Methotrexate in tubal pregnancy (reply)
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Dr Pettinato suggests that the aims of treatment in patients with persistent tubal pregnancy are to achieve haemodynamic stability by inducing abortion and to avoid surgery. However, no such aims are described in the recent study by Hajenius and colleagues.1 Thus, it is misleading to present their data as a comparison with the aim of achieving abortion. Furthermore, the lack of a control group means that no conclusions can be drawn about the relative merits of conservative management and surgery in this group of patients.

A randomised trial comparing laparoscopic salpingostomy and laparotomy for persistent tubal pregnancy was published in 1992.5 The authors concluded that laparoscopic surgery was less painful and caused less involuntary movement. In 1993, another randomised trial comparing laparoscopic salpingectomy and laparotomy for the management of tubal pregnancy was published.6 This randomised trial included patients with tubal rupture and tubal abortion. The authors concluded that laparoscopic salpingectomy was the procedure of choice for persistent tubal pregnancy.

As a health professional, I am concerned about the lack of evidence-based data on the management of persistent tubal pregnancy. I believe that the reported success rate of 77% in the recent study by Hajenius and colleagues is too low. In my opinion, the authors should have used a control group to compare their results with those of previous studies.

I therefore recommend that future studies on the management of persistent tubal pregnancy should include a control group and be conducted in a randomised trial setting.
Watermeyer and Penketh, apart from the use of a vasoconstricting agent because of insufficient to detect persistent trophoblast. Any substantial deviation from the curve indicates the presence of retained trophoblastic tissue. Persistent trophoblast may manifest itself at different moments in the postoperative period: early or late. Therefore, a single cutoff point is insufficient to detect persistent trophoblast. We do agree with Watermeyer and Penketh that not all patients with persistent trophoblast need to be treated. Patients with slow but steadily declining serum hCG concentrations might be managed expectantly, but those with rising or plateaueing concentrations pose a clinical problem, for which systemic methotrexate is an elegant and satisfactory option. Unfortunately, no studies are available comparing expectant management and systemic methotrexate in patients with persistent trophoblast.

The conclusion from our study by Hart and Magos that laparoscopic treatment remains the “optimum treatment” and “standard of care” in patients with ectopic pregnancy, is premature. Apart from medical outcome measures, patients’ health-related quality of life, patient preferences, and costs should also be taken into account in making treatment decisions. We will report on these topics soon, extrapolating the results to those who do not have a preceding laparoscopy. According to our findings, there is a well-defined place for non-invasive management with systemic methotrexate in a selected group of patients. With the results of our study at hand, we agree with Watermeyer and Penketh that future trials should be undertaken without a confirmative laparoscopy.

Fernandez criticises the high rate of persistent trophoblast (20%, not 28%). In our trial, five University Hospitals and one teaching hospital participated and surgery was done or supervised by trained and experienced laparoscopic surgeons. Although much lower rates have been reported by world experts in laparoscopic surgery, we believe our results to be a better reflection of the situation in a training setting, which increases the generalisability of our findings. He also claims the success rate of single dose methotrexate to be similar to the multiple-dose regimen. However, published work shows a primary treatment success of single-dose methotrexate of 75% and of the multiple dose regimen of 95%. As we stated, future studies should focus on varying methotrexate dose, and such studies are being done.

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Folinic acid does not interfere with methotrexate1,2 as Petra Hajenius and colleagues3 suggest it does. Folic acid, which is an analogue of the vitamin folinic acid, can reverse the effects of methotrexate. To reverse the effects of methotrexate, folinic acid has to be given in high doses. Folic acid cannot be obtained over the counter, it must be prescribed.

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**Helicobacter pylori and NSAID-induced ulcers**

SIR—Francis Chan and colleagues (Oct 4, p 975)1 show that Helicobacter pylori eradication is essential to prevent peptic ulcers caused by the use of non-steroidal anti-inflammatory drugs (NSAIDs), whose risk is reduced by almost four-fold after the disappearance of the germ. Accordingly, the investigators conclude that H pylori infection should be sought for and eradicated before the start of NSAID therapy. However, the degree of protection guaranteed by eradication of H pylori is similar to that achieved with two well-known acid-suppressant agents, famotidine and omeprazole. Moreover, both antisecretory drugs are effective even in patients who continue to harbour H pylori in their stomachs. Thus the relevance of H pylori eradication as a prophylactic measure in patients at risk of developing NSAID-associated peptic ulcers is not certain.

On the other hand, H2 blockers have no effect on H pylori and omeprazole alone is only able to determine a temporary suppression, but not a true eradication of H pylori. Moreover, the decrease in gastric acid secretion as result of H pylori eradication can be excluded because the acid output stimulated by pentagastrin, which is the only stimulus capable of exciting the total population of functional parietal cells, does not change even 1 year after H pylori eradication.1 We conclude that the control of gastric-acid secretion is able to prevent NSAID-related ulcers independently of H pylori eradication. If these different pathogenic approaches are equally successful, the mechanism responsible for NSAID-ulcers is not unique and the emphasis placed by Chan and colleagues on the need to eradicate H pylori as the first step to prevent NSAID ulcers should be reduced.

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