

Antibiotic Prophylaxis for Pregnant Women during Peripartum Period

Chinese Eugenics Science Association

ABSTRACT OBJECTIVE To standardize the antibiotic prophylaxis for pregnant women during peripartum and reduce the irrational use of antibiotics. **METHODS** Initiated by the Chinese Eugenics Science Association, and led by the First Affiliated Hospital of PLA Army Military Medical University, clinical, pharmaceutical and evidence-based medicine experts from some Chinese medical institutions jointly developed a tiered program of prophylactic use of antibiotics during the peripartum period aiming at the characteristics of pregnant women during the peripartum period by collecting relevant issues, combining national guiding documents, guidelines, expert consensus and literature. **RESULTS & CONCLUSIONS** A total of 13 consensus opinions were formed on antibiotic regimens for prophylactic use before, during and after delivery for vaginal delivery, cesarean delivery and for pregnant women with related complications or comorbidities (such as obesity, abnormal glucose metabolism, combined autoimmune diseases, etc.). However, to reduce the overall risk of infection in pregnant women, antibiotic prophylaxis is just one of the measures. Medical staff must still pay attention to strict disinfection and standard sterilization, and strictly implement balanced nutrition, reasonable control of blood sugar of pregnant women and other comprehensive measures.

KEYWORDS pregnant women; peripartum period; antibiotics; prophylactic use; infection; rational drug use

In order to promote the rational use of antibiotics in clinical practice and curb bacterial drug resistance, in 2015, the Chinese National Health and Family Planning Commission and other departments jointly issued the 《Guidelines for Clinical Antibiotics use (2015 edition)》^[1] and required the use of relevant indicators to monitor and evaluate antibiotics use, such as antibiotic use density (AUD), defined daily dose (DDD), and defined daily doses (DDD) and other relevant indicators. In 2022, the Chinese Health Commission and other departments released 《National Action Plan for Curbing antibiotic Resistance(2022-2025)》, pointing out that the problem of antibiotic resistance in China has been increasing, the situation remains serious and "adhering to the principle of prevention" should be included as one of the main tasks. It is required to popularize the knowledge of antibiotic resistance and rational antibiotics use to the whole population.

In recent years, the average childbearing age of women in China has been on the rise, and the risk of pregnancy with chronic diseases (e.g. diabetes, immune-related diseases, heart disease, etc.) has increased, and pregnant risk factors have become more complex^[2]. Generally, antibiotics are not required for successful vaginal delivery; however, prophylactic antibiotics may be required in cases of pregnancy complications, (e.g. premature rupture of membranes, cardiac disorders, etc.), or/and special circumstances during delivery (e.g. postpartum hemorrhage, severe injury). Studies show that pregnancy infections caused by drug-resistant bacteria and early antibiotics exposure can adversely affect neonatal immunity, the establishment of self-bacterial flora, and their growth and development^[3-5]. Therefore, effective control of peripartum infection risk and rational antibiotics use have become one of the key tasks of obstetrics and pharmacy departments.

There are existing general principles regarding prophylactic antibiotics during peripartum period issued by certain domestic and foreign guidelines. But specific guidelines are still lacking as to the implementation of stratified management and targeted antibiotics use according to the specific circumstances of perinatal period, the refinement of preventive medicine programmes, and the monitoring and evaluation after prophylaxis is completed to determine whether to add antibiotic therapy. In order to establish a comprehensive, systematic and operable guideline for prophylactic antibiotics during peripartum period, promoting the rational antibiotics use, reducing the risk of infection in mothers and

infants, at the same time reducing unnecessary antibiotics exposure. The Chinese Eugenics Science Association initiated the project of "Expert consensus on the prophylactic use of antibiotics for pregnant women during peripartum period" to formulate an expert consensus on this issue.

1 Development of Expert Consensus

1.1 Methodology and Quality of Evidence, and Basis for Grading the Strength of Recommendations

The development of the Expert Consensus was initiated by the Chinese Eugenics Association and led by the First Affiliated Hospital of the Army Medical University of China, with the participation of 53 experts in the fields of clinics, pharmacy and evidence-based medicine from many medical institutions in China. Firstly, members of the writing expert group conducted a comprehensive and systematic search of national guidance documents, relevant domestic and international guidelines/expert consensus and literature, and initially formulate the clinical problem to be solved. Subsequently, the writing expert group adopted investigation and survey method to solicit opinions from the members of the consensus expert group to identify clinical questions for inclusion in the discussion. Finally, after several rounds of deliberation, discussion, and modification the consensus opinions were finally reached. The quality of evidence and strength of recommendation of each consensus opinion were graded with reference to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) principles (Tables 1 and 2) [6].

Table 1 GRADE quality of evidence and definitions

Level of evidence	Definition
A (high quality)	Further research is very unlikely to change our confidence in the estimate of effect
B (moderate quality)	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
C (low quality)	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
D (very low quality)	Any estimate of effect is very uncertain

Table 2 GRADE Recommended Strength Grading and Description

Recommended Strength	Clarification	This consensus recommendation	Recommended method of expressing strength
Highly recommended	The benefits of the intervention clearly outweigh the disadvantages	testimonials	1
Weakly recommended	Interventions may do more good than harm	suggestion	2
Weak recommendation against use	Interventions may do more harm than good or the relationship between harm and good is not clear	not recommended	2
Strongly recommended against use	Interventions clearly do more harm than good	not recommended	1

1.2 Consensus Registration

This Consensus has been registered bilingually on the International Platform for Registration and Transparency of Practice Guidelines (<http://www.guidelines-registry.cn>) (registration number PREPARE-2024CN355).

1.3 To Whom the Expert Consensus Applies

In this consensus, perinatal period refers to the period from labor to 72h after delivery for vaginal delivery and from 12h before to 72h after cesarean section for termination of pregnancy. The consensus applies to pregnant women with ≥ 28 weeks of gestation and no co-infections; it excludes all pregnant women whose pregnancy risk classification (based on the Chinese Health and Family Planning Commission's 2017 «Norms for Pregnancy Risk Assessment and Management of Pregnancies of Pregnant Mothers») is purple (infectious disease) and all pregnant women with active tuberculosis whose

risk classification are orange (higher risk). This consensus focuses on mothers with green (low risk) pregnancy risk classification or special conditions such as related comorbidities and complications (e.g. obesity, abnormal glucose metabolism, autoimmune diseases, use of immunosuppressive drugs, etc.).

2 Expert Consensus

After the experts' deliberations, the Consensus culminates in 13 recommendations, shown in Table 3.

Table 3 Summary of Expert Consensus Recommendations

Number	Consensus	Strength of Recommendation / Quality of Evidence
1	<p>Indications for antibiotic prophylaxis for premature rupture of membranes in pregnant women:</p> <p>(1) Positive screening for group B Streptococcus (GBS) in the last 5 weeks, GBS bacteriuria in pregnancy, previous history of delivery of GBS-infected neonates, unknown GBS colonization status and premature rupture of membranes ≥ 18h, unknown GBS colonization status and temperature $\geq 38^{\circ}\text{C}$, unknown GBS colonization status and previous GBS positivity in pregnancy</p> <p>(2) Antibiotic prophylaxis should be given as soon as possible for premature rupture of membranes in parturient</p>	-
2	<p>(1) A single dose of 1g of cefazolin prophylaxis in cesarean delivery for a normal woman [body weight ≤ 80kg or body mass index (BMI) ≤ 30kg/m²]</p> <p>(2) A single dose of 2g of cefazolin prophylactic in cesarean delivery for Obesity (weight > 80 kg or BMI > 30 kg/m²)</p>	-
3	Perinatal infections are associated with elevated blood glucose levels, and the goal of glycemic control during labor for pregnant women with abnormal glucose metabolism is 4~7mmol/L; breastfeeding should be encouraged for women with diabetes	-
4	The dosage and course of prophylactic antibiotics should not be increased specifically for perinatal abnormalities of glucose metabolism, autoimmune disorders, anemia, etc.	2C
5	For pregnant women with comorbid heart disease, additional antibiotics should not be administered after cesarean delivery or vaginal delivery specifically to prevent infective endocarditis	-
6	For isolated fever during vaginal delivery, if bacterial infection cannot be ruled out, empirical antibiotic therapy should be considered; if intraamniotic infection is suspected or confirmed, therapeutic antibiotics should be initiated urgently.	-
7	<p>(1) Prophylactic antibiotics are not recommended for patients undergoing episiotomy repair</p> <p>(2) Prophylactic antibiotics are not recommended for patients with I or II degree perineal lacerations</p> <p>(3) For vaginal wall laceration repair or III/IV degree perineal tear repair, a single dose of cefazolin (or cefuroxime) \pm metronidazole may be administered, or a cephamycin antibiotic may be used. For IV degree tear repair with fecal contamination, prophylactic antibiotic coverage may be</p>	2D

	extended up to 48h	
	(4) Prophylactic antibiotics are not recommended for patients undergoing operative vaginal delivery	-
	(5) For vaginal deliveries with postpartum hemorrhage $\geq 1,500\text{mL}$, a single dose of cefazolin (or cefuroxime) \pm metronidazole may be administered	2D
8	For cesarean delivery, the prophylactic antibiotic regimen is cefazolin (or cefuroxime) \pm metronidazole. For patients allergic to cephalosporins, clindamycin + an aminoglycoside or an aminoglycoside + metronidazole may be used. For low-risk patients undergoing scheduled cesarean delivery, a single dose of prophylactic antibiotics is sufficient	-
9	To reduce the risk of cesarean section surgical site infections, soap cleansing of the entire body is recommended prior to delivery, and routine skin preparation is not recommended	-
10	Intraoperative maternal core body temperature not less than 36°C	2B
11	(1) If intraoperative blood loss exceeds $1,500\text{mL}$, administer an additional intraoperative dose of cefazolin/cefuroxime. Continue postoperative dosing every 8h. If metronidazole is used concurrently: administer an additional intraoperative dose of metronidazole. Continue postoperative metronidazole dosing every 6h. Total duration of prophylaxis should not exceed 24h	2C
	(2) If the surgical duration is 3 to 6 hours: administer an additional intraoperative dose of cefazolin/cefuroxime. Continue postoperative dosing every 8 hours. If metronidazole is used concurrently (due to its longer half-life): no additional intraoperative dose of metronidazole is needed. Continue postoperative metronidazole dosing every 6h. Total duration of prophylaxis should not exceed 24 hours	2C
	(3) If intraoperative bowel injury occurs: with spillage of intestinal contents (converting the wound to a Class III/contaminated incision): continue the original prophylactic antibiotic regimen postoperatively. Total duration of prophylaxis should not exceed 48h. Without spillage of intestinal contents (wound remains Class II/clean-contaminated): the prophylactic antibiotic regimen and its duration remain unchanged (i.e., as per the original plan, typically not exceeding 24h)	-
12	Antibiotic therapy is recommended for superficial surgical site infections with signs of systemic infection or deep surgical site infections	2C
13	For those who do not have secondary endometritis or bloodstream infections after delivery, the antibiotic used at the time of delivery for suspected or confirmed amniotic cavity infections should be promptly discontinued antibacterial agent	-

-: Relevant guideline recommendations without grading the quality of evidence and strength of recommendation.

2.1 Perinatal Antibiotic Use Among Pregnant Women with Infection-related Risk Factors

Upon admission to the hospital, the doctor should check the pregnancy health care related data (health care booklet, auxiliary examination results, etc.), ask her medical history, complete physical examination,

auxiliary examination, and complete the assessment of pregnancy risk grading^[7] to confirm the presence of infection, and assess the presence of pregnancy complications, complications, or other special circumstances associated with the infection, (e.g., preterm rupture of membranes, obesity, glucose metabolism abnormality, anemia, cardiac disease, immunosuppressive drugs during pregnancy, etc.)^[8]. Antibiotic regimens vary for different women during the peripartum period.

2.1.1 Premature Rupture of Membranes

Infection prophylaxis regimens differ for women with term preterm rupture of membranes at term versus preterm premature rupture of membranes: term premature rupture of membranes, the rate of infection with the duration of rupture, and early termination of pregnancy is recommended to minimize the risk of infection; prophylactic antibiotic should be given as soon as possible after the onset of preterm premature rupture of membranes. The infection prevention program for premature rupture of membranes is mainly aimed at GBS: for those with term premature rupture of membranes, if GBS screening has been negative in the past 5 weeks, there is no GBS bacteriuria during this pregnancy, and there is no birth history of GBS infection in previous pregnancies, it is not necessary to use antibiotics for GBS prevention^[9-12]. Antibiotic prophylaxis in cases with unknown GBS colonization status and premature rupture of membranes ≥ 18 h (the 10th edition of 《Obstetrics and Gynecology》 states that antibiotics should be used prophylactically in cases of preterm rupture of membranes at full term and rupture of membranes for more than 12h^[13]), in cases with unknown GBS colonization status and a temperature of $\geq 38^{\circ}\text{C}$, and in cases with unknown GBS colonization status and a positive GBS status in a previous pregnancy. Prophylactic antibiotic should be administered as soon as possible in cases of preterm premature rupture of membranes^[9-12]. The prophylaxis options are detailed elaborated in the relevant guidelines^[9,12,14-16].

Consensus opinion 1 above is shown in Table 3.

2.1.2 Obesity

In the past 20 years, the BMI of adults in China has been on the rise, and it is expected that by, about 50% of adults in China will be overweight or obese^[17-18]. The World Health Organization (WHO) defines an adult BMI ≥ 30.0 kg/m² as obese^[19]. Obesity is one of the important risk factors for postoperative infections, and the risk of infection increases with the degree of obesity in patients^[20]. Obesity itself may lead to limited surgical field of view, prolonged operative time, reduced tissue oxygenation, and low tissue antibiotic concentrations, and is a high-risk factor for surgical site infections, maternal infection rates rising with increasing BMI^[21-22]. When standard doses of antibiotic are used, serum and tissue concentrations tend to be lower in obese women than in normal women, especially for cephalosporin; therefore, larger doses of antibiotic prophylaxis need to be used in obese women; however, there is limited evidence on the optimal use and dosage for the antibiotic prophylaxis for cesarean delivery in obese women. The American College of Obstetricians and Gynecologists (ACOG) Guidelines for 《Use of Prophylactic Antibiotics in Labor and Delivery》 recommend a dose of 1 or 2g of cefazolin women weighing ≤ 80 kg, with a dose of 1g being more health-economically advantageous. For women weighing >80 kg or with a BMI >30 kg/m², the dose of cefazolin can be increased to 2g^[23]. In addition, guidelines recommend antibiotic prophylaxis for obstetric surgery as follows: 2g of cefazolin for those weighing <120 kg and 3g for those weighing ≥ 120 kg, but the clinical benefit of the 3g regimen for obese pregnant women is controversial^[23-30]. Prophylactic antibiotic is generally not required for obese women before vaginal delivery, and if prophylactic antibiotic is required, the recommended dosage is the same as for caesarean section operators^[31]. Currently, there is no high-quality evidence to determine the optimal dose-adjustment regimen for the use of cefuroxime and metronidazole for infection prevention in obese pregnant women. The antibiotic prophylaxis regimen for obese women who are allergic to cephalosporin is detailed at in section 2.3.1.

Consensus opinion 2 above is shown in Table 3.

2.1.3 Abnormalities of Glucose Metabolism

Abnormal glucose metabolism during pregnancy is one of the triggers of maternal infections, and women with abnormal glucose metabolism are prone to asymptomatic bacteriuria. Therefore, the assessment of the results of prenatal examination and symptomatic treatment are particularly important, and the clinic should strengthen the monitoring of infections during the labor and delivery examination, routine screening of vaginal secretions, and regular examination of routine urinalysis, and urine culture should be performed if necessary [32], and once diagnosed, asymptomatic bacteriuria during pregnancy is a major concern. Antibiotic should be administered according to the results of pathogenetic cultures and sensitivity tests [33-34]. Antibiotic regimens commonly used for asymptomatic bacteriuria in pregnancy include amoxicillin 500mg q8h orally for 3-5d, cefadroxil 500 mg q8h orally for 3-5d, or fosfomycin trometamol powder 3g orally as a single-dose regimen [35-36].

Perinatal infections are associated with elevated blood glucose levels, so it is necessary to manage perinatal blood glucose levels appropriately [23, 37]. The goal of glycemic control during labor for pregnant women with abnormal glucose metabolism is 4-7 mmol/L [38-39]. For pregnant women with hyperglycemia who are using hypoglycemic drugs, the number of hypoglycemic drugs should be reduced or discontinued during labor and delivery according to blood glucose monitoring; for pregnant women who do not need hypoglycemic drugs during pregnancy, they can return to a normal diet during labor and delivery, avoiding a diet that is high in sugar and fat. Clinical monitoring of pre-breakfast (fasting blood glucose) and postprandial blood glucose in diabetic pregnant women should be performed 24 hours after delivery, and blood glucose monitoring can be discontinued 24 hours after delivery if the blood glucose is within the normal range. Encourage and support breastfeeding in diabetic pregnant women for at least 6 months. Breastfeeding reduces the long-term risk of type 2 diabetes mellitus in diabetic pregnant women and improves maternal and infant metabolism [39-40].

Consensus opinion 3 above is shown in Table 3.

2.1.4 Anemia

Women with anemia have poor tolerance to childbirth, surgery, and anesthesia, and are prone to hemorrhagic shock; severe anemia can cause myocardial hypoxia, which can lead to anemic heart disease; in addition, anemia lowers the resistance of pregnant women, making her susceptible to puerperal infections [13]. When pregnant women with anemia are advised to raise their hemoglobin level through dietary modification and medication as soon as possible in order to correct the anemia [41-46]. Regarding the specific plan for the prophylactic use of antibiotics during the perinatal period in pregnant women with anemia, there is no clear opinion in the current domestic and international guidelines, and it is recommended that clinics should take into account other risk factors and use antibiotics according to the indications for prophylactic use.

2.1.5 Combined Use of Immunosuppressive Drugs

Immunosuppressive drugs (e.g., prednisone, hydroxychloroquine, cyclosporine, etc.) are the mainstay of therapy for immune system disorders. Currently, there is no high-quality evidence confirming that the prophylactic antibiotic regimen for peripartum pregnant women using immunosuppressants differs from that for general pregnant women. Because immunosuppressive drugs can weaken the body's ability to fight infection, pregnant women on immunosuppressive drugs should be closely monitored for signs of postoperative infection, and if there is a suspicion of infection, a personalized diagnosis and treatment plan should be formulated in conjunction with multidisciplinary experts from the departments of pharmacy, rheumatology and immunology, and infectious diseases.

Consensus opinion 4 above is shown in Table 3.

2.1.6 Combined Heart Disease

《China's Expert Consensus on the Diagnosis and Treatment of Combined Heart Disease in Pregnancy》 suggests that pregnant women with combined structural heart disease should continue to use antibiotic medications for 5-10 d after cesarean section to prevent infection, but it does not specify the specific types of medications and their use^[47]. The 2018 ACOG, the 2017 Society of Obstetricians and Gynecologists of Canada (SOGC) guidelines all point out that pregnant women with combined heart disease have already received routine prophylactic medications before cesarean section and do not need to use additional antibiotics to prevent infective endocarditis. Antibiotics (ampicillin, amoxicillin, cefazolin, ceftriaxone, clindamycin, or azithromycin) should be administered prophylactically 0.5 to 1h before vaginal delivery, and should not be continued after delivery^[23,48], but vaginal delivery is not recommended for this group.

Consensus opinion 5 is shown in Table 3.

2.2 Perinatal Antibiotic Use in Vaginally Delivered Pregnant Women

2.2.1 Intrapartum Antibiotic Use for Intrapartum Fever

Intrapartum fever is defined as a maternal oral temperature of $\geq 38^{\circ}\text{C}$ (axillary temperature is 0.2~0.3 $^{\circ}\text{C}$ lower than oral temperature) at the time of delivery. For mothers with intact membranes and no infection-related complications, temperature should be assessed every 4 hours during labor; for those with ruptured membranes, temperature should be assessed every 1-2 hours. Fever during labor can increase the incidence of infection-related diseases in both mother and child^[49]. Common causes of fever include infectious (e.g., amniotic cavity, urinary or respiratory infections) and non-infectious (e.g., use of epidural analgesia, maternal dehydration, or high ambient temperature). Epidural analgesia (painless labor) can produce multiple effects on the body, resulting in more heat production than heat dissipation^[50-51], but it does not usually result in a fever greater than 38 $^{\circ}\text{C}$; amniotic infection is the most common cause of a fever greater than 38 $^{\circ}\text{C}$ ^[52]. Because it is difficult to clearly distinguish the cause of maternal temperature (amniotic infection or epidural analgesia), the empirical use of antibiotic during labor is recommended for isolated maternal fever, unless it is clear that the fever is caused by other factors^[53-55]. If the patient feels fever, frequent fetal movement, abdominal tightness, abdominal pain, abnormal vaginal discharge (odor, dirt, etc.), and abdominal and fundal pressure pain, relevant tests (blood test, urine test, vaginal or cervical secretion test, etc.) should be performed to clarify the diagnosis and timely management.

Consensus opinion 6 is shown in Table 3.

2.2.2 Antibiotic Use in Pregnant Women Undergoing Balloon Induction, Forceps/Vacuum-Assisted Delivery, or Manual Placenta Removal

Balloon induction of labor is contraindicated in cases of premature rupture of membranes and lower genital tract infections (e.g., cervicitis, vulvovaginitis, etc.). In GBS carriers with intact membranes, the balloon may be used to promote cervical ripening, and antibiotic should be administered prophylactically as early as possible after labor or rupture of membranes^[56-57]. Different guidelines have inconsistent recommendations regarding the prophylactic use of antimicrobial agents for instrumental delivery^[58-59]. A 2020 meta-analysis showed that a single dose of antibiotic in women with instrumental delivery reduced the risk of poor postpartum wound healing and infection, but the quality of the included studies was low^[60]. The need for prophylactic use of antibiotic in women with abruptio placenta at delivery is controversial: the WHO recommends a single dose of ampicillin or a first-generation cephalosporin before abruptio placenta to prevent infection, but the SOGC has concluded that there is insufficient evidence to support or oppose the prophylactic use of antibiotic in women with abruptio placenta, or in women who undergo removal of placental remnants^[48,61].

2.2.3 Use of Antibiotics in Women with Perineal Lacerations after Delivery

The 2022 Chinese 《Clinical Practice Guidelines for the Prevention and Management of Perineal Laceration in Vaginal Delivery》 suggest that routine prophylactic use of antibiotics is not necessary after repair of perineal laceration^[62], and that appropriate perineal care and healthy lifestyle management (e.g., local

cleansing, analgesia, decongestion, reasonable diet, avoidance of urinary retention and constipation, and early initiation of postnatal activities, etc.) are effective in decreasing maternal anxiety and thrombosis, and promoting uterine involution to reduce the risk of postnatal hemorrhage and infection^[63-64].

Antibacterial drugs should be given according to the degree of perineal laceration: for episiotomy and closure of perineal laceration of I or II degree, preventive use of antibiotics is not needed; for vaginal wall laceration and closure, antibiotics can be given to prevent infection^[65]. The guidelines issued by the Obstetrics and Gynecology Pharmacy Group of the Hospital Pharmacy Committee of the Chinese Pharmaceutical Society recommend the following regimens for infection prevention in women with vaginal wall lacerations: (1) first- and second-generation cephalosporins ± metronidazole; (2) cephamycins (e.g., cefoxitin, cefmetazole, etc.)^[66]. Among them, first- and second-generation cephalosporins supported by evidence-based medicine include cefazolin and cefuroxime, and cefazolin is the first-line drug^[1,67]. The most common contaminants in third- and fourth-degree perineal lacerations are Gram-negative rods, enterococci, streptococci, and anaerobes (e.g., *Bacteroides fragilis*), and the prophylactic regimen is cefazolin or cefuroxime ± metronidazole for 24h, or 48h in cases of contamination with intestinal contents. Clindamycin + aminoglycosides or aminoglycosides + metronidazole may be used in combination in cases of allergy to cephalosporins^[1, 23, 48]. Studies have shown that prophylactic use of a single dose of cephamycins is associated with a lower complication rate when repairing perineal lacerations of degrees III and IV compared with those who do not receive prophylaxis^[68]. If vacuum extraction or forceps are used during vaginal delivery, combined with any of the following conditions: prolonged labor, second-degree perineal laceration, or urinary catheterization, the risk of postpartum infection increases. Close clinical monitoring is necessary, but the use of prophylactic antibiotics remains controversial.

Postpartum hemorrhage is a major cause of maternal mortality, and co-infection may lead to further exacerbation of the condition. Antibiotic can be given as single-dose prophylaxis for postpartum hemorrhage $\geq 1,500$ mL after vaginal delivery^[69].

Consensus opinion 7 is shown in Table 3.

2.2.4 Perineal Wound Management and Follow-up after Delivery

Factors influencing perineal wound infections include the type and duration of the delivery procedure, the amount of bleeding, and other susceptibility factors, such as smoking, obesity, malnutrition, dysglycemia, imbalances in the vaginal microecosystem, and immunologic abnormalities^[63,70]. The causative organisms may come from the mother herself or from healthcare workers, equipment, and the delivery room environment. Therefore, a multidisciplinary approach is needed to minimize the incidence of infection.

Perineal infection is usually confined to the laceration or incision site, but may spread and present as cellulitis or abscess^[71-72]. The infection may spread upward to the sciorectal fossa, presenting with perineal and buttock pain, bowel discomfort, and a sense of urgency. Multidisciplinary consultation may be necessary to assess the extent of the infection, and debridement and drainage of the abscess may be indicated; antibiotic should be used when accompanied by fever or other systemic signs of infection.

Perineal infections may present clinically up to 1 week after delivery, by which time the woman is usually discharged from the hospital. Therefore, healthcare workers should provide health guidance to mothers before they leave the hospital, informing them of the signs and symptoms of infection and consulting a doctor when symptoms appear; the relevant departments should establish a postnatal follow-up mechanism to routinely review and assess uterine regrowth and perineal wound healing at one week after delivery. In accordance with the requirements for postnatal visits set out in the national Code of Practice for Maternal Health Management Services, postnatal home visits should be carried out by community staff, so communities should pay attention to strengthening staff training in order to meet the requirements for

homogenized management.

2.3 Perioperative Antibiotic Prophylaxis for Cesarean Delivery

The perioperative antibiotic prophylaxis during cesarean delivery reduces the incidence of infection-related complications such as maternal incisional infections, endometritis, and myometritis. The newborns will have a lower birth rate and a lower risk of neonatal infections, especially in the case of non-elective (emergency) cesarean deliveries.

2.3.1 Pre-operative Prophylactic Use of Antibiotics for Cesarean Delivery

Antibiotics should be administered within 0.5-1h before skin incision for cesarean section to ensure that adequate tissue drug concentrations are achieved [1,63,73]. Compared with the use of antibiotic after cord clamping, the use of antibiotic prior to skinning is more effective in preventing infections and does not increase the risk of asthma and eczema in the neonate in the long term [73-74]. The timing of preoperative prophylactic antibiotic is critical, and coordination between the surgeon, anesthesiologist, and operating room nursing staff is needed to ensure that they are administered at the right time. For emergency cesarean sections, antibiotic should be administered as soon as possible after skin incision if they are not given preoperatively [66].

The main microorganisms causing postpartum fever, incision infection, and endometritis include gram-negative bacilli, enterococci, streptococci, and anaerobes [1], so the prophylactic regimen for cesarean section is: first- and second-generation cephalosporins ± metronidazole [1,75-76]. For cephalosporin allergy, 《China's Guiding Principles for the Clinical Application of Antibiotics (2015 edition)》 recommends the use of clindamycin + aminoglycosides or aminoglycosides + metronidazole [1]. Among them, it is not necessary to adjust the dose of clindamycin for obese pregnant women according to their body weight, i.e., 900 mg can be used for women of different body weights; however, it is necessary to determine the dosage of aminoglycosides according to the actual body weight of the pregnant women [23]. Because aminoglycosides have ototoxicity and can penetrate the placenta, which may cause fetal hearing damage [77], for pregnant women who are not suitable for the use of cephalosporins, the prophylaxis of cesarean section is usually clindamycin + aztreonam, but some medical institutions in some regions of China have designated aztreonam as a “special-use class of antibacterial drugs” [66]. The 2018 ACOG guidelines suggest that azithromycin can be an alternative to cefazolin [23, 78-79].

The 2018 ACOG guidelines recommend cefazolin+ azithromycin [23] as a prophylactic regimen for infection prevention in those with non-elective cesarean sections (transplacental cesarean section with vaginal delivery, combined with preterm rupture of membranes). This combination reduces the incidence of infections (wound infections, endometritis, etc.) in patients undergoing elective cesarean section compared with cefazolin alone [78]. Currently, there are no recommendations in China.

Perioperative prophylactic use of antibiotics recommended by the relevant guidelines in China is 24 hours [1], while U.S. and Canadian guidelines recommend a single dose of antibiotic prophylaxis before cesarean delivery as sufficient. [23,48]. A single prophylactic dose of antibiotic for elective cesarean delivery in low-risk pregnancies is effective, inexpensive, has fewer side effects, and is less likely to induce resistance [80-81]. Continued postoperative antibiotic prophylaxis does not reduce incidence of surgical site infections in women who are already following the principles of prophylaxis, and may even increase the risk of adverse events [82].

Consensus opinion 8 is shown in Table 3.

2.3.2 Comprehensive Measures to Reduce the Risk of Perioperative Infections during Cesarean Delivery

The prophylactic use of antibiotics is not the only way to reduce the incidence of perioperative infections;

preoperative skin cleansing, intraoperative warming, health education, universal dissemination of knowledge about microbial resistance and the rational use of antibiotics, as well as the strengthening of healthcare and doctor-patient communication and cooperation are all very important.

The 2019 《Chinese Guidelines for the Prevention of Surgical Site Infections》 recommend that pregnant women use soap to clean the whole body 1d before cesarean section, which can effectively reduce infections^[83]; Relevant guidelines do not recommend routine shaving; if necessary, clipping hair is sufficient^[84]; in addition, the rational use of the electrosurgical unit, layered closure, and appropriate surgical drainage techniques are equally important in preventing surgical site infections^[85-86]. Studies have also shown that hypothermia is associated with decreased immune function, cardiovascular complications, and impaired coagulation, which increases the risk of surgical site infections; therefore, insulation (e.g., thermal blankets or heated fluids) should be used during surgery to maintain the core maternal body temperature (not less than 36°C)^[64,87-88].

Consensus opinions 9 and 10 above are shown in Table 3.

2.3.3 Use of Antibiotic in Special Circumstances such as Severe Bleeding and Prolonged Surgery

If maternal intraoperative hemorrhage during cesarean section is >1,500mL, the duration of surgery is >3h, or the duration of surgery is more than twice the half-life of the drug used, one additional dose of antibiotic is required intraoperatively (e.g., cefazolin has a half-life of 1.5h, and one additional dose should be given intraoperatively when the length of surgery is more than 3h); if the duration of surgery continues to be prolonged, one additional dose of antibiotic is required intraoperatively every 3h or every two times the half-life of the drug, so that serum and tissue drug concentrations exceed the minimum inhibitory concentration^[1, 63]. Since the amount of maternal hemorrhage estimated by healthcare professionals is usually much lower than the actual amount of bleeding, especially in the early stage of hemorrhage when the blood is concentrated, the recent hemoglobin level of the mother does not truly reflect her actual bleeding status, the clinicians should consider whether to add antibiotics in a timely manner when post-partum hemorrhage occurs, and monitor the signs of maternal infection closely after delivery, so that the antibiotic regimen can be adjusted in a timely manner.

Studies have shown that other uterine sutures (e.g., the B-Lynch suture) performed during cesarean section may lead to uterine ischemia, which may result in endometrial and myometrial necrosis and infection, and the incidence of postoperative complications after the B-Lynch suture varies in the literature^[89-91]. The B-Lynch suture is safer than other sutures, but it should be actively evaluated for secondary myometritis and endometritis, and should be treated with anti-infective therapy if necessary^[92].

If there is intraoperative intestinal damage, contamination of intestinal contents, the incision is converted to a class III incision (contaminated incision), the original prophylactic regimen can be continued, and the total duration of treatment should not be more than 48h. If there is intestinal damage without contamination of intestinal contents and the surgical incision is still a class II incision, the prophylactic regimen and time duration will remain unchanged^[1, 93].

Consensus opinion 11 is shown in Table 3.

2.3.4 Comprehensive Management of Cesarean Section Sites

Surgical site infections are associated with a number of factors, including the type and number of microorganisms contaminating the surgical site, maternal health, and surgeon's technique (e.g., good surgical technique, including gentle retraction, effective hemostasis, removal of necrotic tissue, saline irrigation to avoid over-drying of the tissue, reduced wound tension, and shorter placement of drain tubes can help to reduce the risk of surgical site infections)^[28, 94]. The incision dressing can be changed and the healing of the incision can be observed 24-48 hours after cesarean section. The symptoms of superficial

surgical site infection include localized swelling, elevated skin temperature, fluid exudation, incision cracking, and pain, and the clinic needs to perform local debridement without the use of antibiotics; if the mother has systemic signs of infection (e.g., fever, abnormal infection indexes, etc.), the clinic should take the incisional exudate and venous blood for pathogenetic examination and antimicrobial susceptibility testing before treatment, and should consider empirically administering antibiotics, which can be based on the healing status of the incision. According to the healing condition of the incision and the mother's wish, rhubarb and mannite can be used externally to shorten the healing time and treat incision infection^[95]. Deep surgical site infections may cause fascial and/or muscle infections, which can be difficult to diagnose and require more than one patient. It is difficult to diagnose and requires multidisciplinary collaboration. Especially in obese women, a high degree of clinical vigilance is required, and diagnosis can be aided by imaging techniques such as ultrasound, computed tomography, and magnetic resonance imaging. For deep surgical site infections, early antibiotic therapy should be used along with aggressive wound management.

Consensus opinion 12 is shown in Table 3.

2.4 Timing of Antibiotic Use in the Postpartum Period

For postpartum patients who do not develop secondary endometritis or bloodstream infection, antimicrobial agents administered during labor for suspected or confirmed intra-amniotic infection should be promptly discontinued. For those who develop postpartum fever with suspected or diagnosed endometritis or myometritis, antimicrobial therapy should be initiated as early as possible^[53]. Postpartum infection should not be determined solely on the basis of an elevated leukocyte count, as a leukocyte count of 15×10^9 - 25×10^9 L⁻¹ may be a physiologic response to pregnancy^[13]. Clinical diagnosis of infection is mainly based on maternal signs and symptoms, and imaging techniques can also be used.

Consensus opinion 13 is shown in Table 3.

3 Comprehensive Prevention and Control of Perinatal Infections and Health Education

The prevention and control of perinatal infection is a complex systematic project, and 《National Action Plan for Curbing Microbial Resistance (2022-2025)》 emphasizes the principle of "prevention as the mainstay, combining prevention and treatment with a comprehensive approach", and that antibiotics cannot substitute for strict disinfection and sterilization, meticulous aseptic operation, and comprehensive maternal health care. Effective prevention and control of perinatal infections require a comprehensive, scientific and integrated management strategy, and relying only on antibiotics cannot meet the needs.

Perinatal management covers a number of key areas, including maternal nutrition management, blood glucose control, anemia prevention, skin cleansing, preoperative fasting, pain management, catheterization, thrombosis prevention, etc., as well as post-delivery rehabilitation care, breastfeeding feeding, doing more activities, and personal healthy lifestyle development, etc.^[96]. At the same time, attention to maternal mental health, the use of effective emotional management methods, active intervention in insomnia, anxiety and other problems, can also effectively reduce the risk of perinatal infection to ensure maternal and neonatal safety and health.

4 Conclusion

The irrational use of antibiotic has become a global problem, and maternal special populations may be at increased risk of drug resistance and unnecessary antibiotic exposures for mothers and infants. Although antibiotic prophylaxis can effectively reduce the incidence of specific infections, it is not the only measure to effectively control the risk of maternal infections. Strict disinfection and sterilization, standardized aseptic practices, comprehensive maternal management, and enhanced recovery after surgery are closely related and irreplaceable in reducing the incidence of infections. Healthcare workers should not use antibiotic or prolong the course of prophylaxis for fear of secondary infections, poor incision healing and

other related complications. For high-risk individuals for infection, the prophylactic use of antimicrobial agents should be standardized. Following discontinuation, close monitoring for signs of infection is essential, with prompt evaluation and initiation of antimicrobial therapy if necessary. The hospital's multidisciplinary team (MDT), including departments such as Infection Control, Central Sterile Supply, Anesthesiology, Obstetrics & Gynecology, Pediatrics, Pharmacy, and Laboratory Medicine, should conduct regular analyses and maintain close collaboration to implement a prevention-focused antimicrobial strategy. Rational antimicrobial use in pregnant and postpartum women is a systematic project that requires a concerted effort from the whole society, aiming to achieve the "lowest effective dose, shortest necessary duration, and minimal toxic side effects." Healthcare professionals must strengthen science-based public education to enhance public awareness of rational antimicrobial use and reinforce patients' self-management. This is essential to minimize drug-induced harm and effectively safeguard maternal and infant health.

5 Consensus Dissemination and Updates

After the release of this consensus, the consensus will be disseminated and promoted through the following ways: presentations and interpretations at relevant academic conferences, and promotion at special Expert Consensus Promotion sessions held in some regions of China, to ensure that obstetricians and gynecologists, nursing staff, midwives, and relevant pharmacy staff fully understand and correctly apply the consensus. The Consensus Writing Group will regularly consult and track relevant high-quality evidence-based evidence, organize the Consensus Expert Group to assess the possibility of changing the recommendations, and update the consensus of when necessary.

6 Conflict of Interest

All authors of this Consensus and participating experts declare that they have no conflict of interest.

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