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REVIEW

Acupuncture's Immunomodulatory Effects on Macrophages in Allergic Disorders: A Systematic Review

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Abstract: The incidence of allergic diseases has been increasing annually, severely affecting the quality of life of patients. With the growing recognition of traditional medicine, acupuncture, an ancient Chinese therapeutic method, has gradually gained attention for its potential in immune modulation. Studies have shown that macrophages play a crucial role in the development of allergic diseases, and acupuncture may influence allergic reactions by modulating the function of macrophages. This article aims to systematically evaluate the regulatory effects of acupuncture on macrophages in allergic diseases and the corresponding mechanisms. It analyzes existing research findings and explores the clinical application prospects of acupuncture in this context. By understanding how acupuncture affects the activation, secretion, and role of macrophages in immune responses, we hope to provide new insights and directions for the treatment of allergic diseases.

Keywords: acupuncture, macrophages, allergic diseases, immune regulation, allergic asthma, allergic rhinitis, allergic skin diseases

Introduction

Allergic diseases refer to a group of conditions caused by an abnormal immune response to typically harmless substances, such as pollen, food, and others. These diseases mainly include allergic rhinitis, asthma, atopic dermatitis, and so on.[1–3] The pathogenesis of these diseases is typically associated with immune system dysregulation, genetic factors, and environmental influences. According to global epidemiological data on allergic diseases, their incidence has significantly increased in recent years, particularly among children and adolescents.[4,5] For example, in Western countries, the prevalence of allergic rhinitis has reached 20% to 30%, while the prevalence of asthma continues to rise.[6–8] This trend poses a major challenge to public health and underscores the urgent need for new and effective treatment options.[8,9]

Traditional treatment methods for allergic diseases mainly include pharmacological therapy and immunotherapy.[10–12] Pharmacological treatment typically involves antihistamines, corticosteroids, and other medications, but these drugs often only alleviate symptoms without curing the disease, and they may be associated with certain side effects.[13,14] Furthermore, although immunotherapy has shown good efficacy in some patients, the treatment process is lengthy and carries the risk of allergic reactions, which can affect patient compliance.[6,15] Therefore, the limitations of traditional treatment methods have prompted researchers to explore new therapeutic approaches to improve the quality of life for patients with allergic diseases.[16]

Acupuncture, as a traditional Chinese medicine therapy, has gained attention in recent years for its application in immune regulation.[17,18] Studies have shown that acupuncture can positively influence allergic diseases by modulating the function of macrophages and promoting immune system balance.[19] Specifically, acupuncture can improve allergic reactions by downregulating pro-inflammatory M1-type macrophages and upregulating anti-inflammatory M2-type

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macrophages.[20] This regulatory effect may be achieved by influencing the interactions between the neuroendocrine and immune systems, offering new insights into the treatment of allergic diseases.[21,22]

This review aims to explore the role of acupuncture in regulating macrophages and its potential mechanisms in the treatment of allergic diseases. Through a systematic analysis of existing literature, we hope to provide theoretical support for the application of acupuncture in the treatment of allergic diseases and guide future research directions. The immune-regulatory effects of acupuncture not only offer new possibilities for the treatment of allergic diseases but also pave the way for the integration of traditional and modern medicine.

Method

Search Strategy

To identify published research, we conducted a comprehensive search of the PubMed and Embase databases, covering records up to December 2024. Our search strategy incorporated the following keyword sets: [“acupuncture” or “electro-acupuncture”], [“allergic disease” or “asthma” or “allergic rhinitis” or “dermatitis” or “urticaria”], [“macrophages”]. We restricted the search to English - language publications. Initial screening was carried out using the search engines provided by the respective databases. After eliminating 734 duplicate records, we identified 6692 relevant articles.

Study Selection

Before reading the full text of a given paper, we manually select references that are relevant to the topic using Excel software. Among them, 251 articles lacked full text abstracts, 1132 articles unrelated to acupuncture and allergic disease, 1982 reviews or meta-analysis, 1682 clinical research articles, and 529 articles related to acupuncture combined with other therapies. Finally, 382 full-text basic research papers that are relevant to the topic were included. The flowchart of the search process is shown in Figure 1.

Data Extraction

Given the overlapping nature of several studies, we adopted a targeted approach. We selected typical published works and extracted key data on how acupuncture and moxibustion treat allergic diseases via macrophage regulation. To ensure systematic and accurate data collection, we employed a predefined data extraction table This table was structured to categorize data into specific fields: the type of allergic disease, intervention details (including treatment methods, acupoints selected, and acupuncture and moxibustion parameters), and outcome measurements (covering inflammation - related behaviors and mechanism - specific indicators). Prior to analyzing the therapeutic effects and underlying mechanisms of acupuncture and moxibustion in allergic diseases, one author was tasked with data extraction. Subsequently, other authors cross - checked the extracted data to maintain data integrity and reliability.

Immune Mechanism of Allergic Diseases

Allergic diseases are caused by the immune system’s abnormal response to external substances, commonly known as allergens. The mechanisms involved are complex interactions between immune cells and molecular signals.[23,24] In recent decades, with the rapid growth of the global economy, allergic diseases have become one of the most prevalent diseases in society,[25,26] with a significant increase in incidence in both developed and developing countries, particularly in developed nations.[27,28] The pathogenesis of allergic diseases has long been a focus of immunological research, as the occurrence of these diseases is closely related to the immune system.[29] The pathophysiology of allergic diseases primarily involves immunoglobulin E (IgE)-mediated inflammation and type 2 immune responses.[30] Th2 cells play a crucial role in the development of type 2 immune responses by releasing cytokines such as IL-4, IL-5, and IL-13.[31–33] Allergic reactions are generally classified into two types: immediate-type and delayed-type reactions.[34] Immediate-type reactions are primarily IgE-mediated and involve the activation of mast cells and eosinophils, leading to tissue swelling, redness, and other allergic symptoms.[35] Delayed-type reactions, on the other hand, are mainly T cell-mediated and typically occur hours to days after exposure to the allergen.[36] Recent studies have shown that various cell types in the immune system, such as dendritic cells, T cells, and B cells, play important roles in allergic reactions.[37]

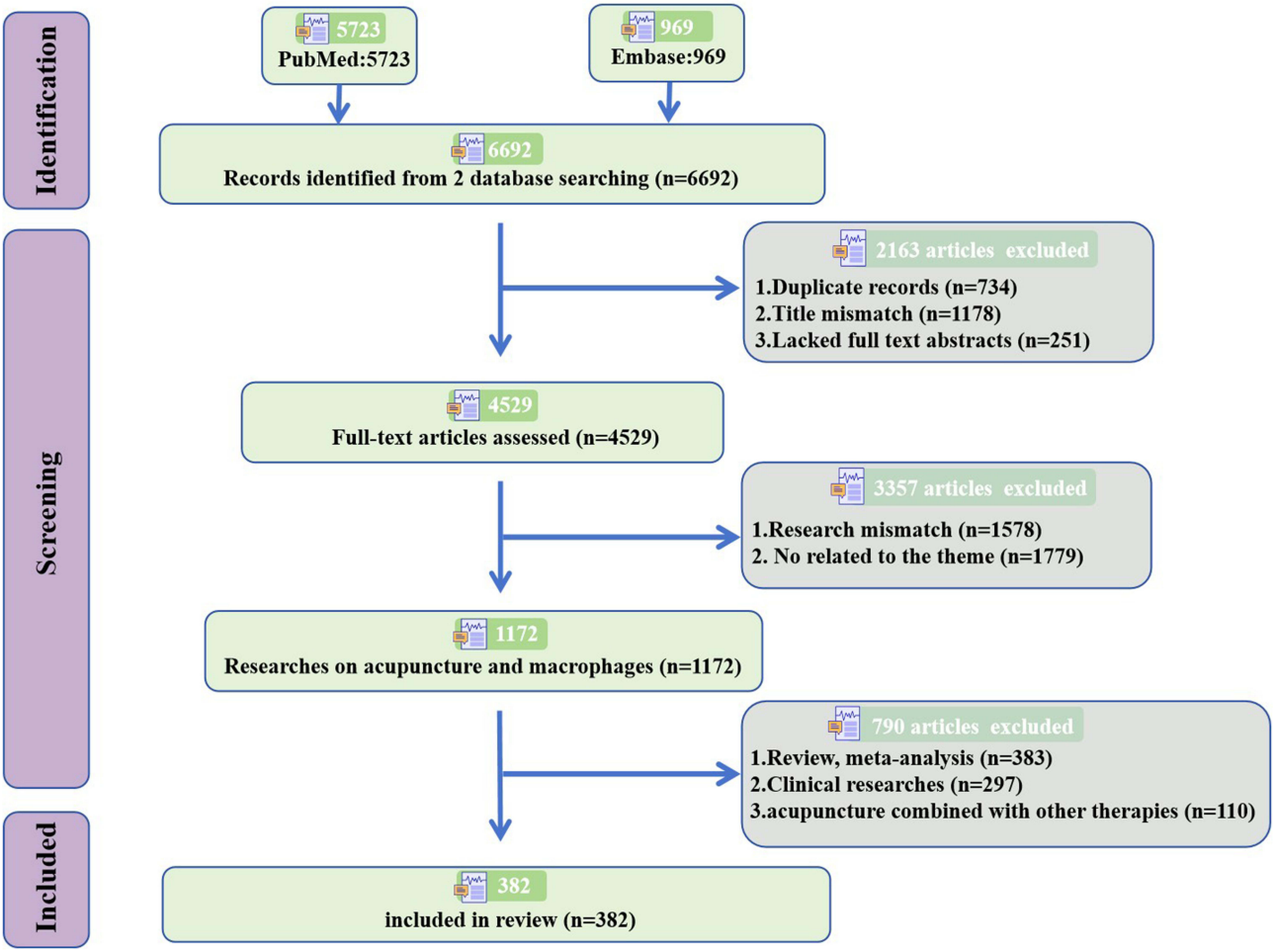

Figure 1 Flow chart of the search strategy and process.

The basic process of an allergic reaction can be divided into two stages: the initial contact and the subsequent re-exposure. In the initial contact phase, allergens are captured by dendritic cells and presented to T cells, promoting their differentiation into Th2 cells.[38] The Th2 cells then secrete cytokines such as IL-4, IL-5, and IL-13, which stimulate B cells to produce IgE antibodies.[39–41] IgE antibodies bind to mast cells, sensitizing them for re-exposure to the same allergen.[42] In the re-exposure phase, when the allergen enters the body again, mast cells release mediators such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and leukotrienes, which recruit and enhance the function of other immune cells, such as macrophages and dendritic cells, thereby establishing a link between innate and adaptive immunity.[43,44] The bound IgE triggers mast cells to release inflammatory mediators, including histamine, proteases, and tryptase, leading to the allergic response.[45–47] The regulation of this process involves the interplay of various cytokines and signaling pathways, with IL-4 and IL-13 playing a key role in promoting IgE synthesis and the activation of eosinophils.[37,39,48]

Macrophages are essential immune cells, present in almost every tissue of the body.[49] Macrophages play a dual role in allergic diseases, both promoting and inhibiting the development of allergic reactions.[50] As key coordinators of immune responses, macrophages can be classified into M1 and M2 types based on their activation state.[51,52] M1 macrophages primarily produce pro-inflammatory cytokines such as TNF-α and IL-6, contributing to the inflammatory response.[53] In inflammatory diseases, M1 macrophages can recruit eosinophils, neutrophils, and monocytes, and activate effector Th cells, leading to the production of mediators such as TNF-α, IL-1β, and MMPs, which cause lung structural cell damage and remodeling, further amplifying the inflammation.[54–58] Dysfunctional exocytosis results in the persistent presence of necrotic cells in lung tissue, releasing damage signals that further enhance inflammation.[59] M2 macrophages are divided

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into three subtypes: M2a, M2b, and M2c.[60] M2a macrophages are induced by IL-4 and/or IL-13, secrete IL-10, enhance arginase-1 (Arg-1) expression, and play an important role in the anti-allergic inflammatory response and wound healing.[19] M2b macrophages are induced by immune complexes or Toll-like receptors, which increase the release of IL-10, TNF-α, IL-6, and IL-1β, inhibit acute inflammation induced by bacterial endotoxins, and promote tissue repair and regeneration.[53,61] M2c macrophages are induced by IL-10 and TGF-β, and produce a large amount of IL-10 and TGF-β to inhibit inflammation.[51,62] By releasing mediators such as IL-10 and TGF-β, M2 macrophages help restore lung structural integrity and reduce inflammation through the phagocytosis of apoptotic cells, thus promoting the resolution of inflammation.[63,64] In allergic diseases, M2a macrophages activate Th2 cells through CCL17- and MRC1-mediated production of IL-4 and IL-13, leading to the development of allergic asthma. M2b macrophages activate Treg cells through CCL24- and MRC1-mediated production of IL-10 and TGF-β, leading to the development of allergic tolerance and dampening inflammation.[63,65] Additionally, macrophages influence the strength and duration of allergic responses by modulating the function of other immune cells.[66] As shown in Figure 2. Studies suggest that the polarization state and function of macrophages play a crucial role in the onset and progression of allergic diseases, and therapeutic strategies targeting macrophages may provide a new direction for the management of allergic diseases in the future.[67]

Basic Principle and Mechanism of Acupuncture

Acupuncture, as a traditional Chinese medicine (TCM) therapy, has a history that dates back thousands of years. As early as around 1050 BC during the Zhou Dynasty, acupuncture was used to treat equine diseases, indicating a long-standing application of acupuncture in veterinary practices.[68] In the 20th century, especially between 1958 and 1960, the promotion and popularization of acupuncture were supported by national policies, making it an integral part of modern Chinese

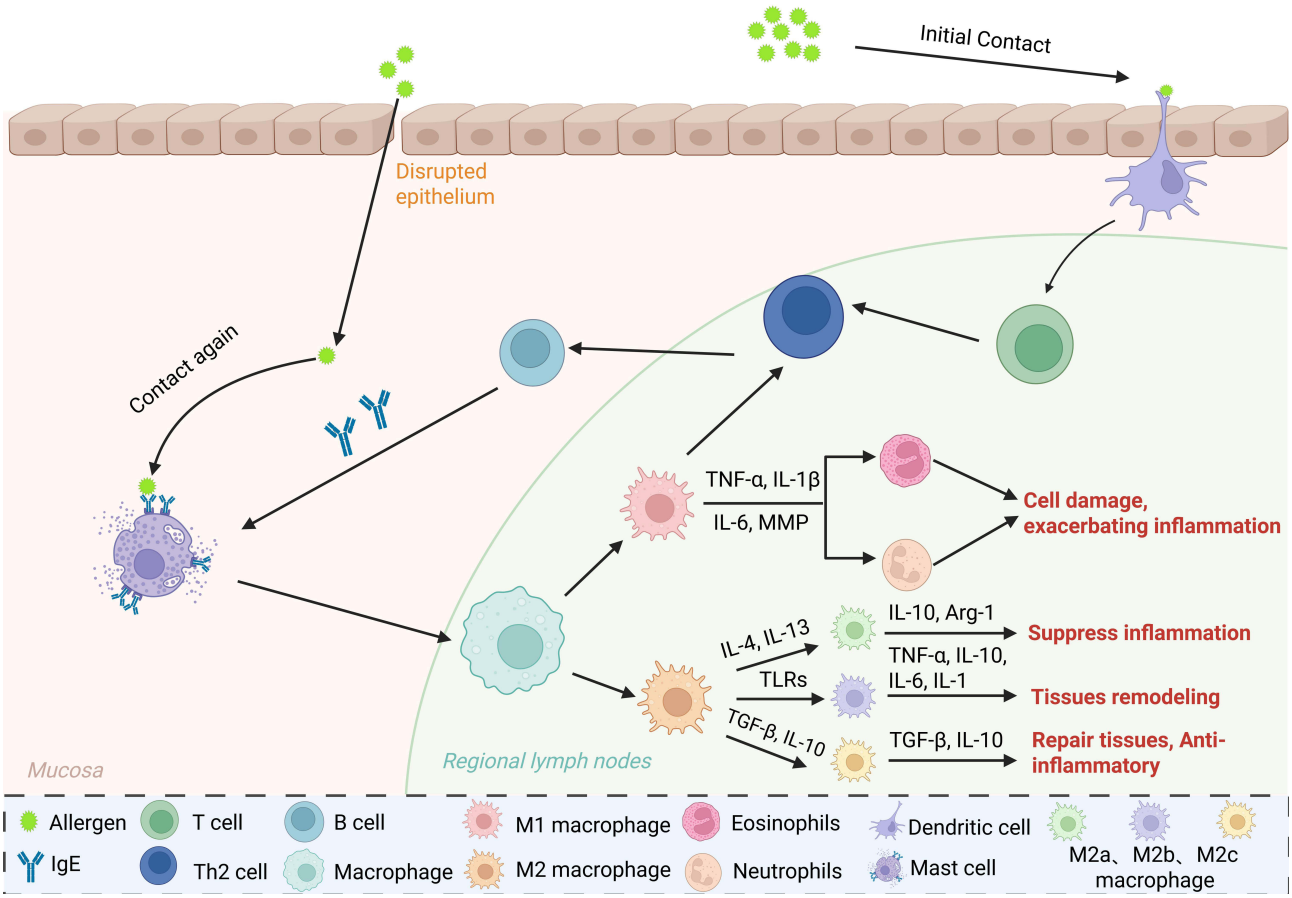

Figure 2 The mechanism of action of macrophages in allergic diseases. Created in BioRender. Zhangyu, X. (2025) https://BioRender.com/o89l798.

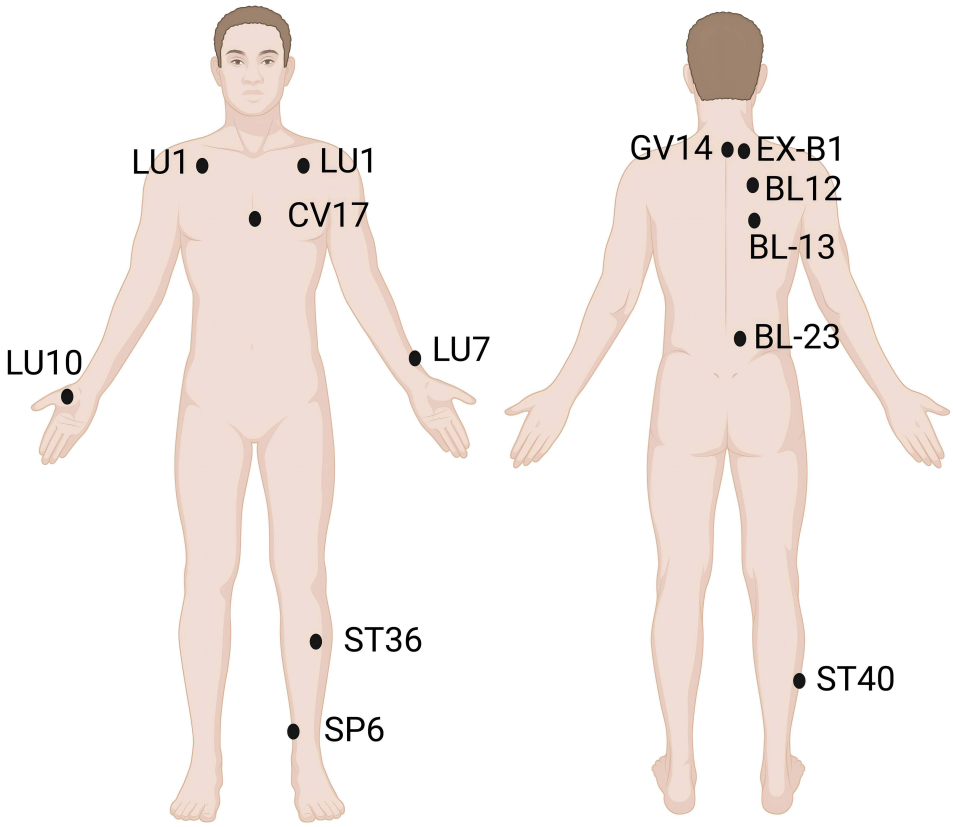

Figure 3 The commonly used acupoint map of acupuncture and moxibustion for treating allergic diseases. Created in BioRender. Lv, J. (2025) https://BioRender.com/qo5sr8c.

medicine.[69] Today, acupuncture is not only widely practiced in China but is also increasingly recognized and accepted worldwide, becoming an international therapeutic method. According to clinical reports,[70–72] the effective acupuncture points for treating allergic diseases include Dazhui (GV14), Danzhong (CV17), Feishui (BL13), Zhongfu (LU1), Zusanli (ST36), Dingchuan (EX-B1), Sanyinjiao (SP6), and Fengmen (BL12).[72] These points are primarily located along the lung meridian, conception vessel, stomach meridian, and bladder meridian, which is consistent with the findings from meta-analyses and clinical data in Chinese practice. In addition to the commonly used acupuncture points mentioned above, other supplementary points are also essential for alleviating allergic diseases, such as Yuji (LU10), Lieque (LU7), Fenglong (ST40), and Fuliu (KI7).[73–75] These points are mainly distributed in the back region and the limbs of the body (Figure 3).

The impact of acupuncture on the immune system has become a hot research topic in recent years. Studies have shown that acupuncture can regulate immune responses to maintain immune homeostasis, thereby influencing the occurrence and progression of various diseases. Acupuncture at ST36 and SP6 with 11 EA has been shown to promote the proliferation and differentiation of regulatory T cells (Treg) in the spleen of CFA rats, leading to increased expression of the anti-inflammatory cytokine IL-10 in the local hind paw and spinal cord tissues. This, in turn, inhibits macrophages and neutrophils, reducing the secretion of IL-1β, NOD-like receptor protein 3 (NLRP3), and TNF-α.[76] Furthermore, in immune-suppressive diseases such as cancer, acupuncture has been found to enhance the body's immune function, promoting the activity of natural killer (NK) cells and CD8+ T cells.[77] In contrast, in autoimmune diseases such as rheumatoid arthritis, acupuncture has shown immune-suppressive effects, helping to restore normal immune tolerance.[77] Notably, acupuncture also affects the body's stress response and endocrine system by modulating the hypothalamic-pituitary-adrenal (HPA) axis, thereby indirectly regulating immune function.[78] These mechanisms suggest that acupuncture is not only a local therapeutic approach but also a comprehensive therapy that can systematically regulate the body's immune function, offering broad clinical applications.

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Regulation of Acupuncture on Macrophage Function

Acupuncture, as a traditional Chinese therapeutic approach, has been shown to exert its anti-inflammatory effects by modulating the polarization of macrophages.[79] Studies have demonstrated that acupuncture promotes the transition of macrophages from the pro-inflammatory M1 phenotype to the anti-inflammatory M2 phenotype, a process that is crucial for alleviating inflammation and promoting tissue repair.[20] Specifically, acupuncture stimulation can activate the NF-κB and MAPK signaling pathways, inhibiting the production of pro-inflammatory cytokines, thereby reducing the number of M1 macrophages and increasing the proportion of M2 macrophages.[80] Furthermore, acupuncture has been found to regulate the macrophage microenvironment, facilitating the conversion to an anti-inflammatory phenotype, which has shown positive effects in the treatment of various chronic inflammatory and autoimmune diseases.[81] By regulating macrophage polarization, acupuncture not only improves local inflammatory responses but also enhances systemic immune function, offering new insights and approaches for clinical treatment.

Acupuncture also exerts a significant regulatory effect on the secretory function of macrophages. Research has shown that acupuncture can promote the secretion of various anti-inflammatory cytokines by macrophages, such as IL-10 and TGF-β, which play crucial roles in suppressing inflammation and promoting tissue healing.[82] In addition, acupuncture can reduce the levels of pro-inflammatory factors (such as TNF-α and IL-1β) secreted by M1 macrophages, thereby alleviating inflammation.[83] In this way, acupuncture not only improves the inflammatory state of local tissues but also regulates immune responses systemically, enhancing the body's resistance to external stimuli.[84] This regulatory mechanism of macrophage secretion provides scientific evidence for the application of acupuncture in the treatment of various inflammatory diseases, highlighting its potential as an effective adjunctive therapeutic approach.

Research on the Application of Acupuncture in Allergic Diseases

Analysis of Therapeutic Effect of Acupuncture on Asthma

In recent years, acupuncture, as a traditional Chinese medical treatment, has gained increasing attention in the management of asthma. Several clinical studies have demonstrated that acupuncture can effectively improve symptoms in asthma patients and enhance their quality of life. For example, a systematic review on cough-variant asthma showed that acupuncture treatment significantly improved clinical efficacy, alleviated symptoms such as cough, sputum production, and shortness of breath, and improved lung function-related parameters.[85] Moreover, acupuncture's positive effects on immune-inflammatory markers have also been confirmed, suggesting that it may exert its therapeutic effects by modulating immune responses.[86] We have collected relevant animal model studies on acupuncture treatment for asthma, as shown in Table 1. These animal models indicate that stimulation of GV14, BL12, and BL13 can reduce the expression of various cytokines such as IL-4, IL-5, and IL-13.[87,88] Furthermore, studies on existing asthma animal models suggest that the therapeutic effect of acupuncture in asthma is due to the inhibition of various cytokines (IL-17, IL-25, IFN-γ) produced by airway smooth muscle cells and inflammatory cells, and this mechanism may be related to the downregulation of autophagy-related proteins (ATG5, Beclin-1, p62, LC3B).[3,89] However, the current research quality is inconsistent, and many studies suffer from issues such as poor design and small sample sizes. Therefore, more high-quality randomized controlled trials are needed to verify the long-term effects and safety of acupuncture in the treatment of asthma.[90]

Analysis of Therapeutic Effect of Acupuncture on Allergic Rhinitis

Allergic rhinitis is a common allergic disease, and traditional treatment methods often rely on medications. However, acupuncture, as a non-pharmacological treatment, has gradually been applied in the management of allergic rhinitis. Studies on various acupuncture techniques for the treatment of allergic asthma are summarized in Table 2. Multiple clinical studies have shown that acupuncture can not only effectively alleviate nasal symptoms of allergic rhinitis, such as nasal congestion, rhinorrhea, and sneezing, but also significantly reduce the levels of inflammatory markers such as IL-4, IL-6, IL-8, and TNF-α[97,98] A systematic review indicated that the acupuncture treatment group significantly outperformed the control group in both nasal symptom scores and quality of life.[99] Furthermore, different forms of acupuncture treatment, such as auricular acupuncture and warm acupuncture, also demonstrated good therapeutic effects with fewer side effects.[100] In animal models of allergic rhinitis, acupuncture was shown to alleviate symptoms of allergic rhinitis in

Table 1 Research and Mechanism of Acupuncture Treatment for Asthma

Reference	Model	Interventions	Acupoints	Acupuncture Parameters	Cytokine	Results
Yu, 2023[87]	Rats	MA	GV14, BL12, BL13	Once every other day	p-p38MAPK↓	Inhibit the proliferation of ASMCs
Tang, 2023[88]	Mouse	MA	GV14, BL12, BL13	Once a day for 3 days	IL-4↓, IL-13↓, MDA↓, ACSL4-15-LO1↓	Acupuncture alleviated the deterioration of pulmonary inflammation and lipid peroxidation in iron death induced by erastin.
Zhao, 2021[89]	Mouse	MA	GV14, BL13, ST36	Every other day for 13 days	ATG5↓, Beclin-1↓, p62↓, LC3B↓, p-PERK↓, p-IRE-1↓, Grp78↓, ATF6↓, IFN-γ↑, IL-4↓, IL-17↓, TGF-β↓	Regulating endoplasmic reticulum stress and CD4+T lymphocyte differentiation by inhibiting ATG5 mediated autophagy, thereby reducing airway inflammation and AHR in asthma.
Cui,2020[91]	Rats	MA	GV14, BL12, BL13	Twisted 360°, 60 times/min, 5 times, 20 min	IL-5↓, IL-9↓, IL-13↓, IL-25↓, IL- 33↓, sST2↑	The inhibition of acupuncture on ILC2 may be related to the IL-33/ST2 signaling pathway and the level of IL-25, thus preventing asthma related airway inflammation.
Dong, 2019[3]	Rats	MA	GV14, BL12, BL13	30 min x3/week for 4 weeks.	IL-10↑, IL-5↓, IL- 13↓, IL-17↓, p-p38↓, p-p44/ 42↓	Acupuncture can alleviate allergic airway inflammation by enhancing the activities of Th1 and Treg, thus regulating the balance of CD4+T cell subtypes in experimental asthma mice.
Dong, 2018[92]	Rats	MA	GV14, BL12, BL13	Manual manipulations every 10 min in 30 min	TNF-α↓, IL-1β↓, IL-33↓, sST2↑	Acupuncture can effectively protect lung function and reduce airway inflammation in OVA induced asthma mouse model.
Nurwati, 2018[93]	Rats	MA	BL13, ST36	15 min x3/ week, 6 weeks from 21st day after modeling	Neutrophil↓, Eosinophil↓	Acupuncture can reduce inflammatory reaction and prevent airway remodeling in chronic asthma mouse model.
Liu, 2018[94]	Rats	MA	BL13	3 weeks	ChAT↓, AchE↑, mAchRs M1-M3↑	Acupuncture may treat allergic asthma by inhibiting the synthesis and release of Ach signal
Wei, 2015[95]	Mouse	MA	GV14, BL13, BL12	Every other day for 4 weeks	IL-17A↓, IL-17F↓, IL-22↓, IgE↓,IL-17R↓, RORγt↓, p65↓, IKKα↓	Acupuncture may treat asthma by regulating Th17, Treg activity and NF - κ B pathway
Carneiro, 2010[96]	Rats	EA	GV14, BL13, EX-B1, LU1, CV17, ST36, SP6	Every other day for 2 weeks	IL-1↑, IFN-γ↑, IL-4↑, NO↓, IL-10↓, LTB↓	The beneficial anti-inflammatory effect of EA on asthma is related to the balance of Th1/Th2 response and the reduction of LTB4 and NO.

Abbreviations: MA, Manual acupuncture; EA, Electroacupuncture; EX-HN9, Neiyingxiang; GV 14, Dazhui; BL 12, Bilateral Fengmen; BL 13, Feishu; ST36, Zusanli; EX-B1, Dingchuan; LU1, Zhongfu; SP6, Sanyinjiao; CV17, Danzhong; ChAT, Synthetase; Ach, Acetylcholine; AchE, Ach hydrolase; mAchRs, Muscarinic receptors; IKKα, NF-κB kinase-α; ASMCs, Airway smooth muscle cells.

rats and suppress nasal mucosal inflammation. This may be associated with the inhibition of TLR4/MyD88/NF-κB signaling, the balance of Th1/Th2 and Treg/Th17 cytokine levels, as well as the regulation of T-bet/GATA-3 expression.[101] However, existing studies generally have small sample sizes and lack standardized treatment protocols. Therefore, larger-scale, multicenter clinical trials are needed in the future to further validate the effectiveness and safety of acupuncture in the treatment of allergic rhinitis.[102]

Table 2 Research and Mechanism of Acupuncture Treatment for Allergic Rhinitis

Reference	Model	Interventions	Acupoints	Acupuncture Parameters	Cytokine	Results
Tian, 2024[101]	Rats	MA	BL13, BL23, DU14	10 days	IgE↓, OVA-sIgE↓, IL-4↓, IL-17↓, GATA-3↓, TLR4↓, MyD88↓, NF-κB↓, IFN-γ↑, IL-10↑	Acupuncture can alleviate the symptoms of allergic rhinitis in rats and inhibit the inflammation of nasal mucosa, which may be related to the inhibition of TLR4/MyD88/NF - κB signal transduction and the balance of Th1/Th2 and Treg/Th17 cytokine levels as well as T-bet/GATA-3.
Wang, 2023[103]	Human	MA	Xinwu, Xiaguan	2/week for 2 weeks	Histamine↓, IgE↓	Acupuncture at Xinwu acupoint combined with loratadine and fluticasone propionate can deliver a powerful efficacy on AR and alleviate the clinical symptoms, without increasing adverse reactions.
Liu, 2023[104]	Human	MA	EX-HN9, Biqiu	20 min x3/week for 2 weeks	——	Intranasal acupuncture has good efficacy and safety in the treatment of PAR. Acupuncture has a good effect on improving nasal congestion, olfactory function and sleep.
Sun, 2023[97]	Human	WA	MH-N-3, LI20, GB20, LI4, Baihui, Taiyang, Shangyingxiang	20 min x7/week	IgE↓, IL-6↓, IL-8↓, TNF-α↓	Warm needle therapy can effectively improve the clinical symptoms of AR patients with lung qi deficiency and cold type, reduce inflammation, and enhance immune function.
Gellrich, 2022[105]	Human	MA	LI4, LI11, LI20, MH-N-3, GB20, SP6, ST36, BL13	2/week for 4 weeks	IL-1b↓, IL-8↓, IP-10↓, MIP-1b↓, MCP-1↓	Acupuncture reduces the intranasal unspecific inflammation.
Li, 2022[98]	Human	MA, INA	EX-HN9, LI20, GV23, LI4, Biqiu	7/week for 2 weeks	IL-4↓, IL-6↓, IL-10↑	Acupuncture can effectively alleviate the symptoms of allergic rhinitis, and IA and moxibustion is more effective.
Gong, 2021[106]	Rabbits	INA	EX-HN9	20 min, once every other day for 7 days.	IL-4↓, IgE↓, IFN-γ↑	INA treatment can relieve symptoms of AR in AR rabbits.
Tu, 2020[107]	Rats	AAT	DU14, BL12, BL13, BL20	28 days	NGF↓, IL-4↓, IL-5↓, IL-13↓, IgE↓, IFN-γ↑	AAT can alleviate allergic inflammation by inhibiting the expression of NGF and its downstream pathways.
Yang, 2018[108]	Rats	CIAA	LI20, ST36	14 consecutive days	IL-4↓, IgE↓, IFN-γ↑	CIAA can effectively alleviate allergic symptoms and inflammatory parameters in AR rat models.

Abbreviations: MA, Manual acupuncture; WA, Warm Acupuncture; INA, intranasal acupuncture; AAT, Acupoint application therapy; CIAA, Catgut implantation at acupoint; LI11, Quchi; EX-HN9, Neiyingxiang; LI20, Yingxiang; MH-N-3, Yintang; GV23, Shangxing; GB20, Fenchi; LI4, Hegu; DU14, Dazhui; BL12, Fengmen; BL13, Feishu; BL20, Pishu; BL23, Shen shu; ST36, Zusanli; EX-B1, Dingchuan; SP6, Sanyinjiao; NGF, Nerve growth factor.

Efficacy Analysis of Acupuncture on Allergic Skin Diseases

Allergic skin diseases, such as atopic dermatitis and urticaria, significantly impact the quality of life of patients. Acupuncture has shown potential in the treatment of these conditions. Relevant studies on various acupuncture techniques for treating allergic skin diseases are summarized in Table 3. In an animal study of skin inflammation induced by 1-chloro-2,4-dinitrobenzene (DNCB), acupuncture at LI11 significantly inhibited skin hyperplasia, serum IgE levels, and the expression of pro-inflammatory cytokine (IL-4, IL-8, and TNF-α) mRNA, as well as NF-κB, ERK1/2, JNK, and p38 proteins.[109,110] Moreover, acupuncture can improve symptoms of allergic skin diseases by modulating the

Table 3 Research and Mechanism of Acupuncture Treatment for Allergic Skin Diseases

Reference	Disease type	Model	Interventions	Acupoints	Acupuncture Parameters	Cytokine	Results
Li, 2024[109]	Urticaria	Rats	EA	LI11, SP10	20 min x1/day for 10 days	IgE↓, HIS↓, 5-HT↓, NLRP3↓, ASC↓, IL-1β↓, IL-18↓, Caspase-1↓	EA pretreatment can prevent and treat UR by inhibiting inflammatory response, which is related to the regulation of pyroptosis.
Liu, 2023[113]	Urticaria	Rats	EA	LI11, SP10	20 min x7/week	IgE↓, Histamine↓, IL-33↓, ST2↓	EA pretreatment can prevent urticaria in rats, which may be related to its function of reducing IgE levels by inhibiting IL-33 and ST2.
Shi, 2023[114]	Chronic spontaneous urticaria	Human	MA	LI11, LI4, SP10, ST36, SP6, Zhongwan, Tianshu, Guanyuan, Yinlingquan,	Twisted 360°, 60 times/min, once every other day for 12 days.	IL-4↓, IgE↓, IFN-γ↑	Acupuncture can significantly alleviate the symptoms and negative emotions of patients, and improve their quality of life, sleep quality and balance of Th1/Th2 cytokines.
Zeng, 2022[110]	Atopic dermatitis	Mouse	A-AHT	ST36, LI11	Once every other day for 28 days	IL-4↓, IgE↓, IFN-γ↑, T-bet↑	A-AHT has shown significant effectiveness in AD model mice by regulating Th1/Th2 immune responses.
Zhang, 2020[115]	Urticaria	Rats	EA	ST36, LI11, SP10	20 min x7/week	NF-α↓, IL-6↓, p-ERK↓, JNK↓, p-JNK↓, p-P38MAPK↓	EA can reduce skin allergic reaction in rats with urticaria
Wang, 2017[116]	Allergic contact dermatitis	Rats	EA	ST36	1/week	IgE↓, p38 MAPK↓, IL-10↑	EA therapy may improve ACD related inflammation by triggering local IL-10 production and inhibiting p38 MAPK activation.
Park, 2013[117]	Atopic dermatitis	Mouse	MA	LI11	1/week	IgE↓, IL-4↓, IL-8↓, TNF-α↓, NF-κ B↓, ERK1/2↓, JNK↓, p38↓	Acupuncture can effectively alleviate allergic contact dermatitis by reducing proinflammatory cytokines and proteins.

Abbreviations: MA, Manual acupuncture; A-AHT, Acupoint autohemotherapy; AAT, Acupoint application therapy; LI11, Quchi; LI4, Hegu; ST36, Zusanli; SP6, Sanyinjiao; SP10, Xuehai.

immune response and alleviating inflammation. For instance, acupuncture has been shown to significantly reduce skin itching, erythema, and other symptoms, while also improving patients' quality of life.[111] Additionally, acupuncture is considered to be relatively safe with fewer side effects, making it a promising adjunctive therapy. However, current research on acupuncture for allergic skin diseases remains limited, with a lack of large-scale randomized controlled trials. Therefore, further high-quality studies are urgently needed to explore its mechanisms and clinical applications.[112]

Potential Mechanism of Acupuncture Regulating Macrophages

Modern medical research has confirmed that acupuncture and moxibustion, as a traditional therapy, has shown good clinical effects in treating allergic diseases by regulating the human immune system. As shown in Figure 4. T lymphocyte

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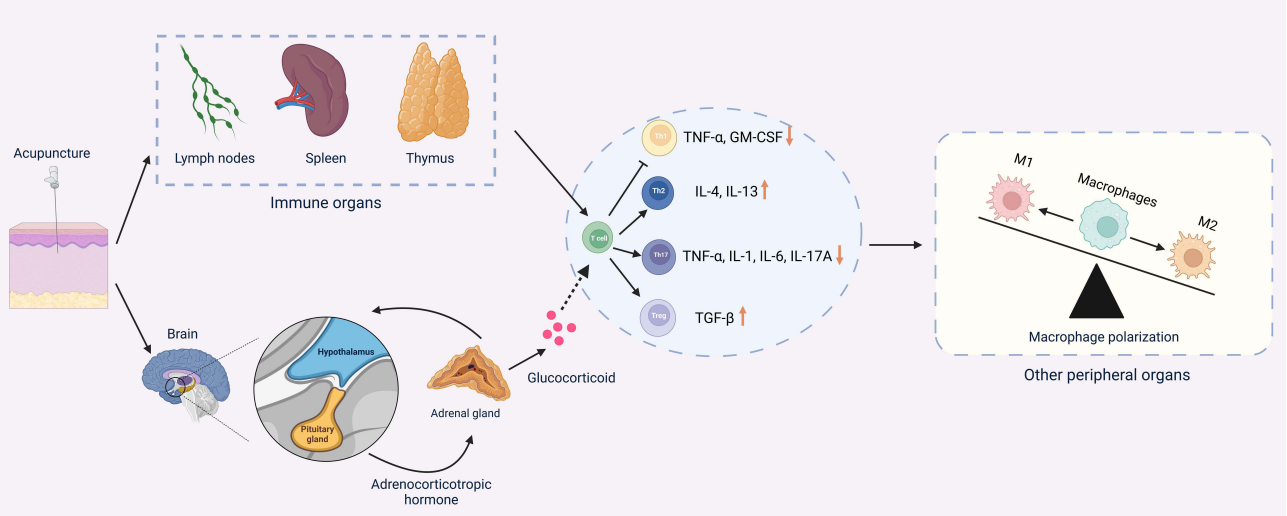

Figure 4 The mechanism of acupuncture regulating macrophage polarization in the treatment of allergic diseases. Created in BioRender. Zhangyu, X. (2025) https://BioRender.com/qlu34am.

subpopulations interact with each other in the body to maintain relatively normal immune function. In allergic diseases, typical helper T cells can polarize, recruit, activate, or differentiate macrophages.[118] Th1, Th2, Th17, and Treg are subpopulations of T cells with distinct functions. During the inflammatory process, Th1 cells produce cytokines, such as TNF-α and granulocyte-macrophage colony-stimulating factor, which mediate M1 macrophage polarization, while Th2 cytokines IL-4 and IL-13 drive macrophage polarization toward the M2 phenotype.[119] Th17-mediated cytokine IL-17A can induce elevated levels of IL-1, TNF-α, and IL-6.[120] Choo et al[121] found that an increase in Treg cell numbers leads to macrophage polarization towards the M2 phenotype, which results in ventricular remodeling. Research shows that acupuncture and moxibustion can improve the inflammatory state in allergic diseases by influencing the cytokine network and promoting the polarization of macrophages. For example, acupuncture can downregulate pro-inflammatory cytokines (such as TNF-α and IL-1β), while upregulating anti-inflammatory cytokines (such as IL-10 and TGF-β), indicating that acupuncture plays a crucial role in regulating the M1 and M2 polarization of macrophages.[122,123] Moreover, acupuncture also promotes the balance of the immune response by modulating the interaction between macrophages and other immune cells, thereby affecting the overall immune status.[66] McDonald et al found that acupuncture increased the release of macrophages by up regulating the expression of CXCL10, thereby inhibiting the production of proinflammatory cytokines, and thus playing an anti-inflammatory role in allergic diseases. In research on diabetes and its related complications, acupuncture has been found to improve the inflammatory response in the pancreatic islets by regulating the function of islet macrophages and promote the functional recovery of islet β cells. The core mechanism involves the network interactions between macrophages, pancreatic adipocytes, and islet β cells, suggesting the potential application of acupuncture in diabetes treatment.[81] In allergic diseases, acupuncture can not only improve local inflammation by regulating cytokine network, but also produce systemic immune regulation, providing a new treatment method for clinical practice.

Neuroimmune interactions are one of the key mechanisms by which acupuncture regulates macrophage function. Recent studies have demonstrated that the interaction between the nervous system and the immune system plays a crucial role in maintaining tissue homeostasis and regulating immune responses.[124] Acupuncture induces mechanical stimulation at acupoints, activating afferent nerves that transmit information to the sensory center in the central nervous system. For example, EA regulates the trigeminal nerve adjacent to the trigeminal nucleus in the medulla oblongata by stimulating ST36, which activates the nucleus of the solitary tract. Subsequently, the NTS directly or indirectly coordinates efferent pathways. Direct neural regulation involves specific activation of the hypothalamic-pituitary-adrenal (HPA) axis and the parasympathetic nervous system, while indirect regulation is mediated by the sympathetic nervous system through the rostral ventrolateral medulla.[125] Acupuncture stimulation can also activate the vagus nerve, initiating the neuroimmune pathway, thereby influencing macrophage function. Wang et al[67]

found that acupuncture significantly reduces the inflammatory response of macrophages by activating the cholinergic anti-inflammatory pathway, promoting the polarization of M2 macrophages, and alleviating both local and systemic inflammation.

Furthermore, the hypothalamus-pituitary-adrenal (HPA) axis plays a crucial role in the process of acupuncture-mediated macrophage polarization. Under stress, corticotropin-releasing hormone (CRH) neurons synthesize and release CRH into the pituitary, stimulating the secretion of adrenocorticotropic hormone (ACTH), which then acts on the adrenal glands to promote the synthesis and secretion of glucocorticoids. Simultaneously, through feedback regulation of the HPA axis, glucocorticoids modulate CRH secretion in the paraventricular nucleus (PVN) of the hypothalamus, thus attenuating the stress response. The release of CRH, ACTH, and glucocorticoids via the HPA axis also suppresses the activation of NF-κB signaling in immune cells, thereby reducing the gene expression of pro-inflammatory cytokines such as IL-1, TNF-α, IL-6, and IL-8, while stimulating the synthesis of anti-inflammatory cytokines.[126] Studies have shown that in deeply anesthetized rats, electroacupuncture (EA) increased plasma concentrations of ACTH and β-endorphins, while c-fos expression was enhanced in the arcuate nucleus and paraventricular nucleus, which contain CRH neurons.[127] Furthermore, after EA treatment at GB30, plasma levels of ACTH and corticosterone were increased in AIA rats, and CRH-containing neurons in the PVN were activated. Pre-treatment with CRH and ACTH antagonists blocked the anti-edema effect induced by EA, indicating that HPA axis activation mediates the anti-inflammatory effects of EA.[128] These findings suggest that EA activates the HPA axis by releasing anti-inflammatory hormones or neuropeptides that target immune organs or damaged tissues.

Conclusion

When exploring the potential applications of acupuncture in allergic diseases, it is evident that this traditional therapy is gaining increasing recognition within the modern medical community. Research indicates that acupuncture not only alleviates allergic symptoms but also exerts potential therapeutic effects by modulating immune responses. Of particular note is the crucial role of macrophages in this process. These cells, often referred to as the "gatekeepers" of the immune system, play an active role in regulating a range of physiological and pathological responses, thereby influencing the onset and progression of allergic diseases.

Although numerous studies have supported the effectiveness of acupuncture in the treatment of allergic diseases, the results across different studies show some variability. On one hand, this may be attributed to differences in research design, sample sizes, and assessment criteria. On the other hand, the effects of acupuncture may also be influenced by individual differences, disease types, and disease stages. Therefore, future studies need to adopt more systematic and standardized approaches to ensure the comparability and reliability of the research findings.

In addition, future research should focus on exploring how acupuncture influences allergic responses by modulating the function of macrophages. This not only provides a deeper understanding of the mechanisms underlying acupuncture but also could offer new therapeutic targets for clinical applications. Furthermore, recommendations for clinical practice should include the integration of acupuncture into standard treatment protocols, providing patients with a more comprehensive range of therapeutic options. However, the promotion of acupuncture also requires enhanced training and certification for clinicians to ensure the safety and effectiveness of the treatment.

In conclusion, acupuncture, as a highly promising therapeutic approach, holds great potential for the treatment of allergic diseases. By deeply studying the mechanisms of macrophage function and standardizing clinical practices, we can better reconcile the diverse perspectives and findings from different studies, thereby advancing the integration of acupuncture into modern medicine.

Disclosure

The authors report no conflicts of interest in this work.

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