

Report of the External Peer Review of CCID's Unexplained Dermopathy (UD) Project

Date Sept 24, 2009

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The CDC continues to receive reports of an unexplained skin condition in which patients report a range of dermatologic symptoms such as crawling, biting and stinging sensations; granules, threads, fibers, or black speck-like materials on or beneath the skin; and/or skin rashes or sores. In addition to dermatologic complaints, some sufferers also report fatigue, mental confusion, short-term memory loss, joint pain, and changes in vision.

Many patients refer to this condition as "Morgellons," however, for the purposes of this document, it will be called Unexplained Dermopathy (UD). At this time, the biomedical community does not know what causes UD or if it is indeed a new condition. Scientists and physicians do not know if the people who report the condition have common risk factors or if there is a common cause for the symptoms. The factors associated with acquiring this condition are unknown and it is not known if UD is communicable.

After receiving an increased number of reports from persons who describe a similar complex of signs and symptoms, the CDC conducted an investigation, in collaboration with Northern California Kaiser Permanente's Division of Research and the Armed Forces Institute of Pathology to learn more about UD. The case definition used to review medical records was description of a symptomatic skin lesion with fibers, threads, specks, dots, fuzzballs, granules or other forms of solid material coming out of the patient's skin within the preceding three months. The descriptions also had to include presence within the last three months of a skin lesion such as a rash, wound, ulcer, or nodule or the patient had to describe skin symptoms such as pruritus, feeling that something is crawling on top of or under the skin, or a stinging, biting, or a pins and

needles sensation in the skin. If additional information were needed, the patient was questioned by phone. The primary goals of the study were to determine who is affected by UD, the symptoms they are having, and what factors may contribute to the condition. The study involved: determining the clinical and epidemiologic features of this condition; examining skin biopsies from affected patients; characterizing foreign material such as fibers or threads obtained from persons with the condition; and estimating rates of illness among the study population.

During the first part of the study, the investigators identified and recruited eligible study participants. Information was collected from participants, detailing symptoms and potential factors or exposures that may contribute to the condition. In the second part of the study, eligible participants underwent detailed clinical evaluations, including a general medical examination, a dermatology examination, a mental health examination, skin biopsies, and multiple blood tests.

On Sept 24, 2009, CDC convened an external panel of experts to provide feedback on the UD study activities conducted to date, including scientific quality and approach; relevance to CCID's mission; and research gaps and opportunities; and to provide recommendations for future study and research. This report summarizes the panel's findings and recommendations to the Agency.

Below are specific questions posed to the panel and the panel's responses:

1. Have the project's goals and priorities been addressed?

The goals were to determine the clinical and epidemiologic features of the condition, to estimate the prevalence and to generate factors that might cause or contribute to the condition.

This was a well-designed initial study of an unexplained syndrome. The target population was carefully chosen but certain limitations were encountered that may restrict the generalizability of the findings. Additional analyses of the data are needed in order to extract the maximum amount of information needed for publication.

2. What are the study's strengths?

This is the largest and most in-depth study conducted to date of this condition. Selection of the study population was done with a minimum of selection bias and detailed epidemiologic and clinical data were gathered. Study of the skin by photography, biopsy and fiber analysis was exceptionally good. The performance-based neurocognitive and self-administered screening psychiatric tests were state-of-the-art.

3 What are the study's limitations?

- a. There is no universal agreement as to how to define the condition; nor is there is a diagnostic test. The case definition used in the study was broad in order to include patients who may have – or believe they may have -- a condition that is popularly referred to as “Morgellons.” Although the definition required fibers or particles to be coming out of their skin, no patient had a fiber extruding from normal skin or visible within normal skin. If there are such patients, the study did not identify them.
- b. This was a descriptive case series, with no control population. One hundred four patients were identified by a retrospective search of electronic medical records for symptoms or signs consistent with an unexplained dermopathy, specifically including fibers extruding from skin. An additional 11 cases were self-identified. All 115 patients met the case definition after screening using a standardized tool.
- c. Participants were all selected from the Northern California KP database, excluding children under 13, and required to be English speaking.
- d. Only one time point was studied and this required illness within three months. Patients were excluded who no longer had the condition, preventing a comparison of those self-resolving and those with persisting illness. The natural history of the condition remains unclear.
- e. The self-administered screening psychiatric profile did not provide as much in-depth information as an interview with a psychiatrist could have, leaving open an assessment as to how much psychiatric co-morbidity is associated with this condition.
- f. The selection process for different aspects of the study may have progressively selected against patients who were busier, less mobile, or less concerned about their health. Of 115 cases identified, 70 completed a detailed Internet-based survey; 41 of

these completed the clinical evaluation and 27 had skin biopsies. Factors leading to the progressive attrition were not studied.

4. Are there gaps of concern or a need for additional study
 - a. Any fibers collected should to be correlated with skin photographs and biopsy reports. Preliminary evidence, suggests that the fibers were all obtained from ulcers, perhaps entrapped in serum or eschar. Many of the skin biopsy specimens showed marked solar elastosis in the upper dermis. This is a common finding in sun-exposed skin of middle-aged and elderly Caucasians but this association of solar elastosis with sun exposure might be verified with the photos of biopsy sites.
 - b. Estimated rates of the condition need to be adjusted for the size and distribution of the KPNC population in the area, rather than using the entire population base.
 - c. Abnormal laboratory values need to be reported to indicate the degree of abnormality.
 - d. It would be important to understand the temporal relationship between the dermatopathy and the neuropsychiatric findings. Employment and health utilization data might address activity levels of the patients prior to disease onset. Current data on employment might be correlated with severity of skin lesions to see how illness is related to disability or activities of daily living.

5. What findings can be communicated to the public, medical community and stakeholder community?

Patients meeting the case definition adopted for this study were recruited in a search of medical records from a large, English-speaking, adult population in Northern California. It should be noted that a single, widely agreed upon case definition does not exist. Consequently, persons enrolled in this study may not unequivocally meet all possible criteria for the condition popularly called "Morgellons." Approximately 50% of patients who underwent clinical examinations had fibers in or on skin lesions, all of which were open or crusted sores. Fibers and other particles collected from participants were photographed and analyzed by infrared spectroscopy for molecular characteristics and scanning electron microscopy with energy dispersive X-ray analysis for elemental

composition. The fibers were found to be hairs, cellulose, or polyester. There was no suggestion in the data collected that the fibers preceded the lesions, caused the lesions, or occurred in normal skin. Blinded samples representing extensive systematic photographs of the participants' skin were reviewed by an independent dermatologist who identified no primary lesions. Visual inspection of the skin and biopsies from multiple sites were interpreted to mean that the lesions were indistinguishable from common superficial erosions or excoriations of the skin.

6. What is the public health impact of this study?

This study could not provide a true prevalence rate, but the condition appears to be uncommon. The extent to which the syndrome disrupts daily activities cannot be estimated but the personality assessment collected on 41 patients suggests a possible elevated rate of psychopathology. Thus far, there is no suggestion that the condition is transmitted person-to-person, within family members, from pets or related to travel or specific environmental exposures. Also, there is no evidence of Lyme disease, or infection by parasites, mycobacteria or fungi.

7. What should the priorities be in the future?

a. Resources should provide for the study's completion.

b. Physicians encountering patients who may have this condition should be encouraged to publish in a peer-reviewed medical journal a description of a carefully documented case. Photographs of fibers extruding from (or present within) normal intact skin, detailed histopathologic examination of biopsied skin specimens, and thorough analysis of the fibers will be especially helpful in clarifying several lingering questions.

c. In the absence of a single, well-described published case with fibers emerging from intact skin, it is difficult to justify the resources needed to start a new study. If a new study is done, access to the study needs to be easier in order to decrease biased participation based on leisure time, disability, transportation, age and motivation. Study personnel may need to conduct interviews in participants' homes, for example. More employed participants might also be included this way.

d. A more wide-ranging mental health study could help define how many of the symptoms are commonly seen in well-characterized neuropsychiatric conditions. Inclusion of healed cases may be useful. A control group might be devised. Additional study populations might be considered to broaden the population characteristics geographically and demographically.

e. What organizations may have a mission relevant to this condition?
Any new study of this condition at CDC or elsewhere should be done by a group with extensive experience in complex conditions of undefined etiology.