UNIT: DNA

LESSON 1: ARSENIC AND EPIGENETICS: A DNA STORY

TEXAS BIOMEDICAL RESEARCH INSTITUTE
HEALTH STARTS WITH SCIENCE

Objectives:

The Student Will Be Able To:

1. Evaluate science research for context clues to demonstrate the interconnectedness of body systems through epigenetic terms. **(1A)**
2. Evaluate data to assess presence or absence of toxins from water samples. **(1B)**
3. Analyze the effects of runoff on sources of drinking water. **(1B)**
4. Interpret evidence from science research to discuss potential adverse epigenetic effects of toxins in water.**(1A, 1B)**
5. Design, test, and evaluate a water treatment strategy. **(1B)**

General Information

Minerals are important elements our bodies need to live. Some of the essential elements our bodies need include:

Mineral/Element (Symbol)	Body Function	Mineral/Element (Symbol)	Body Function
Na Sodium	Muscle contraction, nerve transmission	Fe Iron	Red blood cells, oxygenation
Ca Calcium	Bones, teeth, muscle relaxation	Zn Zinc	Protein synthesis, immune system health
Mg Magnesium	Immune system, protein synthesis	Cr Chromium	Regulates blood sugar
P Phosphorus	Bones, teeth, homeostasis	Cu Copper	Enzyme function, metabolize Fe
K Potassium	Muscle contraction, nerve transmission	I Iodine	Regulates growth and development

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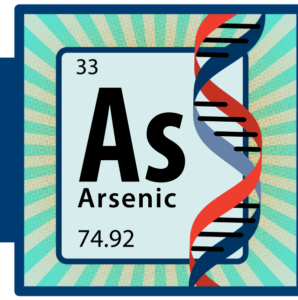

States and Properties of Metals, Nonmetals, and Metalloids

All matter is classified by one of three states, its physical properties and chemical properties. The three states of matter are: solid, liquid, and gas. In a solid, the particles (atoms, ions, or molecules) are tightly packed together and can only "vibrate" in place. In other words, they cannot move apart from one another because they have very low kinetic energy. Unlike solids whose particles are held together, liquids have no defined shape and take the shape of the container, filling from the bottom up (thanks to gravity). Liquids have a higher kinetic energy than solids, meaning the particles are able to move around one another. Matter in the gaseous state have high kinetic energy. The kinetic energy is so high that the particles can spread out and away from one another. Unlike liquids which fill a container from the bottom up, gases will spread out, filling the entire container. If the container does not have a lid, the gas will escape.

There are two properties of matter: physical properties and chemical properties. Physical properties include color, hardness, density, melting and boiling points, and conductivity. Chemical properties include reactivity, flammability, toxicity, and acidity.

Physical Properties of Matter		
Metals	***Nonmetals***	***Metalloids***
Malleable (*hammered into sheets*)	Brittle	Not malleable, not brittle
Ductile (*drawn into a wire*)	Brittle	Not ductile
Shiny, luster	Not shiny, dull	Some are shiny; some are dull
Good conductors of heat	Poor conductors of heat (*good insulators*)	Poor conductor of heat
Good conductors of electricity	Poor conductors of electricity (*good insulators*)	Semi-conductors
Most are magnetic	Not magnetic	Not magnetic
State of Matter – room temperature		
Solid [*except mercury (Hg) which is liquid at room temperature*]	Gas (*oxygen*) Solid (*carbon*) Liquid (*bromine*)	Solid

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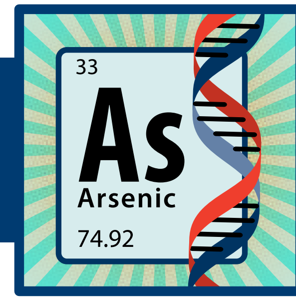

These elements occur naturally in the ground. But how do these minerals get into our bodies? Simply put, plants have symbiotic relationships with fungus. The plural for fungus is fungi ***(FUN-guy)***. The fungi attach themselves to the roots of plants. Once attached to the plant root, the fungi obtain sugars and other nutrients from the plant. In return, the fungi break down the soil, extracting vital minerals from the ground which are then absorbed by the roots of plants. Unlike plants that need fungi to obtain minerals, water erodes the ground which releases minerals. These minerals are then carried by the water. When animals, including humans, eat the plants and drink water, these minerals are absorbed and used by body systems to maintain homeostasis.

But not all elements in the environment are good for us. Some elements are toxic and can be fatal to humans. One such element is arsenic (As). In nature, arsenic is generally found attached or chemically bonded to other elements, primarily metals, forming a substance called "ores". There are different ores, such as iron ore and copper ore. Various methods are used to extract metals from ore but each method releases the other elements found in the ore, including arsenic. When arsenic is bonded to other elements, it is stable and relatively harmless. But when the bonds that attach arsenic to other elements are broken, the highly toxic arsenic is released. The freed arsenic can float in the air, settle on topsoil, or land in water where it can be carried downstream by water.

Threats of Arsenic

Arsenic can naturally be present at toxic levels in groundwater. To address this health threat, communities treat water sources, including groundwater, to remove pollutants and toxins, making the water safe to drink. But not every community has water treatment facilities. This includes indigenous people in rural communities in the western US. Without water treatment facilities, untreated water is used for drinking, cooking, and crop irrigation increasing health risks from exposure to toxins, including arsenic.

Arsenic is associated with various diseases; however, there is evidence that exposure to arsenic during pregnancy increases the risk of offspring developing metabolic diseases later in life. Metabolic diseases are defined as a disease or syndrome that disrupts normal metabolism. A metabolic disease results when abnormal chemical reactions disrupt normal metabolic processes such as converting food to energy at the cellular level. Type 2 diabetes (T2D) is an example of a ***metabolic disease*** while insulin resistance is a ***metabolic disorder***. In general, a metabolic disorder is reversable with changes in lifestyle but a metabolic disease is not.

Exposure to arsenic while in utero (when developing within the mother's uterus) does not automatically mean children will develop metabolic diseases later in life, but it does increase their risk.

Epigenetics: Connecting Arsenic and DNA

Epigenetics is the study of changes in gene expression, specifically what determines when a gene is activated or not activated. The DNA strand resembles a twisted ladder. The rungs of the ladder are made of four molecules called bases: adenine, thymine, cytosine, and guanine. When DNA is exposed to arsenic during development, a methyl group (CH_3) attaches itself to the cytosine base. The attachment of the methyl group, called DNA methylation (DNAm) does not change the DNA, but affects when genes are activated or not activated. This change in gene activation can disrupt metabolic processes and lead to the development of metabolic disease

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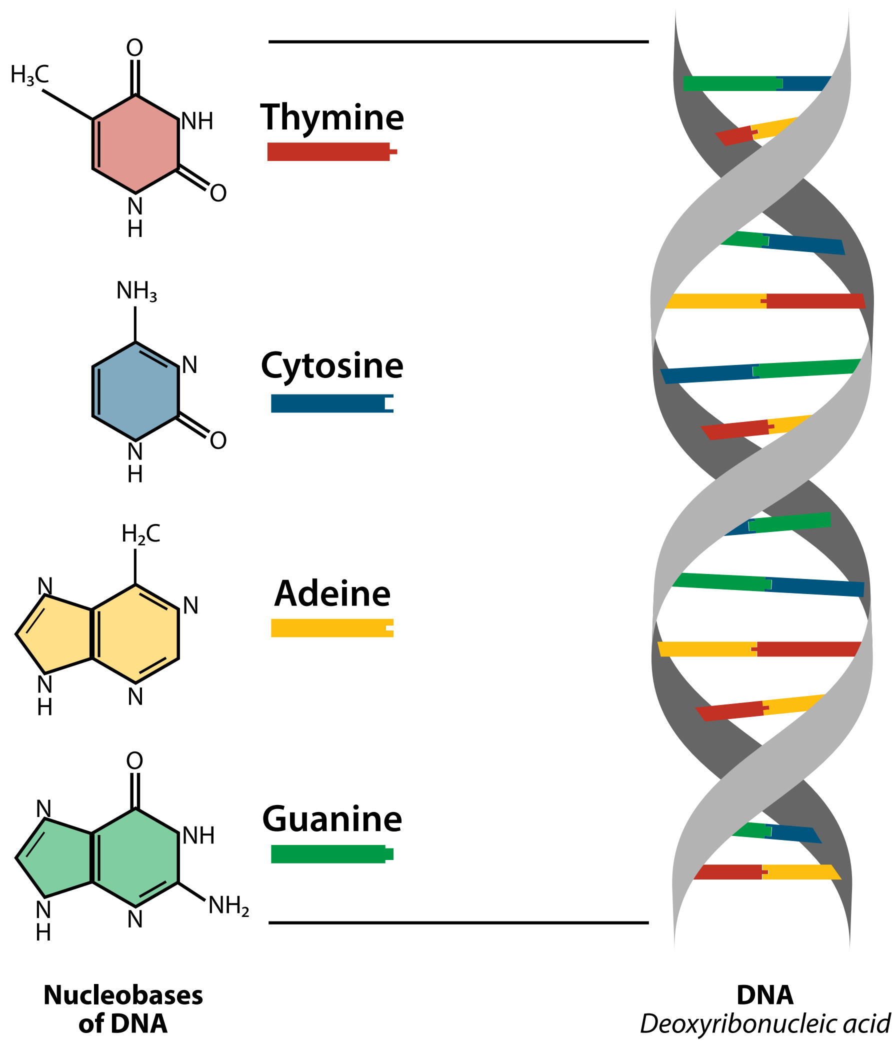
later in life. For example, when an individual with DNAm lives with environmental risk factors such as smoking or obesity, the gene which codes for specific proteins to help metabolize sugars is not activated. Without these proteins, sugar is not effectively metabolized by cells increasing the risk of insulin resistance or type 2 diabetes.

This study seeks to assess the risk of metabolic diseases for individuals known to have been exposed to arsenic in utero. To do so, scientists consulted data from women and their grown offspring in communities with arsenic in the drinking water. The scientists compiled a list of known risk factors which contribute to type 2 diabetes. The data and risk factors are shown in the following table.



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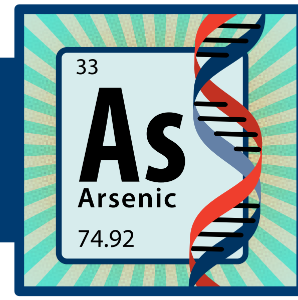

Table 1: Participant Baseline Characteristics

	SHS Mothers (n=119)	Offspring (n=226)
Aqe (years)	54.4 (49.3, 61.6)	40.4 (35.5, 47.2)
Sex (Male)	----	82 (36.2%)
Smoking Status	----	----
Never	44 (37.0%)	78 (34.4%)
Ever	32 (26.9%)	55 (24.3%)
Current	43 (36.1%)	93 (41.2%)
Waist Circumference (cm)	105.0 (98.0 116.0)	100.0(92.0 111.0)
BMI (kg/m^2)	30.9 (27.2, 35.2)	30.4 (26.8, 34.9)
Diabetes Status (diabetic)	44 (37.0%)	0 (0.0%)
Follow-up Diabetes Status	41 (41.2%)	41 (18.1%)
Fasting Glucose (ma/dl)	111.0(99.0, 168.0)	94.0 (87.0 103.0)
Follow-Up Fasting Glucose (ma/dl)	113.0 (98.0, 171.0)	94.0 (86.0, 106.3)
HOMA2-IR (optimal score 1.4)	3.7 (2.4, 5.5)	1.5 (1.0, 2.5)
Follow-up HOMA2-IR (optimal score 1.4)	3.5 (1.9, 6.0)	1.6 (0.9, 2.7)
Total Arsenic (µg/g creatinine)	7.3 (5.0, 13.8)	4.6 (3.0, 8.4)

! **NOTE:** In the above table risk factors of offspring were gathered: waist circumference, BMI, smoking status and glucose (blood sugar) levels. The initial or baseline data were gathered for mothers and their adult offspring (diabetes status and fasting glucose). The "follow-up" data were gathered five years after the initial visit.

Of the mothers, 37% initially tested positive for T2D but five years later, the number increased to 41%. Of their adult offspring, 0% initially had T2D but five years later,18% were diagnosed with T2D. It should be noted that at the start of the study, both mothers and adult offspring had an insulin resistant indicator which was above normal, 3.7 and 1.5 respectively. To understand the table, it is important to note the numbers in the parentheses represent the lowest and highest values obtained while the number outside the parentheses represents the mode or most frequent value measured. It is important to stress this number is not the average value.

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