Rehmannia Six Formula (Liuwei Dihuang Wan) is one of the most commonly used Chinese herb formulas in the world. It serves as a stand-alone remedy, as a base formula from which to make numerous modifications (mostly by additions, occasionally one or two herbs are deleted when others are added), and as an adjunct to other formulas. The fact of its wide-spread use, given the limited scope of application when it was first described, is itself a reasonable subject of investigation. There must be certain properties of the herbs and valuable aspects of the formulation principles that lend to such flexibility in its use.

The formula was introduced initially as a pediatric remedy, mainly for infants, in the book Xiaoer Yaozhen Zhixue (Key to Syndrome Identification and Therapeutics of Children's Diseases) by physician Qian Yi during the Song Dynasty (1, 13). Although the book has not been translated into English, it is frequently referenced as a source of certain valuable formulas and as a basis for understanding ancient concepts of pediatrics.

Qian Yi was born in 1032 A.D. in Yuncheng, a small village in Shandong Province. His father was an acupuncturist and a traveler; in fact, he set off wandering one day and never returned. Soon after his father disappeared from his life, Qian’s mother died of disease. Qian Yi was adopted by his father’s sister, whose husband was a physician with a good reputation. Qian began learning medicine from his new father. Qian read medical books describing the different schools of thought and studied with current teachers of the various schools. As a result of his persistent studies, Qian’s medical skills became quite well recognized and he was eventually invited to treat members of the Imperial Court. His primary area of interest was pediatrics, for which he devoted forty years of his life. His teachings on pediatrics were compiled and organized by one of his students, Yan Xiaozhong, and published in 1114 A.D. in Qian’s name soon after Qian’s death. Xiaoer Yaozhen Zhixue is comprised of three volumes. The first deals with treatments according to the various syndromes that can be differentiated in children. The second reports on 23 cases treated by Qian. The third lists commonly used formulas, the formulation principles (such as interactions and relationships between herbs in a formula), and their method of administration.

The most important diagnostic procedure for children, according to Qian, was observation, particularly assessing the vitality of the infant by the appearance of the complexion and the eyes. According to his understanding, the physiology of infants is dominated by the fact that the internal organs (zangfu) are not fully developed and can easily become weak. “An infant’s five zang and six fu organs have come into shape but are not fully developed, or are fully developed but not yet strong.” Thus, the infant is prone to suffer from deficiency or excess, cold or heat, or other disharmony. These disorders would then manifest in the spirit and appearance of the child, particularly as revealed by the face. As to therapeutics, he considered drastic measures, such as use of strong purging herbs and strong tonic herbs, as commonly used at that time for adults and also given in smaller doses to children, to be inappropriate. A balance of gentle purging and gentle tonification should be the principle of formulation. He recommended relying primarily on herbs that had a mild and moist nature, selecting those that would regulate the functions of the stomach and spleen and benefit the kidney. That is, he focused on the treating the organs that were involved in the nourishment and development of the child.

Among his famous formulas still used today are Yi Gong San (Powder of Extraordinary Merit; used for indigestion associated with weak stomach/spleen functions); Dao Chi San (Powder to Guide out the Red; used for urinary tract infection with bleeding);
and, Liuwei Dihuang Wan (Pill of Six Ingredients Headed by Rehmannia; used for kidney deficiency leading to impaired maturation of infants). The primary use of Rehmannia Six Formula described by Qian was the treatment of the group of developmental disorders called the five delays: delay in standing up, delay in walking, delay in growth of hair on the head, delay in development of the teeth, and delay in speech development. In addition, the formula was indicated for delay in closure of the fontanel.

Although there had been some previous texts on pediatrics, Xiaoyao Yaozheng Zhixue is the earliest pediatric book to be preserved in its original form in China. It played a guiding role in pediatrics throughout the following centuries until the modern era. For example, Wan Quan (1495–1585) was a famous pediatric physician of the Ming Dynasty. He wrote many books and expounded on Qian Yi's theory of differentiation of syndromes in infants according to the zang organs. Like Qian Yi, Wan emphasized nourishing the spleen and stomach and advocated using purgation and tonification at the same time. In turn, many physicians of later generations quoted Wan Quan's books, and his teachings were introduced into Japan and Korea. As a result of his influence, Qian Yi is regarded as the founder of pediatrics in the Chinese medical tradition. Several other books on pediatrics were published in the latter part of the Song Dynasty, including books that focused on treatment of chicken pox, measles, tetanus, and small pox. However, new books on these subjects appeared later with relatively little reference to the basic theories in the earlier works.

THE STRUCTURE OF REHMANNIA SIX FORMULA

Rehmannia Six Formula is comprised of three pairs of herbs, each pair incorporating an herb that gently tonifies and an herb that gently drains or disperses (these actions often referred to as “purging”). The pairs are typically presented:

<table>
<thead>
<tr>
<th>Tonic Herb</th>
<th>Action</th>
<th>Draining Herb</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rehmannia</td>
<td>warms and nourishes kidney</td>
<td>Alisma</td>
<td>cools kidney and drains moisture</td>
</tr>
<tr>
<td>Cornus</td>
<td>warms and nourishes liver</td>
<td>Moutan</td>
<td>cools liver and moves blood</td>
</tr>
<tr>
<td>Dioscorea</td>
<td>warms and nourishes spleen</td>
<td>Hoelen</td>
<td>moves splenic moisture</td>
</tr>
</tbody>
</table>

Aside from the formula's balancing of tonification and dispersing actions on the organs, the dispersing herbs are seen as preventing adverse effects of the tonic herbs: alisma and hoelen prevent the greasy quality of rehmannia from causing indigestion; moutan prevents excessive warming of the liver by cornus (2, 14). Further, one can depict a nutritive scheme encompassing these ingredients:

1. Dioscorea and hoelen improve the function of the spleen, thereby enhancing the extraction of nutrients from food and nourishing the blood, which improves the liver function.

2. Cornus and moutan, in combination with enriched blood, improve the liver function, which provides a moistening action to the kidney.

3. Rehmannia and alisma, along with the moist essence from the liver and spleen, restore the kidney yin and essence and normalize the kidney functions.

Thus, the ultimate aim of the formula is to replenish the kidney, and this is accomplished by addressing each requisite step involved in the normal process of gaining “postnatal” kidney essence. The relationship of the spleen, liver, and kidney are further elucidated by this explanation of the kidney essence (13):

Essence is the material basis of qi. Qi derives from essence, and the functional activity of qi, in turn, produces essence. For example, primordial qi is transformed from congenital essence, while acquired essence is derived from food through the function of the stomach and spleen. Abundant congenital essence leads to vigorous primordial qi, promotes the stomach and spleen's functional activity and enhances acquired essence. In this way, congenital essence is continuously replenished.

Essence and blood can mutually transform into each other. Essence and blood are stored in the
kidney and liver respectively. Abundant essence in the kidney ensures rich blood in the liver. Abundant blood in the liver generates more essence for the kidney.

For infants who have a deficiency of congenital essence, leading to impaired development or failure to thrive, the stomach and spleen activity are weakened by the lack of qi derived from essence, and the liver blood is deficient due to the lack of enrichment from both the kidney essence and the spleen’s digestive and absorptive functions. Therefore, the aim of therapy is to improve the spleen, liver, and kidney so as to boost up the acquired essence—taking the place of deficient congenital essence—and restoring the secondary deficiencies that have arisen from the initial essence deficiency.

DOSAGE AND ADMINISTRATION OF THE HERBS

Rehmannia Six Formula was an adaptation, made by Quan Yi, of an earlier formula: Rehmannia Eight Formula (Bawei Dihuang Wan), described in the Shanghan Lun and Jingui Yaolue. Two herbs included in Rehmannia Eight Formula for strongly warming up the yang, aconite and cinnamon bark, were deleted, and the proportions of the herbs were adjusted to produce the pediatric formula. A typical presentation for Rehmannia Six Formula is this one in Thousand Formulas and Thousand Herbs of Traditional Chinese Medicine (3):

- Rehmannia: 24 grams
- Cornus: 12 grams
- Dioscorea: 12 grams
- Alisma: 9 grams
- Moutan: 9 grams
- Hoelen: 9 grams

The herbs are to be powdered and made into pills with honey. For adults, 9 gram pills (which contain about 6 grams of herbs) are administered, one pill each time, 2–3 times per day (usually, just 2 times). The pills are either chewed and swallowed, or put into water and decocted. For infants, the dosage is about 1 gram each time. Alternatively, the formula can be made as a decoction, with modifications as deemed necessary. In decoction form, it is common to use the amount of herbs specified above for a one day dose for adults, though the amount of cooked rehmannia may be lowered slightly to avoid digestive disturbance. When administered as a dried decoction (granules), about 12 grams of the granules are consumed in one day, usually in two divided doses, with a lower dose for children.

CHANGING APPLICATIONS OF THE FORMULA

The use of Rehmannia Six Formula as a pediatric remedy may have been popular after the publication of Qian Yi’s medical theories and formulas, but treatment of infants is a relatively limited medical area and would not be sufficient to yield such broad appeal for the formula as is seen today. Instead, the transformation of Rehmannia Six Formula from a prescription for infants to one for the adult suffering from disorders of aging was the critical factor that made the formula one which is frequently used.

There is no mention of this formula in books relaying the general practice of Chinese medicine until the latter part of the Qing Dynasty (1644–1911 A.D.). Thus, for example, the book Danxi Zhifa Xinyao (Heart and Essence of Danxi’s Method of Treatment) describing the teachings of Zhu Danxi (1281–1358 A.D.) did not include mention of this formula (4). Zhu was the head of the “yin nourishing school,” propounding the
theory that yin deficiency was a common outcome of pathological processes or basic cause of pathology, so that yin nourishing therapies were a critical means of treatment many diseases. Similarly Li Dongyuan (1180–1251 A.D.), the head of the stomach/spleen school, didn’t include the formula in his famous work Pi Wei Lun (Treatise on the Stomach and Spleen; 5). He advocated use of formulas for improving digestion to nourish all organs and prevent, as well as treat, many diseases.

There is a brief mention of Rehmannia Six Formula in Yinhai Jingwei (Essential Subtleties on the Silver Sea), a text of ophthalmology. Unfortunately, it is difficult to pin down the date of the book or to know if some materials were added later. According to Kovacs and Unschuld, who translated the work to English (16), the earliest existent version was printed around 1550 A.D. There is a question/answer section in the modern version available to Kovacs and Unschuld which says:

Question: To be able to see what is far, but not be able to see what is near, why is that? Answer: This is because qi flourishes, while the blood is weak. The Classic [Neijing] states: ‘When near vision is unclear, this is because of lack of water [kidney essence/kidney yin].’ For treatment, one should take Rehmannia Six Formula and Bushen Wan [pills to supplement the kidney]. All herbs that supplement the yin qi can be used.

The condition described here is consistent with the farsightedness that develops with old age. Regarding the formula, the text continues: Rehmannia Six Pills are effective against depletion of the kidney, and when the eyes cannot see, and their luster is insufficient. Another prescription adds cnidium (chaunxiong), tang-kuei (dangui), and cassia seed (manjingzi).

Zhang Jingyue (1563–1640 A.D.), a well-known physician living at the end of the Ming Dynasty, specialized in rehmannia-based formulas. A review of his teachings about rehmannia, found in his 1624 A.D. publication Jingyue Quanshu (Complete Works of Jingyue), was produced by Huang Baoming and translated to English (17). Zhang believed that the yin qi is never in excess and that diseases associated with yin are deficiency syndromes. He observed that, during his lifetime, most diseases involved yin deficiency to some extent and, frequently, there was an accompanying yin deficiency fire. Rehmannia was, for him, the ideal herb to use in such cases, stating that:

Rehmannia is needed to guard the yin in cases of deficiency that involve scattering of the spirit; the heaviness of rehmannia is needed to counter the rising fire of yin deficiency; the calming quality of rehmannia is needed for pacifying the agitation of yin deficiency; the mild sweetness of rehmannia is needed for relaxing the impulsive nature of yin deficiency; rehmannia is needed to restrict the flooding of water evil in cases of yin deficiency; rehmannia is needed to retrieve the scattered genuine qi back to its origin in the kidney; in yin deficiency with damage to the essence-blood and extreme emaciation, it is used to thicken the gastro-intestinal tract; rehmannia used with dispersing agents is indicated for diaphoresis; rehmannia used with warming agents is indicated for retrieving yang qi.

Zhang had organized 186 prescriptions of his own of which 48 contained rehmannia. In Huang's extensive discussion of rehmannia formulas used by Zhang, including traditional formulas by previous authorities, Rehmannia Six Formula is not mentioned at all. The Rehmannia Eight Formula of the Shanghan Lun received passing mention in the description of an elderly patient being treated. It is evident that the Rehmannia Six Formula had simply not gained much attention at this time.

It was not until the Qing Dynasty that modifications of the Rehmannia Six Formula, intended for use in adults, were mentioned as major formulas, indicating that the transition in use away from pediatrics had occurred by then. For example, Wang Ang, in his Yifang Jijie (1682 A.D.) added schizandra to treat wheezing disorders; Qin Jingming, in his Zheng Yin Mai Zhi (1702 A.D.) added anemarrhena and phellodendron to treat kidney fire; Dai Tianzhang, in his Guangwen Yilun (1722 A.D.) added acorus, schizandra, and magnetite to treat hearing loss and tinnitus; Wu
Qian, in his Yizong Jinjian (1742 A.D.) added schizandra and ophiopogon to treat tuberculosis; and Dong Xiyuan, in his Yiji Baojian (1777 A.D.) added lycium and chrysanthemum to treat eye disorders (see Table).

It is possible that Wang Ang (1615–1680) was primarily responsible for the transformation of Rehmannia Six Formula to one that could be broadly utilized for adults. According to Unschuld (15), “Wang Ang can probably be considered the most successful medical writer of the Qing period.” His variant of Rehmannia Six Formula, Duqi Wan, made by adding schizandra, was published in his books Yifang Jijie (Analytic Collection of Medicinal Formulas) and Tangtou Gejue (Lyrical Prescriptions), the latter being designed to help practitioners memorize 300 valuable prescriptions by presenting the information in simple, logical, and easy-to-understand poems.

His work likely encouraged others to look more closely at this prescription. In Heart Transmission of Medicine (6) by Liu Yiren, written around 1850 A.D., there is brief mention of Rehmannia Six Formula for treatment of dizziness, one of the indications still mentioned in many modern texts, with reference to the following statement in the Ling Shu (ca. 100 B.C.):

The brain is the sea of marrow. When the sea of marrow is superabundant, the person is nimble, energetic, and strong, and can accomplish what is normally beyond the ability of an ordinary person. If the sea of marrow is insufficient, there will be brain spinning [dizziness], ringing in the ears, aching in the legs, fainting, loss of vision, fatigue, and somnolence.

Liu saw that the symptoms of dizziness, ringing in the ears, fainting, and dim vision as signs of modifications of Rehmannia Six Formula commonly mentioned in modern texts.

<table>
<thead>
<tr>
<th>Formula</th>
<th>Additions</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qi Ju Dihuang Wan</td>
<td>lycium, chrysanthemum</td>
<td>eye disorders, particularly with dryness</td>
</tr>
<tr>
<td>Gui Shao Dihuang Tang</td>
<td>tang-kuei, peony</td>
<td>blood deficiency, particularly skin dryness</td>
</tr>
<tr>
<td>Zhi Bai Dihuang Wan</td>
<td>anemarrhena, phellodendron</td>
<td>deficiency fire of the kidney; especially warmth in the palms and soles, sore throat, sweating</td>
</tr>
<tr>
<td>Duqi Wan aka Qiwei Duqi Wan</td>
<td>schizandra</td>
<td>asthma due to yin deficiency</td>
</tr>
<tr>
<td>Mai Wei Dihuang Wan aka Baxian Changshou Wan</td>
<td>ophiopogon, schizandra</td>
<td>asthma and cough, with consumptive syndrome (sweating, tidal fever)</td>
</tr>
<tr>
<td>Gui Fu Dihuang Wan</td>
<td>cinnamon bark, aconite</td>
<td>yang deficiency, with frequent urination and back pain</td>
</tr>
<tr>
<td>Erlong Zuoci Wan</td>
<td>schizandra, acorus, and magnetite</td>
<td>continuous tinnitus like chirping of cicadas, hearing loss</td>
</tr>
<tr>
<td>Erlong Dihuang Wan</td>
<td>bupleurum, magnetite</td>
<td>ringing in the ears due to liver/kidney yin deficiency</td>
</tr>
<tr>
<td>Niu Chen Dihuang Tang</td>
<td>achyranthes, plantago, cinnamon, aconite</td>
<td>weakness and numbness in the legs</td>
</tr>
</tbody>
</table>
fire flaming upward from the deficient kidney. Therefore, nourishing the kidney yin and cleansing the deficiency fire was the requisite therapy, and Rehmannia Six Formula fit this application (he also liked to add deer antler to nourish the kidney along with the pills). Placing the formula in the category of treatments for the elderly suffering from liver/kidney deficiency opened up a broad new area of application for Rehmannia Six Formula.

By the 20th Century, use of Rehmannia Six Formula for adults with severe yin-deficiency syndrome had become the dominant application, overshadowing its pediatric applications. Qin Bowei, a physician who helped the transition of traditional medicine from its early forms to the modern TCM mentioned the formula in his teachings. He wrote that Rehmannia Six Formula could treat “the depletion of kidney water, with head and eye dizziness, soreness and frailty of the lumbar region and legs, yin deficiency engendering fire, spontaneous sweats, emaciation, and lassitude (7).” He summarized the effects of the formula were to treat insufficiency of kidney and liver, mainly applied to treating symptoms of emaciation and lumbar pain.

The Advanced Textbook on Traditional Chinese Medicine and Pharmacology (8) presents the current explanation of the formula based on the TCM principles:

This prescription is indicated for disorders due to kidney yin insufficiency and upward attack of deficiency fire. The lumbus houses the kidney, which controls the growth of bones, marrow, and teeth, so insufficient kidney yin may give rise to soreness and weakness of the lumbus and knees and loose teeth. The brain is the ‘sea of marrow,’ and kidney yin deficiency may impede the production of marrow and the function of the brain, causing dizziness. When kidney yin is deficient, the essence cannot be sent to the ears, resulting in tinnitus and deafness. Since the kidney stores the essence, the ministerial fire may disturb the spermatic chamber when kidney yin is deficient, leading to nocturnal emission. Yin deficiency may lead to internal heat generation, resulting in hectic fever, a hot sensation in the soles and palms, diabetes, and night sweating. Yin deficiency in the lower body may induce an upward attack of deficiency fire, causing dry throat and red and dry tongue with little coating. The principle of treatment is to nourish yin and invigorate the kidney.

**MODERN SITUATION**

During the 1950s and after, physicians working at the rapidly constructed new Chinese hospitals found that they had huge patient loads and barely enough time to make a comprehensive diagnosis and therapeutic plan. By 1980, there were only about 25 traditional medicine doctors per 100,000 people (9). To manage the patient load, which often involved spending less than 5 minutes with each patient, they tended to get an overall picture of the patient requirements by tongue and pulse diagnosis and a quick review of symptoms, and fit a prescription to a relatively small group of basic categories.

Rehmannia Six Formula suited the yin-deficiency category and became the first formula considered within that category. Rehmannia Six Formula could thus be considered the constitutional base formula for most yin-deficiency cases. The formula was easily modified because of its small number of versatile ingredients. Typically, only 1–4 herbs would be added to treat the specific disease manifestation. As stated in an article on the nature and treatment of the kidney in modern TCM (14), under the heading kidney yin deficiency: “The basic prescription of choice is Rehmannia Six Formula. Alterations are made to this prescription according to additional symptoms and signs.”

The clinicians at the hospitals were free to mix any herbs together, because their patients generally went straight to the pharmacy to pick up the crude herb mixtures for preparing decoctions. However, for cases where long-term therapy was deemed important, it was impractical for patients to keep returning to the clinic, and, instead, the doctors encouraged their hospital pharmacies to stock pills, which could be manufactured at the affiliated hospital factory. Eventually, the large-
scale patent medicine factories became the main suppliers, rather than the smaller manufacturing facilities at the hospital: the patent medicine products could be purchased at numerous stores throughout China, not just at the clinical facilities.

With the pills readily available over the counter as well as by prescription, the applications could be further expanded beyond treatment of severe diseases. Thus, proponents of the patent pills began prescribing Rehmannia Six Formula, and its derivatives, for a wide range of preventive health care applications. Additionally, research centers in China began studying a variety of possible new uses of the formula.

Based on an overview of literature from China, it appears that the formula became especially popular about 30 years ago. In the book 100 Famous and Effective Prescriptions of Ancient and Modern Times (10) published in English in 1990, Rehmannia Six Formula was reported to be “often used” to treat: chronic nephritis, hypertension, esophageal epithelial hyperplasia, diabetes, infantile mal-development, and general yin-deficiency syndromes in gynecology, ophthalmology, surgical disorders, and ear, nose, and throat disorders. The book presented a review of experimental and clinical studies published during the period 1977–1981, in which the formula was reported to reduce the incidence of induced cancers and promote excretion of urea, while protecting renal functions in laboratory animals, and to help heal early stage esophageal hyperplasia (pre-cancerous conditions) and treat prostate inflammation in humans.

In the book Formulas and Strategies (12), also published in 1990, the formula is said to be suitable for treating the following biomedically-defined disorders, so long as the presentation is appropriate to a yin-deficiency category: neurasthenia, pulmonary tuberculosis, diabetes mellitus, hyperthyroidism, chronic nephritis, chronic glomerulonephritis, urinary tract infection, hypertension, failure to thrive, functional uterine bleeding, optic neuritis, optic nerve atrophy, and central retinitis.

In a more recent review of the pharmacology studies of the formula reported during the period 1987–1996 (11), Rehmannia Six Formula was reported to have beneficial effects on immune functions and help prevent tumors; to improve digestion and regulate sugar metabolism; to enhance cardiac function and provide general antiaging activity as well as to treat urogenital disorders.

These findings, as well as continued clinical use of the formula in Chinese hospitals and mass production of the formula in many of China’s patent medicine factories, has led to a world-wide demand for the prescription. The production of small pills that are more acceptable to Westerners than the original honey-bolus (see Figures 2 and 3), and production of dried extracts (granules), have made the formula very convenient to use. Based on its record of being safe, having few adverse effects or contraindications, and suited to long-term administration, the formula is worthy of careful study by practitioners to learn of its full potential.

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