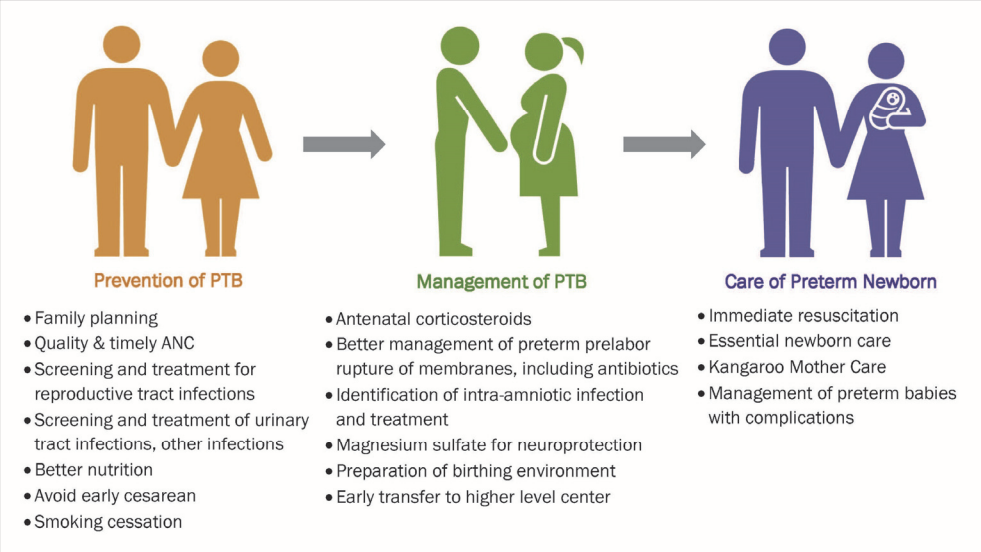
ADMINISTRATION OF ANTENATAL CORTICOSTEROIDS

Technical Guidance for Program Implementation

Preterm Birth: Epidemiology and Consequences

Babies born before 37 completed weeks of gestation are considered preterm babies. More than one in ten babies are born preterm. Preterm birth (PTB) and the complications arising from PTB are the leading causes of newborn deaths worldwide, resulting in more than one million deaths per year. Preterm babies have numerous challenges including difficulty feeding and maintaining body temperature. More serious complications can develop such as necrotizing enterocolitis (death of intestinal tissue) and intraventricular hemorrhage (bleeding into the brain). The primary cause of newborn death and disability from PTB is respiratory distress syndrome (RDS) – difficulty breathing due to underdevelopment of the lungs. Of babies born preterm, survivors may experience lifelong health challenges such as cerebral palsy, impaired learning ability, chronic lung disease, vision and hearing disabilities, and compromised physical health.[i] [ii]

A Three-Phased Approach to Preterm Birth



The Role of Antenatal Corticosteroids

As illustrated in the above graphic, action can be taken to intervene at critical windows of opportunity on the continuum of care from preconception through the care of a preterm baby to reduce the consequences of preterm birth. This technical briefer focuses specifically on the use of antenatal corticosteroids as one of the key interventions to be implemented by a skilled birth attendant.

How effective are ACS?
34% reduction in RDS
46% reduction in IVH
54% reduction in NEC
31% reduction in death[i]

Antenatal administration of corticosteroids to women at risk of imminent preterm birth is the single most beneficial intervention for improving outcomes among babies born prematurely.[iii] Near universal coverage of ACS across 75 priority countries may result in a 40% reduction in newborn death due to complications associated with prematurity.[ii]

ACS are extremely effective in reducing RDS severity and mortality. They are inexpensive, available in most settings, and can be administered by all skilled birth attendants.

Best Practice

A single course of antenatal corticosteroids should be given to a mother who is preterm[1] and for whom PTB is anticipated within 7 days. This includes women with preterm labor and preterm prelabor rupture of membranes, as well as women with conditions necessitating delivery for the safety of the mother, such as antepartum hemorrhage or severe pre-eclampsia/eclampsia.[iv] Ideally, the course of ACS should be initiated at least 48 hours prior to delivery to have maximum benefit.

Overview of Antenatal Corticosteroids for PTB	
Medication 	Give **dexamethasone** (or **betamethasone**) 24mg IM in divided doses. A regimen of 12mg IM every 12 hours for two doses is recommended for ease of administration, but other regimens are also acceptable. *Note*: Dexamethasone and betamethasone are clinically equally effective, however dexamethasone is preferable since it is more widely available and less expensive. Give the first dose immediately upon determining that the woman has a condition that increases her chance of preterm birth within the next 7 days. The maximum benefit of the medication is achieved 48 hours after the first injection. However, even a partial or incomplete course provides some benefit. Because the precise time of delivery cannot be predicted, the medication should be initiated immediately when a condition leading to preterm birth is identified. *Note*: There is no evidence to support administering the full 24mg as a single dose prior to an imminent birth.[iii]
Mechanism of Action	Preterm babies do not have enough surfactant in their lungs. Surfactant helps the lungs expand during breathing, and therefore babies who lack surfactant commonly develop RDS. ACS increase the natural production of surfactant, and thus reduce the risk that newborns will develop severe RDS if born early. ACS have also been shown to have a protective effect on cerebral blood vessels, thus reducing the risk of intraventricular hemorrhage, and on the intestines, thus reducing the chance of necrotizing enterocolitis.
Considerations	Any pregnant woman who is preterm and has an increased likelihood of delivery within 7 days should receive ACS. The first dose should be given even if it is believed that the full course is not likely to be completed prior to delivery. Delivery should not be delayed in order to complete the ACS course in cases where delivery should be expedited, such as chorioamnionitis or eclampsia. In women with diabetes, blood sugars should be closely monitored and additional insulin may be required. Women on chronic steroids can be given ACS but may also need a stress dose of their steroids at the time of delivery. There are no absolute contraindications for ACS.
Medication Administration	Corticosteroid injections are given intramuscularly at a 90 degree angle with a 22-25 gauge, 1-1.5 inch long sterile needle into the upper arm, buttock, or thigh. Be sure to document medication, dose, time, and date, as well as the site of administration.
Administering Provider	The decision to give ACS is typically made by a skilled birth attendant. The injection can be administered by personnel trained to give injections, according to local country policy.

[1] Beneficial effects have been observed at all gestational ages, however, evidence is conclusive when ACS are administered to women at risk of imminent preterm birth between 24^{+0} and 34^{+6} weeks gestation at hospital level. When accurate estimation of gestational age is difficult, it is recommended to administer ACS from 24 to 37 weeks. Country guidelines may differ on the recommended gestational age range for administration.

Steps to Administer ACS

Follow these steps for proper administration of ACS.

1. Once a condition increasing the likelihood of PTB in the next 7 days is identified, ACS are indicated.
2. Facilities that provide basic EmONC should be able to initiate a course of ACS by administering the first dose prior to transfer. If referral is needed, follow facility protocol for immediate referral.
3. Follow these steps:
    a. Cousel the woman: explain risks, benefits and what will be done. Ask permission.
    b. Wash and dry hands and put on clean gloves.
    c. Prepare the IM injection site (either the upper arm, buttock, or thigh). Clean the skin with cotton and alcohol or spirits.
    d. Using a small sterile syringe and needle, maintain sterile technique and draw up 12mg of dexamethasone. Discard all opened ampoules.
    e. Tell the woman what will be done and give injection.
    f. Properly dispose of needle and syringe in an appropriate sharps container.
    g. Properly remove gloves and discard appropriately.
    h. Wash and dry hands.
    i. Document medication, dose, site of administration, and time it was given in the patient record. Document the time when the next dose should be administered.
    j. Advise the woman of the timing of the next dose.

Clinical Considerations[2]

Partial dose: If a woman receives only a partial dose of ACS before her baby is born, there is still a reduction of the risk of RDS. Document in the patient record the dose and time of each injection administered.

Single course or repeat courses: If a woman receives a complete course of ACS for threatened PTB but does not give birth, ***one*** additional course can be considered if the prior ACS treatment was given more than 7 days ago, if the woman has intact membranes and if she is assessed to likely give birth in the next 7 days.[v] There is evidence to demonstrate a small additional benefit to the baby from a single additional course of ACS within these parameters. Repeated courses, at weekly or other intervals, however, are not recommended and may cause harm to the baby.[i] [vi]

Challenges to ACS administration: The major difficulty is correctly identifying women who have an increased risk of imminent PTB in time to administer ACS. Timely and appropriate diagnosis is critical through immediate assessment of women who present for evaluation with complaints of bleeding, contractions or loss of fluid, or symptoms of pre-eclampsia/eclampsia. Clinical teams must develop a "heightened awareness" of the conditions that lead to preterm birth and must be able to initiate therapy to those women with an increased likelihood of imminent PTB.

Giving ACS when there are other complications of pregnancy: Administration of ACS is recommended to speed fetal lung maturity in all women who are preterm and have an increased likelihood of giving birth within 7 days, regardless of other complications of pregnancy. ACS should be initiated even if it is believed that the full course may not be completed prior to delivery. Delivery should not be delayed in order to complete the ACS course in cases where delivery should be expedited, such as chorioamnionitis or severe pre-eclampsia/eclampsia. In women with diabetes, blood sugars should be closely monitored and additional insulin may be required. Women on chronic steroids can receive ACS but may also need a stress dose of their steroids at the time of delivery. There are no absolute contraindications for ACS.

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[2] It is anticipated that in 2013 WHO will convene a guidelines development committee to produce new guidelines on management of prematurity.

Additional Care for Woman with Threatened PTB

Tocolysis: Medications to stop uterine contractions (such as nifedipine or indomethacin) may be useful to prolong pregnancy for a short time (up to 48 hours) to allow administration of ACS or transfer to a higher level facility. Tocolysis has not been shown to reduce rates of preterm birth.[vii] [iii]

Transfer to a higher level facility: A woman with an increased likelihood of a preterm birth should be cared for in a facility where both the mother and baby can receive appropriate care. If a lower level facility is unable to provide adequate care, and if the mother is stable, transfer should take place while the baby is still in utero. Otherwise, stabilize the newborn and transfer to a higher facility.

Antibiotics: There is strong evidence supporting antibiotic use for preterm prelabor rupture of membranes (PPROM) because it delays labor and reduces neonatal infection rates.[ii] Antibiotics should be given to women with PPROM. Give ampicillin 2gms IV twice daily and erythromycin 250mg orally three times daily for two days, followed by amoxicillin 500mg orally and erythromycin 250mg orally three times daily to complete 7 days of therapy. Multiple studies have shown no improvement in outcomes from the use of antibiotics in women with intact membranes and preterm labor.[viii] [iii]

Supportive Environment Needed to Implement ACS as Best Practice

- Establish national service delivery guidelines/protocols for use of dexamethasone in PTB management or ensure it is integrated into existing guidelines.
- Ensure functioning supply and delivery systems in place to support a continuous supply of necessary medication and supplies.
- Incorporate updated guidelines for administration of dexamethasone into pre-service education for skilled birth attendants and other healthcare providers. Ensure education includes didactic and practical learning based on nationally standardized competencies.
- Engage professional associations of healthcare cadres who manage preterm birth or care for newborns born preterm to support the dissemination and adoption of ACS as best practice.
- Provide in-service training on use of dexamethasone for all skilled birth attendants and provide necessary supportive supervision to ensure best practice is integrated into care.
- Strengthen antenatal screening to include messages that all women should report to a facility if conditions that predispose her to PTB occur, such as preterm uterine contractions, preterm rupture of membranes, and symptoms of pre-eclampsia/eclampsia.[ix]
- Increase community awareness of the importance of preterm birth prevention and the signs of threatened preterm birth to encourage early and appropriate referral of women and babies needing preterm birth care.
- Support the provision of essential newborn care after delivery, including Kangaroo Mother Care or other appropriate services or referrals for babies born prematurely.

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[i] Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No: CD004454. DOI: 10.1002/14651858.CD004454.pub.2.
[ii] Born Too Soon: The Global Action Report on Preterm Birth. World Health Organization. Geneva, 2012.
[iii] ACOG Practice Bulletin No. 127. Management of preterm labor. *Obstetrics & Gynecology,* 2012. 119 (6); 1308-1317.
[iv] NIH Consensus Statement, Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes. 1994 Feb 28-Mar 2; 12(2): 1-24.
[v] ACOG Practice Bulletin No. 127. Management of preterm labor. *Obstetrics & Gynecology,* 2012. 119 (6); 1308-1317.
[vi] Crowther CA, McKinlay CJ, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal outcomes. *Cochrane Database of Systematic Reviews* 2011, Issue 6. Art. No: CD003935. DOI: 10.1002/14651858.CD003935.pub3.
[vii] Hearne, AE, Nagley, DA. Therapeutic agents in preterm labor: tocolytic agents. *Clinical Obstetrics and Gynecology*, 2000; 43:787-801.
[viii] King, JF, Flenady V, Murray L. Prophylactic antibiotics for inhibiting preterm labour with intact membranes. Cochrane Database of Systematic Reviews 2002, Issue 4. Art. No.:CD000246. DOI: 10.1002/14651858. CD000246. (Meta-analysis)
[ix] Hofmeyr GJ. Antenatal corticosteroids for women at risk of preterm birth: RHL commentary (last revised: 2 February 2009).*The WHO Reproductive Health Library*; Geneva: World Health Organization.