









# Guidelines of the Polish Society of Gynecologists and Obstetricians on the diagnosis and management of pregnancies complicated by prelabor rupture of the membranes

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The guidelines of the Polish Society of Gynecologists and Obstetricians present the current recommendations about management, which may be modified in justified cases and after a thorough analysis of the clinical context, which in turn may constitute grounds for future modifications and updates.

## INTRODUCTION

Prelabor rupture of the membranes (PROM), defined as rupture of the amniotic membranes before the onset of regular uterine contractility, may occur at term ( $\geq 37 + 0$  weeks gestation) or prematurely ( $< 37 + 0$  weeks of gestation). The latter is known as preterm prelabor rupture of the

membranes (PPROM), and is responsible for approximately 30–40% of all preterm deliveries. PPRM constitutes the most common, identifiable factor for preterm labor and may cause significant morbidity and mortality, mainly due to prematurity, sepsis, cord prolapse, and pulmonary hypoplasia. Additionally, it is associated with elevated risk for intraamniotic

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infection. The management of patients with PPRM and PROM varies and depends on the gestational age as well as other risk factors, chief among them: intraamniotic infection and/or abnormal findings for fetal wellbeing. A thorough assessment of the gestational age and knowledge about the risk factors are vital to achieve accurate diagnosis and offer adequate care to women with PPRM.

### RISK FACTORS

The pathogenesis of prelabor rupture of the membranes remains to be fully elucidated. Various pathological events (e.g. subclinical or symptomatic, bleeding) may initiate the cascade of biochemical changes (metalloproteinase activation, oxidative stress) which will result in PROM. The risk factors are similar to those for preterm labor (Tab. 1), but many patients are free of any risk factors. A strong association with PPRM has been confirmed for the following factors: PPRM in previous pregnancy, genital tract infection, bleeding in the first, second, and third trimester, and smoking [1–3].

### DIAGNOSTICS

The diagnosis of PPRM is based on the characteristic findings in patient medical history and physical examination: the patient presents with symptoms of amniotic fluid leakage and amniotic fluid pooling in the posterior fornix of the vagina is observed during the sterile speculum exam — which remains the gold standard. If the amniotic fluid pooling is not visible at the time of the exam, pressure should be applied to the uterine fundus and the patient should be instructed to cough and lean forward, which might increase the leakage of the amniotic fluid, thus confirming the diagnosis.

When in doubt whether the fluid is indeed amniotic, fluid pH may be checked using a litmus paper. Normal vaginal fluid pH ranges from 3.8 to 4.5 (litmus paper will turn yellow), while amniotic fluid pH is typically 7.1–7.3 (litmus paper will turn dark blue). False positive results of the strip test may be found if the sample is contaminated by blood, semen, alkaline antiseptics, some lubricants or bacterial vaginosis (BV).

If the amniotic fluid leakage cannot be conclusively diagnosed, tests for the presence of insulin growth factor binding protein-1 (IGFBP-1) or placental alpha microglobulin-1 (PAMG-1) in cervical discharge might be considered, if available. Studies on these biochemical markers have demonstrated their high sensitivity and specificity for the diagnosis of PPRM [4, 5].

Fetal fibronectin measurement is a sensitive, non-specific test used to confirm amniotic fluid leakage. A negative test is highly predictive of intact fetal membranes but a positive test result is not fully diagnostic. Therefore, fetal fibronectin should not be routinely used in the diagnostic process for PPRM.

**Table 1. Risk factors for preterm labor/prelabor rupture of the membranes (PROM)**

<b>Obstetric/gynecologic history</b> <ul style="list-style-type: none"> <li>• History of preterm labor/PROM</li> <li>• Cervical interventions (e.g. conization)</li> <li>• Numerous dilation and curettage procedures</li> <li>• Anatomical defects of the uterus</li> </ul>
<b>Maternal demographic characteristics</b> <ul style="list-style-type: none"> <li>• Age &lt; 17 or &gt; 35 years</li> <li>• Low level of education</li> <li>• Single parenthood</li> <li>• Low socioeconomic status</li> <li>• Short &lt; 18 months interval between pregnancies</li> <li>• Other socioeconomic factors — e.g. access to medical care, disability</li> </ul>
<b>Nutritional status/physical activity</b> <ul style="list-style-type: none"> <li>• BMI &lt; 18.5 kg/m<sup>2</sup></li> <li>• 80+ hour work week</li> <li>• Heavy physical labor</li> </ul>
<b>Medical history for the current pregnancy</b> <ul style="list-style-type: none"> <li>• Assisted reproduction technology methods</li> <li>• Multiple gestation</li> <li>• Fetal factors (chromosomal abnormalities, structural defects, fetal growth restriction, fetal demise)</li> <li>• Bleeding from the genital tract — including placenta previa, placental abruption</li> <li>• Polyhydramnios or oligohydramnios</li> <li>• Chronic maternal conditions — hypertension, diabetes, thyroid diseases, connective tissue disorders</li> <li>• Surgical interventions in the abdominal cavity during pregnancy</li> <li>• Psychogenic factors — stress, depression, mood disorders</li> <li>• Stimulants — tobacco, alcohol, psychoactive substances</li> <li>• Infections — bacterial vaginosis, trichomoniasis, chlamydia, gonorrhea, syphilis, urinary tract infections, intraamniotic infection</li> <li>• Cervical length of &lt; 25 mm between 14–28 weeks of gestation</li> <li>• High concentration of fetal fibronectin between 22 and 34 weeks of gestation</li> <li>• Uterine contractility</li> </ul>

BMI — body mass index

Oligohydramnios or anhydramnios on ultrasound may be helpful when attempting to confirm the clinical diagnosis of PPRM but they are not diagnostic.

### MANAGEMENT

Management of patients with PPRM remains to be one of the most controversial topics in perinatal medicine. The following issues are the main causes for debate:

- accurate diagnosis in ambiguous cases,
- expectant management versus intervention,
- use of tocolytics,
- duration and type of antibiotic prophylaxis,
- rationale behind corticosteroid therapy,
- testing methods for maternal/fetal infection,
- timing of delivery.

### Hospitalization

In patients with PPRM, hospitalization and periodic monitoring of maternal and fetal wellbeing are advised.

Gestational age should be determined in all women with PPROM, with additional assessment of fetal presentation and wellbeing in pregnancies > 22 + 6 weeks of gestation. It is vital to be vigilant for symptoms of chorioamnionitis or placental abruption.

In expectant management, it is important to monitor the mother's well-being based on daily values of clinical parameters (heart rate, blood pressure, body temperature). Laboratory parameters should be measured at baseline, *i.e.* upon admission to hospital, and then checked at least twice weekly, depending on clinical results (WBC, CRP, coagulation test and procalcitonin (PCT) if available).

4–6 hours after administration of antibiotics, WBC and CRP should be monitored. If the patient's clinical condition is stable and inflammatory markers do not indicate progression, peripheral blood leukocyte counts and C-reactive protein should be monitored at least twice weekly. In the case of increased levels of inflammatory markers, treatment should be modified accordingly (administration of other antibiotics/antibiotics with a broader spectrum of action and/or planned delivery should be considered).

Infection leading to intraamniotic infection (intrauterine infection) is one of the major threats associated with PPROM.

According to Gibbs, the clinical symptoms of intraamniotic infection are as follows:

- fever (> 38°C),
- leukocytosis (> 15 G/L),
- maternal tachycardia (heart rate > 100 BPM),
- fetal tachycardia (heart rate > 160 BPM),
- uterine tenderness,
- foul-smelling amniotic fluid.

The clinical diagnosis of **chorioamnionitis** may be made if two of the abovementioned symptoms are confirmed [6].

Symptoms of intraamniotic infection and/or abnormal findings for fetal wellbeing are an indication for elective delivery. In particular, maternal septicemia and symptoms of septic shock are indications for immediate delivery and hysterectomy, if necessary, to remove the source of the infection or bleeding.

During hospitalization, if the uterine cervix is closed, absolute bedrest is not recommended — instead, the patient is advised to restrict physical activity. Bedrest regime does not lower the risk for preterm labor but increases the risk for venous thromboembolism, from 0.8/1000 to 15.6/1000 in patients immobilized for over 3 days. In patients with advanced obstetric status (the risk for umbilical cord prolapse at high cervical dilation), restriction of the physical activity (mix of sedentary behavior and bedrest) is advised — anti-thrombotic prophylactic treatment is recommended in such

cases due to the risk for developing deep vein thrombosis and pulmonary embolism. Compression therapy and/or low-molecular-weight heparin at a prophylactic dose might be considered in patients with low or moderate risk for venous thromboembolism [7].

**After hospitalization**, ambulatory care may be implemented **in some cases** (< 22 + 6 weeks of gestation). However, such management of patients with PPROM is associated with high risk for maternal infection and **is not recommended**. **Ambulatory care** may be considered after the clinical condition of the patient was evaluated, the patient and her family were made aware of the seriousness of the condition, and written informed request was submitted by the patient. Expectant ambulatory care should include:

- monitoring of the body temperature (twice/day),
- monitoring of the inflammatory markers (twice/week),
- clear instructions how to monitor for worrisome symptoms (*e.g.* abdominal pain, vaginal bleeding, vaginal discharge, fever, chills, flue-like symptoms),
- frequent check-up tests performed by a physician (min. 1/week).

Another hospitalization is recommended after 22 + 6 weeks of gestation. Hospitalization at a tertiary care center is not required before 22 + 6 weeks of gestation.

Of note, PPROM at this stage of pregnancy is closely correlated with the risk for intraamniotic infection, which in turn might lead to general infection, with septicemia, septic shock, and multiorgan failure. Therefore, it is serious health concern and a life-threatening condition for the mother.

In case of PPROM after 22 + 6 weeks of gestation, the patient needs to be hospitalized at a tertiary care center, whereas women with PPROM after 34 weeks of gestation should be admitted to a secondary care center.

#### Recommended biochemical and biophysical tests after the diagnosis of preterm prelabor rupture of the membranes (PPROM) — summary

Monitoring of maternal wellbeing (heart rate, blood pressure, body temperature)

WBC, CRP\*, clotting test (at baseline — upon admission — followed by twice/week or more), leukocytosis, PCT\*, if available

Vaginal and rectal culture for type B streptococci after 22 + 6 weeks of gestation

Vaginal and cervical culture at baseline — upon admission — and later on, depending on patient condition

Cardiotocography (ideally computerized CTG) after 26 weeks of gestation (1/day)

Transabdominal ultrasound

\*CRP and PCT do not apply to patients with prelabor rupture of the membranes (PPROM) > 37 weeks of gestation; WBC — white blood cell; CRP — C-reactive protein; PCT — procalcitonin

### Prophylactic antibiotic therapy

Intraamniotic infection may be the cause of or the consequence of PPROM. The goal of the antibiotic therapy is to lower the incidence of maternal and fetal infections, thus delaying the onset of preterm labor or the need to induce labor. In a Cochrane review about the role of antibiotics in women with PPROM, antibiotic therapy was found to be associated with statistically significantly lower incidence of chorioamnionitis (RR 0.66; 95% CI 0.46–0.96). Statistically significantly lower rates of neonates born within 48 h (RR 0.71; 95% CI 0.58–0.87) and within 7 days (RR 0.79; 95% CI 0.71–0.89) have been reported. Also, lower rates of neonatal infections, the need for surfactant and oxygen therapy, and abnormal ultrasound findings of the neonatal brain before discharge were reported [8].

Reports about the optimal antibiotic therapy and its duration remain conflicting. Various associations of gynecologists and obstetricians recommend different treatments, and the available data are insufficient to determine which antibiotic regimen (drug, dosage, duration) is superior to other antibiotic protocols. According to the guidelines of the **National Medicines Institute**, the following antibiotic therapy is recommended for patients with PPROM (without contraindications for prolonged antibiotic treatment) for 7 days [9]:

- azithromycin 1 g *p.o.* (single dose) + Ampicillin 2 g *i.v.* every 6 hours for 48 hours, followed by Amoxicillin 500 mg *p.o.* every 8 hours for the next 5 days; additionally, Metronidazole 500 mg *i.v.* may also be considered;
- since anaerobic bacteria (*Ureaplasma*, *Gardnerella*, etc.) play a significant role in the pathophysiologic mechanism of membrane rupture, it is prudent to include into the protocol a chemotherapeutic agent with high success rate for treating such infections;
- antibiotics used if a patient has an **allergic reaction to penicillin**:
- type I allergic response (anaphylaxis):
  - Azithromycin 1 g *p.o.* (single dose) + Clindamycin 900 mg every 8 hours *i.v.* for 48 hours, followed by Clindamycin 300 mg every 8 hours *p.o.* for 5 days,
  - type I allergic response and Group B streptococcus (GBS) resistance to Clindamycin.

Azithromycin 1 g *p.o.* (single dose) + Vancomycin 20 mg/kg every 8 hours *i.v.* (max. one-time dose of 2 g for 48 hours).

Further use of antibiotics should be based on the clinical condition of the patient, laboratory test result and culture results (in accordance with the antibiogram).

### Corticosteroid therapy

Corticosteroid therapy in patients with PPROM was researched extensively by various clinical trials and was found to lower neonatal mortality rates, respiratory distress, in-

traventricular hemorrhage, and necrotizing enterocolitis. According to the literature, corticosteroid therapy is not associated with elevated risk for maternal and/or neonatal infection, irrespective of the gestational age. The following regimen is recommended:

- 2 doses of betamethasone (12 mg) *i.m.* every 24 hours,
- 4 doses of dexamethasone (6 mg) *i.m.* every 12 hours.

A full-course corticosteroid regimen is recommended in pregnant patients with PPROM without intraamniotic infection, between 24 + 0 and 33 + 6 weeks of gestation.

It may be considered in patients with PPROM who are **at risk for preterm labor within 7 days**, as early as from 23 + 0 weeks of gestation. In extreme cases (high risk for preterm labor), a single maintenance dose may be administered up to 33 + 6 weeks of gestation, if the previous course was completed at least 14 days earlier. A routine repetition of a full-course corticosteroid regimen is not recommended [10].

According to the guidelines of the World Association of Perinatal Medicine (2022) and the Perinatal Medicine Foundation (2022), a full-course corticosteroid regimen is not recommended between 34 + 0 and 36 + 6 weeks of gestation since its benefits remain unclear. The use of glucocorticosteroids is also not recommended in patients with intrauterine infection. Also, the delivery should not be delayed to administer corticosteroids [10] (Tab. 2).

**Of note:** transient leukocytosis is observed in pregnant women who received corticosteroids.

### Neuroprotection

Randomized studies demonstrated that — administration of magnesium sulphate for fetal neuroprotection before 32 + 0 weeks of gestation lowers the risk for neonatal cerebral palsy (RR 0.71; 95% CI 0.55–0.91) and motor dysfunction (RR 0.6; 95% CI 0.6–0.88) if the delivery is expected within 24 hours. The dosing should be as follows: loading dose of 4 g of magnesium sulphate over 30 minutes, followed by a maintenance dose of 1 g/hour for max. 24 hours. A repeat course at a later time is possible if the delivery did not take place [11].

Irrespective of the protocol, patients with PPROM between 24 + 0 and 32 + 0 weeks of gestation and at high risk for preterm delivery within 24 hours, should receive neuroprotective treatment using magnesium sulphate, which is compliant with the FIGO guidelines [11]. Magnesium

**Table 2. Corticosteroid therapy**

In patients with PPROM, corticosteroid should be:	
Considered	Between 23 + 0–23 + 6 weeks of gestation
Recommended	Between 24 + 0–33 + 6 weeks of gestation
Not recommended	Between 34 + 0–36 + 6 weeks of gestation

sulphate, min. 4 hours before delivery, should also be administered if elective cesarean section is planned. Magnesium sulphate is contraindicated in patients with myasthenia gravis as it may result in a myasthenic crisis, and in patients with renal disorders, as magnesium is predominantly excreted by the kidneys. If kidney function is normal, there is no need to monitor maternal magnesium levels. However, blood pressure, heart beat, respiratory rate, and tendon reflexes (e.g. patellar reflex) need to be monitored every 4 hours [11].

### Tocolysis

Routine tocolysis in patients with PPRM is a controversial issue and is not recommended. According to a Cochrane review, tocolysis as compared to placebo in patients with PPRM is associated with mean pregnancy prolongation of 73 hours (95% CI 20–126) and lower rate of deliveries within the next 48 h (RR 0.55; 95% CI 0.32–0.95). Still, it increases the risk for intraamniotic infection. Also, tocolytic therapy was found to be associated with lower Apgar score at birth (Apgar score of < 7 points was more often observed) and more frequent need for mechanical ventilation in the neonates. The conclusion of the review was that there are not enough data to support the use of tocolytics in women with PPRM. Despite the lack of conclusive evidence that tocolytics significantly prolong pregnancy or improve the neonatal outcome, tocolytic therapy may still be taken into consideration in patients with PPRM in active preterm labor to implement the corticosteroids or to transport the mother to a higher level of care perinatal center. As a rule, tocolytics should not be administered for longer than 48 hours. Also, they should not be administered to patients in advanced stages of labor (dilation of > 4 cm) or those presenting with subclinical or manifest symptoms of intraamniotic infection [1–3]. Atosiban is contraindicated in patients with PROM after 30 weeks of gestation.

### Amnioinfusion

In certain cases of PPRM before 22 + 6 weeks of gestation, continuous or intermittent amnioinfusion is recommended, as the literature offers an increasing number of reports about high success rates for amnioinfusion. Lack of reliable data prevents such management being introduced into daily obstetric practice [12]. Similar management may also be considered in the third trimester. In a systematic Cochrane review of five studies, amnioinfusion in the third trimester was found to be associated with improved pH in fetal umbilical artery during labor, lower incidence of variable decelerations during labor, as well as lower risk for neonatal death, sepsis, pulmonary hypoplasia, and puerperal sepsis. As some of these benefits were reported for only one study, the authors of the review concluded that further research

was necessary before amnioinfusion may be incorporated into routine clinical practice for patients with PPRM in the third trimester [13]. In light of the above, amnioinfusion in PPRM is not recommended at any stage of pregnancy.

### The cervical cerclage

There is no conclusive evidence to establish the management standards for patients with PPRM and cervical incompetence treated by cerclage. The findings of retrospective studies remain inconsistent, but the main conclusion is that if the cerclage is left in place for > 24 hours after PPRM, it may indeed prolong the pregnancy, allowing to administer corticosteroid therapy (max. 48 hours) [14]. It is not possible to clearly determine whether the cerclage should be removed in PPRM; it is not a mistake to remove or leave it, the decision should be made individually, depending on the clinical situation.

### Delivery

#### *PROM after 37 weeks of gestation*

Prelabor rupture of the membranes is observed in approximately 8% of term pregnancies. With expectant management, spontaneous contractile activity within 72 hours develops in 95% of the women. Active management, *i.v.* administration of oxytocin or prostaglandin to induce contractile activity, lowers the risk for maternal inflammatory complications, without increasing the rate of operative delivery. Randomized studies also demonstrated that induced labor was associated with lower demand for antibiotic therapy and fewer admissions to the intensive care unit, for the mother and the neonate. In order to lower the risk for maternal and neonatal complications, induction of labor is recommended in pregnant women with amniotic fluid leakage at > 37 weeks of gestation. Expectant management (up to 48 hours) is also possible in those patients if there are no symptoms of intraamniotic infection. The abovementioned recommendations are compliant with the current guidelines of the Polish Society of Gynecologists and Obstetricians (“Induction of labor”, “Induction of labor — clinical algorithms”) [15–18].

#### *PPROM between 34 + 0 and 36 + 6 weeks of gestation*

According to the guidelines of the Polish Society of Gynecologists and Obstetricians, in patients with PPRM between 34–37 weeks of gestation but with no symptoms of intraamniotic infection, induction of labor is not recommended as it does not lower the risk for systemic infection (neonatal sepsis) and may be associated with higher risk for neonatal respiratory distress. Expectant management, combined with antibiotic prophylaxis, is advised. In case of PPRM with symptoms of intraamniotic infections, delivery (cesarean section or vaginal delivery) is recommended [15, 16].

**Management of PROM, depending on gestational age — summary**

≥ 37 + 0 weeks of gestation:

- delivery (induction of labor or cesarean section, as indicated)
- GBS prophylaxis, as indicated

34 + 0 to 36 + 6 weeks of gestation:

- expectant management, if there are no symptoms of intraamniotic infection
- prophylactic antibiotic therapy
- GBS screening test and GBS prophylaxis, as indicated
- treatment of intraamniotic infection (if applicable) and delivery

22 + 6 to 33 + 6 weeks of gestation:

- expectant management, if there are no symptoms of intraamniotic infection
- prophylactic antibiotic therapy
- full-course of corticosteroids (24 + 0–33 + 6)
- treatment of intraamniotic infection (if applicable) and delivery
- vaginal and rectal culture for GBS and GBS prophylaxis, in accordance with the guidelines
- magnesium sulphate for neuroprotection (24 + 0–31 + 6), unless contraindicated

< 22 + 6 weeks of gestation:

- patient counseling: consultation with neonatology and maternal-fetal medicine team
- the patient should be informed about low probability for fetal survival and normal development and high risk for complications (intrauterine infection, septic shock, uterine atony, hemorrhage, death)
- management depends on the clinical condition of the patient (presence or absence of intraamniotic infection) and patient wishes:
  - pregnancy may be continued if there is no threat to maternal health and if informed written maternal decision has been obtained
  - termination of pregnancy due to the fact that criteria for threat to maternal health and life have been met
  - if the pregnancy is to be continued:
    - \* prophylactic antibiotic regimen;
    - \* GBS prophylaxis is not recommended;
    - \* corticosteroids are not recommended;
    - \* tocolysis is not recommended;
    - \* magnesium sulphate for neuroprotection is not recommended;
    - \* hospitalization at a tertiary center of perinatal care after 22+6 weeks of gestation.

Irrespective of the nature of maternal decision, written record of the decision — signed by the patient and the obstetrics and gynecology specialist — should always be included in the patient medical records

GBS — Group B streptococcus

*PPROM between 22 + 0 and 33 + 6 weeks of gestation*

Induction of labor before 34 weeks of gestation is not recommended in patients with PPRM but without symptoms of intraamniotic infection due to high risk for complications of prematurity. Expectant management — combined with a course of steroids, prophylactic antibiotic therapy and neuroprotection (advised <32 weeks of gestation). Elective delivery (cesarean section or vaginal delivery) is recommended to patients with PPRM and symptoms of intraamniotic infection [15, 16].

*PPROM before 22 + 6 weeks of gestation*

Patients with PPRM before 22 + 6 weeks of gestation should be informed about the risks and benefits connected with expectant management as compared to elective delivery. Of note, long-term amniotic leakage is associated with the risk for systemic intraamniotic infection, which may result in systemic infection (sepsis), septic shock, and maternal death. Also, patient counseling needs to include realistic evaluation of the neonatal outcome, presented by an **obstetric-neonatal team**, who need to supply the patient with the most up-to-date information about the prognosis. Depending on the obstetric status and patient (parents)

wishes, either expectant management or induction of a miscarriage need to be offered. Such management is compliant with the current eligibility criteria for induced miscarriage due to a direct threat to maternal health and life.

According to Sklar et al. [19], expectant management at this stage of pregnancy is associated with higher risk for intraamniotic infection, postpartum hemorrhage, admission to the Intensive Care Unit, and hysterectomy. Total maternal morbidity in case of expectant management is approximately two-fold higher as compared to elective delivery (60.2% vs 33%, respectively). Additionally, the survival rate of extremely premature (< 22 + 6 weeks of gestation) neonates has been estimated at 1%.

Although most studies on antibiotic prophylaxis in PPRM focused on patients at > 22 weeks of gestation, we recommend to use broad-spectrum antibiotics to prolong the pregnancy in patients with PPRM and expectant management due to the risk for intraamniotic infection. The antibiotic regimen is the same before and after 22 + 6 weeks of gestation. Of note, expectant management in patients with amniotic leakage at > 22 + 6 weeks of gestation is associated with the risk for systemic infection, sepsis, and septic shock.

If a patient presents with symptoms of intraamniotic infection and elevated procalcitonin levels (higher risk for systemic infection — sepsis), immediate delivery is necessary, either using pharmacotherapy to induce a miscarriage and, if that proves ineffective or if the maternal condition is deteriorating, using surgical methods (fetal extraction using obstetric instruments or hysterotomy). Progressive symptoms of a septic shock after curettage and despite intensive antibiotic therapy is an indication for immediate hysterectomy to remove the source of the infection. Before 22 + 6 weeks of gestation, the patient **does not need to be hospitalized at a tertiary center for perinatal care**. After 22 + 6 weeks of gestation, hospitalization at a tertiary referral center of perinatal care is recommended.

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