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WEB PAPER

A game for teaching antimicrobial mechanisms of action

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Abstract

Background: Alternative teaching tools have proved to enhance students' interest and knowledge skills.

Aim: To integrate basic Bacteriology with mechanisms of action of antimicrobial agents.

Methods: The board has 121 squares, including squares with question marks and antimicrobial agents. Each student receives a card with a clinical case, identification of the bacterium and its resistance to antimicrobials. The student rolls a dice and moves the corresponding number of squares. The game depends on the dice values rolled, the bacterial resistance profile, and the questions the student has to answer each time he/she lands on a question mark. Previously, the students were given a lecture about the subject. On the day of the game, students answered a pre-test and a post-test. The paired *t*-test was used for the statistical analysis.

Results: The game was applied to 78 students of the Medicine and Pharmacy undergraduate courses of the Universidade Federal do Rio Grande do Sul, Brazil. There was an increase in the number of right answers and a decrease in the number of unknown answers. There were no significant differences between the courses.

Conclusion: The game could be applied to other undergraduate courses in the field of Health Sciences.

Introduction

One of the main problems in medical teaching is the huge quantity of knowledge students have to acquire in a limited amount of time. Medical curricula have been modified and alternative ways of teaching are being applied in order to overcome this problem and to achieve long-lasting global knowledge, which is required for a good professional practice. Among the alternative ways of teaching there are web-based tools (Lin et al. 2005), role playing games (Fernando et al. 2007), card games (Colombo et al. 1998; Da Rosa et al. 2006) and board games (Scroferneker et al. 1995; Da Rosa et al. 2003; Eckert et al. 2004; Girardi et al. 2006; Beylefeld & Struwig 2007). Bochennek et al. (2007) reviewed card and board games applied to medical teaching and found that these games cover several medical topics, even though many of these games deal with the immune system. Although some authors have reported difficulties associated with the use of games, such as low interest in obtaining deep knowledge about the contents (Lin et al. 2005), and influence of the students' prior experiences (Nestel & Tierney 2007), in general, alternative teaching tools have proved to enhance students' interest and knowledge of the formal contents and interpretation skills.

Although antimicrobial agents and microbial resistance are among the most important medical issues nowadays, medical students have adopted an attitude of indifference towards these topics. In many undergraduate courses, students are first introduced to antimicrobial agents in Microbiology classes, and they have difficulty in understanding that the mechanisms of action of antimicrobial agents and microbial resistance are correlated with Basic Microbiology aspects, such as bacterial cytology. Therefore, the purpose of the proposed game is to integrate these aspects of the microbiological knowledge. The game is intended to be a supplemental tool for the formal learning of the subject.

Practice points

- Alternative teaching tools have proved to enhance students' interest and knowledge of the formal contents and interpretation skills.
- Students have difficulty in correlating Basic Microbiology (i.e. bacterial cytology) with applied aspects of mechanisms of action of antimicrobial agents and microbial resistance.
- The game could be applied to any undergraduate course in the field of Healthy Sciences, and is intended to be applied to students that are at the beginning of their courses.

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Methods

About the game

The game consists of an illustrated board (47.62 × 63.49 cm) (Figure 1) and is played with dice and pawns. The background represents structures of the bacterial cell which can be used as targets for antibiotics. At the center of the game board, there is a path with a total of 119 squares, in addition to the squares in the beginning and the end (cure) along which the players are supposed to move their pawns. This path contains 60 numbered squares, 22 squares with names of antibiotics and 36 squares with a question mark. There is a square marked as mutation (square 11).

Each player receives a red card containing a clinical case, the microorganism which was isolated and its susceptibility profile to the antibiotics that will be mentioned in the game (Figure 2). All information contained in this card is fictional. In this red card, there is also information concerning the susceptibility change in case of mutation of the microorganism. The players roll the dice to decide who starts the game. The player with the highest number is first. Each player moves his or her pawn according to the number rolled. Whenever a player lands on a square with the name of an antibiotic on it, he/she has to check his/her red card in order to decide whether the bacterium is susceptible, resistant, or has intermediate resistance to the corresponding antibiotic. If the bacterium is susceptible, the player moves ahead three squares; if it is resistant, the player moves back one square; and if it has intermediate resistance, the player remains on the same square.

Whenever the player lands on a square with a question mark, the player immediately on his/her left must take a yellow card from the top of a stack, and read the question that is written on it (Figure 3). All questions are based on textbooks about the subject. The player who lands on the square with the question mark can try to answer the question or can pass his/her turn. If he/she passes his/her turn, another player can try to answer the question, except the one holding the yellow card. After an answer is obtained, the player with the yellow card should read the right answer to the question, which is also written on the yellow card, and everybody decides whether the given answer is correct or not. If it is correct, the player who gave the answer moves ahead six squares; otherwise, he/she moves back two squares. The yellow card is then placed at the bottom of the yellow card stack.

Whenever a player lands on the mutation square, he/she has to return to the initial square, and should proceed as explained above, except that he/she must use the antibiotic susceptibility profile corresponding to the mutation the bacterium suffered. This new susceptibility profile is written on the red card the player receives at the beginning of the game. The game is over when a player gets to the last square on the board (cure).

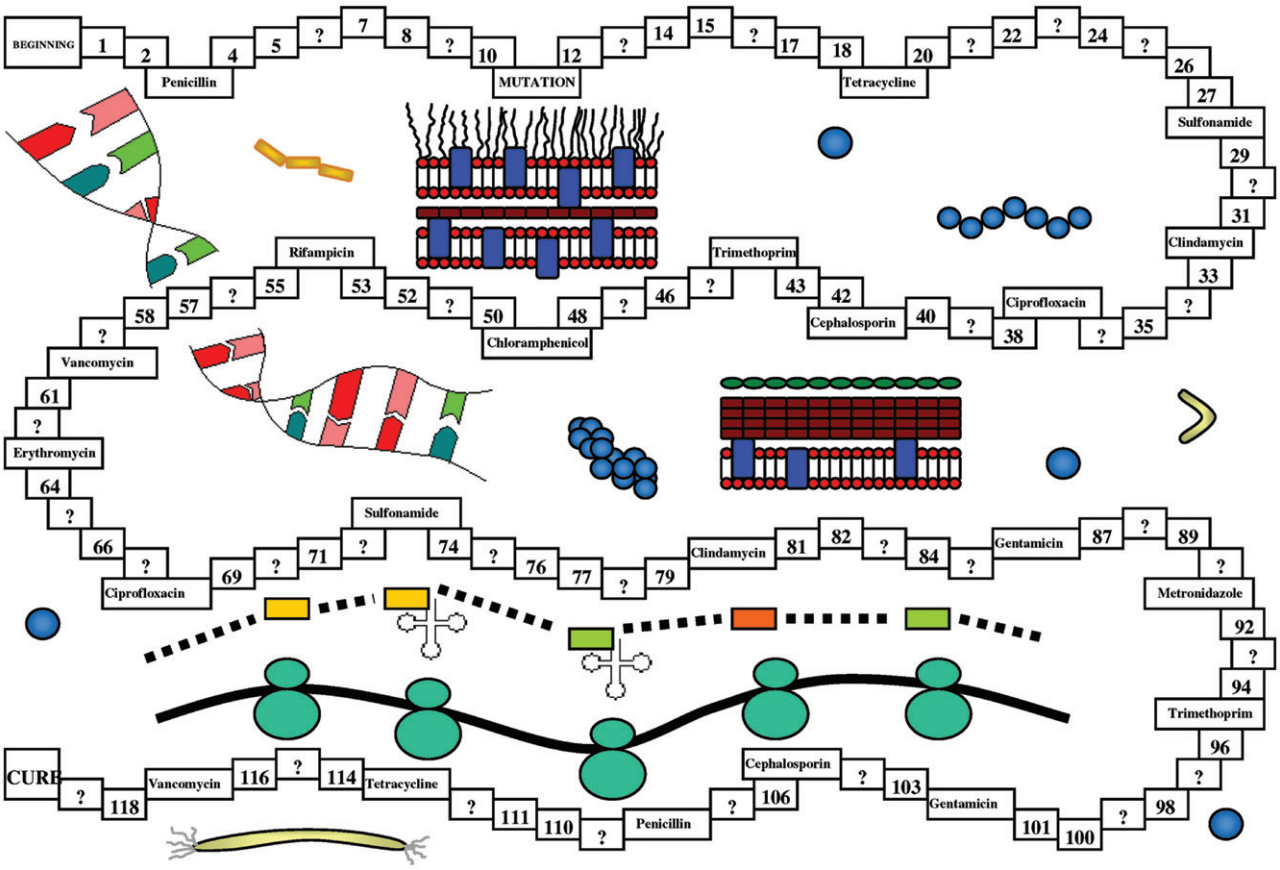

Figure 1. Game board.

Four-year old child is admitted to the ER with diarrhea and fever. Coproculture was performed.
Etiologic agent: *Salmonella* sp. (gram-negative rod)

Antibiogram:

Penicillin	R
Cephalosporin	I
Gentamicin	S
Ciprofloxacin	I
Tetracycline	S
Erythromycin	S
Chloramphenicol	S
Clindamycin	S
Metronidazole	I
Sulfonamide	S
Trimethoprim	S
Vancomycin	R
Rifampicin	S

Mutation: Tetracycline R

Child presents cough with yellow expectoration and fever. Sputum culture was performed.
Etiologic agent: *Haemophilus influenzae* (gram-negative rod)

Antibiogram:

Penicillin	I
Cephalosporin	S
Gentamicin	S
Ciprofloxacin	S
Tetracycline	R
Erythromycin	I
Chloramphenicol	S
Clindamycin	S
Metronidazole	I
Sulfonamide	S
Trimethoprim	S
Vancomycin	R
Rifampicin	S

Mutation: Ciprofloxacin R

Child was admitted to the ER with earache for two days. Ear swab culture was performed.
Etiologic agent: *Streptococcus pneumoniae* (gram-positive cocci)

Antibiogram:

Penicillin	S
Cephalosporin	S
Gentamicin	S
Ciprofloxacin	I
Tetracycline	R
Erythromycin	R
Chloramphenicol	S
Clindamycin	I
Metronidazole	S
Sulfonamide	S
Trimethoprim	S
Vancomycin	S
Rifampicin	I

Mutation: Sulfonamide R

40 year-old woman has pain on urinating. Urine culture was performed.
Etiologic agent: *Escherichia coli* (gram-negative rod).

Antibiogram:

Penicillin	S
Cephalosporin	S
Gentamicin	S
Ciprofloxacin	S
Tetracycline	R
Erythromycin	S
Chloramphenicol	S
Clindamycin	S
Metronidazole	S
Sulfonamide	I
Trimethoprim	I
Vancomycin	R
Rifampicin	I

Mutation: Penicillin R

Figure 2. Red cards containing a clinical case, the microorganism that was isolated and its susceptibility profile to the antibiotics.

Woman presents disseminated infection associated with the use of catheters. Blood culture was performed.
Etiologic agent: *Staphylococcus aureus* (gram-positive cocci)

Antibiogram:

Penicillin	R
Cephalosporin	R
Gentamicin	S
Ciprofloxacin	I
Tetracycline	I
Erythromycin	S
Chloramphenicol	S
Clindamycin	S
Metronidazole	S
Sulfonamide	S
Trimethoprim	I
Vancomycin	S
Rifampicin	S

Mutation: Vancomycin R

25 years-old man has urethral secretion with pain on urinating. The secretion was collected and examined under the microscope.
Etiologic agent: *Neisseria gonorrhoeae* (gram-negative cocci)

Antibiogram:

Penicillin	S
Cephalosporin	S
Gentamicin	R
Ciprofloxacin	S
Tetracycline	I
Erythromycin	S
Chloramphenicol	S
Clindamycin	I
Metronidazole	I
Sulfonamide	S
Trimethoprim	S
Vancomycin	R
Rifampicin	S

Mutation: Penicillin R

70 years-old woman presents edema on her right thigh with a blister containing a red fluid. The fluid was aspirated.
Etiologic agent: *Clostridium perfringens* (gram-positive rod)

Antibiogram:

Penicillin	S
Cephalosporin	S
Gentamicin	I
Ciprofloxacin	R
Tetracycline	S
Erythromycin	I
Chloramphenicol	R
Clindamycin	S
Metronidazole	S
Sulfonamide	S
Trimethoprim	S
Vancomycin	S
Rifampicin	I

Mutation: Clindamycin R

43 years-old man presents cough with sputum, chest pain and fever. Physician requested X ray, blood and sputum culture.
Etiologic agent: *Streptococcus pneumoniae* (gram-positive cocci)

Antibiogram:

Penicillin	S
Cephalosporin	S
Gentamicin	S
Ciprofloxacin	R
Tetracycline	S
Erythromycin	R
Chloramphenicol	S
Clindamycin	S
Metronidazole	S
Sulfonamide	I
Trimethoprim	I
Vancomycin	I
Rifampicin	S

Mutation: Gentamicin R

Figure 2. Continued.

7 year-old child presents prostration, anorexia, vomiting and sleepiness. Lumbar puncture was performed and empirical antibiotic treatment was administered.
Etiologic agent: *Neisseria meningitidis* (gram-negative cocci)

Antibiogram:

Penicillin	S
Cephalosporin	S
Gentamicin	S
Ciprofloxacin	S
Tetracycline	R
Erythromycin	S
Chloramphenicol	S
Clindamycin	I
Metronidazole	I
Sulfonamide	S
Trimethoprim	S
Vancomycin	R
Rifampicin	I

Mutation: Erythromycin R

48 year-old man, after an intestinal operation, presents fever and a purulent secretion in the surgical scar. Culture of the secretion was performed.
Etiologic agent: *Enterococcus faecalis* (gram-positive cocci)

Antibiogram:

Penicillin	I
Cephalosporin	S
Gentamicin	S
Ciprofloxacin	I
Tetracycline	R
Erythromycin	S
Chloramphenicol	I
Clindamycin	S
Metronidazole	S
Sulfonamide	S
Trimethoprim	S
Vancomycin	R
Rifampicin	S

Mutation: Trimethoprim R

Woman, in a coma for two months due to a car accident, presents disseminated infection. Blood culture was performed.
Etiologic agent: *Pseudomonas aeruginosa* (gram-negative rod)

Antibiogram:

Penicillin	S
Cephalosporin	S
Gentamicin	S
Ciprofloxacin	S
Tetracycline	S
Erythromycin	S
Chloramphenicol	I
Clindamycin	S
Metronidazole	R
Sulfonamide	I
Trimethoprim	I
Vancomycin	R
Rifampicin	S

Mutation: Tetracycline R

32 years-old man reports high fever and pain in his left leg, which presents a reddish, swollen and hot lesion. Material was aspirated from the lesion.
Etiologic agent: *Streptococcus pyogenes* group A (gram-positive cocci)

Antibiogram:

Penicillin	S
Cephalosporin	S
Gentamicin	R
Ciprofloxacin	S
Tetracycline	R
Erythromycin	I
Chloramphenicol	S
Clindamycin	I
Metronidazole	I
Sulfonamide	S
Trimethoprim	S
Vancomycin	S
Rifampicin	S

Mutation: Cephalosporin R

Figure 2. Continued.

QUESTION: Why are gram negative bacteria usually more resistant to antibiotics than gram positive ones? ANSWER: Due to their external membrane, which hinders the entry of antibiotics.	QUESTION: What is the mechanism of action of penicillin? ANSWER: Binding to penicillin-binding proteins (PBPs), which are enzymes that act in the synthesis of bacterial cell wall, and activation of autolysins.	QUESTION: Why are bacteria which are cell-wall deficient, such as the mycoplasmas, not susceptible to the action of the β-lactams? ANSWER: Because the β-lactams act by inhibiting cell wall synthesis.	QUESTION: What are R plasmids (R factors)? ANSWER: Plasmids that possess several genes coding for resistance to antibiotics and other chemical agents. They confer a multiresistant phenotype to the bacteria.	QUESTION: What is the mechanism of action of cephalosporins? ANSWER: Binding to penicillin-binding proteins (PBPs), which are enzymes that act in the synthesis of bacterial cell wall, and activation of autolysins.
QUESTION: Can an antibiotic induce bacterial resistance to other antibiotics that have not been prescribed to the patient? Justify your answer. ANSWER: Yes, if it has a sufficiently similar chemical structure or if it acts at the same site.	QUESTION: What is the mechanism of action of vancomycin? ANSWER: Binding to cell wall precursors (peptidioglycan precursors), preventing their use by penicillin-binding proteins (PBPs) and inhibiting the cell wall synthesis.	QUESTION: What is the main clinical use of vancomycin? ANSWER: Treatment of infections caused by multiresistant gram positive bacteria, including the ones caused by methicillin-resistant *Staphylococcus aureus* (MRSA).	QUESTION: Why is vancomycin not efficient in the treatment of infections caused by gram negative bacteria? ANSWER: The molecule is too large for crossing the external membrane of these bacteria.	QUESTION: Why should vancomycin not be immediately prescribed in the case of *Staphylococcus aureus* infection? ANSWER: Vancomycin should only be prescribed in the case of infection with methicillin-resistant *Staphylococcus aureus* (MRSA) in order to avoid the development and dissemination of resistance to this antibiotic.
QUESTION: Why is polymyxin limited to topical applications? ANSWER: Because it is too toxic to the eukaryotic cell, as it acts upon the cytoplasmic membrane, which does not possess many differences in relation to the prokaryotic cell.	QUESTION: What does selective toxicity of an antibiotic mean? ANSWER: It means that an antibiotic is more toxic to the bacterium that is causing the infection than to the eukaryotic cell.	QUESTION: What is the mechanism of action of polymyxin? ANSWER: It is a cationic polypeptide that acts as a detergent, disrupting the cytoplasmic membrane of the cells.	QUESTION: What is the mechanism of action of metronidazole (nitroimidazole)? ANSWER: After entry into the microbial cell, the nitro group is reduced by a nitroreductase in the cytoplasm, generating cytotoxic intermediate compounds that cause DNA disruption.	QUESTION: What is the clinical importance of the isolation of *Pseudomonas aeruginosa* as the agent of an infection? ANSWER: *Pseudomonas aeruginosa* is multiresistant to antibiotics.
QUESTION: Why is the spectrum of activity of nitroimidazoles (ex: metronidazole) restricted to the bacteria and to some protozoa that grow under anaerobic conditions? ANSWER: Because only these organisms are capable of transforming the antibiotic into its active form.	QUESTION: Is it possible to have cross resistance between antibiotics and other chemical agents for the control of microbial growth? Justify your answer. ANSWER: Yes, when they possess identical target sites. The modification of the target site of a chemical agent can make the bacteria resistant to an antibiotic that acts at the same site.	QUESTION: Why are aminoglycosides inefficient against anaerobic bacteria? ANSWER: Because the entry of the antibiotic into the bacterial cell depends on oxidative phosphorylation. The pathogenic bacteria ferment when they are under anaerobic conditions.	QUESTION: What is the mechanism of action of ciprofloxacin (fluoroquinolone)? ANSWER: Its main target is the bacterial DNA gyrase, the enzyme that is responsible by DNA supercoiling, inhibiting DNA replication.	QUESTION: What is the principle of the selective toxicity of penicillin? ANSWER: The eukaryotic cell does not possess cell wall.
QUESTION: What is the principle of the selective toxicity of ciprofloxacin (fluoroquinolone)? ANSWER: The bacterial DNA gyrase is inhibited by a lower concentration of the antibiotic than the eukaryotic cell topoisomerases.	QUESTION: What is the principle of the selective toxicity of vancomycin? ANSWER: The eukaryotic cell does not possess cell wall.	QUESTION: What is the principle of the selective toxicity of metronidazole (nitroimidazole)? ANSWER: The eukaryotic cell is not capable of transforming the antibiotic into its active form.	QUESTION: What is the mechanism of action of sulfonamides? ANSWER: Inhibition of the synthesis of folic acid, which acts in the synthesis of aminoacids, purines and pyrimidines. Therefore, they inhibit the synthesis of protein and DNA.	QUESTION: What is the principle of the selective toxicity of sulfonamides? ANSWER: Mammalian cells do not synthesize folic acid, and have to obtain it through nutrition.
QUESTION: Is clindamycin (lincosamide) bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bacteriostatic because the binding to the bacterial ribosome is reversible.	QUESTION: What is the principle of the selective toxicity of erythromycin (macrolide)? ANSWER: It has less effect on eukaryotic ribosomes.	QUESTION: What is the principle of the selective toxicity of clindamycin (lincosamide)? ANSWER: It has less effect on eukaryotic ribosomes.	QUESTION: Is erythromycin bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bacteriostatic because the binding to the bacterial ribosome is reversible.	QUESTION: What is the mechanism of action of clindamycin (lincosamide)? ANSWER: Reversible binding to the bacterial ribosome, inhibiting the synthesis of proteins.
QUESTION: What is the mechanism of action of trimethoprim? ANSWER: Inhibition of the enzyme that reduces the folic acid, so that it can act as a coenzyme in the synthesis of aminoacids, purines and pyrimidines. Therefore, it inhibits the synthesis of protein and DNA.	QUESTION: What is the principle of the selective toxicity of trimethoprim? ANSWER: It is less active against the enzyme which reduces the folic acid in mammals.	QUESTION: Why do sulfonamides and trimethoprim have a synergistic effect when used together? ANSWER: Because they inhibit two different enzymes in the folic acid synthesis pathway, therefore, their action when used together makes inhibition more efficient.	QUESTION: What is the mechanism of action of rifampicin (rifamycin)? ANSWER: It makes a stable complex with RNA polymerase, blocking the synthesis of mRNA.	QUESTION: What is the principle of the selective toxicity of rifampicin (rifamycin)? ANSWER: The mammal RNA polymerase is less sensitive to the drug.

Figure 3. Yellow cards with questions concerning the mechanism of action of antimicrobial agents and microbial resistance.

QUESTION: What is the mechanism of action of aminoglycosides? ANSWER: Irreversible binding to the bacterial ribosome, inhibiting the synthesis of proteins.	QUESTION: Is penicillin bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bactericidal because it inhibits cell wall synthesis, causing lysis of the new cells due to the lack of cell wall. Besides, it activates the autolysins, which disintegrate the existing cell walls.	QUESTION: Is vancomycin bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bactericidal because it inhibits cell wall synthesis, causing lysis of the new cells due to the lack of cell wall.	QUESTION: Is polymyxin bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bactericidal because it disrupts the cytoplasmic membrane, causing leakage of cellular content.	QUESTION: Is metronidazole bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bactericidal because it causes disruption of the DNA molecules.
QUESTION: Is ciprofloxacin (fluoroquinolone) bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bactericidal because it inhibits DNA replication and repair.	QUESTION: Can there be cross resistance among antibiotics? Justify your answer. ANSWER: Yes, when the antibiotics have identical targets or chemical structures.	QUESTION: What is methicillin-resistant *Staphylococcus aureus* (MRSA)? ANSWER: They are strains of *Staphylococcus aureus* that possess penicillin-binding proteins (PBPs) with low affinity for β-lactams. They do not respond well to the treatment with any β-lactam antibiotic.	QUESTION: What is the importance of knowing if an antibiotic is bactericidal or bacteriostatic? ANSWER: Bactericidal antibiotics effectively kill the bacteria, while bacteriostatic ones only inhibit their multiplication. Therefore, the bacteriostatic agents count on the immunological system of the patient for the elimination of infection. If the patient is immunologically weak, the bacteriostatic antibiotic may not have the desired effect.	QUESTION: Are aminoglycosides bactericidal or bacteriostatic? Justify your answer. ANSWER: They are bactericidal, because ribosomal binding is irreversible.
QUESTION: Why are aminoglycosides poorly efficient against anaerobic bacteria? ANSWER: Because their mechanism of entry into the bacterial cell depends on oxidative phosphorylation. The pathogenic bacteria perform fermentation when they are under anaerobic conditions.	QUESTION: What is the name of the proteins that are present in the outer membrane of gram-negative bacteria and function as entry channels for some antibiotics? ANSWER: Porines.	QUESTION: What is the principle of the selective toxicity of aminoglycosides? ANSWER: Eukaryotic ribosomes are resistant to these antibiotics. Besides, aminoglycosides are not transported into eukaryotic cells.	QUESTION: What is the most common type of resistance to β-lactam antibiotics? ANSWER: Production of β-lactamases, which cleave the β-lactam ring.	QUESTION: What is the mechanism of action of tetracycline? ANSWER: Reversible binding to the bacterial ribosome, inhibiting the synthesis of proteins.
QUESTION: Is tetracycline bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bacteriostatic because the binding to the bacterial ribosome is reversible.	QUESTION: What is the principle of the selective toxicity of tetracycline? ANSWER: The absorption of the drug is higher in bacterial cells than in eukaryotic ones. Bacterial cells possess an active transportation system for tetracycline, accumulating it in their interior.	QUESTION: Why is the resistance to tetracycline so disseminated? ANSWER: Because there was excessive prescription of this antibiotic in the past.	QUESTION: What is the mechanism of action of chloramphenicol? ANSWER: Reversible binding to the bacterial ribosome, inhibiting the synthesis of proteins.	QUESTION: Is chloramphenicol bactericidal or bacteriostatic? Justify your answer. ANSWER: It is bacteriostatic because the binding to the bacterial ribosome is reversible.
QUESTION: What is the principle of the selective toxicity of chloramphenicol? ANSWER: It has less effect on eukaryotic ribosomes.	QUESTION: What is the function of the administration of β-lactamase inhibitors together with β-lactamic antibiotics? ANSWER: To eliminate the bacterial resistance caused by the production of these enzymes.	QUESTION: What is the mechanism of action of erythromycin (macrolide)? ANSWER: Reversible binding to the bacterial ribosome, inhibiting the synthesis of proteins.		

Figure 3. Continued.

Evaluation of the game effectiveness

The game was separately applied to students of Medicine and Pharmacy undergraduate courses from Universidade Federal do Rio Grande do Sul. These two cohorts were chosen because they represent different courses in the field of Health Sciences, and because they are taught the same basic information about antimicrobial agents. One week before the game, students attended a lecture concerning the subject of the game, and a bibliography was indicated. Attendance to the lecture and reading of the bibliography were not mandatory, but strongly advised.

On the day of the game, students were divided into groups of up to five players, and received a randomly chosen password, which was used to identify each student. Students were asked to complete a test (pre-test) so that their previous knowledge could be checked. This pre-test contained 10 statements concerning the subject of the game, and the students were asked to mark if it was true, false or if the answer was unknown (Table 1). Students were asked to identify their pre-tests using their password in order to compare the results with another test (post-test) to be applied at the end of the game. This pre-test was considered the control group in the statistical analysis since it represented the knowledge a group of students should have after attending the lecture and reading the recommended bibliography. After completing the pre-test, the students read the rules of the game, which were available on a sheet of paper placed next to the game board. Each group of students had its own game board and rule sheets. After playing the game, the students

Table 1. Pre-test and post-test.

Mark if the statement is true (T), false (F) or if you do not know the answer (?):	T	F	?
1. Gram-negative bacteria are normally more resistant to antimicrobial agents than gram-positive ones due to the presence of an outer membrane, which hinders the entry of antibiotics.			
2. Antimicrobial agents do not induce bacterial resistance to other antibiotics that have not been prescribed to the patient.			
3. Vancomycin is prescribed for the treatment of infections caused by multiresistant gram-positive bacteria, including the ones caused by methicillin-resistant *Staphylococcus aureus* (MRSA).			
4. Sulfonamides do not act upon mammal cells due to the fact that these cells do not synthesize folic acid, which must be provided through feeding.			
5. The prescription of bactericidal or bacteriostatic antibiotics achieves the same results: Clearance of infection. Thus, the information concerning the bactericidal or bacteriostatic status of the antimicrobial agent is irrelevant in clinical practice.			
6. The most common type of resistance to aminoglycosides is the production of β-lactamases.			
7. The isolation of *Pseudomonas aeruginosa* as cause of sepsis is worrying because this bacterium is naturally resistant to several antimicrobial agents.			
8. Bacterial resistance to tetracycline is disseminated probably due to the excessive prescription of this agent in the past.			
9. The joint use of sulfonamides and trimethoprim is not advisable because these agents compete for the same target in the bacterial cell.			
10. Aminoglycosides are efficient against obligate anaerobic bacteria.			

Table 2. Students' answers to the evaluation questionnaire about the activity.

	Medicine (n=42)[a]		Pharmacy (n=36)		Total (n=78)	
	Yes	No	Yes	No	Yes	No
1. Is the game interesting?	39	3	36	0	75	3
2. Did the game help you better understand the content of the discipline?	38	4	35	1	73	5
3. Is this content difficult?	30	11	21	14	51	25
4. Was the content studied previously?	10	32	5	30	15	62
5. Do you think the game improved your knowledge about the issue?	41	1	35	1	76	2
6. Was the recommended literature appropriate?	36	1	25	3	61	4
7. Was the design of the game clear?	41	1	35	1	76	2
8. Did the activity encourage clinical thinking?	33	8	35	1	68	9
9. Do you consider the game an important way of enhancing learning?	36	5	35	1	71	6

	Medicine				Pharmacy				Total			
10. How do you classify the activity? (E=excellent; G=good; R=regular; P=poor)	E 20	G 20	R 2	P 0	E 27	G 8	R 1	P 0	E 47	G 28	R 3	P 0

Notes: Whenever the number of answers did not correspond to the n for the group analyzed, this means that some questions were not answered by the student.
[a]Two students did not answer the questionnaire.

were asked to complete the post-test, which contained the same 10 statements of the pre-test, also with the possibility of marking true, false, or unknown. Students were asked to identify their post-tests using the same password with which they identified the pre-test. The post-test was considered to represent the knowledge a group of students should have after attending the lecture, reading the bibliography and playing the game. On the back of the post-test sheet, there was a questionnaire about the students' opinions concerning the activity (Table 2).

The pre-tests and post-tests were corrected and the number of right, wrong and unknown answers was scored. The pre-test and post-test of each student were compared and the number of questions that had a change in answers between the pre-test and the post-test was scored. The answers to the questionnaire about the students' opinions were also scored.

Statistical analysis

The number of right, wrong or unknown answers from the pre-tests and post-tests were compared for each student, as well as between the Medicine and Pharmacy undergraduate courses, using the paired t-test ($p<0.001$). The analysis was performed using the Statistical Package for the Social Sciences (SPSS®) version 12.0.

Results

The overall time for the whole class playing the game and answering the evaluation instruments was 1 h and 30 min, but some groups finished both in 40 min. The mean results for the pre-test and post-test applied to Medicine and Pharmacy undergraduate students can be seen in Table 3. There was a significant increase in the number of right answers and a decrease in the number of unknown answers. The number of wrong answers was a little higher in post-tests, but the difference between the pre-test and the post-test was not significant. There was no statistical difference between the courses ($p<0.001$), thus the game could possibly be applied to any undergraduate course in the field of Healthy Sciences.

Table 3. Average number of answers on the pre-test and post-test for Medicine and Pharmacy students.

	Mean (standard deviation)	
	Medicine	Pharmacy
Pre-test		
Right answers	5.59 (2.1)[a]	5.06 (1.3)[a]
Wrong answers	1.02 (1.1)[b]	1.06 (1.1)[b]
Do not know	3.39 (2.3)[c]	3.89 (1.6)[c]
Post-test		
Right answers	7.43 (1.5)[d]	7.64 (1.4)[d]
Wrong answers	1.36 (1.1)[b]	1.33 (0.9)[b]
Do not know	1.20 (1.3)[e]	1.03 (1.1)[e]

Scores marked with the same letters mean they are not significantly different ($p < 0.001$).

Results from the questionnaire about the students' opinions can be seen in Table 2. More than 96% of the students said the game was interesting, had a clear design and improved their knowledge about the subject. More than 90% said the game helped them to understand the subject, and was an important way of enhancing learning. Most students (87.2%) also thought that the game encouraged clinical thinking, and almost 80% found the recommended literature appropriate, although more than 79% of them admitted not studying the subject prior to the game, and 65.4% did not consider the content difficult. Finally, 96.1% of the students found the game excellent or good, while none of them regarded it as poor. In general, there were no differences in the answers to the questionnaire between the courses evaluated.

Discussion

Both the teaching and learning modes of action of antimicrobial agents are difficult tasks due to the great variety of agents available and to the poor knowledge of students about bacterial cells. The proposed game intends to supply this gap of knowledge by reinforcing the learning skills acquired in class.

Alternative ways of teaching microbiological issues are of great concern, mostly because teaching of Microbiology is limited by the time required for microbial growth, by the huge variety of microorganisms, and by the large number of students per instructor (Sancho et al. 2006). Although these alternative tools do not provide acquisition of manual skills, they are valuable for the improvement of intellectual skills. Beylefeld & Struwig (2007) obtained students' perceptions of their experience of a gaming approach to medical microbiology learning, and reported that the most important finding of their work was that students welcomed the game as a teaching device, especially due to the large volume of content of Medical Microbiology. Lin et al. (2005) developed a game-based e-learning virology lesson on encephalitis, while Da Rosa et al. (2006) developed a card game to improve the knowledge of the immunological aspects of viral hepatitis. Sym et al. (2007) applied a questionnaire to Nurse Practitioner programs in order to analyze whether their curricula included issues related to antimicrobial prescription and resistance, and concluded that an electronic module for antimicrobial resistance could be a useful adjunct to the current curricula; but to our knowledge, there is no board game developed for this purpose. Our game comes to supply the demand for alternative ways of teaching this issue. It can be classified as category IV (quiz games) according to Bochennek et al. (2007).

Although there are several structures that can be used in a game, such as web-based tools, role playing games, card games, and board games, the latter two are the easiest to play. Card games, especially trading card games, such as the one proposed by Steinman & Blastos (2002), are very interactive, but they tend to be limited to asking and answering the questions that are displayed on the cards. Board games have more possibilities of interaction as players have to deal with squares on a path, dices, cards with questions, and so on. Our game tried to take advantage of all these items. It simulates therapeutic situations from diagnosis to the cure, where players deal with hypothetical but realistic medical cases. The cases may influence the position of the player on the board since the antibiotic resistance profiles of the bacteria are different and the player has to go backwards each time he/she gets to a square containing an antimicrobial agent to which his/her bacterium is resistant. There is also the possibility of returning to the beginning of the treatment if the bacterium suffers a mutation and acquires resistance to an antibiotic it was previously susceptible to. This is a real situation that is simulated by the game, and it is important that the students be aware they may face this in real practice. This complexity of situations is more easily dealt using board games than any other kind of games, and this was the reason we chose this particular game structure.

Other board games are available for teaching medical issues, such as the MedGame (former Pediatric Board Game) (Ogershok & Cottrell 2004, http://msig.med.utah.edu/board-game/) and the T and B cell Ontogeny Game (Girardi et al. 2006), but our game includes some aspects that makes it different. Although the MedGame could possibly be adapted for teaching almost every medical issue, the structure of the game is not similar to the board games played by children. The player has to answer a question correctly before he/she gets the right to roll the dice and move along the board. Our game uses a different approach, in which the players roll the dice in order to see if they land on a question square. This means that questions do not need to be answered each turn, making the game more fun and less stressful. Differently from our game, there is no penalty for guessing in the MedGame. We believe this penalty is important because it refrains students from dealing with the game in an uncompromised way, and also because it teaches them not to choose any option if they do not know the correct answer. This will be very important in their professional practice, as they will learn that other physicians may know the answer to a problem they are facing.

The T and B cell Ontogeny Game, on the contrary, has a structure that could not be easily adapted to other medical issues. The board is very specific to that game, and the game is very influenced by the monitor who is helping the students.

We tried to develop a game that could be played by the students on their own, without the need of supervision by teachers or monitors. Another important difference is that in the T cell and B cell Ontogeny Game the questions asked on each square are fixed, whereas they are randomly chosen in our game. We believe this makes our game more interesting to play again and an efficient tool for reinforcing the knowledge the students acquired in class.

When our game was applied to students from two undergraduate courses (Medicine and Pharmacy), there was a significant improvement in the students' answers to specific questions about the subject in both courses. As the evaluation of the students' knowledge about antimicrobials on an average test would comprise three to four out of 10 questions, we believe the number of questions applied in order to evaluate the game was appropriate. From our results, it can be concluded that the game could possibly be applied to any undergraduation course in the field of Healthy Sciences. This may be due to the fact that the game deals with basic knowledge about antimicrobial agents, and is intended to be applied to students that are at the beginning of their courses. The results obtained in the two cohorts would probably be different if the game dealt with more advanced topics, such as pharmacological information about antimicrobial agents. These advanced topics are usually specific to each undergraduate course. The higher number of wrong answers on the post-tests, although not statistically significant, can be attributed to the higher confidence the students had in answering the questions after the game. The satisfaction they demonstrated with the game in the evaluation questionnaire corroborates the conclusion that there was an improvement in the confidence level they had in their knowledge.

The game was designed in order to be applied with the assistance of instructors or during unassisted meetings. So, it is possible for the students to play the game with their colleagues outside the classroom, in order to enhance the knowledge acquired therein.

Conclusion

The game proposed herein proved to be an efficient tool for integrating basic Bacteriology and the skills concerning antimicrobial agents, and can possibly be applied to any undergraduate course in the field of Health Sciences.

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