

Words to the wise: 4 secrets of successful pharmacotherapy

Put to good use the placebo effect, conditioned responses, and the power of suggestion

Any medication's therapeutic success depends on the interaction between its specific biochemical effects and nonspecific factors.¹ Thus, clinical trial designers may view the placebo effect as undesirable, but it can be a valuable response that improves treatment outcomes in clinical practice. As Freud stated, "Expectation colored by hope and faith is an effective force with which we have to reckon ... in all our attempts at treatment and cure."²

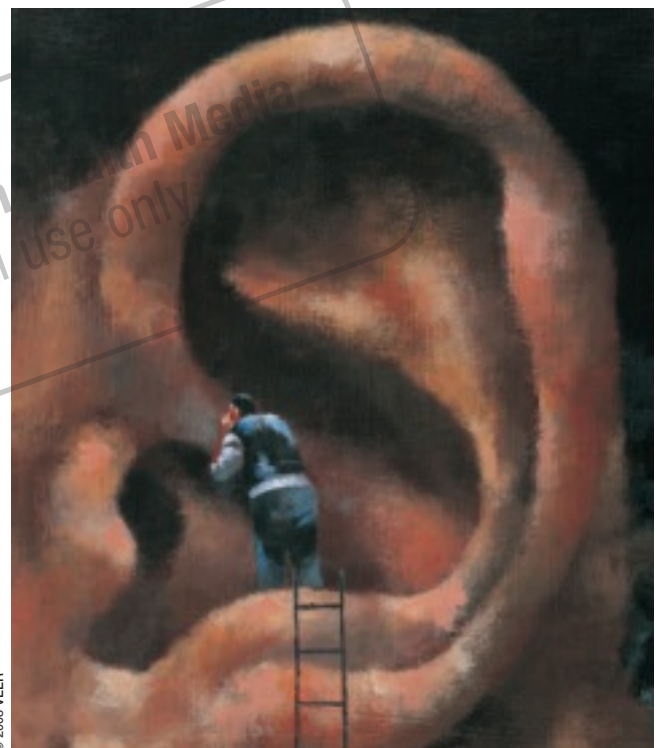
This article describes how experienced clinicians make use of the placebo effect and 3 other powerful, nonspecific elements of successful pharmacotherapy.

The placebo effect

The placebo effect is any effect attributable to a pill or potion that does not originate from its specific pharmacologic properties.³ Its clinical value has been trivialized, in part because of misconceptions (*Table 1, page 20*). For example, the placebo effect is commonly believed to be short-lived, whereas in fact it can last a long time.⁴

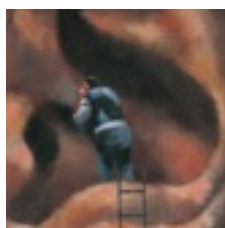
In clinical practice, our goal is to enhance the placebo effect to maximize a desirable therapeutic outcome (*Table 2, page 20*).⁵ Therefore, before I prescribe a medication, I tell my patient that I have selected a particular medication because I have had good results with it in many other patients and I believe it will work well for him or her, too.

Too often, doctors feel pessimistic about a medication's potential therapeutic result and communicate this pessimism. What the patient hears is, "There's



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Clinical Point

Experienced clinicians understand the placebo effect's power and harness it to benefit their patients

Table 1

Correcting misconceptions about the placebo effect

Misconception	What the evidence shows
Placebo effects are short-lived	The placebo effect has been documented to last for a long time
Only complaints that are psychologically originated respond to placebo	Changes after placebo have been documented for most symptoms, including those originating from somatic diseases
Placebo responders are distinctly different from nonresponders	There is no difference between placebo responders and nonresponders
The placebo effect is only about one-third of the total therapeutic effect	The placebo effect can be up to 100% of the total therapeutic effect
Only about one-third of the population responds to placebo	The placebo response is context-dependent and may include >90% of the patient population

Source: Reference 4

Table 2

Clinical strategies to enhance the placebo effect

<ul style="list-style-type: none"> • Develop a sustained therapeutic partnership with the patient
<ul style="list-style-type: none"> • Listen effectively and verify that the patient feels listened to
<ul style="list-style-type: none"> • Provide comprehensible explanations of health problems therapeutically tailored for each patient's needs and personality style
<ul style="list-style-type: none"> • Show empathy, care, and concern for the patient as a person
<ul style="list-style-type: none"> • Enhance patients' sense of control and mastery over their predicament

Source: Reference 5

nothing else I can do for you; why not try this medication, even though I don't believe it's going to work." This may create a negative placebo effect⁶—termed the "nocebo" effect—which gives the patient a negative expectation about the treatment's outcome. The patient internalizes the doctor's words and lives out this negative expectation.

CASE REPORT

Predicting positive results

Mr. B, age 42, has a history of recurrent depression associated with severe insomnia, poor appetite, significant weight loss, and psychosocial withdrawal with feelings of hopelessness. After I take a detailed history and do a mental status examination, I sug-

gest that he be treated with cognitive-behavioral therapy (CBT) and mirtazapine.

I tell Mr. B this antidepressant has excellent potential to help him recover from depression. I also inform him that improved sleep and appetite may be the first effects he experiences. I give Mr. B an appointment for 1 week later, and when he comes in he reports improved sleep and appetite, as expected.

Even though studies of antidepressants rarely show mood improvements within the first 7 days, it is not unusual to hear patients report feeling less depressed within days after they start a new antidepressant. Although the drug's specific chemical effects on the brain may not be sufficient to explain this phenomenon, the explanation probably lies in nonspecific effects—such as the patient expecting that this medication will make him feel better.

The placebo effect can occur as soon as a patient starts a medication. Experienced clinicians understand the placebo effect's power and harness it to benefit their patients.

Conditioned responses

Many biological responses can be associated with visual, auditory, tactile, olfactory, or gustatory stimuli. Nonconditioned physiologic responses paired with conditioned stimuli induce the same biological effects of a drug. Evidence supporting this

phenomenon includes successful conditioning of the immune system.⁷⁻¹⁰ Conditioned responses—as demonstrated in glycemia regulation¹⁰ and with psychopharmacology¹¹—also can enhance the desirable results of pharmacotherapy.

CASE REPORT

A soothing drink

Ms. L, a 22-year-old college student, suffers from obsessive-compulsive disorder associated with anxiety and depression. She arrives at the appointment hurried and worried that she might be late. She is short of breath and looks stressed. The nurse offers Ms. L a cup of tea or water. She chooses a glass of water and is asked to bring it into her session.

Following a comprehensive interview and mental status examination, I recommend CBT plus medication. Considering Ms. L's medication history, we agree to start treatment with sertraline. We review its potential benefits and expectations that it will reduce her anxiety, alleviate her ruminating obsessive worries, and improve her mood. I give her a 50-mg sample and inform her that some patients experience positive effects soon after taking the medication. I then ask her to take the first pill, using her glass of water. She does so and thanks me for being attentive to her needs.

I instruct her to call within 1 week and report on her condition, even if she feels better. Seven days later she reports that she is feeling better and is looking forward to her next appointment. She reports no side effects.

Often patients come to my office feeling thirsty. My staff or I offer them a glass of water or a cup of tea. As patients sip from the cup, they swallow and incorporate the liquid into their bodies. At the same time, I use verbal interventions to make them feel listened to and understood. They internalize this emotional experience in connection with swallowing the liquid.

Later, when swallowing the new medication as instructed, the patient re-experiences the positive therapeutic effect that was internalized in the doctor's office.

The power of suggestion

The power of suggestion has been shown to positively or negatively affect treatment outcomes.^{12,13} In practice, most clinicians give unintentional suggestions by how and what they communicate to the patient.

We make predictions about the patient's disease in terms of progress, severity of symptoms, and expected treatment outcomes, including possible side effects. The patient consciously and subconsciously internalizes these predictions, and then exhibits the outcome predicted by the medical expert. This is compatible with Watzlawick's principle¹⁴ that the prediction of an event may lead to events fulfilling the prediction. In clinical practice, be aware of the power in your words and body language and learn to use them wisely to enhance the positive outcome of pharmacotherapy.

continued

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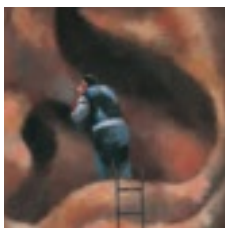
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Reframing a side effect as a sign that recovery has begun sets up a road map of expectations, with more positive changes to come

Box

Using suggestion to reframe initial side effects as positive signs

Ms. M, age 32 and single, has an anxiety disorder associated with bipolar depression. She has discontinued several psychotropics because of uncomfortable side effects, such as constipation.

After taking a detailed history, I decide to prescribe quetiapine. I tell Ms. M about this medication's potential benefits and side effects. One common side effect is dry mouth, which often occurs before patients experience therapeutic effects.

I inform Ms. M that a dry mouth will be her sign that the medication has begun to work, and beneficial effects—such as improved sleep, reduced anxiety, and improved mood—will soon follow. I then instruct her to call my office and report when she experiences a dry mouth.

Discussion. In pharmacotherapy, side effects may appear before patients experience a medication's beneficial/therapeutic effects. Patients' initial experience often determines whether or not they will continue taking a prescribed medication. I know Ms. M may stop taking quetiapine—as she has done with other medications—if she initially has uncomfortable side effects.

Instructing patients to expect a specific side effect (such as a dry mouth with quetiapine) and associating it with a future therapeutic benefit sets up a road map of expectations. They know their experience is compatible with the doctor's predictions. For Ms. M, I reframed the side effect as a positive sign that recovery has begun, with more positive changes to come.

CASE REPORT

Predicting improvement

Mrs. J, age 48, has had dysthymic disorder and fibromyalgia for many years. She describes how various specialists have tried to alleviate her depression and chronic pain. Follow-up questions reveal that whenever she received a new prescription the physician would alert her to all the possible side effects and instruct her to call the office if she developed a problem with the new medication.

Invariably, Mrs. J would call as instructed and describe side effects she developed with the new medication. Often the doctor would discontinue the medication, depriving Mrs. J of benefits she might have derived later.

My approach is different. Although I answer all her questions about potential side effects, I also emphasize this prescription's potential benefits such as improved sleep, appetite, thoughts, and mood. I tell her she may experience improved sleep before improved mood. I then make the following request: "Mrs. J, will you please promise to call me by Tuesday next week even if you begin to feel better?"

When Mrs. J calls to report on her status, she mentions that she is sleeping better and has begun to feel better during the day. She says that her husband told her she has started to smile again.

This vignette illustrates the importance of suggesting to the patient a positive outcome of pharmacotherapy associated with a particular action (calling the doctor's office to report results). When the patient promised to call, she internalized the suggestion that calling would be associated with feeling better—and that is what happened. This intervention contrasts with saying to the patient, "Call me if you have a problem with any of these side effects," which gives the patient a suggestion to call and report a problem.

The suggestion effect also can be used to reframe a predictable side effect as a positive sign that indicates the beginning of change leading to recovery (*Box*).

Participatory pharmacotherapy

Many patients seek ownership in making decisions about their treatment and medications. In participatory pharmacotherapy, patients provide you with data and valuable information—such as family history, personal medical history, and experience with treatment—and inform you about which medications worked best and which did not work. You invite patients to predict how they see themselves getting better and into recovery.

Table 3

Choosing patients for participatory pharmacotherapy

Good candidates

Adults
No history of alcoholism or drug addiction
Average and above intelligence
Intact cognitive function
Not psychotic
Good comprehension of diagnosis and treatment
Therapeutic alliance is present
Personality style or disorder with a need to be in control of treatment, such as obsessive-compulsive personality

Exclusionary qualities

Children, adolescents, and prison inmates
Alcohol dependence or drug addiction
Below-average intelligence
Cognitive deficits, such as dementia
Actively psychotic
Poor comprehension of diagnosis and treatment
Therapeutic alliance is absent
Passive, dependent personality style or disorder; these patients may view a participatory approach as the doctor's lack of confidence

Based on this information and your knowledge, training, and experience, you and the patient create a treatment plan that includes pharmacotherapy tailored to the patient's specific needs. The following case illustrates the use of par-

ticipatory pharmacotherapy to enhance treatment.

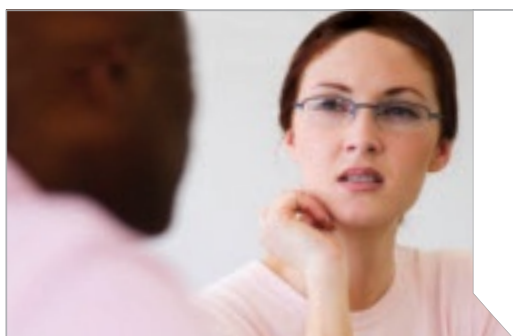
CASE REPORT

All in the family

Mr. A, age 28 and single, has been diagnosed

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Whenever possible, choose medications the patient associates with a positive experience, based on family and personal history



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Not all patients are candidates for participatory pharmacotherapy, but many respond well to it

Related Resources

• Brody H. *The placebo response: how you can release the body's inner pharmacy for better health*. New York, NY: HarperCollins Publishers; 2000.

• Spiro H. *The power of hope: a doctor's perspective*. New Haven, CT: Yale University Press; 1998.

• Ernst E. Placebo: new insights into an old enigma. *Drug Discov Today* 2007;12:413-8.

Drug Brand Names

Lithium • Eskalith, Lithobid Quetiapine • Seroquel
Mirtazapine • Remeron Sertraline • Zoloft

Disclosure

Dr. Torem reports no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

with a bipolar mood disorder. As part of a detailed family history, he reports that his maternal grandfather, mother, and a maternal uncle were diagnosed with mood swings and were successfully treated with medications, specifically lithium. He states that he believes he has the same condition.

I compliment Mr. A for being so well informed about his grandfather and uncle and educate him about mood stabilizers' benefits in bipolar disorder. I tell him about the finding that if lithium has helped his relatives, it will probably help him as well.

I also reassure Mr. A that, in deciding what medications to avoid and what medications to use, I will consider his experience with specific antidepressants that did not help him. He thanks me for considering his suggestion about what medication to use for him.

Inviting patients to be partners in diagnosing their illnesses and formulating treatment plans improves the likelihood of:

- a successful therapeutic alliance
- adherence with prescribed medications

Bottom Line

Nonspecific ingredients of treatment—such as placebo effects, conditioning effects, and suggestion effects—can improve pharmacotherapy results. When prescribing medications, consider utilizing these effects by conveying hope, optimism, and realistic confidence in a desirable therapeutic outcome. The result is often greater therapeutic effectiveness with fewer side effects.

- the best possible outcome with pharmacotherapy.

Not all patients are candidates for participatory pharmacotherapy (*Table 3, page 23*), but many respond well to it. One key is to avoid medications the patient has experienced as unhelpful, ineffective, or associated with side effects. Whenever possible, choose medications the patient associates with a positive experience or expectation, based on family and personal history.

In patients with a defiant-oppositional personality, consider framing the treatment decision as a choice between 2 equally efficacious medications. This gives the patient the sense of control in choosing his or her own medication, which is jointly monitored.

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