

Antenatal corticosteroids to prevent neonatal respiratory distress syndrome

We do not know whether repeated doses are better than a single dose

Administering corticosteroids to pregnant women at risk of preterm birth to reduce the severity of neonatal respiratory distress syndrome is an established intervention. The origins of this practice came in 1972 from the pioneering work of Liggins and Howie, who showed a significant reduction in the incidence of respiratory distress syndrome in preterm babies whose mothers had received antenatal corticosteroids.¹ These agents are thought to improve surfactant production, and there is also an associated reduction in the risk of neonatal intraventricular haemorrhage, necrotising enterocolitis, hyperbilirubinaemia, and neonatal death. What remains unclear, however, is whether repeat doses should be given if delivery does not occur shortly after the initial course.

Most obstetric units in the United Kingdom administer either betamethasone or dexamethasone as a course of two doses over 24 hours. The evidence for this practice is mainly based on only a single course of antenatal corticosteroids in singleton pregnancies given for up to seven days before delivery and included few multiple pregnancies or pregnancies under 28 weeks' gestation.² No adverse maternal or neonatal effects of this treatment have been noted in the 18 randomised trials of antenatal corticosteroid therapy, nor have any long term adverse effects on infant growth or disability rates been observed.²

There is, however, international variation in the use of antenatal corticosteroids: only 45% of pregnant women received them before the birth of preterm infants according to a study in nine Scottish hospitals,³ although these data may have been affected by factors that prevented corticosteroid administration, such as severe antepartum haemorrhage or precipitate labour. A survey found that 97% of Australian obstetricians would prescribe antenatal corticosteroids in the classic setting of uncomplicated preterm labour,⁴ while a North American study of 27 tertiary care hospitals reported that 30% of eligible women received antenatal corticosteroids.⁵ According to a recent study of 210 obstetric units in the United Kingdom, 98% of women at risk of preterm birth receive prophylactic antenatal corticosteroids.⁵

In women who remain undelivered but at continued risk of preterm birth it is common practice to administer repeated doses of corticosteroids every 7-10 days. Some data suggest that 74% of UK maternity units give repeated doses on a weekly basis

to such women.⁶ This practice has arisen because the evidence from randomised trials suggested that infants delivered after seven days of maternal corticosteroid treatment did not have a lower incidence of respiratory distress syndrome, implying that the effect of treatment is short lived.^{1,2} In addition, experiments have shown that the induction of surfactant production in the lung is reversible and that betamethasone is cleared from the fetal circulation 48 hours after maternal administration. More recent observations of preterm infants delivered over seven days after maternal corticosteroid treatment showed that the efficacy of therapy was maintained,⁷ though the effect of increasing gestation confounds these results.

The safety of repeated antenatal corticosteroid therapy has not yet been reported in randomised trials. The results from retrospective observational studies suggest varying maternal and infant effects. Some concerns exist about altered glycaemic control, fluid overload when used in conjunction with tocolytic agents, a transient increase in maternal bone resorption, and osteonecrosis of the maternal femoral head. Other theoretical risks to the mother include pulmonary oedema, exacerbation of hypertension, and an increased risk of maternal sepsis. In neonates serum cortisol levels at birth do suggest some suppression of the fetal pituitary-adrenal axis after exposure to multiple courses of antenatal corticosteroids,⁸ although this does not seem to be deleterious.⁹ Transient hypertrophic cardiomyopathy has also been reported in neonates exposed to multiple courses of maternally administered corticosteroids, but this appears to be temporary.¹⁰ Other adverse effects of repeated corticosteroid use include fetal growth restriction,¹¹ which was reported to be as much as 9% in a recent Australian non-randomised cohort study of 477 neonates born before 33 weeks' gestation.¹²

No trials have been performed which address the hypothesis that repeated courses of corticosteroids given to pregnant women are more effective than single dose therapy. The Royal College of Obstetricians and Gynaecologists' guidelines recommend prophylactic use of corticosteroids up until 36 weeks' gestation. Inevitably, this protocol increases the propensity for repeated courses of corticosteroids in pregnancies complicated by events that may lead to preterm birth, such as recurrent episodes of antepartum haemorrhage or threatened preterm labour.

There is a clear need for a multicentre, randomised trial to assess the risks and benefits—both to mother and fetus—of single versus repeated doses of antenatal corticosteroids. Several such studies, such as the TEAMS (trial of early and multiple steroids) project in the UK, are planned or in progress in several countries, including Australia, New Zealand, Canada, and the United States. Until the results of these studies are available we suggest that only a single course of antenatal corticosteroids should be given to all women at risk of preterm birth at 24-36 weeks' gestation.

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The specialist of the discipline of general practice

Semantics and politics mustn't impede the progress of general practice

Over the past 50 years general practice has established itself not only as an academic discipline with its own curriculum, research base, and peer reviewed journals but also as the cornerstone of most national healthcare systems in Europe. In so doing, general practitioners have shown that the intellectual framework within which they operate is different from, complementary to, but no less demanding than that of specialists. General practitioners must achieve a working diagnostic and therapeutic knowledge across the reach of biomedical science and must be able to forge effective and continuing relationships with an enormous range of individual patients. They need to understand the processes by which illness is socially constructed within the patient's life, and they must mediate between the patient's subjective experience of illness and the scientific explanation.

The breadth and comprehensiveness of its endeavour has made general practice notoriously difficult to define.¹ On p 354 Olesen et al attempt a new definition that emphasises the frontline nature of the care offered and the need to incorporate psychological and sociological perspectives alongside biomedical ones.² Immediately, in using the term "specialist," they have become ensnared at the boundary between semantics and politics.

The English language uses "generalist" and "specialist" as opposites. Other languages may be more obliging, but in the *BMJ* we are stuck with English and must find a way of using it that does not obstruct our purposes. In many European countries general practitioners have needed to claim specialist status to achieve recognition as a separate discipline. In the United Kingdom, however, this recognition has been accomplished through exploiting the notion of opposites and

showing that the expertise of the generalist is complementary to that of the specialist and that the two are profoundly interdependent. Having achieved this, many British general practitioners will find it difficult to accept a definition that includes the word specialist. Yet much rides on the use of this word.

The notion of opposites, with its consequences for optimal (cost) effective health care,³ in fact implicitly underlines the specific virtues of general practice. General practice is special—a specialty—not so much in terms of in depth expertise in the complexity of a defined biomedical area but in the complexity of medical care in the patients' context.⁴ Its focus is on integration and the ability to switch between different perspectives (biomedical, humanities) around patients' health problems.⁵ This relates to a specific set of concepts, rules, and criteria⁶ that appear in the definition of Olesen et al.² Yet the main database for biomedical research, *Index Medicus*, does not accept general practice as a specialty heading and provides an incomplete listing of general practice research journals. This severely impedes academic progress in general practice and is just one, but probably the most important, example of how recognition as a specialty might greatly strengthen the position of general practice.

The situation is further complicated by the complexities of European legislation, which seem to imply that general practitioners must claim specialist status if they are not to be disadvantaged in relation to specialist colleagues. The division between specialist and generalist is enshrined in the European Union Medical Directives, which have separate sections dealing with postgraduate education and training for specialists (title 3) and for general practice/family medicine (title 4). The requirements under title 4 are

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