



ARSENIC
A Global Malediction

THE DETRIMENTAL EFFECT
&
BIOLOGICAL COUNTERACT

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As

*Discovered by Albertus Magnus
in the 13th century*

The name comes from 'arsenikon',
the Greek name for the yellow
pigment orpiment

Although it is now strongly linked with poison, people in the Middle Ages wore arsenic amulets around their necks to ward off the bubonic plague, and women in Victorian times applied arsenic compounds to their faces to whiten their complexion.

It was believed that arsenic was very useful as a topical remedy for skin ulcers and also used widely as a medicine. Dr. Fowler's Solution (potassium arsenate dissolved in water) was a popular cure-all tonic in Victorian times.

Sources:

- ❖ Arsenic is widely distributed throughout the earth's crust.
- ❖ Arsenic is introduced into water through the dissolution of minerals and ores, while elevated concentrations in groundwater is the results of erosion from point sources.
- ❖ Industrial effluents, combustion of fossil fuels, organic arsenic species etc.

Inorganic arsenic can occur in the environment in several forms, but in natural waters (e.g., drinking-water), it is mostly found as trivalent arsenite, As(III) or pentavalent arsenate, As(V). **As(III) is more harmful than that of As(V).**

Organic arsenic species, abundant in seafood, are very much less harmful to health, and are readily eliminated by the body.

Arsenic:
The king of poisons

Acute poisoning

- ✓ Vomiting
- ✓ Oesophageal and abdominal pain
- ✓ Bloody "rice water" diarrhoea
- ✓ Muscular weakness and cramping
- ✓ Erythematous skin eruptions and
- ✓ Swelling of the eyelids, feet and hands

Long-term exposure

- ✓ Atherosclerosis
- ✓ Diabetes
- ✓ Hypertension
- ✓ Anemia
- ✓ Peripheral neuropathy
- ✓ heart diseases
- ✓ Kidney damage
- ✓ Confusion
- ✓ Headache
- ✓ Liver disorders
- ✓ Hyperpigmentation
- ✓ Hyperkeratosis

➤ Cancer is a late phenomenon of arsenic exposure, usually takes more than 10 years to develop.

ARSENIC
&
CANCER

➤ The lung, seems to be a major site of action of ingested arsenic. Lung cancer has been reported as the main cause of arsenic death.

➤ There is evidence that arsenic-exposed people who are predisposed to noncancerous skin lesions may be more vulnerable to other cancers.

➤ Selenium deficiency also enhanced the carcinogenic effects of arsenic.



Over the next decade, skin and internal cancers (bladder, kidney, liver, lung, colon, uterus, prostate, and stomach) are likely to become the principal human health concern arising from arsenic .

❖ Smokers are at an increased risk from arsenic-contaminated drinking water, and there is mounting evidence of a malignant synergy between smoking and arsenic. Here arsenic acts as a **co-carcinogen**, allowing this substance to cause mutations in DNA more effectively.

❖ Although organic arsenic is less poisonous in comparison to inorganic arsenic, but one of the recent reports argues that the organic metabolites of arsenic may be the ultimate carcinogens???

World Exposed

- The majority of harmful arsenic exposure comes from drinking water from wells drilled through arsenic-bearing sediments. In Bangladesh and West Bengal, millions of tube wells were drilled into arsenic-rich sediments; as a result, in many of these wells arsenic levels reach 500-1,000 $\mu\text{g/L}$ and even higher, where **EPA's guideline is 10 $\mu\text{g/L}$.**
- The other major sources of arsenic exposure are through food, soil, and air.
- **PROCESS MAGNIFICATION:** Food processing by arsenic-containing water increases the arsenic content by 10-30% for most foods, and even 200-250% for beans and grains, which absorb cooking water.
- **BIOMAGNIFICATION:** Exposure via food-chain. Several studies in Southeast Asia revealed that arsenic-laced irrigation water can substantially increase the arsenic content of rice and vegetables.

Global Situation

➤ A vast geological zone: Ganga-Meghna-Brahmaputra plains are being exposed to high arsenic levels (all of Bangladesh and most of India), putting more than 500 million people at risk of chronic arsenic poisoning. With 80% of Bangladeshis estimated to be at risk of arsenic-related diseases, the World Health Organization (WHO) has labeled this “the worst mass poisoning in history”.

➤ Large areas of China also face severe arsenic insult from groundwater contamination, with more than 3 million people affected. In Shanxi Province alone, an estimated 900,000 people are at risk of arsenicosis.

➤ More than 100 million people are exposed to underground water with high concentrations of arsenic in Taiwan.

➤ Other countries with arsenic-rich groundwater include Argentina, Chile, Mexico, Cambodia, Vietnam, Thailand, Nepal, and Ghana.





What is endocrine system?

The endocrine system is a network of glands that release many different hormones, sometimes in very tiny amounts.

- ◇ *Hormones control growth, sexual and mental development, and many other functions.*

Endocrine Disrupters ?

An endocrine disrupter is an **exogenous** substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.

In brief, substances that alter normal hormonal levels or activity in the body may be labeled as **Endocrine Disrupting Chemicals (EDCs)**.

EDCs and human health effects

- ◇ Reproductive disorders
- ◇ Immune system malfunction
- ◇ Certain cancers, especially of reproductive organs
- ◇ Birth defects of the penis and falling sperm counts
- ◇ Neurological effects
- ◇ Attention deficit and poor memory
- ◇ Low IQ

Evidences surround us

- Otters from the Lower Columbia River are infertile because the males' penises are too small to mate.
- Alligators affected by EDCs cannot reproduce.
- Male fish develop female hormones.
- In birds, egg-shells turn thin, so chicks cannot survive.

In the mid-20th century, Diethylstilbestrol (DES), a synthetic sex steroid, was used for fattening of cattle as well as to prevent miscarriages in humans, which results in devastating health consequences like vaginal cancer of daughters and reproductive malfunctions of boys in the following decades. Results of this tragic experiences with DES clearly showed that the human body could mistake a man-made estrogenic chemical(s).

Some of the mechanisms by which endocrine-disrupters can interfere with hormones are:

- **Hormone Mimicry:** some chemicals mimic hormones by binding to hormone receptors in cells, and thereby triggering the same biological effect as the hormone.
- **Blocking Hormone Receptors:** some chemicals bind to hormone receptors and block them. This prevents hormones from binding to the receptors and exerting their normal biological effects.
- **Altering Hormone Metabolism:** some chemicals do not directly interfere with hormones or their receptors, but upset the balance of hormones by interfering with their metabolism, i.e., their synthesis or natural breakdown and elimination from the body.

But,

Arsenic appears to act in a different way.

Arsenic

A new type of Endocrine disruptor

❖ *Recent report says that exposure to very low concentrations of arsenic disrupts the function of the **glucocorticoid receptor** via a unique mechanism not previously shown for other EDCs.*

What are Glucocorticoids?

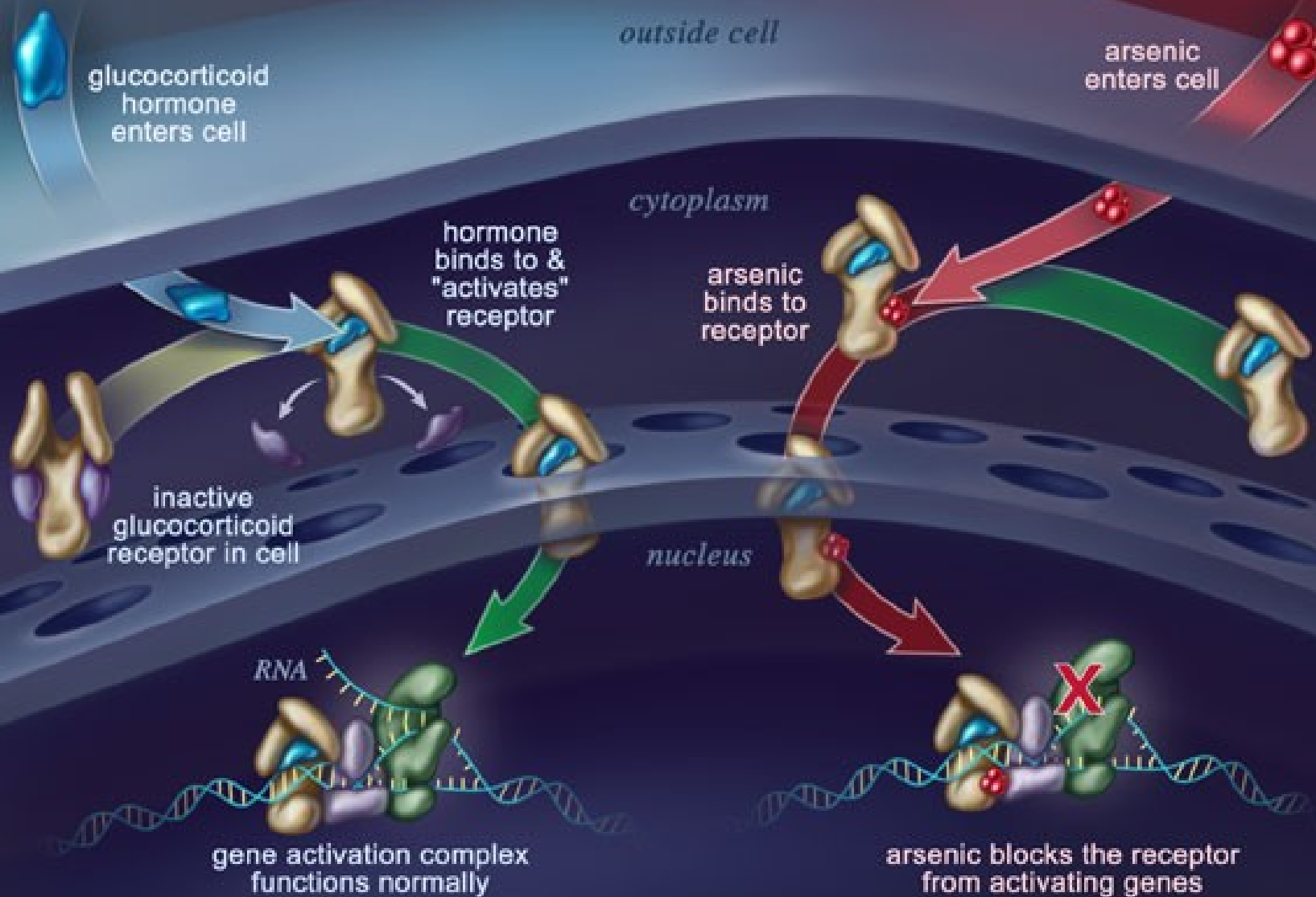
- ❖ Glucocorticoids are steroid hormones in the same class as estrogen, progesterone and testosterone.**
- ❖ Steroid hormones are chemical messengers secreted by glands into the bloodstream and carried to distant cells throughout the body where they help to regulate the body's functions. Each hormone has a specific receptor and it binds to initiate its effects.**
- ❖ Glucocorticoids, acting through their receptor, help to regulate embryo development, stress, blood glucose levels, blood vessel function, lung and skin development, and may also play a key role in suppressing cancer.**

Mechanism of action

- ❖ In the presence of arsenic, the activated receptor is unable to stimulate the correct cascade of signals that usually results from hormone binding, particularly the ability to turn on certain hormone-responsive genes.
- ❖ Arsenic's disruption of the glucocorticoid system takes place after the hormone-receptor complex enters the nucleus.
- ❖ The changes in the system took place within the nucleus and involved selective inhibition of DNA transcription that normally would have been stimulated by the glucocorticoid-GR complex.

Normal Gene Activation

Gene Activation Inhibited by Arsenic



Inside the nucleus, arsenic interferes the glucocorticoid-receptor complex mediated gene activation

In Short,

When arsenic enters the nucleus, the hormone activated GR fails to regulate several normally hormone responsive genes. The investigators postulate that this is a result of arsenic binding directly to GR, at a site other than the site for hormone binding, and blocking its ability to interact with other key proteins that are required for gene regulation inside the nucleus.

After effects :

- **Increase the risk of type 2 diabetes and vascular disease.**
- **Increase the risk of tumor growth.**

The new finding may help to explain how arsenic triggers cancer, and other chronic diseases such as hypertension .

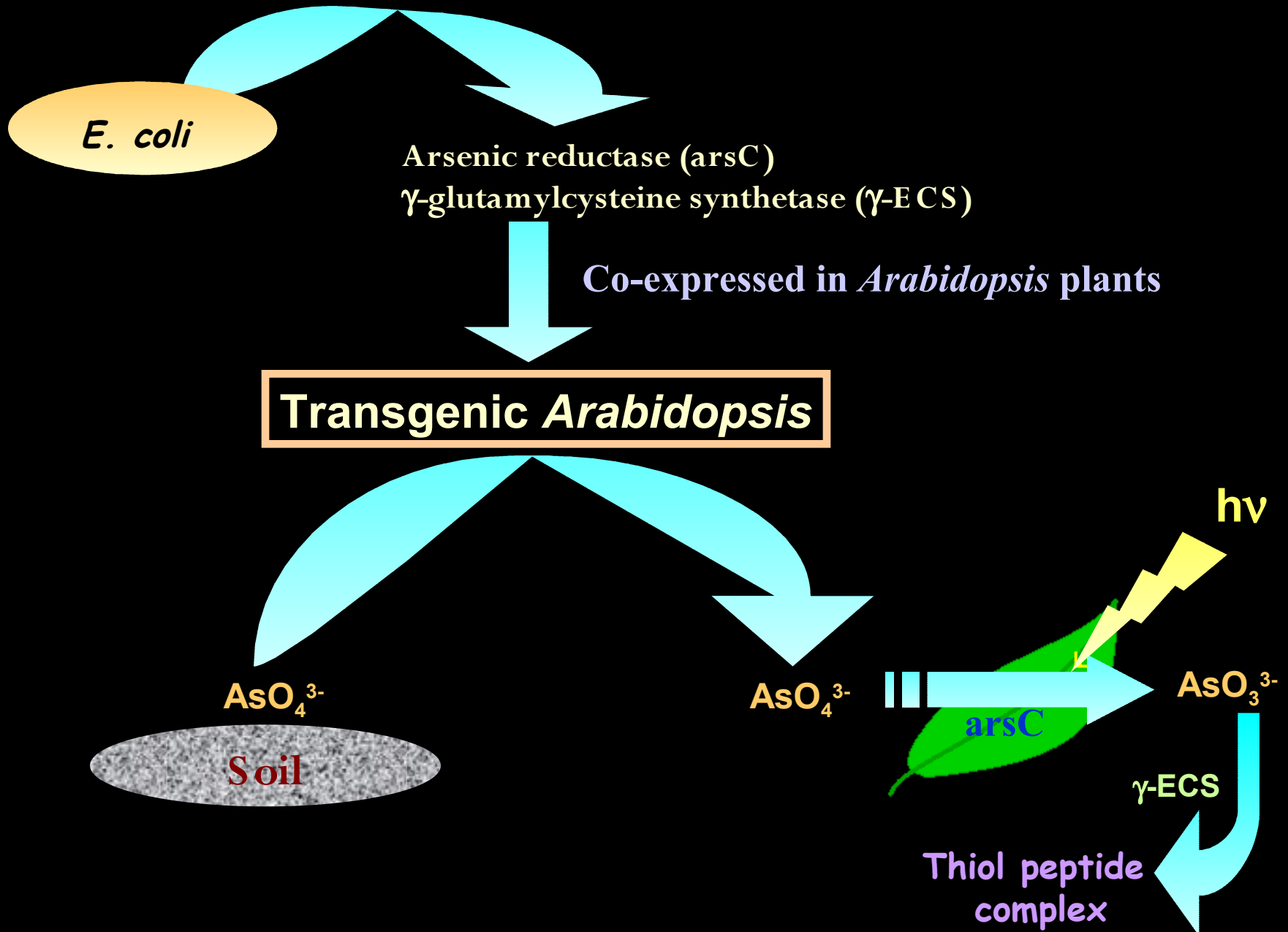
Very recently, it was found that arsenic has the similar effects on other members of the steroid receptor family, such as estrogen and progesterone receptors at very low doses where mechanism remains to be defined.

Future asking :

Arsenic-mediated endocrine disruption need to be explored further to assess the arsenic impact on human health.

**Bioremediation :
Removal of arsenic from
nature**

Phytoremediation :

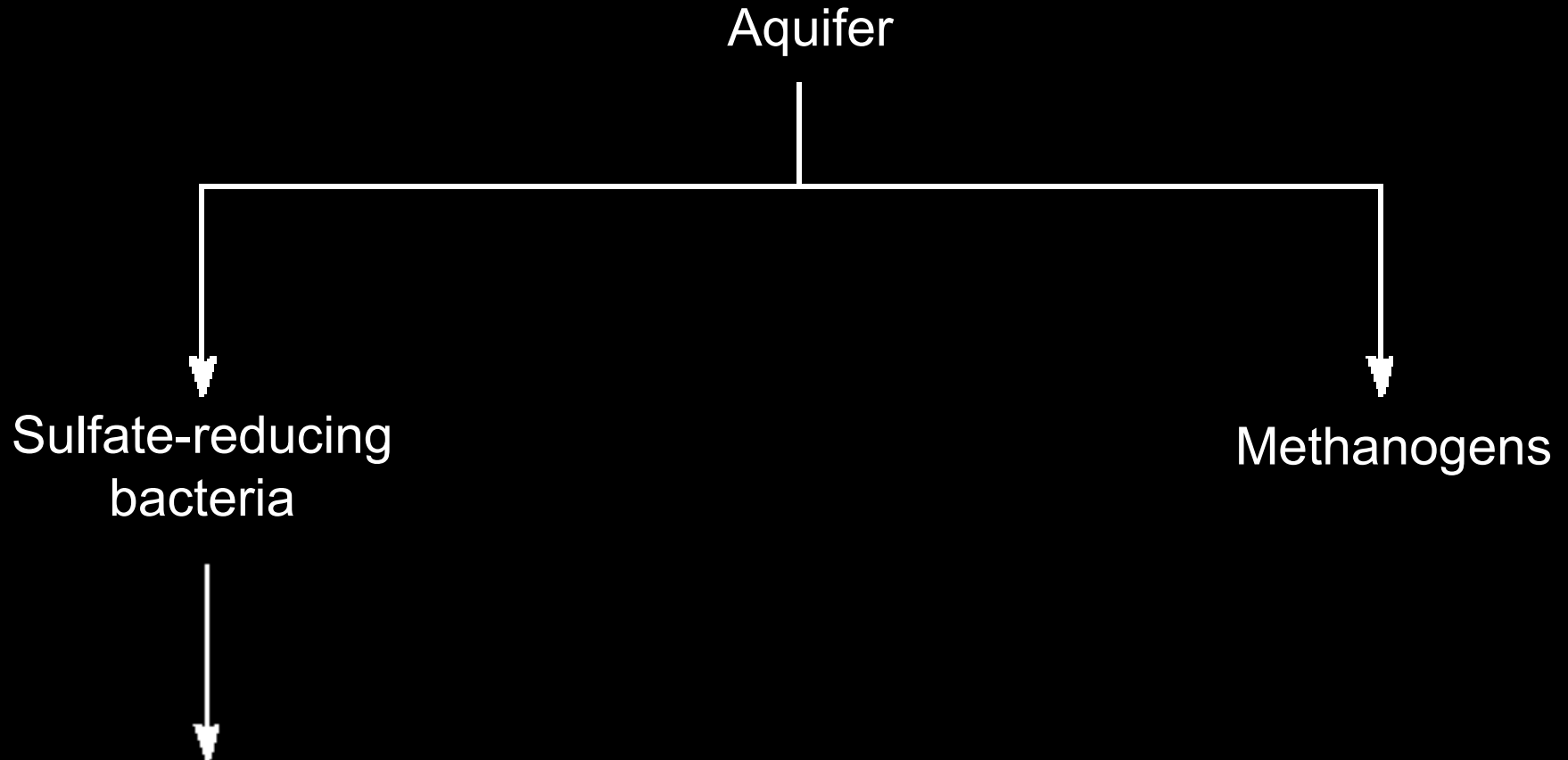


Nitrates Affect Arsenic Pollution?

- ❖ In the June 28, 2002 issue of the journal "Science, MIT engineering professor Hemond said nitrate pollution, which is also associated with noxious impacts such as excessive algal growth, was found to help reduce arsenic pollution in lakes. It reacts with naturally occurring iron to create iron oxides that absorb arsenic.

Microbial Activities

Munching microbes could cleanse Arsenic-contaminated groundwater.



This bacteria will consume sulfate and reduce it into sulfide. The sulfide then reacts to precipitate arsenic, leaving little in solution.

❖ Arsenic eaters:

➤ A new strain of "extremophile" microbe has been discovered in Searles Lake, southwest of Death Valley in California, and it was found that they can eat arsenic(?).

The bacterium, called SLAS-1, metabolize arsenate (terminal electron acceptor in respiratory chain) to gain energy for growth while the arsenite so formed due to the reduction of arsenate is converted to thioarsenite.

➤ So this finding provides a hope that someday microbes may be used to treat arsenic-contaminated drinking water.

Science, 27 May, 2005

Prevention and control

- ❖ The most important remedial action is the prevention of further exposure by providing safe drinking-water.
- ❖ Discrimination between high-arsenic and low-arsenic sources by painting the hand-pumps (e.g. red and green) can be an effective and low cost means to rapidly reduce exposure to arsenic when accompanied by effective health education.
- ❖ Alternative low-arsenic sources such as rain water and treated surface water may be appropriate in some circumstances.
- ❖ The conventional technologies including co-precipitation, ion exchange and activated alumina filtration may be well effective.

❖ Homeopathic solutions for arsenic poisoning?

Researchers from University of Kalyani, W.B. claimed that the potentized homeopathic drug Arsenicum Album has the ability to help remove arsenic from the body and also these drugs in micro doses appear to have the ability to detoxify the ill-effects produced by arsenic in mice.

But the human clinical trial and the mechanisms of action are not yet reported.

❖ Research on **BIOREMEDIATION**, the most promising alternative to control arsenic pollution.

THANK YOU

