In this lesson we continue the discussion of medication adherence. The goal is to concentrate upon the pharmacist’s perspective. This lesson provides 2.5 hours (0.25 CEUs) of credit, and is intended for pharmacists in all practice settings. The program ID # for this lesson is 707-000-11-011-H01-P. Pharmacists completing this lesson by November 30, 2014 may receive full credit.

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page (for continuous participants only).

The objectives of this lesson are such that upon completion the participant will be able to:

1. Describe the importance of medication adherence.
2. List methods to assess patient non-adherence.
3. Describe strategies that pharmacists can incorporate to improve adherence.
4. Provide examples of pharmacist interventions that improve adherence.

All opinions expressed by the author/authors are strictly their own and are not necessarily approved or endorsed by W-F Professional Associates, Inc. Consult full prescribing information on any drugs or devices discussed.
INTRODUCTION

In a recent lesson (September, 2011) we discussed “Medication Adherence.” Among other issues, we defined adherence, described its difference from compliance, summarized factors that impact upon adherence, and included illustrations of pharmacists promoting adherence.

Your responses and input to that lesson were incredibly positive. In fact, it was overwhelmingly requested that we expand the presentation. Therefore, herein we offer additional considerations. Included are: descriptions of the importance of adherence, methods to assess non-adherence, strategies to improve adherence, and demonstration of additional interventions whereby pharmacists can improve adherence.

The World Health Organization (WHO) has defined adherence as the extent to which a person’s behavior – taking medication, following a diet and/or executing lifestyle changes - corresponds with agreed upon recommendations from a health care provider. It is estimated that among patients with chronic illnesses up to 50% are non-adherent to prescribed medications. Poor adherence can lead to increased morbidity and mortality. Some estimates suggest that non-adherence can lead to increased healthcare costs of up to $100 billion per year. This lesson focuses on the general aspects of medication adherence and strategies to improve non-adherence in cardiovascular disease, diabetes and HIV management.

Adherence rate is usually defined as the percentage of prescribed doses of the medication taken by the patient over a specified period. In general adherence rates are higher in clinical trials as well as in patients with acute conditions when compared to those with chronic conditions. The improved adherence seen in clinical trials can be attributed to selection of motivated patients and the additional attention that study patients receive. Specifically, there is an increased frequency of clinic visits and patients know that their medications adherence is being assessed. Even during these circumstances, adherence rates average 43 to 78% in patients with chronic conditions. Unfortunately, there is not a standard for the optimal adherence rate. Some clinical trials suggest that at least 80% adherence to medications is required for optimal clinical effect. There are data that suggest adherence rates up to 90% are required for viral suppression of the human immunodeficiency virus (HIV).

There are several terms used in the adherence literature. The term compliance has been used to define the extent to which a patient’s behavior coincides with the clinical prescription. However, it does not take into account the complex interplay between the patient, provider, and health care system. Concordance is another term which refers to the process of discussion between health care providers and patients to reach an agreement on a treatment plan. Lastly, persistence refers to the length of time during which a patient continues to be engaged in adherent behaviors. These terms are sometimes used interchangeably in the literature; however, the most important term for discussion today is adherence.

BARRIERS TO ADHERENCE

Poor adherence to medical therapies compromises patient outcomes. According to the WHO, improving adherence to medical therapy for hypertension, hyperlipidemia, and diabetes would result in significant health and economic benefit. Adherence is a multi-faceted behavioral process determined by many patient-specific and societal factors. To better understand and address adherence in patients, it is important to understand the contributors to non-adherence. The factors for non-adherence can be classified into patient-related factors, physician-related factors and healthcare system factors.

Patient-related factors

Contributors to medication non-adherence include a lack of understanding of the disease state, lack of involvement in the treatment decisions and poor medical literacy. The patient’s beliefs of the efficacy of treatment, previous experiences with medications, and lack of motivation also affect their medication adherence. Treatment for asymptomatic conditions, such as hypertension, often presents a challenge for patients with poor health literacy because the sequelae of the disease may be difficult to conceptualize. Additional patient-related factors that contribute to poor adherence include lower socioeconomic status, high medication costs, lack of transportation, poor understanding of medication details, and long wait times at the pharmacies. Family and social support is also an integral part of improving adherence. Lastly, mental illness (e.g. depression and anxi-
ety) can be predictive of non-adherence to medical recommendations.

**Physician-related factors**

Physicians contribute to non-adherence by not recognizing or acknowledging medication adherence during patient visits. They may contribute by prescribing complex regimens, failing to address the benefits and potential side effects of prescribed medications and failing to consider financial burdens associated with prescribed treatments.1,3 Studies have indicated a correlation between patient adherence and the provider’s communication, namely “positive talk,” and asking specific questions about adherence.1 Patients who feel like partners in the treatment plan and who are actively engaged have better adherence. In addition warmth and empathy of the clinician continues to be a factor that improves adherence.

**Healthcare system-related factors**

Healthcare systems can create barriers to adherence by limiting the healthcare coordination and patient access to care.1,3 Costs of medications can be prohibitive leading to non-adherence. Systems that promote continuity of care, fee structures that reimburse for patient counseling and education facilitate improved adherence. Information sharing between providers and pharmacies has the potential to improve adherence by allowing prescribers to understand the patient’s behavior toward prescription refills. Clinicians often see a large volume of patients without resources to address individual needs. The amount of time spent with a patient may be insufficient to assess and understand medication taking behaviors. Discussions engaging patients about the importance of adherence are vital to improve and sustain appropriate medication taking behaviors.

The ability of physicians to recognize and address adherence is poor. In some circumstances, they may contribute to non-adherence by prescribing complex regimens, failing to explain benefits of therapy and potential adverse effects of a medication effectively and inadequately appreciating the financial burden to the patient.3 Pharmacists have the unique opportunity to address non-adherence in their clinical setting, and contributing to improved outcomes.

**HOW TO ASSESS ADHERENCE**

As stated previously, pharmacists are the perfect healthcare providers to assess adherence. The first step in addressing non-adherence is recognizing the problem. There are several forms of subjective and objective information that could potentially suggest a non-adherence problem. Subjective information is obtained through interaction with the patient. You may discover non-adherence through open ended questions such as:4

- Can you tell me how you take your medications?
- Which medications do you take in the morning?
- How often do you miss doses of medications?

A mix of open ended questioning and closed ended questioning may be best for obtaining information.4 It is important that the pharmacist notice subtle clues of non-adherence:5

- I’m supposed to take it.
- I think they said to take it twice a day.

Few patients will admit to non-adherence freely. Further assessment of these patients through questioning to gain additional subjective information and through collection of objective information can inform the pharmacist of the patient’s adherence status.

Objective information regarding adherence is obtained from a source other than the patient’s statements.5 Forms of objective information that can be used to assess adherence include:

- Computerized medication profiles
- Drug serum concentrations
- Signs and symptoms of disease i.e. uncontrolled hypertension

Computerized medication profiles provide a history of medication refill rates.5 However, this information should be used with the knowledge that patients may refill their medications on time but still not take them appropriately. Drug serum concentrations can be used to monitor a finite number of medications. However, variations in individual metabolism of medications and need for appropriate timing make this difficult. Signs and symptoms of disease progression are commonly used in clinic as predictors of adherence. However, it is possible that the patient is taking their medications appropriately and the disease is progressing despite their efforts. No method of assessing adherence is perfect; therefore, it is important that pharmacists utilize a combination of multiple methods to gather information.

**STRATEGIES TO IMPROVE ADHERENCE**

There are multiple methods to improve adherence. The adherence interventions should be individualized based on the patient’s barriers to adherence. Pharmacists can address many patient related barriers by providing education about the disease state and medications. Costs of medications can be prohibitive to adherence,
so pharmacists can collaborate with physicians to help determine the most cost-effective therapy based on the available funding or insurance program. Medication regimens that require multiple doses throughout the day have been shown to decrease adherence. Data from a meta-analysis indicate there is a 10% decrease in adherence with each additional daily dose. Selection of medication regimens with the least number of pills and least frequent dosing schedule should be attempted for all patients. In some circumstances, complex treatment regimens cannot be avoided; therefore, pharmacists should specifically target these patients for adherence counseling and interventions such as follow-up phone calls, pillboxes and medication teaching. In 2003, Medicare recognized the non-adherence potential with Medicare recipients on multiple medications; therefore, the Medicare Prescription Drug Improvement and Modernization Act mandated a team-based approach of medication therapy management services (MTMS). This program is provided by insurers through community pharmacies. They are designed to provide education and counseling to improve patient understanding, improve medication adherence and detect adverse reactions. The following section discusses specific interventions involving pharmacists that promote adherence assessment and monitoring with the goal of improved outcomes.

**CARDIOVASCULAR DISEASE**

**Statin therapy**

3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitors (statins) are highly effective at reducing cardiovascular disease burden in a wide spectrum of patients. In clinical trials, statins reliably lower low density lipoprotein (LDL) cholesterol and reduce the risk of cardiovascular events such as myocardial infarction and stroke. Despite the well documented efficacy of statin therapy, non-adherence is quite common. Studies have demonstrated that up to 50% of patients are non-adherent with statin therapy. Non-adherence with statin therapy is associated with a significant increase in health risk. Specifically, one study found that patients who took pravastatin less than 75% of the time had event rates for coronary death or nonfatal myocardial infarction similar to that of placebo. In contrast, those patients who take their medication greater than 75% of the time had a significant reduction in event risk. The risk is even more pronounced in patients taking statins after having an MI. Specifically, one study found that patients who do not fill any of their discharge prescriptions have an 80% increase in mortality compared to fully adherent patients. In addition, partial adherence is associated with a 44% increase in mortality.

Several factors have been consistently associated with non-adherence to statin therapy. Generally patients < 50 and ≥ 70 years of age have the poorest adherence rates. In addition, women are less adherent than men, patients with lower income are less adherent than those with higher income, and in general those patients with a diagnosis of myocardial infarction are more likely to be adherent as this is an acute condition.

Perhaps the most important strategy to improve adherence with statin therapy is patient education. Knowledge of the role of cholesterol in heart disease risk is generally poor and this problem is further compounded by the fact that hyperlipidemia is a silent disease. Therefore, many patients do not understand the value of statin therapy. Repeated, brief educational counseling sessions generally appear to improve statin adherence. It is important that the education be simple and jargon-free. It is also important to understand a patient’s anxieties about therapy. Once a pharmacist understands the patient’s specific concerns, they can be addressed through individual counseling sessions.

Patients who experience adverse events with statin therapy are also more likely to be non-adherent. It is important for pharmacists to counsel patients on the muscle related adverse events associated with statin therapy. Specifically, statins can cause myopathy which can progress to rhabdomyolysis which is a life threatening condition that can cause acute renal failure. Specifically, patients should be counseled to monitor for unexplained muscle pain or weakness and to report this to a healthcare provider. Patients who experience this adverse effect with a higher potency statin can often receive lower doses of the same statin or a lower potency statin without problem. However, if patients lack awareness or understanding of this adverse event, they may simply self-discontinue the drug or take it less regularly. Pharmacists play a very important role in counseling patients on medications and adverse events.

One novel way to improve compliance to statin therapy is through non-invasive imaging studies. Carotid ultrasound for intima-medial thickness and coronary computerized tomography producing a coronary calcium score both show the volume of coronary artery disease. These tools have been used to show asymptomatic patients that they truly do have cardiovascular disease and this leads to increased adherence rates with medications. The cost of these interventions makes their use uncommon. However, pharmacists can discuss results from these tests with patients and use them to support the need for adherence to statin therapy.

**Hypertension**

According to data from 2005-2008, approximately 34% of American adults have hypertension. However, only approximately 80% are aware of their condition, only 71% are taking antihypertensives, and only...
48% are at their goal blood pressure. This is despite the knowledge that blood pressure control significantly decreases the risk of cardiovascular disease and stroke. One major contributor to the number of patients who have not reached their target blood pressure is non-adherence with medication therapy. The guidelines for hypertension management highlight the importance of improving patient adherence with these medications and the role of pharmacists. In addition, the American Society of Hypertension recently released a position paper on the importance of adherence with anti-hypertensive therapy. Patients are non-adherent with anti-hypertensive therapy for many reasons. However, some of the most common reasons are consistent with factors associated with statin non-adherence. Hypertension is a symptomless disease; therefore, patients do not perceive benefit from therapy. In addition, the therapy for hypertension is long term and is often associated with adverse events. Therefore, patient education plays an important role in improving adherence. Patients should be counseled on the positive effects of blood pressure control on heart disease and stroke risk. Improving patient understanding of these points can also help to improve adherence.

Many studies have assessed the ability of healthcare providers to improve adherence with anti-hypertensive therapy and some of the best data are from pharmacist intervention studies. The most effective approaches to improving compliance to these medications are multi-factorial. They include patient education through counseling sessions, provision of written materials, and use of adherence aids such as pill boxes or blister packs. One of the most frequently referenced studies of pharmacist interventions was published in the Journal of the American Medical Association in 2006. The authors studied 200 community-based patients aged 65 years or older taking at least 4 chronic medications at Walter Reed Army Medical Center. After a two month run-in phase of usual care and adherence measures, the patients underwent a 6-month intervention phase (standardized medication education, regular follow-up by pharmacists, and medications dispensed in time-specific packs). They were then transitioned to usual care or continued pharmacist intervention for an additional 6 months. Mean adherence improved from 61% at baseline to 97% after the 6 month pharmacist intervention (p<0.001). Along with this they had a significant drop in systolic blood pressure and LDL cholesterol levels. However, those patients who returned to usual care after the 6 month pharmacist intervention returned to their baseline compliance, blood pressure and cholesterol levels. This study shows that targeted pharmacist education and intervention can significantly improve blood pressure and lipid control.

Diabetes

Diabetes is a chronic medical condition that requires continued medical care, chronic patient self-management, and education and support to prevent acute complication and the risk of long-term sequelae. Diabetes affects 24 million people in the United States resulting in 174 billion dollars in annual healthcare expenditures. The health care system is challenged by this complex patient population.

There have been improvements in the proportion of diabetic patients achieving recommended targets of hemoglobin A1c, blood pressure and LDL cholesterol goals in the last decade. Data from NHANES, National Health and Nutrition Examination Survey, demonstrate that mean A1c has declined from 7.82% (in 1999) to 7.18% (in 2004). In addition, improvements in lipids and blood pressure control have led to reductions in end-stage complications in patients with diabetes. Although this data is encouraging, there are some studies which demonstrate that only 12% of patients achieve all three target hemoglobin A1c, blood pressure and LDL cholesterol goals. Moreover, there is room for improvement in the quality and consistency of diabetes care. Multiple interventions improving adherence to national standards have been implemented, but a major contributor to suboptimal care include a healthcare system that is fragmented. Systems that include multidisciplinary teams are best suited to provide care for patients with diabetes. Increasing amounts of evidence demonstrate that pharmacists, working as patient educators, consultants or clinicians in partnership with other healthcare professionals can improve patient outcomes.

Pharmacists can improve adherence in patients with diabetes which results in improved outcomes. One reason for non-adherence in diabetic patients is lack of knowledge about their disease. Pharmacists can proactively educate patients about their disease, including signs and symptoms of hypoglycemia and hyperglycemia and long-term sequelae of poor glucose control. In addition, pharmacists can educate patients about the medication side effects, administration techniques for insulin and storage requirements. In a study conducted at 16 community health centers, pharmacists developed and established diabetes management programs. The pharmacists provided patient education, monitored adherence, prompted physicians to complete standards of care, and provided education and medication therapy consultations for medical staff. For patients that remained in the program for 6 months, the positive results were impressive. The average HbA1c dropped from 9.1 to 7.7%, (P<0.01). In addition, significant reductions in blood pressure and LDL were achieved. Due to complexity of diabetes management, multi-disciplinary teams are necessary to optimize clinical outcomes.

HIV

Adherence to antiretroviral therapy is associated with improved viral suppression, lower resistance rates,
and increased survival and improved quality of life. Similar to other chronic conditions, lifelong treatment is required for optimal outcomes. Patients must be screened for adherence predictors prior to the initiation of antiretroviral therapy. Predictors for adherence are listed in Table 1. Antiretroviral therapy requires a commitment from the patient as well as the healthcare team.

Prior to initiation of antiretroviral therapy, clinicians must assess a patient’s willingness to take medications. Identifying and addressing social issues prior to initiation of antiretrovirals (such as psychiatric illness, active drug use, and housing) is imperative for successful outcomes and reducing the risk of non-adherence. A pharmacist can assess readiness to start HIV medications by:

- Assessing how the medications fit into the patient’s lifestyle and work schedule
- Assessing adherence by using a trial with candy
- Making a contingency plan during schedule changes, such as weekends and holidays
- Assess the patient’s understanding and acceptance of the regimens

Deferring therapy may be required until social support and co-morbidities are addressed; therefore, several office visits may be required before therapy is initiated. As has been stated with other disease states, patients often comply with regimens when they are involved with the treatment decisions. Because there are multiple first-line regimens for HIV with different dosing frequencies, pill size, and side effects, patients are more likely to commit to a regimen that they selected. Pharmacists can assist by educating patients about the pill size, dosing frequency and potential side effects to foster adherence and acceptance. Many of the HIV medications are available as a combination product. Pharmacists can help reduce pill burden and potentially pill fatigue by suggesting these alternatives (Table 2). There are many online resources available for patient education, including photographs of the medications. (See http://aidsinfo.nih.gov).

Multiple interventions have demonstrated efficacy including pharmacist-led individualized interventions, cognitive-behavior therapy, peer support groups, and reminder strategies. Reminder strategies include alarms, watches, pagers, or cell phone alarms. In addition, it is vital to involve family and friends as a support system. Maintenance of adherence requires close follow-up with the healthcare team, whether it involves a phone follow-up, house visits, or more frequent clinic visits. Adherence should be addressed and emphasized at every clinic visit. In addition, it is important to review adverse effects about the medications at every visit to assure that adverse effects are not a barrier to adherence.

**Table 1: Predictors for poor adherence in HIV patients**

- Low levels of literacy
- Age-related challenges: vision loss, cognitive impairment
- Psychosocial issues: depression, homelessness, inadequate social support, stressful life-events, dementia, psychosis
- Current substance abuse (History of substance abuse is not a risk factor)
- Stigma of the disease
- Difficulty with swallowing medications
- Complex regimens with multiple pills and multiple daily dosing
- Adverse drug effect
- Treatment fatigue

Adapted from DHHS guidelines

**Table 2: Fixed-dose combinations for HIV**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Truvada ®</td>
<td>Dose: 1 tablet daily. Preferred agent for combination therapy for HIV.</td>
</tr>
<tr>
<td>Tenofovir 300mg</td>
<td></td>
</tr>
<tr>
<td>Emtricitabine 200mg</td>
<td></td>
</tr>
<tr>
<td>Epzicom ®</td>
<td>Dose: 1 tablet daily. Alternative agent for combination therapy for HIV.</td>
</tr>
<tr>
<td>Abacavir 600mg</td>
<td></td>
</tr>
<tr>
<td>Lamivudine 300mg</td>
<td></td>
</tr>
<tr>
<td>Combidir ®</td>
<td>Dose: 1 tablet twice daily. Alternative agent for combination therapy for HIV.</td>
</tr>
<tr>
<td>Zidovudine 300mg</td>
<td></td>
</tr>
<tr>
<td>Lamivudine 150mg</td>
<td></td>
</tr>
<tr>
<td>Atripla ®</td>
<td>Dose: 1 tablet at bedtime. Only fixed dose combination that includes 2 classes of antiretrovirals. Preferred agent for HIV therapy.</td>
</tr>
<tr>
<td>Tenofovir 300mg</td>
<td></td>
</tr>
<tr>
<td>Emtricitabine 200mg</td>
<td></td>
</tr>
<tr>
<td>Efavirenz 600mg</td>
<td></td>
</tr>
<tr>
<td>Kaletra ®</td>
<td>Dose: 4 tablets daily or 2 tablets twice daily. Alternative agent for combination therapy for HIV.</td>
</tr>
<tr>
<td>Lopinavir 200mg</td>
<td></td>
</tr>
<tr>
<td>Ritonavir 50mg</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from DHHS guidelines
CONCLUSION

Poor adherence to medication regimens is common. Lack of adherence contributes significantly to increased medical costs and increased morbidity and mortality. Healthcare providers should always address adherence by emphasizing the value of the medication regimen and assessing for barriers to adherence. Simplifying and customizing the regimen to a patient’s lifestyle is imperative for adherence and acceptance by the patient. Nonjudgmental questions about patient’s adherence are a simple way for pharmacists to identify non-adherence. Multi-disciplinary teams also enhance adherence interventions. As medication regimens become more complex and patients continue to have more chronic conditions, pharmacists must remain an integral part of adherence assessment and patient education.

REFERENCES

16. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. JAMA 2006;296:2563-71.

ANNOUNCEMENTS

Credit statements for 2011 will be mailed near the end of the year. Deadline for us to receive quizzes & have them appear on that statement is Friday December 9, 2011.
Credit for quizzes received after December 9, 2011 (but before January 1, 2012) will still be applied to 2011, and will appear on additional statements that will be mailed after January 1st.

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LESSON EVALUATION

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?
   - Describe importance of adherence: 
     - Yes
     - No
   - List methods to assess non-adherence: 
     - Yes
     - No
   - Describe strategies to improve adherence: 
     - Yes
     - No
   - Provide examples of interventions that improve adherence: 
     - Yes
     - No

2. Was the program independent & non-commercial: 
   - Yes
   - No

3. Relevance of topic: 
   - Poor
   - Average
   - Excellent

4. What did you like most about this lesson?: 
   - [Your answer here]

5. What did you like least about this lesson?: 
   - [Your answer here]

Please Select the Most Correct Answer(s)

1. Poor adherence can lead to:
   - A. Increased healthcare costs
   - B. Improved overall patient outcomes
   - C. Decreased mortality
   - D. A & C
   - E. None of these

2. For patients with chronic diseases, what is the estimated adherence rate?
   - A. 100%
   - B. 90%
   - C. 20 %
   - D. 50%
   - E. None of these

3. A patient with poor literacy & poor understanding of his/her disease is considered to have which type of adherence barrier?
   - A. Patient-related
   - B. Healthcare system-related
   - C. Physician-related
   - D. Pharmacy-related

4. Healthcare system-related adherence barriers include:
   - A. MDs seeing a high volume of patients
   - B. High costs of medications
   - C. Lack of reimbursement for patient counseling
   - D. All of these

5. Which of these are strategies to improve adherence?
   - A. Targeted patient education
   - B. Decreasing pill burden
   - C. Follow-up phone calls
   - D. Medication counseling
   - E. All of these

6. How is adherence measured objectively?
   - A. Computerized medication profiles
   - B. Drug serum concentrations
   - C. Signs & symptoms of disease
   - D. Pill counting
   - E. All of these

7. Which of these is an open ended question?
   - A. Can you tell me how you take your meds?
   - B. Do you take your medications every day?
   - C. How often do you miss doses of your meds?
   - D. A & C

8. Which of these are causes of non-adherence for both antihypertensives & statins?
   - A. Both treat asymptomatic disease states
   - B. Both have risk of causing ADRs
   - C. Both are used to treat chronic conditions
   - D. Patients don’t understand underlying disease
   - E. All of these

9. Which of these is the most effective method for pharmacists to improve medication adherence in cardiovascular diseases such as hypertension & hyperlipidemia?
   - A. Verbal patient education only
   - B. Written education only
   - C. Adherence aids only
   - D. All of these

10. What are some adherence barriers specific to patients with HIV?
    - A. Low levels of literacy
    - B. Current substance abuse
    - C. Multiple daily dosing
    - D. Adverse drug effects
    - E. All of these
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