Sex and health

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In the UK, sexually transmitted infections (STIs) of all kinds are rising ever upward in incidence and prevalence. Complicated STIs can present in a number of guises to a wide range of different specialties. Human immunodeficiency virus (HIV) is the 'great mimicker' of our times, and unfortunately the original 'great mimicker' (syphilis) is back with us too.

This conference was addressed to general physicians and those in genitourinary (GU) medicine as an update on how we can expect sexually transmitted infections and related problems to present to non-GU physicians.

Explosion of STIs – why you should be worried about your teenager

The programme was opened by Dr Kevin Fenton, who had received unprecedented media interest in his lecture, resulting in an article in the previous day's *Daily Mail* urging that we encourage teenagers to abstain from sex.

Rates of all sexually transmitted infections are increasing by alarming proportions in the UK. In the last six years, chlamydia has increased by 108%, gonorrhoea by 87% and infectious syphilis by 486%. The burden of this falls on young people. In 2001, 42% of women with gonorrhoea and 36% of women with chlamydia were under 20 years of age.

Risk of acquisition of an STI is strongly predicted by sexual behaviour and, using information from the National Survey of Sexual Attitudes and Lifestyles (NATSSAL), it is possible to pick out the trends driving the epidemic in younger age groups. These include lower age at first intercourse, frequent changes of partner, increased likelihood of concurrent partnerships (overlapping of sexual partners), inconsistent condom use, and increased likelihood of having a partner from a high-risk area of the world outside the UK. Young age is also a predictor of increased likelihood of re-presenting with an STI.

Because of high rates of STI carriage and their sexual behaviours, young people act as a 'core group' for the risk of onward transmission to other groups. In order to plan interventions to prevent these transmissions, it is this core group that needs to be targeted. Economic benefits would follow from the prevention of STIs and their sequelae, with likely positive overlap to areas such as teenage pregnancy, substance abuse and social exclusion.

The young must be specifically targeted. The timely start of the national chlamydia screening programme for young women should be helpful. The reasons why young people are at such increased risk of STI needs to be further researched.

Hepatitis B and C co-infection with HIV

Hepatitis B and HIV

Before the availability of anti-retrovirals (ARVs), hepatitis B was of little relevance to HIV-infected patients, as a functioning immune system is necessary for the adverse clinical effects of this virus. Now, with longer lifespan and an effective immune system in patients being treated for HIV, the hepatitis B virus is causing hepatotoxicity. This is further complicated by the fact that many HIV drugs are in themselves hepatotoxic.

Lamivudine and tenofovir are drugs with good activity against both HIV and hepatitis B. There is no clear consensus as to when they are best used in co-infection. Current thinking suggests that if they are to be used in dual-infected patients, they should be used together to avoid development of lamivudine-resistant virus. It is important to remember that suddenly stopping lamivudine is likely to cause a flare in active hepatitis.

Hepatitis C and HIV

Hepatitis C is not very efficiently transmitted through sex. Gay men are probably at greater risk than heterosexuals, with a prevalence rate of 4–8%. Acute hepatitis C is easily missed, especially as the antibody test can take months to become positive. If in doubt, a PCR test (a nucleic acid based test) should be done.

HIV affects hepatitis C by hastening progression to liver disease. Hepatitis C has an adverse affect on the expected CD4 cell rise when a person is commenced on anti-retrovirals. In addition, anti-retrovirals are more likely to be toxic in someone with pre-existing liver disease.

Gold standard therapy for someone with hepatitis C alone is ribavirin (RBV) and pegylated interferon

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This joint conference with the Medical Society for the Study of Venereal Diseases was held at the Royal College of Physicians on 30 September 2003

Clin Med 2004;**4**:181–4

(PEGinf). Trials are ongoing to see whether this is also the case with dual infection with HIV. Results of the APRICOT (AIDS Pegasys Ribavirin International Co-infection Trial) study comparing PEGinf/RBV with Interferon/RBV are expected in 2004. Previous trials have shown a 33% sustained response with PEGinf/RBV in co-infected patients compared with 55% in non-HIV patients.

Key elements of treatment for hepatitis C co-infection are:

- to work closely with liver units where there is liver disease
- to treat where there is a moderate degree of liver disease
- 48 weeks of therapy for hepatitis C genotypes 1 and 4, as opposed to 24 weeks for genotypes 2 and 3
- optimise HIV therapy prior to commencing hepatitis C treatment, or treat hepatitis C before HIV if the CD4 count is good.

The results of the APRICOT study should improve understanding of how best to treat this group. There is also hope in the development of new drugs such as new protease inhibitors and helicase inhibitors.

Conference programme

- **Explosion of STIs – why you should be worried about your teenager**
  Dr Kevin Fenton, Royal Free and University College Medical School, London
- **Hepatitis B and C and co-infection with HIV**
  Dr Janice Main, Imperial College, St Mary's Hospital, London
- **What the general physician should know about the metabolic complications of anti-retroviral therapy**
  Dr Edmund Wilkins, North Manchester General Hospital
- **Syphilis in the twenty-first century: the great imitator returns (again)**
  Professor Edward Hook III, University of Alabama, Birmingham, USA
- **How to take a sexual history in a general medicine setting**
  Dr Simon Barton, Chelsea and Westminster Hospital, London
- **Recognising STIs and HIV on the acute medical take**
  Dr George Kinghorn, Sheffield Teaching Hospitals NHS Trust
- **Mycoplasmas as sexually transmitted infections – where we are now?**
  Dr Patrick Horner, Bristol Royal Infirmary
- **Sexually acquired reactive arthritis**
  Dr Andrew Keat, Northwick Park Hospital, Harrow
- **Debate – 'Health promotion is a waste of time'**
  Proposer: Professor Graham Hart, MRC Social and Public Health Sciences Unit, Glasgow
  Opposer: Dr Judith Stephenson, Royal Free and University College Medical School, London

What the general physician should know about the metabolic complications of anti-retroviral therapy

ARV drug therapy has had a massive positive effect on patient care since the advent of triple therapy. However, it is important to remember that there are many potentially serious toxicities of the drugs in both the long- and the short-term, with metabolic complications being some of the most important.

There are three main classes of anti-HIV drugs with different and overlapping toxicities. There are two major mechanisms for metabolic toxicity:

1 Mitochondrial toxicity – mainly from nucleoside reverse transcriptase inhibitors (NRTIs) – causes pancreatitis, lactic acidosis and hepatic steatosis.

2 Insulin resistance – mainly from protease inhibitors (PIs) – causes hyperglycaemia/diabetes, hyperlipidaemia and cardiovascular disease.

See Table 1 for a full list of toxicities secondary to anti-retroviral drugs.

Many of these toxicities overlap in the resultant diseases they cause, with lipid abnormalities, insulin resistance and diabetes all being major risk factors for cardiovascular disease. Indeed, the recently published DAD (Data collection on Adverse events of anti-HIV Drugs) study has shown an increasing incidence of myocardial infarctions as patients spend longer on ARVs. This means very aggressive steps need to be taken to reduce as many cardiovascular risk factors as possible, particularly in patients on PIs.

Syphilis in the twenty-first century: the great imitator returns (again)

Treponema pallidum is a tricky organism. It can only be seen with dark field microscopy, as it is too narrow for standard light microscopy. It cannot be cultured, limiting our understanding. It has a division time of 33 hours to five days, giving it a very long incubation period and necessitating that treatment is a prolonged course of antibiotics.

Today's serologic tests are based on those devised in the 1930s, and not very much has changed since. The tests are good for the majority but have problems with biological false-positives, false-negatives in early infection, and difficult interpretation in pregnancy, in those with collagen diseases and in the previously infected (one in five of all new diagnoses in the USA).

The genetic sequence of syphilis is now known and it is hoped that this will provide a gateway to new and more accurate ways of testing.

The best and recommended treatment for syphilis is penicillin, which has been used for decades with no development of resistance. Administration has to be intramuscular (IM) or intravenous (IV) and is therefore painful. The oral alternative is a prolonged course of doxycycline, which is difficult to take and has a higher rate of treatment failure. New therapies are emerging, with limited data showing efficacy of daily IM injections of ceftriaxone 1 g. Azithromycin shows great promise in early syphilis, compares well with standard therapy and has the

advantage of being an oral preparation with only one or two doses a day. Results of large multi-centre trials are awaited.

Syphilis is an eminently controllable illness. There is no animal reservoir; we have reliable diagnostic tests; and there is safe and effective treatment, which is both curative and preventive. So why are we in the upsurge phase of yet another epidemic? In both the USA and the UK, men who have sex with men (MSM) largely account for this most recent outbreak, with some spread to the heterosexual community. Elimination of the infection requires enhanced surveillance and strengthened community involvement, alongside intervention strategies, including rapid outbreak response services, expanded laboratory services and increased education and health promotion for professionals and at-risk groups. However, there are still barriers to this process. We have limited understanding of endemic syphilis from which all epidemics arise. And until the ignorance and stigma associated with sexually transmitted infections can be dispelled, we will continue to have these epidemics.

Table 1. Fatal, irreversible and reversible effects of anti-retroviral drugs.

Toxicities	Nucleoside reverse transcriptase inhibitors	Protease inhibitors
Fatal toxicities		
Pancreatitis	Stavudine/didanosine	
Lactic acidosis	Stavudine/didanosine	
MI or CVA		APV/IDV/LPV/NFV/RTV/SQV*
Guillan-Barré	Stavudine/didanosine	
Irreversible toxicities		
Lipoatrophy		APV/IDV/LPV/NFV/RTV/SQV*
Buffalo hump		APV/IDV/LPV/NFV/RTV/SQV*
Avascular necrosis		Possible PI effect
Peripheral neuropathy	**Zalcitabine/stavudine**	
Mainly reversible toxicities		
Central fat accumulation		APV/IDV/LPV/NFV/RTV/SQV*
Hypercholesterolaemia		APV/IDV/LPV/NFV/RTV/SQV*
Hypertriglyceridaemia		APV/IDV/LPV/NFV/RTV/SQV*
Hyperglycaemia/ diabetes		APV/IDV/LPV/NFV/RTV/SQV*
Renal tubular dysfunction	Nucleotide RTIs, eg tenofovir	
Hepatic steatosis	All, particularly stavudine	

CVA = cerebrovascular accident; MI = myocardial infarction; RTI = reverse transcriptase inhibitor.
*Key to abbreviated protease inhibitor names: APV = amprenavir; IDV = indinavir; LPV = lopinavir; NFV = nelfinavir; RTV = ritonavir; SQV = saquinavir.

Recognising STIs and HIV on the acute medical take

Sexual health workers often refer to 'risky sex', but what is it? Sexual activity is a normal human behaviour and probably most sex that occurs does so with some degree of risk. So if all sexually active people are potentially at risk, how do we judge when a symptom or sign should result in including an STI in the differential diagnosis, other than to ask the specific sticky questions that physicians might prefer to avoid? The mantra on this seems to be: never pre-judge a patient's sexual history or orientation from superficial appearances.

STI complications can present anywhere: to the urologist with epidydimitis; to the gynaecologist with a Bartholin's cyst; or to a surgeon who has a young woman apparently with appendicitis or cholecystitis when in fact she has peri-appendicitis or perihepatitis secondary to *Chlamydia trachomatis*. Systemic manifestations of STIs are perhaps more likely to present to general physicians. Genital symptoms may be absent and the sexual contact leading to infection may have occurred some time before.

Disseminated gonococcal infection can present as a flitting polyarthralgia mainly affecting peripheral joints. The typical pustular skin lesions may be present, and rarely septic arthritis, meningitis or endocarditis can occur. Genital symptoms are generally absent, but the best chance of diagnosis comes from genital sampling.

Syphilis has been discussed above but some clinical aspects, such as the secondary and later stages of syphilis, have widespread manifestations. Acute infectious syphilis in the secondary phase may show features of fever, malaise, generalised macular-papular rash, mucous membrane ulceration, iritis and neurological problems such as meningoencephalitis and transverse myelitis. Late stage neuro-syphilis with Argyll-Robertson pupils and tabetic crises are largely a thing of the past. Patients may present with a more insidious onset of neurosyphilis, with mild confusion and disorientation.

HIV seroconversion can be a non-specific illness which may present with rash, sore throat, fever, lymphadenopathy, encephalitis/meningitis or thrombocytopenia. It is an important diagnosis as it may be years before the patient would next present, leaving a missed opportunity for prevention of onwards transmission and optimum treatment of that patient. Late stage HIV can present in a myriad of ways affecting any system. It is unusual to find anyone with late stage HIV who has no skin problems. Facial molluscum, herpes simplex and multidermatomal zoster are all common. Oral hairy leukoplakia and candidiasis are easy signs to spot in the mouth. It is well documented that patients with HIV can present on numerous occasions to different doctors before the diagnosis is made.

Keeping an open mind and asking the right questions will often be the key to this diagnosis.

Sexually acquired reactive arthritis (SARA)

Reactive arthritis is defined as an arthritis caused by a localised infection elsewhere in the body. The link between STIs and arthritis has been known for nearly 200 years, but there is still much that is unknown about this phenomenon. Reiter's syndrome (the classic triad of urethritis, arthritis and conjunctivitis) is a term we think specific, but in fact it is only part of the spectrum of spondylo-arthropathies which all share similar features.

The diagnosis of sexually acquired reactive arthritis is still mainly clinical, based on signs and a good sexual history, with recently diagnosed or likely STI. Most reactive arthritis is seen within one month of acquisition of an STI, although there are no hard data to back this up.

All spondylo-arthropathies are associated with HLA-B27, but it is not generally helpful in diagnosis. As for management of this problem, there is conflicting evidence. Studies seem to show that early effective STI treatment is helpful in preventing SARA, but that once the problem has been acquired, long-term antibiotics are of little benefit.

Sexual history taking in a general medical setting

The information given above should be a convincing argument for the taking of a sexual history in a general medical setting. This is not an easy task, as privacy on a ward can be difficult to secure, and patients may be embarrassed and suspicious of the questions. The sexual history enables a judgement to be made of someone's risk of STI and also allows feedback to be given about risk-taking behaviour.

Important questions to ask may be: When did you last have sex? Was that with a man or a woman? Did you use condoms? What kind of sex did you have – vaginal/oral/anal? How long have you been with your partner? When did you last have sex with a different partner?

An eight-point plan on how to go about sexual history taking is as follows:

1. Ensure privacy and confidentiality.
2. Act in a professional manner.
3. Be open minded and non-judgemental at all times.
4. Try to recognise any non-verbal clues.
5. Do not over-medicalise the terms that you use.
6. Only ask appropriate questions; you should be able to explain the rationale behind every question.
7. Explain procedures/treatments thoroughly.
8. Use the time to promote risk reduction and good sexual health.

Mycoplasmas as sexually transmitted infections – where are we now?

An update on the roles of mycoplasmas and ureaplasmas in the causation of genital tract disease was given. The pathogenesis of these organisms is still not clear. *Mycoplasma genitalium* has a definite association with pelvic inflammatory disease and probably causes urethritis in males. Ureaplasma may cause urethritis but is more usually just a commensal.

These organisms are not routinely tested for at present. Routine diagnostic testing for *M genitalium* would benefit patient care, but it is still unclear whether testing would be cost-effective.

'Health promotion is a waste of time' – a debate

This was the motion debated by two of the UK's leading researchers into health promotion. It was a humorous, lively and fascinating half hour. Although he lost, top marks should go to Professor Graham Hart who convincingly argued for something he obviously believes passionately. Dr Judith Stephenson won, arguing against the motion. Interestingly, most of her points were to do with the success of smoking cessation campaigns, as opposed to data regarding STIs/HIV. The key with the anti-smoking campaigns has been sustained, large-scale and increasingly brutal campaigns. Dr Stephenson concluded that, with the correct message put across simply and consistently, health promotion can be an effective tool in improving the health of the public.