LETTERS

Bacterial vaginosis and preterm delivery

Bacteria may contribute to lung disease in neonates

EDITOR,—Phillip E Hay and colleagues' report on abnormal bacterial colonisation of the genital tract and preterm labour.[1] The association between infection and preterm labour has been widely reported, with the genital mycoplasmas *(Ureaplasma urealyticum* and *Mycoplasma hominis)* often being implicated.[2] Many of the preterm infants need ventilation, and a considerable number develop chronic lung disease. In our unit in 1993 there were 84 survivors of ≤30 weeks' gestation, of whom 41 developed chronic lung disease. The aetiology of this disease is multifactorial, with gestation and positive pressure ventilation being the most important determinants.

In a pilot study of the incidence of ureaplasma and mycoplasma infections the endotracheal secretions of all intubated neonates of ≤30 weeks' gestation (n=63) were examined weekly from birth while the neonates remained intubated. Sixteen of the infants were positive for one or both organisms, with 11 yielding positive results on the first culture. Fifteen (94%) of these 16 infants with positive cultures went on to develop chronic lung disease whereas only 18 (38%) of the 47 infants for whom culture yielded negative results developed the disease ($P<0.001$). There were no significant differences between the two groups in gestation, birth weight, and duration of positive pressure ventilation.

These data agree with data from the United States.[3] It has been suggested not only that these organisms induce preterm labour but that their presence in the lungs causes a low grade inflammatory response, increasing the need for ventilation and hence increasing the degree of damage done by the ventilator, resulting in chronic lung disease. The presence of an inflammatory response in the development of chronic lung disease from the respiratory distress syndrome is well recognised,[4] and we have found an association between high levels of the cytokine interleukin-8 (as a marker of inflammatory response) on day 2 of life and subsequent chronic lung disease (J McColm, N McIntosh, unpublished observations).

We have started an intervention study looking at the relation between infection, acute inflammatory response, and chronic lung disease and the effect of early treatment with erythromycin. Chronic lung disease has a high mortality and morbidity, and any intervention that reduces its incidence and severity will have important implications in neonatal care.

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1 Hay PE, Lamont RF, Taylor-Robinson D, Morgan DJ, Ison C, Pearson J. Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage. *BMJ* 1994;308:295-8. (29 January.)
2 Cassell GH, Waites KB, Watson H-L, Crouse DT, Harasawa R. Ureaplasma urealyticum intrauterine infection: role in prematurity and disease in newborns. *Clin Microbiol Rev* 1993;6: 69-87.
3 Cassell GH, Waites KB, Crouse DT, Rudd PT, Canupp KC, Stagno S, *et al.* Association of Ureaplasma urealyticum infection of the lower respiratory tract with chronic lung disease and death in very-low-birth-weight infants. *Lancet* 1988;ii:240-5.
4 Robertson B. The evolution of neonatal respiratory distress syndrome into chronic lung disease. *Eur Respir J* 1989; 2(suppl):33-7.

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Little evidence of causal association

EDITOR,—Phillip E Hay and colleagues report an association between bacterial vaginosis in early pregnancy and subsequent late miscarriage and preterm delivery.[1] Although a causal effect has yet to be shown, many people have quoted previous studies with similar findings[2]—and will no doubt quote this study—as evidence that bacterial vaginosis in asymptomatic women should be treated.

Bacterial vaginosis often has an identifiable underlying cause. It can be associated with the presence of an infection such as *Chlamydia trachomatis* infection, which itself has been associated with adverse outcome of pregnancy.[3] In non-pregnant women the vaginal flora may alter cyclically, and bacterial vaginosis is uncommon in prepubertal girls and postmenopausal women[4]; this suggests that hormonal changes may result in alteration of the vaginal flora. Other women find that unprotected sexual intercourse precipitates symptoms. There is no good evidence that bacterial vaginosis is a sexually transmitted disease, and it has been suggested that semen, by altering the pH of the vagina, can lead to an alteration in the flora. We note that in Hay and colleagues' study the presence of sperm in the Gram stained slides was recorded, although any correlation between this and the presence of bacterial vaginosis was not reported.

It is conceivable that hormonal factors or frequent sexual intercourse, or both, could precipitate preterm labour; certainly, women known to be at risk of miscarriage are commonly advised not to have intercourse in the early stages of pregnancy, and women at term are often encouraged to have intercourse to try to precipitate labour (although scientific evidence supporting this advice is lacking). The finding of increased prostaglandin concentrations in the cervical mucosa of pregnant women with bacterial vaginosis[5] has led to the postulation of a mechanism by which bacterial vaginosis could provoke preterm labour. It is equally conceivable, however, that coitus could stimulate both production of prostaglandin and bacterial vaginosis. Thus bacterial vaginosis could be a marker of risk rather than a cause of adverse outcome of pregnancy.

Because of this the results of controlled interventional studies, such as the one currently being undertaken by Hay and colleagues, should be awaited and the risks and benefits of intervention established before a potentially large number of asymptomatic women are treated, especially during pregnancy, when the use of drugs should be minimised.

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1 Hay PE, Lamont RF, Taylor-Robinson D, Morgan DJ, Ison C, Pearson J. Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage. *BMJ* 1994;308:295-8. (29 January.)
2 Gravett MG, Hummel D, Eschenbach DA, Holmes KK. Preterm labour associated with subclinical amniotic fluid infection and bacterial vaginosis. *Obstet Gynecol* 1986;67: 229-37.
3 Ryan GM, Abdella TN, McNeelley SG, Baselski VS, Drummond DE. Chlamydia trachomatis infection in pregnancy and effect of treatment on outcome. *Am J Obstet Gynecol* 1990;162:34-9.
4 Mardh PA. The definition and epidemiology of bacterial vaginosis. *Rev Fr Gynecol Obstet* 1993;88:195-7.
5 Platz-Christensen JJ, Brandberg A, Wiqvist N. Increased prostaglandin concentrations in the cervical mucosa of pregnant women with bacterial vaginosis. *Prostaglandins* 1992;43:133-4.

Spurious link may lead to overtreatment

EDITOR,—Phillip E Hay and colleagues confirm[1] the well known and highly significant relation between previous preterm delivery and preterm delivery.[2-5] It has been inferred from this relation that an underlying factor leads to preterm delivery in the index case and recurs with the occurrence of further preterm deliveries. Consequently it is surprising that the authors did not publish an analysis of their data on primiparous singleton pregnancies and show the association between bacterial vaginosis and preterm labour in these pregnancies.

Hay and colleagues' work shows that the association between previous preterm delivery and preterm delivery ($P<0.001$) is much greater than the association between preterm delivery and bacterial vaginosis at the initial antenatal visit ($P=0.04$). Unusually, previous preterm delivery and bacterial vaginosis were considered to be independent predicting variables; this is surprising because bacterial vaginosis, which is a chronic recurrent condition, is postulated to be a causative factor in repeated preterm labour. If bacterial vaginosis is truly predictive of preterm delivery the logistic regression analysis should be expected to show that preterm delivery is more strongly associated with bacterial vaginosis than previous preterm delivery as bacterial vaginosis will be a factor occurring in index cases but previous preterm delivery will not.

These findings therefore question whether bacterial vaginosis is implicated as a cause of preterm delivery. The assumption that bacterial vaginosis leads to preterm labour will lead to a false sense of security among those mothers who do not have bacterial vaginosis as well as to unnecessary antibiotic treatment in mothers with bacterial vaginosis.

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1 Hay PE, Lamont RF, Taylor-Robinson D, Morgan DJ, Ison C, Pearson J. Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage. *BMJ* 1994;308:295-8. (29 January.)
2 Kaminski M, Goujard J, Rumeau-Rouquette C. Prediction of low birth weight and prematurity by a multiple regression analysis with maternal characteristics known since the beginning of pregnancy. *Int J Epidemiol* 1973;2:195-204.