THE NORTHERN HOSPITAL

MERCURY POISONING

"Girl with a Red Hat", oil on oak panel, Johannes Vermeer, c. 1665-66, National Gallery of Art Washington D.C

"A work of art is the only means of regaining a lost time… Thanks to art instead of seeing one world, our own, we see it multiplied, and we have at our disposal as many worlds as there are original artists, worlds that differ more widely from each other than those which revolve in infinite space, worlds which, whether their name be Rembrandt or Vermeer, send us their special radiance centuries after the fire from which it emanated was extinguished."

Marcel Proust, "Time Regained", 1922

This is Johannes Vermeer's haunting "Girl with a Red Hat", painted around 1665. She stares out at us from across the abyss of centuries with unseeing eyes, the only record we have that she ever existed. Before the photographic age the only visual records we have of our forebears are recorded in paint. It is for this reason, among many, that we owe a profound debt to the great masters, not the least of whom was Vermeer who recorded for posterity everyday scenes from the Dutch Golden Age of culture and sea-borne world empire. Images from these times of everyday life are rare. The paintings of Vermeer himself are very rare, there being fewer than 40 genuine works known in the world today. Precious as the image of the girl he left us is however, it only provides the vanishingly smallest glimpse of those far distant times, a fleeting instant in time of a look given toward the painter. We do not know who the girl was or what her relationship with Vermeer was. It has been suggested that she may have been a household servant, but we will never know.

The great painters of the seventeenth century were masters in many more ways that it is possible to appreciate in the 21st century. The brilliance of the work itself is plain to see but what is lost to modern sensibilities is the Herculean effort that went into the production of each work in those times, for not only did the artist have to be a great painter, they had to be great scientist (or "alchemist" in seventeenth century parlance) and technician as well. Paints and materials were not got from the supermarket, more often than not the artist themselves would need to produce the pigments they wanted. In the Seventeenth century this meant delving into the "alchemic art" a very hazardous process involving extremely toxic elements and compounds the hazards of which were barely recognized. Lead and arsenic were commonly used in the preparation of these pigments, toxic enough but none were more so than mercury. Vermillion was the most prized pigment of Vermeer's time. It was made from mercuric sulphide, the mercury had to be extracted from the mineral cinnabar then combined with another toxic element sulphur by heating the two. Inhaled mercury vapor would have posed a significant threat to the health of anyone involved in the process. The result however was the most brilliant red, no better example of which are the glorious red hat and glistening lips of Vermeer's model.

The vermillion had to be prepared and painted onto the work in the most precisely prescribed manner wherein lies some of the true mastery of the works of Vermeer's day. If not carefully prepared and applied the red may turn to black, especially if the cinnabar contains too much "met-cinnabar", with fatal consequences for the painting. What Vermeer probably did not appreciate was the potential fatal consequences to himself, let alone to his painting, by working with mercury. He died at the tragically young age of just 43 years, not unheard of in the context of the times, but there is no recorded description of any particular illness and the death certificate does not shed any light, merely recording the fact of his death. There was sufficient concern at the time for the Dutch High Court to enquire into the nature of his death. His wife

Catharina stated to the court that her husband had lately "lapsed into decay and decadence" and "fallen into a frenzy" but it is unclear from the records what was meant by this. Could Vermeer's alchemic works have contributed or in fact caused his death? If they did not, it would be a surprise given the nature of the substances he was using. Still this would not have even been considered in his day. It would not be until the Nineteenth century that the full extent of dangers of mercury would be finally realized. It was recognized that many milliners (or hatters) where developing brain damage in the form of personality changes and memory deterioration in addition to skin rashes, the erythema of which became known as the "pink" disease. The cause was the mercury nitrate that was used to remove fur from animal skins in order to produce felt hats. Lewis Carroll's "mad hatter" in Alice in Wonderland is a direct allusion to the milliners' illness.

In Tracy Chevalier's international best selling novel (later made into film) "The Girl with a Pearl Earring" she suggests that Vermeer used his maid / model to assist him in the preparation of his pigments. In the context of the times it seems a more than reasonable bet that he would indeed have used his servants to assist in many of the "mechanical" aspects of preparing his pigments. The mysterious "girl in the red hat" appears to show a pinkish erythema of the lips and face. This is of course likely to be makeup or simply a "healthy glow"…or is it? She looks a little sad, even somewhat distant. Does the girl in the "red hat" in fact look back at us from the past with the first signs of the "pink" disease, her brilliant red hat hinting hauntingly at the fearful toll in store for British milliners of the Nineteenth century?

Mercury poisoning in the 21st century is, like a genuine Vermeer, extremely rare. Like a genuine Vermeer however it is extremely important to recognize! We must take what lessons we can from the past and be ever alert to the possible clues left to us by the "girl in the red hat".

Cinnabar

MERCURY POISONING

Introduction

Mercury has no natural biological functions.

Although it has had and continues to have many useful purposes it is an extremely toxic element.

Its toxicity depends largely on the form in which it is encountered, the route of exposure and the duration and intensity of exposure.

Sources of mercury:

Elemental mercury (Hg^0):

- Dental amalgam
- Thermometers
- Barometers
- Manufacture of chlorine and caustic soda, paints, pigments and gold mining

Inorganic mercury:

- Mercuric acetate
- Mercuric arsenate
- Mercuric bromide
- Mercuric chloride
- Mercuric potassium cyanide,
- Mercuric sulfide
- Disinfectants
- Fireworks and explosives
- Processing of fur and leather
- Waterproofing and antifouling paints
- Photographic plates
- Batteries

Organic mercury (alkoxyalkyl mercury, alkyl mercury, methyl mercury):

- Embalming fluid
- Fungicides / pesticides
- Wood preservatives
- Contaminated seafood

Merbromin (i.e. "Mercurochrome")

History

Mercury has been known for millennia. Spain has mercury mines that have been operating continuously since the Roman Republic. Today it is mainly produced in Spain and Italy.

Historical uses of "medicinal" mercury included:

- Calomel, (mercurous chloride) was used as a "purgative" and in the treatment of syphilis. (It has also been used as a pesticide!)
- Mercurial compounds were once used as diuretic agents.
- "Mercurochrome", a mercury based compound that was used as a topical antiseptic agent, (banned by the American FDA in 1997)

Chemistry

Mercury exists in three forms:

- **Elemental (H^0)**
- **Inorganic**
- **Organic**

It is however rarely found as a pure metal in nature and does not readily combine with other elements under natural conditions.

Cinnabar (mercuric sulphide) is the commonest of only a small number of naturally occurring ores. It is from this ore that most mercury is obtained.

Mercury is sold and traded on world markets in units called "flasks", one flask being equal to 76 pounds.

Uses include:

1. **Elemental** (Hg^0)

   Uses include:

- Thermometers.
- Sphygmomanometers, (older types).
- Barometers
- Some thermostats
- Mercury alloys, known as “amalgams”. Mercury has a particular ability to dissolve other metals. This property was of significant importance in the medieval art of “alchemy”. In more recent times the silver-mercury amalgam was used by dentists as tooth fillings.

2. **Inorganic**

As salt compounds, including Mercurous, (Hg +) compounds and Mercuric (Hg ++) compounds.

Uses include:

- Various salts are used in industrial processes, primarily as catalytic agents.
- The electronics industry, in particular the mercury battery, which consists of a zinc anode and a mercuric oxide cathode.
- Mercuric sulphide, HgS, (the mineral ore cinnabar from which vermilion coloring pigment was derived in the past)
- Mercuric nitrate was once used in the manufacture of felt hats. Workers in long term contact with this compound suffered neuropsychiatric disorders. This was the basis of the expression “mad as a hatter”.
- Mercuric chloride ($HgCl_2$) is a poison used as a fungicide and pesticide. Mercurous chloride (HgCl) is not quite as soluble as the mercuric form and hence is not quite as toxic. Its common terminology is calomel and it also has been used as a pesticide. (As mentioned above it was also once used for medicinal purposes!)
- Mercury fulminate, $Hg(ONC)_2$, (a detonator used in explosives).

3. **Organic**

These are mercury-hydrocarbon compounds occurring in 3 forms, aryl and short and long chain alkyl compounds.

- A particular hazard involves the discharge of mercury containing compounds into lakes and rivers.

Certain aquatic microorganisms can take up and metabolize mercury into extremely toxic **methyl mercury** compounds, which then get passed upward through the food chain.

Fish feeding on these on these microorganisms accumulate these compounds in their tissues. Larger fish may then be consumed by humans with major adverse health effects.

- **Ethyl mercury** is a constituent of thimerosal, a preservative once used in many vaccines.

Toxicology

Mercury is a metal element with no biological function.

It binds to sulfhydryl groups in many intracellular sites resulting in enzyme dysfunction as well as disruption of cellular membranes.

Elemental mercury

Elemental mercury exposures are usually the result of spillages, from breakage of a thermometer for example.

Elemental mercury can be absorbed into the body by:

- Inhalation of its vapour, (produced especially when heated).
- Dermal absorption in cases of skin contact.

Elemental mercury readily crosses the blood-brain barrier, where it becomes ionized and trapped.

GIT absorption of elemental mercury is negligible.

Inorganic mercury

Exposure to inorganic mercury compounds is usually the result of industrial processes.

Mercuric salts do not readily cross the blood-brain barrier, which limits CNS toxicity.

However chronic exposure and the slow elimination half-life means significant accumulation of mercury ions can occur within the CNS.

They tend to accumulate predominantly within the **kidney**, and to a lesser extent within the liver and spleen.

Organic mercury

The most predominant exposure to organic mercury compounds by far, is that of methyl mercury contained within contaminated fish.

Short chained organic mercury compounds readily cross the blood-brain barrier to produce CNS toxicity.

Pharmacokinetics

Absorption:

- Elemental:

  Elemental mercury is **not** readily absorbed from the gut.

  In contrast it **is** well absorbed from the respiratory tract when inhaled as:

  - An aerosol (which may be produced when it is vacuumed)
  - As a vapour when heated.

- Inorganic mercury:

  Inorganic mercury is absorbed from the gut, (about **10%**).

  It can also be absorbed via the skin or mucous membranes.

- Organic mercury:

  Organic mercury is **well** absorbed from the gut or the respiratory tree, or through disrupted skin.

Distribution:

- Mercury has a large volume of distribution.

  It is distributed in particular to the kidneys, liver, spleen, and the CNS.

- The high lipid solubility of elemental and organic mercury especially favors distribution into the CNS.

- Organic mercury is excreted in breast milk and can produce toxicity in infants.

Metabolism and excretion:

- Mercuric ions are excreted in the kidney and by the gut.

- The elimination half-life of elemental and inorganic mercury is about 30-60 days.

- The elimination half-life of organic mercury is more prolonged - in the order of 70 days, and is excreted primarily via the gut, where some enterohepatic re-circulation can occur.

Risk Assessment

Negligible Risk:

- Elemental mercury (e.g. from a broken older style thermometer) is not significantly absorbed from a normal GIT.
- Older style mercury containing dental amalgams do not pose a risk

Potentially Serious Toxicity:

- Inhalation of aerosolized elemental mercury can potentially cause serious toxicity, resulting in pneumonitis, ARDS, or neurological injury.
- Ingestion of inorganic mercury salts can result in in significant hemorrhagic gastroenteritis. The potentially lethal dose is **20 - 30 mg/kg.**
- Any dermal or ingestion exposure to organic mercury compounds can result in serious neurological injury.

Uncertain Risk:

- IV, IM or SC injection of mercury can result in mercuric pulmonary emboli, from which distribution to the brain may then follow in the longer term
- Intentional ingestion of merbromin (i.e. "Mercurochrome") can result in high mercury levels, though the consequences are uncertain via this from and route of exposure.

Clinical Features

The clinical effects of mercury exposure will depend on:

1. The form of the mercury.
2. The route of exposure.
3. The amount and duration of the exposure.

Elemental mercury poisoning

Acute exposure:

Inhalation of mercury vapor or significant skin absorption may result in:

1. Metallic taste, stomatitis and gingivitis.
2. Non-specific constitutional symptoms:
    - Nausea/ vomiting

- Headache
- Chills/ fever

3. Visual disturbances

4. Pulmonary symptoms:

    - Ranging from mild hypersalivation and bronchial irritation to pneumonitis to florid ARDS.

Chronic exposure:

Erethism

This is a systemic manifestation of chronic exposure characterized by the insidious onset of

- Neuropsychiatric symptoms, **(insomnia, memory loss, personality changes, psychiatric manifestations**).
- Delirium
- Tremor.
- Peripheral neuropathies.

Inorganic mercury poisoning

Skin contact may result in:

1. Dermatitis reactions.
2. Vesication.

Ingestion may result in:

1. Metallic taste, stomatitis and gingivitis.
2. GIT upset

    - This can range from mild to severe hemorrhagic gastroenteritis with fluid loss and shock.

3. Renal impairment/ failure.
4. Erethism (as above)
5. **Acrodynia**

This is an inorganic mercury salt induced systemic illness due to chronic exposure, now largely of historical interest only. It is thought that it was due to a type of hypersensitivity reaction. It was also known as **"pink" disease**, probably due to the associated erythematous skin changes that could occur.

Features included:

- Rash, desquamating together with erythema particularly of the palms and soles.
- Hair loss
- Hypertension
- Anorexia
- CNS features, in particular insomnia and "irritability" later progressing to more severe neuropsychiatric and encephalopathic manifestations.

Organic mercury poisoning

Organic mercury can be found mainly in 3 forms, aryl, short and long chain compounds.

The longer chain and aryl forms of organic mercury are metabolised to mercury ions and so have similar characteristics to inorganic mercury toxicity.

Short chain organic mercury poisoning (methyl or ethyl compounds) on the other hand may result in **severe neurological disease**.

Features of short chain organic mercury poisoning include:

Acute manifestations:

1. GIT symptoms
2. Tremor
3. Respiratory distress
4. Dermatitis
5. Renal tubular dysfunction:
6. ECG (ST segment) changes

Chronic manifestations:

Delayed neurotoxicity develops weeks or months after initial exposure and is usually permanent.

It is most severe in children who have suffered prenatal exposure.

Features include:

1. CNS
    - Confusion
    - Short and long term memory loss
    - Cerebellar signs, especially ataxia.
    - Cranial nerve disturbances:
        - ♥ Tunnel vision
        - ♥ Deafness
        - ♥ Anosmia
    - Extrapyramidal effects, including tremor.
    - Peripheral neuropathies
2. Renal impairment

Mercury toxicity in pregnancy

All forms of mercury are toxic to the fetus, but methyl mercury most readily passes through the placenta.

Investigations

Blood tests:

1. FBE
2. U&Es / glucose
3. Consider pregnancy tests in women of childbearing age.
4. LFTs
5. Whole blood mercury levels: [6]

    Levels reflect recent exposure, but not necessarily total body burden.

    - Normal levels are < 20 microgram/L or 100 nanomols/L.
    - Signs of mercury poisoning may occur at levels > 200 micrograms/L or > 1000 nanomols/L

- Following acute inorganic mercury exposure levels may be > 500 micrograms/L or 2500 nanomols/L

Urine mercury levels:

Normal 24 hour levels are < 10 micrograms/L (or 50 nanomols/L)

Levels > 100 micrograms/L (or 500 nanomols/L) are associated with neuropsychiatric signs.

Atmospheric mercury levels:

Toxic atmospheric mercury levels are considered to be > 50 micrograms/ m^3.

Radiology:

Elemental mercury is radio-opaque.

See Appendix 1 below

Endoscopy:

This may be required to assess GIT injury in cases of mercury ingestion.

Management

Mercury poisoning is rare and unlikely to be diagnosed unless there is a clear history of exposure.

Note that for any patient you suspect may have significant mercury poisoning, the case should be discussed with a clinical toxicologist.

Mercury Spills

The main danger here is mercury vapor that can be inhaled due to its high volatility.

Additionally the mercury tends to disperse into multiple small and even microscopic droplets, because of its high surface tension.

The amount that can be vaporized is thus greatly increased due to the larger combined surface area of multiple droplets

Important points to note in dealing with a mercury spill include:

- Gloves should be worn, (this is to avoid dermal absorption but also to protect jewellery. Mercury will cause discoloration of many metals used in jewellery)

- Droplets may be gathered with a syringe using a no touch technique. Alternatively heavy piece of cardboard (eg playing cards) can be used to scoop up larger droplets.

- Do **not** use vacuum cleaners, which will disperse mercury droplets into the atmosphere.

- Mercury spills onto to carpet are particularly problematic due to the porous nature of the carpet. Once all visible mercury has been removed a mercury absorbent (such as "Hg absorb") should be applied to the site and left for 24 hours in order to form an "amalgam". This can then be collected using a dust pan and brush.

- All mercury droplets (and amalgams) should then be placed into a sealed screw top specimen container.

- **Specialized mercury "spillage kits" which contain equipment and Hg absorbing material should be used where available.**

- Major spills should be reported to the Work Environment Manager to organise for the appropriate disposal of the mercury.

Elemental Mercury

Ingested elemental Hg is not significantly absorbed from the GIT, and so does not pose a significant health risk.

The most common setting for ingested Hg is accidental ingestion by small children who have broken a thermometer. This will not require any special treatment.

Inhalation from elemental Hg vapor is more problematic, with respiratory symptoms being the most immediate concern. Treatment will be symptomatic in these cases.

Wash thoroughly any contaminated skin.

Inorganic Mercury

1. Charcoal may be useful, but emesis should be avoided, (mercury salts are caustic)

2. Oral polyethylene glycol solution enhances removal from the GIT tract following deliberate ingestion of large volumes.

3. Chelating agents:

   Poisoning from inorganic mercury is treated with chelating agents

   A number of agents are available including:

   - Dimercaprol, (BAL) given as IM injections.

     Note that dimercaprol is only indicated for **inorganic** mercury poisoning. It is *contra-indicated* following *elemental or organic* mercury poisoning as there are concerns that this merely mobilizes tissue

mercury into the blood making it more available for distribution into the CNS.

- Succimer (DMSA or meso 2,3- dimercaptosuccinic acid), given orally
- Penicillamine, given orally, usually for those requiring chronic treatment.

Note that chelation therapy can remove mercury from the plasma very well, however Hg ligands can persist in the tissues and recovery from mercury poisoning can be protracted, taking months or even years and is often incomplete.

Chelation therapy is only effective once the patient has been removed from the source of exposure.

Any chelation therapy must only be under the direction of a specialist toxicologist

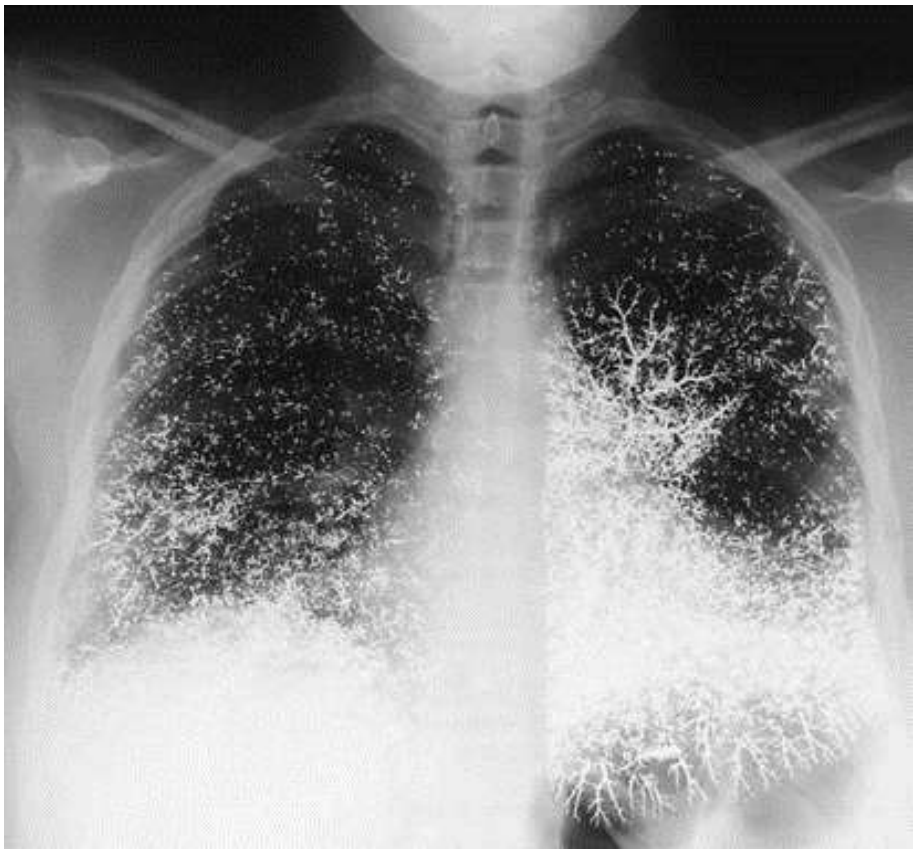
Organic Mercury

Chelation therapies are not as effective for organic mercury poisoning as they are for inorganic mercury poisoning.

Again specialist toxicologist advice must be sought.

Appendix 1

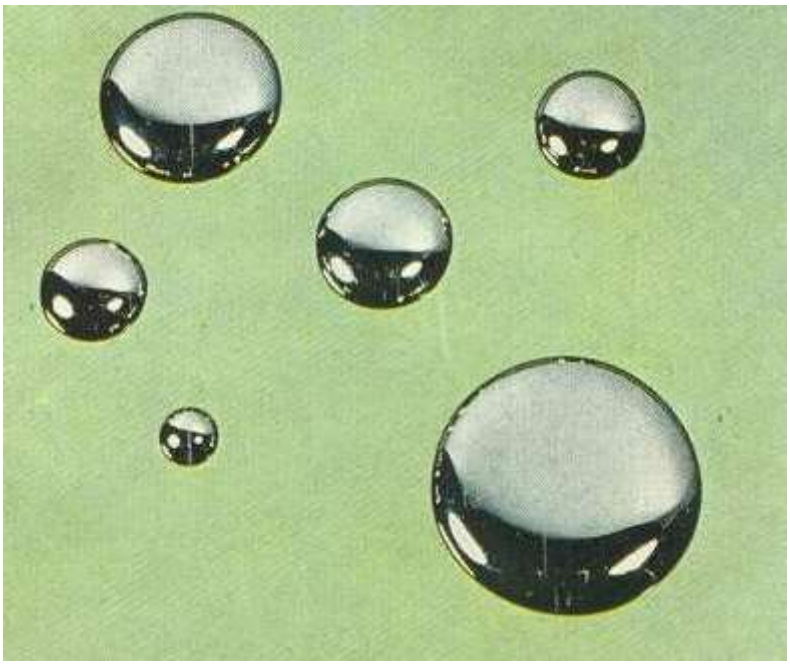
Left: Ingested Elemental Mercury, Right: Inhaled Elemental Mercury



Attempted suicide by intravenously injected Elemental Mercury

Appendix 2

Chemistry of Mercury

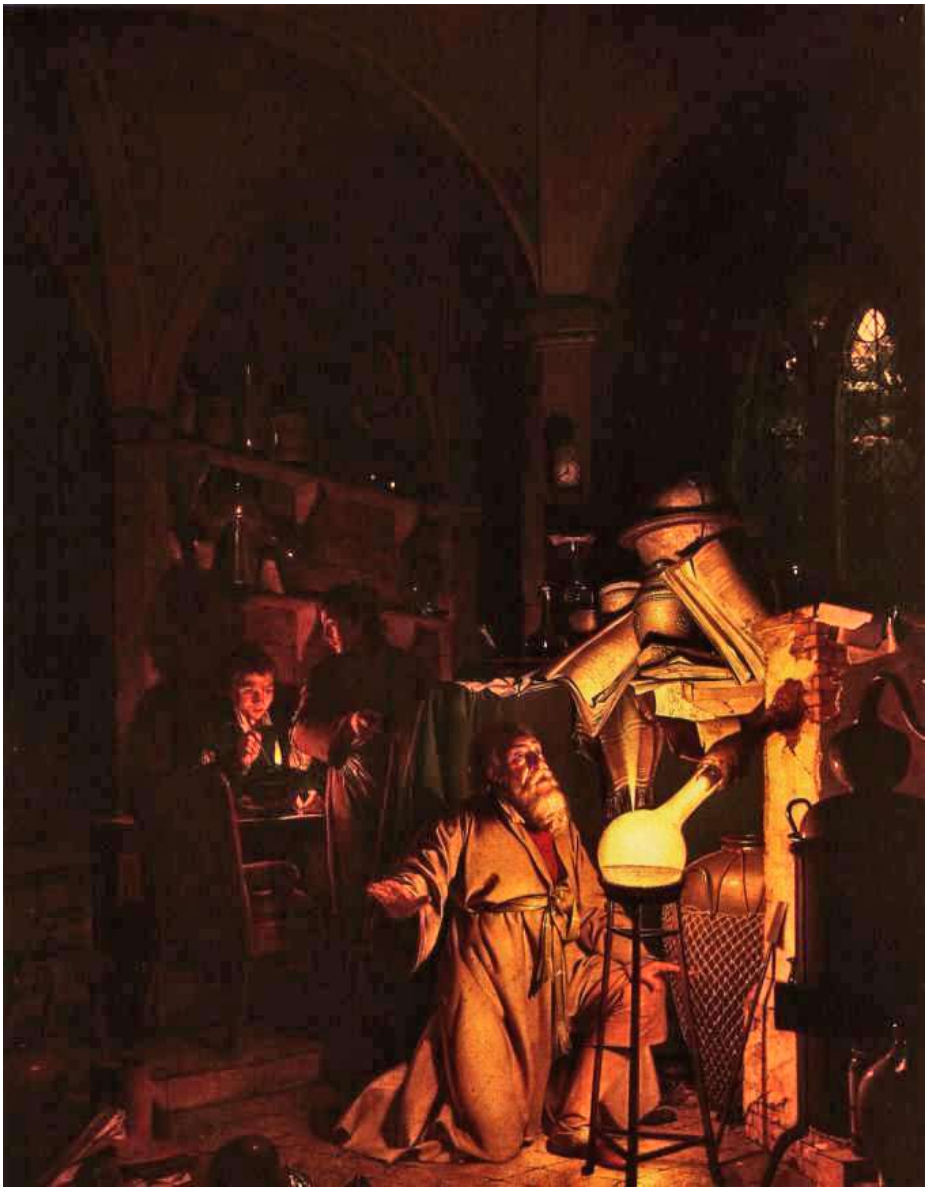


Elemental Mercury, (Life Science Library, "Matter", 1963).

Physical Properties:

Elemental symbol	**Hg**. It is named after the planet Mercury. The origin of the symbol is the Latin word "hydrargyrum" meaning liquid silver.
Atomic number	80
Atomic weight	200.59
Boiling point	It is the only metal that is liquid at room temperature. It freezes at –38.9 degrees Celsius and boils at +357 degrees Celsius. This wide range makes it suitable for use in thermometers.
Surface Tension	This is high in mercury, such that it forms into small discrete globules, rather than "runs" as does water.
Classification	Mercury is a *transitional metallic* element. Like most metals it is a good conductor of electricity, however unlike most metals is a relatively poor conductor of heat.
Alchemy symbol	

Physical Appearance	A silvery white color, traditionally referred to as “quicksilver”
Volatility	Elemental mercury is **very volatile**, dangerous levels are readily attained in air, especially within non-ventilated closed environments.



The Alchemist in Search of the Philosopher's Stone, oil on canvas,
Joseph Wright of Derby.

Take two parts Quicksilver (liquid metallic mercury) and a third part Sulphur, put it in a pot, smelt the Sulphur and the Quicksilver under a weight, when cold, grind well together. Then put it in a Glass, which is already completely covered a finger breadth thick with hairy Loam (a combination of sand and cow's hair). Previously prepare an Oven of the width of your Glass or Retort. Set this Glass on the Oven. Or put it on an iron Tripod or in another little distiller's oven, make a little Tin lid over the basket of the Retort, and a little hole in the middle of the lid, seal it well with the prescribed Loam, push an iron in through this hole that you may stir all with it. First make a small fire under it of dry wood and gradually increase it. And take great note of the Glass too,, for out of it you may see smoke, and steam also from out the Glass, but take no head of it, but mind that you keep a steady fire under it without ceasing until you see that the smoke is as red as blood, then it suffices. Then let it get cold and so you have good vermilion.

!7th Century Recipe for the making of Vermilion

References:

1. Mercury Poisoning, in Ellenhorn, Medical Toxicology, 2nd ed 1997, p. 1588-1599, (1589)

2. Clarkson T.W. The Toxicology of Mercury: NEJM 349 (18) October 30, 2003, p. 1731-37.

3. Elemental Mercury Embolism to the Lung, Images in Clinical Medicine, vol 342 (24), NEJM, 2000

4. Stwertka A, Guide to the Elements, Oxford 2nd edition, 1998, p.181.

5. Mercury Poisoning in Murray L et al. Toxicology Handbook 3rd ed 2015

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