

A Review on Diagnosis, Pathophysiology and Effective Management Strategies of Scabies

Shafkat Hussain Malik¹, Sheikh Irshad Ul Haq², Riyaz Ahmad Bhat³, Hanumanthrao C Patil⁴, Rajesh Kumari Patil⁵

¹Pharm.D Scholar, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda

²Pharm.D Scholar, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda

³Pharm.D Scholar, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda

⁴Professor and HOD, Department of Pharmacy Practice, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda

⁵Professor & Principal, Department of Pharmacy Practice, Adesh Institute of Pharmacy and Biomedical Sciences, Adesh University, Bathinda

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Corresponding author: Rajesh Kumari Patil

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Abstract:

The contagious parasite dermatosis known as scabies is widespread. In addition to skin-to-skin contact, the mite *Sarcoptes scabiei* var. *Homospains* can spread through faces, infected bedding, or infected clothing in cases of crusted scabies. The diagnosis is frequently clinical. The management of scabies is based on topical scabicides, mostly 5% permethrin, according to an updated Cochrane review published in 2010. Although it is illegal in many nations, oral ivermectin may still be helpful, especially for patients who are unable to tolerate or adhere to topical medication and in situations when there is an outbreak of scabies in a particular institution. To prevent the infection from growing further, patients should also be informed in-depth about it. Even in the absence of symptoms, cases brought on by close physical or sexual contact need to be treated methodically. Following therapy, hygienic measures ought to be taken. Little ones are most profoundly affected by it, making it the most influential factor. It continues to receive insufficient attention as a significant community fitness matter.

Keywords: Benzyl benzoate, ivermectin, permethrin, scabicides, scabies, plaques, papules and nodules, glomerulonephritis; rheumatic fever.

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Introduction

The itch mite is the common source of the pruritic skin condition known as scabies. About 300 million people are thought to contract scabies annually in the entire world. Scabies is a serious health issue in numerous underdeveloped nations.[3] The availability of scabies therapy has not changed significantly during the past ten years. Instead, there is emerging evidence from clinical research that the medicines already on the market have limits, and there is still some debate about their safety. Similar to that, clinical judgement is nearly always used to determine the scabies diagnosis. The most recent Cochrane evaluation of scabies treatments found.[1] According to diverse environmental conditions, symptoms can manifest as shallow, elevated, or deep-pitted corky lesions. The presence of common scab in the field typically has no impact on agricultural output, and eating scab-contaminated food may not be harmful to human health. However, because the general appearance of products, like potatoes, determines their quality, their market value

is directly impacted by the extent of common scab infection. For instance, common scab on potato tubers has been observed to cause economic losses in Quebec, Canada, of about 15%.[2] However, they cannot jump or fly. Female mites can move up to 2.5 cm per minute. Mites have a 30-minute window after exposure to the skin to reach the epidermis. Direct skin-to-skin contact is the method of transmission. In order to spread the mite to another person, a person with traditional scabies must come in close contact with them for 15 to 20 minutes.[9] Scabies is challenging to get rid of since cured patients frequently relapse. The use of community based drug intervention tactics, involves the simultaneous treatment of total populace, is one of the treatment option. Ivermectin is an oral medication that is also available in a variety of topical forms.[12]

Form of Transmission

The transmission of scabies occurs through digging of itching mite into the outermost layer of the dermis. 0–4 eggs are laid every day for up to 6 weeks by fertilised gravid sow tick as they dig into the keratinized layer. The complete developmental life cycle from zygote to mature consists of three active transitional phase, also known as developmental stages. This process typically takes approximately two weeks, Three active intermediate stages, or instars, make up the full developmental life cycle from egg to adult, which takes about two weeks. The first adult female was observed 3 weeks after the initial colonisation, according to traditional transmission studies. With the development of host immunity, *S. scabiei* numbers in first infestations have been seen to grow for up to 4 weeks before gradually declining to about 10–12 mites. In contrast, the intense manifestation of the condition, referred to as hyperkeratotic scabies, is characterized by an exceptionally large number of acarid and notable cutaneous scabbing. Prolonged close bodily contact with an afflicted individual (such as clutching hands, bedding, etc.) is the most typical way for this disease to spread. Scabies is also regarded as a sexually transmitted illness since successful direct transmission requires about 15–20 minutes of intimate contact. Many documented instances of transmission within families provide evidence that the spread of Human itch mite tends to occur within specific time periods or locations, with the kindred or residence serving as the primary site of dis-semination. Genetic profiling results also support these theories.

According to earlier studies, it was suggested that the newly fertilized adult female mite is predominantly responsible for transmission, as around 90% of developing acarid do not survive to reach the fully grown stage.

Only the adult females need to be removed in order to cure someone with a low parasite burden, and Keneath Mellanby's attempts to induce an invasion solely using Juvenile acarid proved unsuccessful. The energetic, less advanced forms may be in charge of spread, whereas the fully grown feminine uncommonly exits the tunnel. The argument that the early stages of development may be capable of spread is supported by the observation that invasion with abundance of parasites (>100 fully developed feminine) will have a proportionately large quantity of developing phases than developed feminine. There is no convincing evidence to imply that cleaning blankets and clothing is necessary to stop the spread of the disease, even if these items do not appear to be crucial in the transmission process. From the houses of scabetic patients, live mites have been found. Since it is a parasite that must have its host, the mite is extremely vulnerable to dehydration when it is not present. Mites are almost completely immobile below 20 degrees Celsius. Importantly, it

has been discovered that female mites may survive off the host for 55–67 hours in equatorial climate (thirty degree celsius and seventy five percent moisture level). This finding raises the possibility that female mites could be a source of transmission in these areas.[4]

Clinical Features

The subjects sensitization response to the acarid is what causes one symptoms among scabies infection. Up to six weeks pass after the first infestation before symptoms start to manifest. Subsequent Infections show symptoms sooner after exposure. The observable features of conventional human itch include papules or tunnels in usual areas such the interdigital spaces and phalanges, carpus, gluteal region, chest in female gender, and private parts. The scalp, soles, and palms of younger children and older persons may be more extensively affected. Although thecranio-cervical region frequently spared (especially in babies), the trunk as well as limbs are severely irritating when scabies is present. At night, itches are at their worst. Up to 79% of studies have found that bacterial skin infections occur in conjunction with skin breaches caused by mite burrows and excoriation from scratching an itch. Whenscabetic lesions contain surrounding erythema, yellow crusting, or pus, it is important to examine bacterial skin infection. Plaques, a thick layer of scale, and, in more severe cases, profound fissures, are the hallmarks of scabies that has been crusted. Crusty scabies may not itch like traditional scabies.[5]

Clinical Manifestation

In many areas of resource-poor societies, scabies continues to be one of the most prevalent skin diseases for people of all ages. In contrast, in industrialised societies, scabies manifests differently and affects a specific population, such as young adults or the senior citizens in bodies like assisted living facilities. The occurrence of staphylococcal and group A streptococcal secondary infections exacerbates the scabies problem in locations with limited resources. The mature acarid entry within epidermis is followed by the clinical signs of scabies. The main symptom is irritation, that can be highly intense also is usually tightened in nocturnal hours. It can take up to two weeks or longer earlier than symptoms like irritation are observed after the initial infection and before the incubation period ends. Scabies typically affects a number of skin areas, primarily interdigital spaces, carpal regions, cubital region, and scapular areas. It can also affect the genital region, inclusive of the phallus, inferior limbs, especially hocks, scrotal sac in men, as well as chest within femmes. Scrapes are frequently extra prevalent.

In the tropics, secondary infections remain also typical, and the major affected areas, or the child's

face, may develop inflamed eruptions and crusted scales. These lesions may mimic impetigo, and group A streptococci or *Staphylococcus aureus* are typically the causative agents. Other clinical variations of scabies include the crusted variety, commonly known as Norwegian scabies, which affects immunocompromised or seriously unwell people. Additionally, it has been linked to Down's syndrome. Adults and kids who have the Human Immunodeficiency Virus may, nevertheless, look same.

Although there is less itching, the same places are affected as in typical scabies; other family members also experience the typical manifestation. The symptomatology of Norwegian scabies include the development of flaky skin also scaly patches, which account for the majority noticeable on significance namely wrists, ears, and finger exteriors. One or more nails exhibit thickening and hyperkeratosis, and the face may be affected. [4]

The two primary clinical subtypes of scabies are crusted and classic. 2–6 weeks following an infestation, symptoms usually start to show. The most typical manifestation of scabies, known as classic scabies, is connected to a very light mite burden of 10-15 mites per square inch of skin. Contrarily, crusted scabies typically affects elderly or immuno-compromised people and is linked to a larger mite burden.[10]

Epidemiology

Scabies affects people of all racial backgrounds, socioeconomic statuses, and ages, and it is prevalent around the world. "The *Acarusscabiei* [*Sarcoptes scabiei*] is notorious for its lack of respect for person, age, sex, or race," reported Freidman in 1941. Irrespective of whether it emerges on the skin of a ruler, a servant, a century-old individual, or an infant, scabies assumes its presence with equal impertinence and audacity, paying no heed to the identity of its host. Globally, approximately three hundred million instances of scabies occur annually. Prevalence of the disease is approximately 100% in some Indian communities, and it is most prevalent in developing nations where it is endemic. Scabies is an epidemic that affects hospitals, nursing homes, and long-term care institutions in affluent countries.[6]

Pathogenesis

There are numerous intricate immunological and inflammatory mechanisms involved in the aetiology of scabies, some of which we are only now beginning to comprehend. A delayed hypersensitivity reaction to an antigen induced by the immune system causes skin inflammation, papules, and itching. Initial symptoms normally disappear 3–4 weeks after the main infestation.

However, symptoms return significantly more quickly during subsequent infestations, in just a matter of days. Keneath Mellanby made efforts to deliberately expose patients who had previously encountered the infection, but only 40% of his victims were successful, showing the emergence of a protective immunity. Two primary types of scabies, namely typical scabies and Norwegian scabies, are acknowledged within the realm of this disease. They are connected to defensive and detrimental host reactions, individually. The clinical manifestations of scabies are determined by the type and potency of the natural, cytotoxic, and antibody-mediated responses triggered by acarid antigens. The scabies gene discovery initiative has now helped to identify some of the potential allergens that could be triggering this immune response. Several S. Studies have indicated that scabies mite proteins, which share similarities with allergens found in dermato-phagoidespteronysinus, elicit cytotoxic and antibody-mediated responses strong in individuals affected by both typical scabies and Norwegian scabies. The severe form of hyperkeratotic scabies characterized by an inadequate allergic cytokine profile, and there is evidence suggesting that cytotoxic T cells play a predominant role as functional cells in the skin. In contrast, typical scabies exhibits a protective immune response dominated by a cell-mediated cytokine profile, primarily associated with helper T cells. Cytokine analysis has revealed that stimulated peripheral blood mononuclear cells from hyperkeratotic scabies patients have a significantly augmented Interferon- γ /IL-4 ratio compared to ordinary scabies patients. Furthermore, the levels of IL-5 and IL-13 were found to be elevated in the latter group.

Interestingly, healthy patients' PBMCs treated with scabies mite extracts demonstrated heightened production of the regulatory IL-10 levels. Elevated eosinophil levels and the production of Overall and antigen-specific IgE are observed in both types of scabies, but their intensity is notably higher in cases of hyperkeratotic scabies. The immediate cell toxicity effect on Epidermal cells, primarily executed by Cytotoxic T cells, and the secretion of Immunomodulatory molecules that amplify the Inflammation response by targeting Resident skin cells are additional mechanisms at play.

Skin epithelial cells eosinophils, and basophils have important but poorly understood roles in the immunological response to scabies. Due to inherent immunological responses from the host, tissue-feeding parasites pose severe risks to their early survival. Scabies mites are subject to both internal and external host defence mechanisms while feeding on host plasma and epidermal protein. Uncharacterized mite proteins have been shown in studies to have immunomodulatory qualities that

facilitate parasite invasion of the host by modulating or reducing the inflammation mechanisms of skin epithelial cells, scabies mites may hinder the inflammation pathways of these indigenous cells within the cutaneous layer. Additionally, they might influence a postponed immune response

Research conducted using in vitro skin models has demonstrated that scabies mites can suppress the expression of various immune signaling molecules and cell adhesion proteins in fibrocytes of the dermis, endothelial cells of microvessels in the dermis, and keratinocytes of the skin's outer layer. Interestingly, a protein called peritrophin, found in the mite gut, has recently been found to potentially activate the mannose-binding lectin pathway in human complement activation. The identification of a family of allergenic serine proteases with inactive counterparts in the scabies mite has led to the hypothesis of their involvement in blocking all three pathways of the human complement system. After recombinant expression, it was discovered that two of these scabies mite-inactivated protease paralogs exhibit this inhibitory effect. Additionally, a significant subset of T lymphocytes known as Th17 cells plays a role in activating various cells of the innate immune system. They attract and stimulate polymorphonuclear neutrophils at sites of inflammation and induce endothelial and epithelial cells to produce inflammatory mediators such as IL-1, IL-6, and tumor necrosis factor- α . In contrast to the enhanced proliferation of Th17 cells seen in psoriasis lesions, the IL-17 pathway is impaired in individuals with Job syndrome (hyper-IgE disease). Recent evidence suggests that dysregulated immune responses in the pathophysiology of crusted scabies may involve cytokines associated with Th17 cells, contributing to a better understanding of this condition. This has been shown by preliminary observations of increased interleukin-17 and interleukin-23 in Norwegian scabies. The unique behavior of scabies mites on hosts that are not their natural hosts, as well as the transient nature of cross-infestation, suggest the existence of additional factors influencing host protection and disease outcomes, beyond just the immune response. When a parasite comes into close contact with a potential host, achieving host-pathogen interaction becomes crucial.

This entails creating an environment with favorable physical, chemical, and immunological conditions that support the parasite's development and proliferation, as well as ensuring the availability of necessary nutrients. Additionally, scabies mite proteases play a role in utilizing the proteolytic feeding facilitating the invasion of host tissues and

aiding in activities such as dermal invasion and tissue dissemination. Gaining a deeper understanding of the intricate relationships between hosts and parasites relies on studying and characterizing the excretory/secretory products of the parasite. The requirement to develop the efficient anthelmintic therapies is highlighted by the emergence of *S.scabiei* resistance to current therapies and worries over the impact of medication residues on consumer health. Development of vaccinations or innovative therapeutic treatments for susceptible groups will be aided by a better understanding of the scabies pathogenesis. [7].

Diagnosis

The diagnosis of scabies in dermatology is one of the simplest and yet most challenging. The basis for the diagnosis is the epidemiological history, how often lesions itch, where they are located, and how pruritus feels. A definitive diagnosis can be achieved by examining dermatological specimens or using dermoscopy to detect arachnids, ova, scabies droppings under a microscope. Although it takes expertise and practice, it is possible to remove the scabies mite from the end of the burrow. Diagnoses of scabies can be made using skin scrapings from the burrow or papule. The first step is to scrape five to six suspicious lesions with a sterile scalpel blade and a drop of mineral oil. In order to examine the scrapings and oil, a cover slip is placed over the glass slide. Any mite stage can be used as a diagnostic indicator. Despite how straightforward this treatment is, for optimum results a knowledgeable technician or dermatologist is needed. These facilities are lacking in many nations where scabies is widespread, so the diagnosis is determined based on the Client's medical history and phenotypic traits. Additionally, if there is a clinical indication, the clinical assessment is scabies unless proven otherwise. [7]

Treatment

The diagnosis of itch mite is crucial, but so is the therapy. Topical scabicide medicines are the mainstay of treatment. [6] Treatment for scabies has generally involved applying an acaricide topically, while ivermectin taken orally is becoming more common. Patients are instructed to cover their entire body, from the neck down, with cream before leaving it on for a long time (often overnight), then rinsing it off. Due to more widespread skin involvement in these patient populations, paediatric and geriatric patients also receive treatment for their faces.[1]

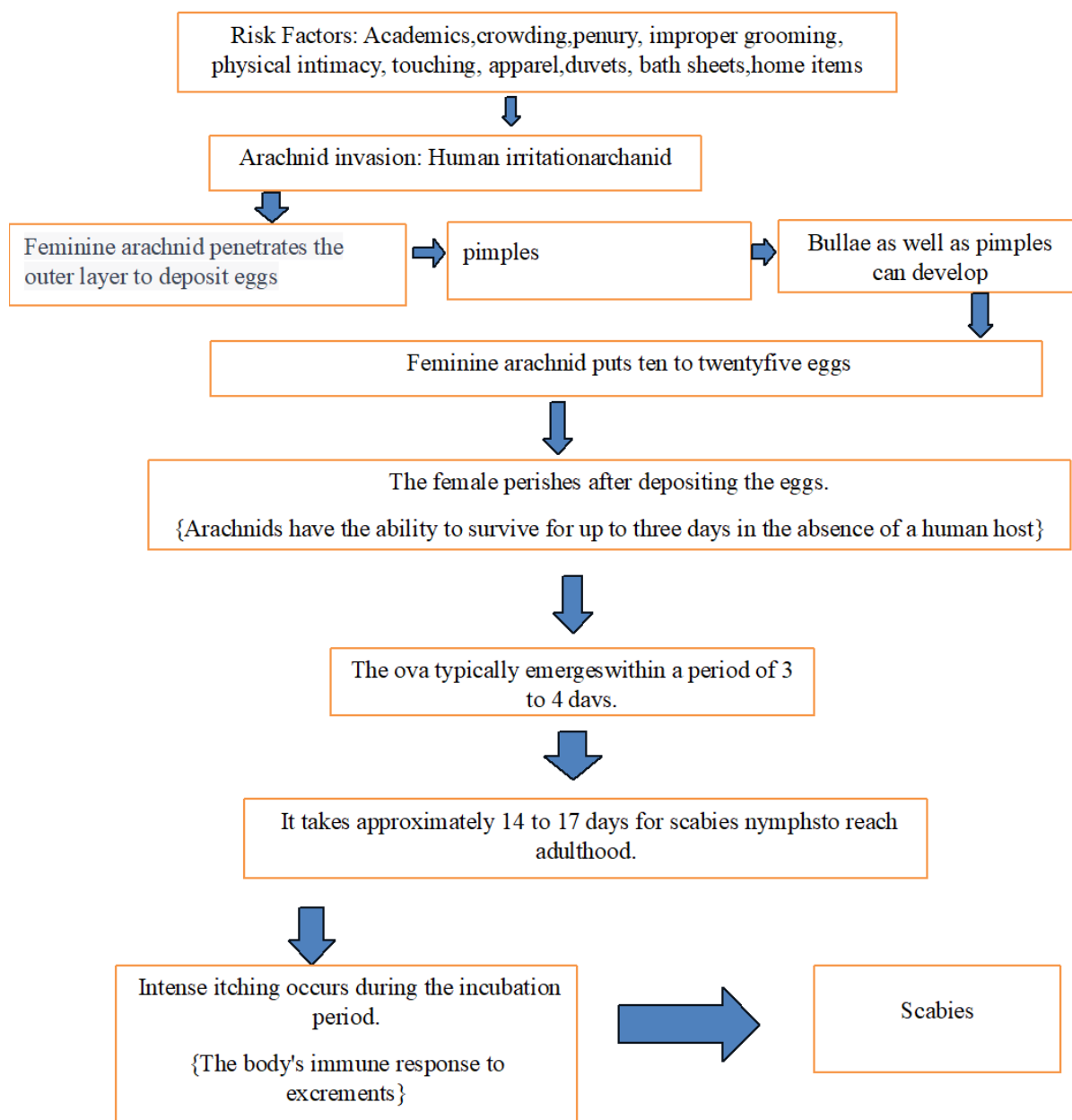


Figure 1: Pathophysiology flowchart of scabies

Topical Medications

Permethrin

In many nations, including the US, Australia, and the UK, synthetic pyrethroid 5% permethrin is the first line of defence against acaricides. In terms of safety and low toxicity, it has a stellar reputation. The most successful scabies treatment now available, according to a Cochrane review, Recent research supports earlier findings, with over 90% of 14 or 28 day cures reported in all investigations. Although its efficiency as an ovicide has been shown to be satisfactory when used as directed in many cases, it is advised to provide a second treatment one week later to eliminate any remaining developed eggs.

The cost of permethrin, which is substantially greater than that of other topical therapies, and the fact that it is not available everywhere, particularly in under developed countries where the occurrence of scabies is probably higher, are significant barriers to its wider usage. [1]

Infants older than two months old are allowed to use the permethrin cream at a concentration of 5%. The cream needs to be applied to the head, neck, and body of children under the age of five, in addition to the body.[8]

Permethrin can be used topically to pregnant and nursing women, and in rare situations, ivermectin can be administered as an off-label medication (i.e.,

without official clearance) following a thorough analysis of the advantages and dangers and with the patient's informed agreement.[16]

Benzyl Benzoate

In adults, benzyl benzoate is used at a concentration of 25%; in children, the concentration is 10% or 12.5%. Its benefits include its inexpensive cost, good efficacy, particularly at 25%, and the absence of known resistance. Because of this, it is a very popular treatment in Africa and some of Europe, but it is not offered in the US. The medicine has a restriction in that it is likely to cause severe acute skin irritation, which limits tolerance; diluting it to lessen this risk may decrease efficacy. The recommended application regimen for benzyl benzoate is more extensive than that for permethrin, for example. It calls for leaving it on for 24 hours and/or using it repeatedly on consecutive days. The reasoning behind this suggestion is unclear given that 25% benzyl benzoate acts in vitro far more quickly than other commercially available acaricides, with mite mortality happening within 30 minutes.[1]

The parasites can be killed by benzyl benzoate application B.N.F. and sulphur ointment B.P. For older children, they are administered at half strength, and for infants, at quarter strength. Sulphur is seen to be more certain and less prone to irritate people. Benzylate is friendlier to garments as well as more enjoyable into use. Keneath Mellanby thought they were both equally successful.

With the exception of newborns, the individuals who need treatment for their heads should be attended to, Apply the medication evenly to all areas of the surface, paying close attention to ensure that no fold or crease is missing and that the foot bottoms are covered. Applications are submitted three evenings in a row. It is advisable to take a bath the night before the initial application and another the next day.[13]

Monosulfiram

Tetraethyl thiurammonosulphide is the term given to monosulfiram in a chemical sense. It was used to treat human scabies for the first time by Percival in 1942 After taking a bath, apply tetraethyl thiurammonosulphide emulsion to the entire body and thoroughly rub it in. Repeat this procedure once each day for two or three days in a row. Alcohol should be avoided while receiving treatment or just after since tetraethyl thiurammonosulphide and antabuse share chemical similarities. Past preventive measures in afflicted communities have included the use of soaps containing tetraethyl thiurammonosulphide.[17]

Other Topical Agents

Despite being effective, topical application of 8–10% precipitated sulphur is rarely chosen because of

how messy and unpleasant it is to use. Due to its inexpensive cost and high margin of safety for infants and pregnant women, it is still utilised in some locations. According to a recent study, application for three straight days is necessary for the best results. Another outdated medication, N-ethyl-o-crotonotoluidide, offers a large margin of safety when administered at a concentration of 10% and is appropriate for newborns. Despite having effective acaricidal capabilities in a test tube, N-ethyl-o-crotonotoluidide. [1] 10% Crotamiton cream N-ethyl-o-crotonotoluidide has been proved to be a safe option for newborns, but its exact mode of action is uncertain, therefore numerous treatments are necessary. It needs to be applied all over the body for 24 hours, cleaned off, and then reapplied all over for 3 to 5 days. According to certain research, daily application for 10 to 14 days may increase the effectiveness of the treatment. Uncommon side effects could include allergic contact dermatitis and methemoglobinemia in youngsters. [14] At a concentration of 0.5%, the organophosphate pesticide malathion is said to be effective against scabies. There are currently few published clinical trial results to support its usage in Britain, despite the actuality that it is advised as a second-line treatment.[1]

Tea tree oil In vitro tests using gel containing melaleuca oil 0.002-2% indicates both antibacterial and miticidal action. An Australian Aboriginal child's scabies can be treated with a gel that contains tea tree oil, according to current research. Alternative remedies apply enhance more standard therapy options in multicultural moreover aid-limited local inhabitants alongside the intent of improving Individuality and community management of this condition in regions of require, albeit real-world use has not yet been shown. [14]

Oral Anti Scabies Agent

As per the Centres for Malady Manage as well Protection, oral ivermectin medication is an option for treating scabies (0.2 mg per 1000 gm, double dosage administered fourteen days time), while charge and presence frequently restrict it to alternative treatment option if topical permethrin remediation is failed. [11]

New Treatments

For the treatment of scabies, longer-acting medications or those with ovicidal qualities would be revolutionary. Since pigs and people have comparable genetic make-ups, physiologies of the skin, and immune systems, new anti-scabies medications are currently being researched and tested on porcine hosts. A single dose of the new acaricide afoxolaner or the extremely fat affinitive largecyclic lactone moxidectin was found to be greater efficacy instead of twin dosing of ivermectin in two pre-clinical experiments.[15]

Complications

While itching is the primary cause of the scabies-related disability in many nations, such as sleep loss, the condition presents differently in places with little resources because secondary infections result in a number of additional problems. Of them, the group A streptococci secondary infection is the most well-documented. The possibility that glomerulonephritis could occur as a result of a streptococcal infection has long been known. In various degrees of individuals affected, primarily youngsters, this can be found through screening testing. In a survey conducted in northern Australia, 10% of children were found to have symptomatic acute glomerulonephritis, but moreover 24% showed microscopic haematuria. As a result, kidney damage without symptoms is also possible. Scabies was shown to be the primary source of the infection, which had a close relationship to skin sores. Streptococci infection can even happen when scabies are not present. In the tropics, acute post-streptococcal glomerulonephritis differs because the skin, not the pharynx, seems to be the primary site of infection. Moreover, it has been demonstrated that in regions where scabies-associated infection is prevalent, presence of protein in the urine can be observed for up to sixteen years following the primary infection in thirteen percent of individuals with documented Postinfectious glomerulonephritis compared to four percent of control subjects. The potential for long-term damage to the kidney's glomeruli due to the renal injury incurred after an initial scabies infestation followed by infection poses a serious risk. Notably, treatment with ivermectin for scabies has been associated with a substantial decrease in blood in the urine and the seclusion of streptococcus bacteria from dermatological wounds according to a subsequent study. It is evident that more details, based on extensive scientific research, are required about the prevalence, geographic distribution, and long-term effects of these renal problems. A link between acute rheumatic fever and streptococcal infections caused by scabies has also been suggested. This is based on the finding that group A streptococcal throat infection, the conventional source of infection linked to rheumatic fever, is uncommon in many locations where rheumatic fever remains a serious issue in children. In contrast, cutaneous infection from group A strains occurs often Streptococcus dysgalactiae and Streptococcus anginosus group, however, are hardly associated with, acute rheumatism despite the fact that in tropical regions, gullet can serve as a potential location for the presence of these variants. Hence, there is a possibility that the tonsillar microbes present in the throat could exchange pathogenicity factors with the prevalent dermal flora, potentially leading to the development of acute rheumatism. Infant septicaemia brought on by *Staphylococcus aureus* is

another instance where a connection between scabies and bacterial sepsis may exist. Although there is currently no evidence to support this claim, scabies-like skin rashes have been linked to life-threatening bacterial bloodstream infection in newborns brought on by golden staph in Gambia. Not all scabies consequences solely from contamination, and household financial hardship is a prevalent issue in areas with few resources. Family expenditure on unsuccessful scabies treatment (\$24 over a 3-month period) was shown to account for a sizeable portion of household income in rural Mexico, according to a study. Due to this, the family was unable to buy other necessities, such as nourishment for their households. As a result, scabies in underdeveloped areas poses a risk for a health impact and financial hardship, exacerbates the effects of the sickness brought on by this straightforward infection in underdeveloped areas. [4]

Conclusions

Scabies is a widespread condition that frequently predominates the skin infection pattern in poor nations, where it distresses and discomforts children and families. Families are compelled to use a significant portion of their limited resources to try to treat this infection, largely as a result of inadequate treatment. In this setting, secondary bacterial infection is nearly a given, with possibly negative health effects on the individual. Controlling scabies should now be a top priority in nations where it seriously affects public health. One of the persistent issues with this illness is that there is a strong correlation between scabies and human louse infestations across multiple geographical areas worldwide, and that ivermectin treatment may be used to effectively eradicate both. The next step in the process involves the creation and evaluation of appropriate protocols for managing scabies within communities, using both ivermectin and dermal medications. Additionally, further investigation should be conducted to explore topics such as the potential persistent health consequences of sarcoptic infestation and the underlying causes of periodic occurrence. This action plan aims to ensure originality in the wording while maintaining the core ideas and suggestions.

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