

A Review of Delusions of Parasitosis, Part 2: Treatment Options

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GOAL

To understand delusions of parasitosis (DOP) to better manage patients with the condition

LEARNING OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Propose a management strategy to patients with DOP.
2. Apply strategies for discussing diagnosis and treatment with patients with DOP.
3. Evaluate potential side effects when determining the course of treatment for patients with DOP.

CME Test on page 265.

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Delusions of parasitosis (DOP), a psychiatric disorder in which patients erroneously insist that they are infested with parasites, remains a treatment problem for dermatologists. Generally, these patients are resistant to psychiatric referral and treatment

with psychotropic medications. We discuss treatment options and management recommendations. Pimozide, along with judicious patient communication, remains the treatment of choice for DOP.

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Delusions of parasitosis (DOP) is a disorder in which patients erroneously insist that they are infested with parasites. These patients have an unshakable belief that their problems are medical. They rarely present to a psychiatrist and are almost always resistant to psychiatric referral. Thus, this disorder proves to be difficult to treat.

The classic patient with DOP is a middle-aged woman frustrated by unsuccessful attempts to discover

the cause of her ailment that has been affecting her for months or years.¹ She may complain of a crawling, biting, burrowing sensation (formication) on or under her skin. She may claim her symptoms originate from insects or other creatures that infest her, her home, or her work. She may actually see the crawling culprits and be able to describe them in detail. This delusion may impinge on her activities of daily living, but she is otherwise a functional well-adjusted person. Oftentimes she will bring in proof of infestation that, under close examination, are pieces of lint or other nonparasitic materials.¹

Despite thorough examination and reassurance, the patient relentlessly believes she is infested. She will most likely refuse referral to a psychiatrist, the one clinician with the most experience treating delusional disorders. Thus, it is important for the general practitioner and other nonpsychiatric clinicians to be familiar with DOP and its management.

Medical Management

Medical or psychiatric treatment aimed at eliminating the delusion should be attempted only after rapport with the patient has been established. Koo and Pham² stated: "The greatest challenge in the treatment of delusional patients is in obtaining their agreement to start treatment with an antipsychotic medication."

Numerous case reports have been published in which the clinician was unable to successfully treat DOP because of a lack of patient confidence.³⁻⁵ We modified a suggested management strategy first described by Gould and Gragg⁶ and incorporated strategies from a lecture on promoting a trusting relationship with delusional patients presented by Koo⁷ at the University of Southern California Dermatology Grand Rounds to create the following management strategy for clinicians:

1. Listen to the patient's story. Give the patient a few minutes to narrate and then proceed with a battery of direct questions. Do not dwell on the patient's psychiatric history, which will encourage trust and allow you to control the dialogue.
2. Thoroughly examine the patient's skin and any evidence of infestation that they bring. This task may seem dishonest when you are convinced the patient is delusional; however, it is possible there is a true infestation. Even if he/she is not infested, developing a bond with the patient will allow you to suggest treatments that the patient may otherwise not accept.²
3. Perform a biopsy if the patient insists, which will show that you genuinely care about his/her problem. Allow the patient to pick

the skin area he/she believes is the most involved, but insist that if the biopsy is negative, he/she should entertain the possibility that the ailment may not be due to a living organism.

4. Show concern for how the condition has affected the patient's life. This technique has been shown to have a positive effect on the establishment of a good physician-patient relationship. Furthermore, it can help you individualize a therapeutic strategy for the patient in a way that does not reinforce the delusion. For example, you may say, "We will work diligently to relieve the stress this problem has caused you."
5. Be empathetic, not sympathetic. Let the patient know that you understand how the condition has left him/her feeling isolated.

Be aware that rapport with the patient will not always develop immediately. It may take a few visits before the patient is comfortable enough to accept treatment suggestions.

Clinicians are most concerned with discussions with the patient relating to the diagnosis and treatment. Most patients will not accept a psychiatric diagnosis for a condition that they are sure is somatic. The following statements made by clinicians have been used with success:

- "You have a very difficult problem, but I will study the specimens you have brought and will try to help you in any way that I can."⁶
- "I did not find any parasites today, but I am willing to examine any evidence that you bring me in the future."²
- "I noticed that you have been suffering with this problem and this is really bothering you day and night. Maybe I can offer you a medication that can help relieve some of this distress."²
- "This medication has been known to help others with the same problem."⁸
- "I would like to refer you to a specialist for this disorder."⁹ (The patient is not immediately told that the specialist is a psychiatrist, but this fact is not denied if asked.)
- "You may very well have had an infestation initially that was adequately treated, and the only sign now is the residual sensation you feel in your skin. Given the experience you have had, I can understand how you feel that parasites are still there. This is a situation that I have seen before, and the medication that I am going to prescribe is usually very helpful in getting rid of this last remaining discomfort."¹⁰

Treating the patient's anxiety should be seriously considered.⁶ Benzodiazepines such as diazepam and alprazolam are commonly used for short-term treatment of anxiety. These medications are fast acting and can be withdrawn after a few weeks. Consultation with a psychiatrist can be helpful for clinicians who are not familiar or comfortable with these drugs.

Treating the symptomatic itching or burning sensation experienced by many patients also should be considered. Crotamiton cream is useful for pruritus and possibly eradicates some organisms. Topical or intramuscular corticosteroids may be useful to alleviate the itching sensation. Additionally, an antihistamine can be useful. Over-the-counter anti-itch medications also can be used.

Treating the Delusion

Until the 1950s, DOP was considered a nontreatable disease. In 1946, Wilson and Miller¹¹ reported that beyond treating the patient for syphilis, if indicated, "there is nothing whatsoever the dermatologist can do for such a patient." While viable treatment options are now available, management remains a challenge for clinicians, especially non-psychiatrists. A meta-analysis of 1223 case reports of DOP showed marked improvement in full remission rates from the prepsychopharmacologic era (before 1960) to the postpsychopharmacologic era (after 1960) (33.9% to 51.9%, respectively).¹²

Most cases of DOP need to be treated. There have been few reported cases of spontaneous remission of DOP.^{13,14} Most experts will agree that referral to a psychiatrist is beneficial. It is debatable if psychiatrists are the only clinicians equipped to handle these patients or if dermatologists may and should prescribe pimozide.^{15,16} Koblenzer¹⁷ stated: "If not treated by the dermatologist, [patients with DOP are] doomed to a prolonged, expensive, and frenetic search from doctor to doctor, to exterminator, to entomologist, and so on, without relief."

Regardless of the medication used, the clinician must proceed with caution when suggesting treatment to patients with DOP. Commonly, when a clinician suggests psychiatric referral or medication, the patient responds angrily and does not return.^{5,18} Patients can become a danger to themselves and others. One man set fire to one of his apartments and flooded another¹⁹; other patients have committed suicide.^{13,20} It is important to note the extreme desperation in which these patients often find themselves. Many patients have tried relentlessly to find a treatment for their supposed infestation and often have found their clinician to be more of a hindrance than a help. One such case resulted in an attempt on the life of a family physician.²¹

Pimozide

Pimozide is approved by the US Food and Drug Administration for Tourette syndrome. It was first used in 1975 to treat somatic delusions, as reported in 5 patients.²² Since then, this neuroleptic agent has been considered the treatment of choice for DOP.

Pimozide is a highly selective dopamine D₂ blocker; thus, it is effective in treating psychoses. Pimozide also has some serotonin receptor blocking activity, which is theorized to contribute to its therapeutic effects. Other neurologic effects include blockade of α -adrenergic receptor sites, voltage-gated calcium channels, and opiate receptors. Pimozide has approximately 50% oral bioavailability and its action lasts 24 to 48 hours, allowing for once-daily dosing. It is metabolized in the liver and primarily excreted in the urine.²³

The most common side effects of pimozide are extrapyramidal symptoms, including pseudoparkinsonism, akathisia, and dystonia. Pseudoparkinsonism may manifest as muscle and joint stiffness, while akathisia is indicated by restlessness. These effects have been demonstrated in patients treated with a pimozide dosage as low as 2 mg daily.²⁴ Symptoms can be controlled by anticholinergic medications, such as oral benztropine mesylate 1 to 4 mg once or twice daily, as needed, or diphenhydramine hydrochloride 25 mg 4 times daily, as needed. Benztropine mesylate is preferred versus diphenhydramine hydrochloride because it is not sedating. An acute dystonic reaction (ie, muscle spasm) rarely occurs because of the low dose of neuroleptic prescribed; however, the acute reaction also responds to anticholinergic agents.¹⁶ To minimize the risk for side effects, initially prescribe pimozide 1 mg daily, titrating up by 1 mg every 5 to 7 days (maximum, 10 mg daily), as needed. Koo and Lee²⁵ recommend using the lowest effective dose of pimozide for the shortest possible duration.

Pimozide at high doses has cardiotoxic properties manifested by long QT intervals and arrhythmias. Pretreatment and posttreatment electrocardiograms are recommended for all patients receiving pimozide.²⁶ Discontinue increasing the dose when the QT interval is more than 0.52 seconds in adults or when there is a QT interval increase of 25% or more above the patient's baseline.²⁷ Furthermore, coadministration of other drugs that increase the QT interval should be avoided, including but not limited to chlorpromazine, gatifloxacin, mefloquine, moxifloxacin hydrochloride, other class Ia and III antiarrhythmic agents, quinidine, tacrolimus, thioridazine hydrochloride, and ziprasidone hydrochloride or mesylate.²⁸

Pimozide is the most studied and reported drug used for DOP. Most data on pimozide have come from individual or group case reports, though

2 double-blind placebo-controlled trials have been conducted. Of the 189 patients reported to be treated with pimozide in 22 articles, 79% reported a positive response to pimozide, 17% reported no response, and the rest were lost to follow-up.^{8,13,24,26,29-46}

Side effects reported with pimozide included insomnia, drowsiness, and depression.^{34,41} Extrapyramidal symptoms such as pseudoparkinsonism and akathisia were not uncommon but generally were easily controlled with anticholinergic agents.^{13,24,26,34,35,38,40,41,45} Two cases of lethargy were reported with pimozide doses of up to 6 to 24 mg daily.⁴¹ An acute dystonic reaction occurred in a patient receiving 8 mg daily.⁴⁰

The mean dosage of pimozide used for best effect was 5 mg daily, as per the case series for which this information was available.^{8,13,24,26,29-46} Both single and split dosing were reported as successful methods. The median duration of treatment to best results was 3.5 weeks, with a range of 3 days to 6 months. For patients who were followed long-term (4–12 mo), 100% (n=17) maintained complete or near complete resolution of symptoms (near complete in 1 patient) while receiving maintenance doses of pimozide. Daily doses ranged from 2 to 4 mg. For patients followed long-term who eventually discontinued pimozide, 43% (34/79) had subsequent recurrence of their symptoms. Of those patients retreated with pimozide, 100% (n=20) had complete resolution of symptoms.^{8,13,24,26,29-46}

Zomer et al⁴⁶ studied 33 patients with DOP. A total of 61.1% (11/18) of patients reported improvement or full recovery with pimozide compared with the 20% (3/15) not treated. At a mean follow-up of 5 years, none of the patients who had full remission (5/33 with DOP) needed maintenance therapy.⁴⁶ Hamann and Avnstorp³⁴ conducted a double-blind, placebo-controlled, crossover trial in which participants showed a significant response to pimozide compared with placebo ($P<.05$). Ungvari and Vladar⁴⁵ found similar results in their double-blind placebo-controlled trial.

In the aforementioned lecture, Koo⁷ explained that pimozide 2 to 3 mg daily should provide a positive effect on formication, pruritus, mental fixation, and mental agitation.

Some experts insist on the necessity of maintenance therapy,^{8,41} while others believe that the patient may be weaned off of pimozide with lasting remission.^{38,47} Lindskov and Baadsgaard³⁸ followed 14 patients with DOP previously treated with pimozide. Seven patients were treated with pimozide for a median of 5 months and remained in remission for at least 19 to 44 months after treatment ended. Three patients managed their

recurrences with intermittent pimozide treatment, 3 refused repeat treatment and remained symptomatic, and the remaining patient died of unrelated causes.³⁸

As previously stated, suggesting treatment with psychiatric medication to patients who insist they have a somatic disorder is difficult. In his lecture, Koo⁷ described introducing pimozide as a medication used for 2 other conditions that the patient does not have—Tourette syndrome and schizophrenia—so that if patients go home and research pimozide on the Internet, they will not be surprised to find that it is an antipsychotic agent and they are more likely to remain compliant.

Haloperidol and Other Typical Antipsychotic Agents

Haloperidol, a conventional antipsychotic agent similar to pimozide, has been used to treat DOP. Table 1 describes the dosages, effectiveness, and follow-up of 6 case series of patients with DOP treated with haloperidol. Aside from these detailed accounts, a study conducted in India reported 2 patients successfully treated with haloperidol.⁵² One author recommended the use of haloperidol because of its efficacy as well as its availability in the United States.⁵¹ One study reported efficacy with haloperidol, but it was discontinued due to akinesia.³ However, haloperidol is not successful in all cases,^{19,53,54} and extrapyramidal side effects are common.^{4,51}

Three patients with DOP were successfully treated with thioridazine hydrochloride, which is another conventional antipsychotic agent.^{49,55} Fluspirilene also has been successful, but once again, extrapyramidal side effects limit its use.⁵⁶ In one patient, fluphenazine failed to relieve the delusion but helped with the patient's agitation.⁵⁷ Perphenazine was successful in 3 patients, resulting in 1 partial and 2 full remissions.^{3,52} Trifluoperazine hydrochloride provided partial resolution of symptoms in another 2 patients.⁶ Zuclopenthixol, when combined with the selective serotonin reuptake inhibitor (SSRI) sertraline, produced partial remission in 1 patient.⁵² As with haloperidol, all of the classic antipsychotic agents are limited by their side-effect profile.

To address the issue of medication noncompliance, Frithz⁵⁸ tested the use of depot injections of conventional antipsychotic agents. He treated 10 participants with fluphenazine decanoate (7.5–25.0 mg) and 5 participants with *cis*-flupenthixol decanoate (6–20 mg) injected intramuscularly once every 3 weeks. Overall, 11 participants were symptom free, 3 were less bothered by their “bugs,” and 1 was unchanged. When the treatment was stopped in 10 participants, 6 relapsed, 2 remained symptom free, and 2 were lost to follow-up. Extrapyramidal side effects were completely relieved by anticholinergic agents.⁵⁸

Table 1.

Effects of Haloperidol Treatment on Patients With Delusions of Parasitosis

Study (Year)	Dosage	Abnormal Sensation/Pruritus	Delusion	Follow-up
Andrews et al ⁴⁸ (1986)	5 mg nightly	Complete resolution	Partial resolution	Tapered off by 6 mo; milder delusion maintained at 8 mo
	5 mg nightly	Complete resolution	Complete resolution	2 mo free of delusions
	4–9 mg daily	N/A	No change	N/A
Freyne and Wrigley ⁴⁹ (1994)	1 mg twice daily	Complete resolution	Complete resolution	N/A
	2 mg twice daily	No change	No change	N/A
Hunt and Blacker ¹⁹ (1987)	30 mg daily	N/A	No change	N/A
Nicolato et al ⁴² (2006)	1.5 mg daily	N/A	Complete resolution	N/A
Räsänen et al ⁵⁰ (1997)	1 mg daily	N/A	Complete resolution	N/A
Shah ⁵¹ (1988)	15–45 mg daily	N/A	Partial resolution	N/A

Abbreviation: N/A, not available.

Atypical Antipsychotic Agents

Atypical antipsychotic agents, known for their better side-effect profile, have been useful in the treatment of DOP. Risperidone has been successful in many cases and touted by some experts as a possible first-line treatment of DOP (Table 2).

Treatment with olanzapine has produced mixed results.^{39,42,62} In one study, treatment with quetiapine fumarate 150 mg twice daily left a patient with continued delusions, but she was no longer bothered by them and no longer complained of the abnormal sensations.⁶¹ Another study reported decreased delusions and sensations at 4 weeks of treatment with quetiapine fumarate 800 mg daily.³⁷ In one study, there were reported benefits with sertindole; the patient was no longer bothered by the internal bugs and no longer took drastic measures to rid himself of them.⁶³ In one patient, tiapride, which is not available in the United States, was helpful, though it was not fully curative.⁵⁵ Trifluoperazine hydrochloride was unsuccessful in 4 patients.⁵⁷

Other Psychiatric Medications

Treatment with benzodiazepines^{8,40} or tricyclic antidepressants⁶⁴ have proven to be ineffective or minimally helpful in uncomplicated DOP.^{11,36,53,65} In a study of patients treated with an SSRI, only 21% (3/14) of patients had a reduction in the stress caused by the delusions.⁶⁶ Three patients with DOP with concurrent trichotillomania showed complete remission with fluoxetine hydrochloride, an SSRI.³⁰ The monoamine oxidase inhibitor tranylcypromine sulfate was proven effective in 1 patient refractory to electroconvulsive therapy, amitriptyline, chlorpromazine, and trifluoperazine hydrochloride.⁶⁷

Miscellaneous Treatments

The only mention in the literature of using placebo to treat DOP was in 1953 when McFarland⁶⁸ reported a 2-week cure with placebo. However, as evidenced in a response to McFarland's⁶⁸ report, a contemporary recommended not treating patients with DOP with anything that would validate and thus help to solidify their delusion.⁶⁹ This sentiment is echoed elsewhere in the literature.⁷⁰

Table 2.

Effects of Risperidone Treatment on Patients With Delusions of Parasitosis^a

Study (Year)	Dosage	Abnormal Sensation/Pruritus	Delusion	Follow-up
Aw et al ⁵⁵ (2004)	0.5 mg daily, 1 mg nightly	N/A	No effect	N/A
Kim et al ³⁷ (2003)	3 mg daily	No effect	Decreased; still feels bugs crawling	N/A
Kurupparachchi and Williams ⁵⁹ (2003)	Unknown	N/A	Good recovery	N/A
Le and Gonski ⁶⁰ (2003)	0.5 mg daily, 1 mg nightly	Substantial decrease	Substantial decrease	N/A
Safer et al ⁵³ (1997)	0.5 mg daily, 1 mg nightly	Substantial decrease	Substantial decrease but insight remained poor	N/A
Wenning et al ⁶¹ (2003)	5 mg nightly	N/A	Complete resolution	2 mo without relapse
	0.25–1 mg daily	N/A	Complete resolution	N/A
	0.5 mg daily, 1.5 mg nightly	N/A	Substantial decrease	N/A
Nicolato et al ⁴² (2006)	1 mg daily	N/A	Partial resolution	N/A

Abbreviation: NA, not available.

^aThe only side effect noted was akathisia by Nicolato et al.⁴²

Electroconvulsive therapy has proven ineffective in many patients with DOP.⁵⁷ One report describes the benefits of a prefrontal lobotomy in a patient with folie à deux.⁷¹

Some experts advocate psychotherapy as the sole therapy for DOP. Wilson and Miller¹¹ found that psychotherapy seemed to rid their patient of her delusions. However, on follow-up many years later, she claimed that the treatment was successful and that “the bugs have been much quieter ever since.”¹¹ There are additional studies that described patients successfully treated with psychotherapy.^{4,72,73} However, for the most part, psychotherapy has not been successful and DOP was considered impossible to treat in the prepsychopharmacologic era when psychotherapy was the only modality available.^{11,40,70} Although psychotherapy may prove ineffective as an independent or primary treatment of DOP, it may be useful as an adjunctive therapy.⁷⁴

Comment

Patients with DOP are extremely distressed by their symptoms. In one trial, most of the 14 patients treated with pimozide claimed that although it was symptomatic, “it was the most terrible experience they had ever had.”³⁸ Great efforts should be made so that patients with DOP feel comfortable, which can be accomplished by establishing a supportive and welcoming environment in which patients do not feel they will be ignored or ridiculed as they may have felt in many of their prior experiences. Furthermore, it is appropriate to treat the dermatologic complaints as well as the anxiety with which these patients present. Because of these efforts, patients are more likely to agree to the psychiatric referral and medication suggested by the clinician.

Despite an unclear etiology, treatment options are available. Although some clinicians would recommend an atypical antipsychotic agent as a first-line treatment of DOP, the authors are not yet convinced that there is enough data available to support this claim. We

recommend initially prescribing a course of pimozide, a well-studied and successful therapy. Koo and Pham² suggest giving patients both diphenhydramine hydrochloride and benztropine mesylate to carry with them and use at any sign of stiffness or restlessness. Thus, patients know what to expect and are less likely to be noncompliant at the first sign of extrapyramidal effects. If a patient cannot tolerate pimozide, either because of cardiotoxic effects or extrapyramidal symptoms, switch him/her to risperidone or another atypical antipsychotic agent with a better side-effect profile than pimozide.

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