risk group)</th>
<th>Number declined test (% of risk group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDUs</td>
<td>191(44)</td>
<td>100(52)</td>
<td>5(3)</td>
</tr>
<tr>
<td>Sex with an IDUs</td>
<td>88(20)</td>
<td>6(7)</td>
<td>3(3)</td>
</tr>
<tr>
<td>Ho/bi</td>
<td>40(9)</td>
<td>4(10)</td>
<td>3(8)</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>53(12)</td>
<td>0(0)</td>
<td>5(9)</td>
</tr>
<tr>
<td>Other</td>
<td>69(16)</td>
<td>4(6)*</td>
<td>14(20)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>441(100)</td>
<td>114(26)</td>
<td>30(7)</td>
</tr>
</tbody>
</table>

* all related to iatrogenic blood products

**Risk groups**

- **IDUs** injection drug users
- **Ho/bi** homosexuals or bisexuals
- **Sex with an IDUs** sexual intercourse with a known IDUs
- **Heterosexual** heterosexual intercourse other than with IDUs

One hundred and fourteen (26%) HIV positive individuals were counselled, 100 (88%) of whom were current or ex injection drug users. There were a total of 191 patients who admitted to injection drug use, 119 (62%) males and 72 (38%) females and the seropositivity rate was 52%. None of the drug users admitted to homosexuality. The mean age of drug users was 26 years, 25 years for those found to be seropositive and 27.5 years for those found to be seronegative (p<0.01). The
mean age of onset of injection drug use was 20 years, 18 years for those found to be seropositive and 22 years for those found to be seronegative (p<0.0001). The Male/Female ratio was 1.6/1, 1.3/1 for those found to be seropositive for HIV and 2.1/1 for those seronegative. Forty three (60.5%) of the females were HIV antibody positive compared to 57 (49.5%) of the males but this difference was not significant.

On 1st January 1986 the family clinic for seropositive mothers and their new-born children was established and by 30th September 1986, 23 at risk babies and their mothers had been counselled and examined.

The total cost of this counselling and screening service in the first year was £27,000 made up of £18,500 in salaries, £3,000 in initial equipment, £2,500 in consumables and £3,000 for HIV and Hepatitis B testing. The cost per patient in the first year was therefore, £61.22 or £27.55 per attendance. The total number of hours available for counselling per year were 2080. Allowing approximately one hour for counselling each patient, a 15% time loss for holidays and 40% for default appointments, approximately 1000 patients could have attended. This number of patients in subsequent years would cost £21,000 for counselling and £7,300 for HIV/Hepatitis B testing or £28.3 per patient. A more compliant population would reduce costs even further to approximately £20 per patient made up of £12 for counselling and £8 for HIV/Hepatitis B testing.

Discussion

The demand for this type of facility was confirmed by the fact that 441 new patients attended in the first year, 64% being either injection drug users or their sexual contacts. In Edinburgh 5 of 7 HIV positive donors identified by the Blood Transfusion Service were ex-injection drug users and this further emphasises the importance of alternative testing sites. The clinic had counselled a total of 114 (26%) HIV positive individuals 88% of whom were injection drug users. It confirmed the fact that HIV infection was commonplace (52%) amongst drug users but less so amongst their sexual contacts (7%). This supported previous work suggesting that this infection in drug users was spread by needle sharing rather than as a sexually transmitted disease.

Those affected in Edinburgh are characteristically younger, have markers of current or past infection with Hepatitis B virus and are more likely to share needles/syringes frequently.
Not surprisingly those individuals with the least risk were most likely to decline the test after counselling, 20% in the miscellaneous group versus 2.6% in drug users. Overall 7% declined testing compared to 16% in the USA where the positivity rate was 17% compared to Edinburgh's 26% \(^6\). The post testing default rate was 21% which compared favourably with 30% in the USA \(^6\). An overall default rate of 42% is a matter of concern, since this means that counsellors are under-utilised. Cost and distance appear not to be factors in the default rate and it may be a feature of either lifestyle or the anxiety associated with screening for this particular virus.

The majority of HIV counselling and screening in the United Kingdom had been undertaken by Genito-Urinary Medicine clinics and since this had been an additional workload separate costing had not been readily available. This HIV counselling and screening clinic was set up de novo for a particularly difficult risk group. For a variety of reasons it was felt necessary to have a medical officer on site at all times and this obviously added to the expense. A realistic estimate of the cost of providing a counselling and screening service was however possible as a result of setting up a new service. In the first year the cost was £61.22 per patient without taking into account the cost of premises which were available at no extra cost to the Health Board. This cost could fall with increased numbers of patients and a better default rate to around £20 per patient.

**Conclusions**

The demand for an alternate site HIV counselling and testing facility was confirmed by the attendance of over 400 patients in its first year of operation, 64% being either injection drug users or their sexual contacts. It confirmed the fact that HIV infection was commonplace (52%) amongst drug users but less so amongst their sexual contacts (7%).

Not surprisingly those individuals with the least risk were most likely to decline HIV testing after counselling. The post testing default rate compared favourably with that reported from the USA but the high overall default rate was a matter of concern, since this meant that counsellors were under-utilised and costs increased. The cost of attendance and or distance appeared not to be factors in the default rate and it may be a feature of either lifestyle or the anxiety associated with screening for this particular virus are the most important factors.
References for Chapter 5

1. Personal Communication, Dr. D. B. L. McClelland, Director, South East Regional Blood Transfusion Service, Royal Infirmary, Edinburgh.


CHAPTER 6

Hospital Health care for HIV Infection with particular reference to Injecting Drug Users - a review of services outside the UK

Introduction

Models of health care developed for HIV and AIDS tend to reflect the experience of San Francisco or London where the majority of affected patients have been homosexual or bisexual\(^1,2\). The services developed in such areas may not necessarily apply to injection drug users. As a group injection drug users exhibit poor utilisation of existing services although some of this chaotic behaviour is more a characteristic of their community than drug use per se\(^3\). The medical services dealing with drug users have, until recently, concentrated on and or specialised in their addiction rather than their physical problems. Health care services have not been developed to manage chronic ill health in drug users and behaviour change with respect to HIV in drug users has been modest and rather difficult to initiate\(^4-6\). In view of the problems associated with IDU related HIV, which are both physical and psychological, the experience of other centres in developing services was important. This chapter details IDU related services, some experienced in HIV others not, in three other centres.

Method

During October and November 1988 the author undertook a travel fellowship to compare and contrast medical services for injecting drug users with particular reference to HIV and AIDS. During this fellowship I visited Amsterdam and a number of centres in the USA notably the Montefiore Medical Centre, Beth Israel Hospital, St Lukes-Roosevelt Hospital, Memorial Sloan Kettering Cancer Hospital, Beth Abraham Hospice and Bailey House residential facility in New York as well as the University of California San Francisco Medical Centre, San Francisco General Hospital and San Francisco Department of Health. Whilst there are many centres dealing with the problem of IDU related HIV I chose Amsterdam because of their model of care for IDU, San Francisco because of their model of care for AIDS and New York because of the size and length of their experience with IDU related HIV.

Results

The shape of any medical service is very much related to local demography and as a consequence the services for AIDS have developed along different lines in New York
and San Francisco. In New York City, IDU has been implicated in 34% of the male and in 60% of the female patients whereas in San Francisco only 1.7% of San Francisco's cases have been in drug users although a further 11.5% have involved drug use in homosexual/bisexuals\textsuperscript{7,8}. New York has had to cope with over 3 times as many patients with very different characteristics\textsuperscript{7}. In San Francisco 82% of the patients have been white, 99% male, 97% gay and only 1.7% heterosexual drug users\textsuperscript{8}. By comparison in New York only 46% of the patients have been white, 90% male, 64% gay and 28% heterosexual drug users\textsuperscript{8}. The medical problems are also very different for instance, 15% of IDU related AIDS have developed tuberculosis and this obviously requires very different nursing facilities\textsuperscript{9}. In addition there has been a dramatic increase in non-AIDS deaths such as pneumonia, tuberculosis, endocarditis etc. amongst injecting drug users\textsuperscript{10}.

It is estimated that New York has some 200,000 injecting drug users for its 7.5 million inhabitants and that around 50% have been infected with HIV\textsuperscript{7}. There are around 35,000 places for drug treatment, approximately 30,000 Methadone treatment slots and about 5,000 drug free treatment slots\textsuperscript{9}. San Francisco by comparison to New York has a much smaller injecting drug problem of approximately 14,000 users for a population of 750,000\textsuperscript{11}. As in New York however the majority are Black or Hispanic.

Methadone maintenance treatment programmes (MMTP) in the USA are regulated by the Federal Drug Administration (FDA) and perhaps the most stringent rule is that for every 50-60 patients attending a programme there should be one drug counsellor. In addition it is required that there be various support services such as day programmes. By law MMTP must also provide patients with an admission medical examination as well as an annual medical examination. The medical examinations vary however from a few minutes to 45-60 minutes depending upon the centres. The majority of patients attend daily to receive their methadone dose on site. In order to get into MMTP the patients need a one to two year history of drug use from court or medical reports, previous failed detoxification attempts and have to be greater than 18 years of age. For most patients there is a 3-4 month waiting list and at the admission physical the doctor will then decide on the dose of Methadone which was usually about 30 mg. He will also decide on the final dose depending upon the patient's history and every two to three days the dispensing nurses can increase the dose by 10 mg provided the patient is having withdrawal symptoms backed up by clinical signs such as dilated pupils, sweating etc. The doctors in the clinic provided primary
care and refer to local hospitals if the patients are at all ill. Payment for the MMTP service is according to income. The support system used relies on role model counselling, from ex-addicts or stable addicts. The underlying philosophy is re socialisation and to this end they are allowed take home privileges as far as Methadone was concerned in an attempt to re stabilise or re socialise the patients9,12.

Whilst New York City has had the largest number of AIDS patients in the USA, it was in San Francisco that an AIDS dedicated medical service began which is described below.

San Francisco

The San Francisco General Hospital (SFGH) AIDS Care system goes back to 1979-80 when Dr Abrams and Dr Volberding began a clinic for gay men with unexplained lymphadenopathy. The AIDS Clinic was set-up in Ward 86 of the SFGH in 1981-82 initially as an oncology clinic and then also as an opportunistic infection clinic. In 1988 it was open 5 days per week, had 2000 attendance's per month, over 120 staff and provided the following functions; a Nurse Screening Clinic, an AIDS/ARC Clinic, an Opportunistic Infection Clinic, a Kaposi’s Sarcoma Clinic and a Prescription Refill Clinic. In addition procedures such as blood transfusions, intravenous rehydration, intravenous chemotherapy etc. were undertaken in the clinic in order to avoid the need for admission13.

Whilst injecting drug users did receive medical and HIV care at this clinic, because of Federal regulations they also had either to attend a separate clinic in the same building for methadone or alternatively a methadone clinic elsewhere in the City. Not surprisingly therefore the follow up of injecting drug users was made more difficult by the need for multiple attendance's12.

In 1983 the in-patient Unit was established initially with 12 beds and latterly because of the increased workload with 18 beds. The hospital had about 30 AIDS patients in each day (or 27% of medical beds) and the AIDS Unit was virtually always full14.

Patients were admitted via the AIDS clinic or arrived via the emergency room and were admitted under the care of one of the general medical teams. There were eight such teams providing medical care for general as well as AIDS patients. The Consultants for the medical teams rotated monthly and provided inpatient care for
between 2-4 months of each year. Thus patients with multiple admissions were under different medical teams for each admission\textsuperscript{14}.

In 1985-86 SFGH created an inpatient AIDS Team made up of an AIDS Specialist (from the AIDS clinic) together with a third year resident (usually a visiting elective resident from another medical school) and visiting medical students. The AIDS Team provided back-up advise for the general medical teams and the AIDS Specialist did 2 ward rounds per week with these teams\textsuperscript{14}.

By comparison the rest of the care provided for the AIDS patients was very much via dedicated workers. For instance there were specialised social workers, counsellors, drug counsellors, physiotherapists, psychologists etc.

It is important to remember that SFGH is a City Hospital and therefore many patients with private health insurance would not utilise these inpatient services until they had exhausted their medical insurance. Patients with private health care insurance might utilise the expertise of the AIDS clinic but still attend their private physician and be admitted to private hospitals for their inpatient care\textsuperscript{14}.

\textit{New York}

In March 1988 1513 or 6.4\% of the acute medical and surgical beds in the municipal or voluntary hospitals were occupied by AIDS patients. At that time the Municipal system was caring for 36\% of the AIDS patients although in fact it only had 16\% of the medical and surgical beds in the City. Whilst overall only 13\% of AIDS patients in New York hospitals were related to IDU, in the Health and Hospital Corporation facilities 75\% of the cases were related to IDU. Thus a disproportionate share of the IDU problems gravitated to the Municipal hospitals\textsuperscript{7}.

In 1986 the New York State Department of Health proposed a system of Specialised AIDS Units. The idea was to provide a comprehensive care model for AIDS patients and by 1988 22 Specialised AIDS Units had been designated together with their associated AIDS Teams. In order to persuade hospitals to set up AIDS Units and Teams the Department of Health offered an increase rate of reimbursement if the patients were consulted on by an AIDS team.

In setting up AIDS centres the New York State Department of Health formulated a set of standards which facilities had to meet in order to be designated an AIDS unit. Essentially in order to claim increased reimbursement for the care of AIDS patients
hospitals had to designate a Unit for the care of AIDS patients which could provide a 24 hour emergency service and an outpatient facility. These units were expected to offer a broad range of services for a range of AIDS patients with differing needs including diagnostic services, inpatient care, hospice and residential care, counselling and educational programmes. The care of the patients in the Units was to be via a multi-disciplinary team providing individual case management. The Units were also expected to participate in clinical research and provide educational programmes for the general public including those at increased risk of acquiring HIV.\textsuperscript{15}

The teams were headed by an AIDS specialist who would rotate monthly but the rest of the staff were dedicated full time to the AIDS patients. There were social workers and nurse practitioners on all teams but the rest of the teams composition then depended upon the particular Unit. Most teams had dieticians, psychiatrists and or psychologists, the Unit head nurse and an administrator the latter because of the importance of identifying AIDS patients in the hospitals in order to obtain increased reimbursement. Others also had occupational therapists or lawyers (because of the problems of Do Not Resuscitate Orders and or living wills).

St Lukes and Beth Israel Hospital utilised dedicated medical staff that rotated monthly but other Units such as at the Montefiore Medical Centre in the Bronx did not have dedicated medical staff and as in SFGH each general medical team cared for its own AIDS patients in the Unit. In both systems there were a large number of Consultants involved in the care of the patients and the AIDS team co-ordinated their care.\textsuperscript{14,15,16,17}

Some Units such as at Montefiore utilised a written admission policy not only for AIDS but also for substance users, whilst others did not. They all tended to admit the sickest and most difficult patients or any patient that might benefit from admission to the Unit. Because the Units were designated as AIDS wards all patients had to volunteer for admission because it revealed their diagnosis.

Security was a problem for many Units and it was not uncommon for the hospitals to have security guards who might visit the Units as often as two hourly. The security staff were however rarely called upon and in fact had a good relationship with many of the patients. Their presence was however appreciated by the staff.

The out-patient AIDS clinics in New York provided care for the non-private patients. The New York Health Department's plan was to provide a similar structure to the
inpatient model of care for out-patient care but by December 1988 most of the AIDS Units had not fully established these specialised clinics. In general anyone not being followed by a private physician or a Methadone Treatment Programme was seen after discharge in an AIDS clinic.

Amsterdam

By 1988 Holland had reported 605 AIDS patients and of these 2.5% were drug users in 1986, 5% in 1987 and 8% in 1988. There were no special facilities available for AIDS in Amsterdam and at that time none were planned18,19.

The Municipal Medical Health Care Service had 5 major departments, one of them known as the Public Health and Environment Department (GG&GD) which had the function of running out-patient clinics, offering vaccinations, controlling infectious diseases, running laboratory services, combating AIDS and drug treatment for drug users.

Amsterdam's programme of drug treatment had 3 levels described as low, middle and high threshold. The Methadone bus was the low threshold system, the Methadone clinics were the middle system and drug detoxification, therapeutic communities etc. the high threshold system. The low level system had little in the way of regulations whilst the high level system was very strict as far as the use of other drugs was concerned. The GG&GD estimate that they reached 70% of the 6000-8000 addicts in Amsterdam (approximately 1/3 of Dutch users) and 40% of these were injecting drugs. Eight hundred individuals or 1/3 of the injecting drug users in Amsterdam had been found to be seropositive and were in touch with authorities. Approximately 50% of these were German or Italian18,19.

The Health care system of the Netherlands was based on an insurance system such that if one was in receipt of social security then the social security system directly paid for the services used by the patient. There were however a large number of uninsured individuals (very often foreign drug users) and if admitted to hospital then the insurance was initially paid by the social services only if it was a life threatening illness. As the patients get better however they become liable for the bills and therefore often self discharge.

A team of psycho-social nurses visited all the drug users in the general hospitals and saw between 300 and 400 patients per year. The team provided crisis intervention
for the patient during the first 2-3 hours in order to avoid a lack of methadone and because the patient's drug problem was usually of such a long standing nature they tried to persuade the staff not to embark on detoxification20.

The patients might well have aggressive, paranoid features or even frank psychiatric problems. The psycho-social nurses evaluated the drug history, the psychiatric history and the social circumstances as well as managed numerous crises between patients and staff. The major problems seen in hospitals with drug users centred around their visitors, their interaction with other patients and continued injection drug use. The nurses tried to place patients in treatment programmes and whilst previously they discharged them as soon as they left the hospital, with AIDS patients they offered outpatient follow up.

Some years ago Amsterdam experienced the effects of poisoned heroin and all those cases were managed in one ward to facilitate care. Thus they had developed a model for how to deal with drug users in hospital utilising a concentrated model of care but in 1988 they had not utilised this model for AIDS or HIV infection20. Similarly the methadone bus and clinics were not directly involved in HIV health care.

Discussion

The accepted model of health care for HIV and AIDS was developed in San Francisco and London and was based on a homosexual or bisexual population. The evolving HIV health care system was characterised by the involvement of voluntary groups, most but not all from the homosexual community, an emphasis on home and/or community care to return the patient to a non-hospital environment, a rapidly evolving health consciousness over HIV and a positive response to risk reduction measures.

This model of care does not necessarily apply to injecting drug users since the current drug user may have a continuing involvement in illegal or criminal activities, manipulative tendencies in dealing with statutory agencies, a dislike or distrust of official organisations and a similar dislike or distrust by those organisations of the clients. As a group they exhibit poor utilisation of existing services although some of this chaotic behaviour is more a characteristic of their community than drug use per se. There are in addition a relative lack of self help groups within the community and a relatively weak community voice. Their home environment is often not ideal or
suited to home care and to date behaviour change with respect to HIV has been modest and difficult to initiate\textsuperscript{4, 5}.

The medical care of patients with AIDS is complicated by a number of medico-social problems which are further compounded by the problem of IDU. Homelessness is extremely common in New York and San Francisco, and the accommodation of those that are not homeless is often unsatisfactory in relationship to their medical condition. Thus the existing situation is simply worsened with the development of AIDS and consequently many patients remain in hospital solely because of their unsatisfactory accommodation.

In the USA continuity of care does not necessarily occur within the voluntary or municipal medical system unless the individual has private medical insurance. Private medical insurance ensures that the same doctor cares for the individual as both outpatient and inpatient but this is not the case for those lacking insurance. Deteriorating health often results in an inability to generate an income or eventual unemployment. When combined with high medical costs this often results in a lack of basic health insurance. Amongst injecting drug users there is not only the problem of the high cost of medical care but also a lack of initial basic health care insurance. This lack of health insurance further reduces continuity of care because individuals may move from hospital to hospital using false names in order to avoid the problem of payment. Without doubt in both New York and San Francisco, as in the rest of the world, the cracks in the medical system are exposed by drug users. Continuity of care in New York or San Francisco was almost non-existent for IDU related HIV unless the patients were in a methadone programme and in this respect those enrolled in programmes may be better off than the ex-users or heterosexuals with HIV.

The inability to generate an income however affects not only those in regular employment but also those with an illegal income. In the case of an injecting drug user this might be because of an inability to continue criminal activities. The resulting poverty often precipitates an additional crisis when the individuals can no longer afford their drug habit. Consequently IDU related AIDS and HIV patients were more often in need of drug treatment programmes as their health deteriorated. As a consequence of the shortage of places in methadone treatment programmes and the priority given to IDU related AIDS or HIV these programmes are rapidly being saturated. Since these programmes were not established to deal with medical problems it created further problems for an over stretched service. In addition it
further reduced the available places for the uninfected drug users and this in turn further reduced the effectiveness of the prevention aspects of methadone programmes.

The San Francisco model for AIDS care whilst providing excellent continuity of care for out patients did not provide continuity of care for the numerous in-patient admissions unless the patient had private medical insurance. The SFGH inpatient model of care was adopted because it was felt that AIDS should be looked after by general physicians (despite the presence of an AIDS clinic). It was an attempt to avoid burnout in the carers and to educate more doctors in the principles of care of AIDS patients. However it did not address the problems of the patients. Continuity of care could not be provided by the Consultants since they were only on service for an average of about 2 months per year. The junior doctors also rotated frequently and thus it was quite possible for an individual to have a number of admissions and to be looked after by a variety of medical teams.

The New York health care system provided some continuity of care via the AIDS teams but even here the AIDS specialists rotated. Thus true continuity of care for inpatients was not available because subsequent admissions were under different Consultants. This contrasts with the UK medical care system where Consultants are on service for the majority of the year and provide both inpatient and outpatient care. A lack of continuity of care or its provision has not been evaluated as a possible factor in the difficulties of delivering health care to injecting drug users.

At present there are relatively few specialised AIDS out patient services in New York but the AIDS teams were an improvement on the way patients are generally managed in the United States in the public sector system. When viewed from this perspective it was of course an extremely good system. However when viewed from a private health care system or a European perspective there is no doubt that it had considerable deficiencies which could be remedied. For instance the creation of dedicated inpatient medical teams supervised by AIDS specialists as seen in some of the New York AIDS Units would provide better care for the patient without sacrificing the training of staff.

As a consequence of the enormous psycho-social problems, the drug dependence problems and the relative lack of a community network or movement to deal with these problems, more than any other group, the management of IDU related HIV requires a multi-disciplinary approach. IDU related HIV is a chronic debilitating
disease of the young who are in addition socio-economically deprived and their care is as much about HIV as about how to deliver that care in the presence of extreme poverty.

The USA experience does emphasises the importance of dedicated HIV services to cope with the problems. The San Francisco experience suggests that it is more efficient to provide all the relevant specialities in one area; thus the specialities of Infectious Diseases, Oncology and Neurology will all be required in the HIV/AIDS outpatient department.

The Amsterdam Municipal Medical Health Care Service provided excellent continuity of care for drug problems but had not yet been utilised for IDU related HIV problems. This despite the fact that Amsterdam had previously used a specialised inpatient service for an epidemic of poisoned heroin. The SFGH and Amsterdam experience of using specialised substance abuse counsellors or psychosocial nurses to help the patients and staff seems to be well worth considering for General Hospitals in the UK. Alternatively inpatient services which are experienced in the care of both HIV and injection drug use are required because the problems and solutions are so different from the services already established.

Conclusions

The model of health care for HIV and AIDS has been developed from the experience of San Francisco and London where the majority of patients have been homosexual or bisexual. This model of care did not apply to injecting drug users who have very different characteristics to other risk groups affected by HIV.

The medical care of patients with AIDS and HIV is complicated by a number of medico-social problems which are further compounded by the problem of IDU. In the USA continuity of care did not necessarily occur unless the individual had private medical insurance and was almost non existent for IDU related HIV unless the patients were in a methadone programme. The San Francisco model for AIDS care provided excellent out patient medical care but continuity of care was not available for the numerous in-patient admissions unless the patient had private medical insurance. The New York health care system provided some continuity of care via the AIDS teams but even the AIDS specialists rotated. Thus true continuity of care for inpatients was not available because subsequent admissions were under different Consultants. This is in contrast to the UK system where Consultants were and are on
service for the majority of the year and provide both inpatient and outpatient care. The USA experience did however emphasise the importance of a dedicated HIV service. The San Francisco experience suggested that it was more efficient to provide all the relevant specialities in one area.

The Amsterdam Municipal Medical Health Care Service provided excellent continuity of care for drug problems but it had not been utilised for IDU related HIV problems. The SFGH and Amsterdam experience of using specialised substance abuse counsellors or psycho-social nurses to help the patients and staff seems to be well worth considering for General Hospitals in the UK. Alternatively inpatient services are required experienced in the care of both HIV and injection drug use because the problems and solutions are so different from the services already established.
References for Chapter 6


9. Drucker E, 1988, Department of Social Medicine, Montefiore Hospital and Medical Center, 111 East 210th Street, Bronx, NY 10467, USA. Personal communication.


15. Friedland G, 1988, Department of Medicine, Montefiore Hospital and Medical Center, 111 East 210th Street, Bronx, NY 10467, USA. Personal communication.


CHAPTER 7

Outpatient medical care of HIV Infection with particular reference to Injecting Drug Users

Introduction

Unlike other UK centres, in the early 1980's Edinburgh had little in the way of specialist services for drug users\(^1\). Whilst Edinburgh had a voluntary sector for dealing with injecting drug users, during the 1970's and early 1980's there had been a gradual reduction in the prescribing of substitute drugs by general practitioners and psychiatrists based on the assumption that spontaneous resolution of addiction would occur with a small overall mortality of around 1% per year\(^2-5\).

The Advisory Council on the Misuse of Drugs (ACMD) report in 1988 noted that in Scotland, and in Edinburgh in particular, there were four notable features of the drug services. Firstly a dearth of psychiatric input with virtually no specialist support which undoubtedly contributed to the unwillingness of general practitioners to provide care for drug users; secondly a limited range of treatment options; thirdly limited community based services and lastly pilot syringe exchange schemes which were not "user friendly"\(^1\). Thus when the epidemic of injection drug use occurred in the early 1980's there were little or no medical provisions for dealing with the problem and as a consequence the initial management of IDU related HIV in 1985 and 1986 utilised only the offer of medical care. In addition the recognised models of health care for HIV and AIDS were based on clinics where the majority of patients affected had been homosexual or bisexual\(^6,7\).

The aims of an IDU related service should be to initiate and then maintain contact, but this may require diverse initiatives such as methadone, pyschological and social provisions as well as medical care. This concept has recently been more widely advocated by the ACMD\(^1\). However to date there has been little if any assessment of the success or failure of IDU related HIV medical services in achieving these aims, the majority of papers proposing various theories of care but rarely providing factual evidence of success or failure.

The aims of medical care are to reduce if possible progression to AIDS, to initiate the early treatment and prevention of OIs and where possible to initiate anti-retroviral therapy. In order to achieve some of these goals regular immunological monitoring of the patients is important in order to provide both the patient and the service, of an
early warning of deterioration. Lastly having established contact an attempt is made to reduce the spread of HIV by behaviour modification achieved via health education.

Since 1985, services for individuals with HIV or AIDS have been developed at the RIDU, City Hospital, Edinburgh. The considerable psychosocial and physical problems associated with HIV infected patients necessitated the development in Edinburgh of a multi-disciplinary team able both to manage patients and co-ordinate their care. This chapter describes that team, its approach to the care of HIV infected drug users and, perhaps more importantly, the results.

Patients and Methods

The RIDU has since the early 1960's provided Urinary Tract Infection (UTI) clinics which are held on one specific day staffed primarily by the Consultant staff. On other days there were Infectious Disease (ID) clinics providing outpatient consultations and care for patients with suspected infections including patients returning from abroad. These clinics were staffed by Consultants and junior medical staff. The HIV medical clinics were also established in October 1985. Initially a single clinic was held in the Out Patient Department of the RIDU of the City Hospital, Edinburgh staffed by one Consultant (RPB) and one part time medical officer. In November 1986 an all day clinic was established and staffing gradually increased to a research registrar and another full time medical officer. In May 1989 an additional consultant (CLSL) was appointed and specific clinics on other days were established

A retrospective analysis of out patient records was undertaken from 1985-90 to assess the effectiveness of this service. In addition to providing medical care some assessment of risk behaviour modification was also made at each clinic visit by recording self reported IDU behaviour. Those patients who did not attend for more than one year were flagged with the Registrar General to provide ongoing information concerning date and cause of death.

In order to re-arrange an appointment it was and remains necessary for defaulting patients to contact the clinic since appointments are not routinely sent out by post. Because the phenomenon of re-attendance after missed appointments is so common, patients were defined as lost to follow up if they had not re-attended before the 31st December 1991 and were not known to have died.
A confidential prospective database containing an assessment of clinical staging, injection drug use, oral drug use, weight as well as biochemical, haematological and immunological parameters is maintained on all patients attending the City Hospital. The patients are identified on the database by hospital number only and the cross link between hospital number and name is stored on a separate database file which is kept on a removable "floppy disc".

**HIV service at the City Hospital**

The general RIDU clinics had been faced with large numbers of HIV infected drug users with no management options for their addiction other than abstinence. There were very few general practitioners or psychiatrists, with notable exceptions, willing to prescribe oral opiate substitutes and it was obvious that the previous philosophy of awaiting spontaneous resolution of addiction was no longer practicable with the advent of HIV. In 1986 it was also suggested that continued IDU was associated with an accelerated loss of CD4 lymphocytes in HIV infected patients and therefore, as an HIV management strategy, the prescribing of oral methadone was commenced.

Patients were evaluated for their HIV problems and those found to be injecting drugs were offered a methadone maintenance programme. Methadone, initially in daily instalments of "DTF" 1 mg/ml solution (an elixir which includes chloroform to induce vomiting if injected), was provided via a hospital prescription which could be taken to any dispensing pharmacist. The cost however was paid for by the hospital rather than the general practitioner budget. The majority of initial prescriptions were, and still are, written for daily dispensing but variations such as two or three times per week are also used. No other drugs of addiction such as dihydrocodeine, buprenorphine, prochlorperazine or benzodiazepines were provided. Initially the majority of patients were in receipt of hospital methadone prescriptions, but with time, more general practitioners have taken on long term opiate substitute prescribing.

As a consequence of the lack of drug services in Edinburgh there was a rise in the number of uninfected injection drug users seeking treatment, until in June 1987 they accounted for over one third of the referrals. Unfortunately, the response of the management to this problem was to restrict the service at the City Hospital to only HIV seropositives rather than to increase the available resources. This created a two tier system such that it was easier to obtain oral drugs if infected and resulted, not
surprisingly, in critical comments from the ACMD\(^1\). Eventually this illogical situation was rectified with the creation of the Community Drug Problem Service or CDPS in April 1988\(^10\).

Patients were provided with other medication such as zidovudine, antibiotics etc. as necessary. Initially \textit{Pneumocystis carinii} pneumonia (PCP) prophylaxis was organised using inhaled pentamidine via the district nurse service although latterly cotrimoxazole has been used more extensively. Generally, however, other than methadone and zidovudine, the majority of prescribing was done by general practitioners with advice from the hospital clinic.

As a consequence of disruption to the general clinics and the large number of missed appointments it was decided in November 1986 to provide IDU related HIV medical care at a separate all day clinic. Provided the patients attend at some time on that day, they are seen by a doctor. This overcame the problem of patients arriving late for morning clinics and being sent away. The busiest time for the clinic was between 11 am and 3 pm and consultations often continued through lunch time. Additional help came from the establishment of a voluntary organisation to offer practical help for HIV positive individuals (including transportation to hospital appointments so that ambulances have not been required except for emergencies).

Patients were offered routine medical surveillance for their HIV infection, methadone maintenance therapy where necessary, as well as advice on their drug problems. As far as possible a number of other facilities such as counselling, contraceptive advice and supplies, inhaled pentamidine, dental care and refunding of bus fares were also provided on site. Paediatric follow up was available in the community or via a combined family HIV clinic from the same out patient department.

The majority of IDU related AIDS or HIV problems have, when necessary, been admitted to the RIDU and were generally nursed in single rooms. There was no written admission policy and there were no security staff. There was however a dedicated HIV team, both medical, paramedical and nursing, but no other specialised drug dependence staff. In general, the problems associated with drug using patients have settled with time. Many of the early admissions allowed patients and staff to get to know each other such that by the time the patient were seriously ill an understanding and trust have developed. Each week there were two multi-disciplinary meetings, one for inpatients and the other for outpatients, which were attended by the team together with inpatient and out patient nurses. The consultant
staff provided medical continuity of care for both in and out patients. Continuity of nursing care was achieved wherever possible by re-admitting patients to the same ward.

The majority of the paediatric HIV patients in Edinburgh had also been admitted to the paediatric ward of the RIDU, initially under the care of the Infectious Disease Consultants but latterly under the care of the Community Paediatrician who also provided the paediatric HIV out patient care. On occasions this allowed both mother and child to be admitted to the same unit. However, when the mother had advanced or serious disease, she was usually too ill to care for the child. Whilst, in emergency situations, an admission to the Unit was offered for the child, the preferred solution was identification, via Social Services, of long term voluntary foster mothers available at short notice.

All these changes were introduced gradually over the time period and are probably also important in maintaining contact. Unfortunately it was more difficult to measure their effect on either attendance and or the missed appointment (MA) rate.

The problems encountered on the wards were more to do with drug use than HIV. The concern about HIV amongst general patients was not so much of a problem as the unsociable and disruptive behaviour connected with drug use which caused considerable distress to other patients as well as difficulties for the staff. The need for specialised AIDS Units may be as much to do with this difficult behaviour as the need to provide specialised HIV medical care. Continued non prescribed drug use either orally or by injection cannot be eliminated whatever the level of supervision. Not surprisingly it was less of a problem the more seriously ill was the patient but even then total immediate withdrawal was impossible despite respiratory failure. Unlike Drug Detoxification Units, restricted visiting and body searches were not possible for visitors and or patients who were seriously ill.

Other major problems were verbal abuse towards other patients and staff, unsociable behaviour at unsociable hours, theft from other patients, as well as the ward's property and violent behaviour. This later problem was not often directed towards the staff. Commonly there were old scores to settle between patients and unfortunately staff have been injured in the attempts to halt the fighting.
Results

By the end of March 1990 contact had been made with 470 HIV seropositive patients, 77% (363) of whom were IDU related, 13% (60) were homosexual and 8% (37) were heterosexually related. The male to female ratio was 2:1 (312/158), the median length of follow up at that time was 21.5 months and 25% of the patients had been followed up for at least 36 months. Only 49 (10%) patients had attended for only a single clinic visit whilst 274 (58%) patients had attended for at least 5 and 48 (10%) patients for at least 20 clinic visits.

One hundred and sixty nine or 47% of the drug using individuals were considered to be definitely injecting at their initial clinic visit compared to 36 (10%) at their last clinic visit. One hundred and twenty nine (36%) of the drug users were in receipt of methadone prescribed from the clinic at their last clinic visit.

An additional 71 HIV seronegative but at risk individuals had also been seen during this time, 66% (47) of whom were drug users, 4% (3) were homosexuals and 21% (15) were heterosexuals mostly the partners of seropositive patients. The male to female ratio for seronegative patients was 1.8:1 (46/25).

The overall mean age of the patients was 27.5 years (SD. 6.5, range 16-57) and 90% of the patients were between 19 and 39 years of age. The mean age of the patients was 27.7 years for the HIV seropositives compared to 26.8 years for the HIV seronegative patients. The mean age for male HIV seropositives was 28.6 years compared to 25.9 years for the HIV seropositive females. This difference was largely accounted for by the fact that the mean age for the male homosexuals was 34.5 years. The mean age for IDU related HIV seropositive patients was 26.9 years for males and 26.0 years for females.

There were 158 (25%) patients who had failed to attend for at least 1 year and 83 (15%) patients who had not attended for 1.5 years by the end of March 1990. However a total of 79 patients were known to have reappeared after a 1 year absence and 37 patients after a 1.5 year absence. The cumulative loss to follow up of HIV seropositive patients between 1985 and 1988 was 20%. Thirty four (6%) patients were also known to have died, 20 after the diagnosis of AIDS, 12 of drug overdoses and 2 of unknown causes.

Of the living patients 80 (18%) patients had been classified as being in CDC stage II, 187 (43%) in CDC stage III and 142 (33%) in CDC stage IV at their last clinic visit.
Initiating and Maintaining Contact

The total attendance for two months (May and November) of each year from 1985-89 together with the number of missed appointments (MA) are shown in Table 7.1. In November 1985 HIV appointments accounted for only 3% (13/426) of the outpatient workload but by November 1989 this had risen to 39% (246/637). The MA rate for the HIV clinic was not constant ($\chi^2(8)$ = 52.6, $P<0.001$) whereas over the 4 year period the MA rate had remained constant for the UTI ($\chi^2(8)$ = 10.26) and ID ($\chi^2(8)$ = 3.12) clinics. Whilst there was a significant linear trend in the reduction of the HIV missed appointment rate ($\chi^2(1) = 21.6, P<0.001$) there was also a highly significant departure from linearity ($\chi^2(7) = 31, P<0.001$).

The data were examined to see if the MA rate changed significantly after the introduction of methadone and an all day HIV clinic. The change in the MA rate after November 1986 was significant ($\chi^2(1) = 38.94, P<0.001$). The introduction of methadone and the all day clinic explains the observed variation (residual variation $\chi^2(7) = 13.7, P>0.05$).

Table 7.1: Actual and missed appointments (MA) for 2 months of each year, 1985-1989

| Month   | UTI Clinics | | ID Clinics | | HIV Clinics | |
|---------|-------------|-----------------|-------------|-----------------|-----------------|
|         | Total       | MA (%)          | Total       | MA (%)          | Total            |
|         |             |                 |             |                 | (%)             |
| Nov. 85 | 359         | 52 (14)         | 122         | 16 (13)         | 19              |
|         |             |                 |             |                 | 6 (32)          |
| May 86  | 306         | 52 (17)         | 123         | 21 (17)         | 28              |
|         |             |                 |             |                 | 17 (61)         |
| Nov. 86 | 304         | 38 (13)         | 127         | 20 (16)         | 77              |
|         |             |                 |             |                 | 27 (35)         |
| May 87  | 283         | 47 (17)         | 103         | 12 (12)         | 172             |
|         |             |                 |             |                 | 31 (18)         |
| Nov. 87 | 275         | 55 (20)         | 112         | 13 (12)         | 152             |
|         |             |                 |             |                 | 26 (17)         |
| May 88  | 321         | 50 (16)         | 63          | 8 (13)          | 192             |
|         |             |                 |             |                 | 42 (22)         |
| Nov. 88 | 269         | 34 (13)         | 153         | 24 (16)         | 213             |
|         |             |                 |             |                 | 36 (17)         |
| May 89  | 225         | 33 (15)         | 152         | 21 (14)         | 300             |
|         |             |                 |             |                 | 45 (15)         |
| Nov. 89 | 244         | 32 (13)         | 205         | 26 (13)         | 294             |
|         |             |                 |             |                 | 48 (16)         |
| $\chi^2(8)$ | 10.26 | 3.12 | 52.6 |
| $P<$ | NS | NS | 0.001 |

UTI = Urinary Tract Infection, ID = Infectious Diseases, HIV = Human Immunodeficiency Virus, MA = Did Not Attend, NS = Not Significant
The data were examined in more detail for the time period November 1985 to May 1987 (Table 7.2). There was no homogeneity of the MA rate across the 19 month time period ($\chi^2_{(18)} = 83.96, P<0.001$). As far as the time periods November 1985-June 1986, (no methadone), July 1986-November 1986 (methadone) and December 1986-May 1987 (methadone and an all day clinic) were concerned there were significant differences ($\chi^2_{(2)} = 61.26, P<0.001$) not explained by the introduction of methadone alone (residual variation after allowing for methadone and the all day clinic $\chi^2_{(16)} = 83.96-61.26 = 22.7$, NS at 10% level; residual variation after allowing for methadone alone $\chi^2_{(17)} = 83.96-52.05 = 31.91, p<0.02$).
Table 7.2: Monthly HIV appointments and missed appointments (MA), November 1985-May 1987

<table>
<thead>
<tr>
<th>Month</th>
<th>Total appointments</th>
<th>Missed appointments or MA(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov. 85</td>
<td>19</td>
<td>6 (32)</td>
</tr>
<tr>
<td>Dec. 85</td>
<td>21</td>
<td>13 (63)</td>
</tr>
<tr>
<td>Jan. 86</td>
<td>27</td>
<td>12 (44)</td>
</tr>
<tr>
<td>Feb. 86</td>
<td>19</td>
<td>8 (42)</td>
</tr>
<tr>
<td>Mar 86</td>
<td>32</td>
<td>14 (44)</td>
</tr>
<tr>
<td>Apr. 86</td>
<td>70</td>
<td>31 (44)</td>
</tr>
<tr>
<td>May 86</td>
<td>28</td>
<td>17 (61)</td>
</tr>
<tr>
<td>Jun. 86</td>
<td>62</td>
<td>30 (48)</td>
</tr>
<tr>
<td>Jul. 86</td>
<td>51</td>
<td>16 (31)</td>
</tr>
<tr>
<td>Aug. 86</td>
<td>55</td>
<td>16 (31)</td>
</tr>
<tr>
<td>Sep. 86</td>
<td>57</td>
<td>18 (32)</td>
</tr>
<tr>
<td>Oct. 86</td>
<td>56</td>
<td>17 (30)</td>
</tr>
<tr>
<td>Nov. 86</td>
<td>77</td>
<td>27 (35)</td>
</tr>
<tr>
<td>Dec. 86</td>
<td>78</td>
<td>16 (21)</td>
</tr>
<tr>
<td>Jan. 87</td>
<td>97</td>
<td>22 (23)</td>
</tr>
<tr>
<td>Feb. 87</td>
<td>102</td>
<td>34 (33)</td>
</tr>
<tr>
<td>Mar. 87</td>
<td>172</td>
<td>36 (21)</td>
</tr>
<tr>
<td>Apr. 87</td>
<td>138</td>
<td>30 (22)</td>
</tr>
<tr>
<td>May 87</td>
<td>172</td>
<td>31 (18)</td>
</tr>
<tr>
<td>$\chi^2$(18)</td>
<td>582.8</td>
<td>83.96</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

As a consequence of the problems of trying to manage chaotic drug users in routine clinics considerable disquiet amongst the non drug using patients developed and therefore it was necessary to consider the effect of relatively large numbers of drug users on the other clinics.

Table 7.3 documents the total number of appointments and the number of MA for the two six month periods of 1986 and the first six month period of 1987. There was a significant decline in the total number of UTI appointments ($\chi^2(2) = 21.3, P<0.001$), a highly significant increase in the total number of HIV appointments ($\chi^2(2) = 442, P<0.001$) but little change in the total number of ID appointments. The MA rates were unchanged for the UTI clinic ($\chi^2(2) = 2.45$) and decreased for the HIV clinic ($\chi^2(2) = 57.7, P<0.001$) as previously noted.
The MA rate for the ID clinic significantly increased for the second half of 1986 and then returned to the previous level ($\chi^2(2) = 11.28, P<0.01$). This coincided with the increased attendance of IDU related HIV patients in the general ID clinics which occurred after the introduction of methadone prescriptions between June 1986 and November 1986. The decline in the MA rate in the general ID clinics coincided with the introduction of the all day clinic for HIV infected drug users in November 1986 which was held on one particular day with no additional ID or UTI clinics running concurrently.

**Table 7.3: Total appointments made and missed appointments (MA) for each 6 month period from 1986-1987**

<table>
<thead>
<tr>
<th>Time</th>
<th>UTI Clinic</th>
<th>ID Clinic</th>
<th>HIV Clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month</td>
<td>Total MA (%)</td>
<td>Total MA (%)</td>
<td>Total MA (%)</td>
</tr>
<tr>
<td>1/86-6/86</td>
<td>2179 349 (16)</td>
<td>726 77 (11)</td>
<td>238 112 (47)</td>
</tr>
<tr>
<td>7/86-12/86</td>
<td>1978 322 (16)</td>
<td>797 124 (16)</td>
<td>374 110 (29)</td>
</tr>
<tr>
<td>1/87-6/87</td>
<td>1894 336 (18)</td>
<td>725 77 (11)</td>
<td>865 192 (22)</td>
</tr>
<tr>
<td>$\chi^2(2)$</td>
<td>21.3 2.45</td>
<td>5.12 11.28</td>
<td>442 57.7</td>
</tr>
<tr>
<td>P&lt;</td>
<td>0.0001 NS</td>
<td>0.1 0.01</td>
<td>0.0001 0.001</td>
</tr>
</tbody>
</table>

Table 7.4 details the numbers of new patients referred to the UTI and ID Out Patient Clinic between 1985-89. There appears to be a significant decline in the number of new patients referred to the UTI clinics over the period 1985-1989 ($\chi^2(8) = 60.72, P<0.001$). The decline in the UTI new patients was non linear ($\chi^2(7) = 22.04, P<0.01$) being accentuated after June 1988. The decline in patients referred to the general ID clinics over the same period was only just significant ($\chi^2(8) = 17.96, P<0.05$) and less remarkable in terms of clinical workload. The six monthly acquisition of new HIV patients (Table 7.4) was not at a constant rate over the period ($\chi^2(8) = 36.3, P<0.001$). Much of the variation was however contributed by the first and last time periods. The number of HIV negative but at risk patients (mainly HIV negative drug users seeking methadone) rose significantly until June 1987 and then ceased. This coincided with a management decision that the prescribing of oral methadone should be restricted to HIV seropositive individuals.
### Table 7.4: Number of new patients referred to the RIDU by half year 1985-1989

<table>
<thead>
<tr>
<th>Time period</th>
<th>UTI</th>
<th>ID</th>
<th>HIV + ve</th>
<th>HIV-ve high risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>July-Dec. 85</td>
<td>108</td>
<td>119</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td>Jan.-June 86</td>
<td>142</td>
<td>102</td>
<td>47</td>
<td>3</td>
</tr>
<tr>
<td>June-Dec. 86</td>
<td>116</td>
<td>130</td>
<td>58</td>
<td>16</td>
</tr>
<tr>
<td>Jan.-June 87</td>
<td>107</td>
<td>122</td>
<td>65</td>
<td>24</td>
</tr>
<tr>
<td>July-Dec. 87</td>
<td>105</td>
<td>107</td>
<td>40</td>
<td>3</td>
</tr>
<tr>
<td>Jan.-June 88</td>
<td>114</td>
<td>114</td>
<td>56</td>
<td>6</td>
</tr>
<tr>
<td>July-Dec. 88</td>
<td>61</td>
<td>96</td>
<td>43</td>
<td>6</td>
</tr>
<tr>
<td>Jan.-June 89</td>
<td>85</td>
<td>85</td>
<td>63</td>
<td>7</td>
</tr>
<tr>
<td>July-Dec. 89</td>
<td>56</td>
<td>88</td>
<td>33</td>
<td>2</td>
</tr>
<tr>
<td>$\chi^2$(8)</td>
<td>60.72</td>
<td>17.96</td>
<td>36.3</td>
<td>70.6</td>
</tr>
<tr>
<td>p&lt;</td>
<td>0.0001</td>
<td>0.05</td>
<td>0.001</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

By the end of 1990 contact had been initiated with 511 HIV positive individuals and 68 HIV negative individuals, 75% IDU related. However 64 of the HIV positive and 3 of the HIV negative individuals had died by the end of 1990. As detailed above a significant reduction in the ratio of missed appointments to total appointments booked, had occurred between 1986 and 1989 coincident with the introduction of methadone and an all day clinic. However between 1989 and 1990 the MA rate rose again from 17% to 25%, but a significant increase in the number of MA was not seen amongst patients attending the all day clinic ($\chi^2(3) = 1.91$) only amongst patients booked for other clinics ($\chi^2(3) = 121.3$, p<0.001, Table 7.5).
Table 7.5: HIV appointments by half year during 1989 and 1990

<table>
<thead>
<tr>
<th>Time</th>
<th>All Day Clinic</th>
<th>Other Clinics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Actual</td>
<td>MA(%)</td>
</tr>
<tr>
<td>Jan.-June 89</td>
<td>818 (164)</td>
<td>164(17)</td>
</tr>
<tr>
<td>July-Dec. 89</td>
<td>836 (153)</td>
<td>153(15)</td>
</tr>
<tr>
<td>Jan.-June 90</td>
<td>889 (182)</td>
<td>182(17)</td>
</tr>
<tr>
<td>July-Dec. 90</td>
<td>864 (186)</td>
<td>186(18)</td>
</tr>
<tr>
<td>Total</td>
<td>3407 (685)</td>
<td>685(17)</td>
</tr>
</tbody>
</table>

\(\chi^2(3) = 1.91\)

\(\chi^2(3) = 121.29, \ p< 0.001.\)

There was, however, no significant change in the number of patients who missed medical appointments between 1989 and 1990 (Table 7.6). In 1989, 263 (65%) of 436 individuals missed 537 (29%) appointments out of 1826 visits where laboratory monitoring occurred (mean number of missed appointments = 2/patient with MA, range 1-8). In 1990, 254 (60%) of 454 individuals missed 621 (24%) appointments out of 2556 visits where laboratory monitoring occurred (mean number of MA = 2.4/patient with MA, range 1-12). There were in addition 19 new patients in 1989 and 14 new patients in 1990 who were referred to the clinic but never attended. There was no male/female difference in the population with missed appointments (data not shown). Only 68 of the patients who missed appointments in 1989 (26% of those patients with missed appointments or 15.5% of the total patients attending in 1989) accounted for 50% of the total number of missed appointments. Looked at another way, 39.5% missed no appointments and 45% missed only one or two appointments per year and only 34/436 (8%) of the patients failed to receive any laboratory monitoring during 1989 at the City Hospital (Table 7.6). During 1990, 88 of the defaulting patients (34.5% of those patients with missed appointments or 19% of the total patients attending in 1990) accounted for 62% of the missed appointments. Again 44% missed no appointments, 36% missed only one or two appointments in the year and only 25/454 (5.5%) of the patients failed to receive any laboratory monitoring during 1990 at the City Hospital.
Table 7.6: Frequency tabulation of missed appointments (MA) during 1989-90

<table>
<thead>
<tr>
<th>Frequency of MA</th>
<th>1989</th>
<th>1990</th>
<th>1990</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of patients</td>
<td>Number of MA</td>
<td>Number of patients</td>
</tr>
<tr>
<td>0</td>
<td>173</td>
<td>0</td>
<td>200</td>
</tr>
<tr>
<td>1</td>
<td>121</td>
<td>121</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>74</td>
<td>148</td>
<td>68</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>108</td>
<td>31</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>60</td>
<td>26</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>30</td>
<td>14</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>48</td>
<td>7</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
Table 7.7: Summary of missed appointments during 1989-90

<table>
<thead>
<tr>
<th></th>
<th>1989</th>
<th>1990</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. patient missing apps</td>
<td>263</td>
<td>254</td>
</tr>
<tr>
<td>Total No. patients</td>
<td>436</td>
<td>454</td>
</tr>
<tr>
<td>Total No. missed apps</td>
<td>537</td>
<td>621</td>
</tr>
<tr>
<td>Mean No. of MAs/patient with MAs</td>
<td>2.04</td>
<td>2.44</td>
</tr>
<tr>
<td>No. of visits where laboratory monitoring occurred</td>
<td>1826</td>
<td>2556</td>
</tr>
<tr>
<td>Mean no. MAs/episode of laboratory monitoring</td>
<td>0.3</td>
<td>0.2</td>
</tr>
</tbody>
</table>

An analysis of patients who missed appointments in both 1989 and 1990 is shown in Table 7.8. This analysis does not include a number of patients; any new patients who first attended in 1990, those that attended in 1989 but had no visits or requests for appointments in 1990, those dying in 1989. Essentially 45% of the patients who missed appointments were consistent in their behaviour, 29% improved their attendance behaviour and 26% worsened over the two years. Of patients who attended in both years only 2.5% with 3 or more missed appointments in a year had no missed appointments in the other year and only 2% accounted for 3 or more missed appointments in both years. In addition, 58% of these patients in 1989 and 64% in 1990 missed appointments in the other year.
Table 7.8: Cross tabulation of the number of patients attending during 1989 and 1990 categorised by the number of missed appointments during 1989-90

<table>
<thead>
<tr>
<th></th>
<th>1990</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>1989</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>69</td>
</tr>
<tr>
<td>1-2</td>
<td>77</td>
</tr>
<tr>
<td>&gt;3</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
</tr>
<tr>
<td>(%)</td>
<td>(41.5)</td>
</tr>
</tbody>
</table>

The number of individuals lost to follow up during 1986-90 varied between 8-11% per year and did not change significantly over time (Table 7.9, \( \chi^2(4)=1.21 \)). The cumulative lost to follow up rate between 1986-90 was 124/582 or 21%. This figure includes the lost to follow up patients who died after missing appointments at the clinic. Amongst the HIV negative individuals the overall lost to follow up rate was worse at 51/68 or 75% whilst for the HIV infected individuals the overall loss to follow up was actually 73/511 or only 14%. A total of 64 HIV infected patients had died by the end of 1990, a rate of 64/511 or 12.5%. Amongst the HIV negative individuals the rate was 3/68 or 4.4%. The deaths in the HIV negative patients were in fact all drug users and a comparison of death rates amongst drug users revealed 38/385 deaths or 10% in HIV infected drug users and 3/50 deaths or 6% in uninfected drug users.

The number of lost to follow up are those patients not seen by 31/12/91 and not notified as having died by the Registrar General Scotland. By the end of 1990 232/511 (45%) patients had commenced treatment with zidovudine and of these 166 (72%) had acquired HIV by IDU.
Table 7.9: Annual number of patients lost to follow up by year

<table>
<thead>
<tr>
<th>Year</th>
<th>Number patients lost(%)</th>
<th>Total patients seen in year</th>
</tr>
</thead>
<tbody>
<tr>
<td>1986</td>
<td>10(7)</td>
<td>143</td>
</tr>
<tr>
<td>1987</td>
<td>28(11)</td>
<td>258</td>
</tr>
<tr>
<td>1988</td>
<td>30(9)</td>
<td>330</td>
</tr>
<tr>
<td>1989</td>
<td>34(8)</td>
<td>436</td>
</tr>
<tr>
<td>1990</td>
<td>41(9)</td>
<td>454</td>
</tr>
</tbody>
</table>

$\chi^2(4)=1.21$, $p=\text{NS}$.

**Risk behaviour**

The self reported injecting behaviour of drug users attending the clinics each year is documented in Tables 7.10, figures 7.1 and 7.2. Amongst HIV infected patients the percentage reporting injecting at more than 50% of the visits during a year fell from 42% in 1986 to 6.5% in 1990 ($\chi^2(4)=93.75$, $p<0.001$) and those reporting injecting at one visit during a year fell from 51% in 1986 to 23% in 1990 ($\chi^2(4)=60.9$, $p<0.001$). Amongst the uninfected drug users the percentage reporting injecting at more than 50% of the visits during a year fell from 73% in 1986 to 35% in 1990 ($\chi^2(4)=7.6$) and those reporting injecting at one visit during a year fell from 72% in 1986 to 50% in 1990 ($\chi^2(4)=12.99$, $p<0.05$).

Table 7.10: Drug users attending the City Hospital assessed as injecting more than 50% of the visits during the year or at least once during the year

<table>
<thead>
<tr>
<th>Year</th>
<th>More than 50% of the year</th>
<th>At least once during the year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV positive (%)</td>
<td>HIV negative (%)</td>
</tr>
<tr>
<td>1986</td>
<td>47/111(42)</td>
<td>8/11(73)</td>
</tr>
<tr>
<td>1987</td>
<td>51/159(32)</td>
<td>13/27(48)</td>
</tr>
<tr>
<td>1988</td>
<td>50/228(22)</td>
<td>7/21(33)</td>
</tr>
<tr>
<td>1989</td>
<td>40/286(14)</td>
<td>3/13(23)</td>
</tr>
<tr>
<td>1990</td>
<td>20/307(7)</td>
<td>6/17(35)</td>
</tr>
</tbody>
</table>

$\chi^2(4)=93.75$, $p<0.0001$  
$\text{At least once}: \chi^2(4)=7.6$, $p=0.1$  
$\text{HIV negative}: \chi^2(4)=60.9$, $p<0.001$  
$\text{HIV negative}: \chi^2(4)=12.99$, $p<0.05$
Injecting Drug Use

More than 50% of the year

Figure 7.1: Drug users attending the City Hospital assessed as injecting more than 50% of the visits during the year.
Injecting Drug Use
At least once during the year

Figure 7.2: Drug users attending the City Hospital assessed as injecting at least once during the year
The self reported use of opiates is documented in Tables 7.11. Amongst HIV infected patients the percentage reporting opiate use for more than 50% of the visits during a year rose from 54% in 1986 to a peak of 70% in 1989 ($\chi^2(4) = 10.22$, p<0.05) and those reporting opiate use at least once during the year rose from 57% in 1986 to a peak of 75% in 1989 ($\chi^2(4) = 14.3$, p=0.006). Amongst the uninfected drug users the percentage reporting using opiates for more than 50% of the visits during a year rose from 50% in 1986 to a peak of 100% in 1990 ($\chi^2(4) = 9.3$, p=0.054) and those reporting opiate use at least once per year rose from 50% in 1986 to a peak of 100% in 1989 ($\chi^2(4) = 9.6$, p=0.05).

Table 7.11: Drug users attending the City Hospital assessed as using opiates more than 50% of the visits during the year and at least once during the year

<table>
<thead>
<tr>
<th>Year</th>
<th>More than 50% of the year</th>
<th>At least once during the year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV positive (%)</td>
<td>HIV negative (%)</td>
</tr>
<tr>
<td>1986</td>
<td>51/95 (54)</td>
<td>3/6 (50)</td>
</tr>
<tr>
<td>1987</td>
<td>95/144 (66)</td>
<td>16/18 (89)</td>
</tr>
<tr>
<td>1988</td>
<td>110/184 (60)</td>
<td>5/9 (56)</td>
</tr>
<tr>
<td>1989</td>
<td>164/233 (70)</td>
<td>9/9 (100)</td>
</tr>
<tr>
<td>1990</td>
<td>153/237 (65)</td>
<td>7/9 (78)</td>
</tr>
</tbody>
</table>

$x^2(4) =$

|      | 10.22 | 9.3 | 14.3 | 9.6 |
|      | <0.05 | =0.054 | =0.006 | =0.05 |

**Discussion**

Traditionally health care for drug users has been based on psychiatric models developed for the management of addiction and has not concentrated on the physical aspects of care. Models for the treatment of drug addiction have utilised a variety of different regimens including contracts, therapeutic communities, substitution therapy etc. Whilst such regimens have been evaluated for the treatment of addiction this has not been the case for the management of IDU related HIV. In addition, unrealistic behaviour change is sometimes expected of drug users such as cure of addiction, before offering treatment modalities like zidovudine. Similar constraints on the behaviour of other risk groups are not however imposed before offering medical care.
The aim of any IDU service should be to initiate and maintain contact in order to deliver health care and health education. This initiation and maintenance of contact may require a variety of initiatives such as needle exchange, methadone, social provisions as well as medical care which may have to be delivered in ways that fit in with the injection drug users life style.

Problems of health care for drug users

The difficulties of engaging drug users however should not be underestimated. IDU has a number of characteristics which provide problems for any health service. For instance it is an illegal, often violent and expensive activity. It may be funded by theft, cheque book or credit card fraud, drug dealing on a minor or major basis or via prostitution. Depending upon the geographical location in general around 2/3 of drug users are male and 1/3 are female. Up to 70% of drug users in Edinburgh may have a criminal record and or be "working the system" i.e. committing DSS fraud. They have a manipulative tendency in their dealings with individuals and society.

The particular problems that make engaging drug users difficult for a health service are a crisis type of lifestyle with little planning other than for the next supply of drugs. Since on average heroin drug users require 3-4 doses per day their horizons may be limited to at the most 24 hours. They are not health conscious as demonstrated by their overwhelming addiction and injection drug use which is demonstrably a dangerous life choice. Lastly they have a tendency for a high MA rate in terms of the health care system probably because the priorities of addiction come before all else.

The consequences of IDU related HIV are also important to bear in mind because they interact with the health care system. As illness occurs the patients suffer a falling income because they are less physically fit, mentally slower and consequently are more likely to be apprehended in criminal activities. This produces what could be described as "criminal unemployment" which results in difficulties of funding a habit. Consequently as HIV progresses there may be a need to become "legal" as regards the DSS in order to obtain some revenue. There may also be considerable pressure to prescribe drugs from the NHS. There is certainly a continual pressure to find other sources of income and this may result in further difficulties for the health service such as drug dealing in hospitals, requests for help in making fraudulent DSS claims or even just for inappropriate hospitalisation because this saves money which would be spent on food, heating etc.
IDU related HIV is accompanied by physical weakness and mental slowing which may result in the patient being victimised and or exploited possibly because of their previous position in the drug culture. This can result in an inability to cope out of hospital but difficulty in accepting a hospital regime. This unwillingness or inability to adapt to changed circumstances results in revolving door type admissions to hospital with considerable frustration for patient, relatives and staff.

In managing HIV patients it may also be necessary to manage the problems of a patients' visitors. There may be unexplained absences from wards by patients, frequent self discharges and perhaps most importantly for the ward routine the problem of day/night reversal as a result of drug use. In addition the ward and areas dealing with drug users are faced with the problems of theft, frequent noise disturbance, victimisation of patients, manipulation of staff or other patients and attention seeking behaviour, aggression or assaults both verbal and or physical on staff and other patients. Other problems noted are those of self medication and drug dealing in the wards by both patients and visitors. Staff are naturally alarmed by the problems of patients carrying offensive weapons such as knives and even on rare occasions guns. This is however usually because of fear of peers rather than staff. It is often not appreciated that the patients are more frightened of each other rather than the staff. Many sworn enemies such as rival drug dealers may be bought together by HIV and the need to visit the hospital. The staff of course may be entirely unaware of these ongoing difficulties.

*Edinburgh model of care for HIV infected drug users*

The initiation and maintenance of contact in Edinburgh has relied on the use of combined medical and drug clinics which are able to deliver both drug services, physical health care and psycho-social services at the same site. The drug services developed at the RIDU in Edinburgh are generally based on the principles of harm reduction. This has meant providing injecting equipment (needles etc.) when requested but mostly it has meant providing an oral non injectable substitute i.e. methadone.

The health care delivered has consisted of routine medical care for HIV and drug problems, prison medical care, dental service, colposcopy, contraception and other services. The psycho-social services consist of counselling and support for infected and affected individuals, welfare rights, social services, child care etc. and other services.
A review of the systems developed in Edinburgh and at the Montefiore Medical Centre in the Bronx of substitute drug prescribing and HIV services delivered from the same site by the same doctors (Chapter 6) suggested that this was the most effective model of care for injecting drug users. It would appear that a particular skill mix is required of psycho-social and physical care which is accentuated for HIV infected drug users. The San Francisco and Amsterdam experiences of providing services at two distinct physical sites seemed to provide either a poor medical and or a poor HIV service for drug users - possibly by not achieving the best skill mix. Whilst combined clinics appeared to be the most efficient service they had not been systematically evaluated. This current analysis of the Edinburgh service supports the contention that combined medical and drug services are able to deliver care to drug users.

In Edinburgh, the initial lack of specialised medical services for drug users required the development of a service which provides not only inpatient and outpatient continuity of care but also delivered both drug and HIV services at the same site. In June of 1986 evidence suggesting that accelerated loss of CD4 cells was associated with continued IDU was presented at the 2nd International Conference on AIDS in Paris9. It had also become obvious that it was necessary to provide a drug service before being able to provide health care for HIV. The provision of oral methadone from the HIV clinics after June 1986 improved not only the numbers attending but also the MA rate achieving the aims of initiating and maintaining contact with IDU related HIV.

As a consequence of the disruption to the general ID clinics and the continuing high MA rates for the HIV patients it became necessary to offer IDU related HIV medical care on separate days from the ID clinics. The use of a specific IDU related HIV clinic which lasted for the whole day, was not only associated with improved total attendance but also a reduction in the MA rate. From an analysis of the MA rates it appears that the organisational changes made in the HIV clinic are as important if not more important than the introduction of methadone in explaining the heterogeneity of the MA rate. Thus the MA rate amongst injection drug users has been steadily reduced by a number of measures including the use of a dedicated all day clinic, on site prescribing of substitute methadone for opiate addiction and a multi-disciplinary approach to care.
As a consequence of the almost total lack of drug services in Edinburgh there was a rise in the number of uninfected injection drug users seeking treatment at the City Hospital. In June 1987 the response of the management to this problem was to restrict the drug prescribing service to only known HIV seropositives rather than to increase the available resources. This not surprisingly created a two tier system such that it was easier to obtain prescribed oral drugs if infected and resulted in critical comments from the ACMD\textsuperscript{1}.

"In practice this has led to the absurd position whereby treatment involving substitute prescribing is mostly available only to those already infected with HIV. Its use to prevent a seronegative drug misuser from engaging in HIV risk behaviour and acquiring the virus is virtually non-existent".

The illogical and damaging situation for the spread of HIV via IDU was rectified eventually with the creation of the Community Drug Problem Service in April of 1988\textsuperscript{10}.

Evaluation of the Aim of Initiating and Maintaining Contact

Despite the difficulties, the measures adopted have enabled us to initiate and maintain contact with large numbers of HIV positive patients, 77% IDU related and at least half injecting at their first visit. This is surprising in view of what is known of drug users and the health care system. The reasons for the loss to follow up are not totally known but seem to include unforeseen prison sentences, dislike of the methadone being prescribed, a dislike of being associated with an HIV clinic for fear of losing confidentiality, and a dislike of currently chaotic drug users.

The subsequent rise in the number of missed appointments between 1989 and 1990 was of some concern but on further analysis was only significant in those patients not utilising the all day clinic. This rise may have occurred because more clinics are now available and are being utilised by the most chaotic patients or because of increasing ill health of the cohort associated with more difficulties in attending hospital.

Despite the fact that non attendance occurred in 24% of booked appointments in 1990, laboratory monitoring of HIV was still achieved in 95% of the patients who missed appointments. In fact an analysis of the MA pattern for 1989 and 1990 revealed that a relatively small number of the total patients (15-19%) accounted for between 50-60% of the missed appointments. In addition, around 60% of these patients missed appointments in both years but only 2% of such patients consistently
miss 3 or more appointments per year. This supports the idea that a particular sub
group of patients account for most of the problem of missed appointments. In both
years an average of 41% of the patients attending missed only 1-2 appointments per
year which seems acceptable and 45% of the patients were consistent in their
behaviour from year to year. Thus a relatively inefficient system from the health
service point of view does achieve laboratory monitoring of HIV in even the most
difficult drug users.

The annual lost to follow up rate for individuals of around 8-11% seems very
acceptable and has remained constant since the clinic opened. The long term follow
up on these patients and the loss to follow up rate is now not significantly different
from the non HIV clinics. The phenomena of re-attendance even after a number of
years explains the lower than expected cumulative lost to follow up rate of 14%. Not
surprisingly it is lower than the 81% lost to follow up rate in HIV negative patients
since the clinic system is very much geared towards HIV infected individuals. The
lost to follow up rate amongst HIV negative patients also of course reflects the
establishment of an alternative substitute prescribing clinic (the CDPS) in Edinburgh.
It does however suggest that clinics offering medical care for drug users can achieve
reasonable follow up provided they are adapted to the patient's needs. The flagging
of defaulters with the Registrar General has allowed us to be very confident that the
lost to follow up rate is accurate and is not obscured by covert deaths.

The effect of HIV Clinics on other medical services

The establishment of an IDU related HIV medical service however appeared to have
an effect on existing medical clinics. The success of methadone prescribing resulted
in an influx of chaotic drug users into the general ID clinics. Until the establishment
of a specific IDU related HIV clinic day there was an increase in the MA rate of
general ID patients presumably as a consequence of the disruption at these clinics
since no change was noted in the MA rate for the UTI clinic which is held on a
separate day. The establishment of a specific all day IDU related HIV clinic
appeared to reverse this trend by removing chaotic drug users from the ID clinics.

Over a 4 year period a gradual decline in the number of new patients referred by
general practitioners for both the ID and UTI clinics was noted suggesting a possible
reluctance by doctors to refer to, or patients to attend, the Unit. This was particularly
notable from the second half of 1988 and might be as a consequence of the City
Hospital, and the RIDU in particular, being identified with AIDS. It was also more
notable for the UTI patients and one might expect such patients to be accommodated more easily in other medical/surgical units. The new patient referral rate for general ID clinics seemed to have been affected less and this was perhaps because these services were not duplicated elsewhere in the region. Thus the establishment of an IDU related HIV service appears to have an effect on other patient services and in order to avoid either separate facilities or separation of clinics, much more in the way of education for the general public is required.

Risk Behaviour

An assessment of risk activity based on self reported behaviour suggested that IDU declined between 1986-90 and that this decline was more common in HIV positive than HIV negative drug users. The decline in IDU can only be attributed in part to the medical clinics since there has also been general campaign in Edinburgh to reduce IDU. During the same time period the use of oral opiates increased suggesting a change of route of administration rather than abstinence.

Conclusion

Whilst there are considerable problems for a health care service in engaging drug users it is possible. In three areas an IDU related HIV medical service delivering substitute drugs and HIV medical services at the same site has been demonstrated to be effective: the ability to initiate contact, the ability to maintain that contact and the ability to help modify high risk IDU. Other proposed systems which separate addiction from HIV medical care should also evaluate their results in order that medical care for HIV infected drug users can be based on facts rather than dogmas.

A medical care system which is experienced in the care of both HIV and injection drug use is able to deliver health care to injection drug users. The system used at the Montefiore Medical Centre in the Bronx and in Edinburgh of drug prescribing and HIV services delivered from the same site by the same doctors seems to provide the best model of care for injecting drug users. The San Francisco and Amsterdam experience of providing these services at two distinct physical sites reveals this to be an inefficient system providing either a poor medical and or a poor HIV service for drug users. Thus HIV and drug dependency specialists need to exchange and acquire each others skills as well as utilising the primary care services.

It is possible to adapt an existing health care system to be more "user friendly" for the lifestyle of injection drug users fulfilling the important aims of initiating and
maintaining contact with health care services although there may be effects on the established service in terms of MA rate for existing patients and the referral of new patients.

Dedicated clinics offering both drug management and medical care are able to initiate and maintain contact with drug users as well as reduce their high risk IDU behaviour. Although there was a large number of missed appointments, the majority of these were in fact related to less than 10% of the patient population. Whilst such a system is inefficient from the health services point of view, it may be necessary in order to maintain contact with the most difficult drug users.
References for Chapter 7


CHAPTER 8

Harm Reduction for IDU Related HIV

Introduction

Drug use related HIV is a continuing problem not only for important areas of the developed world such as the USA and Europe but also for the developing world such as South East Asia and South America. It is a crucial issue because Drug Use related HIV in some areas of the world is the fastest growing risk group and in addition it is associated with a substantial amount of vertical and heterosexual spread of HIV. A number of studies in the USA and the United Kingdom have shown that between 60-100% of heterosexually acquired HIV is related to IDU and at least 40% of injection drug users are in relationships with non users\(^1-4\). Approximately one third of injection drug users are female and vertical spread to new-born children occurs\(^4-6\). Consequently the reduction and control of Drug Use related HIV can have a substantial impact not only on transmission amongst drug users but also on the heterosexual and vertical spread of HIV.

The major public policy issues concerning the prevention of Drug Use related HIV are,

- persuading society and governments that Drug Use is a key element in the spread of HIV,
- that AIDS is a greater threat than Drug Use itself,
- that harm reduction as a strategy in preventing the acquisition of HIV is compatible with the aim of primary Drug Use prevention and
- that there is no one single measure, such as methadone, needles or bleach, that makes up a harm reduction strategy i.e. harm reduction must be multi faceted.

The importance of drug use in the spread of HIV was underlined by the Presidential Commission on HIV in the USA which recognised that "the future course of the HIV epidemic depends greatly on the effectiveness of our nations ability to address IV drug use"\(^7\). In the UK the Advisory Council on the Misuse of Drugs (ACDM) in its report on AIDS and Drug Misuse warned that "The spread of HIV is a greater danger to individual and public health than drug misuse. Accordingly, we believe
that services which aim to minimise HIV risk behaviour by all available means should take precedence in development plans.\textsuperscript{8} Thus it is important to develop drug therapies and care systems that address the problems of IDU related HIV and to reconsider the approach to drug use in the light of HIV. This new position was recently summarised by John Strang and Gerry Stimson "We are at a point of change - a point of crisis between old ways of viewing drug problems and new ones forced on us by HIV\textsuperscript{9}.

Before the advent of HIV infection, drug use itself had a relatively low mortality with alternating periods of abstinence and drug use together with natural recovery \textsuperscript{10-13}. In New York however there was a rapid increase in both AIDS and non AIDS narcotic related deaths such that by 1986, for every AIDS related death in a drug user, there was one other as a consequence of such conditions as tuberculosis, endocarditis and bacterial pneumonia\textsuperscript{14}. Similar data have been reported from Europe\textsuperscript{15,16}. This increase in mortality for drug users is the driving force behind harm reduction and the reason society can no longer rely on spontaneous recovery for drug users.

Harm reduction has recently been described thus "the harm minimisation approach echoes the safer-sex campaigns...people will not want to abstain from sexual activity, therefore they must be encouraged to engage in safer sex. The idea has now been extended to drug injectors - if they won't stop injecting, they should and could inject drugs in a safer way\textsuperscript{17}. There are legitimate but unproved concerns however that harm reduction for IDU related HIV will help to initiate new drug users. Similar concerns are voiced over increasing the availability of injecting drug equipment or teaching safer injecting techniques.

Perhaps one reason for this concern is the difficulty of demonstrating that harm reduction is an effective method of preventing the spread of HIV amongst drug users. However the intense debate over injection equipment availability, especially in the USA, has interesting parallels with the debate that surrounded Methadone Maintenance Treatment Programmes (MMTP) in the management of drug dependency. In 1957 the Council on Mental Health of the American Medical Association concluded that "The advisability of establishing clinics... to dispense opiates to addicts cannot be settled on the basis of objective facts",\textsuperscript{18}. This debate was in fact primarily centred on the health of society rather than around an

211
individuals physical health and is still continuing\textsuperscript{19}. Can society wait however, for the arrival of definitive proof where HIV is concerned?

Previous reviews of harm reduction have tended to concentrate on only one modality such as methadone or injection equipment availability\textsuperscript{20,21}. By comparison this review seeks not to examine the evidence for and against harm reduction with regard to the treatment of drug dependency, but whether harm reduction can have a substantial impact on the spread of HIV. It is necessarily biased because the author is an Infectious Disease physician concerned with the problem of HIV and AIDS rather than a specialist in drug dependency.

**The History of Harm Reduction**

*Maintenance Methadone Treatment Programmes*

The use of methadone, a long acting opiate, allowed the development of maintenance programmes for drug users based on daily administration because they were no longer reliant on the self administration of short acting opiates. MMTP for drug use have been evaluated over a number of years but the these studies have concentrated upon retention rates, frequency and prevention of illicit drug use, reduction of criminal behaviour, the return to normal social activities and/or the possibility of curing drug use\textsuperscript{18,19,22-26}. MMTP were very much seen as harm reduction for society usually in terms of the reduction of crime or reintegration into society. Harm reduction for the individual was seen in terms of psycho social issues such as emotional stabilisation, work record and retention in the programme.

Whilst some improvement in physical health was assumed it is rarely mentioned in reports other than in respect of the safety of methadone maintenance\textsuperscript{18,19,22-26}. For instance the medical side effects of methadone such as constipation or the death rate were published but no other measures of improved physical health\textsuperscript{26}. In addition the initial criteria for selection into MMTP concentrated on defining addiction and specifically excluded patients with serious medical problems although eventually separate programmes for patients with tuberculosis were established\textsuperscript{18,19,22,26}. Lack of venous access or health problems related to injection drug use were not considered as entry criteria.
Amsterdam

The concept of harm reduction for a drug users physical health grew out of Amsterdam's Municipal Health Service Drug Department's (GG&GD) approach to the drug problem. Amsterdam's approach to IDU recognises the fact that it is a relapsing disease and that harm reduction means providing medical and social care whilst waiting for natural recovery from IDU in order to avoid some of the more harmful consequences of injecting drug use27,28.

Amsterdam's programme of drug treatment has been described in Chapter 6. Needle exchanges in Amsterdam began in 1984 after the Junky Union agitated for and then initiated the first needle exchange27,28. There were initially 10 centres for distributing needles and included the Methadone Bus, Methadone Out-Patient Clinics and the Junky Union although this latter site has now been discontinued. There was no enrolment or clinical examination but this was eventually tightened up in order to evaluate the return rate of equipment.

Amsterdam takes a pragmatic and non-moralistic attitude towards drugs and this has resulted in a pleuriform system which now offers harm reduction and/or drug free treatment. The prime goal was to make contact, to provide information on a personal level and to try and produce attitudinal and behavioural change by the use of condoms, drug free treatment programmes with short waiting lists, methadone and needle exchange systems.

The link between IDU related HIV and equipment availability

Whilst there is as yet no direct evidence on the effectiveness of increased injecting equipment availability in stemming the tide of IDU related HIV there is evidence of what happens when the supply is very limited. Edinburgh has perhaps one of the best documented examples of a temporal relationship between a policy of restricting injecting equipment during an epidemic of drug use and a subsequent epidemic of hepatitis B and HIV which started around 1980 and peaked in 1983-8429-31.

Further evidence for this IDU epidemic and the associated sharing of injecting equipment is provided by the concurrent epidemic of injection related medical conditions including Hepatitis B between 1980-8532. This epidemic of IDU related medical conditions was associated with a poor supply of injecting equipment and high levels of sharing (Chapter 4)33-35.
Glasgow had a smaller IDU related HIV problem despite a larger number of drug users than Edinburgh and comparisons of self reported habits between Edinburgh and Glasgow or Edinburgh and London reveal considerably more sharing of needles and syringes in Edinburgh\textsuperscript{5,30,36,37}. The absence of an epidemic cannot necessarily be used as proof of effectiveness but it is interesting to note that many conurbations in England and Wales with larger drug populations than Edinburgh did not have an HIV epidemic. In the main these areas did not restrict equipment availability and some areas such as Liverpool had a well developed strategy for dealing with drug users which was able to adapt rapidly to the problem of HIV\textsuperscript{38}. In 1986 as a consequence of the AIDS epidemic the restriction on the sale of needles and syringes imposed by the pharmacists' professional association was withdrawn\textsuperscript{33,34}. The ACMD in its report on AIDS and Drug Misuse in 1988 noted that "The opportunity to take preventative action must be seized now if the tragedy of Edinburgh is not to be repeated throughout the UK"\textsuperscript{48}.

Similar restrictions on equipment availability existed in other countries such as Australia and New Zealand until 1987 and 1988\textsuperscript{20,39}. They remain in force in many parts of the USA where the connection with blood borne virus epidemics amongst drug users has not been so well documented\textsuperscript{20}.

A significant link between needle sharing and the risk of acquisition of HIV has been established\textsuperscript{6,31,36,40-46}. More recently HIV has been cultured from needles and syringes collected from a shooting gallery in Miami, Florida confirming the infection risk\textsuperscript{47}. Less well recognised is the importance of the type of drug used. Links between HIV infection and the use of intravenous cocaine or amphetamines has been reported \textsuperscript{48-56}. Drug users often inject cocaine intravenously mixed with heroin and do so far more frequently than when they inject heroin alone\textsuperscript{4}. Additionally the sharing of equipment is more often associated with cocaine use and the difficulty in obtaining such equipment\textsuperscript{57-60}.

**Is Harm Reduction effective?**

Whilst there is strong and compelling evidence linking the spread of HIV amongst drug users with the use of contaminated equipment, is there any evidence suggesting that harm reduction measures are effective in preventing the spread of IDU related HIV or even in changing high risk drug use behaviour?
Methadone

There are now data which support the effectiveness of oral opiate substitute programmes in reducing high risk injecting behaviour as well as reducing the risk of acquisition of HIV or AIDS.

Modification of Injecting Behaviour

In a 3 year study of MMTP in New York, Philadelphia and Baltimore 715 clients who remained in MMTP for more than 1 year gave up injection drug use. By comparison, 82% of those who left the programme continued to inject drugs. Additionally, only 10% of clients in MMTP shared equipment during the study period compared to 27% amongst dropouts. This latter figure increased to 48% once individuals had been out of treatment for longer than 1 year. In the Treatment Outcome Prospective Study organised by the National Institute on Drug Abuse (NIDA) 4184 clients from 12 MMTP, 2891 clients from 14 residential programmes and 2914 clients from 11 outpatient drug free programmes were interviewed at admission between 1979 and 1981. One year follow up interviews were reported on 1310 clients from 1979 and 2300 clients from 1980. Whilst none of the treatment approaches had much effect on cocaine use, continuous long term maintenance methadone was the most effective method of reducing the risk of heroin use, 74% effective compared to 68% for residential treatment of greater than 3 months but only 56% for outpatient drug free treatment. These differences were statistically significant at p<0.001 level. The author's conclusion was that the decline in regular drug use after treatment, particularly for longer treatment stays, indicates that drug abuse treatment can be effective in reducing major risk behaviour for HIV.

Another New York study looked at clients on the waiting list for MMTP. These clients were randomly divided into 2 groups to receive counselling, methadone and biweekly urine toxicology or, counselling and biweekly urine toxicology only until they were admitted to the regular MMTP. Initial needle use was identical for each group at 95 injections per month, but at entry into MMTP only 33% of those on methadone were injecting compared to 82% of those in the counselling group. In San Francisco self reported needle sharing amongst 7660 drug users admitted to 28 day out patient methadone detoxification clinics decreased from 50% in 1986 to 28% in 1988 (p<0.001). A study of 42 HIV positive individuals in a San Francisco MMTP assessed via self reporting as well as urine tests and clinical examination found that heroin use decreased significantly during the first 3 months and that the
early gains were generally maintained 12 months after entry \((p<0.0001)\). A Seattle study noted that individuals in a MMTP for longer than six months shared less than those in treatment for less than six months and a study of New York and New Jersey drug users in MMTP noted that older users with more years in treatment were more likely to have changed their needle cleaning habits. In West Germany the majority of 30 HIV positive drug users in a MMTP stopped IDU whilst in Vienna of 180 drug users in MMTP more than one third of poly-drug users and more than one quarter of HIV positive drug users were consuming only methadone after an average of 11.2 months of treatment.

**Effect on HIV acquisition**

A survey of 28 MMTP clinics in New York city revealed that HIV seropositivity in established clients was 27.2% compared to 45.9% in new clients. In 68 long term MMTP patients in New York with a mean length of treatment of 16.9 years but 10.3 years of IDU before enrolment none had HIV antibodies. In San Francisco there was a significant difference between HIV serostatus for individuals in MMTP for more or less than 60 months (8% versus 14%, \(p<0.001\)) although this difference was only for White and Hispanic drug users. There was no difference however for black drug users and this is a matter of concern. It further underlines the fact that behavioural characteristics of drug users vary with race and geographical location and must be taken into account in harm reduction.

In Swedish MMTP, the HIV seroprevalance was only 3% for those admitted in 1983, 16% for those admitted in 1984-1986, and 57% for those admitted in 1988, suggesting a highly protective effect for the acquisition of HIV related to MMTP. In Geneva the HIV seroprevalence for those admitted to MMTP before 1980 was only 12% compared to 47% between 1980 and 1986 \((p=0.02)\). In addition the HIV seroprevalence of drug users admitted to MMTP between 1987-89 had fallen to 22% and this was coincident with a dramatic fall in needle sharing behaviour which fell from 90% to 5% for HIV seropositives and from 80% to 29% for seronegative individuals. During this time period only one out of 155 seronegative patients seroconverted to HIV suggesting that MMTP is able to modify high risk IDU related behaviour. Similar results were obtained from another methadone programme which was able to demonstrate prospectively a reduction in high risk behaviour and a correspondingly low HIV seroconversion rate for HIV. HIV serostatus was recently evaluated for low threshold MMTP in Amsterdam, which enables contact to
be made but has little in the way of counselling, and showed that long term clients did not have a lower seroprevalence for HIV\textsuperscript{75}.

**Effect on Progression to AIDS and Immune activation**

There is a suggestion that continued IDU may accelerate progression of HIV to AIDS; one study reported a relationship between the frequency of IDU and the loss of T4 lymphocytes whilst another study noted a similar increased rate of decline of T4 lymphocytes amongst a group of injectors compared to a group of non injectors\textsuperscript{76,77}. There was also a lower probability of disease progression amongst methadone users or ex users compared to those that continued IDU reported from Switzerland. In that study progression to AIDS after 3 years was 24\% in the methadone group, 19\% in the ex users but 41\% in the persistent IDU group (p<0.05). Multivariate analysis showed a relative risk of 1.76 for persistent users\textsuperscript{78}. However other groups have not found an increased risk for continued IDU\textsuperscript{79-81}. The incidence of AIDS in the Bronx was reported to be lower (11.4 v 33 per hundred patient years) for entrance to the Montefiore MMTP before and after 1983\textsuperscript{82}. Similarly the proportion of drug users attending MMTP in Italy was inversely related to the cumulative incidence of AIDS. The highest AIDS incidence rates were seen in the regions with the lowest proportions of injection drug users attending MMTP. Nearly 40\% of the variability of AIDS incidence was explainable by attendance in MMTP\textsuperscript{83}. The reasons why continued drug use might predispose to accelerated immune decline are unknown but one suggestion is that the drift in molecular composition demonstrated in different HIV isolates could result in an individual acquiring more infection with differing strains of HIV which might hasten disease progression\textsuperscript{84}.

Another possible explanation would be that IDU itself might significantly affect the immune system, for instance frequent IDU is associated with depressed lymphocyte function irrespective of HIV serostatus\textsuperscript{142,143}. IDU has been associated with higher levels of β-2-microglobulin and activated T cells and IDU related HIV is associated with more immune stimulation\textsuperscript{85-88}. HIV serostatus may not be known for most patients and therefore measures, such as the cessation of injection drug use if necessary via MMTP, that are thought to reduce progression to AIDS should be applied to all drug users.

By August, 1987, 241 patients had been examined at the HIV clinics at the City Hospital, 196 of whom were seropositive. Eighty-eight per cent or 172 of these were
injection drug users and 55 per cent or 95 were current users at the initial evaluation. A total of 107 HIV antibody seropositive patients with a history of intravenous drug misuse had attended two or more follow-up appointments by the time of the evaluation. The 107 injection drug users attending the RIDU were classified as follows:

**Group 1:** Those thought to be persistently using illicit injection drugs and who were not prescribed methadone.

**Group 2:** Those considered to have ceased illicit drug use and to have been prescribed methadone.

**Group 3:** Those considered to be utilising both oral methadone and illicit injection drugs.

**Group 4:** Those who were observed not to be using illicit drugs by injection and not in receipt of methadone either from ourselves or from general practitioners.

Significantly, more patients on methadone were noted to register a net gain in weight during the follow-up period. Overall, all methadone users were found to have a mean net weight increase of 2.5 kg. versus 0.2 kg. \((p = 0.02)\) for those patients who received no methadone. There was no significant difference in the follow-up period for these patients (8.1 months versus 7.6 months). When the patients were divided into groups according to their drug use, a significant increase in weight of 3.7 kg. was noted for Group 2 or methadone only users on two sample analysis (Table 8.1). Over the short follow up period there was no significant difference in the initial and final T4 counts, IgG, IgA, IgM levels between the groups.
Table 8.1: IDU related HIV and the use of methadone

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Follow up in months (range)</th>
<th>Net weight change in Kg (range)</th>
<th>P (two sample analysis compared to group 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (IDU)</td>
<td>19</td>
<td>6.5 (1 - 14)</td>
<td>- 0.4 (- 9.3 to 8.0)</td>
<td>= 0.005</td>
</tr>
<tr>
<td>2 (Methadone)</td>
<td>38</td>
<td>8.3 (2 - 19)</td>
<td>+ 3.7 (- 10.6 to 24.8)</td>
<td>NA</td>
</tr>
<tr>
<td>3 (Methadone + IDU)</td>
<td>12</td>
<td>8.1 (2 - 20)</td>
<td>- 1.2 (- 5.8 to 3.4)</td>
<td>= 0.002</td>
</tr>
<tr>
<td>4 (Nil)</td>
<td>38</td>
<td>8.1 (2 - 19)</td>
<td>+ 0.6 (- 10.5 to 21.5)</td>
<td>= 0.01</td>
</tr>
</tbody>
</table>

**Footnote:** IDU = continued injection drug use, Methadone = use of oral drugs including Methadone, Methadone + IDU = use of oral drugs including Methadone as well as continued injection drug use, Nil = use of oral drugs from general practitioners but not Methadone or abstinence from drugs, NA = Not applicable

The physical improvement in those patients giving up injection drug use was impressive but the improvement was difficult to measure and weight gain provided one objective measure of improvement in general health. The weight gain associated with methadone use was almost certainly associated with the cessation of IDU and has been historically reported to us in those patients giving up IDU by other means. A general improvement in health is important in those infected with HIV and the regular attendance of those on oral methadone makes them available for other health education messages.

Although methadone mixture DTF is not the only oral substitute therapy available it does have a number of advantages. In modest doses of 40-60 ml, it prevents withdrawal symptoms but does not provide significant euphoria. It is thus suitable for those not willing to suffer withdrawal symptoms. Whilst the drug may enter the 'Black Market', its dilution and constituents discourage its use by injection. This is in contrast to opiates in tablet form for which there is a ready 'Black Market' because of the ease with which tablets may be dissolved and then injected.

**Injecting equipment**

The most controversial harm reduction measure especially in the USA and certain parts of Europe is the availability of clean injecting equipment.
Modification of Injecting Behaviour

It appears that drug users change their high risk injecting behaviour if given both information and equipment. In Amsterdam this behaviour change was more effective and more likely to occur in the context of individual counselling than in the context of mass campaigns. Specifically over time there was a reduction in risk behaviour amongst those enrolled in a cohort study but no reduction over the same time period in the risk behaviour of the new entrants to the cohort. Others have shown that information and counselling alone can produce risk reduction but equipment alone seems not to be enough since in New Orleans and Portland, Oregon, areas where needles are not controlled by prescriptions, needle sharing still occurred. Similarly the widespread availability in Italy of sterile injecting equipment and water which was introduced as a preventative strategy to combat the heroin and hepatitis B epidemic in the mid 1970's failed to prevent not only hepatitis B but also the spread of HIV.

Behaviour change has however been shown to occur more often amongst those attending needle exchanges than amongst non-attendees. In Amsterdam only 10% of exchange attendees were sharing equipment in the previous 6 months compared to 24% of non-attendees. Similarly, 74% of attendees were using equipment only once, compared to 27% of non-attendees. Comparable results have been reported from Glasgow, Scotland where less risk reduction occurred amongst individuals obtaining supplies from pharmacies compared to needle exchanges. Even stimulant users are able to change behaviour if they can be retained in treatment programmes.

Partly as a consequence of the Amsterdam experience, UK practitioners began to exchange injecting equipment and, under pressure from the McClelland report which called for greater availability of injecting equipment, the UK Government set up 15 experimental needle exchanges in early 1987 which have now been evaluated.

The final report on 2449 clients concluded that these schemes reached a considerable number of injection drug users, the majority living within two miles of the schemes. Forty per cent had never been in a treatment programme and nearly 75% were not in a current treatment programme. The attendees were however older opiate users with a mean age of 27.8 years, mostly male (78%) and had an initial lower level of risk behaviour compared to injectors who did not attend. For instance only 36% had shared equipment within the previous four weeks and only 19% had shared with
more than two individuals in the last four weeks. By comparison 62% of a group of non attendees were injecting in the previous four weeks and 36% with more than two individuals. Thus non attendees at exchange schemes had riskier injecting behaviour despite the fact that this sample was interviewed after the Government publicity campaign. The commonest reason for sharing was difficulty in obtaining equipment and this did not differ between attendees or non attendees. The non attendees however paid more attention to the cleaning of equipment than the attendees.

The major problems for needle exchanges were the high turnover of clients which varied from a low of 25% to a high of 85% returning for a second visit. The average retention rate was 61% for the second visit falling to 17% for the tenth visit and only 1% returning for more than 40 visits. The exchange rate also varied from 23% to 100% with a mean of 62%. The number of syringes/needles issued per visit varied from three (the legal maximum per visit in Scotland) to 30, with a mean of nine per visit.

Amongst clients who continued to attend there was evidence of self reported reduction in needle related risk behaviour. For instance sharing in the previous four weeks declined from 34% to 27% and the percent sharing with two or more individuals declined from 17% to 11%. Over 70% of attendees and non attendees reported that as a consequence of AIDS they had made some change in their drug use usually a reduction in sharing or an increase in using clean equipment.

Interestingly clients in Scotland, possibly because the schemes ran under stricter legal controls with fewer needles and syringes given out per visit and shorter opening hours, showed greater sharing compared to their English counterparts. For instance 76% of Scottish injectors had shared equipment in the previous four weeks compared to only 52% in English injectors. In Scotland injectors found equipment harder to obtain, were more likely to find the exchanges closed or to share in custody.

An evaluation of a central London exchange scheme was able to demonstrate after 3 months a fall in median injecting from 56 to 48.5 per month (p<0.001), sharing from 15 to 11% of the time, equipment borrowing on two or more occasions from 8 to 6% and equipment lending on two or more occasions from 10 to 6%101. This improvement in high risk behaviour was associated with a self reported decrease in skin abscesses in the previous 3 months from 14% to 9%101.
The first North American needle exchange scheme in Tacoma, Washington State was also able to demonstrate change towards safer injecting practices. Lending equipment either to a close or casual friend significantly declined from 64 to 44 times/month and 48 to 32 times/month respectively (p<0.05)102. There are reports that stimulant users, who are known to inject more often and to be more at risk for HIV, are additionally more resistant to behaviour change and this is one important area that requires additional information96.

Effect on Acquisition of HIV

Interestingly diabetic drug users in Baltimore were noted to have a lower than expected incidence of HIV. The explanation offered for this lowered incidence of HIV amongst diabetics was the fact that these individuals have had preferential access to clean injecting equipment103.

Needle exchanges are beginning to provide data that they can prevent acquisition of HIV. This is mostly in the form of stable HIV prevalence rates over time and unfortunately it is difficult to use the absence of an event as positive data. For instance in London the prevalence of HIV in attendees at a needle exchange was 6% at the beginning and 7% at the end of the year of follow up101. In Australia the seroprevalence as judged by anonymous testing of returned equipment remained stable at 1.5% in 1987 compared to 1% in 1986104,105. The seroprevalence rates in Amsterdam have risen from 3.4% in 1983 to between 27-31% in 1987 even in the face of harm reduction27. But how fast would the seroprevalence of HIV have risen without these measures and how much of this is new infection as opposed to the movement of infected drug users into Amsterdam? Careful longitudinal studies are required to answer these questions.

Outreach education, intervention programmes and cleaning of equipment

One of the major criticisms of harm reduction measures based on treatment facilities is the fact that many drug users are not in contact with treatment facilities. Amsterdam's Municipal Health Service Drug Department (GG&GD) is unusual in being in contact with at least 70% of its estimated 6-8000 drug users27,28. Unlike the gay community collective organisations with an educational role have not flourished with the exception of the Junky Union in the Netherlands27,28.
Outreach intervention programmes have been developed most extensively in the United States probably as a consequence of the early involvement of drug users in the AIDS epidemic, the paucity of treatment facilities and the political climate in relation to either increased treatment facilities or other harm reduction measures. In the early 1980's New Jersey began to hire ex-addicts to teach safer injecting techniques which had the unexpected result of increasing the demand for drug treatment facilities. New Jersey had instituted charges for drug treatment in the early 1980's but then in response to the increased demand began to issue coupons for free treatment via outreach workers. Of 1884 drug users interviewed by the Newark and Jersey City Health Behaviour Project 49% subsequently entered methadone treatment programmes. Outreach intervention programmes were also developed in San Francisco and New York City to provide initially basic information concerning safer injecting practices and then the distribution of condoms, cleaning solutions and even injecting equipment despite the fact that this latter event remains illegal. In San Francisco the early message of "Don't Share Needles!" utilised by the Haight-Ashbury Free Medical Clinic in 1983 was extended by the San Francisco Aids Foundation in 1985 into a larger campaign to raise the general consciousness of drug users towards AIDS. This was then augmented by the use of Community Health Outreach Workers to develop trusting relationships with drug users and deliver both the message and simple practical help in the form of bleach.

The campaigns to teach cleaning of injection equipment have concentrated on commonly available disinfectants such as bleach, alcohol, and detergent. Whilst whole blood is protective against disinfection of HIV, dilute household bleach, 70% isopropyl alcohol and dilute detergent remain effective even in the presence of whole blood and such compounds should be available to the majority of injection drug users. Street based education, utilising outreach workers and free one ounce bottles of bleach have successfully improved 'safe' needle hygiene. In San Francisco the combination of Community Health Outreach Workers and bleach raised the use of bleach for equipment cleaning from 3% to 76%. Compliance with the bleach disinfection protocol was associated with access to a Community Health Outreach Worker.

A NIDA funded study of drug users not enrolled in treatment was able to demonstrate that outreach and intervention could influence entry into drug treatment.
and reduce high risk drug injecting behaviour\textsuperscript{107}. The study enrolled 30,000 drug users and their sexual partners and the preliminary report was on 1584 injection drug users, the majority black and male in 5 US cities (Chicago, Houston, Miami, Philadelphia and San Francisco). The recruitment was via community based outreach workers and those eligible were those injecting drugs for at least the previous 6 months and not enrolled in a treatment programme during the previous 1 month. The interventions used included some or all of the following; counselling both individual and peer counselling, efforts to build peer support for behaviour change, demonstrations and practice of safer injecting techniques. The safer injecting practices that were encouraged included; not sharing equipment, use of sterile equipment and or the cleaning of equipment with disinfectants. At follow up 6 months later 14-35\% of the drug users had entered a drug treatment programme and between 49-75\% reported either stopping or reducing their frequency of drug injecting. Amongst those who continued to inject 20-39\% reported an increase in the use of cleaning of equipment. There are also data to suggest that intervention programmes improve the behaviour of users not directly involved in the programmes\textsuperscript{107}.

However much more in the way of outreach and contact is required because in a study of over 15000 US drug users whilst 85\% of users were aware of the benefits of clean equipment only 17\% always cleaned their equipment and only a further 20\% always used new equipment leaving 63\% using high risk injecting techniques\textsuperscript{113}.

Effect on Acquisition of HIV

There is as yet little scientific data to prove that outreach is effective in preventing IDU related HIV although it is popular with clients. In San Francisco where individuals self-reported an improvement in risk behaviour this improvement was noted to coincide with an aggressive prevention campaign directed at drug users which began in mid-1986. Subsequently a flattening of the Hepatitis B and HIV seroprevalence curves has occurred since 1986 amongst drug users\textsuperscript{114,115}. Similar flattening of HIV incidence in drug users has been reported from Baltimore and Amsterdam\textsuperscript{116,117}. It may be that campaigns detailing cleaning techniques could be used effectively in areas such as prisons where needle exchange is unlikely to occur because of security reasons. Perhaps the innovative use of graffiti demonstrated to be effective at reaching drug users in Denver should be considered by others\textsuperscript{118}.  

224
Skin cleaning whilst not protective for HIV has been shown to reduce the risks of endocarditis and skin abscesses. In 110 active drug users in San Francisco reporting on skin cleaning and past infections only 4.2% of those who skin cleaned some of the time reported endocarditis compared to 14.5% in those who did not skin clean. Forty eight percent of those who never skin cleaned had suffered skin abscesses compared to 24% for those who sometimes cleaned. In view of the seriousness of these infections harm reduction measures for bacterial infections are needed and even more so for HIV seropositive users in view of their increased susceptibility to bacterial infections.

Safety of Harm Reduction

A major concern of harm reduction for HIV is the concern that it may encourage existing as well as primary or new drug use. There was no evidence for an increase in the total number of injection drug users as a consequence of one needle exchange programme. Needle exchanges also do not seem to encourage more drug use amongst existing users. In Amsterdam those attending exchanges were compared with those recruited from other areas such as hospitals or police stations. Only 29% of attendees compared to 50% of the non-attendees had increased their injecting during a 6 month period. Similarly with the UK exchanges increased injection behaviour in the attendees was not reported. The opening of a needle exchange scheme next door to a MMTP did not increase or decrease the number of illegal substances found in the urine of the MMTP patients.

Studies in Amsterdam have also shown that new users, that is people who had never injected, were not attracted into the system. The mean age of those attending rose with time from 26.4 years in 1981 to 30.1 years in 1987 and the proportion under 22 years fell from 14.4 to 4.8%. If new, younger users were being attracted to drug use one would expect the average age of the group to fall with time. The length of injection drug use was also greater at 9 years for exchangers compared to 7 years for non exchangers. Comparable data has been reported from the underground needle exchange scheme in San Francisco. The use of bleach for disinfection of injecting equipment has met some resistance especially in the UK on the grounds of safety despite the fact that even full strength bleach has been shown to be relatively non-toxic when injected in small amounts intravenously.

Reasonable return rates have been recorded even for underground and illegal exchanges although static sites were better than mobile sites (60% vs. 30%).
Return rates and public safety can be assured by public health initiatives such as disposal bins in public places and providing portable plastic disposal containers to exchangers. These techniques increased the return rate from 25% to 64% over 14 months in Sydney. More importantly there are studies on the infectivity of discarded needles which suggest that lymphocytes can only be infected with HIV from needles exposed to room temperature for 4 hours or less. Thus discarded equipment may not be as much a danger as previously imagined for the general public.

**Limitations of Harm Reduction**

Harm reduction for injection drug use is not the only solution for IDU related HIV but it is a useful intermediate goal although for many progression beyond safe injection drug use or oral opiate therapy is unlikely. It is important to remember that IDU itself is an immunostimulant which in the context of HIV is a disadvantage and that opiates not only increase susceptibility for bacterial infections but also promote the growth of HIV in cell cultures.

Blanket harm reduction measures applied in the absence of effective counselling and health education are not effective in achieving behaviour change. Needle sharing still occurred in New Orleans and Portland, Oregon despite the fact that needles were not controlled by prescriptions. Similarly the widespread availability in Italy of sterile injecting equipment and water which was introduced as a preventative strategy to combat the fast growing heroin and hepatitis B epidemic in the mid 1970's failed to prevent not only hepatitis B but also the spread of HIV. The data from Amsterdam would suggest that it is not methadone availability alone that is protective but the programme as a whole whilst the data from New York suggests that counselling alone is equally ineffective.

The development and marketing of harm reduction strategies has also to take into account the particular drug problem prevalent in a community as well as the demographic and legal characteristics of that community. For example MMTP are not successful in managing stimulant drug problems or it seems in preventing the acquisition of HIV in black drug users in San Francisco. In those circumstances other measures such as clean equipment or the distribution of stimulants in a non injectable form might be more effective but one also has to remember the variations in safe injecting practices in differing racial groups around the USA. In an assessment of 7835 out of treatment injection drug users in 15 US cities Blacks in
the Northeast and the West reported significantly (p<0.05) greater use of new needles than Whites or Chicanos whereas in the Southwest both Blacks and Chicanos were reporting the use of more new needles than Whites. In the same study the use of cleaning agents was significantly (p<0.05) more likely amongst Blacks in the Northeast or Blacks and Whites in the Southwest and West. In the UK the original needle exchanges failed to attract young or female injection drug users and were less effective at reducing high risk behaviour in Scotland presumably because of greater legal restrictions. Only time will tell whether behaviour change brought about by harm reduction campaigns can be maintained although individuals retained in the UK needle exchanges continued with their behaviour modification.

Despite major efforts with the homosexual community there is evidence that the incidence of rectal gonorrhoea is rising again suggesting that the safe sex message with regard to anal intercourse has not been maintained. Harm reduction for IDU cannot prevent sexual transmission of HIV and in many communities such as the UK, the rate of increase in heterosexual AIDS has equalled or overtaken the rate for IDU related AIDS. It appears that the general heterosexual population as judged by the sexual behaviour of college women in the USA between 1975 and 1989 has not as yet changed significantly. It is not surprising therefore that drug users also need to take on board the need to modify sexual behaviour.

Outreach programmes especially those based on ex or stable drug users also have their problems. Whilst outreach may be viewed as work and part of a drug users reintegration into society it suffers from often being part time, associated with low pay and a high turnover of staff. There is also the concern that the ex drug user will be drawn back into drug use as a consequence of the work. There are no estimates of the risks involved for such workers but it is thought that they are not insubstantial and this must be considered in the overall cost benefit analysis of such harm reduction programmes.

Perhaps the major limitation concerning IDU harm reduction concerns the methodology used to assess its effectiveness. Much of the work quoted here is only in abstract form and close scrutiny of methodology is impossible although it does illustrate the speed of change and the recent nature of the work.

The evidence concerning MMTP and the acquisition of HIV is mostly retrospective but consistent differences continue to emerge and prospective data on the effectiveness of MMTP with regard to low rates of acquisition of HIV, corroborated...
with a self reported reduction in high risk behaviour, is now available\textsuperscript{68,69,70,72,73,74}.

Much of the data from needle exchanges and outreach intervention programmes on behaviour change for injecting drug users is however subject to the criticism that it is based on a purely self reported behaviour change. Such studies often do not assess the changes that occurred in a control group and are thus unable to attribute general from specific behaviour change. The evaluation of the UK and Amsterdam needle exchanges did attempt such assessments\textsuperscript{27,89,94,98-100}. There is as yet little prospective data available on the acquisition of HIV. San Francisco however has noted a fall of annual seroconversion rates amongst drug users from 9 to 3\% as a consequence of a general media campaign, HIV testing, increased availability of drug treatment and outreach programmes\textsuperscript{136}. The newer and hopefully more acceptable methods of anonymous testing such as salivary or urine HIV testing or HIV testing of blood from returned injecting equipment need to be utilised to assess the effectiveness of intervention campaigns\textsuperscript{101,104,137-139}.

Self reported data are used for assessing the sexual behaviour changes of heterosexuals or homosexuals but are usually backed up by more objective measurement parameters such as rates of sexually transmitted diseases or of rectal gonorrhoea\textsuperscript{132}. IDU related research needs to find similar objective measures of reduced risk behaviour. Frequency of injection drug injuries and or skin infections can be used as markers of IDU. A self reported decrease in abscesses was associated with self reported reduction in IDU\textsuperscript{101}. Serum $\beta$-2-microglobulin levels have recently been shown to be increased in HIV negative drug users compared to non drug users. They are also increased in HIV positive injecting drug users compared to HIV positive non injecting drug users\textsuperscript{85-88}. Whilst absolute levels in HIV positive individuals could not differentiate injectors from non injectors trends would provide confirmation of self reported behaviour change. Hair analysis has been shown to be an effective method of detecting drug use and could be utilised on a wider scale to corroborate self reported behaviour change\textsuperscript{140}.

Another major difficulty is to find objective measures of reduced equipment sharing as opposed to IDU. Hepatitis B infection rates are sometimes quoted but these data must be treated with caution because of the saturation effect in a community as a consequence of the development of immunity\textsuperscript{114}. Falling rates of Hepatitis B need to be quoted together with the prevalence rates for markers of past Hepatitis B

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image.png}
\caption{Caption}
\end{figure}

228
infection. Studies of returned equipment from needle exchanges have tended to concentrate on the isolation of HIV in order to demonstrate the potential for spread. However the detection of more than one blood group from such equipment would provide an objective assessment of sharing and if used randomly could be used to corroborate self reported behaviour change.

Conclusion

It would appear that harm reduction measures such as oral opiate substitution therapy and needle exchange when provided in the context of counselling and health education are able to initiate contact with drug users, to maintain that contact and to get across health education and prevention messages. There are preliminary data to show that such measures are safe in that they do not increase drug use or initiate drug use, are effective in changing high risk drug behaviour and that oral substitute prescribing such as methadone is protective against acquisition of HIV and may also be protective against progression to AIDS. It seems however that methadone or needles provided without counselling or health education are not effective. The evidence that needle exchanges are directly protective for acquisition of HIV is not yet available. However there is indirect evidence in the form of an improvement in high risk behaviour and highly suggestive evidence from those localities such as Edinburgh where needle availability was actively reduced. Not only did reduced needle availability fail to prevent an IDU epidemic it facilitated IDU related Hepatitis B and HIV epidemics.

Thus a harm reduction strategy for IDU related HIV should incorporate; outreach health education and counselling to initiate contact with and reduce high risk behaviour amongst drug users not in treatment, increased needle availability in the context of exchanges to reduce the sharing of equipment, increased availability of oral substitute prescribing to reduce IDU and increased availability of drug treatment hopefully to achieve eventual abstinence. There would appear at present to be no overwhelming reasons for society to avoid harm reduction for IDU and in view of the consequences of IDU related HIV for drug users as well as for vertical and heterosexual transmission of HIV every reason to increase such harm reduction programmes. Those of us involved in the care of individuals infected with HIV remain extremely concerned over society's continued opposition, either overtly or by omission, to harm reduction. It is perhaps significant that a recent journal article concerning the report "Treating Drug Problems" from the Institute of Medicine of the National Academy of Sciences dealt with effectiveness, cost benefit and the
recommendations for both public and private treatment systems\textsuperscript{141}. However there was no discussion about the importance of drug treatment with respect to the control of HIV and what effect the HIV epidemic might have on need for drug treatment facilities!
References for Chapter 8


11. Robertson JR & Bucknall AB. Heroin users in a Scottish City - Edinburgh Drug Addiction Study 1986. West Granton Medical Group, 1 Muirhouse Avenue, Edinburgh, EH4 4PL.


74. Schoenbaum EE, Hartel D, Selwyn PA, Klein RS, Friedland GH et al. Low seroconversion and change in high risk behaviour in intravenous drug users (IVDUs) from 1985-88 in the Bronx, NYC. Vth International Conference on AIDS, June 1989 Montreal, Canada: Abstract Th DP 59


83. Diego S and Franceschi S. Methadone maintenance programmes and AIDS in North Italy. VIth International Conference on AIDS, June 1990, San Francisco, USA: Abstract SD 125


238


CHAPTER 9
Inpatient Health Care Utilisation for HIV Infection with particular reference to Injecting Drug Users

Introduction
The published models of health care for HIV and AIDS reflect the experience of those centres where the majority of patients affected have been homosexual or bisexual and there is little in the way of experience of injection drug users (IDUs). Equally the health service resource utilisation for IDUs such as number of admissions (NOA), average length of stay (ALOS), annual bed days etc. may be different to other risk groups. There has also been little published on the health care resource utilisation for early HIV infection and/or the effect, if any, of drug use.

The epidemic of injection drug use which began in Edinburgh around 1980, peaked in 1983-84, was associated with intense sharing of injecting equipment and a concurrent epidemic of injection related medical conditions including Hepatitis B. In 1985 and 1986 surveys found that between 38% and 52% of Edinburgh drug users had been infected with HIV and the Regional Infectious Disease Unit (RIDU) began to admit increasing numbers of drug users. This chapter details the health care utilisation of patients attending the RIDU with respect to HIV and AIDS between 1985 and 1992.

Method
The voluntary self referral HIV Counselling clinic established in the Edinburgh Regional Infectious Disease Unit (RIDU) was described in Chapter 5 and the accompanying out patient services in Chapter 7. Full details of the clinics have been previously published. A confidential prospective database containing an assessment of clinical staging, injection drug use, oral drug use, weight as well as biochemical, haematological and immunological parameters is maintained on all patients attending the City Hospital. The patients are identified on the database by hospital number only and the cross link between hospital number and name is stored on a separate database file which is kept on a removable "floppy disc". A retrospective review of the inpatient care of HIV infected patients at the City Hospital was undertaken from the start of the epidemic until 31st December 1989. Thereafter data on admissions were collected prospectively.

The clinical status of the patients was defined by the 1987 CDC definitions of AIDS (as detailed in Chapter 1) and the immunological status was defined by a CD4 count.
of greater than or less than 200 cells/cumm during any calendar year of attendance. The criterion for fulfilling a CD200 diagnosis was the first of two consecutive CD4 counts < 200 cells/cumm. If an individual fulfilled the criterion before or during an admission, or had an AIDS diagnosis before or during an admission, the admission was classified as such. The average length of stay was calculated by subtracting the date of admission from the date of discharge.

Analyses of Variance were carried out on all data unless otherwise indicated and statistical tests were carried out utilising SPSS/PC.

Results

Between the onset of the HIV epidemic in Edinburgh in early 1983 and the end of the study on 31st December 1992, 624 known HIV seropositive patients had attended the out patient department at the Regional Infectious Diseases Unit of the City Hospital, Edinburgh. Of these, 436 (70%) were IDUs. By the end of the study period 373 (60%) of all out-patients had been admitted to the RIDU at some point and 154 had developed AIDS. The 373 patients had been admitted on 2,069 occasions, (5.5/admitted patient, 3.3/clinic patient or 0.5/clinic patient/year) of which 146 were one day admissions of day patients. The number of admissions for each individual ranged from 1 to 35. The total number of bed days utilised was 21,934 (59 bed days/admitted patient, 35.2 bed days/clinic patient or 5.0 bed days/clinic patient per year. There were 879 (42.5%) admissions attributable to 141 patients with a diagnosis of AIDS and accounted for 11,461 (52%) bed days.

The total number of admissions to the RIDU during 1989, were 2,196; 336 or 15% of which were HIV related. The occupied bed days during this year were 14,860, 3,651 or 25% of which were HIV related. The ALOS for HIV admissions was 10.9 days whilst for non HIV admissions it was 5.8 days. By 1992 the total number of admissions to the RIDU were 1,999; 423, or 21% of which were HIV related. The bed days utilised during this year were 14,424, 4,653 or 32% of which were HIV related. The ALOS for HIV admissions was 11.0 days whilst for non-HIV admissions it was 6.2 days.

Two hundred and fifty one (40%) HIV positive patients were not admitted during the study period, 105 were admitted once, 51 were admitted twice, and 217 admitted three times or more (maximum number of admissions = 35).

Table 9.1, figures 9.1 and 9.2 shows the characteristics of the HIV positive population by Risk Activity of Injecting Drug User (IDU), Heterosexual (Het)
Homo/Bisexual (Ho/Bi) and Transfusion (Tran) and by sex and age at time of admission. Risk was undetermined for five individuals. Analyses of variance indicated significant differences between the ages of different transmission categories ($F = 103.3 \ p < .0001$) and gender ($F = 117.8 \ p < .0001$).
Table 9.1: Transmission category (TC) and gender of all out patients, number admitted (IP) and mean age at admission

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>IDU</th>
<th>Het</th>
<th>Ho/Bi</th>
<th>Trans</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>OP</td>
<td>624</td>
<td>436</td>
<td>85</td>
<td>93</td>
<td>6</td>
<td>433</td>
<td>191</td>
</tr>
<tr>
<td>%</td>
<td></td>
<td>70 %</td>
<td>13.6%</td>
<td>14.9%</td>
<td>1.0 %</td>
<td>69.4 %</td>
<td>30.6 %</td>
</tr>
<tr>
<td>IP</td>
<td>373</td>
<td>267</td>
<td>35</td>
<td>66</td>
<td>3</td>
<td>267</td>
<td>106</td>
</tr>
<tr>
<td>%</td>
<td></td>
<td>71.6%</td>
<td>9.4 %</td>
<td>17.7%</td>
<td>0.8 %</td>
<td>71.6 %</td>
<td>28.4 %</td>
</tr>
<tr>
<td>MeanAge</td>
<td>31.7</td>
<td>30.1</td>
<td>33.0</td>
<td>36.7</td>
<td>45.5</td>
<td>32.8</td>
<td>29.3</td>
</tr>
<tr>
<td>SD</td>
<td>7.2</td>
<td>5.4</td>
<td>10.7</td>
<td>8.6</td>
<td>5.1</td>
<td>7.5</td>
<td>5.8</td>
</tr>
</tbody>
</table>
City Hospital Cohort
Risk activity of patients

December 1992

Figure 9.1: Transmission category or risk activity of City Hospital Cohort
Figure 9.2: Gender of City Hospital Cohort
Table 9.2 (figures 9.3 and 9.4) shows the Number of Admissions (NOA) per year, the number of patients attending the clinic each year and the mean number of admissions per year per patient, by clinical and immunological category. These include the admissions to the ward which did not result in an overnight stay. The mean number of admissions per patient gradually increased over time, up to 1990 for all categories, but particularly for AIDS admissions. Over the time period the percentage of admissions for AIDS increased from 8.7% before 1987 to about 50% in 1990 and 1991 and decreased in 1992 to 41%. This was probably due to the large increase in deaths which occurred in 1990-1991. Similarly, those with a CD200 diagnosis increased from 7% before 1987 to about 75% from 1990 to 1992. The decrease in the total number of admissions after 1990 was contributed to by the opening of a separate facility for respite, convalescence and terminal care (Milestone House).
<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>CD4&gt;200</th>
<th>AIDS</th>
<th>Non-AIDS</th>
<th>CD4&lt;200</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>1988</td>
<td>26</td>
<td>22</td>
<td>3.7</td>
<td>23</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>1989</td>
<td>64</td>
<td>26</td>
<td>0.37</td>
<td>207</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>1990</td>
<td>68</td>
<td>30</td>
<td>0.36</td>
<td>189</td>
<td>0.36</td>
<td>0.36</td>
</tr>
<tr>
<td>1991</td>
<td>103</td>
<td>110</td>
<td>0.23</td>
<td>250</td>
<td>0.23</td>
<td>0.23</td>
</tr>
<tr>
<td>1992</td>
<td>138</td>
<td>127</td>
<td>0.47</td>
<td>219</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>Total</td>
<td>694</td>
<td>550</td>
<td>0.45</td>
<td>434</td>
<td>0.45</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Table 9.2: Total number of admissions (A), number of people attending the clinic (B) and mean number of admissions per patient (C=A/B) by clinical (AIDS and Non-AIDS) and immunological staging (CD4 count of greater or less than 200 cells/μm).
Admissions
Clinical staging and year

Figure 9.3: Mean number of admissions per patient by clinical staging (AIDS and Non-AIDS)

December 1992
Admissions
Immunological staging and year

![Bar chart showing mean number of admissions per patient by immunological staging (CD4 counts of greater or less than 200 cells/cumm)]

December 1992

Figure 9.4: Mean number of admissions per patient by immunological staging (CD4 counts of greater or less than 200 cells/cumm)
Bed Days

The annual number of bed days used for HIV steadily increased over time until 1991, when there was a decrease, for the reasons already given. The ALOS from 1986 to 1992 are shown in Table 9.3 (figures 9.5 and 9.6). These exclude admissions where there was no overnight stay. The overall ALOS decreased from 1987 to 1991 (16 vs. 10 days) but increased again in 1992 to 11.3 days. The ALOS of those with a CD200 diagnosis, however, continued to decrease over the study period although the ALOS for AIDS or HIV (non-AIDS) admissions also showed a nadir in 1991. By comparison admissions of those without a CD200 diagnosis, however, continued to decrease in 1992, although non-AIDS admissions did not.
Table 9.3: Average length of stay (ALOS) per admission by clinical (AIDS or Non-AIDS) and immunological staging (CD4 count of less than or greater 200 cells/cumm) as well as by year of admission

<table>
<thead>
<tr>
<th></th>
<th>AIDS</th>
<th>Non-AIDS</th>
<th>CD4≤200</th>
<th>CD4&gt;200</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>MEAN</td>
<td>SD</td>
<td>N</td>
<td>MEAN</td>
</tr>
<tr>
<td>&lt;1987</td>
<td>6</td>
<td>34.8</td>
<td>26</td>
<td>63</td>
<td>14.1</td>
</tr>
<tr>
<td>1987</td>
<td>26</td>
<td>18.4</td>
<td>16</td>
<td>76</td>
<td>11.7</td>
</tr>
<tr>
<td>1988</td>
<td>62</td>
<td>11.8</td>
<td>15</td>
<td>128</td>
<td>10.2</td>
</tr>
<tr>
<td>1989</td>
<td>124</td>
<td>15.0</td>
<td>16</td>
<td>186</td>
<td>9.7</td>
</tr>
<tr>
<td>1990</td>
<td>233</td>
<td>14.8</td>
<td>20</td>
<td>214</td>
<td>8.4</td>
</tr>
<tr>
<td>1991</td>
<td>194</td>
<td>12.6</td>
<td>14</td>
<td>199</td>
<td>7.2</td>
</tr>
<tr>
<td>1992</td>
<td>170</td>
<td>13.5</td>
<td>15</td>
<td>242</td>
<td>9.7</td>
</tr>
<tr>
<td>Total</td>
<td>815</td>
<td>14.0</td>
<td>17</td>
<td>1108</td>
<td>9.5</td>
</tr>
</tbody>
</table>
Figure 9.5: Average length of stay (ALOS) by clinical staging (AIDS and Non-AIDS) and year of admission
Figure 9.6: Average length of stay (ALOS) by immunological staging (CD4 count of less than or greater 200 cells/cumm) and year of admission
Over the study period 815 admissions occurred in 140 patients with a diagnosis of AIDS and accounted for 11,461 bed days with an average length of stay of 14 days. By comparison there were 1,108 non AIDS but HIV positive admissions of 292 patients, accounting for 10,473 bed days, with an ALOS of approximately 10 days. Table 9.4 (figure 9.7 and 9.8) shows the ALOS per patient admitted, by clinical and immunological category, risk activity and gender.
Table 9.4: Average length of stay by clinical (AIDS and Non-AIDS) and immunological staging (< or >CD200) for transmission category and gender

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>AIDS</th>
<th>Non-AIDS</th>
<th>CD4&lt;200</th>
<th>CD4&gt;200</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
<td>SD</td>
<td>N</td>
<td>Mean</td>
</tr>
<tr>
<td>IDU</td>
<td>454</td>
<td>13.0</td>
<td>14.4</td>
<td>988</td>
<td>9.3</td>
</tr>
<tr>
<td>Het</td>
<td>61</td>
<td>13.8</td>
<td>15.7</td>
<td>65</td>
<td>10.5</td>
</tr>
<tr>
<td>Ho/bi</td>
<td>298</td>
<td>15.7</td>
<td>19.9</td>
<td>43</td>
<td>13.6</td>
</tr>
<tr>
<td>Trans</td>
<td>0</td>
<td></td>
<td></td>
<td>10</td>
<td>5.0</td>
</tr>
<tr>
<td>Male</td>
<td>623</td>
<td>14.2</td>
<td>17.4</td>
<td>683</td>
<td>9.2</td>
</tr>
<tr>
<td>Female</td>
<td>192</td>
<td>13.5</td>
<td>14.2</td>
<td>425</td>
<td>9.8</td>
</tr>
<tr>
<td>Totals</td>
<td>815</td>
<td>14.1</td>
<td>16.7</td>
<td>1108</td>
<td>9.5</td>
</tr>
</tbody>
</table>
Figure 9.7: Average length of stay for AIDS and Non AIDS by transmission category and gender
ALOS
Immunological staging, risk activity and gender

<table>
<thead>
<tr>
<th></th>
<th>IDU</th>
<th>Het</th>
<th>Ho/bi</th>
<th>Trans</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>&lt;CD200</td>
<td>&gt;CD200</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dec 92</td>
<td>261</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 9.8: Average length of stay by CD200 status, transmission category and gender

December 1992
Analyses of variance were carried out examining the effect of risk, sex and AIDS or CD4 status on average length of stay. There were no significant interactions between AIDS or CD4 status with either risk or sex. There was a significant main effect of AIDS status ($F = 23.1 \ p < 0.0001$) and a weaker but significant main effect of CD4 count on ALOS ($F = 4.7 \ p < 0.05$). There was a significant effect of risk ($F = 3.8 \ p < 0.05$) and individual comparisons using the test of Modified Least Significant Difference showed significantly longer lengths of stay for homosexual/bisexual men than for drug users. There was no significant effect of sex ($F = 0.86$).

**Annual Bed Day Use**

The average annual number of bed days utilised per living patient by clinical or immunological staging, risk activity and gender are shown in Table 9.5. Drug users utilised more days than the other risk groups for AIDS and non-AIDS admissions (59.9 vs. 44.7 vs. 52.0 and 5.4 vs. 3.3 vs. 4.4 days) although not when analysed by with or without a CD200 diagnosis (20.4 vs. 23.6 vs. 39.8 and 4.2 vs. 1.6 vs. 7.0 days). Over all and by CD200 diagnosis, homosexual men used more bed days. This is at least partly a reflection of the fact that homosexual men tended to become known to the clinic at a later stage than the drug users. The average time from first visit to the clinic to death or the end of the study for homosexual/bisexual men was 28 months with 40% of that time being with AIDS. This compared to 49 months for drug users with only 5.5% with AIDS. Females utilised more annual bed days per year per patient than males for AIDS or HIV (non-AIDS) admissions (64.2 vs. 52.7 and 5.4 vs. 4.8) but not apparently when analysed by with or without a CD200 diagnosis (22.0 vs. 24.1 and 4.5 vs. 3.9).
Table 9.5: Average annual bed days per living patient for clinical (AIDS or Non-AIDS) or immunological staging (< or > CD200) by transmission category and gender

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>AIDS</th>
<th>Non-AIDS</th>
<th>CD4&lt;200</th>
<th>CD4&gt;200</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDU</td>
<td>59.9</td>
<td>5.4</td>
<td>20.4</td>
<td>4.2</td>
<td>8.4</td>
</tr>
<tr>
<td>Het</td>
<td>44.7</td>
<td>3.3</td>
<td>23.6</td>
<td>1.6</td>
<td>6.7</td>
</tr>
<tr>
<td>Ho/bi</td>
<td>52.0</td>
<td>4.4</td>
<td>39.8</td>
<td>7.0</td>
<td>23.5</td>
</tr>
<tr>
<td>Trans</td>
<td>0.0</td>
<td>2.1</td>
<td>2.2</td>
<td>1.7</td>
<td>2.0</td>
</tr>
<tr>
<td>Male</td>
<td>52.7</td>
<td>4.8</td>
<td>24.1</td>
<td>3.9</td>
<td>10.3</td>
</tr>
<tr>
<td>Female</td>
<td>64.2</td>
<td>5.4</td>
<td>22.0</td>
<td>4.5</td>
<td>8.3</td>
</tr>
<tr>
<td>Total</td>
<td>59.9</td>
<td>5.0</td>
<td>23.5</td>
<td>4.1</td>
<td>9.6</td>
</tr>
</tbody>
</table>
Annual bed days per living patient
Clinical staging, risk activity and gender

December 1992

Figure 9.9: Average annual bed days per living patient for AIDS or Non-AIDS by transmission category and gender
Annual bed days per living patient
Immunological staging, risk activity and gender

Figure 9.10: Average annual bed days per living patient for immunological staging (< or > CD200) by transmission category and gender

December 1992

265
First Admissions

The clinical status of patients on their first admission was also investigated. Table 9.6 shows the AIDS and CD200 diagnosis of the transmission categories and genders on first admission. Significant differences were found on chi square tests between the transmission categories (IDU, Het and Homo/BI) for AIDS versus Non-AIDS admissions (chi$^2 = 93.9, p<0.0001$), and also between sexes. (chi$^2 = 7.48, p<0.01$). Differences were also found between transmission categories for CD200 diagnosis at first admission (chi$^2 = 8.8, p<0.05$), but not between sexes. (chi$^2 = 1.95$).

Further investigation showed that of 41 individuals whose first admission was the first time that they had been seen at RIDU, 24 were homosexual men, (34% of all homo/bisexual men seen) 10 were drug users (2.6%) and 7 were heterosexual (12.7%). Drug users were more likely to be admitted prior to an AIDS or CD200 diagnosis than, particularly, homosexual men. Generally, females were more likely to be admitted at an earlier stage than males, though there was no gender difference, when homosexual men were excluded from the analysis.

Sixty eight of the admissions (3.3%) were as a direct result of injecting drugs, (for instance injection injuries such as abscesses or cellulitis) and were unrelated to HIV infection or any other medical condition. A further 65 admissions (3.1%) were drug related (usually detoxification or stabilisation of drug use). The ALOS for both was 12 days; 22.75 days reducing to 7.2 days in 1992. The number of admissions each year was similar, with twenty admissions in 1988, 22 in 1990 and 28 in 1992.
Table 9.6: Clinical and immunological status on first admission for transmission category and gender

<table>
<thead>
<tr>
<th>Status</th>
<th>IDU</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>AIDS</td>
<td>16</td>
<td>8</td>
<td>6</td>
<td>38</td>
<td>37</td>
<td>70</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-AIDS</td>
<td>190</td>
<td>92</td>
<td>10</td>
<td>62</td>
<td>16</td>
<td>30</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4&lt;200</td>
<td>51</td>
<td>25</td>
<td>3</td>
<td>19</td>
<td>20</td>
<td>38</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4&gt;200</td>
<td>155</td>
<td>75</td>
<td>13</td>
<td>81</td>
<td>33</td>
<td>62</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>206</td>
<td>74</td>
<td>16</td>
<td>6</td>
<td>53</td>
<td>19</td>
<td>2</td>
<td>0.7</td>
</tr>
</tbody>
</table>

267
Discussion

In view of the dramatic onset in 1983 of the Edinburgh HIV epidemic in injection drug users 4,8, it is not surprising that the utilisation of HIV inpatient services increased over time. The early stage of the Edinburgh drug related HIV epidemic is demonstrated by the fact that 75% of drug users and 62% of homosexuals did not have a CD200 diagnosis at first admission, though there were other major differences between these transmission categories, as discussed below. The relatively early stage of the Edinburgh epidemic, in health care resource terms, is also exemplified by the fact that 40% of HIV positive patients in contact with the hospital did not require an admission, and only 35% had required 3 or more admissions. By the end of 1989 there were still only 51 patients with AIDS attending the clinic, less than 14% of all HIV positive patients attending in that year. This had risen to 154 (25%) by the end of 1992.

Clinical Staging: AIDS and Non AIDS

Among the AIDS patients in this study, 141 out of the 154 (92%) had been admitted at some point and 92 (60%) had three or more admissions. The ALOS for each AIDS admission in Edinburgh decreased from 35 days to 13.5 days whilst the number of admissions rose from 1.5 to 2.6 per AIDS patient. The reduction in ALOS is likely to be as a result of increased familiarity with the disease whilst the increase in the number of admissions is probably associated with increased survival. These results are comparable with a study of 863 patients with AIDS from North California where 99.5% had at least one admission and 57.7% had 3 or more admissions 10. The non profit prepaid group practice in Northern California, which may be closer to NHS medical practice than other US practices, reported a mean number of admissions of 3.3 and an ALOS of 17 days in 1983 which had fallen to 10.7 days by 1987 for AIDS patients 10. The reduction in ALOS is likely to be as a result of the increased familiarity of the treating physicians with the disease and the increase in the number of admissions may well be associated with increased survival.

Considerable variations in the ALOS for AIDS have been reported between various geographical areas; the ALOS for 1983-86 was 22.3 days for New York but only 13.5 days for San Francisco whilst in 1988 it was 9.7 days for Washington State, 32 days in Boston and 18.5 days in New Jersey 11-14. The number of admissions and the ALOS for AIDS are affected by local demography, health care systems, stages of the HIV epidemic, familiarity with the problems, anti-retroviral therapy and the use
of newer therapies for opportunistic infections. There is also evidence of the increasing incidence of conditions such as TB, lymphoma etc., which are likely to require more protracted hospital stays, as other opportunistic diseases, such as PCP, cytomegalovirus and toxoplasmosis become more treatable 15.

Without a doubt however, the major difference between New York and San Francisco or the East and West Coasts of the USA in terms of health care are related to differences in demography. In New York City, IDU has been implicated in 34% of the male and 60% of the female patients whereas in San Francisco only 1.7% of cases have been in drug users although a further 11.5% have involved drug use in homosexual or bisexuals 16,17.

The ALOS in Edinburgh for HIV (non-AIDS) admissions decreased from 14 days to 7 days in 1991 whilst the number of admissions per clinic patient clinic increased by a factor of 1.6 from 0.47 to 0.75 admissions per patient. It is unclear why the ALOS in 1992 was longer than in the preceding three years, but may reflect the fact that prophylaxis for opportunistic infections delays the onset of AIDS defining illnesses, but does not prevent immunological decline as indicated by a CD200 diagnosis and the onset of serious non AIDS ailments.

There were 1,108 (57.6%) HIV (non-AIDS) admissions in 220 patients, accounting for 10,473 (48%) bed days. The fall in the proportion of HIV (non-AIDS) admissions to AIDS admissions from 1987 to 1990 reflects the development of the epidemic in IDUs. The proportion of bed days used by HIV (non-AIDS) patients also steadily decreased up to 1990.

There is unfortunately a paucity of data on non AIDS admissions compared to AIDS admissions. In New Jersey the admission rate for HIV (non-AIDS) was 1.25 admissions/year/patient with an ALOS for HIV admissions of 12.7 days 18. In the Montefiore Methadone cohort for the years 1986 and 1987 the admission rates were 0.22 and 0.27/patient/year 19. AIDS accounted for only 14 and 16% of the Montefiore Methadone cohort admissions. Only 8% of the Edinburgh cohorts first admissions were for AIDS suggesting that the Edinburgh and Bronx cohorts are broadly comparable. The ALOS for non AIDS, HIV admissions for the whole of the USA was 17.1 days in 1985 and 14.1 days in 1988 for HIV admissions 20.
Immunological Staging

CD200 diagnosis based on falling below a level of 200 CD4 cells/cumm was predictive of the number of admissions and the ALOS. There were nearly three times as many admissions for those with a CD200 diagnosis than for those without by 1992. There was a significant difference in ALOS between the two groups when looked at over the whole length of the study (12.1 vs. 10.0). This was less marked than the difference between AIDS and non AIDS admissions, but became longer over the last 12 months of the study. It is probable that physicians were more likely to admit those with a CD200 diagnosis who were exhibiting some symptoms for investigation than those with a higher count with similar symptoms. Such admissions, where no opportunistic infection was found, would be of short duration compared with admissions of those who were known to have AIDS and this factor probably explains the relatively small difference in ALOS by CD200 diagnosis. These admissions could be considered as a form of "prophylaxis" for opportunistic infections in a population with poor compliance for standard prophylactic treatment for Pneumocystis Pneumonia and who have a high incidence of bacterial pneumonia and chronic obstructive airways disease.

Both clinical and laboratory staging of immunodeficiency provide useful indications of health care resource utilisation, but the fact that those who have a relatively healthy status with regard to their immunology and clinical status consume significant health care resources in terms of in patient care cannot be ignored. It is also important to note that, in Edinburgh by 1992,Whilst HIV patients accounted for 21% of the admissions they occupied 32% of the bed days utilised in the Unit. This increased length of stay compared to other patients and the increased likelihood of admission with advancing immunodeficiency must be taken into account in health care planning terms.

Gender

There was no significant difference for gender in ALOS whether analysed by AIDS or CD200 diagnosis but females were more likely than males to have their first admission prior to an AIDS diagnosis. This difference disappeared when drug users alone were examined suggesting that the result has more to do with times at which the different risk groups accessed health care rather than a gender difference. Women with AIDS used more bed days per year per living patient than men (64.2 vs. 52.7) but the difference was not statistically significant. The situation in Edinburgh is
in stark contrast to that in the USA where there are studies demonstrating that US women present late for medical care; 39% of women had a CD4 count of less than 200/cumm mm at presentation and in Minnesota two thirds of women with HIV were detected by neonatal screening rather than as a result of medical care \(^{21,22}\). In New Jersey women presented with more advanced disease, with more symptoms and a greater duration of symptoms (59.75 versus 24.5 weeks) than did men \(^{23}\).

**Risk Activity**

Between 6-7% of both admissions and bed days in HIV positive patients could be identified as being solely related to the effects of drug use rather than to HIV infection. By comparison a similar survey amongst the Montefiore Methadone programme revealed that 30-40% of the admissions in 1986-87 were drug related, suggesting perhaps that our cohort are less chaotic in terms of drug use than in the Bronx\(^{14}\).

Drug users and those infected heterosexually had a shorter ALOS than homosexual men (15.4 vs. 10.4 vs. 12.1 days). This may be related to the finding that drug users were more likely to be admitted at an earlier stage in their illness than homosexual men; only 8% of IDUs had AIDS on their first hospital admission compared with 70% of homosexuals. IDUs attend earlier in the illness, are more familiar with the clinic and may be more likely to attend at an early stage when ill. The reasons for this are unclear, but contributory factors may have been the early knowledge of HIV status in the IDU related HIV patients following massive publicity about the epidemic in drug users in Lothian Region. Such local factors need to be taken in to account in evaluating resource utilisation. Another local factor which may have affected the presentation of individuals was advice about testing among the gay community and the fact that some received their care as out patients from the GUM clinic but transferred to the RIDU when they became more ill. The fact that the counselling and medical clinics at RIDU were particularly associated with IDU patients and offered a prescribing service in the early stages of the epidemic no doubt also facilitated access of IDU patients at an earlier stage of disease. Certainly the IDU population attending RIDU is over represented within the tested population within Edinburgh. The Official Scottish figures \(^{24}\) show that IDUs were 60% of the tested population in 1992 but they have constituted between 70 and 80% of clinic attenders in most years. It is clear from an earlier study that hospital admissions for
drug users, prior to an AIDS diagnosis, can be largely accounted for by admissions with bacterial chest infections.

A more difficult question to answer is what effect concurrent drug use or risk activity has on health care resource utilisation since the main risk groups are usually not comparable socio-economically. In 1989 and 1992 AIDS patients attending RIDU on average utilised 15 and 13.5 bed days per admission, compared to 5.8 and 6.2 for non HIV patients. In Switzerland, where only 31% were drug users, AIDS patients utilised 23.3 days compared to 12.4 days per admission, suggesting that drug use per se does not have a major effect. The effect of lower socio-economic status on non HIV admissions has been shown in the USA to increase ALOS by 3 to 30%.

Two US studies have compared ALOS for AIDS for various risk groups; homosexuals (16.23 days), heterosexuals (21.54 days) and drug using heterosexuals (19.27 days). A further report showed an ALOS for homosexuals (13.8 days), drug using homosexuals (11.1), heterosexuals (17.0 days) and drug using heterosexuals (19.4 days). In Switzerland by comparison no significant difference could be detected between the ALOS for homosexuals (18.5 days) or drug users (21 days) with AIDS.

In Edinburgh, when considering equivalent clinical or immunological stages, IDUs did not use excessive resources as judged by ALOS compared with other groups. Drug users were shown to make up 70% of the total population and, in any one year, they constituted from 70% to 84% of the cohort. Over all they constituted 72% of all those persons admitted and 69% of all days spent in hospital. However the average number of bed days used per living AIDS patient was greatest for drug users (60 days vs. 52 days for homo/bisexuals). It seems that drug users overall do utilise more bed days per year than other risk groups although each admission tends to be shorter than other risk groups.

**Conclusion**

By 1992 each member of the clinic was on average utilising 1 admission per year and 11.6 bed days per year. In Edinburgh, both clinical and immunological staging, were predictive of resource utilisation. Gender however was not predictive and the effect of risk activity was complex possibly because of differing socio-economic status. The extra hospital resources for drug use related HIV appears to be in the form of more frequent admissions at all stages of HIV disease rather than in an increased ALOS per admission.
Whilst the increased use of resources with AIDS or CD200 diagnosis is not unexpected it does underline the fact that the allocation of resources needs to be based on both clinical and laboratory measures of immunodeficiency since neither are sufficient to predict all the health care needs of a population.
References for Chapter 9


CHAPTER 10

The health service problems of IDU related health care

Introduction

By the end of 1991 35% of the AIDS cases and 50% of those infected with HIV in Scotland were related to IDU. Some 52% of Scottish HIV reports have come from Lothian where 57% of the Lothian HIV cases have involved drug use, the highest percentage in the UK for this particular risk group. The extent of the concentration of ill patients in Lothian is seen by the fact that 50% of the reported cases of AIDS in Scotland and 67% of the CD4 200 cases have come from Lothian.

The Regional Infectious Disease Unit has been coping with the injection drug use related hepatitis problems since 1970 and HIV since 1985. It was designated as a Regional AIDS Centre in 1987 and new in-patient and out-patient services were opened in 1991. The initial new facilities provided in London to cope with AIDS were often based on open or Nightingale wards. These facilities were inappropriate for a population where one third of the patients were female and a higher incidence of infectious diseases such as TB and PCP was to be expected. Consequently the majority of Edinburgh's new accommodation was based on cubicles rather than open wards.

Characteristics of IDU which affect the Health Service

Since the major risk group in Lothian affected by HIV/AIDS are drug users, caring for such patients introduces a number of problems, not faced by other AIDS Units in the UK. One of the major problems for a health service is that drug users typically have a crisis type of lifestyle with little planning other than for the next supply of drugs. On average heroin drug users require 3-4 doses per day and therefore their horizons are often limited to the next 24 hours. They are not particularly health conscious as demonstrated by their overwhelming addiction and injection drug use which is demonstrably a dangerous life choice. Lastly they have a tendency for a high default rate in terms of the health care system probably because the priorities of addiction come before all else (Chapter 7).

The characteristics of drug use itself are also important to bear in mind since it is an illegal activity often associated with violence and unpredictable behaviour. The accompanying aggression is often as a consequence of excess (e.g. alcohol/opiates)
or a lack of drugs (e.g. opiates or benzodiazepines). Since recreational drug use (other than of alcohol and nicotine) is an illegal activity in most countries medical care for drug users whether HIV infected or not, is difficult to deliver. Since many individuals come from socio-economically deprived areas there is an associated lack of support in the community which puts a greater strain on the hospital services. These characteristics of the drug using patients are important when considering the problems the RIDU in Edinburgh has had to face. Whilst as a group injection drug users exhibit poor utilisation of existing services it is important to remember that some of this chaotic behaviour is as much a characteristic of their community as their drug use.

**Health Care Service for IDU**

In view of all these problems it is not surprising therefore that the health care system has problems coping with drug users in large numbers. Even more difficulties occur when one is trying to manage a chronic illness that requires regular attendance over many years. Traditionally health care for drug users has been based on psychiatric models developed for the management of addiction rather than the physical aspects of care.

Health care workers themselves, are concerned over the behaviour associated with drug use particularly verbal or physical aggression, disruptive behaviour, theft, the carrying of offensive weapons, drug dealing, self medication, day night reversal (sleeping the day away and being awake all night) etc. Much of the aggression and the carrying of offensive weapons is however connected with the problems of the drug culture and fear of their peers rather than a wish to harm health care workers although they can be caught in the cross fire. An understanding of the reasons for their behaviour helps in managing it in the wards. Without doubt nurses with both physical and psychiatric expertise are essential.

**Health Care Service for IDU related HIV**

Despite the fact that IDU related HIV is becoming more common there are still relatively few units in the UK with a large enough clinical workload to be able to provide advice on the management of problems associated with IDU related HIV. There are two possible methods of delivering care for HIV infected drug users. One relies on physical restraint and coercion but there are very real concerns over the possibility of deliberate infection of staff by patients and this has in fact occurred in
other countries. In addition the system is also interested in increasing harm reduction for both IDU and sexual behaviour by health education and a coercive system is unlikely to succeed in this area. The other method of organising care for HIV patients which was adopted in Edinburgh relies on attracting individuals to the health care system via the facilities. It is hoped that using this method the chance of deliberate infection occurring of the staff is reduced. In addition maintaining contact with the patients over long periods increases the likelihood of harm reduction being adopted. However as a consequence of the need to maintain contact for long periods the health care service may have to tolerate more difficult and problematic behaviour from the patients.

**RIDU Edinburgh**

The difficulties faced by the RIDU in Edinburgh of having a unique population attending the Unit have necessitated a number of changes or alterations in the organisation of the health care system. For outpatients the clinics have been stratified for chaotic and non chaotic days as well as offering both drug and medical services at the same site (Chapter 7). In addition higher staffing levels are required to contain and cope with the problems of this difficult population which stretch from "bad behaviour" to violent aggression and frank psychosis. It was noticed that more of the most difficult problems tend to occur at high levels of occupancy whether this is in the outpatient department or the wards.

Unfortunately only 11 of 15 beds in the new ward dealing with the mainly HIV patients rather than infectious diseases were in the form of cubicles and the pressure for cubicles for medical reasons has necessitated the use of cubicles from adjacent wards. In addition, in order to spread out the different patient populations attending the RIDU and reduce or avoid problems there has been an additional need to utilise more than one area. Consequently the patients have been spread over three wards rather than one in an attempt to reduce behaviour problems. This of course requires more resources and increases the cost of care. Similar problems exist for the outpatient department and in order to spread out the different patient populations attending the RIDU and to avoid problems, more clinics are organised to spread the patient's attendance over the week. This obviously requires a higher staffing level than if fewer mixed clinics were utilised.

Continuity of care from both nurses and doctors has been one of the most effective means of reducing problems and incidents. Prior knowledge of the patient by the
caring team can easily avoid problems. For the new ward dealing mainly with HIV patients rather than infectious diseases this concept has been extended to night duty and all the nursing staff rotate from day to night duty.

**Problems of RIDU, Edinburgh**

Despite the absence of a serious incident even with the current staffing levels problems have occurred.

**Risk of Infection and Isolation requirements**

There are no students on the new ward and there are reduced student numbers on the ID wards because of the problem of untrained individuals dealing with the problem of HIV. As an example, for a medical ward in the City Hospital the usual establishment per ward is around 21 WTE but one third of these are student nurses. By comparison because of HIV the student numbers in the RIDU vary from 0% in Ward 14 to around 10% in the other wards.

A large number of patients require isolation in cubicles because of infectious problems such as salmonella, TB, or infective diarrhoea. Cubicles are also required because of the nature of the patient population i.e. mixed sexes (one third are female) and mixed risk groups (20% homosexuals and 70% drug users). The staffing required for cubicles is higher than for an open ward or Nightingale wards. On an isolation ward nurses are not immediately available since on leaving the cubicle hand washing will usually be required. As a consequence more staff are required to cover an infection ward than a general ward. In 1993 the ratio of the number of staff to the number of beds is 0.79 for a medical ward in the City Hospital with only one or two cubicles, between 1.06-1.11 for the general ID wards where 55% of the beds are single cubicles and 1.7 for our HIV ward where 73% of the beds are single cubicles. Ideally 2 nurses are required for every cubicle.

**Escort duty**

Every patient leaving the unit for any investigation is accompanied by a trained nurse. This was instituted because other units were extremely reluctant to take the patients, and incidents occurred. Also other departments were concerned over spillage of body fluids such as vomiting, disconnected intravenous lines etc. A review of the financial year 1992-3 revealed an average of 2.12 WTE nurses out of the Unit/month covering escort duties. This is equivalent to 0.53 WTE out of the
Unit/day. The grade of staff varied from an average of 7 hours/month of a G grade sister to 33.3 hours of an E grade nurse/month.

**Patient dependency**

The physical care of the patients with HIV especially IDU related HIV varies from mildly ill to high dependency (just short of ITU). The mixture of serious physical ill health combined with serious mental ill health is rarely found in any other area of medicine and as yet there is no dependency scale that easily reflects the problems. This lack of an appropriate indicator for care levels has led to difficulties in justifying resources. Whilst there is a dedicated HIV team, both medical and paramedical and psycho-social, there are no other specialised drug dependence staff as for instance might be available in other centres.

The dependency of the patients is both physical and psychological. On a physical scale it can vary from just short of assisted ventilation because of respiratory failure to the walking well with numerous psychological problems. On the psychological scale the patients can be entirely well or have agitated psychotic states with physical assault on staff (one of the episodes described above).

A 6 month survey of inpatients during 1992 revealed that on average 35.5% of the patients in the wards each day had HIV infection; 89% of the patients in the wards each day required total care (attention every 2 hours) whilst 0.9% of the patients in the ward each day required constant care (one nurse in constant attention). In addition 7% of the HIV patients in the ward each day or 0.8 patients/day in the ward each day required increased supervision as a result of medical or drug related drowsiness or because of psychiatric disturbance (see below).

A survey of dependency was undertaken utilising the Patient Assessment Information System (PAIS); a scoring system which only accurately reflects acute nursing interventions and omits the psychological needs of the patient\(^3\). An assessment was made of the nursing hours needed on 12 randomly chosen HIV and ID discharges. This revealed an estimated requirement for HIV patients of 81.81 hours of nursing on one day with only 47.5 hours actually available compared to an estimated 52.5 hours for ID patients with only 32 hours actually available\(^4\).
Psychiatric problems

HIV related disease may present with apparent psychiatric problems such as psychosis. However the differential diagnosis is extensive including toxic confusional states from drugs or infections, space occupying lesions or HIV related dementia. Admission to the RIDU is commonly requested in HIV positive patients in order to exclude the diagnosis of an organic psychosis.

During a 12 month period (1992) 4 psychotic patients were admitted to the RIDU to exclude organic psychosis rather than be admitted to the local psychiatric hospital. The time the patients have remained in the Unit varied from a few days to over a month and not surprisingly this put considerable strain on the Nursing staff.

Security incidents

Over a 12 month period (from August 1992) the busiest ward for HIV experienced 22 reported security incidents. These consisted of two physical assaults on staff members by patients, one episode of self harm (slashed wrists) by a patient, 11 episodes of verbal aggression towards staff threatening physical assault, 5 episodes of serious self medication requiring medical attention, one episode of theft of a patient's valuables, one episode of the fire alarm being set of by patient's children, and one episode of theft of ward equipment (later returned after lengthy discussions).

The out patient department suffered 12 serious security incidents in the 12 month period consisting of, three episodes of theft of equipment, 4 episodes of verbal assault threatening physical assault, one episode of physical assault on a consultant(RPB), one episode of a fight between two patients which resulted in a slashed face for one patient, one episode of damage to a consulting room as a result of a patient being asked to observe the no smoking policy and at least 2 episodes of unconsciousness requiring several hours of constant care in the day bed area as a result of excess alcohol and drugs. In every year since 1985 the department has had to deal with the problem of concealed offensive weapons such as guns and knives. However the peak of incidents in the out patient department occurred in 1989 when there were 40 security incidents or 3.3 events per month.

There are obviously many more incidents each week, not serious enough to require reporting or the attention of the police, which are safely avoided or defused by the staff. These which take considerable time to manage.
**Selfmedication**

Continued use of non prescribed drugs taken either orally or by injection cannot be totally eliminated in a Unit whatever the level of supervision. Unlike Drug Detoxification Units, restricted visiting and body searches are not possible for visitors nor for patients who are seriously ill. This results in episodes of excess sedation requiring at least constant care or infusions with antidotes and/or the risks of fire from smoking.

**Fire incidents**

The majority of the patients smoke heavily and since they also prefer excessive sedative drugs there is a constant danger of fires started by careless cigarette smoking. Much of the day and night is spent re-enforcing the ward rules with regard to smoking; for instance repeatedly requesting patients not to smoke in bed or when drowsy.

Over a 20 month period (10/91-5/93) there were 34 fire incidents in the City Hospital involving the Fire Brigade. Of these 15/34 or 44% of the fire incidents occurred in the RIDU area. Ten or 66% of the RIDU fire incidents were related to patients smoking. Of the 7 ward evacuations that occurred as a result of fire incidents in the hospital 6 or 86% of the evacuations occurred in the RIDU area. Four or 57% of the RIDU evacuations were as a consequence of smoking. Unfortunately since the patient's addiction to cigarettes is probably greater than or at least equal to opiates it is impossible to enforce a total no smoking policy for the inpatient areas. Smoking is restricted to patients and only in their rooms but problems still arise. Not surprisingly the enforcement of such as policy and coping with the fires requires considerable staff especially since 66% occurred out of office hours.

**Conclusions**

The range of problems which occur with IDU related HIV are not only extensive but also very different to those usually faced by the health service. The RIDU in Edinburgh has had to adapt in order to manage drug users with a chronic illness. This adaptation has required new skills on the part of the staff and the gradual reduction in problems suggests that not only are the staff adapting but possibly the patients are also adapting to the health care system.

Despite this improvement, the RIDU is still having to cope with a considerable amount of disturbed behaviour probably more so than other units managing HIV in
the UK. As IDU related HIV appears in other areas of the UK these Units will need to consider how best to cope with the associated disturbed behaviour. Hopefully Edinburgh's experience of how to adapt and respond to behavioural problems will be of some help to others.

One might question why should a health care system have to cope with this sort of behaviour and there seems no doubt that if the patients were not infectious and capable of infecting other individuals including health care staff it is unlikely that funds would continue to be made available for the current level of service which is extremely expensive (in the region of around £3-4 million per year). HIV/AIDS funds are now being reduced since it appears that the epidemic is about to plateau. However caution is required in the area of health care since any suggestion of lack of caring by society may result in a backlash with the possibility of increased levels of aggression towards the health service. Lower levels of staffing, the use of cheaper methods of staffing such as temporary ("bank") staff, higher turnover of staff with reduced continuity of care and or higher occupancy of difficult patients will and may will lead to an increase of violent behaviour with increased risks for staff.
References for Chapter 10


4. Personal communication from Mrs Heather Coutts and Miss Shirley Parker, Ward 14, City Hospital.
CHAPTER 11

IDU related HIV and prison medical care

Introduction

Unfortunately a considerable proportion of drug users, in Edinburgh perhaps as many as 70%, will spend periods of time in prison. In view of the rising prevalence of drug use related HIV, prisoners constitute a group who are at high risk of HIV infection. Exact figures of HIV seroprevalence within UK prisons are unavailable as screening of individuals on entry to or inside prison is not performed. European figures are available however and give much cause for concern. In Italy, which screens all prison inmates, overall seroprevalence is 16.8% and in some reported studies is around 30%. Small scale studies in other countries have revealed prevalence rates of 26% in Spain, 12.6% in France and 11% in Dutch and Swiss prisons. It is not unreasonable to estimate a United Kingdom seroprevalence of a similar order especially in Scotland. In one study of two Madrid prisons, an overall seroprevalence in males of 55% was found with the highest prevalence (77%) amongst drug users. In the USA, seroprevalence rates of up to 15% have been reported.

One consequence of the high rates of HIV in drug using prisoners is that new infections with HIV are bound to occur because injection drug use continues within the prison environment. Owing to the lack of available injecting equipment, multiple sharing does occur and it has been anecdotally reported that as many as 30 inmates can regularly share a single set of injecting paraphernalia. This obviously puts HIV seronegative drug users at great risk of acquiring HIV. A recent study of prison inmates in one US prison suggested an annual rate of infection of 0.41% per person, and the incidence of seroconversion in Stockholm Central Prison has been estimated to be 1% per year. Obviously higher transmission rates are more likely in regions with high HIV seroprevalence in drug users.

With time it became apparent that as a consequence of HIV infection in addition to trying to reduce the spread of HIV in prison some alteration in the medical care arrangements for prisoners was necessary.
Patients and Methods

As detailed in Chapter 6 during October and November 1988 the author undertook a travel fellowship to compare and contrast medical services for injecting drug users. This included visits to the prison medical services available in New York and San Francisco.

HIV medical care for prisoners in Edinburgh

Health care in Scottish Prisons is provided by the Prison Medical Service. In some of the larger prisons this service employs full time medical officers but often it is based on part time medical officers who are also general practitioners. Daily sick parades or surgeries are undertaken and specialist medical care is provided by referral to local hospitals either as in or out patients. HIV referrals to the City Hospital occurred soon after HIV testing was introduced in October 1985 either because of requests by prisoners or because known HIV seropositive individuals under care at the City Hospital had been sentenced. This was not altogether surprising in view of the fact that in one local study as many as 70% of Edinburgh injection drug users had been in prison.

HMP Saughton caters for adult male remand prisoners from South East of Scotland as well as sentenced prisoners from all of Scotland. It has a maximum occupancy of 600 prisoners who are housed on single cells and only locked up between 20.30 and 6.30 hours. In May 1991 the breakdown of inmates was 20% on remand, 28% serving sentences for less than 18 months and 52% serving sentences of longer than 18 months. There is no segregation of HIV infected individuals although they are excluded from cookhouse duties. The medical facilities consist of one full time and two part-time medical officers, one principal nurse, 2 senior nurses and 16 nurse officers. The prison has 11 "hospital beds", a treatment room, a dental suite and 3 rooms which can be used as consulting rooms. All prisoners are examined within 24 hours of admission to the prison and those identified as being at risk of HIV are offered counselling and or HIV testing.

The health care system for HIV in Edinburgh had to take into account the fact that a significant number of patients with HIV and AIDS were spending some of their time in prison. After discussions with Dr Joliffe, the medical officer and Mr Pearce, Governor at Saughton Prison Edinburgh a specific HIV medical service for the local prison was developed with the aim of improving the HIV medical care for prison
inmates. It was also hoped to reduce the large number of prison inmates and officers attending the outpatient department. This had produced considerable congestion in the outpatient department since each prisoner had to be accompanied by 2 officers. Thus on some mornings there were as many as 12 individuals in the waiting room for 4 consultations. The large number of patients having to attend was also causing staff problems at the prison and the officers accompanying the prisoners were intimidated by the fact that many of the other patients attending the department were ex inmates. It was also hoped that a specific service would reduce the number of patients "lost" to follow up by the department during spells in prison and offer inmates (whether patients of the City Hospital or not) access to the same treatment, whether standard or experimental, as available outside the prison.

In August 1989 a twice monthly HIV medical clinic was established in the infirmary of HMP Saughton. The establishment of the clinic was preceded by an exchange of nurses between the RIDU and the prison infirmary. Patients were either individuals who had already attended the City Hospital HIV clinic or were HIV positive individuals referred by the medical officers of HMP Saughton. Equally all patients known to be HIV seropositive could request a consultation with a visiting consultant via the medical officer.

The service occupied one morning session every two weeks and was undertaken except for holidays by Consultant medical staff (RPB and CLSL). The clinic took place in the prison infirmary but was physically separate from the medical surgery. All consultations were in private without prison officers or nursing staff although recommendations for treatment were passed to the medical officers both verbally and via letters. The hospital notes were used on all occasions to preserve confidentiality and as before this encouraged fuller disclosures concerning current drug use. This latter problem is important in differentiating drug use from HIV problems. The results of the service were assessed up to December 1990.

**Results**

Between August 1989 and December 1990 41 (8%) of the 501 HIV positive patients known to the City Hospital had been seen at the 32 prison clinics (117 attendances). Thirty (73%) of the patients had previously attended the City Hospital outpatient department clinic but 11 (27%) were new to specialist medical care. Twenty eight (68%) of the 41 patients were seen after their discharge from prison at the RIDU outpatient clinic. By comparison in December 1990, 80 or 16% of the City Hospital
cohort had been lost to follow up. From August 1989 to December 1990 7 (17%) of the 41 patients had been admitted to the City Hospital for inpatient treatment and one had been diagnosed with AIDS. This approximates to 11% of the prison population being admitted each year. By comparison approximately 12% of the patients known to the City Hospital were admitted each year for inpatient treatment.

By December 1990 294 (59%) of the 501 patients seen at the City Hospital were in CDC stage II or III and 207 (41%) had progressed to CDC stage IV. The prison population was similar in terms of clinical staging in that 20 (49%) of 41 patients were in CDC stage II or III and 21 (51%) were CDC stage IV.

Four patients or 8% of the 50 patients entered into the MRC\Inserm Zidovudine (Concorde) trial were enrolled from these prison clinics. In addition 14 (9%) of 155 patients who were started on open label zidovudine did so at the prison clinics and one patient continued on his zidovudine after imprisonment. Seven (11%) of 65 patients were commenced on inhaled pentamidine as prophylaxis for PCP in prison.

Review of prison services in the USA

New York

In the 1970's a fear arose in the prison service that a lack of medical care could be regarded as "cruel and unjust treatment". "Cruel and unjust treatment" was unconstitutional and therefore moves began to provide a better prison medical care system. It was decided in New York to offer the service out to tender and the Montefiore Medical Centre provided the only initial bid. Montefiore Rikers Island Health Service (MRIHS) now provides 80% of medical care for the New York City correctional service but none for the State prisons9.

Individuals arrested in New York might spend 3-5 days in Precinct prison cells or "lock ups" where there might be as many as 50 individuals per cell. Prisoners were then moved to either Rikers Island or to what was called the "Tombs" (Manhattan House of Correction for Men) which was above the lock ups in downtown Manhattan. There were 200,000 arrests per year in the lock ups and Rikers Island catered for 100,000 arrests per year of which 70,000 were separate individuals. At any one time there were approximately 11,000 individuals (10,000 males and 1,000 females) on Rikers Island, seventy five percent were under 30 years of age, 19% were under 21 and only 10% were over the age of 40. The mean length of stay on Rikers
Island was only 40 days and 40% only stayed 7 days. The majority of crime in New York is related to drugs or crime against property. It was thought that 40% of the prisoners were drug users and 19% were enrolled in a Methadone Maintenance treatment Program (MMTP) prior to imprisonment.

Rikers Island had three types of prisoners, those on remand awaiting trial, those serving a sentence of less than 1 year and those awaiting transfer to State Prisons. Prisoners sentenced to serve longer than 1 year were transferred to a State prison and at any one time there were between 1,000-5,000 (28%) prisoners awaiting transfer as a result of a lack of accommodation in the State system. Prisoners on remand as in the UK have more rights which essentially means more space, the right to wear their own clothes and the ability to move around with fewer restrictions.

The right to health for prisoners had in fact resulted in access to a better health care system for those on Rikers Island than for those on the outside. The medical system employs about 800 staff for 8 clinics which were open from 8am-4pm with emergency cover at other times provided by part time practitioners. There were approximately 70 full time doctors and physician assistants, 125 part time doctors and 200 nurses or mental health staff. Each clinic was run by a Chief of Medicine (a specialist in Internal Medicine), a Nurse Supervisor, a Social Worker and a Pharmacist. MRIHS provides 24 hour, 7 day per week health care including 3 "infirmaries". These infirmaries were not able to cope with iv infusions etc. and patients requiring more intensive medical care were transferred to a number of City Hospitals with locked wards.

All new prisoners were examined before they were assigned a cell. The clinics also provided a comprehensive follow up service of any initial medical problems as well as emergency medical care, daily walk-in clinics and specialist clinics such as Dermatology, ENT, Neurology, Ophthalmology, Orthopaedics and Surgery.

The provision of methadone to substance abuse prisoners depended very much on the sentence. Those awaiting transfer to a State prison were enrolled in a 7 day detoxification programme whilst those already in a MMTP with a discharge date within 21 days were enrolled in a 21 day detoxification programme in order to enable them to return to their programme on discharge. Lastly there was a new programme called "keep" which provided maintenance methadone for those with an early discharge date whilst an attempt was made to enrol them in a MMTP. The prisoners
had to demonstrate addiction from their past medical or prison history and current state but on the whole the programme was fairly liberal\(^9,10\).

One infirmary had recently been converted to an AIDS dormitory because the correctional system wished to house AIDS patients separately in order to avoid victimisation. There was no programme of HIV screening (unlike the federal system) unless the prisoner requested it but there were probably a lot of HIV patients in the system as judged by the medical problems being treated. The medical officers were seeing an increasing amount of TB and from the medical examinations they concluded that continued drug use was occurring\(^9\). Eight per cent of females were pregnant on admission\(^9\). Six per cent of AIDS cases in inmates in New York have concurrent TB and AIDS now accounts for 70% of inmate deaths\(^9\).

The MRIHS clinics were based on an open plan construction with 5 feet high partitions to provide the necessary confidentiality whilst ensuring security for the staff. There were dentists on site and facility for X-rays but not at all of the clinics. The nurse practitioners and clinic doctors treated patients but not necessarily the chief of the clinic who basically could do only administration if he so wished\(^9\).

\textit{San Francisco}

The SFGH had a separate locked medical ward (Ward 7D) which was part of the county jail. Access was regulated by the police and all acute medical cases, psychiatric cases etc., in police custody needing acute care were admitted there under the general medical teams. There appeared to be no system equivalent to the Montefiore Medical Centres on Rikers Island in San Francisco. Consequently they had little experience of HIV related medical problems in drug users and there was no methadone programme for prisoners\(^11\).

\textbf{Discussion}

Unfortunately to date most of the medical interest has been in the transmission of HIV in prison rather than the medical care for individuals infected with HIV. There are suggestions especially from the USA that prisoners are disadvantaged as far as medical care for HIV is concerned. For instance one study from New York State on the medical care of prisoners revealed that inmates with PCP arrived in a worse physical state than community patients with PCP; only 5% of inmates admitted were on zidovudine compared to 20% for community patients and the mortality for PCP was 23% for the inmates compared to 5% for community patients\(^12\). In addition
prisoners have considerable medical problems relating to their HIV infection; six percent of AIDS cases in inmates in New York have concurrent TB and AIDS now accounts for 70% of inmate deaths\textsuperscript{13}.

The system used in New York whereby medical care is tendered for by health care organisations seems to provide a better health care system than is available to an individual via the municipal health care system when he or she is not in prison. This situation may not of course apply to the UK but it does raise concerns over the access of inmates to specialised HIV medical care.

Efforts to improve inmate's access to specialist care have been tried. For instance in Rhode Island, USA a collaborative effort between the Brown University AIDS Program and the Department of Health and Corrections had managed to evaluate 204 newly diagnosed HIV positive inmates (a policy of mandatory testing is in place) or 3.9% of all male inmates and 12% of all female inmates. They achieved 65% follow up after discharge, improved access of inmates to expert medical care, significantly reduced health care costs by reducing need for specialist consultations outside the correctional facility\textsuperscript{14}. In France two groups, one in Paris and the other in Bordeaux have established similar systems to that in Edinburgh in an attempt to make specialist medical care available to inmates of prison. In Bordeaux 160 HIV positive inmates had received medical consultations (7.5% with AIDS), 13% were on treatment with zidovudine and 6% were receiving inhaled pentamidine\textsuperscript{15}. In Paris over 1000 inmates are HIV positive, 75 already have AIDS and access to zidovudine for advanced disease or PCP prophylaxis has been arranged\textsuperscript{16}. After discharge from prison 20% continued in medical care\textsuperscript{16}.

In Edinburgh approximately 10% of the current HIV clinic population are in Saughton prison at any one time and the clinical stage of these patients reflects that of the population as a whole. It is particularly important to note that the prison population are no sicker than the clinic population and this is in part because of the relatively short sentences that many of the patients had received. One can therefore consider the prison HIV population as a small sample of the Edinburgh HIV population and the results demonstrate that they have access to similar health care to those patients in the community. For instance 8% of the zidovudine trial patients, 9% of the open label zidovudine patients and 11% of the inhaled pentamidine treated patients have been enrolled from the prison HIV population. Disappointingly 32% of inmates were lost to follow up after discharge from prison compared to a lost to
follow up rate of 16% for the City Hospital clinic by December 1990. Thus at present the system is achieving its aims of providing prisoners access to specialised HIV care although it is not yet maintaining that contact. The results are as good as the best of the centres in the USA and apparently better than the French system with respect to follow up\textsuperscript{12,16}. Whilst these centres have reported delivering PCP prophylaxis and zidovudine to inmates to date no other centres have reported enrolment of inmates in clinical trials. In the USA there has been considerable criticism of the HIV/AIDS therapeutic trial programme in not recruiting disadvantaged groups such as women, ethnic minorities and drug users\textsuperscript{17}.

The system adopted in Edinburgh is without doubt expensive in terms of consultant time but it has ensured that patients in prison have the same availability of medical care as those in the community. Whilst not suggesting that the rest of the UK prison service should follow the same system consideration should be given to the Edinburgh model.

**Conclusions**

To date transmission of HIV in prisons has been of more concern than the medical care for individuals infected with HIV. In Edinburgh approximately 10% of the current HIV clinic population are in the local prison at any one time and their clinical stage of HIV reflects that of the HIV population as a whole.

The services instituted have provided inmates with similar access to health care as patients in the community. Thus at present the system is achieving its aim of providing prisoners with access to specialised HIV care although it is not as yet maintaining that contact after the inmate leaves prison. The system adopted in Edinburgh is without doubt expensive in terms of consultant time but it has ensured that patients in prison have the same availability of medical care as those in the community.
References for Chapter 11


8. Robertson JR. Edinburgh Drug Addiction Study. West Granton Medical Group, 1 Muirhouse Avenue, Edinburgh, EH4 4PL. Personal communication.

9. Safyer SM. Deputy Medical Director, Montefiore Medical Center, 15-15 Hazen Street, East Elmhurst, New York 11370, USA. Personal communication.


11. Kantor E. Medical Director, San Francisco County Jails, Ward 7-D, San Francisco General Hospital, Building 80, Ward 84, 995 Potrero Avenue, San Francisco, California 94110. Personal communication.


