the track record of the experimental arms over the past decade?⁵

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Effect of CSM's warning about safety of third generation oral contraceptives

General practitioners in England prescribed second generation pills instead

EDITOR,—On 18 October last year the Committee on Safety of Medicines issued its latest warning on the risk of thromboembolism associated with combined oral contraceptives.¹ It did this after becoming aware of three studies indicating that combined oral contraceptives containing desogestrel and gestodene were likely to be associated with around a twofold increase in the risk of thromboembolism when compared with those containing other progestogens. There was insufficient evidence to know whether norgestimate was also associated with an increased risk. Analysis of the (now published) evidence supports the stand that the committee took over desogestrel and gestodene.

Since the committee's warning, the Prescription Pricing Authority has monitored the use of oral contraceptives on a monthly basis. Use of third generation oral contraceptives containing desogestrel and gestodene fell dramatically: from accounting for about 55% of the total use and 70% of the total costs before the warning they accounted for about 12% and 23% respectively after it. The main change was towards pills containing levonorgestrel, which increased from

30% to 62% of the total use and 16% to 44% of the total costs. Norgestimate was not included in the warning, but its use increased from 7.3% of the total before the warning to 12.3% afterwards and its cost increased from 9.7% of the total to 23%. Figure 1 gives a breakdown of the hormonal contraceptives supplied in September last year (the month before the committee's statement) and February this year.

The average prescription for an oral contraceptive is for 4.5 months, which suggests that roughly equal numbers of prescriptions for three months and six months are supplied. After the Committee on Safety of Medicines' warning the average prescription was for 3.9 months, which suggests that prescribers were trying new products for a shorter period. Prescribing now seems to be returning to its previous pattern.

Because second generation pills are considerably cheaper than third generation pills the costs of oral contraceptives have fallen considerably, though total use has been maintained. Recently, the costs of some oral contraceptives have been increased.

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Contraceptive effectiveness may be being sacrificed for safety

EDITOR,—The Committee on Safety of Medicines recently published a statement about the increased risk of breast cancer associated with oral contraceptives.¹ Have the effects of previous alerts about the contraceptive pill been assessed to show their impact on choices in contraception? Research shows that women primarily choose a contraceptive for its effectiveness and lack of side effects.²

Recently, the Marie Stopes Centre in Leeds reported a rise in the use of condoms by women seeking abortion after the safe sex campaign of the early 1990s³; one possible interpretation of this trend was that women had been influenced in their choice of contraceptive by the huge publicity attendant on that campaign. The use and methods of contraception of women seeking abortion at the centre were surveyed over five years. The percentage of women not using contraception fell over time in direct relation to the rise in the use of condoms.

Figure 1 shows the change in the use of contraceptives by women seeking abortion from January to June for three consecutive years, 1994-6. These findings from the Leeds centre are part of a nationwide study being undertaken by Marie Stopes International. The proportion of women reporting that they used condoms for contraception at the time of unintended or unwanted pregnancy has increased, while the proportion not using contraception has fallen. A similar pattern was found in our previous study.³ Also, the proportion of women choosing to use condoms as their primary method of contraception after abortion has doubled.

No society can attain a situation in which abortion is not required, but the numbers of requests for abortion can be reduced with good provision of contraceptives.⁴ Bromham has highlighted the possibility that misleading information may prevent uptake of new methods of contraception,⁵ but are women also experiencing a reduction in choice in real terms and moving away from more effective methods that are

Fig 1—Change in use of contraceptives by women seeking abortion at one centre during January to June, 1994-6

already available to those methods with fewer perceived side effects but less contraceptive efficacy?

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Abortions increased by nearly 8% in Norway

EDITOR,—The number of women using oral contraceptives in Norway has steadily increased from about 140 000 in 1985 to 160 000 in 1994 (roughly 17% of fertile women). The recent reports of an increased risk of venous thromboembolism associated with third generation compared with second generation oral contraceptives received much attention in the media, and members of the Norwegian parliament demanded that health authorities should take action against the only third generation pill in Norway that contained desogestrel. Last November the Norwegian Medicines Control Authority issued a statement that this pill should be restricted to women who were dissatisfied with second generation pills; this led to a 75% decrease in the use of this particular pill and an 8% decrease in total pill use by late February this year.

In Norway legal abortion has been available on demand up to the end of week 12 since 1978. The annual numbers of these abortions were stable until 1988. Since then there has been a continuous decreasing trend from 15 800 to 14 500 in 1994. The annual number of deliveries has been in the range of 50 000-60 000 in the same period. All legal abortions are performed in public hospitals, each of which serves a well defined geographical area and population.

To study the possible impact of the media scare on the number of abortions we compared the abortion figures for January and February 1996 with those for the same period in 1995 in the nine largest hospitals in Norway (all have more than 2000 births each year; total 29 200 in 1995). With an annual number of abortions of

Fig 1—Use of various types of hormonal contraceptives in September 1995 and February 1996. Figures are numbers of patient months supplied

7560 in 1995, these hospitals performed roughly half of all abortions and deliveries in Norway that year and served a similar proportion of the total population. There are no separate abortion clinics in Norway.

Figure 1 shows that the number of abortions had increased by 5% in January and by 11% in February this year compared with the previous year. For the two months combined the largest increase in one institution was 22%.

Fig 1—Number of legal abortions carried out in the nine largest gynaecological departments in Norway, January and February, 1995 and 1996

We consider that the findings reported here are probably representative of those for Norway as a whole. The downward trend in the number of legal abortions has been replaced by an increase of nearly 8% in the first two months of this year; this equals the reduction seen over the preceding five years.

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Depression in carers of elderly people living at home

EDITOR—We wish to respond to the letters¹ generated by our paper on psychiatric morbidity in carers.² R H Bird raises the interesting suggestion that carers of older people may be at risk of drinking excessively. Possibly because we do not work in a substance misuse service, our clinical impression is that alcohol misuse in this population of carers is rare. Bird is, however, correct in assuming that we did not ask about alcohol misuse in the prevalence study. The spouse carers of people with psychiatric disorders have now been interviewed in more detail as part of a follow up study; none admitted to excessive alcohol consumption, although some of the index cases did.

J M Eagles suggests that we have misrepresented his findings.³ Our point was that his study found that "Supporters of demented relatives showed no increase in psychiatric morbidity on the [general health questionnaire] when compared with the supporters of non-demented elderly." It is possible that our results differed partly because of the differences in settings. It still remains true that Eagles *et al* did not make a formal psychiatric diagnosis in the carers and that a

further possible explanation of the difference in findings between their study and ours lies in the method of ascertaining cases.

The interesting study by Orazio Zanetti and colleagues shows the importance of the characteristics of carers in determining vulnerability to depression; these findings can best be seen as complementary to our results in generating a multifactorial model of carers' vulnerability.

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Transdermal glyceryl trinitrate for dysmenorrhoea

Confidence intervals for glyceryl trinitrate do not suggest a significant effect

EDITOR—Effective treatments for dysmenorrhoea (combined oral contraceptives and non-steroidal anti-inflammatory drugs) are available, but, as R Pittrof and colleagues state, contraindications to non-steroidal anti-inflammatory drugs make them unsuitable in some patients.¹ The authors suggest, on the basis of a small clinical trial, that transdermal glyceryl trinitrate is a clinically useful alternative. They quote P values for different outcome measures (total pain score, $P = 0.059$; pain score on worst day, $P = 0.048$; total headache score and headache score on worst day, $P = 0.4$), which to us hardly suggest a clinically meaningful effect. More importantly, in their table of results none of the confidence intervals suggests a significant effect because the differences in the scores obtained during treatment with glyceryl trinitrate and with placebo range from negative to positive.

The contradictory conclusions drawn from the significance levels and the confidence intervals seem to stem from the use of non-parametric tests (for the P values) and parametric estimation of the confidence intervals. Given the emphasis in the *BMJ* and other journals recently on the use of confidence intervals rather than significance levels,^{2,3} we are surprised that Pittrof and colleagues' conclusions should have been allowed to stand.

A larger trial may well produce a more definitive answer, but on the basis of existing data we believe that the authors' assessment of the efficacy of glyceryl trinitrate is unduly optimistic. We would recommend paracetamol for patients who cannot tolerate non-steroidal anti-inflammatory drugs.

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Authors' reply

EDITOR—We fear that A Li Wan Po and R W Stones have missed the main point of our study. We recruited a small, highly selected group of women with severe dysmenorrhoea primarily to see whether a very small dose of transdermal glyceryl trinitrate had any effect on period pain. Using self score charts and standard statistical techniques, we showed an effect on period pain but not on other variables. In this context it is important to note that headache was included not as an outcome of treatment but as a potential side effect.

Readers vary in their preference for parametric and non-parametric tests, particularly when, as in our study, the scale of measurement is not straightforward. As we gave Wilcoxon P values and tabulated confidence intervals (here equivalent to parametric t tests) the concerns of both groups of readers are met with an economy of space. Different tests will yield slightly different results, which emphasises why one should not to be obsessed with $P = 0.05$ as a critical value or 95% confidence intervals that include or exclude 0. In this case, the results of both tests broadly agree and suggest that the treatment is worthy of further interest.

The magnitude of the response is largely irrelevant as we were primarily interested in investigating a pharmacological therapeutic mechanism. Hence our study has not proved clinical usefulness but has suggested a possible treatment; further studies of efficacy, dose, and safety are needed. As for the suggestion that women with dysmenorrhoea who cannot take non-steroidal anti-inflammatory drugs should take paracetamol—most gynaecologists know that women attending their clinics because of painful periods have tried everything already.

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Contamination of ampicillin was probably due to reuse of disposable stoppers

EDITOR—In July last year a small non-government organisation started to support a 40 bed paediatric unit in Afghanistan. Essential drugs were one of the items provided. These drugs were bought from pharmaceutical wholesalers in Pakistan and transported to Afghanistan. In November the medical staff of the unit suspected that excess deaths were associated with a batch of ampicillin for injection. The aluminium seal of the phials was intact, but the underlying rubber stoppers showed puncture marks.

A review of (imperfect) case notes showed eight unexpected deaths after the use of about 500 suspect phials. All of these children had shown sudden deterioration, resembling that occurring in septic shock, some hours after intravenous