A 66-year-old woman presents to the emergency department with crushing chest pain and ST-segment elevations on ECG. She has left ventricular systolic dysfunction (ejection fraction, 35%) after recent (6 days earlier) non-ST-segment elevation myocardial infarction treated with percutaneous coronary intervention, including 2 drug-eluting stents. She is sent for emergent cardiac catheterization, is found to have in-stent thrombosis, and subsequently is revascularized. After being transferred to the coronary care unit, she undergoes further workup. Before her previous admission, her home medication regimen included aspirin, lisinopril, atenolol, atorvastatin, spironolactone, furosemide, potassium, and sublingual nitroglycerin. At the time of her latest discharge, her medication regimen consisted of an increased dose of aspirin, the addition of clopidogrel, and a change in atenolol dose, in addition to all other previous medications. During the history and physical examination, it is discovered that she had not filled any of her new prescriptions after discharge from the hospital 5 days ago. She explains, “I already had all my drugs in my medicine cabinet at home.”

Nonadherence
Nonadherence to medications has been documented to occur in >60% of cardiovascular patients. Self-reported adherence to cardiovascular medications in patients who have coronary artery disease is <40% for the combination of aspirin, β-blocker, and a lipid-lowering agent in both isolated and long-term follow-up surveys (Table 1).

The immediate discharge period is a time of high risk for nonadherence. Nearly 1 in 4 patients is partially or completely nonadherent in filling prescriptions after discharge. Of the patients who are initially adherent, up to 50% will discontinue antihypertensive medications within 6 to 12 months, and only ≈40% continue statin medications for 2 years after hospitalization for acute coronary syndrome.

Primary nonadherence (not initially filling the prescription written) leads to a significant increase in 1-year mortality after hospitalization for myocardial infarction. Secondary nonadherence (failure to follow the instructions or to refill the prescription) has been shown to increase mortality, hospitalizations, and costs.

Patients with high adherence rates have a significantly lower risk of cardiovascular events compared with those with low adherence rates. Those who filled none of their discharge prescriptions within 120 days after myocardial infarction had an 80% increased odds of death and those who filled only some of their prescriptions had a 44% increased odds of death compared with those who filled most of their prescriptions.

Causes
We care for our patients in a fast-paced, high-level environment. Their medication regimens have become increasingly complex. Factors of nonadherence can be categorized into 3 major groups: socioeconomic, communication-related, and motivational (Figure 1).

Socioeconomic factors are derived from the patients’ inability to afford or difficulty in affording their medications. They may include lack of adequate healthcare coverage, unemployment, retirement, and indigence. Some studies have shown that socioeconomic factors and low health literacy in patients with cardiovascular disease contribute to nonadherence.

Effective communication requires providing medication instructions at a level that the patient can understand. Health illiteracy is a major ongoing problem. Inadequate communication is often multifactorial. Aggravating circumstances include languages other than English as the primary household language, cultural barriers, low functional literacy, substance or alcohol abuse, and mental illness. Those with depression or other significant psychiatric illnesses, heavy drinkers, and nonwhite patients...
have been associated with risk for low adherence rates.\textsuperscript{2,11}

Lack of motivation has been identified as a barrier to medication adherence in patients who are able to effectively communicate and can comfortably afford their medications. These patients’ nonadherence is not due to a choice between affording food or their medication but rather to their lack of understanding the gravity of their illness or the benefit that the medication will provide. This issue is often compounded by a fear of potential side effects or toxicities associated with their medications. Cultural beliefs may also play a role in medication nonadherence.

National patient surveys have shown that patients are less likely to take a medication if it does not correlate with a noticeable beneficial effect. Unlike analgesics, antiemetics, or antibiotics, many medications in the armamentarium against cardiovascular disease have a preventive mechanism that does not demonstrate noticeable symptom relief to the patient. The use of antiplatelet agents to prevent in-stent thrombosis, high-dose statin therapy after acute coronary syndromes, or antihypertensive agents in asymptomatic patients may all be perceived by a patient as not providing benefit because they simply do not feel better.

Finally, a lack of perceived need or concern about adverse effects may also decrease adherence rates. Conflicting information exists on the roles that age and regimen complexity play as risk factors.\textsuperscript{3,12}

Solutions

The reasons for nonadherence are often multifactorial; therefore, multimodal interventions are generally more successful than a unimodal approach.\textsuperscript{13} Solutions to overcoming patient-specific barriers to nonadherence do not have to consume valuable time or resources.

Table 1. Adherence Rates to Common Cardiovascular Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Self-Reported Adherence, %</th>
<th>Consistent Adherence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>83</td>
<td>71</td>
</tr>
<tr>
<td>Lipid-lowering agents</td>
<td>63</td>
<td>46</td>
</tr>
<tr>
<td>β-blockers</td>
<td>61</td>
<td>44</td>
</tr>
<tr>
<td>Aspirin + β-blocker</td>
<td>54</td>
<td>36</td>
</tr>
<tr>
<td>Aspirin + β-blocker + lipid-lowering agent</td>
<td>39</td>
<td>21</td>
</tr>
</tbody>
</table>

\*More than 2 consecutive follow-up surveys over 6±12 months.

Figure 1. Causes of medication nonadherence.
In the Hospital
If therapy is initiated in the hospital, the patient is most likely to relate the drug to the disease; intensive education by the medical team at this opportune time may improve adherence. Patients will have a perceived importance of medications used in the hospital setting and often have more dialogue with physicians, pharmacists, and nurses about medications, including discussions about possible adverse effects. Management strategies should be tailored to patient needs, and patients should be educated about the goals of treatment and potential adverse effects, thus becoming part of the decision-making process.

Methods shown to improve medication adherence are discharge medication counseling, positive interactions between clinician and patient, close follow-up with patients (1 to 2 weeks after discharge), low costs or copayments for prescription medications, and simplified drug regimens. It is helpful to initiate motivational strategies, including daily drug reminder charts, training on self-determination, reminders, social support, nurse telephone calls, family member support, and telephone-linked computer counseling.

In the Office
The first and most crucial step in ensuring medication adherence is to determine whether the patient can communicate and process the information that you are sharing. If you are not able to effectively communicate with the patient, monitoring prescription refills, counting pills, and involving friends or family members are of value when nonadherence is suspected. Once specific factors are identified, an appropriate tool should be used to facilitate understanding (Figure 2).

Once effective communication is achieved, simple attempts to determine the patients’ ability to pay for the medication should be made through a series of questions that ask patients what pharmacy they use, who their insurance carrier is, or what their current profession is. A patient will often give clues that they may not be able to afford their medication. Fortunately, programs continue to emerge that are designed to help patients acquire medication at a fraction of the cost.

Motivation is the most elusive reason for medication nonadherence. Patients will often respond to instructions with a learned series of nods and “yes” responses. Asking patient to explain the reason they are prescribed each medication may reveal their lack of understanding, which predicts a high likelihood of poor adherence.

Conclusions
Nonadherence to medications remains a major problem for cardiovascular
Table 2. Resources to Address Medication Nonadherence

<table>
<thead>
<tr>
<th>Description</th>
<th>Resource/Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Socioeconomic</td>
<td></td>
</tr>
<tr>
<td>Access to no- or low-cost medication and links to patient assistance and disease-based programs</td>
<td><a href="http://www.needymeds.com">http://www.needymeds.com</a></td>
</tr>
<tr>
<td>Access to patient payment assistance programs and discounted prescription medications</td>
<td><a href="http://www.rxassist.com">http://www.rxassist.com</a></td>
</tr>
<tr>
<td>Communication</td>
<td></td>
</tr>
<tr>
<td>Web site</td>
<td><a href="http://clearhealthcommunication.com/public-health-professionals/tips-for-providers.html">http://clearhealthcommunication.com/public-health-professionals/tips-for-providers.html</a></td>
</tr>
<tr>
<td>Link to patient counseling tools in multiple languages</td>
<td><a href="http://www.rxtran.com/">http://www.rxtran.com/</a></td>
</tr>
<tr>
<td>Motivation</td>
<td></td>
</tr>
<tr>
<td>Patient-directed publications for the management of various disease states</td>
<td><a href="http://circ.ahajournals.org/collected/patient.shtml">http://circ.ahajournals.org/collected/patient.shtml</a></td>
</tr>
</tbody>
</table>

Case Presentation
The physician caring for the patient recognized the problem with primary nonadherence and instituted a multimodal approach to increase adherence. Family member support was obtained, and discharge medication counseling and a daily drug reminder chart were provided. In addition, a follow-up appointment 2 weeks after discharge was scheduled with her cardiologist. At her 2-week appointment, she was able to explain the reasons for each medication and describe how she was taking them. She acknowledged that she was able to pay for her medications, and she was motivated by her cardiologist to continue adhering to her medication regimen.

References
Medication Adherence in Cardiovascular Disease
Steven Baroletti and Heather Dell'Orfano

Circulation. 2010;121:1455-1458
doi: 10.1161/CIRCULATIONAHA.109.904003

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