

REVIEW ARTICLE

Review of Mammary Gland Hyperplasia in Classical Chinese Medical Literature

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ABSTRACT

Objective • Mammary gland hyperplasia is a common gynecological disease, which seriously affects the patient's physical and mental health. Therapeutic strategies to treat the disease include endocrine therapy and surgery. Compared to Western treatment, traditional Chinese medicine prescription shows its superiority in treatment. The purpose of this review was to provide a reference for the determination of the pathogenesis, treatment principles, and treatment methods of mammary gland hyperplasia.

Method • This article comprehensively reviewed the records on mammary gland hyperplasia in ancient Chinese medical literature.

Results • The present review discussed the disease and summarizes the information on mammary gland hyperplasia, including the disease name, the traditional Chinese medicine analysis, etiology, pathogenesis, treatment methods, prognosis, and nursing care.

Conclusion • We clearly described the research history of mammary gland hyperplasia, and the analysis and treatment of this disease by physicians in past dynasties. This information will help modern physicians to fully understand the disease development and treatment process. (*Altern Ther Health Med.* 2023;29(6):97-105).

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INTRODUCTION

Hyperplasia of mammary glands (HMGs) is a common gynecological disease, which seriously affects the patients' physical and mental health. Western medicine mainly focuses on endocrine therapy, mostly using hormone or surgical treatment. However, the distribution of hormone receptor targets has multi tissue characteristics, and patients are prone to adverse reactions, such as menstrual disorders, irritability, nausea, liver damage, etc. Surgical treatment has a high recurrence rate, which causes greater trauma to patients.

Hyperplasia of mammary glands is a disease in which traditional Chinese medicine (TCM) prescription shows its superiority in treatment. HMG is related to the stagnation of

liver Qi as well as the disorder of Chong meridian and Ren meridian according to the TCM theory. The main treatment is to tonify liver and kidney and to regulate Chong and Ren meridians. The auxiliary treatment is to soothe liver, regulate the operation of Qi, promote blood circulation, remove blood stasis, resolve phlegm, disperse lumps, clear heat poison, etc. Moreover, multiple treatments are adopted according to the different constitution, etiology, and pathogenesis of patients, which has achieved remarkable curative effects.

The earliest cognition on HMG in TCM can be traced back to the *Sui Dynasty*. After more than a thousand years, the understanding of HMG in TCM has been accumulated and expanded, a relatively perfect knowledge system has formed gradually. To explore its development history and process is of great significance for a comprehensive understanding of the etiology, pathogenesis, and treatment methods of this disease.

Based on the clinical manifestations, the terms *Ru Pi*, *Ru He*, *Ru Li*, *Nai Xian*, *Nai Li*, and breast tuberculosis in ancient Chinese medical textbooks all refer to mammary gland hyperplasia. The present comprehensive literature review and analysis discusses the records of mammary gland hyperplasia in ancient Chinese medical textbooks to provide a reference for modern research.

LITERATURE REVIEW

Descriptions of mammary gland hyperplasia in ancient literature

Before the Sui and Tang dynasties, there was no specific literature on *Ru Pi*, and the relevant descriptions were scattered in various medical works. As *Ru Pi* was not recognized as an independent disease, there were no corresponding theories, treatment methods, or prescriptions.

The earliest recognition of *Ru Pi* was in the Sui dynasty (AD581–AD618). CHAO Yuanfang wrote a chapter on breast disease in *Zhu Bing Yuan Hou Discussion* that described the symptoms of breast tuberculosis.¹ This chapter reported that breast disease was related to the stomach meridian, and that the treatment methods were to activate *Qi*, eliminate scrofula, and alleviate pain. The *Zu Yang Ming Stomach* meridian descends into the breasts from the *Que Pen* acupuncture point; when the *Qi* and blood of the meridian are weak (lack of blood and nutrients in the veins) and cold wind condenses in the blood to generate lumps (external pathogenic factors coagulate in the blood). Over time, the lumps generate heat, and the swelling and heat turn into pus.¹

In the Ming dynasty (AD1368–AD1644), the discussion of *Ru Pi* gradually increased. GONG Juzhong first linked *Ru Pi* to breast lumps and described the condition in an independent chapter in *Wai Ke Huo Ren Ding Ben*. The text stated that *Ru Pi* is born in the breasts, is related to the *Jue Yin* and *Yang Ming* meridians, is hard and not painful, and is caused by stubborn phlegm.^{2,3}

CHEN Shigong wrote an extremely detailed discussion in *Wai Ke Zheng Zong* on the name and clinical characteristics of *Ru Pi*. This text is greatly respected by other physicians and describes *Ru Pi* as breast tuberculosis leading to lesions shaped like pills or eggs with a normal skin color that grow or shrink in accordance with patients' moods. Additionally, it was stated that *Ru Pi* is caused by excessive worry damaging the spleen or excessive anger damaging the liver, causing poisonous turbid stagnation.^{4,5}

In the Qing dynasty (AD1636–AD1912), *Ru Pi* was discussed in many works. The name *Ru Pi* appears many times in *Yang Yi Da Quan*.⁶ This text states that *Ru Pi* mostly occurs in weak individuals and is easy to cure when there is only one lesion, but is difficult to cure if there are three or more lesions.⁶ Furthermore, the text states that *Ru Pi* is most common in women in their 50s or 60s. The text cautions against the use of cooling herbs when there is no pus, as the use of cool herbs in non-purulent cases may force the poisonous evil to penetrate the internal organs and endanger life. Women with *Ru Pi* with wound ulceration rarely survive. This description was very detailed and accurate, and was highly praised by later physicians.

In *Wai Ke Zhen Quan*, ZOU Wufeng described *Ru Pi* as breast tuberculosis that initially presents as a hard lesion as big as a copper coin that gradually enlarges to the size of a peach or egg, but has a normal skin color and is painful when the environmental temperature is cold.⁷ The causes of *Ru Pi* were stated to be stagnation of *Qi*, phlegm, and other fluids.

The manifestations of *Ru Pi* were described as breast lumps with a characteristic hard texture and gradual growth. The text suggests that chronic untreated *Qi* deficiency in older women may become malignant, and proposes methods to prevent malignant transformation.

In 1805, GAO Bingjun published *Yang Ke Xin De Volume*, which contains a separate chapter on *Ru Pi*, *Ru Tan*, and *Ru Yan*. This text reported that the lesions in *Ru Pi* have a clear boundary and regular shape (round or oval). The lesions cause no pain, no changes in skin color, neither cold nor fever, and the size grows or shrinks with mood changes and the menstrual cycle.

Various names for mammary gland hyperplasia

The term *Ru Pi* first appeared in *Zhong Zang Jing* (also known as *Fahrenheit Tripitaka*), but its meaning was not clearly explained. In the Sui dynasty, CHAO Yuanfang wrote *Zhu Bing Yuan Hou Discussion* and described the clinical manifestations of *Ru Pi* as lumps that grow between the flanks and are sometimes painful.

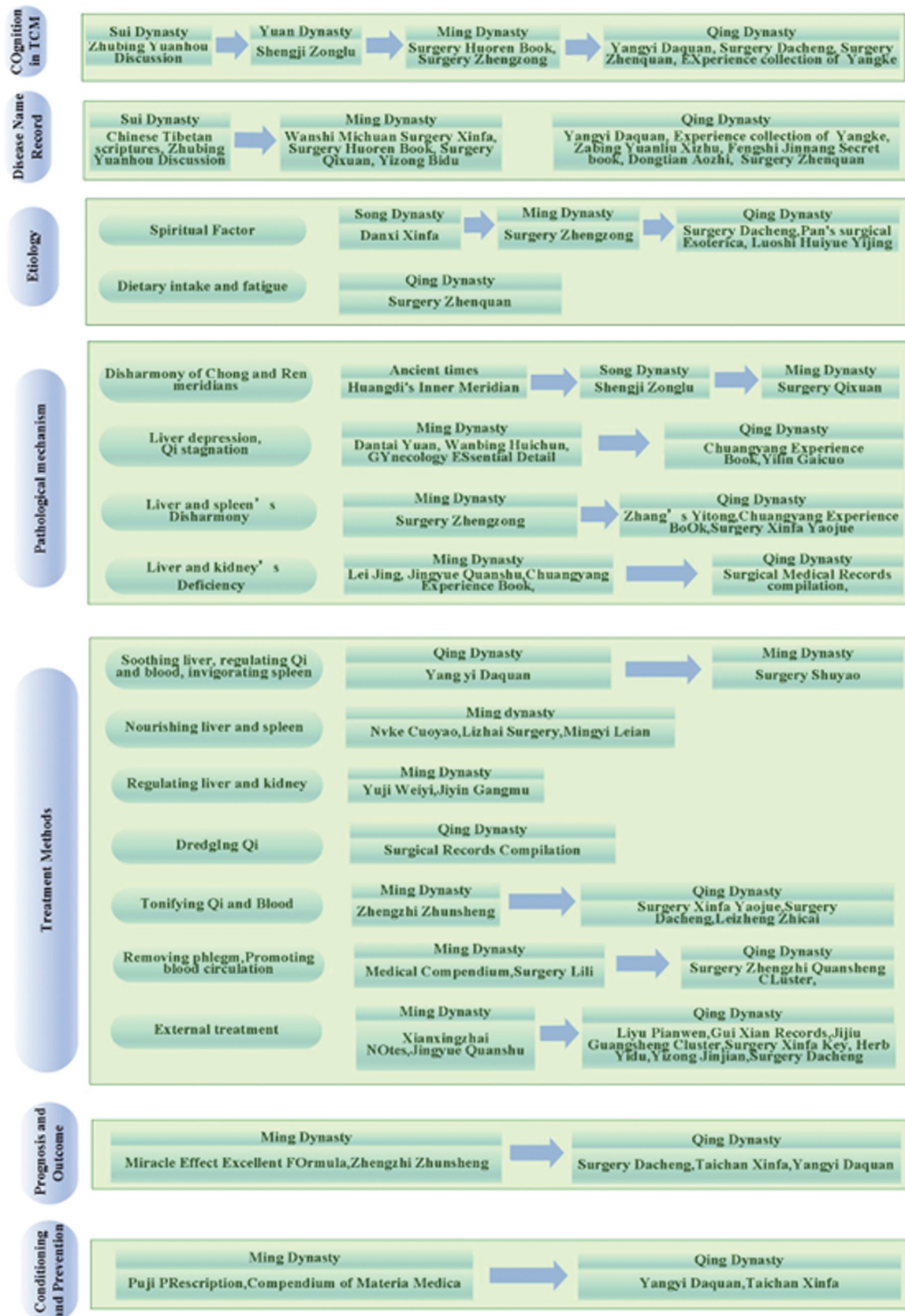
GONG Juzhong first defined *Ru Pi* as breast lumps in *Wai Ke Huo Ren Ding Ben*. The text stated that the masses grow in the breasts, belong to the *Jue Yin* and *Yang Ming* meridians, are hard and not painful, and have a “stubborn” core. In *Wai Ke Qi Xuan* (volume 5), SHEN Douyuan reported that women older than 50 years have decreased *Qi* and blood, often feel depressed, and develop tuberculosis in the breasts (*Ru Pi*), causing pain on cloudy days.⁸ In the Ming dynasty, a famous doctor called LI Zhongzi wrote *Yi Zong Bi Du* and stated that *Ru Pi* grows inside the body and is not visible.

In the Qing dynasty, medical books proliferated and the understanding of *Ru Pi* became more systematic and comprehensive. The condition was discussed as an independent disease, and the term *Ru Pi* has been fixed since then. GAO Bingjun clearly defined *Ru Pi*, *Ru Tan*, and *Ru Yan*, and defined the differences between these three diseases in *Yang Ke Xin De Volume*.⁹ It was recorded in *Za Bing Yuan Liu Xi Zhu* that *Ru Pi* hides in the ribs and cannot be palpated, but sometimes causes pain; *Ru Pi* reflects the characteristics of breast tuberculosis that sometimes disappear and sometimes cause pain in accordance with anger or the menstrual cycle. *Feng Shi Jin Nang Mi Lu: Gynecology Essentials* (volume 16) reported that *Ru Pi* is caused by the blockage of *Qi* and is also known as *Nai Li* or *Ru Li*.¹⁰

Dong Tian Ao Zhi (volume 7) described *Ru Pi* as *Qi* stagnation in older women that results in breast lesions that are painful on cloudy days.¹¹ *Yang Yi Da Quan* reported that *Ru Pi* comprises a small lump in the breast tissue that is neither painful nor itchy and should be treated early, as it is difficult to cure once it becomes a chronic condition (present for 6 or 7 years).¹² In 1872, *Wai Ke Zhen Quan* also referred to *Ru Pi* as breast tuberculosis and described its clinical characteristics.¹³

To sum up, the term *Ru Pi* was first used in *Zhong Zang Jing*. However, it was not until the Ming dynasty that breast lumps were associated with *Ru Pi*, and the name was determined and discussed in separate chapters.

Figure 1. Ancient Chinese Medical Literature of Breast Hyperplasia



Etiology of mammary gland hyperplasia

Emotional factors. Ancient Chinese physicians believed that emotional factors had a great influence on the pathogenesis of *Ru Pi*. In the Yuan dynasty, ZHU Danxi reported that the accumulation of sadness, anger, and depression may cause a woman to become melancholic, which can cause breast lesions with hard cores (the size of big chess pieces) that may be painful or itchy. Sores with sunken skin may appear decades later.

CHEN Shigong believed that *Ru Pi* is related to overthinking and anger. It is reported in *Wai Ke Zheng Zong* that *Ru Pi* is mostly caused by thoughts hurting the spleen, anger hurting the liver, and stagnation of *Qi* and blood; the lumps increase or decrease in accordance with emotional changes.¹⁴

In *Wai Ke Da Cheng*, QI Kun reported that breast tuberculosis is either caused by emotional depression leading to liver *Qi* stagnation that damages the spleen or by depression directly damaging the spleen and stomach.¹⁵ Weakness of the spleen and stomach leads to dysfunction of dietary metabolism, preventing food from being transformed into essence substances to nourish the body. Food is instead transformed into phlegm and dampness, which condense in the breasts to form breast tuberculosis.¹⁵

Nine Types of Pan's Surgical Secret Books stated that *Ru Pi* is formed by stagnation of the *Jue Yin* meridians, causing egg-shaped lesions that dissipate with joy and increase with anger.¹⁶ *Luo Shi-Hui Yue Yi Jing (Breast Diseases)* reported that breast disease is caused by anger and linked to emotions. Chronic depression damages the liver and results in *Qi* stagnation, which accumulates in the breasts and the spleen and stomach meridians. When the spleen and stomach meridians are not functioning smoothly, this may cause liver damage and obstruction of *Qi* and blood. *Qi* stagnation, phlegm coagulation, and blood stasis agglomerate in the breasts.¹⁷

Unhealthy diet. ZOU Yue wrote in *Wai Ke Zhen Quan* that *Ru Pi* is caused by eating cold foods, which causes the accumulation of *Qi* and phlegm in the stomach and related meridians. Long-term consumption of cold, fatty foods might damage the spleen and stomach and reduce the function of these organs. An unhealthy spleen produces dampness and phlegm. The pathogenic stagnation of phlegm and dampness blocks *Qi* movement and blocks the meridians. Moreover, as the breasts belong to the *Foot Yang Ming* stomach meridian, phlegm flows into the stomach meridian and ascends to the breasts to accumulate into lumps, resulting in *Ru Pi*.^{7,18}

Medical cases of *Ru Pi* became more commonly reported in the Ming dynasty. Zheng Zhi Zhun Sheng reported a case in which a woman in her 60s who consumed sweet and fatty foods developed a small and painless lesion (as big as a chess piece) in her left breast, felt lethargic, and lost her sense of taste. The lesion disappeared on day 7 after the administration of a decoction consisting of ginseng, *Citrus aurantium*, minced licorice, and ginger juice five or six times daily.

Pathological mechanism

Ancient Chinese textbooks report that the occurrence of *Ru Pi* is closely related to the liver, spleen, and kidney, as well as the *Chong* and *Ren* meridians.

Disharmony of the Chong and Ren meridians. *Sheng Ji Zong Lu* is a large-scale medical textbook compiled by officials in the Northern Song dynasty (AD1111–AD1125) under the edict of Emperor Huizong. This text states that the *Chong* and *Ren* meridians are the foundation meridians in women. The *Chong* meridian originates from the *Qi Jie* acupoint, travels around the navel, and spreads out in the chest. The blood and energy of the *Chong* and *Ren* meridians act as milk on the upper side, and menstrual blood on the lower side. If the *Chong* and *Ren* meridians are not in harmony and the *Yang Ming* meridian is hot, this leaves women vulnerable to attack by wind evil. The evil of wind and heat is difficult to disperse and accumulates in the breasts, resulting in hardness, swelling, pain, and nucleated lesions. Furthermore, sexual activity or excessive labor deplete the body vitality. The kidneys store essence, which depends on the nutrition supplied by the spleen and stomach. Chronic fatigue damages the spleen and stomach and results in kidney deficiency, which negatively affects the *Chong* and *Ren* meridians and causes *Ru Pi*.¹⁹

It is reported in *Wai Ke Qi Xuan* that *Ru Pi* is caused by high parity, excessive physical labor, and other factors that lead to a lack of *Qi* and blood, as well as an imbalance of the *Chong* and *Ren* meridians in older women.²⁰ A woman older than 50 years who has depression, an imbalance of the *Chong* and *Ren* meridians, and declining *Qi* and blood, may develop lumps in her breasts that are painful on cloudy days.

XUE Lizhai wrote that the *Chong* and *Ren* meridians play an important role in the mammary gland function and that the effect of *Tian Gui* on the mammary gland is mainly implemented through the *Chong* and *Ren* meridians. The roots of the *Chong* and *Ren* meridians lie in the kidneys, and the *Chong*, *Ren*, and kidney meridians intersect. The *Chong* meridian is called the blood sea, and functions only when it is nourished by the kidney essence. The kidneys preside over the metabolism of water and body fluid, collect and store subtle substances of the five systems, and then inject the subtle substances into the *Chong* and *Ren* meridians. Deficiency of *Kidney Yang* leads to the imbalance of *Tian Gui* and insufficiency of the *Chong* and *Ren* meridians; thus, phlegm and dampness may linger along the breast meridians, leading to mammary gland hyperplasia.

Insufficient essence in the kidneys. *Huang Di Nei Jing Su Wen* reports that the full essence of the kidneys can produce another essence named *Tian Gui*. When a woman is 49 years old, the *Ren* and *Tai Chong* meridians are weakened, resulting in *Tian Gui* insufficiency. Older women have insufficient kidney essence, dissonant *Chong* and *Ren* meridians, and insufficient *Yin* nutrient essence in the liver and kidneys; this prevents nourishment of the breast meridians, causing *Ru Pi*.²¹

Medical Records Compilation of Surgical Department elucidates the importance of the kidneys in the pathogenesis of *Ru Pi*. Although breast tuberculosis is commonly thought

to be related to the liver, its root lies in the kidneys. If there is insufficient essence in the kidneys, *Qi* and blood stagnation accumulate in the breasts and uterus, which may manifest as breast pain and swelling or menstrual disorder.²²

ZHANG Jingyue wrote in *Jing Yue Whole Book* that the kidneys are the root of phlegm because the kidneys govern water metabolism and abnormal water metabolism produces phlegm. If the *Kidney Yang* is insufficient, there will be weak water transpiration and gasification. Furthermore, *Yang* deficiency leads to fluid metabolism disorders and the *Ming Men* fire will not be able to warm the spleen (the traditional Chinese medicine (TCM) element of earth), which results in phlegm and dampness condensing in the breasts and relevant meridians.

In the Ming dynasty, DOU Menglin wrote in *Chuang Yang Experience Volume* that a 15–16-year-old girl who has no menstruation or who menstruates only once every 2 or 3 months may develop *Ru Pi*, mostly caused by body weakness and deficiency of *Qi* and blood. This condition is more common in women in their 50s or 60s. The incidence of *Ru Pi* is always related to a congenital insufficiency of the kidney essence *Tian Gui*.

Zhu Bing Yuan Hou Discussion: Zu Shao Yin Kidney reported that meridians run through the liver septum and connect with the breasts. Kidney meridians are directly connected to the breasts. The kidney system directly or indirectly affects breast growth or atrophy and plays an important role in breast function. If the *Kidney Yang* is deficient, the kidney and relevant meridians lose warmth, leading to the accumulation of phlegm and dampness in the breast meridians, which directly results in mammary gland hyperplasia.

Many ancient medical textbooks discuss the correlation between *Tian Gui* and breast diseases. *Tian Gui* is the subtle substances that affect growth and reproduction and is closely related to the breast function of women. *Tian Gui* nourishes the breasts and regulates and restricts the breast meridians. The kidney system is the source of *Tian Gui*, and *Tian Gui* is transformed by kidney *Qi*. If there is insufficient kidney *Qi* and *Yang*, there is less *Tian Gui*, which leads to breast function disorders and blockage of phlegm and dampness in the breast meridians.

Liver dysfunction and Qi stasis. Chapter 6 of *Dan Tai Yu An* states that melancholy hurts the liver and overthinking hurts the spleen, which makes the meridians become astringent and causes the development of lesions that are initially bean-sized and gradually grow to the size of chess pieces.²³

FENG Zhaozhang wrote in *Nv Ke Jing Yao* (chapter 1) that chronic anxiety, anger, and depression affect the function of the spleen in women; the liver *Qi* is overturned, *Qi* and blood are depleted, the tendons are not nourished, and phlegm and blood stasis produce pathological products (lesions). The epidermis over the lesions is not red and there is no pain. The condition develops over a few years; as the accumulation gradually increases, the lumps develop internal ulceration and become deep and rotten. In severe cases, this condition may develop into *Ru Yan*.²⁴

CHEN Shigong wrote that *Ru Pi* is mostly caused by anger damaging the liver, which results in stagnation. The liver governs the dredging of the whole body, which should ideally be smooth. If the emotion is not smooth for a long time, stagnation damages the liver, which may cause *Qi* to accumulate and block the breast meridians, causing breast pain. Prolonged liver *Qi* stagnation produces excessive heat and transforms the liquid essence into phlegm; liver stagnation also disrupts the flow of *Qi* and blood. *Qi* stagnation, phlegm coagulation, and blood stasis agglomerate into lumps that grow or shrink with anger or happiness, respectively.

GAO Bingjun proposed that *Ru Pi* may be caused by the *Jue Yin* meridian rather than the *Yang Ming* meridian because the *Yang Ming* stomach (earth element) is afraid of *Jue Yin* liver (wood element). Therefore, when the liver function is disrupted, it may impair the digestive function of the stomach. If the stomach cannot digest properly, the food is transformed into lumps.²⁵

In the Qing dynasty, WANG Qingren wrote in *Yi Lin Gai Cuo* that *Qi* is invisible and cannot aggregate into lumps individually; lumps are caused by *Qi* stagnation and blood stasis. If the liver function is stagnant, blood cannot flow smoothly, and blood stasis mixed with phlegm stagnates in the breasts to produce lumps.

Incoordination of liver and spleen. In the Qing dynasty, ZHANG Lu wrote in *Zhang Shi Yi Tong* that *Ru Pi* is chronic stagnation of the liver and spleen, which results in loss of *Qi* and blood, causing small lumps to appear in the breasts. This is followed by severe internal heat at night, which manifests as irritation and heat in the precordial area, bilateral palms, and bilateral soles of the feet, limb fatigue, and irregular menstruation. The lesions may resolve with long-term administration of Jia Wei Xiao Yao powder. Additionally, women with *Qi* deficiency should take large doses of ginseng. However, if detoxifying drugs damage the woman's positive energy, this will inevitably lead to corruption and festering of the muscles.²⁶

CHEN Shigong reports that when a woman's desire is unlimited, excessive thinking may damage the spleen. If her desire is difficult to achieve, depression may damage the liver, which causes the meridians to become congested and stagnant. The spleen and stomach are the source of *Qi* and blood. If the spleen is injured, *Ying Qi* is suppressed, blood cannot be metabolized, blood is deficient, and *Qi* loses its carrier; this results in a disorder of *Qi* movement, causing metabolite stagnation. The liver governs dredging and evacuating. If the emotions are not smooth, this causes stagnation of *Qi* and blood, which may damage the liver. Excessive hyperactivity of liver *Yang* leads to *Qi* stagnation, phlegm coagulation, and blood stasis. Affected women may feel pain in the bilateral sides of the torso and swelling of the breasts. If the liver meridians are not smooth, the liver and spleen are out of harmony, and the invisible *Qi* and visible phlegm accumulate in the breasts to form lumps.

Yang Ke Xin De Ji reports that *Ru Pi* is caused by stagnation of the *Jue Yin* meridian. The resultant egg-shaped

masses decrease with happiness and increase with melancholy. Chronic turbulent emotions damage the liver, causing *Qi* to stagnate and accumulate in the meridians of the breasts and stomach. The obstruction of the meridians results in *Qi* stagnation, phlegm coagulation, and causes blood to agglomerate into masses. The spleen and stomach are the source of *Qi* and blood. If the spleen and stomach are weak, the food cannot generate *Qi* and blood, but creates phlegm stasis. Anger may damage the liver; if the subtle substances in the liver are insufficient, the liver cannot function and the spleen will be damaged. When the liver and spleen are out of harmony, *Qi* and phlegm accumulate, causing *Ru Pi*.

Wai Ke Xin Fa Main Skills states that the lesions in breast tuberculosis are shaped like plums, do not move when pressed, and have a normal skin color. The patient may occasionally feel dull pain that worsens with exertion, which is mainly caused by stagnation of the liver and spleen.²⁷ *Lei Zheng Zhi Cai* reports that breast disease is mostly governed by the liver, stomach, and spleen. Stagnation of the liver and spleen meridians frequently results in white-colored breast lesions.²⁸

Deficiency of liver and kidney. The *Compilation of Surgical Records* and ZHANG Jingyue's *Lei Jing* report that although breast tuberculosis is related to the liver system, it is rooted in the kidneys. Both the liver and kidneys are located in the lower part of the body cavity, which is called the homology of *Yi* and *Gui* in TCM theory. The regular dredging function of the liver requires the warming of the kidney *Yang*. Insufficiency of kidney *Yang* may decrease the warming function of the liver and lead to the dysfunction of dredging. In the TCM five-element theory, the mother passes disease to her children. Dysfunction of the liver and kidneys, *Qi* stagnation, and phlegm coagulation lead to *Ru Pi*.^{29,30}

Treatment methods

Oral herbs. In the Ming and Qing dynasties, the understanding of *Ru Pi* was enriched and the principles and methods of prevention and treatment were improved. In the Ming dynasty, the focus was on internal treatment, with particular emphasis placed on the use of empirical prescriptions. In most cases, the treatment of *Ru Pi* was based only on treating the clinical manifestations.

Regulation of liver and spleen. CHEN Yuangong wrote in *Yang Yi Da Quan* that the stomach (earth element) is afraid of the liver (wood element), and *Ru Pi* is caused by liver *Qi* malfunction. Therefore, the treatment of *Ru Pi* does not require adjustment of the stomach, but the liver function must be repaired by Jia Wei Xiao Yao powder to eliminate swelling. *Ru Pi* caused by depression hurting the spleen is treated by soothing the liver and strengthening the spleen. Additionally, *Qi* movement should be adjusted to dissolve agglomeration in the breasts. This is achieved by the administration of Gui Pi decoction and Trigonella powder.

Surgery Shu Yao (chapter 2) states that patients with fire stagnation of the liver meridian and blood deficiency should be treated with Si Wu decoction mixed with ginseng, *Atractylodes*, *Bupleurum*, and *Cimicifuga*. Gui Pi decoction

and *Trichosanthes* powder are used to treat *Ru Pi* caused by spleen injury. If the liver and spleen are hurt by anger, the lumps are non-pruritic and non-painful; this condition is called *Ru Yan* and is more difficult to treat than *Ru Pi*.

Women with chronic depression who develop hard lumps in the breasts should take herbs to relieve depression as well as nourish *Qi* and blood. This may be achieved by the administration of Ginseng Killing Poison powder, Yi Qi Yang Rong decoction, Xiao Chai Hu decoction mixed with *Angelica*, *Citrus citus*, and *Campanulaceae*, or Eight Treasures decoction mixed with *Polygala*, *Fritillaria*, *Bupleurum*, and *C. aurantium*.³¹

Famous Doctor Cases (chapter 10) describes a case of a woman with chronic irritability and depression who developed a lump in her left breast that was slightly painful on palpation. The symptoms were slightly relieved after the administration of more than 20 doses of Lian Qiao Yin Zi. The condition was cured by the administration of more than 20 doses of Ba Zhen decoction mixed with *C. aurantium*, *Cyperus officinalis*, *Campanulaceae*, and *Fritillaria*.³² Similar results are reported in other books. *Wai Ke Da Cheng* (chapter 2) reports that patients with a weak liver and spleen should take Four Jun Zi decoction mixed with *Angelica*, *Cimicifuga*, and *Bupleurum*. Patients with spleen injury caused by depression should be treated with Gui Pi decoction and herbs to soothe the liver and clear phlegm (e.g., *Fritillaria*, *Pinellia*, and *Trigonella*). The removal of phlegm resolves the lumps.³³

Regulation of liver and kidneys. YU Xinhong wrote that a woman's nipples belong to the liver system, while her breasts belong to the stomach system; however, while a man's nipples also belong to the liver system, their breasts belong to the kidney system. Women are dominated by the liver, while the kidneys are the foundation of the body. The exquisite substances of the kidney and liver blood arise from the same source. If the liver fails to evacuate, the kidney essence is insufficient, which leads to disorder of the *Chong* and *Ren* meridians and stagnation of *Qi* and blood in the breasts, causing lumps to form.

Yu Ji Wei Yi (chapter 15) states that *Ru Pi* with liver blood deficiency and wind-heat stagnation is mainly treated with Qing Gan Jie Yu decoction. If the lumps are painful and chronic, the cause may be disorder of the *Qi* and blood of the liver and gallbladder meridians; Nei Tuo Sheng Ma decoction (comprising *Trigonella*, *Forsythia*, licorice, and *C. aurantium*) is very effective for this condition.

Lei Zheng Zhi Cai (chapter 8) states that if the liver and kidneys are damaged by depression, the breast lumps will soften with the administration of Gui Pi decoction mixed with *C. officinalis* juice, *Rehmannia glutinosa*, oyster powder, *Sichuan fritillaria*, and honeysuckle vine.²⁸

Eliminating *Qi*, phlegm, and blood stasis. In the *Compendium of Surgical Medical Records*, YU Xinhong emphasized the importance of regulating *Qi* and dredging the meridians in treating *Ru Pi*. When treating *Ru Pi*, it is best to first regulate *Qi*, regardless of whether the condition is acute or chronic; cold or hot medicine and *Qi*-regulating herbs should be added to the prescription used to dredge the breast

Table 1. Action Mechanism of the Traditional Chinese Medicines Involved in this Research

	Character	Taste	Meridian Attribution	Efficacy	Chemical Composition	Action Mechanism in Treating Mammary Hyperplasia
Ginseng	Mild	Sweet Bitter	Spleen, Lung	Tonifying <i>Yuan Qi</i> , tonifying spleen and lung, producing fluid to quench thirst, calming mind, and increasing wisdom.	Ginsenoside Rd	GSRd can decrease serum estradiol level, decrease acinus number, lobular number and acinus diameter in breast tissue, inhibit ER- α and PR in breast tissue, reduce acinus volume in breast tissue, reduce fibrous tissue in lobular tissue, increase progesterone level.
Attractylodes	Mild	Bitter Sweet	Spleen, Stomach	Invigorating spleen and <i>Qi</i> , clearing wet, preventing excessive sweat, and nourishing fetus.	Attractylodes macrocephala, Koidz polysaccharide	AMP has good scavenging ability on DPPH, ABTS and \cdot OH free radicals, and can reduce the diameter of papillae, reduce the number of acinus, and reduce the abnormal expansion of ducts. AMP has good antioxidant effect and good efficacy in treating mammary hyperplasia, and the activity of AMP is significantly enhanced after esterification modification by sulfuric acid.
Bupleurum	Cold	Bitter	Liver, Gallbladder	Harmonizing the internal and external environment of the body, soothing liver, and raising <i>Yang Qi</i>	Volatile oil, Bupleurumol	Volatile oil can regulate sex hormone metabolism, improve the expression and release of ER, PR, P53, and telomerase in breast tissue.
Cohosh	Cold	Spicy Sweet	Lung, Spleen, Stomach, Large Intestine	Promoting rash penetration, clearing heat, detoxifying, and raising <i>Yang Qi</i> .	Cohosh glycosides, Cohosh terpenes, Ferulic acid	Cohosh plays the role of anti-mammary hyperplasia by promoting apoptosis of mammary epithelial cells or inhibiting excessive proliferation of mammary epithelial cells. The action mechanism is related to the release of cytochrome C, down-regulation of anti-apoptotic protein α B-lens protein (CRYAB), Bcl-2, caspases-8, caspases-9, Bax, and p53 expression.
Ligusticum Hort	Mild	Spicy	Liver, Gallbladder, Pericardium	Promoting <i>Qi</i> and blood movement, dispelling wind, and relieving pain.	Chuanxiongine	Ligustrazine can inhibit the proliferation of MDA-MB-231 cells <i>in vitro</i> . Ligustrazine can retard the cell cycle of MDA-MB-231 in G0/G1 phase and induce apoptosis. Ligustrazine can inhibit cell proliferation and induce apoptosis of mammary cells by blocking cell cycle in G0/G1 phase.
Angelica	Mild	Sweet Spicy	Liver, Heart, Spleen	Tonifying blood, promoting blood circulation, regulating menstruation, relieving pain, moistening bowel, and defecation.	Terpene, Palmitic acid, folic acid, Beta-sitosterol	By promoting the expression of <i>Let-7a</i> gene and reducing the expression of p-ERK, <i>Angelica Sinensis</i> can inhibit the proliferation activity of breast tissue cells, so as to improve the state of breast tissue hyperplasia and achieve the purpose of treating breast hyperplasia. It can promote <i>Let-7</i> gene expression and inhibit P-ERK protein expression in mammary gland hyperplasia epithelial cells, thus inhibit cell proliferation and differentiation, promote cell apoptosis, and improve the hyperplasia of mammary gland tissue.
Citrus Husk	Mild	Bitter Spicy	Spleen, Stomach	Regulating <i>Qi</i> , dredging the thorax, removing stasis, and eliminating fullness.	Volatile oil, flavonoid glycosides	Hesperidin, Glutamic sterol, Chuanpi glycoside and other components of <i>Fructus aurantii</i> can act on HSP90- α , HSP90- α belongs to the heat shock protein family. HSP is related to cell proliferation, apoptosis, differentiation, immunity and drug resistance, and HSP 90 plays a leading role in cell invasion and metastasis. <i>Fructus aurantii</i> can cure breast hyperplasia by inhibiting cell proliferation, mediating gene protein, and different signal transduction.
Campanulaceae	peaceful	Bitter Spicy	Lung	Clearing lungs and throat, removing phlegm, and discharging pus.	Polygonic acid, platycodon saponins, Glucose	<i>Campanulaceae</i> can regulate hormone, IL-2 and TNF- α levels, increase thymus and spleen index, improve immunity. Thymus atrophy was induced by various ways, T cell regeneration was inhibited, and cell-induced immune activity was reduced. It can increase the number of T cell subsets such as CD3+, CD4+, CD4+/CD8+. Its direct or indirect action on endocrine and immune cells, the anti- HMG function can be exerted by multi-pathway and multi-target.
Fritillaria	Cold	Bitter Sweet	Lung, Heart	Clearing heat, moistening lungs, eliminating phlegm, and relieving cough.	Isosteroid alkaloids, steroidal alkaloids	<i>Fritillaria</i> can inhibit serum estradiol and progesterone levels in the mammary gland hyperplasia model. The number of breast acinar was significantly reduced. The mean diameter of breast lobule was decreased significantly, and the damage of breast pathological tissue was alleviated in breast hyperplasia model. It can reduce whole blood viscosity and plasma viscosity.
Citrus	Mild	Bitter Spicy	Liver, Gallbladder, Stomach	Comforting liver, dredging <i>Qi</i> , and eliminating stagnation	Volatile oils, Flavonoids, Amino acids	The effects of volatile oil and flavonoids on mammary gland MDA-MB-231 cells significantly inhibit proliferation and induce apoptosis, and the mechanism was related to the increased expression of Caspase-3 and Caspase-8.
Cyperus officinalis	Peaceful	Spicy Bitter Sweet	Liver, Spleen, Coelom	Promoting the movement of <i>Qi</i> , releasing stagnation, regulating menstruation, and relieving pain.	Glucose, Fructose, Starch, volatile oil	Under the action of sterols, <i>Rhizoma Cyperi</i> can make the DNA of mammary cells division stay in the synthesis phase, inhibit cell proliferation and promote cell apoptosis. Phytosterols can enhance the proliferation of lymphocytes and T cells in human peripheral blood, thus enhances the immune response and avoids the further development of mammary hyperplasia from the direction of immunosuppression. Isorhamnetin inhibits proliferation of mammary gland cells by inhibiting cell growth, producing cytotoxicity, increasing oxidative stress, and blocking cell cycle.
Gardenia	Cold	Bitter	Heart, Lung, Coelom	Purging fire, eliminating boredom, clearing heat and diuresis, cooling blood, and detoxifying	Gardenoside, Geniposide, Shanzhiside, Gardoside,	<i>Gardenia</i> can regulate the body's overall metabolic level. It plays the role of anti-mammary hyperplasia by intervening pyruvate metabolism, tryptophan metabolism, and other metabolic pathways, improving amino acid metabolism, sugar metabolism, fat metabolism, and energy metabolism.
Trichosanthis fructus	cold	Sweet Bitter	Lung, Stomach, Large Intestine	Clearing heat, removing phlegm, dispersing stasis, and moistening intestine	Triterpenoid saponins, Amino acids, Sugars, Organic acids	<i>Trichosanthis Fructus</i> can reduce the plasma viscosity, nipple height, and diameter of mammary gland hyperplasia models. The serum E2 and PRL levels can be decreased and P level can be increased. It can reduce breast coefficient and uterine coefficient improve endocrine disorders, reduce the overexpression of ER and PR in breast tissue, and reduce the overstimulation of estrogen and progesterone to breast tissue. It can reduce breast lobular number and acinar number, shrink the dilated acinar cavity and catheter cavity, reduce intracavitary secretions, and improve the hyperplasia of acinar and catheter.
Pinellia	Mild, Toxic	Spicy	Spleen, Stomach, Lung	Drying dampness, relieving phlegm, reducing retching, and eliminating stasis	Volatile oil, Starch, Nicotine, Aspartic Acid, Glutamic Acid, Arginine	Vascular Endothelial Growth Factor (VEGF) can promote the growth and proliferation of endothelial cells and increase vascular permeability. Fibroblast Growth Factor belongs to Polypeptide growth factors, and there are mainly two forms: acidic (aFGF) and alkaline (bFGF). <i>Pinellia</i> plays the role of anti-mammary hyperplasia by decreasing the expression of VEGF and bFGF in serum and hyperplasia tissues. It plays a role in inhibiting the lesions' location enlargement and improving Microvascular Density (MVD) by inhibiting the transfer of vascular endothelial factors, reducing vascular permeability, and then inhibiting the generation of new blood vessels.
Tangerine peel	Mild	Bitter Spicy	Lung, Spleen	Regulating <i>Qi</i> , invigorating the spleen, drying dampness, and eliminating phlegm.	Flavonoids, Hesperidin	The mechanism of Tangerine peel on mammary hyperplasia is related to reducing the expression of ER and PR in breast tissue. It can enhance the antioxidant capacity, regulate the expression of Bcl-2 and P53 protein, which induces the apoptosis of breast hyperplasia cells.
Paeonia lactiflora	Cold	Bitter	Liver	Clearing heat, cooling blood, dispersing blood stasis, and relieving pain.	Peony glycosides, Peony lac-tone, Carotenoside, Betasitosterol	Paeoniflorin can increase estrogen metabolism in liver and inhibit prolactin secretion, which is beneficial to the recovery of breast hyperplasia tissue.
Licorice	Peaceful	Sweet	Heart, Lung, Spleen, Stomach	Tonifying spleen and <i>Qi</i> , clearing heat and detoxifying, eliminating phlegm, relieving cough and pain, and harmonizing drugs.	Glycyrrhiza polysaccharides, Glycyrrhetic acid, Liquiritin, Liquiritigenin, Glycyrol	Glycyrrhiza polysaccharides can reduce the content of estradiol in plasma, reduce the binding of estradiol to plasma protein, regulate the level of estrogen, thus inhibits the proliferation of mammary cells. By down-regulating the expression of estrogen receptor <i>ESR1</i> gene, estradiol was inhibited from binding to estrogen receptor dimer and ERE element in breast cells. By down-regulating <i>EGFR</i> gene expression, ER phosphorylation and downstream gene transcription are inhibited, and the proliferation of breast tissue cells is weakened. It can regulate gene transcription, regulate estrogen signaling pathway through ligand-dependent pathway and ligand-independent pathway, and improve the symptoms of breast hyperplasia.
Poria Cocos	Peaceful	Sweet	Heart, Lung, Spleen, Kidney	Drying dampness, invigorating spleen, and calming mind.	Poria Polysaccharide, β -poria Polysaccharide, Acetyl Poria Acid, Poria Acid	Poria Polysaccharide in Poria Cocos can improve blood rheology and regulate the endocrine level of the body. By up-regulating the expression of PPARG, cell proliferation and migration are inhibited and cell metabolism is affected. It can promote breast cell apoptosis, inhibit inflammatory response and cytokine synthesis, reduce VEGF expression, inhibit vascular hyperplasia, regulate sex hormones' balance.

Table 1. (continued)

Oyster	Cold	Salty	Liver, Gallbladder, Kidney	Soothing nerves, nourishing Yin, removing stasis, and softening hardness.	Calcium Carbonate, Calcium Phosphate, Calcium Sulfate	The mechanism of Oyster in treating mammary hyperplasia is related to the regulation of endocrine and expression of ERα, PR, PRLR and other hormone receptor proteins in the body, so as to reduce the influence of hormone level disorder on the body.
Honeysuckle	Cold	Sweet	Lung, Heart, Stomach	Clearing heat and detoxifying, dispelling wind and heat	Flavonoids, Triterpenes, Triterpenes Saponins,	Anti-mammary hyperplasia of Honeysuckle involves intervention in hormone metabolism, inflammatory response, signal transduction, and transcription.
Dandelion	Cold	Bitter Sweet	Liver, Stomach	Clearing heat and detoxifying, removing stasis, reducing swelling, and promoting urine discharge.	Dandelion terpenol, Dandelion sterol, Aesculolactone	<i>Dandelion terpenol</i> can inhibit cell proliferation by inducing MCF-7 cells to autophagy, and the mechanism is related to the inhibition of mTOR signaling pathway. Dandelion sterol can inhibit tumor generation, promote and induce cell differentiation. Aescinolactone can induce cytotoxicity involving apoptosis, and its mechanism is related to the reduction of mitochondrial membrane potential, the promotion of cytochrome c release, and the hydrolytic activation of caspase 9/caspase 3 proteins.
Loofah	Peaceful	Sweet	Lung, Stomach, Liver	Dredging meridians, promoting blood circulation, and dispelling wind.	Xylan, Cellulose, Mannan, Galactan, Lignin	Loofah can regulate hormone levels (Estrogen Hormone, Progesterone Hormone, Gonadotropin Releasing Hormone, Luteinizing Hormone, Follicular Stimulating Hormone) and balance endocrine homeostasis.
Perilla terrier	Mild	Spicy	Lung, Spleen	Regulating Qi operation, relieving pain, and nourishing fetus	Perilla ketone, Isoegomaketone, Egomaketone	<i>Perilla terrier</i> can improve immune function, lower serum E2, E3, and P levels, and regulate endocrine imbalance.
Musk	Mild	Spicy	Heart, Spleen	Awakening mind and spirit, promoting blood circulation, dredging meridians, reducing swelling, and relieving pain.	Thymol phenol, Muscopyridine, Cholesterol, Cholesteryl Ester	Thymol phenol plays a therapeutic role by inhibiting inflammatory signaling pathways and by inhibiting bacterial invasion of mammary epithelial cells.
Rehmannia glutinosa	Cold	Sweet Bitter	Heart, Liver, Kidney	Clearing heat, cooling blood, nourishing Yin, and producing fluid.	Rehmannioside, Cyclic Ether, Terpenes, Lactone, Triterpene, Flavone	Rehmannioside plays the role of anti-mammary hyperplasia by inhibiting the activation of the associated nuclear transcription factor Runx2 in breast cells and down-regulating the expression of its target genes <i>MMP-9</i> , <i>MMP-13</i> , <i>OPN</i> and <i>BSP II</i> in breast cells.

meridians. Because *Qi* is the commander of blood, it can move blood. Thus, the addition of *Qi*-regulating herbs dissipates the agglomerated blood, which softens the hard lumps.

In the Qing dynasty, many oral prescriptions for *Ru Pi* were recorded, such as Amber pill, Yi Qi Yang Rong decoction, Six Jun Zi decoction, Four Jun Zi decoction, Gui Pi decoction, Qing Gan Jie Yu decoction, and Xiao Yao powder. The treatment principles and herb selection focused on dredging and nourishing *Qi*. *Angelica*, *C. officinalis*, *Paeonia lactiflora*, *C. aurantium*, ginseng, licorice, *Poria*, and *Trigonella* were frequently used.

It was recorded in *Wan Bing Hui Chun* (chapter 6) that *Ru Pi* is initially a nuclear swelling that is treated with herbs that regulate *Qi* and adjust mood. However, the condition is only curable in patients without epidermal breakage.³⁴

Wai Ke Zheng Zhi Quan Sheng Ji reports that the main pathological factors of *Ru Pi* are phlegm turbidity and blood stagnation. Therefore, *Ru Pi* is effectively treated by clearing cold phlegm with warm herbs and removing blood stasis. However, if the lumps do not disappear, they should be treated from the inside; for example, Shen Xiao *Trigonella* powder can eliminate the root. Nei Tuo Sheng Ma decoction is best for treating women with breast tuberculosis with swelling and pain.³⁵

External treatments. The treatment of *Ru Pi* with Jin Xian paste was recorded in *Li Yu Pian Wen*. Breast lumps (*Qi* and blood stagnation) should be washed with a ginger and scallion decoction, followed by the application of an ointment composed of Patchouli, *Paeonia lactiflora*, *Angelica*, *C. officinalis*, and mastic on the affected area.³⁶

Gui Yan Records recommends treating *Ru Pi* with Clearing Nucleus ointment (a topical paste made of gallnuts powder and vinegar) or Removing Clumping ointment (composed of

C. officinalis, *Ligusticum hort*, *Fritillaria*, honeysuckle, dandelion, *Perilla terrier*, orange leaves, loofah, scallion white, and wine dregs); these ointments are applied to the affected area.³⁷

Physicians in the Qing dynasty attached great importance to external medicines for treating *Ru Pi*. The dosages and forms of these external medicines varied, and acupuncture was also used. *Ji Jiu Guang Sheng Ji* recommends the application of a thin sheet made by blending peeled and washed shrimp membrane mixed with *Pinellia* and musk.³⁸

In *Surgical Xin Fa Tips* (chapter 4), breast tuberculosis is described as initially comprising lumps the size of a jujube or chestnut that gradually increase to the size of a chess piece; the lesions are not red or hot, but sometimes cause dull pain. The recommended treatment is moxibustion and oral blood-nourishing herbs to prevent the poison from attacking internally. The lesions should be treated immediately with the use of bean-sized moxa columns seven times over the lumps.

In other ancient textbooks, external treatments for *Ru Pi* include *Rehmannia glutinosa* powder made into thin sections³⁹ and *Bletilla striata* powder mixed with water.⁴⁰ If the breast lumps are caused by poisonous phlegm, the external application of white mustard seed powder mixed with water or vinegar is very effective.³⁰ Other reported external treatments include Crucian Carp paste and 14 sessions of moxibustion at the *Jian Qian* and *Zu San Li* points.⁴¹

Prognosis and nursing care

Ancient physicians paid attention to treatment adjustment and nursing and had a comprehensive understanding of the prognosis. Chronic *Ru Pi* may transform into *Ru Yan* which frequently ruptures and releases pus, and has a poor prognosis.

Zheng Zhi Zhun Sheng (chapter 3) states that early

treatment can remove the root of *Ru Pi*. The disease can be cured if the patient can get rid of messy thoughts, stay away from fatty and sweet foods, clear stagnation, and nourish *Qi* and blood. However, women may have breast lumps without pain or itching that may remain undetected for 5 or 10 years before the breasts rupture, creating purulent open lesions; this condition is more serious.⁴²

Wai Ke Da Cheng (chapter 2) reports that *Ru Pi* becomes painful over time because of the connection to the heart. This may cause the diseased site to rupture, creating an open lesion that occasionally oozes smelly blood and is difficult to cure.³³ *Qi Xiao Liang Fang* (chapter 54) reports that untreated *Ru Pi* develops into a carbuncle. *Tai Chan Xin Fa* describes *Ru Pi* as small breast lumps initially causing mild symptoms in non-menopausal women, which can be cured; however, the condition is difficult to treat in women in their 50s or 60s who are no longer menstruating.⁴³

Yang Yi Da Quan reports that *Ru Pi* is most likely to develop in women in their 50s or 60s. If there is no pus, cool herbs should not be applied because they may force poison into the viscera.¹²

Pu Ji decoction can be used to cure *Ru Pi* in patients younger than 30 years with strong *Qi* and blood. However, it is difficult to cure those who are over 40 years old and have weak *Qi* and blood.⁴⁴

Physicians in the Ming and Qing dynasties attached great importance to the use of primers and emphasized the use of liquor. MINGLI Shizhen wrote in *Compendium of Materia Medica* that eels like to move through caves and can therefore clear meridians and treat hard breast lumps in women. The eels should be burned to ashes and drunk with warm wine on an empty stomach. The wine is used to increase the potency of the herbs, dredge the meridians, and dissipate breast lumps.

Textbooks written in the Qing dynasty stated that herbs should be dissolved by warm liquor and that herbal powders should be mixed with hot liquor; the intake of herbs with liquor should be continuous and uninterrupted. Other recommended herbal primers include ginger decoction, rice decoction, and wick decoction. The herbal primer should be selected in accordance with the TCM syndrome.

CONCLUSION

The present review summarized the records of mammary gland hyperplasia from ancient times. Various aspects of the condition were comprehensively discussed, including etiology, pathogenesis, treatment, prognosis, and conditioning. This information will help modern physicians to fully understand the disease development and treatment process.

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