## ALLERGEOUS



# Focus on the *non-*T.R.U.E. Test Allergen — GOLD

BY SHARON E. JACOB, M.D., AND PANTA ROUHANI, M.P.H.

since January of 2005, this column has highlighted a different thin-layer rapiduse epicutaneous (T.R.U.E.) Test allergen each month and intended to answer some of the most frequent questions relating to their origin and most common uses. Each column has also highlighted appropriate products that affected patients should avoid, along with tips to avoid cross-reactions and exposures.

This month, we break from the tradition of this column to discuss a non-T.R.U.E. Test allergen. Although the T.R.U.E. test screens for 46 distinct allergens and the Balsam of Peru mixture and it is a valuable first-line screening tool to assess for allergic contact dermatitis, it adequately identifies an allergen in only approximately 24.5% of patients with allergic contact dermatitis. This being said, many relevant allergens are not detected with this screening tool alone and, for this reason the column was





Sharon E. Jacob, M.D.

Panta Rouhani, M.P.H.

expanded this month to cover one of the notorious allergens that has been designated by the American Contact Dermatitis Society as an Allergen of the Year: Gold.

#### THE CONTACT DERMATITIDES

Allergic contact dermatitis is an important disease with high impact both in terms of patient morbidity and economics. The contact dermatitides include allergic contact dermatitis, irritant contact dermatitis and contact urticaria.

*Irritant contact dermatitis*, the most common form, accounts for approximately 80% of environmental-occupational based dermatoses.

Contact urticaria (wheal and flare reaction) represents an IgE and mast cell-mediated immediate-type hypersensitivity reaction that can lead to anaphylaxis, the foremost example of this being latex hypersensitivity. While being beyond the scope of this section, we acknowledge this form of hypersensitivity due to the severity of the potential reactions and direct the reader to key sources.<sup>2-3</sup>

The primary focus of this section is to highlight the educational component of *allergic contact dermatitis*.

#### **CLINICAL ILLUSTRATION**

A patient presented to the University of Miami Contact Dermatitis Clinic for evaluation of her eyelid dermatitis. She had been evaluated by the T.R.U.E. test and no positive allergic reactions were found. Of note, she wore a large amount of gold jewelry and titanium dioxide containing eye make-up and sunscreen.

#### THE HISTORICAL IMPORTANCE OF GOLD

In Voltaire's *Candide*, a satire on the human condition, Candide and Cacambo encountered the utopian land of Eldorado where there was such an abundance of gold on the streets that it held no value.<sup>4</sup> Surprised by the insignif-

icance of gold to the people of Eldorado, Candide and Cacambo loaded their travel sacks with gold before departing. Their actions underscored the broadly accepted real-world value and scarcity of gold.

The word "gold" itself is often used to denote a high level or a reference point for an esteemed time period or object. For example, the metaphor of the Golden Age, a term originated from Greek and Roman poetry, refers to a time when mankind was pure and lived the exalted life.<sup>5</sup>

The original meaning of "the gold standard" referred to a monetary system in which the standard economic unit of account was a fixed weight of gold.<sup>5</sup>

Furthermore, in the clinical setting, the term "gold standard" is used to denote a definitive diagnostic test.<sup>6</sup>

### ANCIENT CULTURES AND THEIR LOVE OF GOLD

Archeologists and anthropologists have traced the use of gold back to the Stone Age.<sup>7-8</sup> It is thought that early man found gold along streams and used it to make jewelry.<sup>9</sup>

Interestingly, the identification and study of Otzi the Iceman, a mummy from about 3300 B.C. who carried with him a copper axe and a flint knife, has led researchers to acknowledge that the transition from the Stone Age to the Bronze Age was a long, gradual process involving gold and copper.<sup>7</sup>

Many historic accounts and tales of Ancient Egypt, Greece and Rome are filled with the legacies of golden treasures.<sup>8</sup> The Nubian (Ethiopian) gold mines were built on one of the earliest discovered natural gold stores.<sup>9</sup> During the XVIII-XX Egyptian Dynasties (ca. 1402-1364 BCE), the Nubian gold became highly prized as a trade commodity.<sup>10</sup>

The Amarna correspondence letters between Egyptian and Canaan/Amurru (present day Israel/Palestine, Jordan, Lebanon and Syria), described this early value of gold<sup>10</sup>:

"Why have you sent me only two mines of gold? My work in the houses of the Gods is abundant, and now I have begun an undertaking: Send much gold! And you, whatever do you need from my land, write and it will be sent to you." 10

In Greek Mythology, gold and golden objects were also revered. Gold symbolized man's lust for power and desire for achievement.

In gratitude for the safekeeping of Silenus, Bacchus offered to grant Midas



APPROXIMATELY

125,000 TONS OF GOLD

HAVE BEEN COLLECTIVELY

MINED.<sup>8</sup> NOTABLY,

ONLY 10,000 TONS

(LESS THAN 1%)

ARE ESTIMATED TO HAVE

BEEN MINED PRIOR TO THE

CALIFORNIA GOLD RUSH!

anything that he may wish for. Midas asked for the power for all that he touched to be changed into gold. Soon Midas realized his demise was imminent, as even his bread and wine turned to gold. With fear of starvation ahead, Midas prayed to Bacchus to have his granted wish reversed. Midas was told to go to the river of Pactolus and wash

away his sins. To this day the sand in the river bed is still golden. 11

The mystical power of gold can also be seen in yet another famous tale. Jason and the Argonauts willingly, and ultimately successfully, traversed the Black Sea and dared the Clashing Islands in pursuit of the "unattainable" Golden Fleece, as this would ensure his inheritance of the throne of Iolcus.<sup>12</sup>

The Romans were also known to go to great lengths for the possession of gold. Under Emperor Nero, Rome possessed low gold content in its coins. Confirmed rumors of gold and other desired valuables in Dacia (modern-day Romania) motivated the new Emperor, Trajan, to prepare for a war against Dacia.<sup>13</sup>

Between 101 AD to 106 AD, Dacia was conquered by the Romans in two subsequent wars for both land acquisition and to secure Roman rights to the Dacian gold mines, an important source of gold for coin tender and assurance of continued growth of the empire.<sup>13</sup>

Not only did the Romans secure the Dacian gold mines, but by the treason of Bacilis (a confidant of the Dacian King), the Romans captured the king's treasure in the river of Sargesia — 364,100 pounds of gold.<sup>13</sup>

To mark the triumphant victory of the Dacian wars, Emperor Trajan declared 123 days of celebration throughout the Empire, a tribute to the acquisition of the financial resources needed to support Rome's future campaigns and expansion.<sup>13</sup>

#### THE CALIFORNIA GOLD RUSH

There are several monumental events in history that had such an impact on mankind that time before and after these events seems to stand divided. For the history of gold, there is a clear distinction between the pre- and post-California Gold Rush of 1849.8

In the last 6,000 years, approximately 125,000 tons of gold have been collectively mined.<sup>8</sup> Notably, only 10,000 tons (less than 1%) are estimated to have been mined prior to the California gold rush!

The vast economic and societal impact distinguished the California Gold Rush from the other great gold frenzies in the history of the world,

which included the Spanish invasion of the Incans and Mayans in the early 16th century and the South African gold rush of 1884.<sup>13-16</sup>

The California Gold Rush impact was so great, that some historians refer to it as "the greatest adventure the world has ever seen." In less than a decade, over a quarter of a million "adventurers" (dubbed the "forty-niners") headed West with dreams of "striking gold".

Sadly, the reality was a 6% mortality rate, with more than 1,500 people dying from cholera, yellow fever and malaria. It is important to note that in 1848 there were less than 12,000 non-Indian inhabitants in the great expanse of California, having just been acquired from Mexico in 1847. By 1849, the number had more than doubled, marking this year as the beginning of the great Western expansion.

"When carpenter James Marshall saw the first glint of gold in a California river on January 24, 1848, it sparked the largest migration in history. For the first time, individuals — not kings or sultans — could have gold for the taking, spurring tens of thousands of people to make the arduous journey by boat or horse-drawn wagon to the sparsely inhabited territory. Virtually overnight the influx drove California to statehood and eventually fueled vast industrial growth in America.

"The Gold Rush created the United States as an industrial power, but it also shaped a fundamental aspect of the American psyche, the whole idea that you could go to California, reinvent yourself and strike it rich." — film director Jeffrey Friedman. 15

There is some speculation that we are on the verge of the fourth, and perhaps greatest, gold frenzy the world has ever seen — the current China gold rush. <sup>16</sup>

Already among the world's largest producers of gold, China incorporates a large under-explored land mass believed to have some of the world's richest gold fields.<sup>16</sup>

#### **GOLD FOR MEDICINAL PURPOSES**

Gold has been long revered by the Chinese people who were the first to prepare red colloidal gold as the alchemical drug for longevity.<sup>17</sup> During the Tang Dynasty, the preparation of the

elixir, obtained from the refining of cinnabar, yielded a "gold" liquid that could be ingested. This preparation technique is still used today by Ayurvedic physicians in India.<sup>17</sup> Furthermore, alchemists worldwide



DURING THE
TANG DYNASTY, THE
PREPARATION OF THE ELIXIR,
OBTAINED FROM THE
REFINING OF CINNABAR,
YIELDED A "GOLD" LIQUID
THAT COULD BE INGESTED.
THIS PREPARATION
TECHNIQUE IS STILL USED
TODAY BY AYURVEDIC
PHYSICIANS IN INDIA.<sup>17</sup>

have used gold as a therapeutic agent for most ailments, as well as, an aphrodisiac.8

According to Wiegleb's History of Alchemy, the ingestion of gold is mentioned in the Bible (Exodus 32:20).<sup>17</sup> While the Israelites awaited for Moses to return from Mount Sinai, Aaron melted gold from the Israelites' jewelry and made a golden calf. Upon his return

from Mount Sinai, Moses burnt the golden calf in a fire, ground it to powder, scattered it on water, and forced the Israelites to drink the water.<sup>18</sup>

During this time, gold gained use in Western Cultures as a "nervine" (therapy for nervous disorders) to cure epilepsy and depression.<sup>17</sup>

As 21st century physicians explored the medical practice of gold, as a drug for rheumatoid arthritis and bronchial asthma, many wealthy individuals were exploring the possibility of replacing their ordinary everyday wares with gold.<sup>8</sup>

The rich and famous, pampered themselves with golden washbasins, gold-plated pianos, and more recently meshed gold coffee filters to preserve coffee's flavor.<sup>8</sup>

In the 1920s business mogul, William Randolph Hearst, alongside architect Julia Morgan, designed the expansive *La Cuesta Encantada*, aka the Hearst Castle, on a 240,000-acre ranch at San Simeon, California.

The gold-leafed Venetian glass "home pool" and eight acres of cultivated gardens were playground to invited guests like President Calvin Coolidge, Winston Churchill, George Bernard Shaw, Charles Lindbergh and Charlie Chaplin.<sup>19</sup>

Entertainment King, Elvis Presley, indulged himself by customizing his three Stutz automobiles with gold details, such as ashtrays, cigarette lighters, steering wheels and pedal surrounds.<sup>8</sup>

#### **ALLERGIES TO GOLD**

Despite the wide range of uses of gold, allergies to gold were thought to be very rare until the 1980s. 20-22 A notable case of severe pulmonary allergy to gold was noted in 1953 and reports of lichenoid dermatitis following gold therapy were soon reported. 23-24

The growing body of evidence suggested a higher sensitization prevalence to gold, which led the North American Contact Dermatitis Group (NACDG) to incorporate gold onto the NACDG Standard. Analysis of the NACDG 1996 to 1998 data demonstrated that it was the sixth-most-frequent allergen.<sup>21</sup>

The further recognition of gold as a significant cause of contact dermatitis and second (only to nickel) in causing

metal allergy, led to gold being designated as the 2001 Allergen of the Year.<sup>25</sup>

It is important to note that a reaction to gold at the contact site of jewelry, such as watches and rings, is rare. Rather, reactions, may been seen on the bridge of the nose, where gold glasses come into contact with eye make-up, foundation, and sunscreens containing harder metals, such as titanium dioxide and zinc oxide. These harder metals abrade the gold and release sensitizing gold particles. Notably, gold is an occupational hazard to jewelers, gold gilders and those who apply gold leafing, such as bookbinders and chocolatiers.

#### TESTING FOR GOLD SENSITIVITY

Patch testing for gold allergy can be accomplished with comprehensive patch testing. Sodium gold thiosulphate 0.5% in petrolatum is used as the screening agent due to the relatively inert nature of gold leaf.

#### THE VALUE OF THIS PATIENT CASE

Our patient unknowingly applied gold particles to her eyelids during application of her titanium dioxide based make-up and sunscreen. This patient chose to regularly rhodium plate her jewelry and her dermatitis resolved.

The importance of appropriate patch testing and subsequent patient education is vital as she was able to resolve her dermatitis with wardrobe modification. Albeit slowly, this patient dramatically improved with gold avoidance, this being consistent with the fact that the mainstay of treatment for allergic contact dermatitis is **avoidance**.

Dr. Jacob is the Director of the Contact Dermatitis Clinic at the University of Miami. She's also an Assistant Clinical Professor in the Department of Dermatology and Cutaneous Surgery.

Panta Rouhani is an M.D./Ph.D. student at the University of Miami — Miller School of Medicine.

#### References:

1. Saripalli YV, Achen F, Belsito DV. The detection of clinically relevant contact allergens using a standard screening tray of twenty-three allergens. *J Am Acad Dermatol.* 2003 July;49(1):65–9.

- 2. Valks R, Conde-Salazar L, Cuevas M. Allergic contact urticaria from natural rubber latex in healthcare and non-healthcare workers. *Contact Dermatitis.* 2004; 50(4): 222-4.
- 3. Warshaw E. Latex allergy. Skinmed. 2003 Nov-Dec;2(6):359-66.
- 4. Voltaire. Candide. New York: Viking Publishers, 1976.
- $5. ``Golden age." \it Wikipedia, The \it Free \it Encyclopedia.$



A REVIEW OF THE
MEDICINAL USES OF
GOLD REVEALED THAT IT
HAS BEEN RECOMMENDED
FOR DEPRESSION,
MIGRAINES, RHEUMATOID
ARTHRITIS, ALCOHOLISM,
EPILEPSY, AMENORRHEA
AND IMPOTENCE.<sup>17</sup>

- 11 Apr 2006, 17:09 UTC. 13 Apr 2006, 02:28 http://en.wikipedia.org/w/index.php?title=Golde n\_age&oldid=47979420.
- 6. "Gold standard." Wikipedia, The Free Encyclopedia. 12 Apr 2006, 17:39 UTC. http://en.wikipedia.org/w/index.php?title=Gold\_standard&oldid=48143334.
- 7. "Stone age." Wikipedia, The Free Encyclopedia. 1 Apr 2002, 15:51 UTC. http://en.wikipedia.org/w/index.php?title=Stone\_age&oldid=15925610.
- 8. "About Gold." World Gold Council. 1 Apr 2006, 16:00 UTC. http://www.gold.org.

- 9. "Gold." *Gold History for Kids!*. 1 Apr 2006, 22:17 UTC. http://www.historyforkids.org/learn/science/mining/gold.htm.
- 10. "Amarna Letters." Ancient Egypt: An Introduction to its History and Culture. 8 Apr 2006, 20:46 UTC.http://nefertiti.iwebland.com/a-burnaburiash3.htm
- 11. Craft C, Craft KY. King Midas and the Golden Touch. New York: Harper Collins, 1999.
- 12. Apollonius of Rhodes, Hunter R. Jason and the Golden Fleece. New York: Oxford University Press, 1998.
- 13. "Dacia." Wikipedia, The Free Encyclopedia. 11 Apr 2006, 18:49 UTC. http://en.wikipedia.org/w/index.php?title=Dacia&oldid=47993417.
- 14. "Gold Rush." *The Columbia Encyclopedia*. 1 Apr 2006, 16:36 UTC. http://www.bartleby.com/65/.
- 15. "The Gold Rush." *Public Broadcasting System*. 1 Apr 2006, 17:51 UTC. http://www.pbs.org/goldrush.
- 16. "China's New Gold Boom." The Stock Analysts Group. Special Report: March 2006.
- 17. Richards DG, McMillin DL, Mein EA, Nelson CD. Gold and its relationship to neurological/glandular conditions. *International Journal of Neuroscience*, 2002;112:31–53.
- 18. Exodus 32:20. *The Holy Bible*, King James Version. New York: The American Bible Society, 1999: 101.
- 19. "Heart San Simeon SHM." California State Parks. 26 Apr 2006, 15:17 UTC. http://www.parks.ca.gov/?page\_id=591.
- 20. Rietschel RL, Fowler JF. Fisher's Contact Dermatitis 5th ed. Lippincott Williams & Wilkins; Philadelphia, PA: 2001.
- 21. Marks JG Jr, Belsito DV, DeLeo VA, Fowler JF Jr, Fransway AF, Maibach HI, Mathias CG, Pratt MD, Rietschel RL, Sherertz EF, Storrs FJ, Taylor JS. North American Contact Dermatitis Group patchetest results, 1996–1998. *Arch Dermatol*. 2000 Feb;136(2):272–3.
- 22. Bruze M, Edman B, Bjorkner B, Moller H. Clinical relevance of contact allergy to gold sodium thiosulfate. *J Am Acad Dermatol*. 1994 Oct;31(4):579–83.
- 23. Bjorkman SE. A case of severe allergic pulmonary reaction to gold. *Acta Allergol*. 1953;6(4):304-11.
- 24. McKenna WB. Lichenoid dermatitis following gold therapy. *Br J Dermatol*. 1957 Feb;69(2):61–5.
- 25. Fowler JF Jr. Gold. Am J Contact Dermat. 2001 Mar; 12(1):1–2.
- 26. Nedorost S, Wagman A. Positive patch-test reactions to gold: patients' perception of relevance and the role of titanium dioxide in cosmetics. *Dermatitis*. 2005 Jun; 16(2):67-70.

**Disclosure:** The authors have no conflict of interest with any subject matter discussed in this month's column.