

**James L. Holly, M.D.**

## **The Story of Coumadin**

**By: Jeff Guillory, RN, MSN, CFNP**

Coumadin is one of those drugs which are frequently considered poisons more than medicines. It is common to hear the word Coumadin in the same sentence with “rat poison.” This is because, it’s true. Coumadin is the brand name for the drug “warfarin.” This is the story of warfarin and how it came from killing cows to becoming the most widely used rat killer in the world, to being one of our greatest drugs used in certain patients for the prevention of strokes.

"All things are poisons, for there is nothing without poisonous qualities. It is only the dose which make a thing a poison . . . a lot kills, a little cures" Aureolus Paraceisus (1493 - 1541) "Grandfather" of Pharmacology

In the early 1900's, the northeastern United States was being plagued with a dreadful cattle disease that was causing cows to die from internal and external hemorrhages. Cattle would be found dead with pools of un-clotted blood around them. The cattle ranchers were at a complete loss to know why this was happening. Veterinarians and scientist began to respond to pleas from the ranchers for an answer.

The cattle’s main source of feed at the time was a plant called Sweet Clover, which was imported from Europe. It grew well in America, was an excellent feed for cattle, and was good for planting fields because it replenished nitrogen in the soil. Cattle that ate sweet clover in the fields seemed to thrive. The Summer of 1933 was hotter and wetter than usual which led to the storing of moist Sweet Clover hay in the farmers silos for Winter use.

One day in the Winter of 1933 a farmer named Ed Carlson, drove to the biochemistry building at the University of Wisconsin with a dead cow, a bucket of un-clotted blood and a truckload of old sweet clover that had been cut and used for hay. He pleaded with the researchers to help him with his dying cattle. Professor Karl-Paul Link did research at the university and began to work on this project.

Professor Link was a biochemist who specialized in agricultural chemistry. He discovered that the rotting sweet clover brought to him by the farmer contained a

compound called “coumarin.” “Coumarin” seemed to be a major active anticoagulant but fresh Sweet Clover did not produce “coumarin.” It was discovered that the recent rainy season had allowed mold in the Sweet clover hay to convert sweet clover into the “coumarin compound. Molds such as *Penicillium nigricans*, *P.jensi*, and *Aspergillus* metabolize the coumarin” into “dicoumarol.” “Dicoumarol” prevents fibrinogen in blood from forming form clots by interfering with vitamin K that the body uses to make blood clots.

This discovery helped farmers save their cattle. The disease was called Sweet Clover Disease and was prevented by not allowing cattle to eat molded Sweet Clover hay. Professor Link had made a cattle-saving discovery but saw no further use of “coumarin”.

Later in Professor Link's career he took a sabbatical from his research because he had tuberculosis and spent time in a sanitarium. While there he read about a troublesome problem with rodent control and thought of a use for the “coumarin” which his team at the university had discovered. Professor Link patented warfarin, which he developed into rat poison. The name warfarin is derived from the Wisconsin Alumni Research Foundation (WARF) which is the foundation that funded Professor Link's work. Warfarin is mixed with a corn base which is still used today as an effective rat poison. Mice and rats like the taste of the bait, while the warfarin prevents their blood from clotting which will kill the rodents within a few days because of bleeding into their brain.

The safety of warfarin was not determined in humans until a farm worker attempted to commit suicide by eating the rat poison. The rat poison did not kill the man immediately. The farm worker was taken to the hospital where doctors administered vitamin K. This counteracted the warfarin and the patient recovered. Now medical researchers knew how to counter-act an overdose.

Now that there was a use for warfarin as rat poison, and it could be safely taken by humans, scientist and medical researchers tried to find a use for this chemical for human health care. If it prevented blood from clotting, perhaps it could be used for people who made too many clots in their body. Medical researchers knew that strokes were caused frequently by clots in the brain. They also found that those with irregular heart rhythms were having strokes due to clots. If they could use warfarin in these patients to decrease the formation of clots, perhaps they could reduce the incidence of strokes. They began to experiment with warfarin to determine the correct safe doses to give to humans. Warfarin was discovered to reduce the chance of stroke in these patients by half.

Coumadin (warfarin) was not used frequently until 1955 when President Dwight D. Eisenhower had a heart attack while on vacation at his in-laws' house in Denver. Coumadin was used to prevent clots from forming in President Eisenhower's damaged and weakened heart. Eisenhower's long term treatment included Coumadin 35 mg per week. Since then, it has been one of the most widely prescribed drugs in the United States.

The FDA approved Coumadin for the treatment of the thromboembolic complications associated with atrial fibrillation in 1955. Since that time, Coumadin has continued to be the best medication for prevention of strokes in people with atrial fibrillation, and with other medical conditions in which clot formation could be detrimental to health.

Coumadin does not actually “thin” the blood, though this term is used frequently and is well understood. It actually lengthens the amount of time it takes for blood to clot. This is beneficial in medical conditions in which the formation of clots would be detrimental. These conditions include Atrial Fibrillation, Deep Vein Thrombosis and heart valve replacements.

Recent changes in Coumadin management include the blood testing to determine how long it takes for blood to clot. In the past the PT (Prothrombin Time) was used. Today we use a more precise test called the INR. INR stands for International Normalized Ratio. This test will provide the same result from anywhere the test is done, unlike the PT which could give a wide range of results.

The average person’s INR is around 1.00. For most Coumadin patients, healthcare providers attempt to keep the INR between 2.00 – 2.50 and 3.00 – 3.50. This means that the blood of people taking Coumadin will take longer to clot than the average persons but will not be at a dangerous level. We want the blood to be thin but not too thin. This test can be measured using a finger stick blood test in approximately one minute.

There are precautions that need to be taken when prescribed Coumadin. Complications that could occur if the blood gets too thin include: bruising for no known reason, nose bleeds, and blood in the urine or stool. If a person is taking Coumadin and any of these things occur, the patient should be checked immediately to determine if your blood is too thin.

Another precaution is the diet. Many daily foods interfere with how Coumadin works in the body. These are foods that are high in Vitamin K. These include: green leafy vegetables, cauliflower, broccoli and herbal teas. Medications can also interfere with Coumadin. It is very important to have your INR checked more frequently when taking new medications, such as antibiotics and anti-fungal medication.

Coumadin can be a dangerous drug, after all it is the same ingredient used in many rat poisons. It can also be a life saving drug. For safety reasons, Coumadin Clinics are available to monitor Coumadin levels and keep those on Coumadin safe. To learn more about Coumadin and the benefits it can offer you see your Primary Care Provider. If you are on Coumadin be sure to have your blood checked at your Coumadin Clinic as directed by your healthcare provider.

Remember, it is your life and it is your health.