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News

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The National Anonymous Tonsil Archive: a resource for Creutzfeldt-Jakob disease studies

The National Anonymous Tonsil Archive (NATA) study will begin tonsil collection and archiving on 1 December 2003, starting in London and the south east of England. The archive will establish an unlinked anonymous collection of prospectively collected tonsil tissue from 100,000 individuals undergoing routine tonsillectomy. This will be used to study the population prevalence of abnormal prion protein, the agent believed to be responsible for variant Creutzfeldt-Jakob disease (vCJD).

The project is to be coordinated by the CJD Team at the Health Protection Agency (HPA) Communicable Disease Surveillance Centre (CDSC) and the TSE (transmissible spongiform encephalopathy) Unit at the Specialist and Reference Microbiology Division and will involve the collaboration of ear, nose, and throat and histopathology departments in approximately 100 hospitals throughout England, with arrangements currently underway to secure the participation of hospitals in Wales, Northern Ireland, and Scotland. It is anticipated that the first hospitals to have tonsil collection procedures implemented will be the London-based hospitals. Between March 2004 and September 2005, the number of participating trust sites will increase to include most NHS trusts that regularly undertake tonsillectomies.

Variant CJD is a TSE first identified in the United Kingdom (UK) in 1996 (1). Data indicate that vCJD is the human manifestation of infection with the abnormal prion protein that causes bovine spongiform encephalopathy (BSE) in cattle, most probably as a result of dietary exposure to the BSE agent before 1996, after which it was effectively prevented from entering the human food chain (2). Unfortunately, predicting the likely number of vCJD cases with any certainty is difficult. Although the number of cases so far identified is relatively small (by 6 October 2003, a total of 143 cases had been reported to the National CJD Surveillance Unit, Edinburgh: <http://www.cjd.ed.ac.uk/>), it is conceivable that a very large number of people are infected. Planning of interventions to limit the impact of the vCJD epidemic, and of care provision for those who will develop the disease, would be greatly improved if reliable estimates of the prevalence of vCJD infection in the population could be derived.

A distinctive feature of vCJD is the widespread distribution of the infective abnormal prion protein in peripheral lymphoid tissue, where it can be best detected in the tonsils (3). This protein may also be detected during pre-clinical infection, so peripheral tissues offer the opportunity to study the population prevalence of asymptomatic vCJD. The potential exposure of the UK population to the BSE agent through diet in the late 1980s and early to mid-1990s was very large. For those born after 1995, this exposure was less likely. As the median age of onset of vCJD is 26 years, it is anticipated that young adults will have the highest prevalence of detectable abnormal prion protein. Unlinked anonymous studies have been carried out since 1997 to look at the prevalence of detectable abnormal prion protein. The largest study undertaken so far detected one positive specimen among 8318 appendix and tonsil specimens removed between 1995 and 1999 from people aged from 10 to 50 years (4). This gave an estimated prevalence of 12 per 100,000 people in this age band, but with very wide 95% confidence intervals. In order to provide more precise prevalence estimates, tonsils from closer to 50,000 patients from this age group would need to be included.

It is proposed that the archive will include tonsil specimens from patients of all ages. Younger children could act as an important negative control group, as they are unlikely to have been exposed to the infective agent through the consumption of contaminated bovine material. The archive team aims to collect tonsils from 100,000 patients. As 49% of tonsillectomies are carried out on children aged under nine years, this total would include sufficient numbers of

patients from the older age groups that are considered most at risk. It is anticipated that the study will need to operate for three years to collect this many specimens. Work on the Tonsil Archive needs to begin as soon as possible because as the cohort of the UK population that was exposed to the BSE agent through its diet grows older, the availability of tonsils from this cohort will diminish.

To ensure patients are not harmed or disadvantaged by the inclusion of their specimens in this study, the archive will be established on an unlinked anonymous basis – a method already used to monitor HIV prevalence in the UK since 1989. This will require that all specimens be irreversibly anonymised before archiving and will ensure that there is no possibility of tracing the identity of the individual from whom the tissue originated. Moreover, only tissue that is removed at routine operation, and not required for further examination as part of the patient's medical care, will be collected for the archive. Residual tonsil tissue remaining in the tonsil bed after surgery is likely to be sufficient to allow a biopsy of tonsil tissue should this be required for a diagnostic purpose at any time in the future. There is no obvious benefit for an individual knowing the result of tests on their own tonsils as the prognostic significance of a positive test for abnormal prion protein in an asymptomatic person is not known and there is no effective treatment for vCJD. Potentially serious psychological harm may, however, arise if an asymptomatic person, positive for abnormal prion protein, is told they might be incubating a fatal and incurable neurological illness.

An opportunity will be provided for patients to object to having their specimens included. An additional paragraph, with an accompanying tick-box, will be incorporated into the operation consent forms should the patient wish to object. The Department of Health and Medical Research Council support the use of the unlinked anonymous technique on tonsil specimens without consent, provided there is an effective means of publicity and opportunities for patients to ask questions (5). Leaflets distributed to healthcare staff, and to patients prior to admission, will provide adequate information on the archive and the mechanism for objecting. Emergency tonsillectomies will be excluded from the study.

More information about NATA can be found on the HPA website at <http://www.hpa.org.uk/infections/topics_az/cjd/tonsil_archive.htm>.

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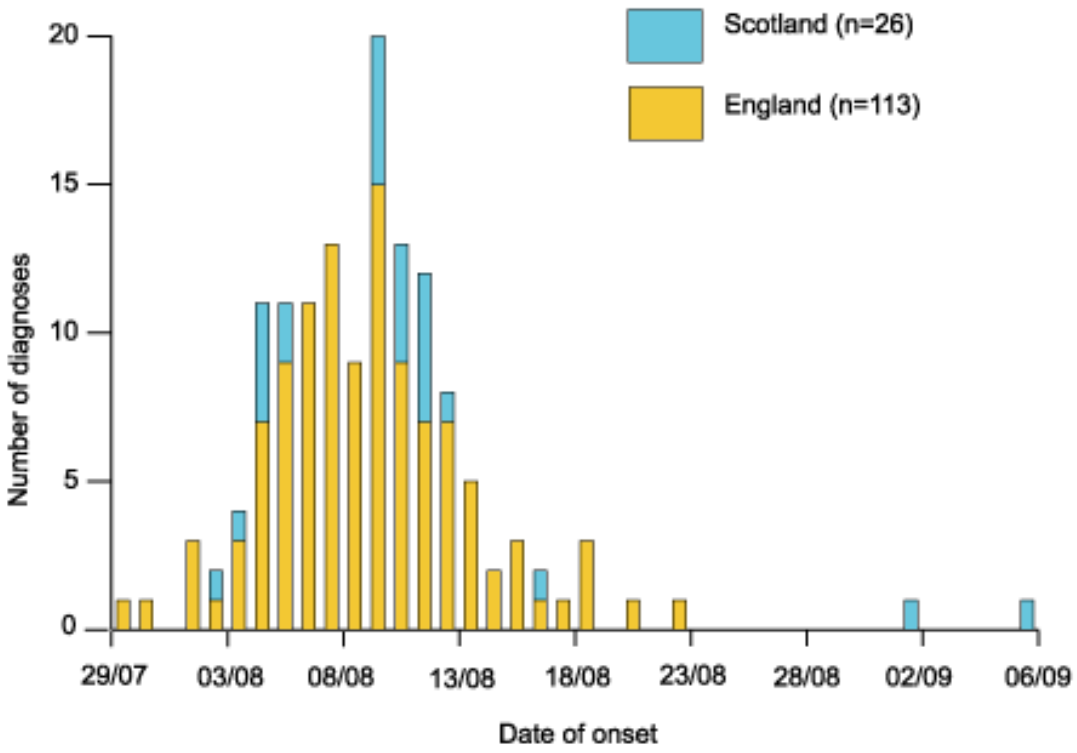
National increase in *Salmonella* Bareilly infection: update

The Great Britain-wide outbreak of *Salmonella* Bareilly infection reported previously (1,2) is now over. One hundred and eighty-six cases were identified: 160 from England and Wales and 26 from Scotland. Cases ranged in age from under 1 year to 93 years. Dates of onset of illness ranged from 29 July and 6 September (figure 1).

Figure 1 Outbreak of *S*. Bareilly infection, Summer 2003. Epidemic curve of 139 cases with known dates of onset



An outbreak control team consisting of representatives from the Scottish Centre for Infection and Environmental Health (SCIEH), the Scottish Salmonella Reference Laboratory, Scottish NHS Boards, Health Protection Agency (HPA) and the Food Standards Agency, was convened to coordinate investigations. Following hypothesis-generating interviews with 31 cases during the last week of August 2003, a matched case-control study was conducted between 30 August and 17 September to determine the vehicle(s) of transmission.

The study team, based, at the HPA and SCIEH conducted telephone interviews with 79 eligible cases and 132 eligible controls. In the statistical analysis, illness was independently associated with the consumption of egg and cress sandwiches bought in plastic packs (MOR 21.75; 95% CI 4.08-115.95; P<0.001), consumption of egg and mayonnaise sandwiches bought in plastic packs (MOR 20.05; 95% CI 1.71-234.49; P=0.017), consumption of mayonnaise (MOR 2.66; 95% CI 1.13-6.25; P=0.025) and buying food from shops in chain Z (MOR 3.86; 95% CI 1.53-9.73; P=0.004). A total of 23/27 (85%) cases who reported consumption of pre-packed egg and cress sandwiches and 5/13 (38%) of cases who reported consumption of egg and mayonnaise sandwiches had bought their sandwiches from shops in chain Z.

Although the descriptive epidemiology and case-control study have identified these items as important (although not necessarily exclusive) vehicles of infection, environmental and microbiological investigations have failed to pinpoint the cause of their contamination.

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1. Health Protection Agency. National increase in *Salmonella* Bareilly. *Commun Dis Rep CDR Wkly* [serial online] 2003 [cited 29 October 2003]; **13**(35): news. Available at <http://www.hpa.org.uk/cdr/PDFfiles/2003/cdr3503.pdf>.
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HIV / STIs

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Sexually transmitted disease quarterly report: genital warts and herpes simplex virus infection in the UK

Summary:
This report summarises the current epidemiology of anogenital warts and anogenital herpes simplex virus infection within the United Kingdom (UK). Data presented consists of all diagnoses of anogenital warts and anogenital herpes simplex infection made in genitourinary medicine (GUM) clinics reported on the statutory quarterly KC60 return and ethnicity data, provided by the Programme for Enhanced Surveillance of Sexually Transmitted Infections (ProgrESS).

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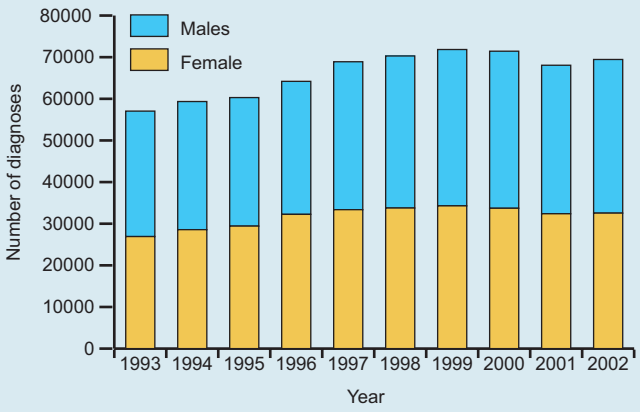
Genital Warts

Genital warts are the most common viral sexually transmitted infection (STI) diagnosed in genitourinary medicine clinics (GUM) clinics in the United Kingdom (UK) (1). Genital warts are the clinically visible manifestations of infection with human papillomavirus (HPV), however, they are only associated with some HPV types. Of the 35 or more HPV serotypes known to infect the genital tract, types six and 11 are the most common cause of visible genital and perianal warts (2). More than 20 different HPV types have been linked to cervical cancer (3), although these types are less frequently associated with the manifestation of genital warts (4) and, therefore, remain undiagnosed. HPV type 16 is the most common HPV type to be linked to cervical cancer (5), and non-cervical anogenital cancers (6). Diagnoses seen in GUM clinics represent a small proportion of the total pool of HPV infection within the population.

In 2002, 69,449 cases of first attack genital warts were diagnosed, of which 53% were among men and 47% among women (figure 1). This represents a one-year increase of 3% in the number of male cases; the number of infections diagnosed in females remained constant between 2001 and 2002. Rates of diagnosed genital warts in GUM clinics are highest among males aged between 20 and 24 years (776 per 100,000 population) and in females in the 16 to 19 years and 20 to 24 age groups, (682 and 672 per 100,000 population respectively) (figures 2 and 3).

The age distribution of diagnoses of genital warts varies by gender. For both males and females, rates of infection remain highest in London at 209/100,000 and 157/100,000 respectively (figure 4 and 5). Elsewhere in

Figure 1 Number of new diagnoses of gential warts (1st attack) by sex, GUM clinics UK*, 1993 to 2002



* Data for Scotland 2001, 2002 are not available.

Figure 2 Males: Rates of diagnoses (per 100, 000) of genital warts (first attack) by sex and age group, GUM clinics, UK: 1993-2002*

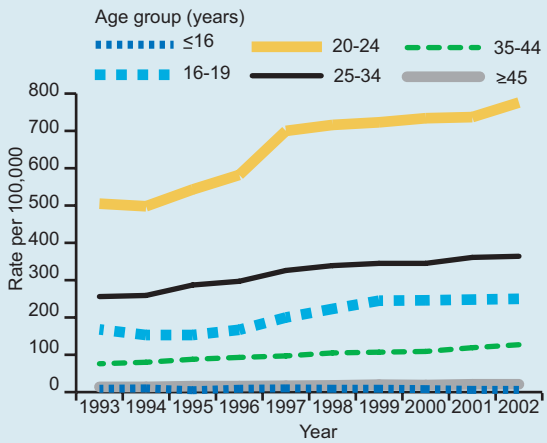
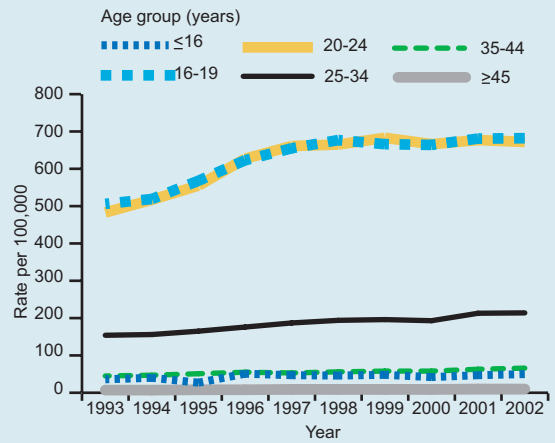
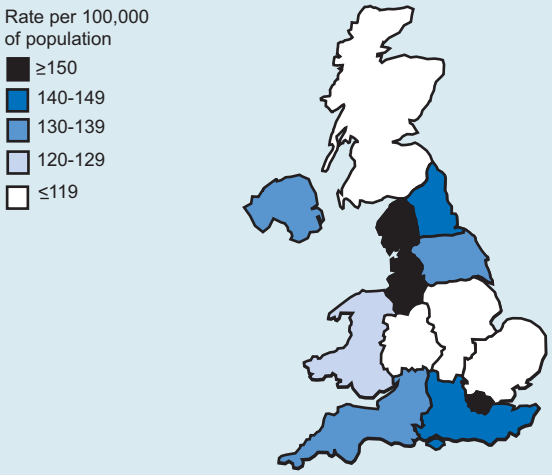


Figure 3 Females: Rates of diagnoses (per 100,000) of genital warts (first attack) by sex and age group, GUM clinics, UK: 1993-2002*



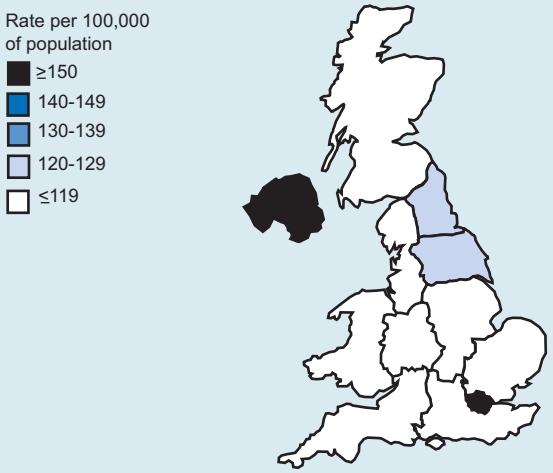
*1995 data not available for Northern Ireland, 2001 and 2002 data not available for Scotland

Figure 4 Males: Rate of diagnoses (per 100,000) of genital warts (first attack) by sex and region*, GUM clinics, UK: 2002



* 2000 Data used for Scotland

Figure 5 Females: Rate of diagnoses (per 100,000) of genital warts (first attack) by sex and region*, GUM clinics, UK: 2002



* 2000 Data used for Scotland

Figure 6 Rates of diagnoses of genital warts in London residents by sex and ethnic group: 2001 (ProgrESS)

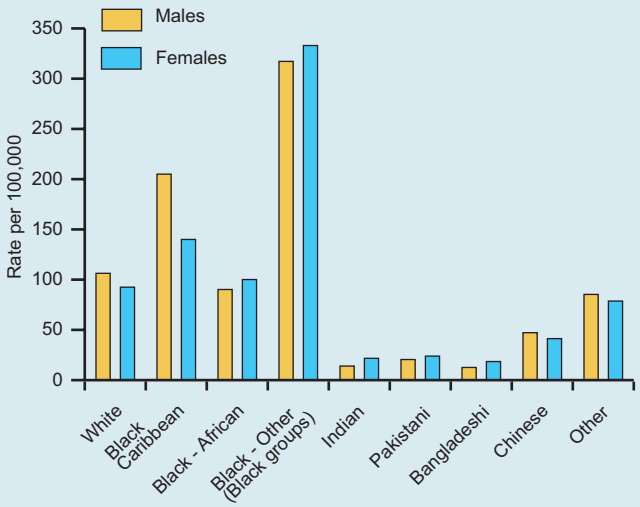
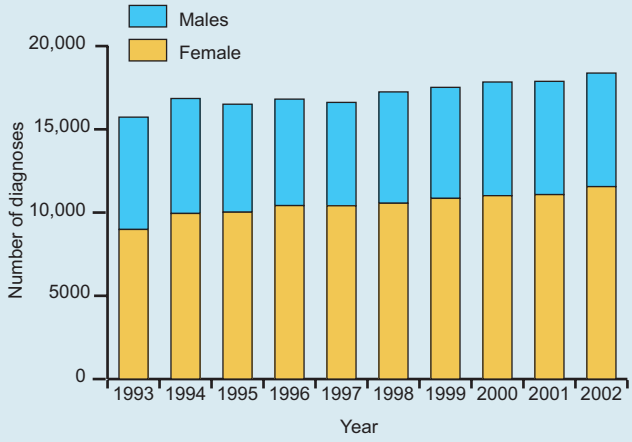


Figure 7 Number of new diagnoses of genital herpes (1st attack) by sex, GUM clinics UK*: 1993 to 2002



*2001-2002 Scottish data not available.

the UK , rates in females were relatively similar across the UK and ranged from 126/100,000 in the North East region to 91/100,000 in the East Midlands. Rates in males show more regional variation, with the highest seen in the North West and North East (151 and 140/100,000 respectively), and South East (141/100,000). Data from the Programme for Enhanced Surveillance of Sexually Transmitted Infections (ProgrESS) illustrate the heterogeneity in the distribution of warts in the population. Data for London residents shows the disproportionately high rate of diagnoses among black ethnic groups, in particular among those identifying as Black Other, with rates of infection of 317/100,000 and 333/100,000 observed in males and females respectively (figure 6).

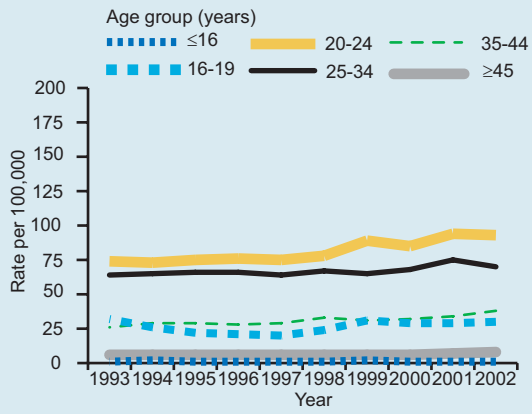
Genital herpes simplex virus

Anogenital herpes simplex virus (HSV) infection is the commonest ulcerative STI in the UK (1) and can cause considerable physical and psychological morbidity. Anogenital HSV infection may facilitate HIV transmission (7), can cause severe systemic disease in people with impaired immunity, and can be potentially fatal in neonates (8).

In 2002, 18,379 diagnoses of genital herpes simplex infection were made in GUM clinics in England, Wales, and Northern Ireland, of which 37% were among men and 63% among women. The number of diagnoses in females increased by 4% between 2001 and 2002, while the number of diagnoses in males increased by less than 1%. In males, however, the proportion of infections homosexually acquired increased by 19%. In 2002, the female to male diagnostic ratio remained at 1:1.6. The consistent excess of diagnoses in females cannot be accounted for in terms of increased case ascertainment alone; it is also likely that changes in sexual behaviour are influencing HSV epidemiology (figure 7).

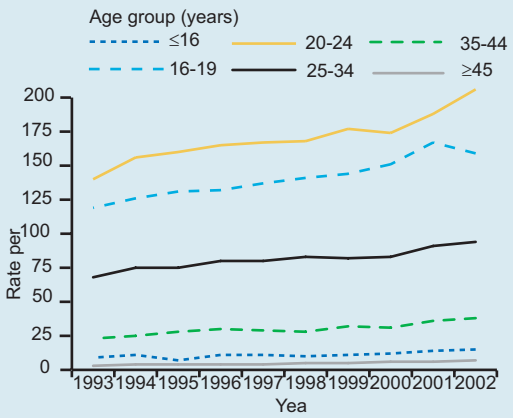
In both males and females diagnostic rates were highest among those aged between 20 and 24 years, at 93 and 206 per 100,000 respectively. Overall, rates

Figure 8 Males: Rates of diagnoses (per 100,000) of genital herpes (first attack) by sex and age group, GUM clinics UK: 1993-2002*



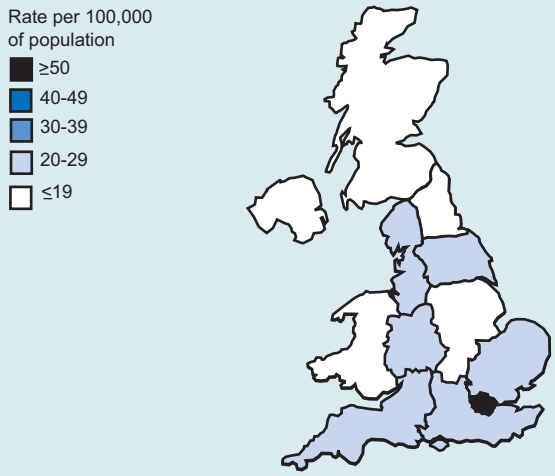
*1995 data not available for Northern Ireland, 2001 and 2002 data not available for Scotland

Figure 9 Females: Rates of diagnoses (per 100,000) of genital herpes (first attack) by sex and age group, GUM clinics UK: 1993-2002*



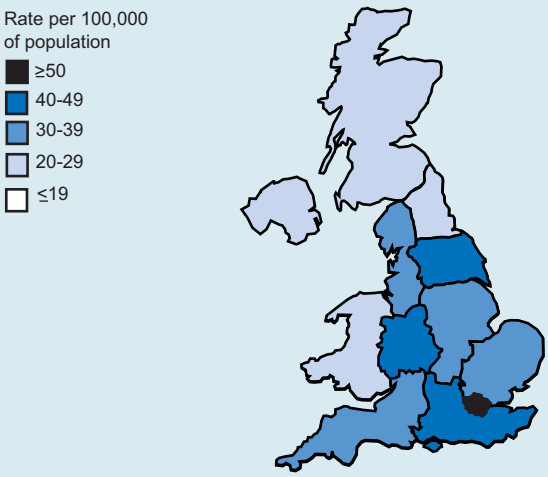
*1995 data not available for Northern Ireland, 2001 and 2002 data not available for Scotland

Figure 10 Males: Rate of diagnoses (per 100, 000) of genital herpes (first attack) by sex and region*, GUM clinics, UK: 2002



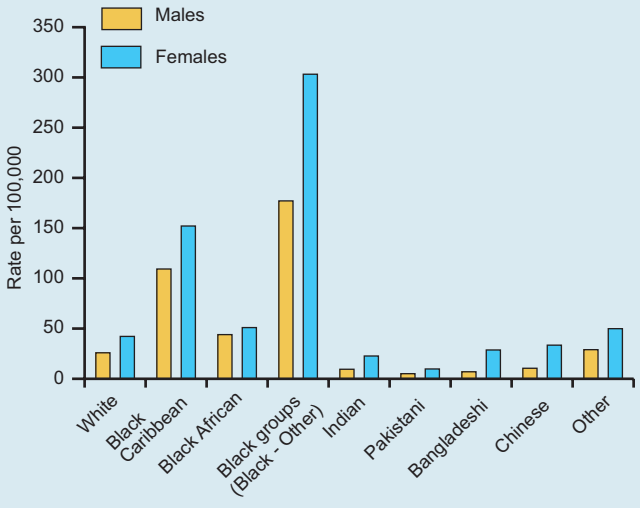
* 2000 Data used for Scotland

Figure 11 Females: Rate of diagnoses (per 100, 000) of genital herpes (first attack) by sex and region*, GUM clinics, UK: 2002



* 2000 Data used for Scotland

Fig 12 Rates of diagnoses of genital herpes in London residents by sex and ethnic group: 2001 (ProgrESS)



continue to be higher for females than males in those aged under 45 years.

Rates of diagnosis of genital herpes are fairly evenly distributed across the UK, with the lowest rates observed in Northern Ireland, North East England and Wales (figure 8 and 9). During 2002, rates were highest in London, at 57/100,000 in males and 78/100,000 in females. London accounted for 31% of male cases and 44% of female cases in 2002 (figures 10 and 11).

As seen with genital warts, ProgrESS data indicate the highest rates of genital herpes (HSV) infection in London are found among black ethnic groups, in particular among those identifying as Black Other. Rates of diagnoses of HSV in GUM attendees were 177/100,000 and 303/100,000 in males and females respectively (figure 12).

Genital HSV infection can be caused by either HSV types 1 or 2. In the past, HSV-1 was mainly associated with oral infection. In the UK, however, the population prevalence of HSV-2 is low, and the proportion of

genital HSV-1 cases is increasing. HSV-1 is now the commonest cause of primary genital HSV infection in GUM clinics. This may be in part due to reduced exposure to HSV-1 during childhood (9). This reduction in the prevalence of HSV-1 antibodies in adolescents may have led to an increase in the pool of adults at risk of disease due to becoming sexually active, while HSV naive. At the same time, studies indicate that oral sex has increased in young people (10). This combination of factors suggest that sexual transmission, particularly orogenital contact, is becoming an increasingly important transmission route for new cases of genital HSV-1 infection(11-13).

Discussion

The data presented here further emphasise the increasing burden of sexually transmitted infections within the population, although the increases in diagnoses seen for HPV and HSV are somewhat lower than in those seen for several of the acute bacterial STIs. These data highlight the burden of genital warts and genital herpes among young people, with the highest rates of infection for both STIs seen in the younger age groups. The changing epidemiology of these STIs are due, in part, to changes in sexual behaviour among young people, leading to a gradual deterioration of sexual health in this population. The physical and psychological morbidity of these recurrent viral sexually transmitted infections are substantial with long-term implications, such as the development of adverse sequelae including cervical and penile cancers (HPV), and the increased risk of HIV transmission with concurrent HSV infection.

Prevention efforts, such as encouraging condom use, could be effective. Studies have shown the regular use of condoms can decrease the rate of transmission of HSV-2 by as much as 50% to 75% (14). Other prevention methods may include selective screening of individuals (14), and in the case of HSV the future development of prophylactic vaccines. Enhanced surveillance data such as that provided by ProgrESS allows a greater understanding of the epidemiology of these sexually transmitted infections and identifies those at risk, to enable specific targeting of future prevention efforts.

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