

# Recent Developments in Psychodermatology and Psychopharmacology for Delusional Patients

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The management of delusional infestation (DI), also known as Morgellons disease or delusional parasitosis, can lead to some of the most difficult and stressful patient encounters in dermatology. As a specialty, dermatology providers are trained to respect scientific objectivity and pride themselves on their visual diagnostic acumen. Therefore, having to accommodate a patient's erroneous ideations and potentially treat a psychiatric pathology poses a challenge for many dermatology providers because it requires shifting their mindset to where the subjective reality becomes the primary issue during the visit. This disconnect may lead to strife between the patient and the provider. All of these issues may make it difficult for dermatologists to connect with DI patients with the usual courtesy and consideration given to other patients. Moreover, some dermatologists find it difficult to respect the chief concern, which often is seen as purely psychological because there may be some lingering bias where psychological concerns perhaps are not seen as bona fide or legitimate disorders.

## Is There a Biologic Basis for DI? A New Theory on the Etiology of Delusional Parasitosis

It is important to distinguish DI phenomenology into primary and secondary causes. Primary DI refers to cases where the delusion and formication occur spontaneously. In contrast, in secondary DI the delusion and other manifestations (eg, formication) happen secondarily to underlying broader diagnoses such as illicit substance abuse, primary psychiatric conditions including schizophrenia, organic brain syndrome, and vitamin B<sub>12</sub> deficiency.

It is well known that primary DI overwhelmingly occurs in older women, whereas secondary DI does not show this same predilection. It has been a big unanswered question as to why primary DI so often occurs not only in women but specifically in older women. The latest theory that has been advancing in Europe and is supported by some data, including magnetic resonance imaging of the brain, involves the dopamine transporter (DAT) system, which is important in making sure the dopamine level in the intersynaptic space is not excessive.<sup>1</sup> The DAT system is much more prominent in woman vs men and deteriorates with age due to declining estrogen levels. This age-related loss of striatal DAT is thought to be one possible etiology of DI. It has been hypothesized that decreased DAT functioning may cause an increase in extracellular striatal dopamine levels in the synapse that can lead to tactile hallucinations and delusions, which are hallmark symptoms seen in DI. Given that women experience a greater age-related DAT decline in striatal subregions than men, it is thought that primary DI mainly affects older women due to the decline of neuroprotective effects of estrogen on DAT activity with age.<sup>2</sup> Further studies should evaluate the possibility of estrogen replacement therapy for treatment of DI.

## Improving Care of Psychodermatology Patients in Clinic

There are several medications that are known to be effective for the treatment of DI, including pimozide, risperidone, aripiprazole, and olanzapine, among others. Pimozide is uniquely accepted by DI patients because it

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has no official psychiatric indication from the US Food and Drug Administration (FDA); it is only indicated in the United States for Tourette syndrome, which is a neurologic disorder. Therefore, pimozide arguably can be disregarded as a true antipsychotic agent. The fact that its chemical structure is similar to those of bona fide antipsychotic medications does not necessarily put it in this same category, as there also are antiemetic and antitussive medications (eg, prochlorperazine, promethazine) with chemical structures similar to antipsychotics, but clinicians generally do not think of these drugs as antipsychotics despite the similarities. This nuanced and admittedly somewhat arbitrary categorization is critical to patient care; in our clinic, we have found that patients who categorically refuse to consider all psychiatric medications are much more willing to try pimozide for this very reason, that this medication can uniquely be presented to the DI patient as an agent not used in psychiatry. We have found great success in treatment with pimozide, even with relatively low doses.<sup>3,4</sup>

One of the main reasons dermatologists are reluctant to prescribe antipsychotic medications or even pimozide is the concern for side effects, especially tardive dyskinesia (TD), which is thought to be irreversible and untreatable. However, after a half century of worldwide use of pimozide in dermatology, a PubMed search of English-language articles indexed for MEDLINE using the terms *pimozide and tardive dyskinesia*, *tardive dyskinesia and delusions of parasitosis*, *tardive dyskinesia and dermatology*, and *tardive dyskinesia and delusional infestation/Morgellons disease* yielded only 1 known case of TD reported in dermatologic use for DI.<sup>5</sup> In this particular case, TD-like symptoms did not appear until after pimozide had been discontinued for 1 month. Therefore, it is not clear if this case was true TD or a condition known as withdrawal dyskinesia, which mimics TD and usually is self-limiting.<sup>5</sup>

The senior author (J.K.) has been using pimozide for treatment of DI for more than 30 years and has not encountered TD or any other notable side effects. The reason for this extremely low incidence of side effects may be due to its high efficacy in treating DI; hence, only a low dose of pimozide usually is needed. At the University of California, San Francisco, Psychodermatology Clinic, pimozide typically is used to treat DI at a low dose of 3 mg or less daily, starting with 0.5 or 1 mg and slowly titrating upward until a clinically effective dose is reached. Pimozide rarely is used long-term; after the resolution of symptoms, the dose usually is continued at the clinically effective dose for a few months and then is slowly tapered off. In contrast, for a condition such as schizophrenia, an antipsychotic medication often is needed at high doses for life, resulting in higher TD occurrences being reported. Therefore, even though the newer antipsychotic agents are preferable to pimozide because of their somewhat

lower risk for TD, in actual clinical practice many, if not most, DI patients detest any suggestion of taking a medication for “crazy people.” Thus, we find that pimozide’s inherent superior acceptability among DI patients often is critical to enabling any effective treatment to occur at all due to the fact that the provider can honestly say that pimozide has no FDA psychiatric indication.

Still, one of the biggest apprehensions with initiating and continuing these medications in dermatology is fear of TD. Now, dermatologists can be made aware that if this very rare side effect occurs, there are medications approved to treat TD, even if the anti-TD therapy is administered by a neurologist. For the first time, 2 medications were approved by the FDA for treatment of TD in 2017, namely valbenazine and deutetrabenazine. These medications represent a class known as vesicular monoamine transporter type 2 inhibitors and function by ultimately reducing the amount of dopamine released from the presynaptic dopaminergic neurons. In phase 3 trials for valbenazine and deutetrabenazine, 40% (N=234) and 34% (N=222) of patients, respectively, achieved a response, which was defined as at least a 50% decrease from baseline on the abnormal involuntary movement scale dyskinesia score in 6 to 12 weeks compared to 9% and 12%, respectively, with placebo. Discontinuation because of an adverse event was seldom encountered with both medications.<sup>6</sup>

## Conclusion

The recent developments in psychodermatology with regard to DI are encouraging. The advent of new evidence and theories suggestive of an organic basis for DI could help this condition become more respected in the eyes of the dermatologist as a bona fide disorder. Moreover, the new developments and availability of medications that can treat TD can further make it easier for dermatologists to consider offering DI patients truly meaningful treatment that they desperately need. Therefore, both of these developments are welcomed for our specialty.

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