Play It Again, Sam — Depression Is Recurring

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Many years ago I read an editorial, author and journal now forgotten, that included in its title the phrase, "Play it again, Sam" — words attributed to, but never actually spoken by, the character played by Humphrey Bogart in the film *Casablanca*. I can think of no better phrase by which to emphasize the point of this editorial: again and again, research has shown that depression is an illness with a high degree of recurrence.

It is difficult to overstate the effect depression has on health. The World Health Organization lists depression as the leading cause worldwide of years lost because of disability.[1] And when depression coexists with other illnesses, such as an acute coronary syndrome,[2] it can be an independent risk factor for death (by means other than suicide).

Every step toward improving the outcome of depression late in life has considerable public health significance. In this issue of the *Journal*, Reynolds et al.[3] report on their follow-up of patients who had a response to treatment for depression. The findings advance our knowledge about the recurrence of depression late in life, and about how to prevent such recurrence, in three main ways. First, the investigators looked for recurrence for two years after the start of treatment, a longer follow-up period than has been studied previously. Second, they found evidence of recurrence in patients who had had their first episode of depression at 70 years of age or older, showing the potentially chronic nature of the illness, even among those with no previous episodes. Third, they found that maintenance therapy with antidepressants during the two years of treatment significantly reduced the rate of recurrence, as compared with therapy that did not involve antidepressants. The finding that only four patients needed to be treated for 2 years to prevent one recurrence brings sharply into question whether the common practice of administering only 6 to 12 months of antidepressant therapy is sufficient.

In the study by Reynolds et al., antidepressant therapy plus monthly contact with a clinician, for either clinical management or psychotherapy, was the intervention most likely to prevent recurrence. The antidepressant the authors chose was paroxetine, but as authors of many reviews have noted, there is no convincing evidence that any particular agent is superior to others.[4] Fortunately, many good antidepressants exist, with short-term, controlled trials showing response rates of 65 to 75 percent. Although manufacturers emphasize what they view to be the uniquely advantageous features of their drug, any of the more widely used agents will usually be effective. Basing the choice of antidepressant on factors such as cost and side effects (e.g., the tendency to cause sedation or weight gain) is reasonable, though one must keep in mind that some patients will not respond to the first agent that is administered and some will be resistant to several medications. The older tricyclic antidepressants are also effective in elderly patients, as has been previously shown by some authors of the current study.[5] Although patients who take newer antidepressant drugs have fewer cardiovascular side effects and are less likely to die from an overdose than those taking older antidepressants,[3] physicians should still think carefully before switching a patient who has been doing well on a tricyclic antidepressant for years to a newer agent.

Two of the four treatments in the study by Reynolds et al. included psychotherapy. Psychotherapy alone was less effective at preventing the recurrence of depression than was therapy involving antidepressant medication, but a benefit from psychotherapy for elderly patients with depression has been noted in another study.[5] The efficacy of psychotherapy is probably of less interest to most physicians than is the efficacy of other nonpharmacologic strategies. Evidence suggests that exercise and increased social and physical activities are reasonable first approaches to treating mild-to-moderate depression.[6,7] These approaches may be particularly useful in patients who have a specific precipitating event, such as the death of a spouse, or in patients who are averse to taking medications. Active follow-up is important, as is encouragement to accept antidepressant therapy if the nonpharmacologic measures prove ineffective.

Electroconvulsive therapy is another option for severely depressed patients. It is well tolerated in older patients[8] and can result in dramatic improvement, but its negative portrayal in movies and the

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opposition to it by critics such as scientologists have led some patients and their families to resist it.

A misstep that physicians may take with regard to depression late in life is to view it as an inevitable consequence of a particular coexisting illness or, even worse, as a normal part of the aging process. It is not uncommon to hear physicians and nonphysicians alike say that if they had cancer (or heart disease, emphysema, or what have you), they would be depressed, too. Many patients with such illnesses are indeed depressed,[9] but most are not. Dismissing depression as inevitable denies the patient a fair chance of recovery from an illness that not only is potentially disabling but also increases the risk of death. The available evidence suggests that advancing age does not diminish the potential for a response to antidepressant medication.

Treatment for depression is effective,[10] and the disease burden depression causes is well documented. But despite this evidence, depression usually goes undetected; even when it is detected, it usually goes untreated; and, as we are learning from the work by Reynolds et al. and others, even when it is treated, it is probably not treated for long enough.

On the basis of the findings of Reynolds et al., it is premature to recommend lifelong antidepressant therapy after a single episode of depression late in life. However, except in patients with irreversible cognitive impairment so severe that the diagnosis of depression is moot, it is not premature to recommend lifelong follow-up. In my judgment, it is better to view an older person who has fully recovered from depression as a patient who is in remission, rather than as a patient who has been cured. Periodic reevaluation is just as important for an elderly patient who has recovered from depression as it is for a patient who has recovered from cancer.

The song that Bogart's character Rick asked Sam to play was, of course, "As Time Goes By." Time has taught us to have a healthy respect for the damage that depression causes and for the potential of depression to recur. Over time, too, comes the knowledge of how to prevent such recurrence.

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The Promise of Single-Embryo Transfer

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Worldwide, the use of assisted reproductive technology is increasing.[1-3] The technology, which includes such treatments for infertility as in vitro fertilization, accounts for 2 to 3 percent of births in many European countries[1] and approximately 1 percent of U.S. births overall, with higher proportions for states, such as Massachusetts, that mandate insurance coverage for the procedures.[2]

Enthusiasm for assisted reproductive technology, however, is tempered by concern about adverse sequelae among the children conceived with the use of these techniques, in particular those associated with multiple births. In the United States, because two or more embryos have been routinely transferred in such procedures, 35 percent of live-birth deliveries resulting from assist-

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