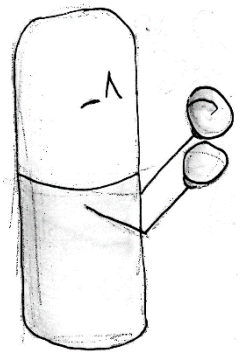
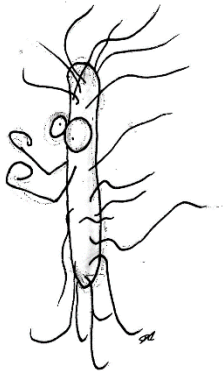


Adapt to Survive: An Antibiotic Story



Overview

In this very simple game, you are a bacterium. You have caused food poisoning in a patient who is being treated with antibiotics. The aim of the game is to survive five rounds of treatment…

Learning Objectives

By the end of this game you will:

1. Recall the mode of action of four antibiotics
2. Describe how different bacterial physiologies affect their resistance to antibiotics
3. Communicate how antibiotic treatment can drive resistance
4. Evaluate why different antibiotics are used in clinical settings

Please complete these questions before playing

What you need

In order to play this game, you will need:

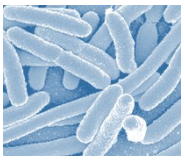
1. The *Antibiotics to Action!* Spreadsheet. (This includes the rules and the phenotype card to record your adaptations)
2. A random number (1-6) generator (e.g. https://pickerwheel.com/tools/random-number-generator/) or D6 die

How the game works

Select your bacterium

To begin the game you must select your starting organism. You have two choices, each has different sensitivities (1-3) to the antibiotics used.

Table 1. The bacteria species that can be selected for this game.

Identifier	Gram-stain	Effect of antibiotic
 *Escherichia coli*[1]	Negative	Ampicillin -25% Chloramphenicol -50% Streptomycin -50% Penicillin 0%
 *Bacillus cereus*[2]	Positive	Ampicillin -50% Chloramphenicol 0%* Streptomycin -25% Penicillin -50%

[1]https://www.nationalgeographic.org/encyclopedia/escherichia-coli-e-coli/; [2]https://en.wikipedia.org/wiki/Bacillus_cereus
*Still affected by bacteriostatic action

Game structure

Once you have selected your bacterium (see below), the rounds progress in the same order: (1) *Growth,* (2) *Adaptation,* (3) *Treatment,* (4) *Resolution*. As the rounds progress the players increase the number of bacterial cells, gain (or lose) useful traits, and respond to the treatment administered.

Growth phase

In this part of the round your bacterial numbers double (unless treated with a bacteriostatic antibiotic), to a maximum of 100. For example, each bacterium begins with a starting inoculum of 25 cells and the carrying capacity (maximum bacterial load) of the system is 100. In round 1, each player doubles their number of bacteria to 50 and follows the remaining phases accordingly. In round 2, the player once again doubles the number of cells, unless a bacteriostatic antibiotic has been used in which case all players with sensitive bacteria cannot grow.

Adaptation phase

In this phase, player roll a dice (D6) or equivalent, and their bacteria gain or lose that specific ability. Any changes in a bacterium's phenotype should be noted on the player's *Phenotype card.*

Table 2. Potential phenotypic changes occurring in the *Adaption phase*

Number	Action	Phenotypic response	Ref
1	Mutation of ribosome	Resistance to Chloramphenicol	(4)
2	Gain plasmid encoding AACs	Resistance to Aminoglycosides	(5)
3	Synonymous mutation	No change to phenotype	
4	Gain plasmid encoding bla_{PC1} or $bla_{CTX\text{-}M}$ enzymes	Resistance to penicillin or all β-lactam antibiotics*	(6)
5	Lose all plasmids	All plasmid-encoded resistance is lost	
6	Establish a biofilm	Resistant to all antibiotics and immune response for this round	(7)

** On the first roll of this action, a Gram positive bacterium gains resistance to penicillin only. If a Gram-negative bacterium rolls this action, or it is the second time this action is rolled for a Gram-positive bacterium, then the bacteria gain resistance to all β-lactam antibiotics*

Treatment phase

Here, your tutor will roll a die (D6) to subject all the bacteria to one of four antibiotics. Each antibiotic affects the types of bacteria differently, and the player must remove the specified cell number from their total.

Table 3. Antibiotics available for treatment phase and the consequences of administration

Number	Antibiotic	Reduction		Other
		Negative	Positive	
1	Ampicillin	-25%	-50%	Bacteriolytic
2,3	Chloramphenicol	-50%	0%	Bactericidal
4,5	Streptomycin	-50%	-25%	Bacteriostatic
6	Penicillin	0%	-50%	Bacteriolytic

Resolution phase

Once the treatment has been administered, it is time to see how this affects your bacteria. If your bacteria is sensitive to the treatment then you must remove the % of cells given in **Table 3.** If your cell number drops below the *Immune Threshold* then you have been eliminated by the immune system. If you are above the threshold, then you progress to the next round.

“Winning” the game

The game ends after 5 rounds. At this point, you will have either been eliminated or survived, and hopefully learnt something! You will be asked to answer questions after the game.

References

1. Frenzel E, Kranzler M, Stark TD, Hofmann T, Ehling-Schulz M. The Endospore-forming pathogen *Bacillus cereus* exploits a small colony variant-based diversification strategy in response to aminoglycoside exposure. *mBio*. 2015;6(6):e01172-15.

2. Fiedler G, Schneider C, Igbinosa EO, Kabisch J, Brinks E, Becker B, *et al.* Antibiotics resistance and toxin profiles of *Bacillus cereus*-group isolates from fresh vegetables from German retail markets. *BMC Microbiology*. 2019;19(1):250.

3. Schroeder CM, Zhao C, DebRoy C, Torcolini J, Zhao S, White DG, et al. Antimicrobial resistance of *Escherichia coli* O157 isolated from humans, cattle, swine, and food. *Applied and Environmental Microbiology*. 2002;68(2):576-81.

4. Baughman GA, Fahnestock SR. Chloramphenicol resistance mutation in *Escherichia coli* which maps in the major ribosomal protein gene cluster. *Journal of Bacteriology*. 1979;137(3):1315-23.

5. Garneau-Tsodikova S, Labby KJ. Mechanisms of resistance to aminoglycoside antibiotics: overview and perspectives. *MedChemComm*. 2016;7(1):11-27.

6. Bush K. Past and Present Perspectives on β-Lactamases. *Antimicrobial Agents and Chemotherapy*. 2018;62(10):e01076-18.

7. Donlan RM, Costerton JW. Biofilms: Survival mechanisms of clinically relevant microorganisms. *Clinical Microbiology Reviews*. 2002;15(2):167-93.