longer regimen was subsequently approved as the standard of care.[1] However, sustained responses remained relatively uncommon in patients who were treated with interferon alfa alone. Sustained virological loss was seen in 6-15% of patients after a six month course and this rose to 13-25% after 12 months of treatment.[1] Recent studies that have carefully assessed virological end points of treatment with different regimens have clearly shown that sustained viral responses to interferon alfa monotherapy are at the lower end of these ranges.[2 3]

It was almost a decade before the next major advance in treatment of chronic hepatitis C emerged, namely, the combination of interferon alfa with the oral nucleoside analogue ribavirin. Although ribavirin alone does not seem to be active against the hepatitis C virus, the combination resulted in much improved and sustained biochemical, virological, and histological response rates.[2 3] The mechanism(s) that accounts for the increased efficacy of ribavirin and interferon as combination therapy for hepatitis C virus infection remains poorly understood. The combination of interferon and ribavirin was approved for treating chronic hepatitis C in 1999. Overall, hepatitis C virus is permanently eradicated in about 40% of patients treated with combination therapy in doses appropriate to viral genotype.[2 3] Obviously, as pointed out in the review by Kjaergard and colleagues in this issue (p 1151),[4] many patients who do not respond optimally to the less effective interferon alfa monotherapy will respond to this more effective combination therapy.[5]

Recent studies have shown that long acting pegylated interferons have better viral responses than standard interferon alfa preparations. Pegylation involves attaching a large inactive molecule, polyethylene glycol, to a protein in order to reduce clearance. This longer half life allows large doses of the drug to be given infrequently—once weekly. The process pays a price in that there is variable loss of activity of the native protein, depending on the size and site of attachment of the polyethylene glycol molecule. Pegylated interferon alone is about twice as effective as monotherapy with interferon, but it is not as effective as the combination of standard interferon and ribavirin.[6 7] However, the combination of pegylated interferon and oral ribavirin considerably improves antiviral activity and results in sustained eradication of hepatitis C virus in 54-56% of treated patients.[8 9] Once again, responses are genotype dependent and are sustained in 42-46% in patients infected with genotype 1 and 76-82% in genotype 2 or 3.[8 9]

Sustained virological response rates are now achievable in more than half of patients with chronic hepatitis C who are candidates for treatment.[8 9] Viral clearance is associated with a reduction of hepatic inflammation and fibrosis on liver biopsy,[10 11] and it is reasonable to assume that viral clearance will translate into a reduction in morbidity and mortality. This has been projected by mathematical modelling and cost benefit analyses.[12 13] A dedicated and vigorous research effort continues in the hope of identifying new agents that will further improve the response and ease of administration of treatment.

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Promoting normality in childbirth

Women and professionals should be encouraged to consider vaginal birth positively

Researchers have shown much interest in possible explanations for rising caesarean section rates.[1] Consumer choice is seen as being very influential. An often cited survey of London obstetricians found that 31% would choose caesarean section as their preferred mode of delivering babies.[2 3] However, there appear to be paradoxes within this decision making process.[4] Professionals choose abdominal delivery, on the basis that it appears to be "easier, less painful and more convenient," even though they consider it to be more expensive and dangerous than a vaginal delivery.[4] A subsequent study, with a

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wider national base, found a more balanced attitude to normal birth, but this has yet to be commented on in the national press.[5] National data in this area have been collected and the results of the national sentinel audit of caesarean section were presented at the Royal College of Obstetricians and Gynaecologists on 26 October 2001. Accurate comparative figures on rates, indications, standards which can be audited, women's views and clinicians' attitudes are available at www.rcog.org.uk/guidelines/nscs-audit.pdf

Although mothers' overall satisfaction with the experience of childbirth is influenced by availability of choice and the sense of control, adverse views undoubtedly correlate significantly with the degree of intervention.[6] There is evidence that obstetric interventions in labour tend to lead from one to another. Women who have labour induced need more help with pain relief, epidurals lead to more instrumental births, and perineal trauma causes dyspareunia. Long term morbidity after childbirth may be significant and is particularly related to instrumental and caesarean delivery. Specific concerns relate to painful intercourse and urinary and anal incontinence. Even elective caesarean section does not avoid these particular complications, which may have a closer relation to pregnancy itself than the mode of delivery.[7] Doctors have a duty not to harm their patients, so must ensure that any care does more good than harm, taking into account long term as well as short term effects.

A focus on reducing caesarean section rates might be perceived as somewhat negative. An alternative approach is to ask what can be done about increasing the numbers of women who have a straightforward vaginal birth, an intact perineum, and a healthy baby. We need to know which systems of care are associated with optimal rates of normal birth.

Provided the baby and the mother are well and not compromised, there is good evidence that avoiding an initial obstetric intervention and providing women with one to one support increases the opportunity that women will give birth spontaneously and avoid the increased risks of surgery, perineal trauma, and separation from their baby associated with more complex births.[8]

A further series of studies have examined the possibility of more extended continuity of care.[9] Disappointingly, although these studies showed significant reductions in interventions such as epidural analgesia and episiotomy, they did not increase rates of normal delivery.[9] The rates of intervention and variations in outcome are far greater between studies than within them,[9] suggesting that factors related to the system have a greater influence on intervention rates than specific midwifery input.

Epidural analgesia rates (69%) in traditional care at Queen Charlotte's Hospital are higher than for those having one to one midwifery care (56%) but contrast dramatically with a rate of 10.5% in the caseload group in North Staffordshire.[9] The audit commission commented on the wide variations in intervention seen around the United Kingdom.[10] Indeed, medicalisation of the environment could be the dominant effect in the United Kingdom, over-riding potential benefits of continuity of support and "knowing your midwife."

Avoiding defensive and medicalised environments may be the most important next step. Initial evaluation of the Edgware birthing centre has been very positive,[11] and successful community focused approaches have been reported from other countries. In the Swedish birthing centre study normal delivery rates of nearly 90% were achieved.[12]

Further work urgently needs to be undertaken to extricate the essential ingredients of success from midwifery units and regions that achieve a high normal delivery rate with few interventions. Expectations and attitudes of the community as well as those of pregnant women and their carers are important. New approaches that examine choice and control need to be examined, particularly in a climate where some women are choosing interventions. Putting evidence into practice could improve the outcome of labour for many thousands of women, and providing there is a commitment to increasing the proportion of straightforward vaginal births, change can be achieved without significant additional funding.

It is important that all women and professionals should be encouraged to consider vaginal birth positively. Women who have had a surgical delivery should be encouraged to consider a trial of scar. Among professional colleagues increasing interest and commitment to external cephalic version for breech pregnancy[13] and implementation of the NICE guidelines on fetal monitoring (www.rcog.org.uk/guidelines/eb-guidelines.html) are likely to be associated with a reduction in unnecessary intervention. At the same time, further research is required on avoiding perineal injury and on appropriate recognition and repair of injuries, with a view to reducing the long term incidence of incontinence. (www.keele.ac.uk/depts/og).

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