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March, 2018

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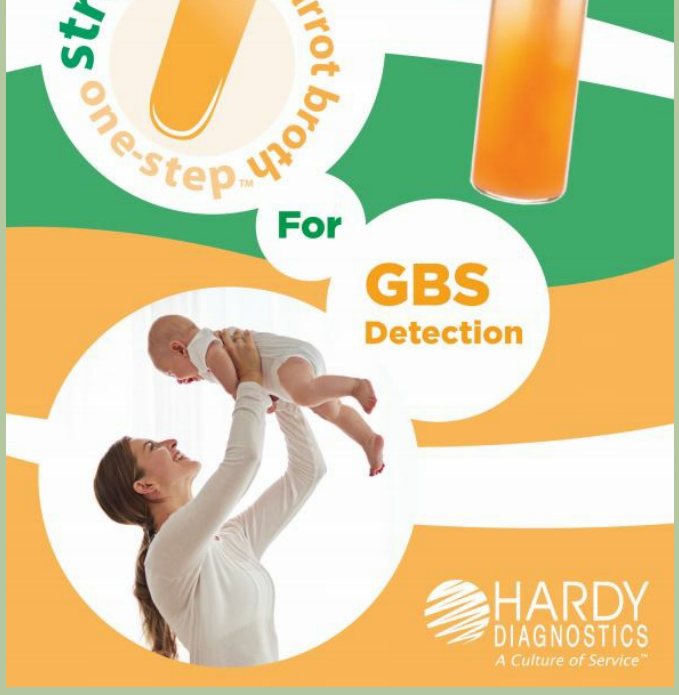
Carrot Broth One-Step

Micro Musings...

Why science teachers should not be given playground duty!

The Incredible Indestructible Tardigrade



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It's Science Project Season!

What doesn't need water, can freeze solid and come back to life, survives intense radiation, and stays alive in the vacuum of space?

Although the answer isn't a cinematic horror, it certainly looks the part. The humble tardigrade (also known as a moss piglet or water bear) is a small-scale animal that rarely grows larger than half a millimeter in length. It is quite possibly the toughest member of the animal kingdom. These water dwelling, eight-legged animals have been found everywhere: from mountain tops to the deep sea and mud volcanoes; from tropical rain forests to the Antarctic. The extreme resiliency of these animals to a wide array of hostile environments, often in combination with one another, has kept them at the center of extremophile research for the last century. Through unique mechanisms and adaptations to stay alive when all normal methods fail, the tardigrade is continually redefining what is possible for multicellular life.

For a typical animal, a lack of water means a lack of life. While a typical animal must either remain hydrated or die, tardigrades have developed numerous strategies to survive even total dehydration. As early as 1922, major conformational changes in dehydrated tardigrades were observed. When water becomes scarce, the already compact

tardigrade forms a structure called a tun, contracting its body and going into a state of dormancy. While in the tun state, the animals don't have functional legs or claws but otherwise appear largely unchanged [1]. This compact body shape reduces surface area, thereby reducing the rate of evaporation. Concurrently, the tardigrade's cuticle becomes much less permeable, retaining more water in the tardigrade's core [2]. the photo below show a tardigrade dehydrated

down to only 3% of its original water volume!

In 2011, a team of Italian researchers found that the dormancy state of the tardigrade can go even further in response to cyclic changes. In the cyclomorphosis process, the animals encase themselves inside of a series of cysts named for their resemblance to ancient Egyptian burials. The outermost cuticle of the animal remains, but inside, the tardigrade is protected by two new layers, named the "sarcophagus" and "mummy" cuticles, respectively [3].

The exterior adaptations to dehydration don't tell the entire story. For the tardigrade to return to life once water is available again requires protective measures for the proteins and organs of the body. In the absence of water, these structures would normally denature and collapse, killing the creature. One suggested preservation mechanism centers around replacing water with the sugar trehalose. In this process, trehalose would be substituted into proteins to form the same hydrogen bonds normally formed by water molecules, allowing the proteins to maintain their structure even in a state of dehydration [4]. Evidence in favor of this mechanism includes the direct observation of trehalose accumulation preceding the ahydrobiotic stage in at least six species of tardigrade [5].

Surviving desiccation would be impressive on its own, but the talents of the tardigrades only start there. These resilient metazoans have adapted to freezing environments as well. Initially, the surprise discovery that tardigrade species were present in polar regions sparked interest in their freeze tolerance. Since then, tardigrades have been shown to survive over 80% of their body water being frozen, as well as being

frozen in their dehydrated state [7, 8]. The precise mechanism by which the animals keep themselves alive is unknown. In other freeze-tolerant creatures, the accumulation of cryoprotectants is used to prevent ice crystals from damaging tissues [9]. Some process is clearly required in order to prepare for extended subzero survival: Hengherr et al demonstrated in 2009 that the survival rate of frozen tardigrades was to some extent dependent on the cooling rate by which they were frozen [10]. In an experiment by Paul Becquerel, tardigrades were briefly brought near absolute zero by use of liquid helium and were subsequently revived. [11]

Tardigrade radiation resilience isn't perfect, but the small creatures do much better than humans or other large animals do when exposed to powerful amounts. Combination experiments that exposed both hydrated and dehydrated animals to gamma radiation and heavy ion bombardment showed mean lethal radiation doses in the thousands of Grays, with hydrated animals actually showing high mean dose tolerance[13]. For humans, a lethal dose of radiation could be as little as 5-10 Grays. It's hard to imagine why such an animal would develop such staggering ionizing radiation resistance, but the same capability may come to humans in the near future. The same experimental group has shown that expression of a damage-suppressing protein from the tardigrade species Ramazzotius varieornatus can be successfully introduced into human culture cells. Once expressed, the protein acts to limit DNA damage, and the modified human cells experience 40% less radiation damage than their unmodified counterparts [14]. Transfer of this radiation resistance has strong possible implications in fields such as long-term spaceflight, where constant exposure to high-energy cosmic rays provides a long-term risk.

For an animal with such a broad array of resistances, the tardigrades lead a relatively sedate life. Their name comes from a Latin term meaning "slow-stepper" and it's difficult to see why they need to be so well prepared for such extreme disasters. Fortunately, this class of animals can serve as a model organism for us to study the limits of animal endurance.

By Weston Mangin
Biomedical engineer at Hardy Diagnostics

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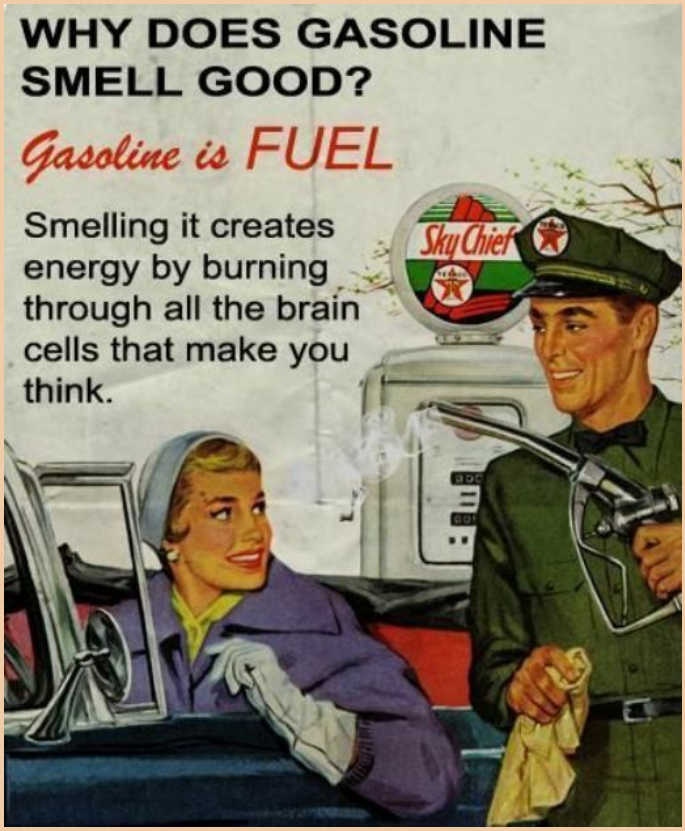

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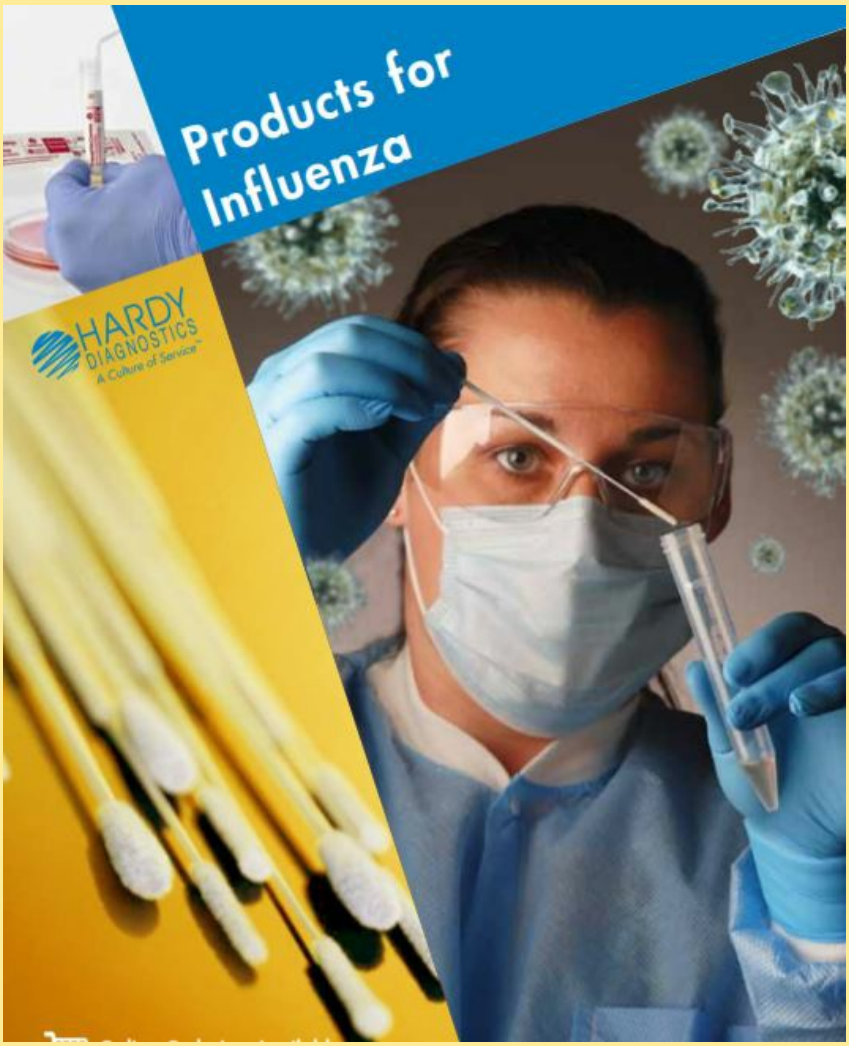

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Trio Bas Air Samplers

* * * * *

Discoverer of Shigella

Dr. Shiga

1871 ~ 1957

Kiyoshi Shiga was born in Sendai, Japan. He graduated from the Medical School of Tokyo Imperial University in 1896 and continued his

studies at the Institute for the Study of Infectious Diseases under Dr. Kitasato Shibasaburō.

Shiga became famous for the discovery of *Shigella dysenteriae*, the bacillus causing dysentery, in 1897, during a severe epidemic in which more than 90,000 cases were reported, with a mortality rate approaching 30%.

The bacterium *Shigella* was thus named after him, as well as the Shiga toxin, which is produced by this bacterium as well as other bacteria, such as *E. coli.*

After the discovery of *Shigella*, Shiga worked with Paul Ehrlich in Germany from 1901 to 1905. After returning to Japan, he resumed the study of infectious diseases with Dr. Kitasato. He became a professor at Keio University in 1920.
From 1929 to 1931, Shiga was the president of Keijō Imperial University in Keijo (Seoul, South Korea).

* * * * *

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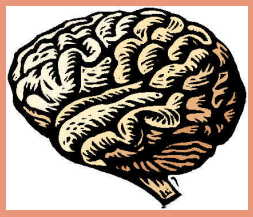

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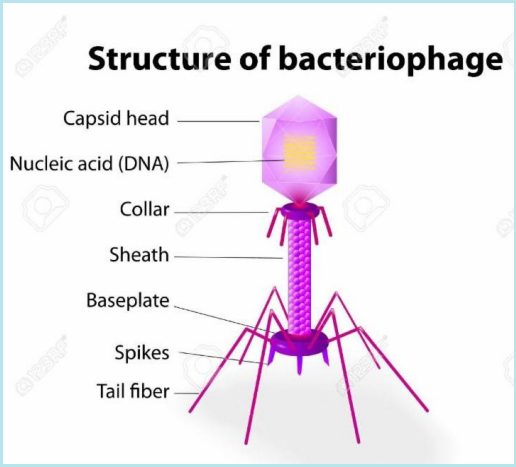
Super Bacteriophage to the Rescue!

We're all aware that one shouldn't fight fire with fire, but microbiologists are challenging that conventional wisdom. Infectious disease researchers are using phage therapy to battle antibiotic-resistant bacteria. Bacteriophages, also known as phages, are viruses that infect bacteria and can be used to treat bacterial infections. Phages enter the target bacteria, replicate, and lyse the cell. They can be observed as clearing zones on agar plates.



Bacteriophages were first identified separately by Felix d'Herelle and Frederick Twort in the early 20th century. The first instance of using phages as a bactericide was when Felix d'Herelle administered a dose to a 12-year-old boy with dysentery in Paris, 1919. In 1921, Richard Bruynoghe and Joseph Maisin used another species-specific phage to treat a skin infection caused by *Staphylococcus*. Trials continued throughout Eastern Europe but were poorly documented. The treatment never caught on in

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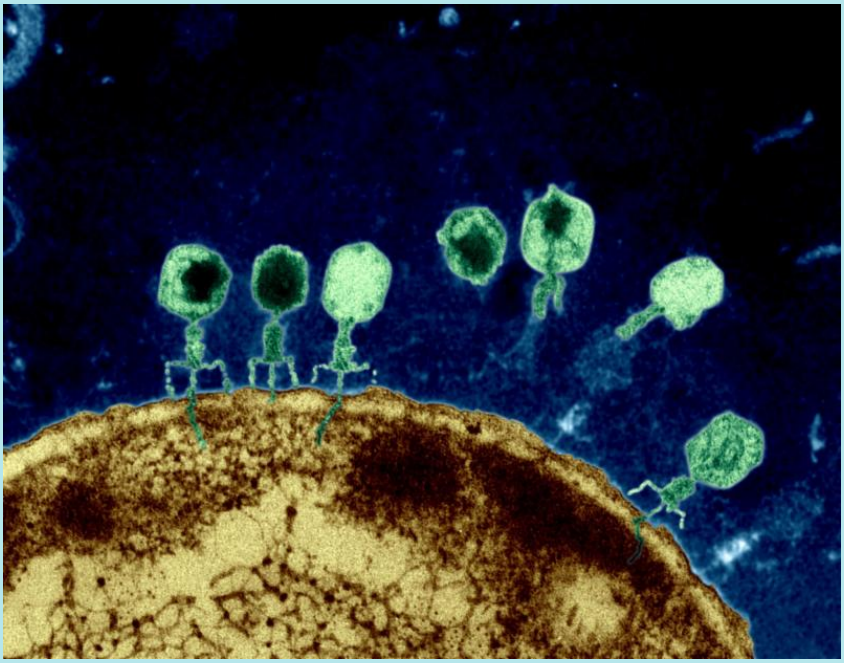
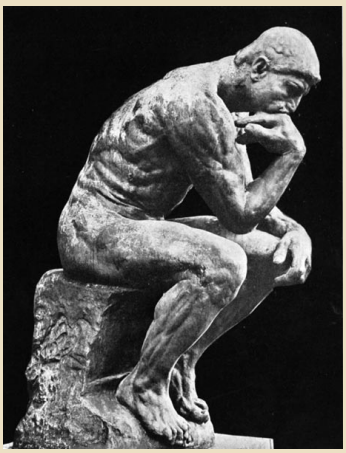
poorly documented. The treatment never caught on in Western Europe or the United States due to the discovery of antibiotics.



Mulitple bacteriophases docking on a bacterium and injecting their DNA into the cell.

It sounds strange; who wants to ingest a cocktail teeming with viruses or apply a topical cream of viruses to an infection? However, bacteriophages are species-specific and won't infect human cells or target any bacterium at random. This eliminates the possibility of killing off natural microflora that leads to opportunistic infections such as *Clostridium difficile*. By nature, they are the only bactericidal therapy that would multiply in the human body before being excreted. Phages gain another advantage since they are able to replicate at the site of infection where treatment is necessary, and can penetrate biofilms. They are also an option for people who are allergic to certain

Think about it...



* If we have finger tips why not toe tips, especially since we tiptoe around?

* Why do Kamikaze pilots wear helmets?

* Whose idea was it to put an 'S' in the word 'lisp'?

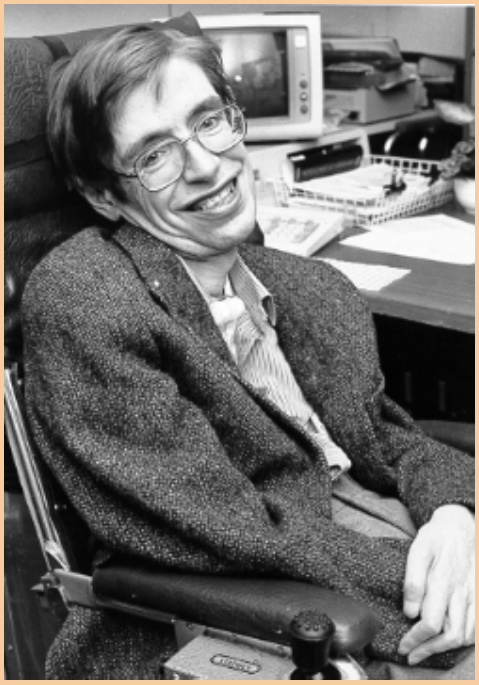
* Why do doctors leave the room while you change? They're going to see you naked anyway...

* Do the Alphabet song and Twinkle, Twinkle Little Star have the same tune?

* Why did you just try singing the two songs above?

* * *

Wisdom to Ponder...



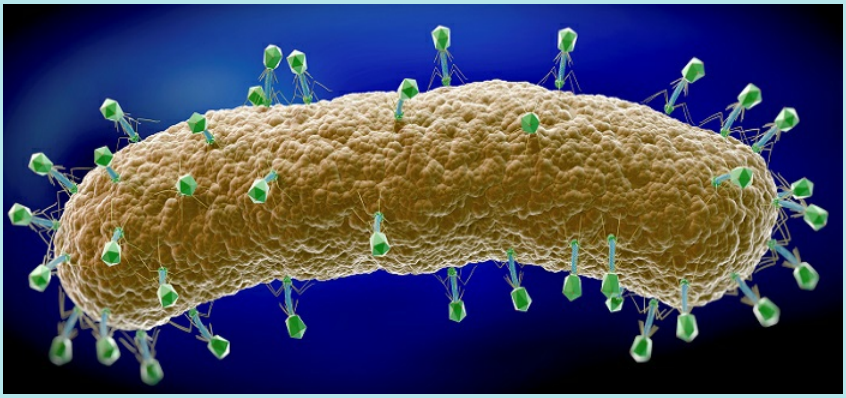
Stephen Hawking
1942 ~ 2018

English theoretical physicist, cosmologist, author, and Director of Theoretical Cosmology at the University of Cambridge

are also an option for people who are allergic to certain antibiotics. Phage strains can be applied in a variety of ways: intravenously, orally, topically, aerosolized, or even integrated into sutures.

Since the discovery of phage therapy, a number of facilities in Eastern Europe have made progress in treatments. The George Eliava Institute of Bacteriophages, Microbiology and Virology (EIBMV) in Tbilisi, Georgia offers options for patients with CRE, ESBL, MRSA, and other infections. The Hirszfeld Institute of Immunology and Experimental Therapy (HIEET) in Wrocław, Poland have been manufacturing phage treatments against *Staphylococcus, Enterococcus, Escherichia, Klebsiella, Serratia,* and *Proteus* infections.

Today, the option of phage therapy has piqued interest in the United States as antibiotic-resistant bacteria become more widespread. In 2016, intravenous dosage of phage cured a multidrug-resistant *Acinetobacter baumannii* infection in a 69-year-old psychiatry professor from UC San Diego. Currently, there are treatments being developed for multidrug-resistant *Pseudomonas aeruginosa* infections found in cystic fibrosis patients. Proposed therapies are a combination of phages and antibiotics.



While phage therapy represents a new frontier in molecular biology and medicine, there are some pros and cons to their use. Only lysogenic viruses may be used, which could lead to the release of endotoxins by certain bacteria during bacterial lysis. A high-purity phage must be ensured to eliminate the possibility of contaminants or endotoxins in the treatment administered. Even though the phages aren't infecting human cells, the body may produce an immune

"Look up at the stars and not down at your feet. Try to make sense of what you see, and wonder about what makes the universe exist. Be curious."

"However difficult life may seem, there is always something you can do and succeed at."

"Life would be tragic if it weren't funny."

"Intelligence is the ability to adapt to change."

"Work gives you meaning and purpose, and life is empty without it."

"I believe alien life is quite common in the universe, although intelligent life is less so. Some say it has yet to appear on planet Earth."

"We are all now connected by the Internet, like neurons in a giant brain."

"I am just a child who has never grown up. I still keep asking these 'how' and 'why' questions. Occasionally, I find an answer."

"Keeping an active mind has been vital to my survival, as has been maintaining a sense of humor."

"I think the human race doesn't have a future if it doesn't go into space."

"I'm not afraid of death, but I'm in no hurry to die. I have so much I want to do first."

response, a problem that has not been widely researched. Additionally, the target bacteria may establish resistance to the phage administered. To counter this, another phage can be given or a phage cocktail used. "Phage typing" must first be performed to determine what bacteriophages can be used effectively against the target bacteria. However, as biologically active agents, viruses are capable of

evolving alongside bacteria, can be manipulated or attenuated in the laboratory, and take far less time to culture or isolate from the environment than to synthesize new antibiotics.

It will take time for the concept of phage therapy to be accepted in the United States. Consequently, there is far more research needed on the pharmacokinetics and toxicology of bacteriophages. Such a unique medical treatment may also require a potential reevaluation of the current medical device regulations. But just as "not all bacteria are bad," not all viruses do us harm; so phages remain a potentially viable option in our race against antibiotic-resistant pathogens.

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Ludwik Hirszfeld Institute of Immunology and Experimental Therapy https://www.iitd.pan.wroc.pl/en/OTF/ZasadyTerapiiFagowej.html

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https://www.technologyreview.com/s/409905/using-viruses-to-kill-bacteria/

By Sarah Hepler
R&D Microbiologist
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Optical oddities...

* * *

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~ Benjamin Franklin ~

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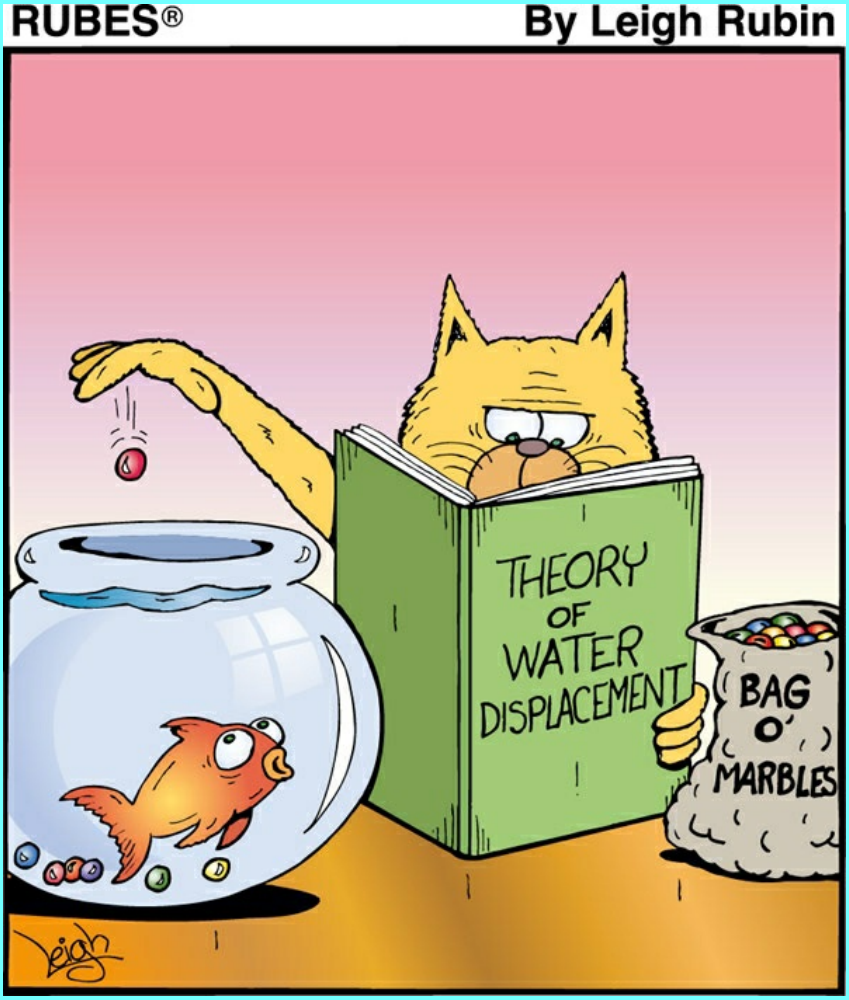

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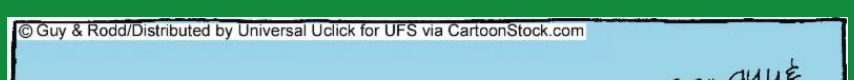

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* I got a job at a bakery because I kneaded dough.

* I'm reading a book about anti-gravity. I just can't put it down.

* I did a theatrical performance about puns. It was a play on words.

* I didn't like my beard at first. Then it grew on me.

* Did you hear about the cross-eyed teacher who lost her job because she couldn't control her pupils?

# # #