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Medication Enhancement

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Synopsis

In every double blind clinical study of therapies, a certain percentage of subjects obtain the same benefit from a placebo, as with the real drug. Using today's advanced brain imaging; we can identify the specific centers that supply the healing effect when it is a placebo [1]. To augment therapy, reduce the amount of drug use and speed time of healing, I suggest we utilize the known principles of placebo physiology.

Medication Enhancement

Today the internet is filled with pleas to reduce medical costs, and develop better means to fight resistant organisms. It would be beneficial to find a way to reduce costs and increase the effectiveness of therapies. We need to increase the actual effectiveness of therapies. How? One suggestion: by applying what we know about Placebo Effect. Placebo effect should enhance almost any therapy and lead to fewer antibiotics and days off work.

Considerable research has been done studying placebo effect. Some 200,000 listings come up with PubMed for Placebo. Today, with the use of brain imaging, the actual changes that take place in the Central Nervous System can be imaged and actually recorded [2].

What We Know

In the best double blind scientific tests, a percentage of placebo patients get the same result as the real pill. This can be 5% or even a much higher percentage. How did the placebo stop the pain and produce chemistry for pain relief? Actually, fMRI demonstrates the changes in the Central Nervous System when placebo effect is active [3].

We know that relaxation makes any condition better and anxiety/stress makes any condition worse. This may explain why the pain stopped when the patient was brought into the ER and the nurse gave her a shot-the pain stopped before the injection had a chance to work. She relaxed, being in the hospital, and this reduced her pain. Another example, a patient comes to emergency room for an extremely rapid pulse. As the tests are being run, his/her pulse returns to normal before he/she has received any medication or therapy [4].

All these examples may also explain, why in a study at the Montefiore Headache Clinic, irrespective of what drug was being used, headache relief was better when the patient was seen every two weeks, and not as effective when the patient was seen every month [5].

But relaxation doesn't explain why the chronic pain patient, who is already in the hospital, after three pain injections, will continue to have complete relief from the fourth injection of plain saline. Nor does stress reduction alone explain why, when the effective medication is suddenly changed from a red pill to a white pill, it no longer works. The evidence is clear: when stress/anxiety is reduced, placebo effect can take place and aid in healing [6]. In order to apply what we know about placebo effect, I recommend these principles be applied. I call this Medication Enhancement.

Knowing What the Pill Does

In the double-blind studies, the patient gets a detailed explanation of what the pill does, how it works, what the mechanism of action is for the drug. Even if the explanation is complex, the patient still understands that the antibiotic kills bacteria, or blocks the renin angiotensin factor for hypertension. When the patient takes the pill 3x a day with a full glass of water before meals, the brain is given a course to follow. The actions of following the program as directed combines with lowered stress/anxiety, allows the full healing power of the body. When specific actions to follow are given, placebo effect may be more effective [7].

Further Proof

A patient receiving intravenous pain therapy

If the medication is given without oral cues, the IV pain medication works. When administered with strong oral cues, the actual medication is far more effective. When the "same" medication is given IV with oral cues, but it is a placebo, this often works effectively.

Example: Patient receives their intravenous pain medication at 10 PM, aiding their sleep. It is effective, enhanced by bringing in a tray set, the nurse carefully measuring the amount from a vial and then taking 2 minutes to administer the intravenous medication. On the fourth dose, a placebo, patient gets exactly the same effect. On the fifth dose, not as effective. On the sixth dose, may not be effective at all.

In many specialty groups, there may be one particular doctor whose patients seem to heal faster, use less pain medication, and are preferred by patients. This is despite the fact that all members of the specialty group are known to be of equal skill, knowledge, and ability. Indeed, most physicians refer themselves or their families to Dr. Jones, rather than to Dr. Goodfellow, the "kind, considerate, caring" one. Why Dr. Goodfellow's patients require less pain medication, and why patients prefer him? Probably because he automatically uses what I refer to as Medication Enhancement.

As doctors, we have read many reports, where Dr. Smith published an 80% cure with the drug, but when other doctors used the same drug, the results were different. The question is raised, "Did Dr. Smith fake his results?" However, there should be a consideration that perhaps Dr. Smith was unconsciously using Medication Enhancement, which explains his higher success rate.

Researchers are aware of possible bias when doctors report on "their" invention/therapy, affecting the patient's course. The enthusiastic doctor may unconsciously be giving clearer directions, getting their patient relaxed, and using patient oriented illustrations to clarify how the medication/therapy works.

Mechanism

The placebo effect is a learned response, whereby various types of cues (verbal, conditioned, and social) trigger expectancies that generate placebo effects via the central nervous system [8]. Using fMRI, the right mid frontal gyrus has been shown to be active in the placebo effect response.

In 2016, a study carried out at Northwestern University in Chicago used an MRI scanner to observe in real time how the brain of patients res-

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ponded to a placebo - in this case, a sugar pill instead of a painkiller. They found that an area within the mid frontal gyrus lit up or, in their own words, "showed a higher functional connectivity" in patients who res-ponded to the placebo, compared with non-responders. The study con-cluded that this brain region seemed to be quite separate from another region of the brain known to be involved in responding to the effects of real pain-killing drugs [9].

Studies using fMRI have shown reduced signals in pain-relevant regions during placebo analgesia, including reductions in insula, primay (S1), secondary (S2) somatosensory cortices, anterior cingulate cortex (ACC), amygdala, and basal ganglia. Further, a recent meta-analysis of fMRI studies on placebo analgesia identified the insula, dorsal ACC, thalamus, amygdala and right lateral prefrontal cortex as consistently less activated during placebo analgesia [10].

Application of Medication Enhancement

On the one hand, do you want to increase placebo effect when you are trying to evaluate a new drug for therapy? When trying to evaluate a new anti-histamine, I am careful to reduce placebo effect, because it might distort the new drug's value to the patient. Once I am familiar enough with the drug, then it is good medicine to use medication enhancement to speed healing and perhaps reduce the dose.

One of our peers is an oncologist. He is totally useless for evaluating new therapies: no matter what he is administering, his patients feel better. However, in daily practice, we feel it is an advantage to engage the entire central nervous system to aid in the therapy. In evaluating the results of double blind studies, the added or subtracted factor of placebo effect needs to be recognized and accounted for.

Anxiety/Stress

Anxiety/stress can make any condition, trauma, and infection worse. Studies have shown reduced complications post-operative when attention is paid to reducing anxiety/stress before surgery. In one study, for a routine series of a standard orthopedic procedure, patients were administered The Minnesota Multiphasic Personality Inventory (MMPI) test. The psychologists reported a significant predictability of which patients would have a surgical complication, as shown by stress and similar behaviors. The MMPI was more accurate in predicting surgical complications than the surgeon [11].

Most otolaryngologists have learned to identify "stressed" patients who come for cosmetic surgery and have refused to perform cosmetic procedures on them. Patient mental stability also prevents medical complications and possible lawsuits. Thus, for any therapy, many patients benefit by instructions that lower stress chemical output. These include:

- **Counted Breathing.** Count inhale 1-4, exhale 1-6. Do this hourly for one minute. When exhalation is longer than inhalation, the amygdala is signaled–there is no tiger. Counting reduces activity from the frontal lobe.
- **Increase exposure to humor.** Some hospitals now have two comedy channels in patient's room.
- **Do you have any questions?** The more staff that ask this, the more relaxed a patient will become with the feeling that this "office" cares about them.
- **Do daily yoga, walking, or deep breathing.** The doctor's personal experience and preference are important in selecting a relaxation technique.

How does the Pill Work?

It is not necessary that the patient understand the biochemistry or pharmacology details of each drug. However, the more insight they have into what the pill does, how it works i.e., this pill opens clogged small arteries for better circulation - or this pill prevents clogged blood vessels leading to blood clots - the better the patient can bring their central nervous system to aid in the healing. Actions of making sketches or writing the instructions, of keeping a diary also help to involve the central nervous system. Keeping a diary is a keystone of many therapies and may be a means of engaging the whole person in the therapy.

The pill/therapy mechanism does not need to be complex, and should be directed to the patient's own background and interest. It may be sufficient to explain, "This pill kills bacteria, making them so sick, that they die off." Then the patient may visualize that the good knights are fighting the bad knights.

Visualization

A significant aid to engaging the central nervous system is to visualize the pill/treatment being effective. The more relaxed, the more senses that can be included, the more effective the placebo effect. "The nasal spray opens the nose, I can feel the air coming through, I can appreciate the increased sense of smell and even taste, now that my nose is wide open". When the patient visualizes the pill/therapy working, fMRI shows that certain areas of the brain light up [12].

Follow the Instructions

"Take one pill before each meal with a full glass of water." Where placebo showed a high cure rate, those patients were shown to have strictly followed the actions prescribes by the doctor. Every orthopedist deals with the same identical shoulder problem but with different patient types such as Jack and Robert:

Jack returns and says that the pill worked to relieve his shoulder pain. Robert states that the pill didn't work.

Doctor: *"Did you take the pill with a full glass of water?"*
Robert: *"No, I usually wasn't near water, and I missed a few doses."*
Doctor: *"Did you do the stretching and heat application that I recommended?"*
Robert: *"Well, we had company and I really didn't have the time..."*

Even when the scientific evidence is clear that the therapy is effective, not following the pattern set out by the doctor, may impair the value of the medication, by failing to involve the central nervous system [13]. In the best scientific double-blind studies, how many subjects failed to follow the instructions, skipped pills, didn't add the water, and reported poor results with the real pill? There may be medications that do require input from the central nervous system. Remember, the patient stated that the pill didn't work, when it was a white pill instead of a red one.

Reward for Success

In the placebo studies, when the patients were offered a reward for the success of achieving pain relief, or other placebo effect therapy, the placebo effect was enhanced.

This can be,

"When you come home from having your tonsils out, you will have ice cream and popsicles."

"After you are cleared up by taking the pills, you can relax at the beach"

"The package insert says it takes two weeks. I'll bet with your visualization, you will feel better much faster."

When the patient knows that when she finishes her therapy, she will finally get that trip to Italy she has longed for all her life, the body's healing mechanism adds to the healing. Every practitioner has a case report that the mother was expected to expire in February. Yet, by some miracle, she lived until the birth of her first grandchild in July. If you read the psychiatry literature, you find dozens of case reports where the psychiatric therapy cured the patient's asthma! Was the mechanism simply reducing the patient's stress level? [14].

Summary

It is Good Medicine to get a patient well as quickly as possible, with as little medication as possible. Through Medication Enhancement, the principles of Placebo Effect, can be added to aid in the healing.
These include:

- Stress reduction
- Enhanced understanding of the medication/therapy
- Visualization or guided visualization
- Recommend a set of actions
- Reward for success

Actually, this is treating the Patient as a Whole.

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