

REVIEW ARTICLE

Delusional Infestation and Chronic Pruritus: A Review

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The literature on chronic pruritus, paresthesia and delusional infestation indicates that a wide variety of conditions ranging from AIDS to vitamin deficiencies may cause these symptoms. In many, or perhaps most of these cases, activation of itch pathways seems to be the underlying cause of the skin sensations and perhaps even the visual hallucinations characteristic of delusional infestation. The principle difference between diagnoses of chronic pruritus and delusional infestation appears to lie in the patient's interpretation of the cause of the symptoms, rather than underlying physiological differences. Delusional infestation, paresthesia and chronic pruritus must be considered symptoms of underlying conditions. Key words: Ekbom's syndrome; Morgellons; delusional parasitosis; self-mutilation; drug abuse.

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Three syndromes, delusional infestation, chronic pruritus and paresthesia often involve unexplained, long-term itching. They share symptomology but differ widely in diagnoses and treatments. Delusional infestation, delusional parasitosis, Morgellon's or Ekbom's syndrome are all names for a disorder where sufferers feel itching, crawling and pinching sensations (paresthesia) that may become chronic. These individuals believe they are infested with parasites, yet no parasites can be found. Chronic pruritus is an itch that persists for 6 weeks or longer (1). It is a major symptom in a diversity of diseases and health issues. Paresthesia is sometimes termed formication, and involves tickling, pinching, burning and/or tingling sensations without obvious physical manifestations or long-term physical effect. A growing literature indicates that a wide variety of conditions can cause chronic pruritus, paresthesia and delusional infestation (Table I). In the case of delusional infestation, the primary difference in final diagnoses seems based on the patient's interpretation of the cause of their paresthesia or pruritus. Many commonly prescribed drugs, including ones used to treat delusional infestation, are known to cause pruritus and paresthesia (Table II).

Table I. Medical conditions reported to cause paresthesia, pruritus and delusional infestation

Condition (Ref.)	Pare- sthesia	Chronic pruritus	Delusional infestation
AIDS/HIV (2, 13, 18, 27, 29)	X	X	X
Alcoholism (29, 30)	X		X
Anemia (13, 27, 31)	X	X	
Autoimmune disease (12, 33)		X	X
Carbon monoxide poisoning (29, 35)	X	X	
Cancer ^a (2, 13, 18, 34, 36)	X	X	X
Cholestasis (2, 13, 18, 27, 34, 36, 37)	X	X	X
Cirrhosis (2, 34, 37)	X	X	
Diabetes mellitus (2, 13, 27, 29, 34, 36)	X	X	X
Drug abuse (2, 29, 36)	X		
Fluoride poisoning (34, 38)	X	X	
Heavy metal toxicity (29, 39)	X	X	
Hemochromatosis (34)	X		
Hepatic disease (12, 34)	X		X
Hepatitis B, C (13, 27, 36)	X	X	X
Hyperthyroidism (2, 13, 27, 34, 36, 37)	X	X	X
Hypoglycemia (29, 34, 40)	X	X	
Hypothyroidism (2, 13, 27, 29, 34)	X	X	X
Lupus erythematosus (2, 29, 41)	X	X	X
Medications ^b (12, 27, 29)	X	X	X
Menopause (29)	X		
Multiple sclerosis (2, 13, 29, 42)	X	X	
Niacin overdose (42)	X	X	
Opioids (1, 18, 36)		X	X
Parkinson's disease (2, 43)			X
Pernicious anemia (29)	X	X	
Peripheral neuropathy (12, 29)	X	X	X
Psoriasis (2, 13)		X	
Renal failure (2, 37)		X	X
Rheumatoid arthritis (29, 44)	X	X	
Stress (1, 34, 45, 46)		X	X
Stroke (2, 27, 29)	X	X	X
Uremia (18, 29)	X	X	
Vitamin B deficiencies (2, 29)	X	X	X

^aCancer is reported by authors as carcinoma, chronic lymphocytic leukemia, lung cancer, multiple myeloma or neoplasia. ^bCommonly prescribed medications causing paresthesia and pruritus are given in Table II.

DELUSIONAL INFESTATION

Delusional infestation is the mistaken belief that the skin and often other parts of the body are infested by parasites. The reported identification of these parasites ranges from insect groups, usually flies or Strepsiptera, to mites, nematodes, "worms" or even new and unknown types of organisms. Individuals suffering from delusional infestation exhibit a number of typical traits (2–5). They have suffered from the problem for a long time (months or longer) and have seen numerous specialists ranging from dermatologists to entomologists.

Table II. Most commonly prescribed U.S. drugs and side effects that cause skin sensations but no physical changes (4, 13, 47)

Generic Name	Drug type or indication	Paresthesia	Pruritus
Acetaminophen/codeine	Analgesic		X
Alprazolam	Sedative	X	X
Amitriptyline	Antidepressant	X	
Amlodipine	Angina	X	X
Amoxicillin	Antibiotic		X
Benazepril	Hypertension	X	X
Cefprozil	Antibiotic		X
Cephalexin	Antibiotic		X
Ciprofloxacin	Antibiotic	X	X
Clomipramine	Antidepressant		X
Diltiazem	Hypertension	X	X
Doxazosin	Hypertension	X	X
Enalapril	Hypertension	X	X
Famotidine	Gastric ulcer	X	X
Fluoxetine	Antidepressant	X	X
Furosemide	Hypertension	X	X
Glipizide	Diabetes mellitus	X	X
Ibuprofen	Analgesic	X	X
Lisinopril	Hypertension	X	X
Loratadine	Antihistamine	X	X
Lovastatin	Cardiovascular	X	X
Nabumetone	Analgesic	X	X
Nifedipine	Hypertension	X	X
Olazipine	Antipsychotic	X	
Omeprazole	Gastric ulcer	X	X
Paroxetine	Antidepressant	X	X
Pimozide	Antipsychotic		X
Pravastatin	Cardiovascular	X	X
Quniapril	Hypertension		X
Risperidone	Antipsychotic		X
Sertraline	Antidepressant	X	X
Simvastatin	Cardiovascular	X	X
Tetrazosin	Cardiovascular	X	X
Tramadol	Analgesic	X	X
Trimeth/Sulfameth	Antibiotic		X
Warfarin	Thrombolytic	X	
Zolpidem	Sedative	X	

Sufferers strongly reject findings that deviate from their perceptions of the infestation. They come from a variety of occupational and socioeconomic backgrounds, generally possess average or above average intelligence, and generally lack a fear of insects. Other than the delusion most sufferers hold reasonable views of reality. They often engage in self-mutilation, which can range from scratches to deep ulcerations, in their attempt to dig out the parasites (2). Unfortunately, the delusion may also result in the use of home remedies, a distrust of prescription drugs and doctors, and exposure to potentially dangerous levels of pesticides and cleaning products, such as bleach. Sufferers may be quite persuasive and convince individuals close to them that they too have symptoms of infestation.

Prevalence. Although prevalence of the syndrome remains unknown, a landmark study sponsored by the Centers for Disease Control (CDC) found the syndrome in 3.7 Kaiser Permanente Healthcare patients per 100,000 in central California (6). Given the prevalence of the syndrome found in the CDC study it is possible

to extrapolate the number of individuals suffering from these symptoms. If the population of the United States as of the 2013 census was 317,294,000 and if 79% of the population is 15 years old or older then there may be an estimated 9,300 individuals with these symptoms in the US (7). However, the Kaiser estimate was based on medically insured individuals. Considering the number of elderly people on public assistance or uninsured individuals using illegal drugs, the two populations most affected by delusional infestation in the U.S., the number potentially ranges much higher. According to the 2012 National Survey on Drug Use and Health approximately 0.4% of the U.S. population reported using methamphetamine in the previous year and in 2013 9.2% of the population over the age of 12 reported using illicit drugs.

Risk factors. Freudenmann & Lepping (2) summarized characteristics of patients suffering from delusional infestation. They listed 4 categories of patients: 1) middle-aged or older women, with no psychiatric history, few social contacts and normal social and cognitive functioning. 2) Delusional infestation secondary to dementia in older patients with dementia, and vision and hearing impairment. 3) Elderly patients with cortical atrophy and vascular encephalopathy. 4) Young male patients with sudden symptoms corresponding with regular use of opiates, amphetamines and/or cocaine. In all cases however, stress was a significant component though it remains unclear whether stress leads to the problem or results from it.

The CDC study (6) also reported a number of clinical characteristics in Kaiser Permanente patients that self-diagnosed skin parasites: the average age was 52, 77% were female and largely Caucasian, multisystem complaints were common, 54% felt their overall health was fair or poor, and 70% reported chronic fatigue. The study detected cognitive deficits in 59% of case patients and 63% had evidence of clinically significant somatic complaints. In terms of externalities, half tested positive for drugs in hair samples and 78% reported exposure to solvents. Finally, skin biopsies in roughly half of the patients showed solar elastosis.

Although the syndrome seems to occur at any age, there is a strong correlation with drug abuse in individuals under 40. Chronic use of stimulant drugs, such as methamphetamine and cocaine, commonly leads to delusional infestation (8, 9). Methamphetamine use generally leads to a syndrome referred to as "meth mites" where the affected person believes they have parasites crawling under their skin. These individuals pick at themselves to remove the "parasites" they feel. Ellison & Eison (10) found that continuous amphetamine intoxication caused measurable, sometimes irreversible alterations in dopaminergic innervations of the caudate nucleus, but not in several other neurotransmitter systems.

Sufferers over 40 typically consist of middle-aged to elderly women. The female to male ratio in this group is

about 5:1. In premenopausal women correlations with delusional infestation include drug abuse, stress and loneliness, divorce with children, low or no income, low self-esteem, feelings of social rejection, and alternate life styles (11). Predisposing factors also exist in postmenopausal women, although drug abuse is less common. These include a diversity of illnesses, prescription drug treatments and long-term skin damage.

Symptoms. Symptoms of delusional infestation are strikingly stereotypic across age and racial groups. Even before the Internet and widespread information sharing, individuals in different parts of the US and other countries used the same terms to describe what they are feeling and seeing (12). This suggests a neurological component involving the skin and visual hallucinations, or at least the association of tiny objects in the sufferer's environment that they correlate with the sensations they are feeling. Many sufferers have a fixed perception of fibers on and in the skin somehow being associated with their skin sensations and samples are often obsessively packaged, with detailed notes on disease history and symptomology. These fibers are sometimes called Morgellons. One of the difficulties in sorting out the cause of these sensations is determining whether or not there are actual parasites. Individuals suffering from chronic pruritus and paresthesia often scratch themselves and self-mutilate, resulting in lesions, scarring and rashes (13). In addition, delusional infestation strongly associates with obsessive-compulsive disorder (14, 15).

SKIN PARASITES

Sufferers of delusional infestation require a causal agent to explain their syndrome. This may be part of the delusion, but it may also be due to a very human need for explanations for the unknown. A number of skin parasites have been suggested as the cause of the problem. In reality, only a few groups of insects live entirely in or on human skin in some life stage, including lice, tunga fleas and maggots (12). Then there are the free-living blood-feeders, including adult flies (mosquitoes, blackflies, sandflies and horseflies), kissing bugs, bedbugs and fleas (12). All are relatively large-bodied and easily detectable. The majority of these insects do not remain on the skin, they simply feed and leave.

Few mites spend their entire life cycle on or in the skin, except hair follicle and scabies mites. Hair follicle mites commonly infest human skin rarely causing disease other than a rosacea-like dermatosis (16). Scabies mites cause extremely itchy rashes and tend to be concentrated in axillary parts of the body, particularly on the feet, hands and wrists (17). Scabies mites are readily detected both from the rash they produce and in skin scrapings. In neither case is the movement of individual mites detectable. Other mites, including chiggers and nest parasitic species, such as tropical

rat mite, remain on the skin only long enough to feed. These mites cannot be felt moving either.

Blood-feeding by these parasites results in an itchy bump at the site of the bite, caused by a reaction to salivary proteins and other compounds injected into the bite wound. The rash caused by their feeding responds to treatment with antihistamines. Paresthesia and pruritus occurring in cases of delusional infestation remain unaffected by direct treatment with antihistamines (2).

A number of support groups have developed explanations for delusional infestation, frequently promoting the idea of Morgellons as a heretofore unrecognized group of causal organisms. Such organizations often treat the inability of the scientific and medical communities to discover such organisms as a conspiracy. Yet this overlooks the scientific drive to discover new organisms and identify agents of disease. Anything new would be a tremendous discovery, but despite decades of searching no one has found an actual organism associated with the syndrome.

CHRONIC PRURITUS AND PARESTHESIA

Chronic pruritus and paresthesia are defined as unpleasant skin sensations, and paresthesia is sometimes treated as a form of chronic pruritus. Pruritus is an unpleasant skin sensation that results in scratching. Typical chronic pruritus has a number of components as outlined by Twycross et al. (18). There may be a periodicity to the sensations. They may occur mostly during the day or more likely at night, and may be intermittent or continuous. The location of the sensations can also be stereotypic focusing on the shoulders, face, arms, hands or feet. These sensations are also typical of delusional infestation including enhanced paresthesia at night (12).

Willan's itch or "senile" pruritus constitutes a syndrome found in elderly patients without primary skin disease, xerosis, drug reaction or underlying systemic causes (13). The pathology of Willan's itch is poorly understood but even in the 19th century a neural mechanism resulting from peripheral neuropathy was proposed (19). More recently, subclinical neuropathy has been demonstrated, which may result in age-related changes in touch and pain thresholds (20).

Paresthesia is a term for sensations associated with the skin that range from crawling, pinching sensations to tingling, burning or "pins and needles". The term formication is used for paresthesia where individuals feel crawling sensations on or under the skin, a common complaint in individuals suffering from delusional infestation.

CAUSES

Quite apart from what we know about skin infesting parasites and delusional infestation a largely separate

literature exists that reports the origins and causes of itch as chronic pruritus or paresthesia (18, 21) (Table I). Itch sensations have been categorized as pruritoceptive (peripheral), or neuropathic, neurogenic or psychogenic (central) (18). However, Ständer et al. (22) classified itch patients into 3 categories, including those with pruritus on diseased skin, with pruritus in non-diseased skin, and those having pruritus with chronic scratch lesions, associated with several categories of disease, including dermatological, systemic, neurological and psychogenic, or combinations thereof. Like all skin sensations, itch originates from the central nervous system (21). Several pain and itch pathways are thought to exist, only one of which is mediated by histamine (21). Itch can be initiated by damage to the nervous system anywhere along the afferent pathway between the skin and the brain. Thus, itch can be caused by issues along the entire neuronal pathway from the skin, peripheral nerve endings and mucous membranes to the brain and spinal cord. Individuals with back injuries may complain of crawling pinching sensations in their backs, particularly across their shoulders (23). Individuals with multiple sclerosis and HIV often make the same complaint (18). Itch can occur without nerve damage but may be caused by clinical administration of opioids; typically via morphine pumps or the use of illegal drugs.

Delusional infestation, chronic pruritus and paresthesia share symptomology and may share root causes. Nerve damage also associates with delusional infestation. One study described a patient with delusional infestation who had lesions at the root of the trigeminal nerve (24). A second study found that chronic pruritus characterized systemic disease in 12 out of 55 patient's examined (25). Underlying causes ranged from diabetes to lung cancer. A third study found delusional infestation in 4 of 636 patients with neurological disease (26). These patients suffered from brain cysticercosis, cerebrovascular disease, pernicious anemia, and peripheral neuropathy. Finally, two studies found that more than half of the population over the age of 70 suffers from itch without obvious cause (18, 27).

TREATMENT

Delusional infestation is largely treated as a dermatological and psychiatric problem. Bernard and others argue that psychogenic itch arises as a purely psychiatric or psychological syndrome (28). However, many individuals suffering from delusional infestation also have underlying medical conditions that may cause pruritus and paresthesia (Table I). Because a specific physiological cause for delusional infestation has not been found does not mean none exists, and in fact a wide variety of conditions can lead to all 3 conditions. Pruritus, paresthesia and delusional infestation all

should be viewed as symptoms, not diseases. Whether caused by drug abuse, or of some other origin, delusional infestation most likely also incorporates neural pathways and receptors between the brain and the skin, and within the brain itself, and thus may be an indicator of underlying disease. In both chronic pruritus and delusional infestation, correlations exist between chronic dopamine potentiation by various categories of drugs including methamphetamine. Because a large number of prescribed medications can cause pruritus and paresthesia as side effects, the patient's medications must be examined as well. Ironically some of the very drugs used in treatment of delusional infestation are known to cause itching (Table II) (2, 13, 27, 29).

Current treatments for delusional infestation include the use of antipsychotics and antidepressants to control the delusions, pruritus and paresthesia. These drugs include Pimazide, Olanzapin and Ziparisidone (30–32). Some antipsychotic drugs used to treat delusional infestation have antihistamine effects as well (Table II). Additional treatments may be necessary for skin damage.

CONCLUSION

Thus, assuming that parasites are not involved, chronic pruritus and delusional infestation arise from an underlying physiological or physical cause that triggers an itch pathway. Additionally, this itch pathway can also be triggered by exogenous causes, such as drug use or abuse. Underlying psychiatric conditions, such as schizophrenia, paranoia, depression, anxiety disorders and obsessional states may be linked to this pathway as well.

Treatment of patients suffering from delusional infestation or from chronic pruritus is largely based on the patient's interpretation of the cause and the physician's response to that interpretation. Patients diagnosed with chronic pruritus or paresthesia may be examined for neurological or physiological origins of the symptoms. Whereas patients claiming parasite infestations are treated as delusional and are sent to dermatologists and psychiatrists, often without further examination for underlying health issues. This group is difficult to treat because of their persistent belief in the parasitic origins of their skin sensations, and they will self-medicate, which can lead to further health issues. Patients suffering from delusional infestation require treatment of underlying causes, the degree of skin involvement and reevaluation of existing medications.

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