ORIGINAL ARTICLE

Bali Dermatology and Venereology Journal (*BDV*) 2020, Volume 3, Number 1, 9-14
P-ISSN.2089-1180, E-ISSN.2302-2914

Published by DiscoverSys

# Trends in the diagnostic approach of scabies as a neglected tropical disease

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## ABSTRACT

Scabies is a parasitic disease of the skin that is difficult to enforce if the clinical symptoms are not typical. The diagnosis relies on clinical symptoms to be less efficient and only has a sensitivity of less than 50% because it is difficult to distinguish active infestations, residual skin reactions, or reinfestations. Misdiagnosis results in wrong treatment and causes the patient to not recover and continues to be a source of infection for the environment. The exact diagnosis of scabies is determined by finding mites or eggs on laboratory tests, but mites are difficult to find because only a few mites infest sufferers. For this reason, various studies in the world have tried to develop diagnostic methods in the enforcement of scabies. This article will describe the trend of establishing a diagnosis of scabies, as well as the advantages and disadvantages in its application.

**Keywords:** scabies, diagnosis method, diagnosis enforcement
**Cite this Article:** Trasia, R.F. 2020. Trends in the diagnostic approach of scabies as a neglected tropical disease. *Bali Dermatology and Venereology Journal* 3(1): 9-14. DOI: 10.15562/bdv.v3i1.26

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## INTRODUCTION

Scabies is a skin disease caused by *Sarcoptes scabiei* infestation and sensitization. The World Health Organization (WHO) in 2017 stated that scabies is included in the neglected tropical disease (NTD), which requires large-scale control. WHO estimates that more than 300 million people, or around 3% of the world's population, are infected with scabies.[1] In Indonesia, according to data from the Indonesian Ministry of Health, the prevalence of scabies in 2017 is 6% of the total population in Indonesia.[2]

Scabies can provide typical symptoms so that they are easily diagnosed; however, if the clinical symptoms are not typical, the diagnosis of scabies is difficult to establish. Typical clinical symptoms are complaints of severe itching at night (nocturnal pruritus) or when the heat is hot, and the sufferer sweats. Typical skin eruptions include tunnels, papules, vesicles, and pustules at the site of predilection. Although the symptoms of scabies are typical, sufferers usually come for treatment when it is already in an advanced stage and do not have any more typical clinical symptoms because excoriation has arisen, secondary infection by bacteria and lichenification.[3]

Another problem in the diagnosis of scabies is that clinical symptoms of scabies can mimic the symptoms of other skin diseases or are covered by other diseases such as eczema and impetigo so that diagnosis becomes difficult. The diagnosis relies on clinical symptoms to be less efficient and only has a sensitivity of less than 50% because it is difficult to distinguish active infestations, residual skin reactions, or reinfestations. Tunnel detection with Indian ink has been done for a long time, but the test is not practical, so it is rarely used.[4] Misdiagnosis results in wrong treatment and causes the patient to not heal and continues to be a source of infection for the environment.

The exact diagnosis of scabies is determined by finding mites or eggs in a laboratory examination, but mites are difficult to find because only a few mites infest sufferers. According to Mellanby,[5] out of 900 scabies sufferers, only found 11 mites per sufferer on average and in most sufferers only found 1-5 mites per sufferer. In a study at a boarding school in Jakarta, the prevalence of scabies was 72.6%, but only 8 mites were found in all sufferers.[3]

If there are no mites or their products found in a laboratory examination, the situation has not been able to get rid of scabies because the mites may be in an unreachable location at the time of sampling. Therefore, the diagnosis of scabies needs to be considered in every patient with persistent complaints of itching, and if the clinical diagnosis has been established then presumptive therapy can be seen and then the response is seen. Patients tested positive for scabies if they respond well to scabies treatment. However, it should be noted that a positive response to the treatment of scabies has

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Received: 2020-01-20
Accepted: 2020-04-22
Published: 2020-06-01

not been able to get rid of other skin diseases that are not scabies, and a negative response has not been able to get rid of scabies because there may be resistance to scabies mites. Because it is difficult to find mites and their products on laboratory tests, a clinical diagnosis can be established if there are two of the four signs of cardinal scabies in patients, namely:

1. Pruritus nocturna
2. There is a group of people who suffer from the same disease, for example, in a family or in a settlement or in a dormitory.
3. There are tunnels, papules, vesicles, or pustules in the predilection site, which are between the fingers, wrists, outer elbows, folding the front armpits, areola mammae (female), umbilicus, buttocks, the external genitalia (male), and lower abdomen. Keep in mind that in infants, scabies can infest the palms and soles of the feet and even the entire body.
4. Find mites on laboratory examination.

## Laboratory tests for detection of mites and their products

Although mites and mite products are difficult to find, laboratory tests should be carried out, especially in cases of suspected atypical scabies. Laboratory tests can be carried out as follows.

## Skin scrapings

Before doing a skin scraping, pay attention to the area where mites are expected to be found, namely the newly formed and intact papules or tunnels. Then the papule or tunnel is dripped with mineral oil and then scraped with a sharp sterile scalpel to lift the top of the papule or tunnel. The scrapings are placed on the slide, dripped with KOH, covered with a cover glass, and then examined under a microscope.

Skin scrapings are the easiest way to do and give the most satisfying results making it suitable for those who have not had much experience in diagnosing scabies. Another advantage that skin scraping can be done in low resource health facilities. Skin scrapings have high specificity, but their sensitivity is low because the number of mites in classic/typical scabies patients is very small. According to Dupuy et al.,[4] the sensitivity and specificity of skin scrapings in diagnosing scabies with typical symptoms are 90% and 100%. There are several factors that can affect sensitivity such as clinical presentation, the number of lesions examined, and examiner experience. Lesions that have never been scratched usually give better results.[4,6]

## Take mites with needles

Intake of needle mites can increase the accuracy of diagnosis from 5% to 95%. To get the mites, the needle stuck in the tunnel in the dark and then lifted up. When the needle is inserted, the mite will usually hold the tip of the needle so that it can be lifted out. Taking mites with a needle is relatively difficult for people who have no experience, especially in patients with scabies whose lesions are no longer typical and many secondary infections by bacteria.[4-6]

## Wipe (swab) the skin

The skin swab examination is carried out with a transparent tape cut to the size of the glass object (25 x 50 mm). To do this procedure, first, determine the location of the skin suspected of being infested with mites. After the skin is cleaned, then sticking tape on the papule or tunnel and then removed quickly. After that, the tape is attached to the glass object, dripped with KOH, covered with a glass lid, and examined under a microscope. From each one lesion, the tape was attached as much six times with six tapes to make six preparations.[7] The preparation can be inspected within three hours after sampling if stored at 10-14ºC. Skin swabs are relatively easy to use and have high positive and negative predictive values, so they can be used for screening in areas with limited facilities.[8]

## Burrow ink test

Scabies papules smeared with Indian ink using a pen then left for 20-30 minutes, then removed with alcohol. Burrow ink test shows positive results when the ink enters the tunnel and forms a typical image in the form of zig-zag lines. Burrow ink test is an examination to detect tunnels, not to detect mites and their products.[4,6-8]

## Histopathological examination

Papules or tunnels that are suspected of containing mites are removed using the thumb and forefinger, then sliced with a scalpel parallel to the surface of the skin. The biopsy is done very superficially so there is no bleeding and no need for anesthesia. The specimen is placed on the slide, dripped with mineral oil, covered with a glass lid, and examined under a microscope.[9]

The histopathological picture of scabies lesions is the presence of tunnels in the stratum corneum, but the end of the tunnel where female mites are located in the dermis slices. The histopathological examination has no diagnostic value unless mites or eggs are found in the examination.[9]

Areas containing mites will show eosinophils that are difficult to distinguish from other arthropodae


Published by DiscoverSys | *BDV* 2020; 3(1): 9-14 | doi: 10.15562/BDV.V3I1.26

bite reactions such as mosquito bites or bed bugs. If the histopathologic features of the epidermal tunnel biopsy are only perivascular inflammatory cell infiltrate with multiple eosinophils, edema, and epidermal pink spongiosis, then it is only suggestive and not a definitive diagnosis of scabies infestation.[9] Histopathological features on skin biopsy showing in a pink pigtail and adheres to the stratum corneum and the presence of an empty mite egg wrap leading to the diagnosis of scabies.

Primary scabies lesions provide hyperkeratosis, spongiosis and vesiculation in the epidermis. Changes in the dermis in the form of perivascular infiltrates, consisting of T lymphocyte cells, little histiocytes, and sometimes eosinophils and neutrophils. In primary lesions, the number of mast cells is higher when compared to secondary lesions and normal skin.[6,9]

Secondary lesions are generally in the form of urtical papules which may occur due to circulating immune complexes or due to cellular immune responses. The presence of circulating immune complexes is evidenced by the increase in C1q binding activity. In secondary lesions, infiltration of cells is milder than primary lesions, and no eosinophils or vasculitis are found.[9]

Biopsy of persistent nodes shows chronic inflammatory infiltrate with or without eosinophils, thickened blood vessels, and vasculitic features. Atypical mononuclear cells are sometimes found. In crusts scabies, the stratum corneum is thickened and filled with mites.[9] Skin biopsy can be used to confirm the diagnosis of scabies if mites or parts of mites are identified from skin scrapings.[6,8,9]

## Dermoscopy

Dermoscopy, also called dermatoscopy or epiluminescence microscopy, is a method used by dermatologists to evaluate the differential diagnosis of pigmented lesions and melanomas, but in its development, dermoscopy can also be used to diagnose scabies. Dermoscopy is a technique of observing superficial dermis skin layers in vivo. Dermoscopy uses a liquid medium which is oil, water or alcohol or polarized light, which allows direct observation to the skin without disturbing light reflection in the skin so that it can provide a detailed picture of each layer of the epidermis to the superficial papillary dermis and identify the presence of tunnels.[4-6,8]

On dermoscopic examination of scabies, mites appear triangular in shape, followed by tunnel lines in the epidermis such as pictures of jet planes, kites, or spermatozoid. The acral area such as between the fingers and wrists is the best place for a dermoscopy examination, but other parts of the skin that have reddish papules with intact tunnels must also be examined.[4,8]

Dermoscopy is a good tool as a diagnostic tool for scabies, but not as good as skin scrapings or biopsies. Dupuy et al. reported that dermoscopy has a sensitivity of 91% and specificity of 86% in experienced examiners with a slightly lower specificity in inexperienced examiners. However, during the study, it was found that diagnostic accuracy by inexperienced dermoscopic continued to increase.[4]

Dermoscopy is able to detect more scabies lesions (84% vs. 47%, $p<0.01$) than skin scrapings and shorter examination time (227 seconds vs. 442 seconds, $p<0.01$). Dermoscopy is more useful in patients with scabies who have non-distinctive, subclinical symptoms, are in the treatment of steroids, nodular scabies, and immunocompromised patients such as infants, elderly, and HIV. The sensitivity of the dermoscopy increases with the severity of the disease, whereas the sensitivity of skin scrapings is not affected.[4-6,8]

Dermoscopic examination procedures do not cause pain so that the patient feels comfortable and is not afraid to be examined (especially in children). The advantage of the dermoscopy technique over skin scrapings in diagnosing scabies is that the patient is preferred, saves time, and is portable so that dermoscopy is preferred for screening in large communities. Barriers to the use of dermoscopy are expensive equipment so that they are not widely used in developing countries.[8] Skin scrapings can also be combined with the dermoscopic examination. The diagnostic method of skin scrapings with dermoscopy is far superior to skin scrapings without dermoscopy in terms of duration of examination and accuracy[6,8,9]

## In vivo *S.scabiei* imaging method

Although this procedure is uncommon in Indonesia, in developed countries such as Europe, imaging methods for scabies that have been carried out in vivo have been developed, namely using optical coherence tomography (OCT) and confocal microscopy (CM).[9,10]

OCT is a non-invasive in vivo imaging technique that has been routinely used in ophthalmology to diagnose retinal disease. In recent years, OCT has begun to be used in the field of dermatology to monitor therapy in cases of non-melanoma skin cancer and actinic keratosis. With 8-μm resolution, OCT can visualize changes in skin morphology due to infestation, the presence of mites and tunnels, and tunnel contents in vivo, making it possible for rapid, non-invasive in vivo diagnosis. In addition, OCT makes it easy to analyze and study the biological

structure of mites and infestation processes in the host, which have been limited to in vitro studies.[10]

Banzhaf et al.[10] succeeded in identifying mites in patients with scabies in vivo with vertical and horizontal cuts. In the vertical picture, the mite looks like an oval (mango/almond-shaped) structure measuring 0.2 x 0.3 mm or less and is located just below the stratum corneum. The density of the mite is similar to the surrounding skin tissue, but the mite appears to be limited or located at the end of the tunnel, which is described as two hyperreflective lines (tunnel walls) flanking the hyporeflective space in the center (lumen of the tunnel). In one case, it was found that mites are not always in the stratum corneum but can dig deeper into the stratum granulosum. In horizontal cuts, mites appear 0.3 x 0.15 mm. Moreover, it can be visualized feces and mite eggs that appear as hyperreflective droplets along the tunnel lumen.[10]

Imaging techniques other than OCT are CM, which provides better resolution and deeper penetration than OCT so that the specific structure of the mite and surrounding tissue can be seen more clearly. CM makes it possible to record video so that CM is more often used in biological studies of scabies mites. The disadvantage of CM examination requires a longer time than OCT, requires higher skills, and cannot make vertical cuts so that it cannot explain the location of mites in detail.[10]

Scabies imaging technique in vivo with OCT and CM is similar to dermoscopy. The advantages of this procedure that it can describe the specific structure of mites and tunnels, the location of mites on the skin, and the condition of the surrounding tissue in more detail than dermoscopy. However, OCT and CM are more difficult to access, require more time, and require high skills, so they are not suitable for mass diagnosis or screening and are more often used for the purpose of the study of mite biology.[9,10]

## Intradermal skin test

The scabies diagnosis method with intradermal tests is still difficult to do because it requires pure mite extracts, while *S. scabiei hominis* varieties are difficult to breed so it is difficult to get mite extracts in sufficient quantities. Research specific immunity with intracutaneous tests and prick tests using scabies mite extracts showed that intracutaneous tests were positive in most scabies patients but prick tests gave negative results. This is due to the insufficient antigen used, which is only 5% of the total weight of scabies mites. Meanwhile, when used all parts of the body of the mite that is destroyed (crude antigen) pyogenic eruption occurs, which is different from classic scabies.[6,7,9]

Until now, the examination of specific immunity using scabies mites is still not satisfactory. That is due to the difficulty of making antigens because *S. scabiei hominis* varieties cannot be propagated both in vivo and in vitro, while the use of *S. scabiei* animal varieties gives different reactions. Mite extracts obtained from animals contain heterogeneously mixed antigens from hosts and parasites. In addition, there are cross-reactions with antigen determinants of house dust mites, composition, and varying potential.[6,9]

Recently there are well-characterized recombinant scabies mite allergens that have been purified with standard protein compositions. The allergen has the potential to be used in intradermal skin tests in the future. This method can facilitate the diagnosis of difficult scabies cases as well as having the potential in the field of immunotherapy.[6,7,9]

## Detection of antibodies with ELISA

Based on the pathogenesis of scabies, mite antigens induce a humoral response to the host, resulting in antibody production. This makes it possible to diagnose scabies using a blood test on the basis of measuring circulating antibodies that react to scabies-specific antigens without cross-reacting with house dust mites. Antibody detection by ELISA (enzyme-linked immunosorbent assay) in *S. scabiei* pigs and dogs that have been widely used in Europe, but the method has not given good results in humans.[11]

Arlian et al. examined IgA, IgD, IgE, IgG, and IgM specific antigen scabies in 91 patients. The results showed that all scabies sufferers have a mixture of IgA, IgG, and IgE antibodies that can recognize scabies mite antigens with a composition of 45%, 27%, and 2.2%, respectively. Apart from that, as much 73.6% of scabies sufferers have serum IgM that can recognize scabies protein but also reacts with house dust mites. There are no serum antibodies that react exclusively to scabies mite antigens. This is due to co-sensitization or an unavoidable cross-reaction between scabies mite antigens and house dust mites in the human immune system so that it still hinders the development of scabies diagnosis methods using human blood tests. As with intradermal tests, antibody detection by ELISA still requires research to look for human-specific scabies antigens that are not found in other types of animal scabies mites or other parasites.[11]

## Polymerase chain reaction

Scabies examination with polymerase chain reaction (PCR) can be one method of detection of *S.scabiei*. With the PCR technique, the diagnosis of scabies is made easier because it is sensitive to

enzymatic amplification of gene fragments from a small amount of parasitic material. PCR is a method for accurate identification of parasites, knowing the characteristics of parasitic genes, diagnosing parasitic infections, knowing the isolation and characteristics of expressed genes, detecting drug resistance, developing recombination of DNA vaccines, and analyzing overall parasitic genomes.[8,9]

The disadvantage of PCR is the dependence of the method on the presence of mites or parts of mites in the preparation, so it is not possible to be widely used because the amount of mites is only small. PCR can be relied upon if other methods cannot diagnose scabies. PCR followed by ELISA detection can increase diagnostic sensitivity in patients with atypical scabies, but this method is very time-consuming and costly.[6,8,9]

### Factors to consider in laboratory examinations

Various methods for diagnosing scabies by finding mites have their advantages and disadvantages. Skin scraping is the easiest method, and the results are more satisfying than other methods. Picking mites using needles is more difficult because it requires special skills and the success rate is low because in darker skin, tunnels difficult to identify. The skin swab method has disadvantages because the examination takes a longer time. This is due to the samples must be taken from various lesion locations and from each lesion, 6 samples need to be prepared. Burrow ink tests rarely give positive results because patients usually come in a chronic state and secondary infections have occurred so that the tunnel is covered by crusting and difficult to evaluate the tunnel using the ink.[5,7,8]

In the diagnosis of skin scrapings, scrapings should not be performed in excoriated lesions because of the possibility that the mites are gone because they are scratched and mechanically removed. Skin scrapings should also not be used in lesions with secondary infections because they can make the infection worse. In addition, in lesions with secondary infections, there is pus that is acaricide so that the mites may no longer exist in these lesions.[12,13]

The best way to do skin scrapings is that scrapings must be done superficially because the mites are in the tunnel in the stratum corneum. Skin scrapings should not bleed because if there is bleeding, it means deeper scrapings than the stratum corneum. A good papule to scrub is a newly formed whole papule, oval-shaped, and not crusted because mites can usually still be found in the papule. Scrubbing of the skin is not only in one lesion but in various lesions because mites are not necessarily in the chosen lesion. Scabies lesions are most often found between the fingers, therefore lesions between the fingers should receive more attention.[5-9]

Before doing a skin scraping, drop mineral oil in the scalpel and in the lesion to be scraped off. The penetration of mineral oil is better than KOH because mites adhere to mineral oil so that it can be removed alive. In addition, microscopic examination is easier on the use of mineral oil because the difference in refraction between mites and mineral oil is greater than that of mites and KOH. Another advantage of using mineral oil is that it does not dissolve fecal pellets, which are useful to help establish the diagnosis.[5-9]

## CONCLUSION

Difficulties in establishing a diagnosis of scabies have triggered various studies in the world to create a diagnostic approach. The definitive diagnosis is to find mites on microscopic examination. However, in practice, it is very difficult to find mites in these skin scrapings. Thus developed scabies diagnosis methods, such as skin swabs, burrow ink tests, histopathological examinations, dermoscopy, *S. scabiei* imaging methods in vivo, intradermal skin tests, antibody detection by ELISA, and PCR. These methods have advantages and disadvantages, depending on their application.

## CONFLICT OF INTEREST

None.

## FUNDING

None.

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