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The Pharmacist

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JAS4QoL

Mini-Review

~ The Pharmacist ~

From God to Neighborhood Chemist and Beyond

Changing image, changing roles, but ever a friendly and informative community figure

The pharmacist has been known through history by a variety of names or titles: shaman, medicine man, witch, healer, wise woman, apothecary, alchemist, druggist, dispenser, or chemist, but the services we provide to the community have remained essentially the same. With a rich knowledge of medications, both natural and synthesized, and well-versed in both their risks and benefits, we have provided the people in our communities with the specific drug or healthcare information that they need: to heal, if they are ill, or enhance their health, if they are not.

For as long as humans have walked this earth, malady has been an unwelcome, yet constant presence in our lives. Ever unwilling to surrender without a struggle, man has fought against premature arrival of the shrouded black figure with his ominous sickle. Prayer, religion, sacrifice, and ritual, herbs or other medicinal plants and animals were searched for some cure, some way to stave off life-threatening illness. In fact, it was the rich earth, the soil itself which contained an organism *Penicillium*, too small for the naked eye, yet potent enough to rescue us from pathogens which had been the main cause of premature death through much of man's history. As alchemy developed from mystique into the science of chemical synthesis, the 20th century enjoyed a golden age of synthetic compounds with miraculous powers that could bring even those on the brink of death back to us.

1. Shinno-san: The Divine Farmer

History suggests the first to provide medicinal products to the community was an emperor, or perhaps a deity, who lived in China around 2700 B.C., nearly 5000 years ago. *Shennong*, or *Shinno-san* as he is fondly called in Japan, literally means, *Divine Farmer*. He taught his people to tame the land, inventing the plow and the burning of fields to make the land more fertile, encouraged hunter-gatherers to cultivate and eat grains instead of relying on a haphazard diet of wild plant and animal life. Wall murals and other depictions passed down over the millennia show him with ox horns on his head, chewing on some vegetation to test it and discover its properties. European artifacts from prehistory have also shown a Horned God, consort of the Great Mother; again we are struck by these similarities among such vastly diverse regions and cultures.

Shennong was said to have had a transparent body which allowed him

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to see exactly how each organ was affected by the plants he sampled. Stories suggest that he had a special red whip which he would use to smack a plant, and taste its juices which had transferred onto the whip. He is said to have tested dozens of plants every day, and used a special antidote, yet another of his important discoveries, which counteracted the toxic effects of as many as 70 different poisons.

His herbal knowledge has been passed down through the generations to form the foundation of what we know as Oriental herbal medicine. It was compiled into the first known book of herbology published sometime around the birth of Christ titled *Divine Farmer's Materia Medica* (*Shennong Ben Cao Jing)* and is believed to have been written by one of his followers or a descendant. It comprises three volumes, classifying plants into the following categories:

- Noble herbs: Volume 1 introduces 120 plants that are harmless to humans and have "stimulating properties" such as reishi, ginseng, Chinese cinnamon, or liquorice root.
- Common herbs: Volume 2 contains 120 plants with therapeutic properties, that are toxic, or potentially toxic and includes ginger, peonies and cucumber.
- Lowly herbs: Volume 3 covers 125 substances with potent or violent effects that can prove poisonous. These include rhubarb, different pitted fruits and peaches.

Shennong died accidentally after eating a weed with yellow flowers which caused his intestines to rupture before he could ingest the antidote

2. Shennong's now-popular "antidote"

Your curiosity is no doubt piqued by Shennong's antidote which could counteract so many poisons. It is in fact something many cultures around the world ingest almost every day! Shennong had instructed his helpers to boil water for drinking since he understood that water was often safer when boiled. A sudden gust blew some leaves from a nearby plant into the boiling water and intrigued, Shennong decided to try it, finding himself delighted by its refreshing fragrance. And thus, tea was born. Tea is believed to have been in use since the first millennia B.C., and written documentation of its use stems back to Emperor Han in the second century B.C.

It arrived in Japan together with Buddhism as the priests carried brought it back with them from China, cultivating the plants in their monasteries in the 6th to 7th century A.D. Almost every culture has a tradition of taking the leaves of the *Camellia sinensis*, steeping them in hot water and enjoying the result, and a cup is often offered to a visitor. Green, unfermented tea contains catechins and caffeine. Fermentation creates many different flavors and colors, all of which are enjoyed around the world. Some teas are flavored such as Earl or Lady Grey, where citrus peel and flowers are added to black tea, or Vietnamese lotus tea, which is green tea flavored with the scent of lotus flowers. In other teas such as Darjeeling and Oolong, the flowery fragrance is a result of fermentation.

Many herbs are enjoyed as teas, such as Peter Rabbit's comforting chamomile, or *Echinacea* to ward off colds, and many are known to have some medicinal effects as well. Much of Kampo medicine, the use of plant and animal-derived ingredients mixed into specific formulations, is founded in Chinese medicine which resulted from Shennong's research. However, over the many centuries since it reached Japan in the 5th century A.D. via Korea, it developed into its own unique form of medicine. Kampo formulations are traditionally administered in the form of a tea. However, the strong tastes and aromas associated with these products are not always palatable, so many are now available in the form of pills or packaged as granule powders for convenience and ease of ingestion.

An impressive oil painting by Hinckley hangs in Harvard Medical School's Countway Library, *The First Operation with Ether* (1893). And yet according to the *Records of the Three Kingdoms*, Hua Tuo 華佗 (c. 140–208) used máfèisàn (麻沸散), a mix of wine and medicinal herbs, to induce general anesthesia as early as the 2nd century A.D. An unparalleled great physician, Hua Tuo was able to use this anesthetic to conduct many surgeries that had previously been impossible. Unfortunately, that knowledge died with him when he was executed for treason when he offered to conduct open brain surgery on the Emperor of his time to treat his migraines. Many attempts were made to recreate the formulation with no success. However, Hua Tuo had already discovered that physical inactivity, a disease of the rich and pampered even in his day, was a major cause of illness and developed *Wu Qin Xi* (Five Animal Frolics), a *Tai Chi*

exercise routine that imitates the physical movement of tigers, deer, monkeys, bears and birds, and this survives to this day.

In Japan, Seishu Hanaoka is known as the Japanese father of anesthesia. In 1804, Hanaoka successfully used 通仙散 Tsu-sen-san, a formulation based on Korean morning glories, to anesthetize and remove a breast tumor from a 60-year-old woman. Hanaoka had lost his beloved sister to the disease and over the course of his career, performed over 150 breast cancer surgeries. His story was fictionalized by Sawako Ariyoshi in *The Doctor's Wife*. With no Good Clinical Practice standards to rely upon in the early 19th century, Hanaoka was forced to use a relative as a healthy volunteer for his anesthetic. Both Hanaoka's mother and wife offered to serve as his human guinea pigs, further upping the stakes of the traditional mother-in-law vs wife standoff. Hanaoka shows where his allegiance lies when he gives his experimental concoction to his wife, while giving his mother a harmless sleeping potion.

In these early days, anesthesia was still a very lengthy process. It took 2 to 4 hours before the patient became impervious to pain and subsequently became unconscious. Depending on the dosage, this effect lasted from 6 to 24 hours. Active ingredients included a number of poisonous ingredients: scopolamine, hyoscyamine/atropine, aconitine and angelicotoxin. In combination, these compounds gave rise to anesthesia, sleep and paralysis—mainly due to atropine and scopolamine—both of which act to inhibit the transmission of stimuli between neurons (as acetylcholine antagonists). Current general anesthesia still involves the use of multiple drugs to induce reversible muscle relaxation, analgesia, amnesia, and depression of consciousness.

Shennong came to Japan together with his teachings and the raw materials for Kampo formulations which continue to be imported from the Asian continent today. From as early as the 16th century during Toyotomi's dynasty, crude drugs from China have been sold in *Doshomachi*, a particular street in Osaka which is the mecca of the pharmaceutical industry. The tributaries of Yodo river ran into central Osaka city bringing ships from mainland China and other regions filled with the crude drugs that supplied Japan. The so-called Big Three Pharma companies: Takeda, Tanabe, and Shionogi, were already in business at that time, serving as trading companies that dealt in these life-saving ingredients.

Tanabe, now Tanabe Mitsubishi, was established in 1678 and is one of the oldest pharmaceutical companies in the world, second only to Merck which was established 10 years earlier in 1668. In fact, historical documents show that the Tokugawa Shogunate granted Tanabe's great grandfather permission to travel to the Philippines and Thailand to procure crude drugs as early as 1604.

They made their mark in society with the historical equivalent of a blockbuster formulation called *Tanabeya's Furidashi Kusuri* (literally, Tanabe's Infusion Drug). According to the curator at Tanabe's museum, the secret formula for this product was based on the special battle medication used by the Shimadzu clan during their wars. It stopped bleeding, healed wounds, and enhanced cures. It was primarily sold for women after childbirth.

As the Edo Era ended and the Meiji Restoration began in 1868, Japan gradually became more attuned to Western culture and medicine was no exception. Pharma companies began importing chemically synthesized drugs from the West. By 1877, Tanabe Gohei decided it was time to begin manufacturing drugs in Japan.

In 1916, Tanabe opened its first factory. Others soon followed. Osaka's Doshomachi now became a street of pharmaceutical manufacturers, not just wholesalers and importers.

Religiosity in the Japanese is ambiguous, but there will always be a strong streak of Shintoism underlying its culture. As such, a shrine dedicated the gods of medicine was set up in Doshomachi in 1780. It is formally called Sukunahikona Shrine but more commonly referred to as Shinno-san after the Chinese God. It houses two gods, Shinno-san and Sukunahikona, Japan's god of healing and medicine. On November 22nd and 23rd, the Shinno Festival is held in Doshomachi and the whole street comes to life, filled with food stalls and visitors and cute dressed-up figures of Shinno-san, other pharma-related characters, and most notably, bright yellow bobble-head paper-mache tiger figures.

The tiger became associated with the shrine during the great cholera epidemic in 1822. A Kampo formulation called *Kotou-sakkiuouen (tiger head kills ogre)* pills were handed out to the public after being blessed at the shrine. Tiger bones, especially those of the skull, have been in use for about 1500 years

and are said to reduce inflammation and pain, and also calms the nerves. Some texts suggest that it can cure dementia. Part of the so-called potency of this ingredient has to do with the image of the tiger. Its magnificent strength is feared by all beings, even supernatural beings such as the oni (Japanese ogres), and so it would surely be effective against disease. Unfortunately, these beliefs have led to widespread poaching of tigers throughout much of Asia so that very few animals remain today. Other bones from mammals such as wolves, bears, and deer, are said to have the same properties as tiger bones. Similar properties have been attributed to *Ryukotsu* or dragon bones which are actually fossilized mammal bones.

3. From Kampo to Modern Pharmacy

Kampo 漢方 is a form of traditional Japanese medicine founded in Chinese Traditional Medicine and imported into Japan in the 5-7th century A.D. together with Buddhism (famous Buddhist priests were often its first proponents).

Currently, it has developed into something quite distinct from its origins. Kampo is generally believed to cause fewer adverse effects than western drugs. Chief among its characteristics is its highly individualized form of treatment. The practitioner conducts a thorough physical exam and based on the patient's unique "type" and "condition", recommends an appropriate mix of crude plant- and animal-based ingredients that are then brewed into a "tea" specific to that patient alone. Although it was mostly abandoned at one time in favor of more "scientific" western medications, Kampo has become increasingly more popular in Japan over the past few decades.

4. Pharmacy in Japan

Shortly after WWII, pharmacy programs were established at the University of Southern California Los Angeles, which were 6-year programs and a focus was placed on clinical pharmacy. Graduates of this program were called Doctors of Pharmacy or PharmD, a clinical degree similar to the Doctor of Medicine or MD degree. Currently, the minimum requirement to take the state-based NAPLEX board examinations to practice as a pharmacist is graduation from a 6-year college of pharmacy. Some students complete a pre-pharmacy bachelor of science degree before entering pharmacy school so the length of education can vary from 2-4 years of undergraduate education (BS) followed by graduate level professional training for 3-4 years, totaling 7-8 years overall.

I received a post-BS-Pharmacy graduate-level PharmD back when a BS in Pharmacy was a 5-year program and the graduate PharmD program was 2 years with a full 1.5 years of clinical rotations which included a 10-week teaching rotation mentoring undergraduate students at a teaching hospital, so it is probably closer to the current 4+4 year program.

5. Why clinical pharmacy?

Tailor-made medicine, individualized medicine has now become fairly commonplace, but even in the mid-20th century they recognized the limitations of the one-prescription-fits-all formula. The idea, was to create a pharmacist who had more in-depth training in the clinical sciences and who would be better attuned to the individual needs of patients in a clinical setting.

The 6-year PharmD program was originally an undergraduate program and graduates wishing to practice clinical pharmacy were encouraged to undergo hospital residencies to bolster their actual experience.

This has increasingly become the norm around the world including Asia and in Japan, the first graduates of the 6-year program graduated 5 years ago. Currently, pharmacy students are required to undergo 22 weeks of practical training at a pharmacy during their 5th and 6th years of college comprising 11 weeks at a community pharmacy and 11 weeks at a hospital pharmacy. A greater focus has been placed on teaching medical pharmacy with the content reflected in the national board examinations for pharmacists.

6. Emerging pharmacist roles

The Ministry of Health, Labour and Welfare have decided that pharmacists should be the providers

of community-based healthcare information. Educating the public will help to reduce unnecessary use of healthcare resources while instilling life-style related guidance to the public may help to prevent lifestyle-related illnesses or achieve better control in chronic disease to improve morbidity and mortality.

7. Why Pharmacists?

People generally feel pharmacists are easier to talk to than their doctors, especially with regard to their medications. They are generally more accessible since walking into a pharmacy is easier, faster, and cheaper than walking into a doctor's office. The informal setting of a shop front has fewer time restraints (i.e., no patients waiting out in the hallway) and makes it easier for patients to open up about any medication-related concerns. In Japan, physicians are viewed with a great deal of respect and many fear insulting the doctor who prescribed the drug if they mention any side effects or other drug-related concerns.

Traditionally, pharmacies and drug stores in the community have been gathering places for the public. Often, before bottling technology was developed in the 1950s, pharmacies housed soda shops since carbonated or fizzy drinks were a luxury that could only be enjoyed at stores. Before the advent of modern pharmaceuticals, many pharmacies had little to offer locals except powders, elixirs, cordials, and curative spring waters, and so it was natural that these would have the facilities to provide carbonated soda drinks which were thought to have some health-related effects.

As scientists have finally unraveled some of the fundamental mysteries of the double-helix and are currently in the process of deciphering the nucleotide codes that make up one of the most basic components of life itself, a door has been opened to a new age of drugs. It holds immense potential for individualized patient care as we discover just how important genetic makeup is, not only that of the patient, but also of the diseases. Many cancers that had previously been "uncurable" are now gradually being conquered thanks to these new weapons man has developed to target specific genotypes within those cancers. Simultaneously, these drugs have become ever more complex and expensive, and the knowledge to wield them ever more challenging. Hence the need for more knowledge and experience on the part of the pharmacist.

What are the qualifications that pharmacists will need in this new era? Kyoto Pharmaceutical University is the second oldest school of pharmacy in Japan, and was established in 1884 by students of a German scholar, Dr. Rudolf Lehmann. Since that time, it has seen its graduates become leading members of society in all walks of life related to pharmacy and medicine. As the world evolves, we peer into a crystal ball trying to foresee the challenges our students will face so that they can be trained to ensure that they are ready.

In other countries around the world, most prominently in North America, pharmacists are proving their worth in helping patients with chronic illnesses. By providing patients who have long-term conditions such as hypertension, diabetes mellitus, and such with an in-depth review of their medications and life-styles including diet, healthfoods, and any OTC products or supplements that they may be taking, pharmacists are showing that they can make an impact.

A review of such services in Canada reveals that patient health outcomes improved by as much as 60% when pharmacists offer these services. In other studies, pharmacist counseling and interventions which may or may not involve a pharmacist contacting the prescriber to suggest prescription changes, has led to better control of high blood pressure or blood sugar to a degree where long-term patient morbidity and mortality are impacted.

8. What are the requirements for a success as a clinical pharmacist?

Clinical competence: The pharmacist must have the necessary professional knowledge and experience to provide appropriate responses in any given situation. To become a better healthcare team member, both sides will need time to accept the roles of a clinical pharmacist. What can s/he offer?

Time is also needed to build a basic relationship based on trust among the team members. The pharmacist also needs to learn not to overstep. The physician will always be the team leader and the pharmacist should never try to diagnose a patient. However, there will be situations when he/she suspects a

drug-related cause and can offer a possible solution. In such cases, the pharmacist will need to employ tact, using evidence in the form of published studies to support her theory. But even this will become easier once she has established a reputation for reliability in the team.

Proving effectiveness and usefulness in solving clinical issues will improve the pharmacist's reputation as a team member.

9. Communication Skills

Japanese, in general, are not very good at verbal communication. There is a sense that it is somehow better to leave many things unsaid. That this is superior to laying things out clearly on the table. However, when it comes to clinical decisions and discussion, pharmacists must be able to provide effective, clear, and concise information that is supported by solid evidence and experience. Unfortunately, pharmacists have a tendency to be reticent and shy. They must learn to overcome this barrier to communication through practice and the building of self-confidence. They are required to show professionalism, self-awareness as a healthcare worker, and as a member of a helping profession. It is also important to develop a clinical sense.

As with any skill, students can only learn through practice with the help of professional mentors and educators. Their most important and effective teachers will be the patients they encounter and are responsible for. A clinician must be able to express understanding, empathy for a patient's suffering, use communication skills to most importantly, listen to the patient, share if it will help the patient, and exercise common sense, offering only what the patient is capable of accepting.

What will it take to change a youth from a student into a clinical pharmacist? Ultimately, the answer is touch. Not physical, but emotional. To touch and be touched by example, by respect, by compassion, and by the humanity of those encountered in the clinical field.