HIV Post-Exposure Prophylaxis:

Guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS

UK HEALTH DEPARTMENTS

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INTRODUCTION

This document updates 1997 guidelines on occupational HIV post exposure prophylaxis (PEP) from the UK Chief Medical Officers' Expert Advisory Group on AIDS (EAGA)[1].

Newly included are sections which consider the issues of health care workers seconded overseas (including medical and dental students), and exposure to HIV outside the health care setting. New annexes refer to recommended drug regimens, drug resistance, drug interactions and special considerations for health care workers who are, or may be pregnant.

The main sections of this guidance apply to occupational exposure in the health care setting of health care workers to material which is known to be, or has the potential to be a source of HIV infection.

However:

Any person significantly exposed to risk of HIV infection in a health care setting (including a domiciliary care situation) should be assessed and managed according to the principles in this guidance, whether or not they are a health care worker. Examples would include relatives or friends providing care in the home, hospital domestic and waste disposal staff. If a child is exposed, specialist advice from a paediatrician with experience in the HIV field should be sought.

Those responsible for occupational health provision to people in professions where there may be a risk of exposure to HIV infected material outside health care settings (eg police, fire service, voluntary aid agencies, armed forces) may wish to use these guidelines as a basis for developing guidance relevant to their own occupational setting.

General principles

Occupational exposure to HIV and other blood-borne viruses is unnecessarily common. Many exposures result from a failure to follow recommended procedures, including the safe handling and disposal of needles and syringes, or wearing personal protective eyewear where indicated.

Prevention of avoidable exposure is of prime importance. The recommendations of EAGA and the Advisory Group on Hepatitis in " Guidance for Clinical Health Care Workers: Protection Against Infection with Blood-borne Viruses"[2], if scrupulously observed will serve to reduce the incidence of occupational exposures to a minimum. All the general principles of those recommendations, set in the context of health and safety legislation are relevant to the issue of blood-borne virus (including HIV) occupational exposure. It is important that they should be read in conjunction with this guidance.

This document concerns exposure to HIV and post-exposure prophylaxis. Any significant exposure to blood, some other body fluids or tissues (see Annex A) has the potential to transmit other blood-borne virus infections, such as hepatitis B (HBV)

and hepatitis C (HCV). Chapter 5, entitled " Management of Blood Exposure Incidents" of the 1998 EAGA/AGH guidance[2] referred to above recommends an integrated approach to post-exposure management with respect to HIV, HBV and HCV.

There will remain occasions where exposure occurs despite careful attention to the correct procedures. All exposure incidents should be reviewed to consider how recurrence might be prevented.

All health care workers in hospital and elsewhere (eg general medical and dental practitioners, community health care workers) should be informed and educated about the possible risks from occupational exposure and should be aware of the importance of seeking urgent advice following any needlestick injury or other occupational exposure. Training should ensure that everyone knows to whom to report. The guidance applies equally to students in health care settings.

Every employer should draw up a policy on the management of exposures. Each Health Authority, Health Board or NHS Trust should designate one or more doctors to whom exposed persons may be referred urgently for advice. Local policies should specify who will be responsible for provision of post-exposure prophylaxis and follow up. Occupational health services should be considered for this role, and accident and emergency departments out of hours. Sources of expert advice may also include consultants in HIV disease, genito-urinary medicine, virology, microbiology, infectious diseases and public health medicine. There should be clear channels for access to any necessary expert advice about HIV and PEP drugs.

HIV and significant occupational exposure

The risk of acquiring HIV infection following occupational exposure to HIV infected blood is **low**. Epidemiological studies have indicated that the average risk for HIV transmission after percutaneous exposure to HIV infected blood in health care settings is about 3 per 1,000 injuries. After a mucocutaneous exposure the average risk is estimated at less than 1 in 1,000. It has been considered that there is no risk of HIV transmission where intact skin is exposed to HIV infected blood.

A case control study[3] conducted by the US Centers for Disease Control (CDC) concluded that the administration of zidovudine prophylaxis to health care workers occupationally exposed to HIV was associated with an 80% reduction in the risk for occupationally acquired HIV infection. Four factors were associated with increased risk of occupationally acquired HIV infection:

1) Deep injury
2) Visible blood on the device which caused the injury
3) Injury with a needle which had been placed in a source patient's artery or vein
4) Terminal HIV-related illness in the source patient

It was estimated that the risk for HIV transmission after percutaneous exposures involving larger volumes of blood, particularly if the source patient's viral load was likely to be high,exceeds the average risk of 3 per 1,000.

Information about primary HIV infection and that derived from animal models indicates that systemic viral dissemination does not occur immediately, leaving a window of opportunity during which post-exposure antiretroviral medication may be beneficial.

In established HIV infection, the use of combinations of antiretroviral drugs are more potent than zidovudine alone in suppressing viral replication. This, together with the increased prevalence of zidovudine resistance amongst HIV infected people, has led to the introduction of combination antiretroviral drug prophylaxis following occupational exposure to HIV.

EAGA has considered the evidence for the efficacy of post-exposure prophylaxis (PEP) with antiretroviral drugs and recommends that their use should be considered in certain circumstances. Additional references[4,5,6,7,8] are included in Annex G for those who seek more detailed consideration of the accumulated evidence supporting efficacy of HIV PEP, and of potential disadvantages.

This document offers guidance on:

- assessing the risk to a health care worker of acquiring HIV infection following occupational exposure
- when to recommend PEP
- the choice of drugs
- how to ensure that all health care workers have **immediate, 24 hour access** to advice on PEP, to drugs and to appropriate support
- devising local PEP policies and protocols
- the issue of health care workers seconded overseas, including medical students on 'electives'
- the issue of PEP in relation to exposure to HIV outside the health care setting
- antiretroviral drug resistance
- laboratory workers (including virologists) who may be exposed to unusual and/or highly resistant viruses
- considerations about PEP for exposed women who are or may be pregnant

-drug interactions

RISK ASSESSMENT

1. Immediate Action

1.1 Immediately following ANY exposure - whether or not the source is known to pose a risk of infection - the site of exposure eg wound or non-intact skin should be washed liberally with soap and water but without scrubbing. Antiseptics and skin washes should not be used - there is no evidence of their efficacy, and their effect on local defences is unknown. Free bleeding of puncture wounds should be encouraged gently but wounds should not be sucked. Exposed mucous membranes including conjunctivae should be irrigated copiously with water, before and after removing any contact lenses.

1.2 The exposed health care worker should be aware about local arrangements for access to urgent advice about occupational exposure and PEP. A risk assessment needs to be made urgently by someone other than the exposed worker about the appropriateness of starting PEP, ideally a doctor designated according to local arrangements for the provision of urgent post-exposure advice. This guidance refers only to the issue of HIV post-exposure prophylaxis. Consideration should also be given to risk of exposure to hepatitis B (if the exposed worker is not immune) and hepatitis C. Guidance on an integrated approach to post-exposure management is provided in 1998 guidance from EAGA and the AGH[2].

Circumstances of Exposure

1.3 The issue of PEP should be considered after an exposure with the potential to transmit HIV, based on the type of body fluid or substance involved, and the route and severity of the exposure.

1.4 The designated doctor or other practitioner should first assess if the exposure reported by the health care worker was **significant –** that is, with the potential to transmit HIV. There are three types of exposure in health care settings associated with significant risk. These are:

a) percutaneous injury (from needles, instruments, bone fragments, significant bites which break the skin, etc);

b) exposure of broken skin (abrasions, cuts, eczema etc);

c) exposure of mucous membranes including the eye.

[Note – the history and examination may highlight the need to institute other prophylactic and investigative regimens eg antibiotic therapy, hepatitis B immunisation]

1.5 Some health care workers may have had occupational exposures which, after careful assessment, are not considered significant - i.e. they do not have the

potential for HIV transmission. Such workers should be advised that the potential side effects and toxicity of taking PEP outweigh the negligible risk of transmission posed by the **type of exposure** because it is considered insignificant, whether or not the source patient is known or considered likely to be HIV infected.

2. The Source Patient

2.1 If initial assessment indicates that an exposure has been **significant** - that is, with the potential for HIV transmission - consideration should then be given to the HIV status of the source patient. It may be possible to ascertain from the medical record that a source patient has established HIV infection. Results from animal studies suggest that HIV PEP is most likely to be efficacious if started within the hour. An urgent preliminary risk assessment therefore should assess if it is appropriate to recommend that the exposed worker takes the first dose of PEP pending the outcome of a more thorough risk assessment to inform a decision whether to continue the regimen (see also paragraphs 4.3 and 4.4).

2.2 The designated doctor should normally make arrangements to approach a source patient whose HIV status is not known and ask for their informed agreement to HIV testing. **This approach should not be undertaken by the exposed worker.** Occasionally, there may be good reason to believe that HIV infection of the source patient is highly unlikely on the basis of personal (including sexual) history, and what is known about local seroprevalence. However, a universal approach to asking source patients to agree to have HIV tests avoids the need to make difficult judgements, simplifies and normalises the process and avoids any appearance of discrimination against people perceived as belonging to groups associated with higher than average HIV prevalence.

2.3 When a source patient is asked to agree to be tested for HIV antibodies, careful pre-test discussion will be needed, as will fully informed consent (in the case of a child, from a person with parental responsibility). This pre-test discussion can be provided by any appropriately trained and competent health care worker[9]. Specialist pre-test counselling may sometimes be considered appropriate if the circumstances of the source patient are unusual or complex.

2.4 As part of pre-test discussion, or prior to asking about a history of possible exposure to HIV, the source patient should first be informed about the incident and the reason for the enquiry and request for a test. The difficulties of the exposed health care worker's situation should be discussed – either in terms of the worker not missing the opportunity to benefit from PEP, or conversely not being subjected unnecessarily to its potentially unpleasant short term and unknown long term side effects. It is understood that consent to HIV testing is rarely withheld in these circumstances, when the approach is made in a sensitive manner.

2.5 The use of codes as identifiers should be considered when requesting HIV testing of source patients and exposed workers in connection with an exposure incident, as an additional safeguard for confidentiality.

2.6 The General Medical Council's ethical statement *Serious Communicable Diseases* includes a section about injuries to health care workers and the issues of source patient testing, consent and testing of existing blood samples. It includes a consideration of situations where consent to testing for serious communicable diseases cannot be obtained, for instance in the unconscious patient. This is reproduced at Annex B and should be read in conjunction with this guidance.

2.7 Any source patient who is newly diagnosed HIV positive as a result of this process will need immediate access to specialist post-test counselling and assurances about confidentiality. Close support and clinical management will be needed on an ongoing basis. Source patients should also be informed promptly of HIV negative results, with any post-test counselling appropriate to individual circumstances.

3. The Unknown Source

If there has been a significant exposure and a source patient cannot be identified, risk assessment should be on an individual basis. This will be informed by a consideration of the circumstances of the exposure, and the epidemiological likelihood of HIV in the source. In the vast majority of such exposures, it would be difficult to justify the use of PEP.

4. PEP – when?

4.1 PEP should be recommended to health care workers if they have had a significant occupational exposure (see 1.4) to blood or another high risk body fluid [see Annex A] from a patient or other source either known to be HIV infected, or considered to be at high risk of HIV infection, but where the result of an HIV test has not or cannot be obtained, for whatever reason.

4.2 PEP should not be offered after exposure through any route with low risk materials (eg urine, vomit, saliva, faeces) unless they are visibly blood stained. Also, PEP should not be offered where testing has shown that the source is HIV negative, or if risk assessment has concluded that HIV infection of the source is highly unlikely.

4.3 When offering PEP it is important to take into account any views of the exposed health care worker. Depending on the outcome of preliminary risk assessment, if the exposure was significant, the exposed health care worker may wish to consider starting PEP until further information is available about the source patient. In this way the option of possible benefit from prompt PEP will have been kept open. Changes can be made to the PEP regimen, including cessation, as appropriate if further information becomes available.

4.4 If the HIV status of the source cannot be established, the exposed health care worker should have the opportunity to consider whether or not to continue PEP, their decision informed by all that is known about the source patient in terms of past exposure to risk of HIV infection and also the nature and severity of the exposure. These aspects should be considered together with the potential for unpleasant short-term adverse effects and unknown long-term effects of taking PEP drugs.

4.5 The relative risk of transmission may be increased considerably if the source patient has a high viral load (eg at the time of seroconversion or in the later stages of HIV disease). There is no reassurance that the converse applies ie when a source patient's viral load was low when last measured.

5. PEP – What?

See Annex C.

6. Management of health care workers occupationally exposed to HIV – further issues

6.1 Occupational exposure to known or suspected HIV infected materials is always stressful and for some, extremely so.

6.2 Although PEP ideally should be commenced as soon as possible after the event, if a longer interval has elapsed following possible exposure this may not be a contra-indication to starting therapy. The kinetics and early pathogenesis of HIV are not fully understood and it may still be worth considering starting PEP even if up to 2 weeks have elapsed since the exposure. The guidance given on risk assessment earlier in this document would still be relevant.

6.3 Following exposures for which PEP is considered appropriate, health care workers should be given time to discuss the balance of risks in their particular situation and they should be offered appropriate psychological support. They should be informed that knowledge about the efficacy and toxicity of drugs used for PEP are limited. It is important that their views about PEP are taken into account and that their preferences about what to discuss and with whom are respected. In particular, there may be someone in whom they have trust and to whom they would like to be referred.

6.4 The evaluation of the health care worker should include a medical history. Details of any existing medication should be established (including oral contraception – see Annex C, 11). Females should be asked specifically about the possibility of pregnancy [see Annex E].

6.5 It is important that all information about the health care worker and the source patient is kept confidential. Arrangements will need to be in place to ensure this, including the use of codes as identifiers where appropriate.

6.6 PEP should normally be continued for 4 weeks. Every effort should be made to facilitate adherence to a full 4-week regimen. This time course, or the drugs used may need to be modified if problems of tolerance and/or toxicity are encountered (see also Annex C). Since nausea is a common problem, the prescription of prophylactic anti-emetics should be considered. If severe nausea is experienced and is a deterrent to taking PEP, expert advice should be sought. Anti-motility drugs may be helpful if diarrhoea develops – a common side effect of nelfinavir.

6.7 Regular medical follow-up during the period of PEP is necessary to monitor acceptability and possible toxicity of the preparation(s). Close follow up and encouragement, ideally on a weekly basis at least, from an experienced occupational health practitioner, is likely to help improve adherence and deal expeditiously with concerns and complications. Any need for sickness absence associated with adverse effects of PEP drugs following an occupational exposure should preferably not contribute to an individual's sickness absence record.

6.8 In line with EAGA's HIV infected health care worker guidance[11] all health care workers occupationally exposed to HIV should have follow-up counselling, post-exposure testing and medical evaluation **whether or not** they have received PEP. All should be encouraged to seek medical advice about any acute illness which occurs during the follow up period. Illnesses characterised by fever, rash, myalgia, fatigue, malaise or lymphadenopathy may represent a seroconversion illness. Some of these symptoms may, however, be side effects of antiretroviral medication – in particular rash associated with nevirapine (a NNRTI), if used in a PEP regimen (see also Annex C, 12).

6.9 Pending follow up and in the absence of seroconversion, health care workers need not be subject to any modification of their working practices, for example avoidance of exposure prone procedures, defined according to criteria given in the guidance referred to above[11]. Advice should, however, be given about safer sex and avoiding blood donation during the follow up period.

HIV seroconversion

6.10 If during the follow up period HIV infection is diagnosed, the health care worker should be advised and managed in line with EAGA recommendations[11]. Although HIV is not a prescribed disease under the Social Security Acts, health care workers who have acquired HIV infection because of exposure to HIV infected material in the workplace may be able to claim Industrial Injuries Disablement Benefit where there has been an accident arising out of and in the course of employment, eg a significant occupational exposure such as a needlestick injury.

6.11 The NHS Injury Benefits Scheme (or HPSS Injury Benefits Scheme in Northern Ireland) provides temporary or permanent benefits for all NHS employees who lose remuneration because of an injury or disease attributable to their NHS employment. The scheme is available also to general medical and dental practitioners working in the NHS. Under the terms of the scheme it must be

established whether, on balance of probabilities, the injury or disease was acquired during the course of NHS work.

6.12 At least 6 months should elapse after cessation of PEP before a negative antibody test is used to reassure the individual that infection has not occurred. Following any occupational exposure to HIV, whether or not PEP was prescribed, health care workers should attend for occupational health follow-up for such a period, and be prepared to report symptoms of concern at any time.

6.13 The use of PEP drugs in special circumstances (eg pregnancy), the place of alternative drug regimens, and viral drug resistance drug interactions are discussed in Annex E. Drug interactions are considered in Annex F.

7. MAKING PEP AVAILABLE: Immediate access

7.1 It is recommended that, for optimal efficacy, PEP should be commenced as soon as possible after the incident and ideally within the hour. There may be circumstances where it is appropriate that the exposed worker is offered the initial doses immediately pending fuller discussion and risk assessment as soon as practicable.

7.2 Starter packs of the recommended drugs should be kept in a number of readily accessible and well advertised places including:

- Occupational Health Department
- Pharmacy
- Accident & Emergency (A&E) Department
- Specific wards or departments

7.3 Each pack should contain a 3 day course of the drugs sufficient to cover weekends and bank holidays, two packs to be given to cover longer bank holiday weekends.

7.4 Arrangements will need to be in place to ensure that starter packs are stored appropriately and that the drugs have not passed their expiry date.

7.5 Training and clear protocols should be given to personnel who might be responsible for initial administration of drugs.

8. MAKING PEP AVAILABLE: Policies and Protocols

8.1 Consultants in Communicable Disease Control or, in Scotland, Consultants in Public Health Medicine (CD & EH) should ensure that the management of Health Authorities, Health Boards, NHS Trusts and other health care settings (including primary care and private facilities) is aware of its responsibility to make adequate arrangements for staff. This would include ensuring that A&E departments are aware of, and have accepted their responsibility to provide cover, where applicable. As part of the contracting process, these arrangements should be audited.

8.2 It is recommended that every NHS Trust or other health care setting should develop a post exposure policy and a protocol. Where appropriate, standard starter packs should be available on site for use following occupational exposure. In those settings where PEP is not available on site the policy and protocol should include information about where the starter pack of drugs may be obtained.

8.3 Managers should ensure that PEP policies and protocols reflect current best practice.

8.4 To minimise delay in seeking advice about PEP it is important that all health care workers are aware of the possible risks from occupational exposure and the need to seek urgent advice following any percutaneous or other potentially significant exposure. All should be aware about how to report an exposure, and to whom. Occupational health departments should issue regular reminders to all those for whom it is responsible, including non-hospital healthcare workers who have contracted cover for post-exposure management (eg general medical and dental practitioners and their staff).

8.5 Local factors will vary between Trusts and other health care settings and first-line provision of PEP will depend on these.

8.6 Sources of expert advice should be indicated in local policies and may include:

- Consultants in Virology, Microbiology, Infectious Diseases, HIV medicine, G.U. Medicine, Occupational Health;

- Public Health Physicians (particularly those with responsibility for infection control such as Consultants in Communicable Disease Control or, in Scotland, Consultants in Public Health Medicine (CD & EH).

8.7 In NHS Trusts where there is a consultant occupational physician in post it is likely that arrangements will be co-ordinated through the occupational health department. Where there is no consultant occupational physician, hospitals may group together on a geographical basis for advice through a central consultant occupational physician.

8.8 Where there is no consultant occupational physician, the policy should specify who is responsible for provision of PEP and its follow-up according to local expertise and logistics.

8.9 In view of the need for very prompt treatment and the serious consequences of HIV seroconversion, significant occupational exposure to known or possible sources of HIV constitutes a medical emergency. Outside normal working hours, A&E Departments normally would be expected to assume responsibility for assessment of occupational exposure and PEP, and will be the first point of contact for any such exposure, whether or not this arose in the hospital. A&E staff such as junior medical staff and triage nurses will require specific training regarding assessment of the need to access immediate expert advice and about supplying an initial dose of PEP, and clear protocols to follow. As key 'stakeholders' it is important that A&E departmental staff are involved in developing and agreeing local PEP policies and protocols

8.10 In other health care settings it will be important for general medical practitioners and dental practitioners, their staff and other community health workers to ensure they have arrangements in place for have rapid access to urgent advice, and PEP where indicated. This will be particularly important for GPs and networks of carers who know they are looking after one or more HIV infected patients – for instance, in the context of terminal illness. If friends or relatives are providing clinical care to HIV infected patients in the community which involves a risk of exposure to HIV infected material, they should be advised about infection control measures to prevent exposure[2,12], and the importance of reporting any exposure incidents to the accident and emergency department without delay.

8.11 Those responsible for occupational health and safety of certain non-health care workers (such as police, fire service and prison service personnel) who may also be at risk of occupational exposure to HIV should ensure there are similar arrangements in place for access to advice in such an emergency, and assessment and treatment where appropriate.

8.12 Backup information for community health care workers via a widely publicised local helpline may be helpful as well as locally disseminated guidelines on appropriate local sources of expert advice as in paragraph 8.6 above.

8.13 It would normally be appropriate for the starter packs of PEP drugs to be made available to community based health workers through A&E Departments on a 24 hour basis.

8.14 It is suggested that local PEP policies should include the following information.

- occupational risks of HIV for health care workers;
- definition of "significant occupational exposure" (see 1.4, 1.5);
- clear protocols for post-exposure assessment, management and prescription of PEP drugs;
- rationale for therapy offered;
- sources of emergency advice and sources of subsequent support for the psychological consequences of the incident;

- out of hours access (eg when occupational health department closed);
- procedures following an occupational exposure;
- timing and duration of PEP;
- sites of starter packs;
- possible side effects of drugs and possible interactions with other medication (including 'over the counter' preparations);
- ensuring that local sources of expertise have access to appropriate training to maintain up to date knowledge of issues surrounding PEP, and to sources of expert advice for consultation where indicated, such as physicians experienced in the treatment of HIV and familiar with considerations for the use of PEP.
- arrangements for follow-up visits, follow-up testing, record keeping and confidentiality;
- voluntary reporting of occupational exposures to PHLS CDSC or, in Scotland, to Scottish Centre for Infection and Environmental Health (SCIEH) (See Annex D, paragraph 1 and 2). Some occupational exposures to HIV may be reportable under the Reporting of Injuries, Diseases and Dangerous Occurrences (RIDDOR) Regulations 1995 (See Annex D, paragraph 3-5);
- local procedures for reporting accidents and keeping lists of workers exposed to Hazard Group 3 pathogens (a requirement under Control of Substances Hazardous to Health (COSHH) Regulations 1994.

8.15 **Staff training** issues include:

- avoidance of occupational exposure to HIV by adherence to safer working practices and use of personal protective equipment as appropriate[2];
- action to be taken following possible exposure including immediate first aid. Clear information should be provided to all health care workers about where emergency advice and assessment can be obtained;
- the importance of reporting all percutaneous and other potentially significant occupational exposures according to local arrangements.
- encouraging health care workers particularly at risk to maintain awareness of the principles of PEP. Some may wish to consider the

pros and cons of PEP before any event, although views may change depending on the particular circumstances of an exposure;

- training of junior staff (eg triage nurses and junior doctors in Accident and Emergency Departments) who may be called upon to assist a colleague immediately after an incident and who may be responsible for supplying a starter pack. Detailed and clear protocols should be available.

8.16 The OH department (or other designated department for reporting blood exposures) should keep a database of exposure incidents. It is very important that all exposure incidents are reviewed, whether or not PEP was prescribed:

- to consider how recurrence might be prevented
- to inform staff training as appropriate.

Responsibility for review should be made clear. It may vary according to local arrangements for provision of occupational health services and management of exposure incidents. Hospital or Community Infection Control Teams should be involved.

9. UK health care workers seconded overseas

9.1 There are occasions when health care workers may leave the UK to work abroad, some of whom intend to return to work in the UK in the future. Included in such a group are those UK medical, dental and nursing students who travel abroad during an 'elective' period to gain experience, often in developing countries.

9.2 In the UK as well as elsewhere, it is important that all who may perform procedures which involve a risk of significant occupational exposure are well versed in the principles of blood-borne virus infection control precautions[2,15]. These principles should be introduced in medical, dental school and nursing training curricula prior to the start of clinical attachments, and as a minimum, prior to the performance of any invasive procedures such as venepuncture. At the same time, all students should be made aware of the importance of reporting any occupational exposure so that consideration can be given to the need for PEP. These messages should be reinforced at regular intervals.

9.3 The prevalence of HIV infection in some areas overseas is relatively much higher than that in the UK[16]. Infection control precautions to prevent possible blood-borne virus exposure may be more difficult to implement in some less developed countries. The likelihood of an occupational exposure, and in turn the likelihood that that exposure will be to HIV infected material, will be considerably higher in some circumstances than in the UK setting[17,18,19].

9.4 Health care workers (including students) intending to work in health care settings overseas should be advised about health and safety issues when working outside the UK, including the risk of occupational and other exposure to HIV. A Health Education Authority booklet on behalf of the UK NGO AIDS Consortium, "HIV/AIDS and working overseas: A guide for employees"[20] provides some

useful general background material, although its reference to PEP is based on the 1997 EAGA guidelines[1] which this document supersedes.

9.5 Medical, dental and nursing schools should consider developing accessible, regularly updated advice for students considering electives overseas, about measures to keep the risk to their health to a minimum. Specific consideration should be given to the risk of occupational exposure to HIV and how to minimise this.

9.6 Advice should include up to date information about the prevalence of HIV infection in the country which a student is considering for an elective. Students considering electives in high HIV prevalence situations should be made aware of the occupational consequences in terms of ability to complete dental, and medical training (if performing exposure prone procedures is necessary to achieve this). Limitation of future career choices in the event of HIV infection for a student who is able to complete training, or other healthcare worker depending on their discipline, should be carefully explained.[11] Some medical schools may advise students against involvement in clinical procedures which carry the highest risk of occupational exposure – for instance in surgery or obstetrics - in areas of high HIV prevalence.

9.7 Pre-travel briefing might include reinforcement of advice on immediate post-exposure first aid measures (see paragraph 1.1), and training on self assessment of occupational exposure as to whether an exposure is, or is not significant with the potential to transmit HIV, as considered earlier in this document (paragraph 1.5). Advice should also be given about how to make some assessment of the likelihood of HIV infection in the source, as many people who are infected with HIV in less developed countries will not have had their infection diagnosed.

9.8 Procedures should be clarified for access to urgent advice in the event of any significant occupational exposure to a source considered likely to have HIV infection. Even if not working in a major centre, it may be possible for arrangements to be in place for advice to be obtained as soon as practicable at the nearest major centre, or alternatively by phone from the UK source of expert advice to their own employer/medical school.

9.9 Employers, medical, dental and nursing schools should consider making 7-day starter packs of PEP drugs available to workers/students travelling to countries where antiretroviral therapy is not commonly available. EAGA recommends that those travelling to, and who may be occupationally exposed in countries where zidovudine resistant virus is much less likely to be encountered, should take PEP starter packs with them containing zidovudine in combination with lamivudine. Difficulties may arise if protease inhibitor drugs are taken unsupervised. Any student/other worker issued with a starter pack including a protease inhibitor should be warned about increased toxicity in the event of dehydration.

9.10 The principles about starting PEP as soon as possible after a significant occupational exposure, and the known short-term and unknown long term adverse effects should be made clear to those issued with PEP drugs.

9.11 In circumstances where it has been considered necessary to start PEP, expert advice by phone will also be needed to help the student/other worker decide whether the regimen needs to be continued for four weeks and if so, about the need for urgent repatriation. This may be appropriate if further treatment and follow up cannot reasonably be accessed in the foreign country. The possibility of insuring against the need for repatriation in the event of a medical emergency requiring treatment should be explored with the travel insurance provider, prior to leaving the UK. EAGA is aware that one medical school has negotiated an inexpensive group arrangement with a travel insurance company for urgent repatriation of students who have had significant occupational exposures overseas. The desirability of adding a protease inhibitor for the remainder of the 4-week regimen can be considered on return to the UK, or if a specialist centre can be accessed overseas.

9.12 It is important that the possibility of occupationally acquired HIV infection is specifically considered after occupational exposure in countries of high HIV prevalence, and excluded before performing exposure prone procedures in the UK[11]. On return from working abroad in countries of high HIV prevalence, health care workers including students should be asked to complete a questionnaire about possible significant exposures in circumstances of high HIV prevalence. This will alert the occupational health department for the need for any more detailed debriefing. After discussion of the risk(s) to which they may have been exposed, HIV testing may be considered appropriate (in reference[11] -paragraphs 4.5-4.6). Of the eight "probable" occupationally acquired HIV infections reported in the UK, seven were associated with exposure in high prevalence areas abroad[7,9] .

9.13 The outcomes of such debriefing will help medical, dental and nursing schools steer future students away from placings for electives where the risks to which they may be exposed – eg, by poor facilities for protecting themselves against BBVs – outweigh the possible benefits otherwise perceived.

10. Exposure outside the health care setting

10.1 For the purposes of this document, exposure outside the health care setting may include sexual exposure to HIV, sharing drug injecting equipment with someone with HIV or significant exposure to material which may be infected with HIV in any other circumstance.

10.2 Those responsible for occupational health provision to people in professions who may be at some risk of exposure to HIV infected material outside health care settings (eg police, fire service, voluntary aid agencies and the armed forces) may wish to use these guidelines as a basis for developing guidance appropriate to the particular occupational setting.

10.3 As for occupational exposure, the most effective methods for preventing HIV infection in all settings are those which protect against exposure to HIV.

10.4 No data exist on the efficacy of antiretroviral post-exposure prophylaxis following exposure to HIV other than for occupational exposure in a health care setting. EAGA is aware that some physicians have prescribed PEP outside the occupational exposure context, on an individual case-by-case basis. However, due to lack of any evidence of efficacy, at present EAGA cannot recommend in favour of, or against its use. A selection of references of relevance to this issue is provided in Annex G[21,22,23].

10.5 Exposures outside the health care setting which may give rise to requests for PEP include: rape (whether or not the HIV status of the source is known), condom breakage during sex between HIV discordant partners, and having shared drug injecting equipment. There are other circumstances where individuals may be exposed to blood or other material which may pose a risk of HIV transmission[24]. Such exposures may give rise to requests for PEP, or the need to consider it. After an exposure outside the health care setting considered to carry a high risk of HIV infection, expert advice should be sought urgently from a physician experienced in the treatment of HIV and familiar with considerations for the use of PEP. If a child has been exposed, specialist advice from a paediatrician experienced in the field of HIV should be sought.

10.6 Sexual exposure can also place a person at risk of other sexually transmitted infections, and of pregnancy. Exposure through sharing drug injecting equipment can expose a person to risk of other blood-borne virus infections (eg hepatitis B and C). Testing and follow up for other infections as appropriate should be undertaken, and the need for post-exposure prophylaxis for hepatitis B should be considered. Where unintended pregnancy is a possible outcome, emergency contraception should be offered.

10.7 Factors influencing the potential efficacy of non-occupational PEP include the probability that the sexual partner, or injecting equipment sharer is HIV infected, the likelihood of transmission by the particular exposure, the interval between the exposure and initiation of PEP, the efficacy of the drugs used, and the exposed person's adherence to the PEP regimen.

10.8 The circumstances of the exposure should inform a discussion about the perceived risk of HIV acquisition. It is recognised that the sexual exposure of greatest risk is receptive anal exposure to an HIV infected partner[24] . The risk associated with receptive vaginal exposure is of a similar order to percutaneous (occupational) exposure[25]. The risk per episode of injecting equipment exposure is probably intermediate[26]. In all circumstances published estimates of overall incidence for a particular exposure can serve only as a guide, since individual factors may increase or decrease risk. If it is known that the viral load of a source had been below the limit of detection around the time of the exposure, or consistently for a period prior to the exposure, it seems likely that the risk of HIV transmission to a sexual or injecting partner would be low[27]. Otherwise, because of the potential for fluctuation of viral load, the fact that viral load was low on the last occasion of testing does not provide reassurance that it would also have been low at the time of the exposure which is being considered.

10.9 Following occupational exposure, source patients and their records including information about past and current antiretroviral therapy and possible resistance are often available. By contrast, even when it is known or considered highly likely that a non-occupational source is HIV infected, such detail may be less readily available. In coercive situations eg rape, scant (if any) detail may be available about the source. Lack of information makes it difficult to tailor antiretroviral therapy if used as PEP for an exposed person, increasing the risk of infection with a drug resistant strain of HIV in the event of PEP failure. This outcome is all the more likely if adherence to the PEP regimen is sub-optimal.

10.10 For optimal efficacy, ideally PEP should be started within an hour of exposure (see 2.1, 7.1). Presentation following a non-occupational exposure is unlikely to be sufficiently prompt to derive maximum benefit from PEP, and the risk of its failure is consequently increased. However, longer periods from exposure are not considered an absolute contraindication to PEP (see 6.2).

10.9 A doctor considering the prescription of PEP after an exposure outside the health care setting should make an individual risk assessment of the circumstances of the exposure. If approaching the source to seek consent to HIV testing is feasible, the considerations earlier in this document (section 2) should apply.

10.10 Doctors should be aware that if PEP has the potential to be effective after non-occupational exposure, benefits are more likely in situations where:

- the risk of HIV transmission is considered high
- such exposure is considered unlikely to be repeated
- PEP can be started promptly
- good adherence to the regimen is considered likely.

10.11 Informed consent should be obtained from the exposed person prior to prescribing PEP. The exposed person's understanding of the following should be documented:

- the need to start or resume relevant measures to reduce risk of exposure to HIV
- lack of evidence of efficacy of PEP in these circumstances and the differing views of experts about its use in this context
- known side effects and unknown toxicity of the drugs to be prescribed
- the importance of close adherence which may improve any efficacy and reduce the risk of infection with drug- resistant HIV, should infection supervene despite PEP
- arrangements for follow up
- symptoms and signs which may be associated with HIV seroconversion.

10.12 All the considerations in this document which apply to the prescription of PEP after occupational exposure apply equally to non-occupational PEP from the point of a decision being reached that it is appropriate to prescribe it. In particular, Annex E is of relevance to exposed women who are or may be pregnant, including any who may become pregnant as a result of the exposure for which PEP is being considered.

10.13 To assist in the accumulation of epidemiological evidence on the use and efficacy of non-occupational PEP, any doctors prescribing it are encouraged to keep well documented records of individual cases on an ongoing basis. Such records should include:

- information about the circumstances of the exposure
- details of the source and their HIV medication if known
- the time between exposure and starting PEP
- drugs prescribed
- compliance with the regimen
- adverse effects of the drugs
- results of follow up testing for HIV infection.

Well documented records would also facilitate responses to any audits and surveillance of non-occupational PEP use in the future.

Annex A

Body fluids etc which may pose a risk of HIV transmission if significant occupational exposure occurs:

Amniotic fluid
Cerebrospinal fluid
Human breast milk
Pericardial fluid
Peritoneal fluid
Pleural fluid
Saliva in association with dentistry (likely to be contaminated with blood, even when not obviously so)
Synovial fluid
Unfixed human tissues and organs
Any other body fluid if visibly bloodstained
Exudative or other tissue fluid from burns or skin lesions
Semen
Vaginal Secretions

Annex B

Extract from *Serious Communicable Diseases*: General Medical Council 1998

Injuries to health care workers

8. *If you or another health care worker has suffered a needlestick injury or other occupational exposure to blood or body fluids and you consider it necessary[1] to test the patient for a serious communicable disease, the patient's consent should be obtained before the test is undertaken. If the patient is unconscious when the injury occurs consent should be sought once the patient has regained full consciousness. If appropriate, the injured person can take prophylactic treatment until consent has been obtained and the test result is known[2].*

9. *If the patient refuses testing, is unable to give or withhold consent because of mental illness or disability, or does not regain full consciousness within 48 hours, you should reconsider the severity of the risk to yourself, or another injured health care worker, or to others. You should not arrange testing against the patient's wishes or without consent other than in exceptional circumstances, for example where you have good reason to think that the patient may have a condition such as HIV for which prophylactic treatment is available. In such cases you may test an existing blood sample, taken for other purposes[3], but you should consult an experienced colleague first. It is possible that a decision to test an existing blood sample without consent could be challenged in the courts, or be the subject of a complaint to your employer or the GMC. You must before be prepared to justify your decision.*

10. *If you decide to test without consent, you must inform the patient of your decision at the earliest opportunity. In such cases*

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[1] Wherever possible you should consult an occupational health physician or other suitably qualified colleague before making a decision about testing.

[2] Post-exposure Prophylaxis for Health Care Workers Exposed Occupationally to HIV. Expert Advisory Group on AIDS, UK Health Department, 1997.

[3]Taking blood from a patient without consent may leave you open to criminal charges.

confidentiality is paramount: only the patient and those who have been exposed to infection may be told about the test and its result. In these exceptional circumstances neither the fact that the test has been undertaken, nor its result, should be entered in the patient's personal medical record without the patient's consent.

11. *If the patient dies you may test for a serious communicable disease if you have good reason to think that the patient may have been infected, and a health care worker has been exposed to the patient's blood or other body fluid. You should usually seek the agreement of a relative before testing. If the test shows the patient was a carrier of the virus, you should follow the guidance in paragraphs 22-23 of this booklet on giving information to patients' close contacts.*

Annex C

PEP – what?

1. Antiretroviral agents from at least 3 classes of drugs have been licensed for the treatment of HIV infection, including:

   - nucleoside analogue reverse transcriptase inhibitors [NRTIs]
   - non-nucleoside reverse transcriptase inhibitors [NNRTIs]
   - protease inhibitors [PIs].

2 .Zidovudine (an NRTI) is the only drug to date which has been studied and for which there is evidence of a reduction of risk of HIV transmission following occupational exposure [3]. It continues to be reasonable that zidovudine is included in all first choice PEP regimens.

3. No antiretroviral drug has been licensed for post-exposure prophylaxis. These drugs can be prescribed for PEP only on an 'off-label' basis since their use in this context is outside approved indications.

4. In HIV infected patients, combination drug therapy has proved more effective than zidovudine alone in reducing viral load. In theory, a combination of drugs could increase potency of post-exposure prophylaxis and offer increased protection, in view of the increased prevalence of resistance to zidovudine and other antiretrovirals.

5. Information about the virus present in the source patient and, if known, any sexual partner of the source patient, will be relevant when choosing appropriate PEP drugs. Similarly, information about the source patient's (and his or her sexual partner's) previous and current antiretroviral therapy may also be important. Any information available in the source patient's medical record about antiretroviral drug resistance should be used to inform choice of PEP drugs [see Annex E]

6. Since 1997 the recommended drugs for PEP starter packs have been zidovudine, lamivudine and indinavir, taken for 4 weeks as follows:

   zidovudine 200mg t.d.s or 250mg b.d.

   <u>plus</u>

   lamivudine 150mg b.d.

   <u>plus</u>

   indinavir 800mg t.d.s.

These drugs are still considered a reasonable choice, but poor tolerability in some circumstances has been considered attributable to indinavir. It is now recommended that the following regimen is an acceptable alternative, and may be considered when starter packs are being renewed:

zidovudine 200mg t.d.s or 250mg b.d.

plus

lamivudine 150mg b.d.

plus

nelfinavir 750mg t.d.s or 1250mg b.d.

7. Nelfinavir, a protease inhibitor has become available since the 1997 EAGA guidelines were issued. In comparison with indinavir, an advantage of nelfinavir is the option of twice-rather than three-times daily dosage, and it need not be taken on an empty stomach. It can, however, cause diarrhoea (see 12).

8. Soft-gel saquinavir (a more bio-available saquinavir formulation) is another possible alternative to indinavir. For tailoring of individual PEP regimens, differences in the side effect profiles of these drugs may influence which is selected. It should be noted that for both nelfinavir and soft-gel saquinavir, more tablets/capsules need to be taken each day (9 or 10, and 16 or 18 respectively) than for indinavir (6). In some cases this factor may affect adherence.

Side effects

9. All of the antiretroviral agents have been associated with side effects. Many of these can be managed symptomatically. Side effects of the NRTIs (eg zidovudine and lamivudine) have been mainly gastrointestinal (eg nausea, vomiting). Malaise, fatigue and headache have also been reported. Some experts consider that stavudine may be substituted for zidovudine as a means of reducing adverse effects, and others consider that zidovudine should not be omitted from any PEP regimen (see 2. above).

10. Those providing advice on and protocols for prescribing PEP should maintain awareness of advances in HIV therapeutics, potential side effects, adverse drug reactions and drug interactions, and seek further expert advice where necessary.

11. Protease inhibitor drugs may have potentially serious interactions with other prescribed drugs. The examples provided below are by no means exhaustive. Some further examples, and sources of further advice about drug interactions are provided at Annex F.

12. Nelfinavir frequently causes diarrhoea. It may accelerate the clearance of certain drugs including oral contraceptives, resulting in reduced contraceptive efficacy. Protease inhibitors have been associated with new onset of, and exacerbation of existing diabetes mellitus. Kidney stones and rare cases of haemolytic anaemia have been associated with indinavir.

13. Both NNRTIs licensed for treatment (nevirapine and efavirenz) are associated with short term toxicity, nevirapine with the potential for severe rashes [which may be confused with rash associated with HIV seroconversion] and sometimes Stevens-Johnson syndrome. Efavirenz is associated with neurological side

effects but has a lower incidence, and severity of rash. For these reasons they have not yet been recommended for inclusion in PEP regimens. There has been some recent interest in the potential for nevirapine for use as PEP in light of published evidence of its efficacy in reducing vertical transmission of HIV[14]. Further evidence in this area will be kept under review.

14. If symptoms believed to arise from PEP are distressing, cannot be managed symptomatically and the health care worker feels unable to continue to adhere to the regimen, expert advice should be sought about suitable substitutions. This process should be informed, as before, by considerations of the source patient's antiretroviral history if known. Adverse reactions associated with anti-retroviral drugs should be reported to:

    HIV Adverse Drug Reactions Reporting Scheme
    Medicines Control Agency
    Market Towers
    1 Nine Elms Lane
    London SW8 5NQ

    Telephone: 0207 273 0710

15. Any drug regimen should take into account the following factors:

- ♦ whether the health care worker is, or may be pregnant (see Annex E);
- ♦ whether the health care worker has an existing medical condition
- ♦ when the potential for interaction with other medications is recognised (see Annex F);
- ♦ when there is a possibility that the virus may be resistant to one or more of the drugs, or where the exposed health care worker has been handling resistant virus in a laboratory (see Annex E).

In all these circumstances expert advice should be sought.

16. There may be local variations in the choice of regimen used. As newer antiretroviral drugs are developed, it is likely that other drugs will become the preferred regimen for PEP. Managers should ensure that PEP policies and protocols reflect current best practice.

Reporting of occupational exposures to HIV

Reporting to PHLS Communicable Disease Surveillance Centre (CDSC) or, in Scotland, to Scottish Centre for Infection & Environmental Health (SCIEH)

1. Occupational health physicians and clinicians involved in the care of health care workers are encouraged to report occupational exposure to HIV (in complete confidence) to CDSC or SCIEH. By doing this, central data can be analysed so that:

- the size of the problem and the degree of risk can be quantified;
- working practices and procedures which are particularly risky may be identified;
- the side effects and benefits of prophylaxis may be assessed.

2. For further details and reporting forms please contact PHLS AIDS Centre, CDSC, 61 Colindale Avenue, London NW9 5EQ (Tel. 020 8200 6868) or, in Scotland, SCIEH, Clifton House, Clifton Place, Glasgow, G3 7LN (Tel. 0141 300 1100).

Reporting of Occupational Exposure to HIV to the Health and Safety Executive (HSE)

3. In the event of exposure to HIV, employers may be required to report the event to HSE under the Reporting of Injuries, Diseases and Dangerous Occurrences (RIDDOR) Regulations 1995. The most likely requirement, if any, may be the need to report a **dangerous occurrence**; namely *"any accident or incident which resulted or could have resulted in the release or escape of a biological agent likely to cause severe human infection or illness"*.

4. Cases of HIV infection resulting from exposure in the health care setting will also normally be reportable as **diseases** within the meaning of RIDDOR.

5. More detailed guidance on the requirements of RIDDOR can be obtained from the HSE [for details of your local HSE, contact Health and Safety Information 0541 545500].

Annex E

PEP: Special circumstances

Viral drug resistance:

Source Patient

Resistance should be suspected if there has been prolonged treatment with any antiretroviral, where there is clinical progression of disease or a persistently increasing viral load and/or a decline in CD4 lymphocyte count despite therapy, or a lack of virological response to a change in therapy. Antiretroviral drug resistance profiling is available in some centres, and its results, if available, should be taken into account when selecting PEP drugs. Specialist advice should be sought.

Laboratory Staff

Similarly, in the case of laboratory-based staff, knowledge about the source virus may be very important. This would be the case particularly if a virus with multiple nucleoside analogue resistance and/or protease inhibitor resistance was being handled.

Pregnancy

Pregnancy does not preclude the use of HIV PEP. Expert advice should always be sought if PEP is considered indicated for a female health care worker who is pregnant, after assessment of the circumstances of the exposure and of the source patient. Urgent pregnancy testing should be arranged for any female worker who cannot rule out the possibility of pregnancy, as part of the evaluation prior to the exposed worker reaching a personal, informed decision about starting PEP.

The available evidence is that zidovudine and lamivudine are not contraindicated in the second and third trimesters of pregnancy. Whilst experience is not extensive, there has been no indication of particular problems for the babies of HIV infected women who have become pregnant whilst already on antiretroviral medication. It should be noted that there is limited experience of the use in pregnancy of some of the newer drugs, including NNRTIs and protease inhibitors.

A pregnant health care worker who has experienced an occupational HIV exposure should be counselled about the risks of HIV infection, about the risks for transmission to her baby, and about everything that is known and not known about the potential benefits and risks of antiretroviral therapy for her and her baby, to help her reach an informed personal decision about the use of PEP.

Decisions on the use of specific drugs in pregnancy may be influenced by their individual adverse effects. For example, drugs which may cause nausea may exacerbate pregnancy-associated nausea.

The British HIV Association has published guidelines for prescribing antiretroviral therapy in pregnancy [13].

Annex F

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