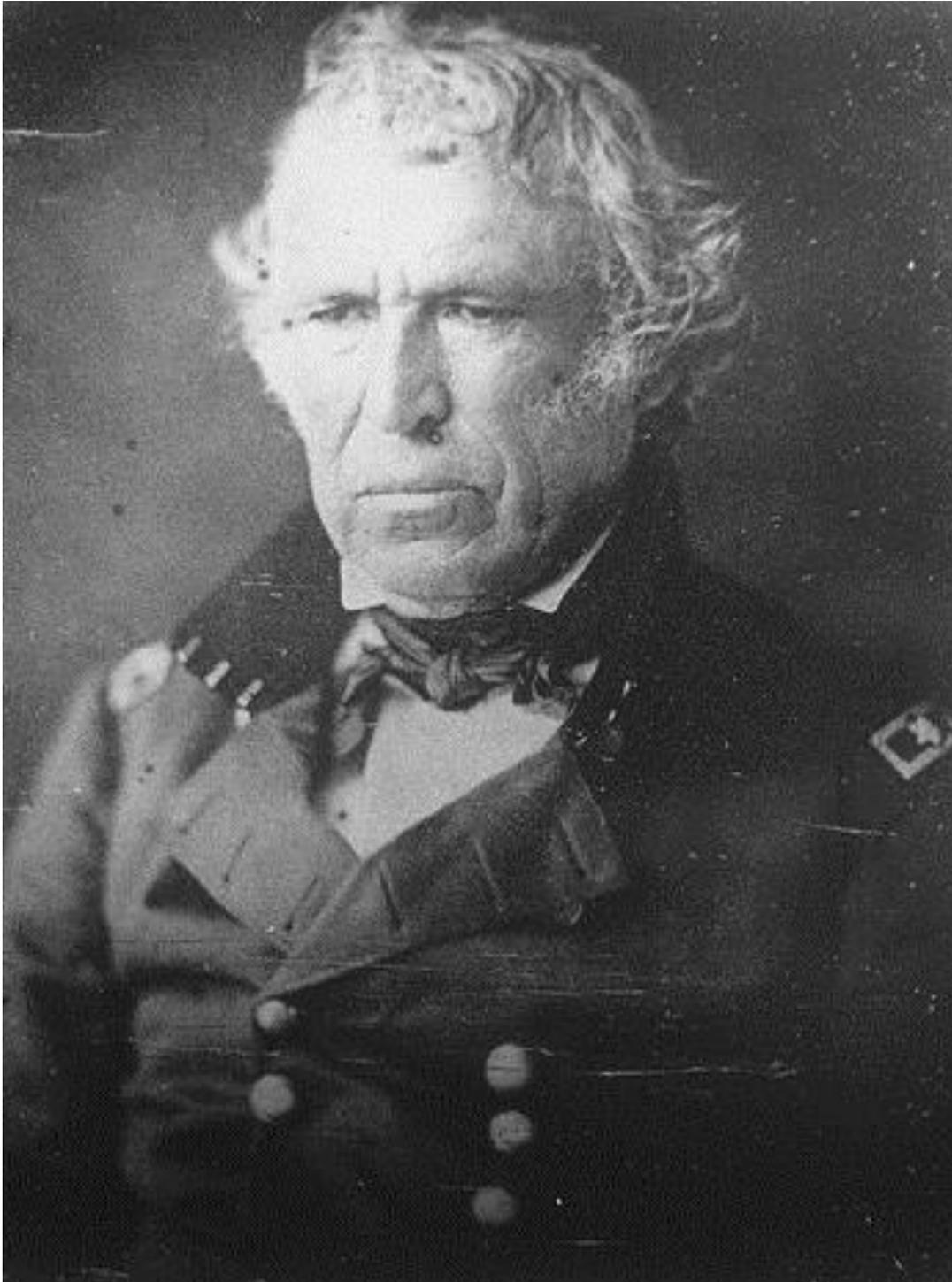


**ARSENIC POISONING**



*Zachary Taylor (1784-1850), 12<sup>th</sup> President of the United States of America.  
Daguerreotype circa 1844-49, Mathew Brady, Library of Congress.*

*“...For more than half a century, during which kingdoms and empires have fallen, this Union has stood unshaken. The patriots who formed it have long since descended to the grave; yet still it remains, the proudest monument to their memory and the object of affection and admiration with everyone worthy to bear the American name. In my judgment its dissolution would be the greatest of calamities, and to avert that should be the study of every American. Upon its preservation must depend our own happiness and that of countless generations to come. Whatever dangers may threaten it, I shall stand by it and maintain it in its integrity to the full extent of the obligations imposed and the powers conferred upon me by the Constitution...”*

*President Zachary Taylor, December 4 1849.*

*Zachary Taylor was one of the true pioneers of the old American West. He joined the army and spent his early years fighting native Indians on the extreme frontiers of what then constituted the United States of America. In the 1830s vast swathes of the distant Northern territories of Mexico that included California, New Mexico and Texas were annexed by the United States in response to these regions' rapidly expanding English speaking populations. The annexation was also felt by many Americans and Taylor in particular to be the fulfillment of the “manifest destiny” of their new nation.*

*Needless to say the Mexican government, itself only recently independent of the vast Spanish American Empire, had ideas of its own in regard to “manifest destiny” and in response to the annexation of Texas, sent an army under General Santa Anna across the Rio Grande in 1846, sparking war with the United States. Zachary Taylor defended the newly acquired lands with such a zealous ferocity that he quickly became a national hero. With Taylor defending the borders, President Polk sent a counter invasion force led by General Winfield Scott into Mexico itself. The invasion was successful, with General Scott capturing Vera Cruz, then Mexico City leading to the capitulation of the Mexican government.*

*Difficult issues soon arose however with respect to how the newly acquired territories where to be governed and how they would fit in with the rest of the United States. Taylor urged the new territories to bypass any preliminary “territorial status” and to apply directly for statehood within the Union. The new territories were eager to do this but fierce disputes then arose with the Northern states over the issue of slavery. The new territories were for slavery but many in the North were vehemently against it. Surprisingly Taylor, whose family owned over 100 slaves, agreed with the government that the new territories should be slave free. This created enormous tensions and in fact laid the foundations for the Civil War that would follow a generation later in which more Americans would die than in both the World Wars of the 20<sup>th</sup> century combined.*

*Taylor saw the issue as so divisive that it threatened the new Union before it had even come into existence. In 1848 he became President and promptly held urgent talks with Southern leaders who were talking secession from the Union. Taylor was not a diplomat, he was primarily a soldier. He was known from his army days as old “rough and ready” in view of his disheveled dress and rough and ready frontier manner acquired over many years fighting the native Indians. In February 1850, an exasperated man, he made his position perfectly clear to the Southerners. He screamed at them that if necessary to enforce the laws, he personally would lead the Army against them and that*

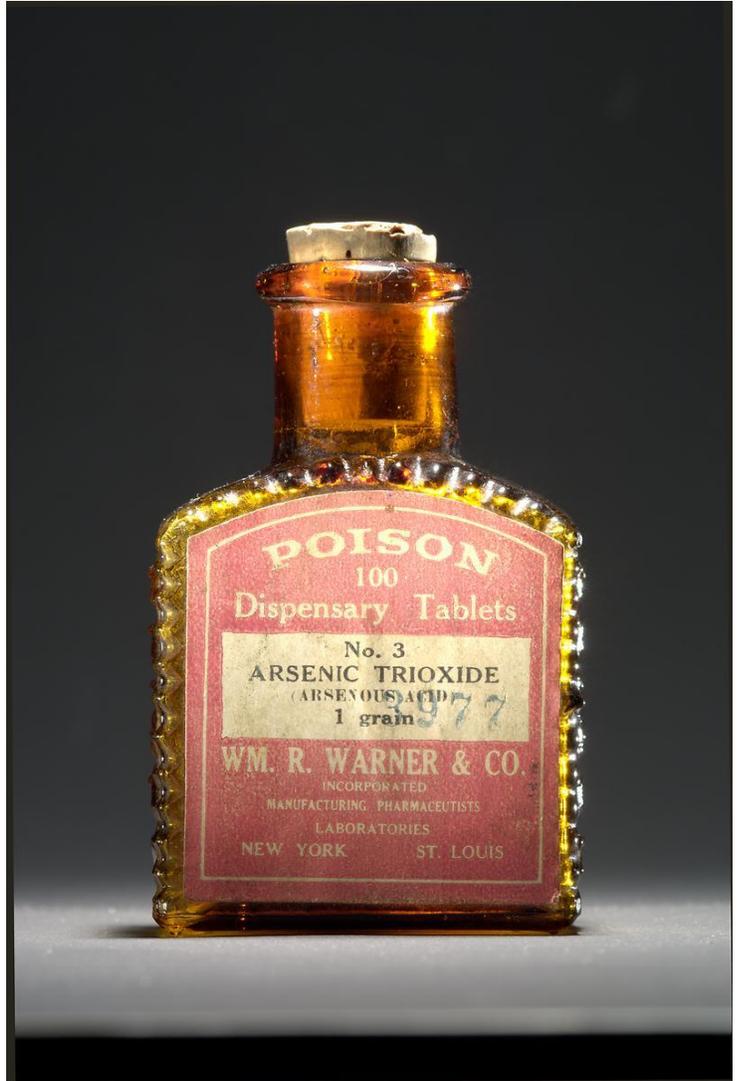
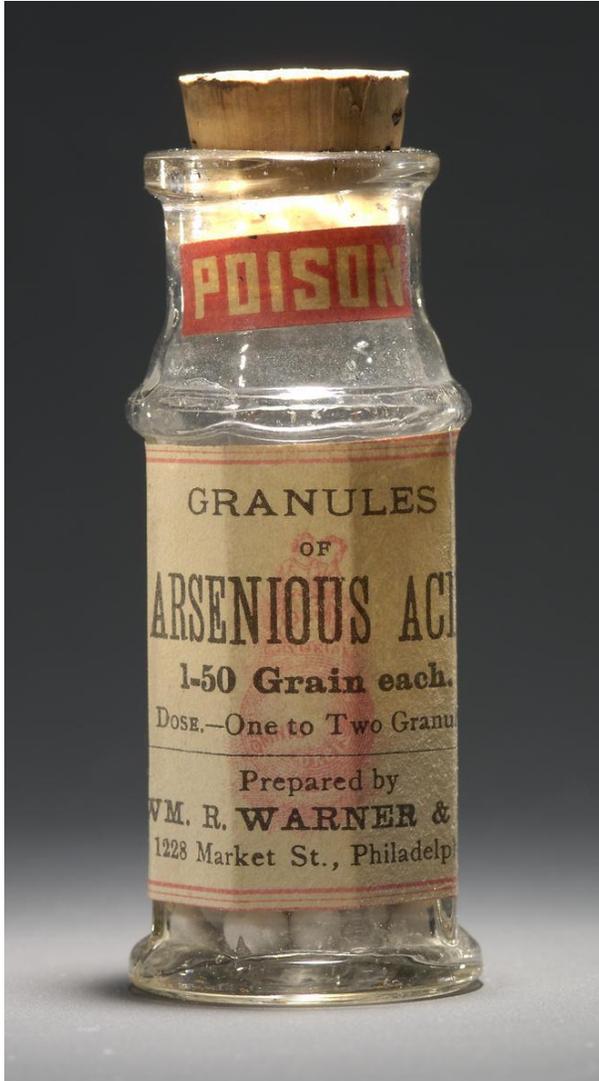
*any persons “taken in rebellion against the Union, he would hang ... with less reluctance than he had hanged deserters and spies in Mexico.” He never wavered from this stance. The Southerners were not prepared to take him on, as they did Abraham Lincoln a generation later. Though they eventually lost the war to Lincoln, things may have been even worse for them had they taken on old “rough and ready” in 1848.*

*One hot July 4<sup>th</sup> afternoon in 1850, during Independence Day celebrations in Washington, Taylor suddenly became quite ill with symptoms of a severe gastroenteritis. Five days later he was dead. The cause of death given at the time was simply a “cholera-like” illness. Taylor, it need hardly be said had many enemies. Almost from the moment of his death there were rumors of foul play with suspicions of arsenic poisoning in view of the prominent gastrointestinal symptoms. These rumors, never proven, persisted long after his death, so much so that in 1991 with permission from family descendents, his body was exhumed and an autopsy was undertaken at the Oak Ridge National Laboratories in Tennessee. Samples of Taylor’s hair and nails, which were well preserved, were taken for highly sophisticated neutron activation analysis for the detection of arsenic.*

*After reviewing the test results, the medical examiner announced that the arsenic levels in the samples were several hundred times less than they would have been if the president had been poisoned with arsenic. The official line therefore is that President Taylor did not die of arsenic poisoning. This would have been expected to put the issue to rest, however surprisingly in many circles it has not. The testing of hair samples is fraught with difficulties. It is more appropriate to testing from chronic as opposed to acute poisoning. It is very open to artifact with respect to false positive results from environmental contamination, (though not obviously in the Taylor case) and results may be influenced by how the sample is actually measured. Apparently President Taylor’s results were the average arsenic levels of the whole sample. Some argue that it is more accurate to look at levels at specific sites on the hair, the base of the hair in the case of acute poisoning for example. As in many good conspiracy stories, even seemingly rigid scientific analysis can remain open to variable interpretation. We will probably never definitively know what Zachary Taylor died from.*

*In the 21<sup>st</sup> century arsenic poisoning is no longer a favorite of the assassin as it once was in centuries gone by. This is primarily because it may be detected by scientific methods where in previous centuries it could not. The testing of blood and urine samples is done in most cases. The testing of hair samples however is not usually included in modern analysis due to its unreliability. In a “cold case” however of 141 years previous this rather “rough and ready” method nonetheless was our only possible method of investigation.*

## ARSENIC POISONING



*Two arsenic based “medicines”, circa 1900, (National Museum of American History, Behring Center, Smithsonian Institution)*

### ACUTE TOXICITY

#### Introduction

**Acute arsenic poisoning** is uncommon but potentially fatal. It can occur from intentional ingestion of arsenic containing compounds.

Acute ingestions result in a severe gastroenteritis followed by potentially fatal multi-organ system failure.

**Chronic arsenic poisoning** is characterized by the insidious onset of multi-system effects. Chronic exposure is most commonly seen in third world countries as a result of long term drinking of contaminated artesian water.

### Sources of Exposure:

1. Inorganic arsenic:

- Industrial sources, including semiconductors, glass, pesticides and wood preservatives.

Note that cutting or burning pine impregnated with chromium-copper-arsenate preservatives may result in mucosal irritation from smoke or sawdust, but does not result in arsenic poisoning.

- Contamination of naturally occurring artesian ground water
- Arsenic trioxide may be an ingredient of some rodenticides or herbicides.
- May be found in a range of “traditional” and “herbal” remedies.

2. Organic arsenic:

- This is predominantly found in fish and shellfish.
- The compounds include arsenobetaine and arsenocholine, both of which are non-toxic.

### History

In past ages arsenic was widely used as a poisoning agent of assassination.

It was however also used in a wide variety of “medicinal” agents that usually resulted in toxicity rather than any medical benefit.

Arsenic sometimes still persists in a range of “traditional” and “herbal” remedies.

### Chemistry

Arsenic exists in three forms:

1. **Elemental**
2. **Inorganic**
3. **Organic**

Inorganic and organic forms may exist as:

1. Arsenite (trivalent)

- Most commercially available arsenic containing products are produced from **arsenic trioxide**, one of the more toxic trivalent inorganic compounds.

2. Arsenate (pentavalent)

### Toxicology

Arsenic binds to numerous intracellular enzymes, and interferes with a range of metabolic processes, including:

- Binding to sulfhydryl groups.
- Interference with oxidative phosphorylation.
- Inhibition of DNA replication and repair mechanisms.
- May produce reactive oxygen intermediaries that cause lipid peroxidation.

### Pharmacokinetics

#### Absorption:

- Absorption can occur via the **GIT, respiratory tract and dermally**.

#### Distribution:

- Initial distribution is to the kidneys and liver.
- In more chronic exposure distribution will also be to the lungs, nervous system, spleen hair and nails.

#### Metabolism and excretion:

- Arsenic undergoes hepatic methylation and these metabolites are excreted in the urine.
- Elimination half-life is 2-5 days following acute ingestion.
- Small amounts of inorganic arsenic are excreted unchanged in the urine.
- The organic arsenoids found in seafoods are excreted in the urine unchanged.

### Risk Assessment

**Acute or subacute ingestion** of **inorganic** arsenic leads to a dose dependent pattern of multi-organ failure.

Dose	Effects
< 0.05 mg / kg	Mild and self-limiting GIT symptoms only without systemic toxicity
0.05 - 1mg/kg	Increasing likelihood of multisystem toxic effects
> 1mg/kg	Potentially lethal.

In children any ingestion of arsenic insecticide should be regarded as potentially lethal.

### Clinical Features

Toxicity can be acute, subacute or chronic.

#### Acute toxicity:

Following large **acute** ingestions toxicity occurs in 3 phases, an initial severe gastroenteritis, followed by multiorgan failure and delayed complications in those that survive.

#### *Rapid onset:*

1. GIT:
  - GIT upset is severe with watery diarrhoea, vomiting and abdominal pain.
  - GIT hemorrhage can occur.
2. Hypersalivation/ possible garlic odour.

#### *Followed in hours by multiorgan failure:*

3. Encephalopathy:
  - Seizures.
4. Cardiac:
  - Arrhythmias/ prolonged QT interval.
5. Respiratory:

- An ARDS type picture.
6. Renal failure
  7. Hepatic impairment

*In survivors later complications may then follow:*

8. Bone marrow depression:
  - This may occur within **24-72 hours**.
  - It becomes maximal within **2-3 weeks**.
9. Alopecia.
10. Peripheral neuropathy:
  - This may develop over the ensuing **1-3 weeks**.
  - It is an ascending motor neuropathy similar to Guillain-Barre syndrome and may progress to respiratory failure.

### Investigations

#### Blood tests:

1. FBE.
2. U&Es/ glucose:
  - Particularly in view of the severe gastrointestinal toxicity.
3. Coagulation profile.
4. LFTs
5. ABGs/ VBGs/ lactate level:
  - In unwell patients.
6. Blood arsenic levels:
  - Limited utility, possible role in the assessment of acute exposure in the anuric patient.

#### Urine:

1. Spot urinary arsenic

- Normal is < 30 microgram/L or < 4.0 micromol/L.
  - Helpful to confirm acute ingestion.
  - Following acute ingestions levels may be as high as 1000 micrograms per liter or more.
2. 24 hour urinary arsenic excretion:
- Normal is < 50 micrograms per 24 hours or 675 nanomols per 24 hours.
  - This better reflects the total body load of arsenic.
  - Amounts may be one to two orders of magnitude higher than normal following acute ingestion.
  - Seafoods ingested 3-4 days before doing a 24 hour urinary arsenic level may falsely elevate readings.

Note that discovery of elevated arsenic levels in asymptomatic patients undergoing a “heavy metal” screen will most commonly reflect increased excretion of non-toxic organic arsenic compounds that may be found in seafoods.

### Hair samples:

General screening of hair samples for metals is very often subject to artefactual results, hence is unreliable and **not** usually recommended.

### Radiology:

CXR/ AXR are useful as inorganic arsenic compounds are radio-opaque.

### ECG:

Prolonged QT and cardiac arrhythmias have been described in acute toxicity.

### Management

1. Immediate attention to any ABC issues:
2. Fluid resuscitation:
  - IV fluid resuscitation to restore circulating volume will be the initial priority.
  - Correction of any hypokalemia.

3. Charcoal:
  - Activated charcoal does **not** bind arsenic and so is not useful
4. Whole bowel irrigation:
  - Alert and cooperative patients who have self poisoned with **arsenic trioxide confirmed on AXR** should undergo whole bowel irrigation.
  - Ongoing therapy may be guided by serial AXRs following the transit of arsenic.
5. Supportive:
  - Supportive measures as clinically indicated.
6. Specific antidotes:

Arsenic is amenable to **chelation** therapy.

This should be commenced when there are **objective clinical signs** of acute arsenic poisoning.

It is not necessary to wait for arsenic level results before commencing therapy.

Agents used are:

- [Succimer](#)

This is the oral agent of choice

*Or*

- [Dimercaprol](#)

This can be given by IM injection in cases where oral administration is not possible.

**See separate documents for these in Drugs folder**

*Disposition:*

**Specialist toxicologist advice should be sort for any suspected acute or chronic arsenic poisoning.**

Patients who are well and symptom free at 12 hours following acute ingestions may be medically cleared.

## CHRONIC TOXICITY

### Introduction

**Chronic arsenic intoxication** most commonly occurs as a result of long term drinking of contaminated artesian water and is characterized by multi-system effects.

### Risk Assessment

Chronic arsenic poisoning most commonly is the result of long term ( > 10 years) drinking of naturally contaminated artesian water in third world countries, particularly Bangladesh. <sup>2</sup>

Immigrants from third world countries, particularly from Bangladesh, with a long term history of drinking water from deep artesian wells, may therefore be at risk of chronic arsenic poisoning.

### Clinical Features

#### Subacute toxicity:

The principle features include:

1. Initial GIT symptoms
2. Leukopenia/ liver function impairment.
3. Hematuria
4. Peripheral neuropathy, (after several weeks).

#### Chronic toxicity:

There is an insidious onset over years of a multi-system disorder:

1. Non-specific constitutional symptoms:
  - Lethargy / malaise
  - Anorexia
  - Weight loss
2. Cutaneous lesions:
  - Hyperkeratosis of palms and soles
  - Hyperpigmentation.

- Nail changes, (**Mees lines**)



*Mees lines are white lines of discolouration running across the nails, (described by Dr R.A Mees a Dutch physician in 1919). They can be produced by a number of causes, including, renal failure, chemotherapy, and heavy metal poisoning, including arsenic poisoning.*

3. Peripheral neuropathy:
  - Painful and in typical “glove and stocking” distribution.
4. Malignancies:
  - Skin/ bladder.

### Investigations

Subacute/ Chronic arsenic poisoning is diagnosed on the basis of:

1. A history of exposure
2. Clinical features consistent with arsenic poisoning.
3. Elevated urinary arsenic levels:
  - Usually > 200 micrograms per liter, (or > 2.7 micromols/L)

Nerve conduction studies will confirm peripheral neuropathy.

### Management

Patients with chronic arsenic intoxication can usually be managed on an outpatient basis.

Chelation therapy is given.

**Specialist toxicologist advice should be sort in any case of suspected chronic arsenic poisoning.**

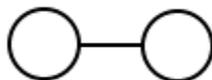
## Appendix 1

### Physical properties:



*Arsenic, (Life Science Library, "Matter", 1963).*

Elemental symbol	<b>As</b>
Discovery	Arsenic compounds have been known since ancient times. It is believed that Albertus Magnus isolated the element in 1250 A.D.
Atomic number	33
Atomic weight	74.92
Melting point	817 degrees Celsius.
Boiling point	614 degrees Celsius, (see appendix 1 below).
Classification	Metal
Alchemy symbol:	Arsenic is one of the elements which has an alchemical symbol, shown below.



Physical Appearance:           Metallic grey.

*Note on the melting and boiling points of arsenic:*

*Arsenic's boiling point is lower than its melting point. This occurs because these two temperatures are measured at different atmospheric pressures. When heated at standard atmospheric pressure, arsenic changes directly from a solid to a gas, or sublimates, at a temperature of 887 K. In order to form liquid arsenic, the atmospheric pressure must be increased. At 28 times standard atmospheric pressure, arsenic melts at a temperature of 1090 K. If it were also measured at a pressure of 28 atmospheres, arsenic's boiling point would be higher than its melting point, as you would expect.*

### References

1.     Arsenic poisoning in: Murray L et al. Toxicology Handbook 3rd ed 2015.
2.     Editorial: Arsenic in drinking water: a natural killer in Bangladesh and beyond, An urgent alternative watershed management strategy is needed. MJA Volume 183 Number 11/12. December 2005

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