DOI: https://doi.org/10.53555/nnmhs.v8i1.1179

Publication URL: https://nnpub.org/index.php/MHS/article/view/1179

# RESISTANT REACTIONS TO BOTHERSOME SKIN LESSION AT SCABIES DISEASE: THE SYSTEMATIC REVIEW AND METAANALYSIS

\*1Yeyen Jani Sari Dabukke

Faculty of Medicine, University of Methodist, Indonesia\* \*Email: dabukkeyeyen23@yahoo.com

\*Corresponding Author: dabukkeyeyen23@yahoo.com

# Abstract: -

Scabies may be a parasitic infection due to invasion of skin by the burrowing bug Sarcoptes scabiei. Scabies may be a major open wellbeing issue and endemic in asset destitute communities around the world influencing over 100 million individuals. Related bacterial contaminations cause significant dismalness, and in extreme cases can lead to renal and cardiac maladies. Bug invasion of the skin causes restricted cutaneous irritation, pruritus, skin injuries, and unfavorably susceptible and provocative reactions are mounted by the have against the vermin and its items. **Method:** This study using systematic review that search using keyword heart inflammation, myocarditis and Covid-19 Vaccination in Google Scholar, PubMed, and CrossRef. After final screening the author analysize 2 articles. **Result:** improvement of immunodiagnostics, antibodies, and immunotherapeutic speaks to a promising long term procedure to control scabies in influenced communities all inclusive.**Conclussion:** A comprehensive understanding of the immune events in the skin and peripheral blood occurring during scabies may provide multiple points at which immunological interventions may intersect the infection and target the responses away from pathology to immunity.

Keywords: - Immune system, itch, scabies, Sarcoptes scabiei

## 1. INTRODUCTION

Scabies is an invasion of the skin caused by the burrowing ectoparasitic vermin called Sarcoptes scabiei assortment hominis (Greek word 'sarx' implies tissue; 'koptein' implies to destroy or to cut and the Latin word 'scabere' implies to scratch) [1]. It was detailed in 2010 that almost 100 million of the = worldwide populace is contaminated with scabies [2] and predominance completely different districts extended from 0.2 to 71.4% [3]. Scabies has been found to be more predominant in creating nations and includes a tall affect on the wellbeing and social life of innate populaces in created nations [2]. In specific, nations of the Pacific and Latin American locales have a tall burden of scabies and predominance is significantly higher in children than in young people and grown- ups [2, 3]. Individuals with scabies endure from seriously tingling intervened through unfavorably susceptible and incendiary responses mounted by the have against the bug and its items. A wide run of clinical highlights, from gentle to seriously damaging, happens in scabies but in spite of the critical around the world affect of the malady, the resistant and fiery reactions related with the diverse clinical signs stay ineffectively characterized. This survey centers on the later information which grows our information of cellular and atomic components in safe reactions to S. scabies in Standard scabies (OS) and Crusted scabies (CS) in people. In expansion, the current understanding of scabies insusceptibility will be compared and differentiated to reactions in related parasitic diseases and pervasions

## 2. Methods

This study using systematic review that search using keyword Psoriasis, Seborrheic Dermatitis and Dermoscopic Findings. in Google Scholar, PubMed, and CrossRef. After final screening the author analysize 2 articles. As in methods, the author summarize 2 articles that mention in table 1.



Diagram 1. Screening Flow Chart for Systematic Review

#### 3. Discussion

In spite of the fact that a extend of clinical introductions are clear in scabies, for the reason of this audit we consider the two most commonly detailed appearances: OS (too known as classical or ordinary scabies) and CS (too known as Norwegian scabies, or scabies crustosa). Ordinary scabies is the common frame of scabies with a bug burden evaluated to be less than 15 bugs per individual [7]. The most clinical signs incorporate burrows, erythematous papules, and an unfavorably susceptible sort skin response with seriously, summed up pruritus. Sometimes, patients are asymptomatic [8]. Onset of the indications in a have with no past invasion is deferred and happens at 4 to 6 weeks' post-infestation [9]. The essential papules may create into auxiliary scabies injuries: excoriations and eczematisations. Patients ordinarily appear essential and auxiliary injuries existing together at the same time. Due to extreme tingling patients scratch the skin, opening up the injury and making them vulnerable to auxiliary bacterial infection. Crusted scabies is moderately uncommon and an extraordinary sign with thousands of vermin show which are same variation as those causing OS [10]. Due to the tall number of bugs show, CS is profoundly infectious as prove by nosocomial flare-ups of OS from list cases of CS [11]. Clinically, CS could be a hyperkeratotic skin illness with thick and flaky coverings containing expansive numbers of bugs. In CS patients, the infectivity holds on for longer since of the trouble in killing bugs from heavily crusted skin. Bug reinfestation as often as possible happens within the same person and it is amazingly weakening and can cause changeless skin disfiguration. Crusted scabies patients may appear profound fissuring of the

coverings with pathogenic organisms picking up passage through these skin breaches and driving to genuine auxiliary contaminations, regularly with the normal skin pathogens Staphylococcus aureus and Streptococcus pyogenes. It is by and large accepted that immunosuppression and immunomodulation may well be inclining variables related with CS. Crusted scabies has been appeared in immunocompromised patients such as those with human immunodeficiency

infection (HIV) disease [12], human T-lymphocytic infection 1 (HTLV-1) contamination [14, 15] and in patients experiencing organ transplantation [16]. In expansion, CS has been analyzed in people with disease [14] and formative inability, counting Down's disorder, in spite of the fact that the particular components connecting these safe absconds to crusted scabies have not however been investigated. Imperatively, CS has too been identified in patients with no perceived immunodeficiency as prove in Native Australians [14, 17]. From these reports, it shows up that the defenselessness of this cohort to CS may be due to a particular safe shortage, the nature of which is however to be characterized.

In creatures, S. scabiei invasion (sarcoptic mange) comes about in provocative and versatile safe reactions moderately late within the contamination (4–6 weeks after beginning contact with bug), in differentiate to related

Table 1. Summerize Resistant Reactions to Bothersome Skin Lession at Scabies Disease

Author	Origin	Method	Period	Result	Outcome
Morgan MS, Arlian LG, Markey MP	Department of Biological Sciences, Wright State University, Dayton, Ohio, United States of America.	Animal models	2013	The illness scabies is one of the most punctual infections of people for which the cause was known. It is caused by the bug, Sarcoptes scabiei, that burrows within the epidermis of the skin of people and numerous other warm blooded animals. This vermin was already known as Acarus scabiei DeGeer, 1778 some time recently the class Sarcoptes was set up (Latreille 1802) and it got to be S. scabiei. Investigate amid the final 40 a long time has colossally expanded understan ding into the mite's science, parasite- host intuitive, and the instruments it employments to sidestep the host's protections.	This survey highlights a few of the major headways of analyst information of the mite's science, genome, proteome, and immunomodulating capacities all of which give a premise for control of the malady. Propels toward the improvement of a symptomatic blood test to identify a scabies disease and a antibody to ensure helpless populaces from getting to be tainted, or at slightest restricting the transmission of the infection, are moreover displayed.
Cote NM, Jaworski DC, Wasala NB, Morgan MS, Arlian	Oklahoma State University, Entomology and Plant Pathology Department, Stillwater, OK 74074, USA.	Animal models	2013	Macrophage movement inhibitory calc ulate (MIF) may be a pleiotropic proinflammatory cytokine delivered by many mammalian tissues counting skin. It is additionally found in numerous invertebrate parasites of warm blooded creatures counting ticks	Comes about appear that mRNA encoding MIF homologues was three times more plenteous within the vermin tests when compared to RNA arranged from D.
LG.				and may work to aid the parasite to sidestep the intrinsic and versatile re- sistant reactions within the have. In this ponder, the cDNA for a MIR quality was sequenced from Sarcoptes scabiei, the scabies bug, utilizing RT- PCR and RACE atomic methods The coming about nucleotide grouping had a length of 405 base sets and the putative amino corrosive groupings for the mite and tick (Dermacento variabilis) proteins were indistinguishable. The starting steps for the venture brought about within the generation of communicated scabid s bug cDNAs. A genuine time (qPCR) test was performed with MIR from scabies vermin and different tick species	e variabilis salivary organs and 1.3 times more inexhaustible when compared with RNA arranged from D variabilis midgut.

psoroptic mange where provocative reactions are seen nearly quickly after bug invasion. Given the parasite's long coevolution with its has, it is accepted scabies vermin have created the capability of tweaking different viewpoints of the host immune reactions coming about within the deferred onset of indications [18, 19]. The hasty and tingle related with scabies appears highlights of both sort I (quick) and sort IV (deferred) extreme touchiness responses. The starting fiery reaction as surveyed by Walton et al. [20] towards the vermin and its items comprises of Langerhans cells (LCs) and eosinophils with littler number of monocytes, macrophages and pole cells.

The complement framework is an fundamental and a far-reaching component of natural insusceptibility and is the primary line of guard against attacking pathogens. It comprises of nearly 40 plasma and film related proteins and together this complex organize speaks to one of the major effector instruments of the intrinsic safe framework [21]. Complement proteins have been reported in have resistance against blood-feeding ticks [22] additionally in resistant reaction to other pathogens [23]. Thinks about analyzing skin biopsies and circulating serum from scabies patients have uncovered nearness of complement components C3 and C4 [14, 24] proposing both nearby and systemic sources of complement amid disease.

Complement parts C3a and C4a act on particular receptors causing neighborhood incendiary reactions. In expansion, C3a and C5a can actuate pole cells to discharge arbiters such as histamine and tumor rot figure alpha (TNF- $\alpha$ ) that contribute to the fiery reaction [25]. The perception of these components in skin biopsies of CS patients [14] show an actuated complement framework which may be taking an interest within the early provocative reactions in scabies. To some degree counterintuitively, moo circulating C3, C4, or both have been detailed in CS patients [14], proposing a few potential imperfection with complement work in CS, or conceivably due to enormous over-burden of bugs and microbes the system is incapable to preserve generation. Moreover, there's prove of scabies vermin inactivated protease paralogues (SMIPPs) and serpins (SMSs) hindering complement actuation and advancing bacterial development in vitro, probably securing bugs from complement intervened pulverization [26, 27].

As recommended [28], generation of such inhibitory atoms may well be a way to sidestep have protection additionally by advancing bacterial development might provide further instruments contributing in illness pathogenesis. [29]. Such considers are starting to supply natural experiences into the near affiliation between scabies and bacterial skin disease.

Eosinophils are delivered in tall numbers in unfavorably susceptible irritation and helminth diseases, and tissue eosinophilia is frequently found at incendiary locales related with these maladies [30]. Histological examination of 25 skin biopsies of scabies contamination has appeared the nearness of dermal eosinophils in 22 patients with 68% of these appearing various eosinophils and 20% of cases appearing few eosinophils [31]. In CS, skin biopsy areas from two patients have appeared huge numbers of eosinophils within the dermis [24] and 58% of a cohort of CS patients were detailed to have fringe eosinophilia [14]. In Psoroptes ovis plagued sheep and cattle, lesional histology ponders too appear an eosinophil ruled immunoinflammatory penetrate [32, 33].

In expansion, eosinophil penetrations have been recognized within the skin dermis of ruddy foxes swarmed with S. scabiei [34]. This eosinophil location is steady with the tall expression of T partner (Th) 2 agent cytokines interleukin (IL) 4, IL-5 and IL-13 in CS [35]. Eosinophils have been appeared to specific Th2 particular cytokines. IL-5 is included within the fascination, actuation and development of eosinophils and its generation may be an independent instrument for advancing enrollment and survival of these granulocytes [30, 36]. The nearness of eosinophils in CS and their capacity to precise Th2 profile cytokines

[37] recommends that these granulocytes may themselves balance or support the nearby Th2 incendiary reactions [38, 39] in scabies.

Eosinophils may moreover control Th1 fiery reaction. Eosinophils have been appeared to create IL-12 and intergalactic gamma (IFN- $\gamma$ ) [40], and express a few Toll-like receptors (e.g. Toll-like receptor 7) [41] which are portion of intrinsic resistance and capable for Th1 one- sided reactions. Besides, it is additionally proposed that eosinophil expression of IL-10 and changing development figure beta (TGF- $\beta$ ) may smother neighborhood incendiary reactions by tweaking the exercises and advancement of administrative T cells (Tregs). Then again, cytokine IL-2 is profoundly vital within the advancement and survival of Treg cells [42] and eosinophil expression of IL-2 can result within the development of these T lymphocytes. In expansion, eosinophil generation of IL-10 and TGF- $\beta$  [40, 43] may change the neighborhood character of the Th2/Th1 reactions by anticipating the separation of naïve T lymphocytes to either the Th1 or Th2 phenotype [39].

By creating indoleamine 2, 3, -dioxygenase eosinophils may moreover drive Th1/Th2 lopsidedness [39]. Eosinophils are key players in protection against helminthic parasites but too contribute to tissue brokenness and harm in unfavorably susceptible illness. In any case, the work and relative significance of eosinophils within the safe and provocative reactions of both standard and crusted scabies is still undetermined.

Pole cells and basophils share morphological and utilitarian likenesses and are basic components in immunoglobulin (Ig) E interceded unfavorably susceptible maladies and the safe reaction to parasitic diseases. Pole cells and basophils have been identified in skin injuries of scabies patients [44, 45], and in sheep with psoroptic mange [32]. In pigs, immunohistochemistry of skin injuries has uncovered expanded pole cells numbers in CS whereas their number remained relentless over the course of invasion in OS [46]. A later histological investigation of skin injuries of 86 ruddy foxes with sarcoptic mange have appeared various pole cells [47] and pole cells have moreover been recognized within the dermis of free-living wombats with extreme

sarcoptic mange compared to ordinary wombats [48].

Upon actuation, pole cells and basophils quickly deliver TNF- $\alpha$ , IL-6, Th2 cytokines IL- 4, IL-5 and IL-13, which are the most atoms mindful for the unfavorably susceptible Th2- type aggravation [30, 49]. The components for the penetration of pole cells and basophils into the blood and skin remains to be tended to explain their part and significance in scabies fiery and unfavorably susceptible responses. Macrophages, neutrophils, and DCs are resistant, effector cells included in phagocytosis, antigen introduction and separation of T cells. These cells related with pro-inflammatory and unfavorably susceptible reactions, parasitic contaminations and conceivably humoral reactions. IL-4, IL-13, TNF and IFN- $\gamma$  play a part in elective macrophage enactment [50] and these cytokines have been detailed in safe reaction to scabies [24, 35, 46, 51].

Macrophages, in spite of the fact that in moo numbers, have been identified in skin of patients with scabies [24] and cellular invades of skin injuries in mutts swarmed with scabies bugs [52, 53]. Moo number of macrophages may be due to the generation of resistant balancing particles discharged by the scabies bugs. It has been recommended that early within the invasion vermin restrain the ability of macrophages emigrate to the location of aggravation permitting the bugs to develop and set up [19].

Neutrophils are an basic portion of the intrinsic safe framework. They drive the start of aggravation and are ensnared as arbiters of tissue-destructive occasions in different provocative maladies as already checked on [54, 55]. In a later ponder, histological discoveries of skin injuries in 44 cases of bullous scabies uncovered neutrophils as the overwhelming fiery cell invades [56]. In another comparative consider, 25 skin biopsies gotten from scabies patients appeared the nearness of dermal neutrophils in 52% of cases [31]. Neutrophils have too been identified in fiery penetrates within the skin of common wombats, sheep and ruddy foxes contaminated with S. scabiei [34, 48, 57]. In an in vitro think about utilizing human entire blood, with Staphylococcus aureus, the recombinant S. scabiei bug protein SMSB4 was found to smother bacterial murdering by restraining opsonisation and phagocytosis by neutrophils [27].

Dendritic cells are among the primary skin antigen displaying cells to come into contact with antigens, relocate to depleting lymph hubs and handle the antigens for introduction to effector T cells which comes about in T cell separation and enactment. These cells are capable for pathologies in diseases, incendiary disarranges and have moreover been embroiled in balancing the adjust between insusceptibility and fringe resistance [58, 59]. Histological examination of the scabietic injuries of mutts have revealed infiltration of DCs within the skin epidermis [53] and DCs determined from human fringe blood mononuclear cells (PBMCs) have been appeared to discharge pro- inflammatory cytokines upon incitement with scabies vermin extricate [60]. This engagement of DCs, neutrophils and macrophages in scabies warrants advance examinations into their work, part and significance in resistant and incendiary reactions in scabies bug invasions.

## 4. Conclussion

In conclusion, improvement of immunodiagnostics, antibodies, and immunotherapeutic speaks to a promising long-term technique to control scabies in influenced communities all inclusive. A comprehensive understanding of the resistant occasions within the skin and fringe blood happening amid scabies may give numerous focuses at which immunological mediations may meet the disease and target the reactions absent from pathology to insusceptibility.

#### **Conflicts of Interest**

The author declares no conflict of interest. The funding sponsors had no role in the writing of the manuscript and in the decision to publish it.

## REFERENCES

- [1] Hicks MI, Elston DM. Scabies. *Dermatol Ther*. 2009;**22**(4):279–292. doi: 10.1111/j.1529 8019.2009.01243.x. [PubMed] [CrossRef] [Google Scholar]
- [2] Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *J Invest Dermatol.*
- 2014;**134**(6):1527–1534. doi: 10.1038/jid.2013.446. [PubMed] [CrossRef] [Google Scholar]
- [3] Romani L, Steer AC, Whitfeld MJ, Kaldor JM. Prevalence of scabies and impetigo worldwide: a systematic review. Lancet Infect Dis. 2015;15(8):960–967. doi: 10.1016/S1473- 3099(15)00132-2. [PubMed]
   [CrossRef] [Google Scholar]
- [4] Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. *Lancet.* 2012;**380**(9859):2197–2223. doi: 10.1016/S0140-6736(12)61689-4. [PubMed] [CrossRef] [Google Scholar]
- [5] Hoy WE, White AV, Dowling A, Sharma SK, Bloomfield H, Tipiloura BT, et al. Post-streptococcal glomerulonephritis is a strong risk factor for chronic kidney disease in later life. *Kidney Int.* 2012;81:1026–1032. doi: 10.1038/ki.2011.478. [PubMed] [CrossRef] [Google Scholar]
- [6] Engelman D, Kiang K, Chosidow O, McCarthy J, Fuller C, Lammie P, et al. Toward the global control of human scabies: introducing the international alliance for the control of scabies. *PLoS Negl Trop Dis.* 2013;7(8):e2167. doi: 10.1371/journal.pntd.0002167. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [7] Mellanby K. Transmission of scabies. Br Med J. 1941;2(4211):405–406. doi: 10.1136/bmj.2.4211.405. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [8] Wendel K, Rompalo A. Scabies and pediculosis pubis: an update of treatment regimens and general review. *Clin Infect Dis.* 2002;**35**(Suppl 2):S146–S151. doi: 10.1086/342102. [PubMed] [CrossRef] [Google Scholar]
- [9] McCarthy JS, Kemp DJ, Walton SF, Currie BJ. Scabies: more than just an irritation. *Postgrad Med J.* 2004;80(945):382–387. doi: 10.1136/pgmj.2003.014563. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [10] Walton SF, Currie BJ, Kemp DJ. A DNA fingerprinting system for the ectoparasite Sarcoptes scabiei. Mol Biochem Parasitol. 1997;85(2):187–196. doi: 10.1016/S0166-6851(96)02825-3. [PubMed] [CrossRef]
   [Google Scholar]
- [11] Mounsey KE, Murray HC, King M, Oprescu F. Retrospective analysis of institutional scabies outbreaks from 1984 to 2013: lessons learned and moving forward. *Epidemiol Infect.* 2016;144(11):2462–2471.doi: 10.1017/S0950268816000443. [PubMed][CrossRef] [Google Scholar]
- [12] Hulbert TV, Larsen RA. Hyperkeratotic (Norwegian) scabies with gram-negative bacteremia as the initial presentation of AIDS. *Clin Infect Dis.* 1992;14(5):1164–1165. doi: 10.1093/clinids/14.5.1164.
   [PubMed] [CrossRef] [Google Scholar]
- [13] Currie BJ, Carapetis JR. Skin infections and infestations in aboriginal communities in northern Australia. Australas J Dermatol. 2000;41(3):139–143. doi: 10.1046/j.1440- 0960.2000.00417.x. [PubMed] [CrossRef]
   [Google Scholar]
- [14] Roberts LJ, Huffam SE, Walton SF, Currie BJ. Crusted scabies: clinical and immunological findings in seventyeight patients and a review of the literature. J Inf Secur. 2005;50(5):375–381. [PubMed] [Google Scholar]
- [15] Einsiedel LJ, Pepperill C, Wilson K. Crusted scabies: a clinical marker of human T-lymphotropic virus type 1 infection in central Australia. *Med J Aust.* 2014;200(11):633–634. doi: 10.5694/mja14.00458.
   [PubMed] [CrossRef] [Google Scholar]
- [16] Youshock E, Glazer SD. Norwegian scabies in a renal transplant patient. JAMA. 1981;246(22):2608–2609. doi: 10.1001/jama.1981.03320220058027. [PubMed] [CrossRef] [Google Scholar]
- [17] Gogna NK, Lee KC, Howe DW. Norwegian scabies in Australian aborigines. Med J Aust. 1985;142(2):140-2. [PubMed]
- [18] Morgan MS, Arlian LG, Markey MP. Sarcoptes scabiei mites modulate gene expression in human skin equivalents. *PLoS One.* 2013;8(8):e71143. doi: 10.1371/journal.pone.0071143. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [19] Cote NM, Jaworski DC, Wasala NB, Morgan MS, Arlian LG. Identification and expression of macrophage migration inhibitory factor in Sarcoptes scabiei. *Exp Parasitol.* 2013;135(1):175–181. doi: 10.1016/j.exppara.2013.06.012. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [20] Walton SF. The immunology of susceptibility and resistance to scabies. *Parasite Immunol.* 2010;**32**(8):532–540. [PubMed] [Google Scholar]
- [21] Ricklin D, Hajishengallis G, Yang K, Lambris JD. Complement: a key system for immune surveillance and homeostasis. *Nat Immunol.* 2010;**11**(9):785–797. doi: 10.1038/ni.1923. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [22] Wikel SK. Acquired resistance to ticks: expression of resistance by C4-deficient guinea pigs. *Am J Trop Med Hyg.* 1979;**28**(3):586–590. doi: 10.4269/ajtmh.1979.28.586. [PubMed] [CrossRef] [Google Scholar]
- [23] Zipfel PF, Wurzner R, Skerka C. Complement evasion of pathogens: common strategies are shared by diverse<br/>organisms.Mol Immunol.2007;44(16):3850–3857.doi:

10.1016/j.molimm.2007.06.149. [PubMed] [CrossRef] [Google Scholar]

- [24] Walton SF, Beroukas D, Roberts-Thomson P, Currie BJ. New insights into disease pathogenesis in crusted (Norwegian) scabies: the skin immune response in crusted scabies. Br J Dermatol. 2008;158(6):1247– 1255. doi: 10.1111/j.1365-2133.2008.08541.x. [PubMed] [CrossRef] [Google Scholar]
- [25] Janeway CAJ, Travers P, Walport M, Shlomchik MJ. The complement system and innate immunity. In: Sarah G, editor. *Immunobiology: the immune system in health and disease*. New York: Garland Science; 2001. [Google Scholar]
- [26] Mika A, Reynolds SL, Pickering D, McMillan D, Sriprakash KS, Kemp DJ, Fischer K. Complement inhibitors from scabies mites promote streptococcal growth - a novel mechanism in infected epidermis? *PLoS Negl Trop Dis.* 2012;6(7):e1563.doi: 10.1371/journal.pntd.0001563. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [27] Swe PM, Fischer K. A scabies mite serpin interferes with complement-mediated neutrophil functions and promotes staphylococcal growth. *PLoS Negl Trop Dis.* 2014;8(6):e2928. doi: 10.1371/journal.pntd.0002928.
   [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [28] Holt DC, Fischer K. Novel insights into an old disease: recent developments in scabies mite biology. *Curr Opin Infect Dis.* 2013;26(2):110–115. doi: 10.1097/QCO.0b013e32835eb986. [PubMed] [CrossRef] [Google Scholar]
- [29] Swe PM, Zakrzewski M, Kelly A, Krause L, Fischer K. Scabies mites alter the skin microbiome and promote growth of opportunistic pathogens in a porcine model. *PLoS Negl Trop Dis.* 2014;8(5) doi: 10.1371/journal.pntd.0002897. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [30] Prussin C, Metcalfe DD. IgE, mast cells, basophils, and eosinophils. J Allergy Clin Immunol. 2006;117(Suppl 2 Mini-Primer):S450–S456. doi: 10.1016/j.jaci.2005.11.016. [PubMed] [CrossRef] [Google Scholar]
- [31] Elwood H, Berry RS, Gardner JM, Shalin SC. Superficial fibrin thrombi ... and other findings: a review of the histopathology of human scabetic infections. *J Cutan Pathol.* 2015;42(5):346–352. doi: 10.1111/cup.12482.
   [PubMed] [CrossRef] [Google Scholar]
- [32] van den Broek AH, Huntley JF, MacHell J, Taylor M, Bates P, Groves B, Miller HR. Cutaneous and systemic responses during primary and challenge infestations of sheep with the sheep scab mite, Psoroptes ovis. *Parasite Immunol.* 2000;22(8):407–414. doi: 10.1046/j.1365-3024.2000.00318.x. [PubMed] [CrossRef]
   [Google Scholar]
- [33] Sarre C, Gonzalez-Hernandez A, Van Coppernolle S, Grit R, Grauwet K, Van Meulder F, et al. Comparative immune responses against Psoroptes ovis in two cattle breeds with different susceptibility to mange. *Vet Res.* 2015;46:131. doi: 10.1186/s13567-015-0277- x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [34] Little SE, Davidson WR, Rakich PM, Nixon TL, Bounous DI, Nettles VF. Responses of red foxes to first and second infection with Sarcoptes scabiei. J Wildl Dis. 1998;34(3):600–611. doi: 10.7589/0090-3558-34.3.600.
   [PubMed] [CrossRef] [Google Scholar]
- [35] Walton SF, Pizzutto S, Slender A, Viberg L, Holt D, Hales BJ, et al. Increased allergic immune response to Sarcoptes scabiei antigens in crusted versus ordinary scabies. *Clin Vaccine Immunol.* 2010;**17**(9):1428– 1438. doi: 10.1128/CVI.00195-10. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [36] Hamelmann E, Gelfand EW. IL-5-induced airway eosinophilia the key to asthma? Immunol Rev. 2001;179:182– 91. [PubMed]
- [37] Voehringer D, Reese TA, Huang X, Shinkai K, Locksley RM. Type 2 immunity is controlled by IL- 4/IL-13 expression in hematopoietic non-eosinophil cells of the innate immune system. J Exp Med. 2006;203(6):1435–1446. doi: 10.1084/jem.20052448. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [38] Cadman ET, Lawrence RA. Granulocytes: effector cells or immunomodulators in the immune response to helminth infection? *Parasite Immunol.* 2010;**32**(1):1–19. doi: 10.1111/j.1365- 3024.2009.01147.x. [PubMed] [CrossRef] [Google Scholar]
- [39] Jacobsen EA, Taranova AG, Lee NA, Lee JJ. Eosinophils: singularly destructive effector cells or purveyors of immunoregulation? J Allergy Clin Immunol. 2007;119(6):1313–1320. doi: 10.1016/j.jaci.2007.03.043.
   [PubMed] [CrossRef] [Google Scholar]
- [40] Lamkhioued B, Gounni AS, Aldebert D, Delaporte E, Prin L, Capron A, Capron M. Synthesis of type 1 (IFN gamma) and type 2 (IL-4, IL-5, and IL-10) cytokines by human eosinophils. Ann NY Acad Sci. 1996;796:203–8. [PubMed]
- [41] Nagase H, Okugawa S, Ota Y, Yamaguchi M, Tomizawa H, Matsushima K, et al. Expression and function of toll-like receptors in eosinophils: activation by toll-like receptor 7 ligand. *J Immunol.* 2003;**171**(8):3977–3982. doi: 10.4049/jimmunol.171.8.3977. [PubMed] [CrossRef] [Google Scholar]
- [42] Boyman O, Sprent J. The role of interleukin-2 during homeostasis and activation of the immune system. Nat Rev Immunol. 2012;12(3):180–190. [PubMed] [Google Scholar]
- [43] Ohno I, Nitta Y, Yamauchi K, Hoshi H, Honma M, Woolley K, et al. Transforming growth factor beta 1 (TGF beta 1) gene expression by eosinophils in asthmatic airway inflammation. *Am J Respir Cell Mol Biol.* 996;15(3):404–409. doi: 10.1165/ajrcmb.15.3.8810646. [PubMed] [CrossRef] [Google Scholar]
- [44] Amer M, Mostafa FF, Nasr AN, el-Harras M. The role of mast cells in treatment of scabies. Int J Dermatol. 1995;34(3):186–189. doi: 10.1111/j.1365-4362.1995.tb01564.x. [PubMed] [CrossRef] [Google Scholar]
- [45] Ito Y, Satoh T, Takayama K, Miyagishi C, Walls AF, Yokozeki H. Basophil recruitment and activation

in

inflammatory skin diseases. *Allergy*. 2011;**66**(8):1107–1113. doi: 10.1111/j.1398-9995.2011.02570.x. [PubMed] [CrossRef] [Google Scholar]

- [46] Mounsey KE, Murray HC, Bielefeldt-Ohmann H, Pasay C, Holt DC, Currie BJ, et al. Prospective study in a porcine model of sarcoptes scabiei indicates the association of Th2 and Th17 pathways with the clinical severity of scabies. *PLoS Negl Trop* Dis. 2015;9(3):e0003498. doi: 10.1371/journal.pntd.0003498. [PMC free article]
  [PubMed] [CrossRef] [Google Scholar]
- [47] Nimmervoll H, Hoby S, Robert N, Lommano E, Welle M, Ryser-Degiorgis MP. Pathology of sarcoptic mange in red foxes (Vulpes vulpes): macroscopic and histologic characterization of three disease stages. *J Wildl Dis.* 2013;**49**(1):91–102. doi: 10.7589/2010-11-316. [PubMed] [CrossRef] [Google Scholar]
- [48] Skerratt LF. Cellular response in the dermis of common wombats (Vombatus ursinus) infected with Sarcoptes scabiei var. wombati. *J Wildl Dis.* 2003;**39**(1):193–202. doi: 10.7589/0090-3558- 39.1.193. [PubMed] [CrossRef] [Google Scholar]
- [49] Schroeder JT. Basophils: emerging roles in the pathogenesis of allergic disease. *Immunol Rev.* 2011;**242**(1):144–160. doi: 10.1111/j.1600-065X.2011.01023.x. [PubMed] [CrossRef] [Google Scholar]
- [50] Brombacher F. The role of interleukin-13 in infectious diseases and allergy. *BioEssays*. 2000;**22**(7):646–656. doi: 10.1002/1521-1878(200007)22:7<646::AID- BIES7>3.0.CO;2-9. [PubMed] [CrossRef] [Google Scholar]
- [51] Abd El-Aal AA, Hassan MA, Gawdat HI, Ali MA, Barakat M. Immunomodulatory impression of anti and proinflammatory cytokines in relation to humoral immunity in human scabies. *Int J Immunopathol Pharmacol.* 2016;**29**(2):188–194. doi: 10.1177/0394632015627464. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [52] Arlian LG, Rapp CM, Stemmer BL, Morgan MS, Moore PF. Characterization of lymphocyte subtypes in scabietic skin lesions of naive and sensitized dogs. *Vet Parasitol*. 1997;**68**(4):347–358. doi: 10.1016/S0304-4017(96)01093-X. [PubMed] [CrossRef] [Google Scholar]
- [53] Stemmer BL, Arlian LG, Morgan MS, Rapp CM, Moore PF. Characterization of antigen presenting cells and T-cells in progressing scabietic skin lesions. *Vet Parasitol.* 1996;**67**(3–4):247–258. doi: 10.1016/S0304-4017(96)01038-2. [PubMed] [CrossRef] [Google Scholar]
- [54] Barrett NA, Austen KF. Innate cells and T helper 2 cell immunity in airway inflammation. *Immunity*. 2009;**31**(3):425–437. doi: 10.1016/j.immuni.2009.08.014. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [55] Hahn J, Knopf J, Maueroder C, Kienhofer D, Leppkes M, Herrmann M. Neutrophils and neutrophil extracellular traps orchestrate initiation and resolution of inflammation. *Clin Exp Rheumatol.* 2016;**34**(4 Suppl 98):6–8. [PubMed] [Google Scholar]
- [56] Luo DQ, Huang MX, Liu JH, Tang W, Zhao YK, Sarkar R. Bullous scabies. *Am J Trop Med Hyg.* 2016;**95**(3):689–693. doi: 10.4269/ajtmh.16-0273. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [57] Dagleish MP, Ali Q, Powell RK, Butz D, Woodford MH. Fatal Sarcoptes scabiei infection of blue sheep (Pseudois nayaur) in Pakistan. *J Wildl Dis.* 2007;**43**(3):512–517. doi: 10.7589/0090-3558- 43.3.512. [PubMed] [CrossRef] [Google Scholar]
- [58] Hunger RE, Sieling PA, Ochoa MT, Sugaya M, Burdick AE, Rea TH, et al. Langerhans cells utilize CD1a and langerin to efficiently present nonpeptide antigens to T cells. J Clin Invest. 2004;13(5):701–708. doi: 10.1172/JCI200419655. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [59] Loser K, Beissert S. Dendritic cells and T cells in the regulation of cutaneous immunity. *Adv Dermatol.* 2007;**23**:307–333. doi: 10.1016/j.yadr.2007.07.014. [PubMed] [CrossRef] [Google Scholar]
- [60] Arlian LG, Morgan MS, Neal JS. Extracts of scabies mites (Sarcoptidae: Sarcoptes scabiei) modulate cytokine expression by human peripheral blood mononuclear cells and dendritic cells. *J Med Entomol.* 2004;41(1):69–73. doi: 10.1603/0022-2585-41.1.69. [PubMed] [CrossRef] [Google Scholar]