

NEWS ROUNDUP

Advertising Yasmin

Yasmin contains the new progestogen drospirenone and 30 µg ethinylloestradiol. Since its launch in April 2002, Yasmin has been promoted as 'the pill for well-being', with a 'demonstrable positive effect' on skin and premenstrual symptoms and 'no associated weight gain'.

While accepting Yasmin's good contraceptive efficacy, some experts are less convinced by the other claims. The *Drugs and Therapeutics Bulletin* (DTB), in its independent review for the Consumer's Association, found 'no compelling published evidence' that Yasmin offers any advantages over established combined oral contraceptives. Bearing in mind its high cost (£59 for 12 cycles), the DTB concluded that it could not recommend Yasmin. National Health Service (NHS) review boards such as the Scottish Medicines Consortium have reached similar conclusions and effectively blocked NHS prescription of Yasmin in many areas of the UK.

Attention has now focused on advertisements for Yasmin. The government's Medicines Control Agency (MCA) and the pharmaceutical industry's own watchdog have agreed that the advertisements are misleading, with insufficient published evidence to support the claims. Schering Health Care has withdrawn the advertisements on a voluntary basis but say they are appealing against the decision and stand by their claims for Yasmin.

Sources: *Is Yasmin a 'truly different' pill?* Drug Ther Bull 2002; 8: 57-59. Revil J. *Health claims for new Pill are 'bogus'*. The Observer, 8 December 2002

Human papilloma virus: what do women know?

Human papilloma virus (HPV) is an important risk factor for cervical cancer. As such it is a focus of current research, including promising trials of a vaccine against HPV16, and use of HPV testing in cervical screening programmes.

Researchers set out to discover how much women in general know about HPV. They surveyed the entire female workforce of an English university. Respondents were manual workers, clerical personnel, academics and managers, with an age range from 19 to 64 years. Knowledge of the cervical screening programme was generally good. However, 70% of the women had not heard of HPV and many had inaccurate knowledge. Only 11% of women knew HPV was a risk factor for cervical cancer. Even women who had attended colposcopy clinics after abnormal smears had poor knowledge of HPV.

The authors suggest that increasing medical knowledge about HPV must be matched by better public understanding in order to achieve real health benefits. They conclude that health professionals need to work harder at informing women about HPV without adding to the considerable anxiety caused by receiving an abnormal smear result.

Source: Pitts M, Clarke T. *Human papillomavirus infections and risks of cervical cancer: what do women know?* Health Educ Res 2002; 17: 706-714

Genital herpes vaccine trials in the US

Genital herpes is common, distressing and highly infectious. Many people shed the virus asymptomatically, contributing significantly to the spread of infection. An effective vaccine could make important contribution to limiting the spread of genital herpes, where other public health measures have failed.

Double-blind randomised trials have recently reported that an HSV2 vaccine reduces the risk of herpes transmission from an infected partner, but only in some circumstances: women who had no pre-existing antibodies to HSV1 or HSV2 derived some protection from the vaccine. However, women who already had antibodies to HSV1 did not derive any extra protection against genital herpes. The vaccine was not effective in men, regardless of HSV serology at baseline.

Following these results, the HERPEVAC Trial for Women was launched in the US in November 2002. GlaxoSmithKline Biologicals are already recruiting into the phase III, double-blind, randomised, placebo-controlled trial across the US.

Sources: Stanberry LR, Spotswood LS, Cunningham AL, et al. *Glycoprotein-D-adjuvant vaccine to prevent genital herpes*. N Engl J Med 2002; 347: 1652-1661. GlaxoSmithKline Biologicals. Rixensart, Belgium, 21 November 2002

Steroidal oestrogens added to list of known human carcinogens

Steroidal oestrogens used in oral contraceptives and hormone replacement therapy (HRT) have been added to the US government's official list of known human carcinogens. The report simply reflects reviews of the medical literature and does not attempt to quantify risks and benefits of oestrogens in different formulations and used for different indications.

Some experts have disagreed with this classification; while oestrogens are implicated in some malignancies they stress that oestrogens are used in many indications that have not been associated with an increased cancer risk. Unopposed oestrogen in HRT increases the risk of endometrial cancer but there is good evidence that the combined oral contraceptive pill significantly reduces the risks of both endometrial and ovarian malignancies.

Coming after the early discontinuation of the Women's Health Initiative Study on long-term HRT, this news can only add to public disquiet about synthetic hormones in contraception and HRT.

Source: Lancet 2002; 360: 2051

Sex lottery campaign and new fpa leaflets

A new £4 million public information campaign has been launched to raise awareness of the risk of sexually transmitted infections (STIs) among 18-30-year-olds. The 2-year drive, 'Don't play the sex lottery - use a condom', is aimed at young adults on low incomes, highlighted as high risk. The campaign is part of the National Strategy for Sexual Health and HIV. To provide information to the target group a new website has been developed at www.playingsafely.co.uk

Funded by this campaign, the fpa has launched new leaflets on gonorrhoea, genital warts and genital herpes to add to the first two in the series on chlamydia and STIs: where to go for advice and help. The leaflets cost £5 plus P&P for 50 leaflets, and are available from: fpa direct, PO Box 1078, East Oxford DO, Oxfordshire OX4 6JE, UK. Tel: +44 (0) 1865 719418.

The beginning of the end for nonoxynol-9?

Nonoxynol-9 (N9) has been widely used in spermicides for contraception over the past 50 years. In the 1970s and 1980s, laboratory tests showed it could destroy the micro-organisms responsible for HIV, gonorrhoea and chlamydia. The initial excitement of this discovery spawned a whole series of clinical investigations of N9's protective effect against transmission of sexually transmitted infections (STIs). Much of this work was necessarily in very high-risk groups such as sex workers, in developing countries with high rates of HIV/AIDS. The results were disappointing, suggesting that N9 might actually increase the risk of HIV transmission in these groups, perhaps by causing mucosal irritation and ulceration. The future of N9 in general contraceptive use was therefore called into question. In October 2001, the World Health Organization (WHO) and the Contraceptive Research and Development Programme (CONRAD) together convened an expert group to review the available evidence and make broad recommendations on the use of N9. These recommendations must be adapted in different countries according to local STI and HIV rates and available contraceptive options.

The group recommended:

- N9 should never be used for the purpose of STI or HIV prevention. Condoms should always be used to prevent infection.
- There is no evidence that N9-lubricated condoms provide any additional protection against pregnancy or STIs compared with condoms lubricated with other products ... such condoms should no longer be promoted. However it is better to use N9-lubricated condoms than no condoms.
- Among women at low risk of HIV infection, the use of N9 remains a contraceptive option. Although its effectiveness is low ... it is generally easily available ... and is a method under the control of the woman.
- Since high-frequency use of N9 products may cause mucosal damage and increase the risk of HIV infection, women who have multiple daily acts of intercourse should choose another method for contraception unless there is no other contraceptive option available and acceptable to them.
- Women at high risk of HIV infection ... should not use N9 for contraception.

In the UK, N9 is already quietly disappearing from condom ranges. N9 is still readily available through family planning clinics and over the counter in spermicidal foams, gels and other vaginal products, and it is still recommended for use with diaphragms and caps, where it does appear to increase contraceptive efficacy.

Source: WHO/CONRAD Technical Consultation on Nonoxynol-9. Summary Report. World Health Organization, Geneva, October 2001 (published June 2002)

Contraception is difficult to obtain

New, as yet, unpublished research shows that over one-third of people calling the fpa helpline have difficulty obtaining local advice on contraception. Another survey found that long-term methods of contraception such as the intrauterine device (IUD), intrauterine system (IUS) and implant were particularly difficult to obtain. The fpa have called for a 'contraceptive champion' in each primary care trust to promote services and ensure that services are properly signposted by all providers of contraception.

Sources: fpa press release 30 January 2003 and www.fpa.org.uk

US Government attacked on sexual health policies

In the US, Democratic Representatives have criticised the administration for eliminating vital information from a government factsheet on HIV and sexually transmitted disease (STD) prevention, including how to use a condom properly, and evidence that educating youngsters about condoms does not foster earlier sexual activity.

The factsheet previously advised abstinence from sex as the best way to avoid sexually transmitted infections (STIs) and HIV but added that 'latex condoms were highly effective when used correctly and consistently'. The revised version says that 'no protective method is 100% effective, and condom use cannot guarantee absolute protection against any STD'.

The alterations and deletions 'appear to be part

of an Orwellian trend', according to 14 Democratic Representatives in a letter to the government's Health and Human Services Department. They allege that 'information that used to be based on science is being systematically removed from the public when it conflicts with the administration's political agenda'.

The Bush administration is also criticised by the American Civil Liberties Union for financially supporting Abstinence Programs in which youngsters are encouraged to 'pledge' to abstain from premarital sex. Abstinence Programs do not teach about contraceptive methods and sometimes link abstinence with fundamentalist Christian messages. A vast questionnaire study of US adolescents has raised serious questions about the impact of Abstinence Programs. Younger adolescents who 'pledge' do delay first intercourse compared with those who

choose not to pledge. However 'pledging' makes no difference to the sexual debut of 18-year-olds, except that 'pledgers' were *less* likely to use contraception at first intercourse.

The International Planned Parenthood Federation (IPPF) General Director, Dr Steven Sinding, spoke recently of George Bush's 'seemingly single-minded determination to strip women of reproductive rights and access to reproductive health services'. IPPF lost \$18 million in US government aid when the Mexico City Policy of January 2001 blocked US government funding of any organisation directly or indirectly involved in abortion-related activity.

Sources: *Associated Press* via CDC Prevention: *News Digest* 2003; 1(308). www.aclu.org. Bearman PS, Bruckner H. Promising the future: virginity pledges and first intercourse. *Am J Sociol* 2001; 106: 859-912

JOURNAL CLUB

A controlled trial of a human papillomavirus type 16 vaccine. Koutsky LA, Ault KA, Wheeler CM, et al. *N Engl J Med* 2002; 347: 1645-1651

Although cervical cancer is now relatively uncommon in the UK, worldwide it is the second most common cause of cancer-related mortality in women. Persistent infection with oncogenic human papilloma virus (HPV) is the single most important factor in the development of pre-invasive and invasive cancer. Oncogenic types of HPV DNA are detected in virtually all cervical cancers and recognition of this crucial role has stimulated the investigation and development of HPV vaccines in both prophylactic and therapeutic settings. Such strategies could prevent cancer deaths, especially in developing countries where population screening is not feasible and therapeutic options can be limited.

This paper presents an interim analysis of a large double-blinded multicentre randomised controlled trial. The aim of this trial is to determine if a HPV 16 virus-like particle (VLP) vaccine will prevent HPV 16 infection. A total of 2392 women aged 16-23 years, recruited by advertising at college campuses in the US, received three doses of either HPV 16 vaccine or placebo. The analysis presented is restricted to 1533 (64%) women who meet the eligibility criteria of having no serological or DNA evidence of either current or previous HPV 16 infection at enrollment or 1 month after completing the vaccination regime. Completion of the trial requires 4 years of follow-up post-vaccination and the median follow-up of this subgroup was 17.4 months. Of the women receiving the active vaccine, 99.7% seroconverted with mean antibody titre of 1510 mMU/ml compared with < 6 mMU/ml in the placebo arm. There were no serious adverse events reported and the most common side effect was pain at the injection site. Thirty-one women subsequently developed a persistent HPV 16 infection and nine women a HPV 16-positive cervical intraepithelial neoplasia (CIN) lesion. All these women had received placebo. This represents an incidence of persistent HPV 16 infection of 3.8 per 100 woman-years for the placebo arm and 0 per 100 woman-years in the vaccination arm ($p = 0.001$). There were also 44 cases of HPV 16-negative CIN lesions, which were equally distributed between the two trial arms.

These early results on prophylactic HPV 16 vaccination of young women are exciting and support the hypothesis that vaccination will prevent persistent HPV 16 infection. The vaccine appears to be safe and able to produce a significant serological response. HPV infection

is extremely common and around 80% of women will have an HPV infection at some time before age 30. For the majority of women, these infections are transient and of no clinical significance and fewer than 10% of women with a persistent HPV infection will subsequently develop cervical cancer.

This study has concentrated on HPV infection but it is fundamental to confirm whether preventing infection will impact on deaths from cervical cancer. The subjects in this study come from a high prevalence group. A public health vaccination programme cannot be directed by sexual behaviour and we need to know the effect of vaccination on a population-based cohort. This is of particular importance in the developing countries where such rigorous selection criteria and evaluation of HPV infection are not practical and the impact on cervical cancer, where screening is not an option, needs to be seen. This will require much larger population-based studies with long-term follow-up. In addition, HPV vaccines are known to be highly specific and vaccinating against one subtype may produce less effect on cervical disease as other HPV infections replace the eliminated type.

Effective vaccination against HPV has been anticipated for a number of years now and this trial demonstrates a highly significant impact on HPV 16 infection. The completion and final analysis of the trial will be as important as these early results and may produce essential data on the duration and protection offered by such a vaccination regime.

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Official warnings on thromboembolism risk with oral contraceptives fail to inform users adequately. Berry DC, Raynor DK, Knapp P, et al. *Contraception* 2002; 66: 305-307

This small study questioned 186 university students on their understanding of the risks of venous thromboembolism (VTE) when taking the combined oral contraceptive (COC). One hundred and thirty-five women in this group were taking the pill or had taken it in the past. The women were randomly divided into two groups. One group had the standard information about the COC and the other group had additional information regarding the risks of VTE following the statement of the Committee on Safety of Medicines (CSM) in 1999, where the previous advice of 1995 was withdrawn. Only about two-thirds of each group could give the correct advice when asked in a questionnaire. The additional information made no difference. The authors are of the opinion that there is very little research done on how to

put information cross to women regarding the risks of the pill, especially when information becomes sensationalised by unbalanced reporting in the press.

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Quick Start: a novel oral contraceptive initiation method. Westhoff C, Kerns J, Morroni C, et al. *Contraception* 2002; 66: 141-145

This paper reviews a method of starting the pill at the first visit to the clinic. The authors describe it as the 'Quick Start' method. They consider that the traditional way of starting the pill on the first day of the menstrual cycle is to avoid an unexpected pregnancy occurring in the first packet of pills. It is now established that taking hormones in early pregnancy are not harmful to the fetus so it does not matter when the pill is started. The authors have used the Quick Start method of starting the combined oral contraceptive (COC) for several years in their clinics and it is offered to patients at the discretion of the provider. How they advised starting the pill was at the preference of the clinician.

The study was not randomised. Two hundred and fifty women were recruited and 62 (25%) took the first pill at the clinic. The study reviewed the continuation rate of the method after one cycle. The strongest association with continuing the COC was if the partner was aware [odds ratio (OR) 3.9; CI 1.9-8.3], this was followed by Quick Start (OR 2.8; CI 1.1-7.3). There were no differences in bleeding pattern when the Quick Start method was used.

This study was not randomised and it depended on the clinician's opinion whether the woman was offered Quick Start. In addition, the follow-up time was very short. So is the analysis reflecting the clinicians' practice rather than the way the pill is started? The authors admit that a randomised trial is needed to see if there is a true effect. Does it have any relevance to our own practice? The authors feel that it reduced the amount of counselling needed at the first visit as the women needed less information about how and when to start the pill and had less chance of forgetting the information. I am sure we all have instances in our own practice where young women have become pregnant after receiving the pills and before starting them. Maybe by getting them to start the pill at the first visit will reduce the chance of pregnancy if they are not already at risk. Would it not be interesting to see when the women want to start the pill rather than when the clinician feels is the best time?

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