Antenatal steroids were first introduced to perinatal practice in 1972 by Liggens and Howie who showed that their use could reduce incidence of respiratory distress syndrome in premature infants. Since their introduction to clinical practice, many randomized controlled studies have confirmed the positive maturation effects of antenatal corticosteroids, which result in lower incidence and severity of respiratory distress syndrome, lower incidence of intraventricular hemorrhage, and decreased mortality.

The notable implications of antenatal corticosteroid therapy resulted in the National Institutes of Health recommending them for routine use at 24 to 34 weeks’ gestation when preterm delivery is anticipated. Use of antenatal steroids is today considered a standard of care and has dramatically increased over the last decade.

Despite the proven benefits of antenatal steroids, there are still controversies regarding their use. Important issues include type of corticosteroid that should be used, timing of administration, duration and number of doses given, whether recent advances in neonatal care have decreased the effectiveness of antenatal steroids, whether corticosteroids should be used when there is premature rupture of membranes (PROM) or preeclampsia, and what the long-term effects of corticosteroids are.

Dexamethasone and betamethasone are the corticosteroids recommended for antenatal therapy. These compounds have similar biologic activity, readily cross the placenta, have no mineralocorticoid activity, and have relatively weak immunosuppressive action.

Do you have questions about the safety of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at (416) 813-7562; they will be addressed in future Motherisk Updates. Published Motherisk Updates are available on the College of Family Physicians of Canada website (www.cfpc.ca). Some articles are published in The Motherisk Newsletter and Motherisk website (www.motherisk.org) also.
For the last two decades, there has been no preference between the two, but a recent study suggests that betamethasone might be the better choice.4 In a large cohort of 881 infants born from 24 to 31 weeks’ gestation, use of betamethasone was found to be associated with a 50% decrease in the rate of cystic periventricular leukomalacia when compared with a control population. There was a trend toward increase in this adverse neurologic outcome among infants exposed antenatally to dexamethasone.

Timing
Timing is an important element in the effectiveness of antenatal corticosteroid treatment. Strong evidence supports the benefits of antenatal steroids starting at 24 hours and lasting at least 7 days after treatment.2,3 There is a demonstrable reduction in morbidity and mortality even when antenatal steroids are given less than 24 hours before delivery. As timing of delivery varies, corticosteroids should be used whenever preterm delivery is expected. There is insufficient evidence to establish a continued effect of antenatal steroids after 7 days. For this reason, some perinatal centres repeat the dose of corticosteroids if preterm delivery is still expected.

Many of the randomized controlled trials evaluating antenatal corticosteroids were completed before use of surfactant for respiratory distress syndrome became the standard of practice. Antenatal corticosteroids have an additive effect when used before surfactant replacement and continue to reduce respiratory distress syndrome, intraventricular hemorrhage, and death.3,5

Effectiveness
The effectiveness of antenatal corticosteroids when pregnancy is complicated by PROM has not been clearly demonstrated. Meta-analysis5 shows that steroids can reduce respiratory distress syndrome, intraventricular hemorrhage, and mortality, but that this result was mainly influenced by one study.7 A more recent observational study found antenatal corticosteroids to be associated with a decrease in intraventricular hemorrhage and death, but not respiratory distress syndrome.8

Despite the possible increased risk of infection when steroids are used in pregnancies complicated by PROM, current guidelines based mainly on expert opinion state that there is a favourable risk-benefit ratio and recommend use of antenatal corticosteroids for this indication.9 Use of antenatal corticosteroids when there is pregnancy-associated hypertension is also controversial, but recent data from a large randomized controlled trial found antenatal steroids decrease neonatal morbidity and mortality in infants born at 26 to 34 weeks’ gestation with no adverse effects on maternal hypertension.10

Antenatal corticosteroids have had a positive effect on the perinatal outcome of preterm infants. Long-term follow-up studies have not demonstrated any adverse neurologic sequelae in preterm survivors up to the age of 12 years.11,14 Antenatal corticosteroids have been found to be associated with higher mean blood pressure levels at 14 years of age in a cohort of 210 preterm survivors, but only a few had blood pressure levels in the hypertensive range.15

Repeated doses
Repeated courses of antenatal corticosteroids are less well studied than single courses and are controversial. The rationale for repeated doses is the decreasing efficacy of antenatal corticosteroids after more than 7 days. Multidose antenatal steroids have been found in one retrospective study to decrease incidence of respiratory distress syndrome.16 Other studies have failed to show any such benefit.17,18 Animal models have shown that repeated betamethasone doses cause growth retardation that persists to term.19 Similar findings have been described in humans.20 When antenatal steroids were used repeatedly every week until 32 weeks’ gestation or delivery, a large observational study demonstrated a negative association between increasing doses of antenatal corticosteroids and birth weight and head circumference.20 Although no association was found at 3 years old, a reduced head circumference could affect later development. Additional adverse effects from multiple corticosteroid courses are adrenal depression17,21 and increased mortality.17

Conclusion
Use of a single course of antenatal corticosteroids when preterm labour is anticipated decreases incidence of respiratory distress syndrome, intraventricular hemorrhage, and death. Long-term follow-up of large cohorts has not shown any adverse neurologic sequelae. There is insufficient evidence to show that multiple courses of antenatal corticosteroids are more effective than a single dose. Serious concerns exist regarding the long-term outcome of infants exposed prenatally to multiple doses of corticosteroids.

References