Multivariate relative risk (95% confidence interval) of pelvic endometriosis according to oral contraceptive use, northern Italy*

	Indication for diagnostic surgery			
	Sterility	Pelvic pain	Other†	Total series
Oral contraceptive use				
Never users	1·00 (n = 67)	1·00 (n = 25)	1·00 (n = 131)	1·00
Current users	2·3 (0·1 to 2·1) (n = 2)	2·7 (0·9 to 7·8) (n = 6)	0·7 (0·2 to 1·8) (n = 7)	0·8 (0·3 to 1·6)
Former users	2·2 (1·3 to 3·7) (n = 53)	2·7 (1·4 to 5·2) (n = 21)	1·5 (1·0 to 2·3) (n = 63)	1·9 (1·4 to 2·6)
Duration of use (years):				
< 3	2·1 (1·2 to 3·2) (n = 37)	2·4 (1·2 to 5·0) (n = 18)	1·6 (1.0 to 2·5) (n = 49)	1·9 (1·3 to 2·7)
⩾ 3	1·5 (0·7 to 3·1) (n = 12)	3·2 (1·3 to 7·7) (n = 9)	1.1 (0·6 to 1·9) (n = 21)	1·4 (0–9 to 2·2)
Time since last use (years):				
< 10	2·4 (1·4 to 4·0) (n = 46)	3·1 (1·6 to 6·2) (n = 18)	1·5 (1·0 to 2·4) (n = 42)	2·0 (1·4 to 2·9)
⩾ 10	1·3 (0·4 to 4·0) (n = 7)	0·7 (0·1 to 5·0) (n = 1)	1·6 (0·9 to 3·0) (n = 21)	1·5 (0·9 to 2·7)
Time since first use (years):				
< 15	1·9 (1·2 to 3·2) (n = 50)	2·8 (1·5 to 5·3) (n = 24)	1·4 (0·9 to 2·1) (n = 53)	1·7 (1·3 to 2·4)
⩾ 15	1·4 (0·3 to 5·7) (n = 4)	1·3 (0·2 to 10·0) (n = 1)	1·4 (0·7 to 3·0) (n = 13)	1·4 (0·7 to 2·8)

*Multivariate estimates adjusted for age, education, parity, and in turn the above indicators of oral contraceptive use.
†Including pelvic masses and incidental diagnosis.

contraceptives. Although the results for current users were compatible with a reduced risk, the estimate was not significant, possibly on account of small absolute numbers of cases. It is interesting to note that in our study an increased risk of endometriosis for former users was evident in women in whom diagnosis of the disease was an incidental finding—that is, in the group in which indication bias should have a minor role. Indication and diagnostic bias may, however, have different roles in different diagnostic subgroups, and it is therefore difficult to quantify their role.

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EDITOR,—M P Vessey and colleagues have shown that current use of oral contraception has a significant protective effect (relative risk 0·4) against endometriosis.[1] The relative risk in women who had stopped taking the pill 25-48 months previously compared with women who had never taken the pill was 1·8. This is inadequate evidence to propose a true worsening of the risk of endometriosis as a rebound effect after the pill is stopped. A more plausible explanation is selection bias: the women in this non-randomised cohort study who chose to take the pill were probably to some extent self selected or selected by their doctor for problems with their periods.

It has long been known that both bleeding and pain are improved by the combined pill; hence women with endometriosis or women likely to develop symptoms of the condition are likely to have been overrepresented in the cohort taking the pill. The endometriosis would generally not become manifest until pill taking stopped, thus producing a higher rate in former users than among those who had never used the pill. If this explanation is true, so that those taking the pill tended to be a higher risk group, the observed beneficial effect of current use of the pill in suppressing symptomatic endometriosis is all the more impressive.

Increased benefit with increasing total duration of use of the pill was not shown in the whole population, but this included both current and former users. Have the authors examined whether, among current users who have never taken a break from the method, increasing duration of use further improves the beneficial effect?

I agree with Eric J Thomas that the main indication for treatment is cyclical pelvic pain and dyspareunia.[2] Because endometriosis is chronic and relapsing, after initial medical or surgical treatment it must be suppressed long term. The combined pill has now been shown to be suitable for that purpose, long term.[1] I also agree that these data "support the hypothesis that the incidence of the disease is related to exposure to menstruation." I have, therefore, for some time recommended maintenance treatment with the "tricycle regimen" first introduced for a different purpose by Loudon *et al*, in which three or four packets of the pill (which should logically be a relatively oestrogen deficient and progestogen dominant formulation) are taken consecutively before each pill free interval.[3] Although pill bleeds are hormone withdrawal bleeds rather than menses, it seems logical to arrange that they are infrequent, occurring four or five rather than 13 times a year, to minimise bleeding into persistent endometrial deposits. A study in which this regimen was used might well show an even greater protective effect.

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Increasing patients' knowledge of secondary contraception

EDITOR,—D R Bromham and R S V Cartmill report the knowledge and use of secondary contraception among patients requesting termination of pregnancy at a fertility control unit.[1] They found that many patients had switched from using the pill to condoms for contraception, hoping to decrease any risk of contracting AIDS. A considerable number of the women said that a condom had leaked and some that one had split. The authors concluded that an increasing proportion of unplanned pregnancies were due to condom failure. They also found that many women were unaware of the availability of the postcoital pill—popularly and perhaps misleadingly called the morning after pill, although it is recommended for use up to 72 hours after any risk.

This exactly reflects my experience in seeing a large number of women who have sought a termination of pregnancy in Liverpool. I wrote to two large manufacturers of condoms, pointed out my findings, and suggested that it would be helpful if they included in their product's leaflet information about the postcoital pill, how to obtain it, and in what circumstances to use it. This was in July 1989, and by November I had received considered replies from both manufacturers.

One manufacturer wrote: "To incorporate such wording as you suggest within our instructions would imply that the product has a higher failure rate than is actually the case and cast doubt upon the advisability of its use." The other, having said that most "failures" (its inverted commas) are really related to the users and not the product, went on to say: "I find it hard to envisage how such advice could be given without causing potential damage to our own product's reputation." Manufacturers competing in the market may well have a problem, but surely a form of words could be agreed and, with government help, made mandatory for inclusion in all manufacturers' information sheets.

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Re-emergence of tuberculosis

EDITOR,—John M Watson's editorial and M Kennedy and colleagues' letter draw attention to the danger of multidrug resistant tuberculosis, particularly in HIV positive patients.[1 2] We have completed a bacteriological survey of tuberculosis in south east England from 1984 to 1991.[3] This survey included a study of the prevalence of drug resistance in different ethnic groups. The table summarises the findings, which may prove useful for comparative purposes in future surveys. The overall distribution of resistance was not signi-

Prevalence of tuberculosis due to drug resistant strains of Mycobacterium tuberculosis in south east England, 1984-91

	Ethnic origin of patients		
Type of resistance	European (n = 4594)	Indian subcontinent (n = 4099)	Other (n = 625)
1 Drug:			
Isoniazid	60	119	16
Streptomycin	30	72	21
Pyrazinamide	15	12	2
Rifampicin	3	5	1
Ethambutol	1		
2 Drugs:			
Isoniazid and streptomycin	16	83	22
Isoniazid and rifampicin	4	4	4
Other	1	7	
3 Drugs	1	28	1
4 Drugs	1	14	5
5 Drugs	1	3	1
6 Drugs		1	
Total (%) resistant	133 (2·9)	348 (8·5)	73* (11·7)

*35 African, 31 from Far East, seven other.

ficantly different from that in a similar survey in 1977-83.[4]

By the end of 1992 we had received strains of *Mycobacterium tuberculosis* from 167 HIV seropositive patients. Nine of these strains (six from African and three from European patients) were drug resistant: six to isoniazid, one to streptomycin, one to rifampicin, and one to both isoniazid and streptomycin. The prevalence of drug resistance in these HIV positive patients was not significantly different from that in other patients in these ethnic groups, and no multidrug resistant strains (resistant to three or more drugs) were isolated. Thus we have not yet experienced the serious problem of multidrug resistant tuberculosis related to HIV encountered in the United States.

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EDITOR,—Chris Hayward attributes the low level of tuberculosis in people with AIDS in Britain to "the high proportion of [BCG] vaccinated people in the United Kingdom and the limited overlap between the population with HIV and those at risk of mycobacterial reactivation."[1] There is little if any evidence that previous BCG vaccination would protect an HIV infected person against tuberculosis, so it is difficult to see how the fact that a high proportion of people have had BCG vaccination could be directly responsible for the low incidence of tuberculosis in those with AIDS. More probably this low incidence is due to the fact that a high proportion have never been infected with *Mycobacterium tuberculosis*, coupled with the limited overlap between the groups most at risk of tuberculosis and those most at risk of HIV infection.

Hayward bases the plea for the continuation of the schools BCG vaccination programme on a causative link between the high level of BCG vaccination in Britain and the low level of tuberculosis in those with AIDS. If the only link between BCG vaccination and the low level of tuberculosis in those with AIDS is the indirect one based on any epidemiological effect of BCG vaccination in reducing the risk of infection with *M tuberculosis* then the effect is small compared with other influences, including chemotherapy. The size of the effect of BCG vaccination in reducing the risk of infection[2] has been allowed for in papers discussing the effects of stopping BCG vaccination in schools.[3,4] These papers also take into account the probable effect of AIDS on the number of notifications of tuberculosis in the future and show that stopping the schools BCG vaccination scheme would probably give rise to a limited number of additional cases.

Though the recent cessation in the decline in notifications of tuberculosis is unexplained, it remains reasonable to examine closely the contribution of each of the available methods of control, including BCG vaccination of all schoolchildren, and to be prepared to stop any that are shown to be no longer playing a worthwhile part in controlling the disease.

Jacques Germanaud is to be supported in his plea that all health workers should receive BCG vaccination because of their greater than average risk of exposure to infection with *M tuberculosis*.[5] It is difficult to accept his further suggestion that tuberculin testing, leading to repeat BCG vaccination if the result is negative, should be carried out at two year intervals. The Medical Research Council's study showed that a high level of protection was maintained for 15 years, after which no reliable assessment could be made because of the small number of cases occurring.[6] The recommendation of the Joint Committee on Vaccination and Immunisation—that no repeat vaccination is required[7]—or that of the joint tuberculosis committee of the British Thoracic Society—that repeat BCG vaccination should be undertaken after 25 years[8]—seems better justified than repeated tuberculin testing and possibly repeat BCG vaccination at two year intervals.

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EDITOR,—In his editorial on tuberculosis John M Watson discusses the association between it and HIV infection.[1] Recent reports have highlighted the risk of transmission of tuberculosis both between patients infected with HIV[2] and from such patients to health care workers.[3]

We report on an HIV positive patient with pulmonary and extrapulmonary tuberculosis who presented with fever, weight loss, and productive cough. Sputum and a supraclavicular lymph node specimen stained positive for acid fast bacilli, and triple treatment of rifampicin, isoniazid, and pyrazinamide was started. Sputum samples taken on days 18, 19, and 21 after the start of treatment showed multiple acid fast bacilli on staining and were all positive on culture, indicating a continued risk of infection to others. Further sputum samples were not taken until day 42, by which time they were negative on culture.

The organism cultured was fully sensitive in vitro to standard antituberculous agents; the patient had no vomiting or evidence of malabsorption to suggest subtherapeutic drug concentrations, and his drug treatment was supervised by nursing staff so that poor compliance was not a factor in his slow response to treatment.

Current recommendations from the joint tuberculosis committee of the British Thoracic Society on protective isolation of patients whose sputum smears are positive for *Mycobacterium tuberculosis* are that patients should be segregated in a single room for two weeks after the start of treatment.[4] This time has been shown to be adequate in patients not infected with HIV.[5] Clearly, in our patient two weeks of protective isolation would have allowed at least one week of potential transmission to others.

Risk of transmission of tuberculosis is influenced by poor compliance with treatment, by resistant organisms, and, in patients also infected with HIV, by procedures that induce cough such as induction of sputum and use of nebulised pentamidine as well as the presence of cavitating lung disease.[6] One of the hallmarks of HIV infection is progressive depletion of the CD4+ lymphocytes together with defects in the function of macrophages.[7] This may well delay the clearance of live, potentially infectious organisms from sputum and other sites despite treatment with bactericidal agents, particularly in those with advanced disease.

Current recommendations for isolating patients with tuberculosis and HIV infection may well be inadequate. A systematic study looking at the period of infectivity after the start of treatment is needed urgently to reduce the risk of further outbreaks of tuberculosis in HIV units and transmission to health care workers.

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BCG vaccination and health care workers

EDITOR,—Jacques Germanaud states that in his study 62 cases of occupationally acquired tuberculosis occurred in hospital employees between 1984 and 1992.[1] Of these, 44 were detected by routine chest *x* ray examination. To evaluate his statement that chest *x* ray screening is more effective than skin testing, information is needed on the frequency of the routine chest *x* ray examinations, the frequency of the skin testing, and the number of employees who had either or both procedures.

Germanaud recommends that health care workers should have a tuberculin test at least every two years, which should be followed by revaccination with BCG vaccine if the result is negative. This procedure, if adopted, could lead to a hospital employee receiving BCG vaccine several times during his or her working life. If BCG vaccine offers protection for up to 15 years, and if BCG vaccination is compulsory for hospital employees in France,[1] there is no good reason for advocating tuberculin tests at this frequency. The British experience also shows that BCG vaccine provides high and consistent protection against tuberculosis.[2] The British Joint Committee on Vaccination and Immunisation has indicated that immunisation with BCG vaccine produces a high tuberculin conversion rate and that further tuberculin testing is not recommended.[3] Even for health care staff judged to be at high risk, reimmunisation with BCG vaccine recommended for only one further occasion under specific circumstances.