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EDUCATION RESEARCH

What happens to misunderstandings of biomedical concepts across a medical curriculum?

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Abstract

Research on the extent and nature of commonly misunderstood fundamental biomedical concepts across a medical curriculum is scarce. These misunderstandings could point toward robust misconceptions. We examined first whether common misunderstandings persist throughout a medical curriculum, followed by a fine-grained analysis to identify their nature. We designed and administered a 2-tier test to 987 medical students across our curriculum, with 8 questions covering the respiratory and cardiovascular systems, cell division, and homeostatic processes. Proportions of incorrect responses were computed. Four questions where misunderstandings persisted were further qualitatively analyzed. A one-way ANOVA showed the proportion of incorrect responses decreased significantly by students' academic year [$F(6, 986) = 96.05$, $P < 0.001$]. While novices and end-of -first-year students showed similar proportion of incorrect responses ($P > 0.05$), incorrect responses decreased significantly between first years and second years ($P < 0.001$). Thereafter, the proportion of incorrect responses remained stable from second to final year ($P > 0.05$), with ~35% of incorrect responses. Five questions showed no decrease of incorrect responses between second and final years, with two questions where final year students performed marginally better than novices. A Chi-square analysis, with Bonferroni post hoc test, showed certain misunderstandings appeared frequently across the curriculum. The qualitative analysis of the open-ended questions yielded 15 categories of common misunderstandings of fundamental biomedical concepts in all years of training. If educators become aware of commonly misunderstood biomedical concepts, preventative measures could be taken to prevent robust misconceptions.

biomedical misconceptions; cardiovascular system; medical curriculum; physiology

INTRODUCTION

What if a significant proportion of senior medical students still hold incoherent and unscientific biomedical ideas that remain unresolved through training? While researchers disagree on the role of biomedical knowledge in clinical reasoning, they concur that basic sciences are fundamental to a coherent conceptual understanding of the human body (1–6). It is possible that, as medical students progress through the curriculum, there are moments when complex content related to biomedical sciences may be misunderstood. Usually, training will assist with the process of constructing largely accurate mental models. However, if misconceptions are not specifically addressed, they remain.

Misconceptions are persistent and robust unscientific ideas that survive education (7–9) and may become part of a medical student's knowledge base if not timely addressed. For example, the belief that blood flows from the heart to the extremities and back, ignoring the interaction between the cardiovascular and the respiratory systems, is a typical misconception among medical students (8). The problem with misconceptions is that students are unaware that they hold these beliefs, and therefore, it is difficult for educators to detect and repair them (10). In addition, if everyday life experiences continuously confirm a belief, it becomes deeply rooted in a person's mental models (8, 9). Under these conditions it begins to resist change and therefore impacts negatively on learning (7–11).

There is empirical evidence of the existence of misconceptions in medical education. Biomedical misconceptions have been investigated mainly in physiology, particularly in the respiratory (12–16) and cardiovascular systems (11, 13, 17–24).

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The cardiovascular system poses particular conceptual difficulties, specifically with integrating anatomical and physiological knowledge (23), assimilating the role of biochemical and physiological processes (18, 19), and drawing on a coherent understanding of physics and chemistry (21). Studies about respiratory misconceptions found that medical students draw on teleological explanations to describe breathing (12, 25), they struggle to understand the mechanics of breathing (9, 12), and they have misconceptions related to the underlying physiological processes (15, 26). Research on misconceptions in the field of cell biology and histology is limited and mainly focuses on conceptual difficulties students experience with regards to cell processes, genes, and chromosomes (27–30).

While there is empirical evidence of medical students presenting with misconceptions in certain knowledge domains, research on their durability in a curriculum is scarce. Most of the above-mentioned studies focused on identifying misconceptions at specific points in time, that is, not throughout an entire curriculum, or demonstrated their resistance to teaching in short intervention studies. In one of the few studies of misconceptions surviving instruction and the implications of those misconceptions (17), researchers found that students with misconceptions about the cardiovascular system performed poorly during clinical reasoning. Misconceptions therefore potentially have implications for patient care. However, it remains to be detected whether certain fundamental biomedical concepts are commonly misunderstood by some medical students throughout their years of training. These misunderstandings could potentially point toward misconceptions. If there are commonly misunderstood biomedical concepts (potential misconceptions), what is their nature and why do students hold onto certain incorrect understandings despite training? If educators become aware of this, preventative measures could become part of their curricula to ensure coherent biomedical knowledge construction.

The present cross-sectional study addressed these questions. To this end, we designed and administered a set of eight probing two-tier questions to undergraduate medical students in all years of study at one institution to investigate the extent and nature of some commonly misunderstood biomedical concepts in in four domains. By employing a mixed methods design, we first examined the prevalence of these misunderstood concepts across all years of the curriculum, followed by an in-depth qualitative analysis to explore what underlies students reasoning in the most prevalent incorrect answers.

MATERIALS AND METHODS

The present study was conducted at the University of Cape Town, Cape Town, South Africa, where ~1,300 students enroll in the medical curriculum from *years 1* to *6*. This institution has been consistently evaluated as the top university in Africa by the Center for World University Ranking (31). Similar to many other universities, in South Africa, students who have met the necessary entrance criteria for a medical degree can register straight after secondary school. Selection into the medical school at the University of Cape Town is highly competitive, and only top achievers are offered places. From the 9,000 applicants from all over South Africa, only between 220 to 250 students are selected. Selection is based on top grades, where science and mathematics are prerequisites. All students were electronically invited to participate in a study purportedly to explore reasoning processes in physiology and anatomy, and 987 enrolled (see Table 1). The study spanned two academic years. The academic year runs from January to December, and the first cohort of first to final year students were recruited from July to October. The following year, the incoming first years were recruited at the start of the academic year before classes commenced. This group will be referred to as "novices." Two first-year classes were thus surveyed, one as entering novices and one halfway through their first academic year. First-, second-, and third-year students were recruited during class activities. Fourth-, fifth-, and final-year students were recruited through clinical rotation blocks. Progressively fewer students participated in more advanced cohorts. The Faculty of Health Sciences Research Ethics Committee at the University of Cape Town, Cape Town, South Africa approved the study.

Probing Questions

The set of eight questions probing misunderstandings addressed content on the respiratory and cardiovascular systems, homeostatic processes, and cell division. To design the eight questions, the principal investigator and a team of four discipline experts (two physiologists and two clinicians) revisited data from a previous study (13) exploring lecturers' perceptions of misconceptions. The eight questions were developed to address misconceptions that were repeatedly mentioned by the lecturers in this previous study (13) and appear to have been detected in other studies (8, 9, 11–28, 30, 32–35). The developers of the questions ensured that students would have been exposed to the knowledge required to answer them. First, drawing on content covered in secondary school biology, we designed the questions so that all novices could provide a relatively coherent answer. Second, by checking the content of the curriculum, we were able to ensure that the relevant knowledge had been addressed in the first year of the curriculum. The institution has a spiral curriculum, and the content probed by all questions is introduced in the first year (either *semester 1* or *2*), with a return to it in the second and third years, moving gradually from physiology to pathophysiology and the clinical dimensions.

Table 1. *Number of students who participated in the study per training year per gender and percentage of the total number of registered students per year*

Years	Male	Female	Total	Percentage Registered 2017
Novices*	90	137	227	100%
1	76	134	210	77%
2	58	100	158	67%
3	54	84	138	66%
4	33	57	90	40%
5	34	48	82	40%
6	41	41	82	44%
Total	386	601	987	

*Students who had just entered the medical school and had no formal teaching yet.

The whole cohort of students were therefore exposed to the relevant content knowledge required to provide correct answers to the questions. Please see the eight questions below, with the correct response in bold.

1. During normal quiet breathing (eupnea) air moves out of the lungs because:
   a. The gas pressure in the lungs is less than the outside pressure.
   b. **The volume of the lungs decreases with expiration.**
   c. Contraction of the diaphragm decreases the volume of the pleural cavity.
   d. PCO_2 is high inside the lungs compared to PO_2.
2. If a person is stabbed in the chest and the intrapleural space is punctured, the lung collapses because:
   a. The pressure in the intrapleural space decreases as air leaves.
   b. **The pressure around the lung increases.**
   c. The external intercostal muscles are damaged.
   d. The patient does not breathe as deeply because of pain.
3. When blood leaves the arterial system it enters the venous system via:
   a. **A closed system of capillaries.**
   b. The organs that they supply.
   c. Arterioles and venules.
   d. The interstitial fluid.
4. As blood circulates from arteries into capillaries, the total cross-sectional area of capillaries
   a. Decreases and causes the blood velocity to decrease.
   b. Increases and causes the blood velocity to increase.
   c. **Increases and causes the blood velocity to decrease.**
   d. Decreases and causes the blood velocity to increase.
5. If a human egg and sperm joined together to start forming a zygote, its cells will divide to
   a. **Copy each chromotid precisely.**
   b. Pair maternal chromosomes with corresponding paternal chromosome.
   c. Let chromosomes undergo crossing over.
   d. Form four daughter cells.
6. A patient is diagnosed with deep vein thrombosis (DVT) on his left calve. If a clot breaks away, it could lodge
   a. In his brain.
   b. **In his lung.**
   c. In his heart muscle.
   d. In his liver, via the portal venous system.
7. If a patient is sweating profusely and not drinking any water
   a. **Osmosis moves water from the ICF to the ECF.**
   b. There is an increase in the volume of the ICF.
   c. Both the ECF and the ICF become more dilute.
   d. the osmolarity of the ECF falls.
8. If a child has a temperature of 40 degrees Celsius, you should do the following to reduce the fever:
   a. Give her something hot to drink.
   b. Sponge her with cold water.
   c. Wrap her in a woollen blanket.
   d. **Sponge her with luke-warm water.**

Research indicates that multiple-tier, multiple-choice questions provide the best lens to distinguish real misconceptions from lack of knowledge (36, 37). Therefore, we developed two-tier questions, with a multiple-choice option in the first part of the question, followed by a free-text rationale for choosing the option to give insight into participants' reasoning processes.

The questions were answered anonymously and administered during a 45-min designated teaching activity, either electronically (students from *years 1* to *3*) or in an identical paper-based version (students from *years 4* to *6*).

Data Analysis

Quantitative analysis to establish the prevalence of misunderstandings.

We scored responses for each of the eight multiple-choice tier questions as correct, incorrect, or absent and computed the proportion of incorrect responses (thus excluding absent responses) for each participant, and, subsequently, the mean proportion of incorrect responses for each training year. A one-way ANOVA with training year as a "between-subjects" factor was performed on the mean proportion of incorrect responses. Post hoc tests with Bonferroni correction were performed to further explore significant differences. This analysis checked for differences in the frequency of incorrect responses between years of training. Its purpose was to examine whether misconceptions persist throughout the curriculum years, despite students' exposure to relevant knowledge.

A subsequent analysis checked whether the pattern across years differed between questions, i.e., whether specific misunderstandings persisted whereas others disappeared as the curriculum progressed. The mean proportion of incorrect responses given to each question in each year of training was compared in eight separate one-way ANOVAs. Post hoc tests with Bonferroni correction identified which pairs of years significantly differed in the proportion of incorrect responses. This analysis allowed for the identification of questions to which the proportion of incorrect responses did not progressively decrease across years, i.e., a similar proportion of incorrect responses triggered by misconceptions persisted even in more advanced cohort of students.

As the number of participants in *years 1* to *3* differed substantially from *years 4* to *6*, we performed additional analyses to check whether this difference had influenced the findings. Conducting these sensitivity analyses (38) allowed us to examine whether our results would have been different if we had been able to recruit different samples of students. We first performed the analyses on the entire data set and second on a similar number of students in each year. For this latter analysis, we randomly numbered participants from *years 1* to *3* and selected participants to match the number of participants in *years 4* to *6*. Random selection of subgroups was considered appropriate, as all participants were volunteers, ruling out systematic a priori differences between groups.

Another possibility was that the findings would have been affected by dropout. A third analysis took into account that the medical curriculum studied loses ~10% of its students in the first year due to insufficient performance (39, 40). As the data were collected anonymously, we were unable to check which students in the first year in our sample actually dropped out. Therefore, we performed the analyses again after removing the poorest 10% of our first-year participants to check whether this would affect our initial findings.

Qualitative analysis to establish what underlies the misunderstandings.

In four of the questions incorrect responses did not decrease between the second and the two final years of training (5th and 6th yr). These questions probed misconceptions related to the cardiovascular system (*question 4*), cell division (*question 5*), and homeostasis (*questions 7* and *8*). In questions referring to cell division (*question 5*) and homeostasis (*question 7*), students from the fifth and the sixth year performed better only relative to novice students, and in *question 8* on thermoregulation, the proportion of incorrect responses increased between the fourth and the final year. This subset of questions (*questions 4*, *5*, *7*, and *8*) were therefore selected for a fine-grained analysis of *1*) the pattern of the incorrect options chosen by the students in the multiple-choice part of the question across years of training, followed by *2*) a qualitative analysis of the rationale provided by the students in the second part of the question for choosing that incorrect option. For the analysis of the multiple-choice options, we first computed the frequencies of the three incorrect options chosen to *questions 4*, *5*, *7*, and *8* when students from all years were combined. Chi-square tests were performed, for each question, to check whether the frequency with which each incorrect option was chosen differed significantly. Subsequently, we checked whether the incorrect options chosen showed a different pattern across the years of training (i.e., similar or different incorrect options were chosen) and therefore whether similar or different misconceptions existed across years of training. We compared the percentages of each incorrect option chosen per question across years of training. In all pairwise comparisons, Bonferroni correction was used to further explore significant differences. This was followed by inductive qualitative analysis of the data from the second part (the open-ended free-text rationale given by participants) to uncover whether there were common incorrect reasoning patterns underpinning participants' answers. Looking at all the incorrect options chosen for the four questions, three scientists and three clinicians individually analyzed the rationale provided to freely code the data and arrive at a codebook with a clear definition of each code and example quotes from the data. Second, a coding-consensus meeting was held with the six raters and the first author to agree on a set of similar categories that emerged from the coding. Clustering together common themes in the rationale given by participants who chose the wrong options, each question thus had an agreed-on set of categories speaking to common misunderstandings. Third, two scientists and two clinicians individually analyzed the rationale for each response to find examples of the agreed-on categories of common misunderstanding in the data. Interrater agreement was computed.

RESULTS

Prevalence of Misunderstandings

The proportion of incorrect responses as a function of training year is presented in Fig. 1. The one-way ANOVA showed a significant effect of training year on the proportion of incorrect responses [$F(6, 986) = 96.05$, $P < 0.001$]. The post hoc analysis indicated that the proportion of incorrect responses did not consistently decrease by training year. The proportion of incorrect responses was similar for novices and those completing their first year ($P > 0.05$) and decreased significantly between first year and second year ($P < 0.001$). After the first year, however, the proportion of incorrect responses remained stable across years ($P > 0.05$ for all comparisons between pairs of years from the 2nd to the 6th year). Around 35% of the responses were incorrect in each of these years.

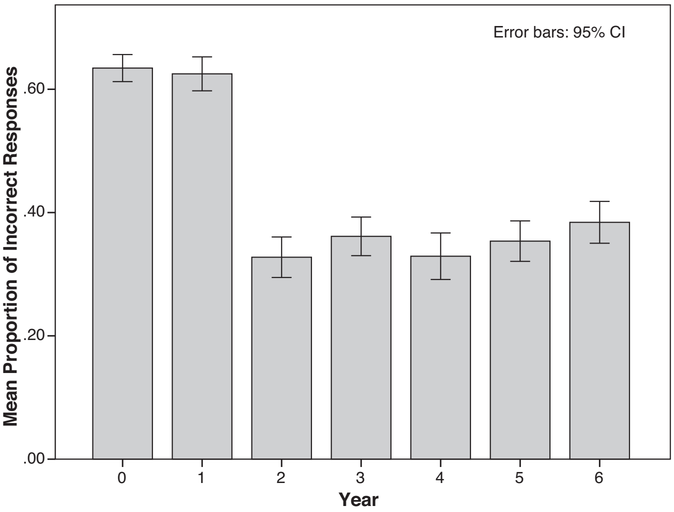

Figure 1. The proportion of incorrect responses as a function of training year. CI, confidence interval.

Table 2 presents the results of the analysis of incorrect responses for each question by year of training. This is depicted in Fig. 2. Results of the analysis of the proportion of incorrect responses for each question separately showed that for all the questions, except *question 6*, which probed the "single loop misconception" (8), there was no decrease between the second and the two final years of training (5th and 6th years). *Question 5*, which probed cell division, and *question 7*, which probed homeostatic processes, showed that students in their final 2 yr of training performed better only relative to novice students who had just entered the medical program. *Question 8*, which probed thermoregulation, showed a very high proportion of incorrect responses across all years of training, surprisingly with an increase between the fourth and the final year.

It is noteworthy that at the end of the medical training >60% of the responses were incorrect for *question 5* probing cell division.

Results from the smaller subset ($n = 549$), randomly selected from the original set to deal with unequal numbers of students in the various years, yielded similar results. Analysis showed the proportion of incorrect responses decreased significantly by students' academic year [$F(6, 542) = 40.91$, $P < 0.001$]. As with the full data set, the proportion of incorrect responses did not decrease significantly between novices and first-year students ($P > 0.05$). However, there was a significant decrease between first-year and

Table 2. *Mean proportion of incorrect responses provided by the students for each question per year of training and results of the statistical analysis checking for differences between years*

	Year of Training							
Question	***0***	***1***	***2***	***3***	***4***	***5***	***6***	**Statistic Test**
1	0.68 (0.47)^{a}	0.67 (0.47)^{b}	0.23 (0.42)^{a,b,c,d}	0.41 (0.49)^{a,b,c}	0.28 (0.45)^{a,b}	0.32 (0.47)^{a,b}	0.45 (0.50)^{a,b,d}	$F(6, 980) = 25.9; P < 0.001$
2	0.76 (0.43)^{a}	0.67 (0.47)^{b}	0.40 (0.49)^{a,b,c,d}	0.35 (0.48)^{a,b}	0.19 (0.39)^{a,b,c}	0.18 (0.39)^{a,b,d}	0.28 (0.45)^{a,b}	$F(6, 980) = 37.3; P < 0.001$
3	0.44 (0.50)^{a}	0.50 (0.50)^{b}	0.27 (0.44)^{a,b}	0.18 (0.39)^{a,b}	0.20 (0.40)^{a,b}	0.11 (0.32)^{a,b}	0.10 (0.30)^{a,b}	$F(6, 980) = 18.96; P < 0.001$
4	0.79 (0.41)^{a}	0.78 (0.42)^{b}	0.39 (0.49)^{a,b}	0.49 (0.50)^{a,b}	0.48 (0.50)^{a,b}	0.56 (0.50)^{a,b}	0.49 (0.49)^{a,b}	$F(6, 980) = 20.14; P < 0.001$
5	0.38 (0.49)^{a}	0.56 (0.50)^{b}	0.44 (0.50)	0.50 (0.50)	0.57 (0.50)^{a}	0.60 (0.49)^{a}	0.63 (0.50)^{a}	$F(6, 980) = 4.90; P < 0.001$
6	0.87 (0.34)^{a}	0.78 (0.42)^{b}	0.21 (0.41)^{a,b,c,d,e}	0.07 (0.26)^{a,b,c}	0.07 (0.25)^{a,b,d}	0.04 (0.19)^{a,b,e}	0.06 (0.24)^{a,b,f}	$F(6, 980) = 195.40; P < 0.001$
7	0.41 (0.49)^{a}	0.32 (0.47)^{b}	0.16 (0.37)^{a,b}	0.12 (0.32)^{a,b}	0.14 (0.35)^{a,b}	0.22 (0.42)^{a}	0.22 (0.42)^{a}	$F(6, 980) = 10.85; P < 0.001$
8	0.74 (0.44)^{a}	0.73 (0.45)^{b}	0.52 (0.50)^{a,b,c,d,e,f}	0.78 (0.42)^{c}	0.71 (0.46)^{d}	0.80 (0.40)^{e}	0.84 (0.37)^{f}	$F(6, 980) = 7.40; P < 0.001$

Values are means (SD). ^{a,b,c,d,e,f}Significant differences in pairwise comparisons. $^{*}P < 0.001$.

second-year students ($P < 0.001$). For all comparisons, the proportion of incorrect responses between pairs of years from the second to the sixth year remained stable from the second year onwards ($P > 0.05$).

Finally, we removed 10% of our poorest performing students from the first-year sample to simulate the effect of dropout in that year. This measure did not affect our findings; the proportions of incorrect responses did not differ among novices and first-year students. Again, analysis showed the proportion of incorrect responses decreased by training year [$F(6, 955) = 93.34$, $P < 0.001$].

Further analysis indicated that these proportions did not decrease progressively. There were similar proportions of novices and first-year students with incorrect responses ($P > 0.05$), followed by a significant decrease between first-year and second-year students ($P < 0.001$). However, the proportion of incorrect responses did not differ from the second year onwards ($P > 0.05$) for all comparisons between pairs of years from the second to the sixth year.

What Underlies These Misunderstandings?

The frequencies of incorrect options chosen in *questions 4*, *5*, *7*, and *8* are presented in Fig. 3. There was a significant difference between options chosen for all four questions [*question 1*: $x^2(2) = 35.98$, $P < 0.001$; *question 2*: $x^2(2) = 106.51$, $P < 0.001$; *question 3*: $x^2(2) = 59.36$, $P < 0.001$; *question 4*: $x^2(2) = 1001.75$, $P < 0.001$]. Results showed that in all the questions the incorrect options chosen were not evenly, or randomly distributed. Statistically significant differences emerged between their distributions; some incorrect choices were more prevalent.

The percentages of incorrect options per question across years of training are presented in Fig. 4. Only for *question 4* was there a significant difference in the frequency of the options chosen between novices and *year 1* students ($P < 0.01$), without significant differences between *year 1* and the subsequent years. For all the other questions, there were no significant differences in the incorrect options chosen between years of training (all $P > 0.05$). Please see Supplemental Table S1 (all Supplemental material is available at https://doi.org/10.6084/m9.figshare.14572773) for full results of the eight MCQs.

The qualitative analysis of the free-text rationale given by participants yielded a range of common misunderstanding pertaining to the domains of cell division, homeostasis, and the cardiovascular system. The researchers identified in total 15 common themes of discipline-specific misunderstandings. While the examples from these responses are not exhaustive or mutually exclusive, they are presented here to best articulate the specific themes that arose from the data. See Table 3 for a summary of common themes indicating incorrect reasoning clustered per question.

Percentages were calculated where there was consensus in allocating the rationale given by participants, to the common themes among the four raters. Table 4 presents the scores in percentages per category from high to low with interrater reliability.

DISCUSSION

The present study investigated, first, the extent to which biomedical misunderstandings, in four domains, the respiratory and cardiovascular systems, cell division, and homeostasis, persist throughout our medical curriculum. Furthermore, we examined whether certain misunderstandings appeared more frequently than others across all years of training, thus potentially becoming more resistant to instruction. In addition, we explored the nature of these resistant misconceptions, to gain insight into the way students reason incorrectly.

Regarding the first question explored in this study, three key findings emerged: *1*) there was no difference in performance between novice and end of first-year students; *2*) there was a significant drop in proportion of incorrect responses from first year to second year; and *3*) there was a stability of incorrect responses from the second to sixth year of training.

The similar proportions of incorrect responses in the novice and first-year group indicate that in first year certain biomedical misunderstandings persist. However, incorrect responses significantly decreased in the second year. Interestingly, despite basic science and clinical teaching, from the second-year onwards, the proportion of incorrect responses remained stable across years of training, which indicates that surviving misunderstandings in more advanced years remain high, at 35%, and may even increase as it happened with *question 7*.

A first, and perhaps obvious, reason for the decrease in percentage of incorrect responses after the first year would be that poor students drop out at the end of the first year (as is the case in many European medical schools), leaving only the better students in the second year. Such state of affairs would explain why students do not seem to learn anything

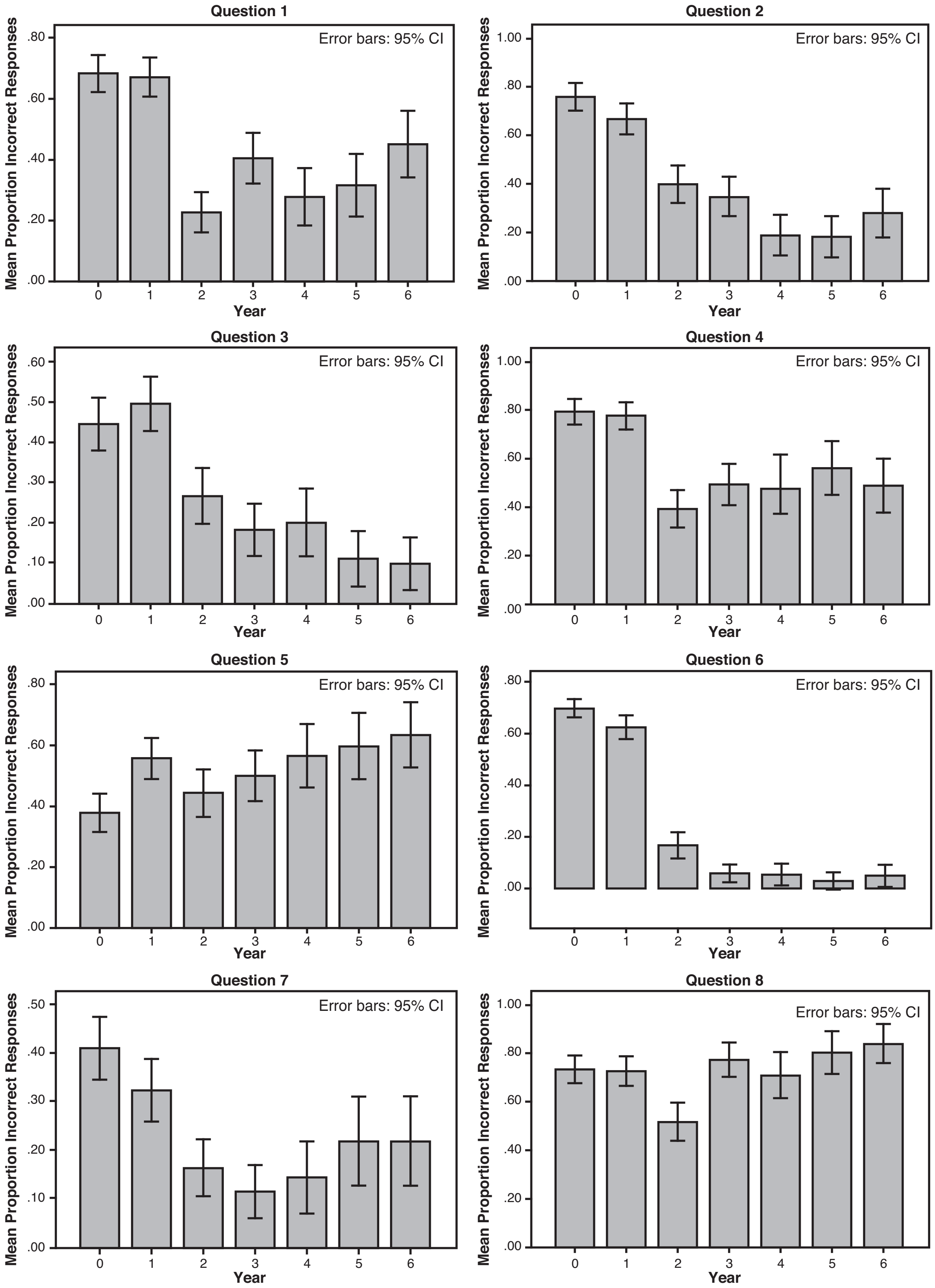

Figure 2. Proportions of incorrect responses for *questions 1* to *4* in each year of training. Proportions of incorrect responses for *questions 5* to *8* in each year of training. CI, confidence interval.

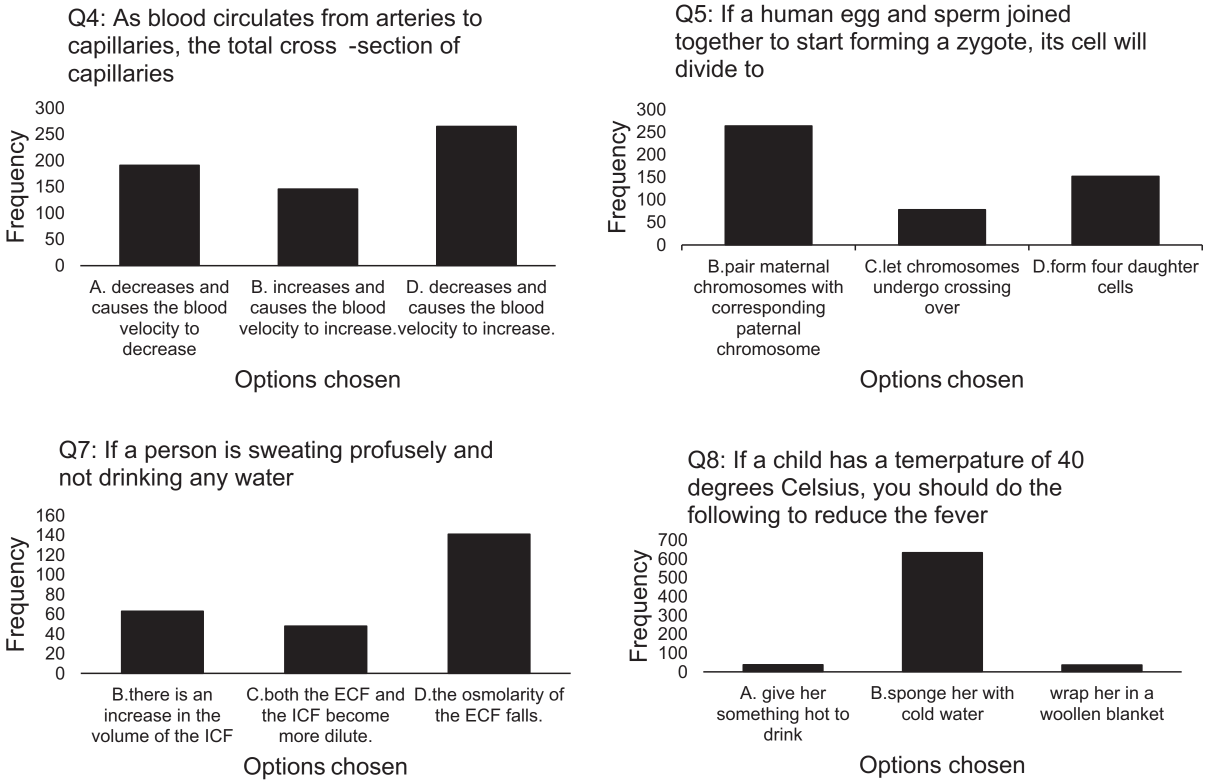

Figure 3. Frequencies of incorrect options chosen per question for all participants. ECF, extracellular fluid; ICF, intracellular fluid.

useful in the first year but then understanding improves dramatically in the second year. However, at the Faculty of Health Sciences at the University of Cape Town, first-year students who failed their first semester enter an extended support program to address learning barriers, which makes drop out in the first year very limited (39). Indeed, we simulated the effect of such dropout in our first-year sample but found that it did not affect our findings.

A possible explanation for the apparent lack of learning in the first year and a rather sudden drop in incorrect answers in the second, is that learning to apply biomedical concepts to medical problems (such as the ones presented in our questions) takes some time to manifest itself. The first-year curriculum focuses on normal developmental processes in the body and an introduction to body systems. It is therefore unlikely that students would be able to coherently solve problems, even though they are familiar with underlying concepts. In the second-year students are introduced to more complex material. It is therefore possible that knowledge gained in the first year only becomes meaningful through application in the second year of study. Such explanation for the drop in incorrect responses after the first year comes close to the knowledge-in-pieces theory (24, 41–43), suggesting that knowledge is first acquired as individual and rather isolated pieces ("phenomenological primitives") (42). Only after a period of application of these pieces do they become integrated into larger wholes. Take for example, the question on why a lung would collapse when the intrapleural space is punctured (*question 2*). To answer this question, students must organize fragmented bits of naïve knowledge (what happens if you puncture something filled with air) into a more complex knowledge system (the interaction between negative intrathoracic pressure and atmospheric pressure and the subsequent recoil of elastic lungs resulting in a pneumothorax). It is possible that this knowledge integration only takes place when application to pathophysiological conditions is required in second year. This seems to imply that learning complex materials requires a latency period during which no change in performance is observed. While this abrupt change remains an enigma, a plausible explanation is that many of the concepts and processes learned in the second year facilitate the better understanding of concepts learned in first year.

Our third finding is the relative consistency with which second- to sixth-year students chose incorrect options. If this was simply due to forgetting over time, one would expect the number of incorrect answers to increase gradually. For the majority of the questions, this was not the case. This suggests that these incorrect responses could potentially be manifestations of deep-seated misconceptions embedded in students' mental models. Research suggests this could be because everyday life experiences confirmed these beliefs, regardless of scientific evidence (8–11, 13). Some students, for example, hold onto false unscientific anatomical understandings that the diaphragm contracts to push air out of the lungs (*question 2*); blood leaving the arterial system enters the venous system via organs (*question 3*); and venous return to the heart traverses the liver (*question 6*). It could be that in these situations, students had no need for conceptual understanding, and intuitive explanations that did not clash with

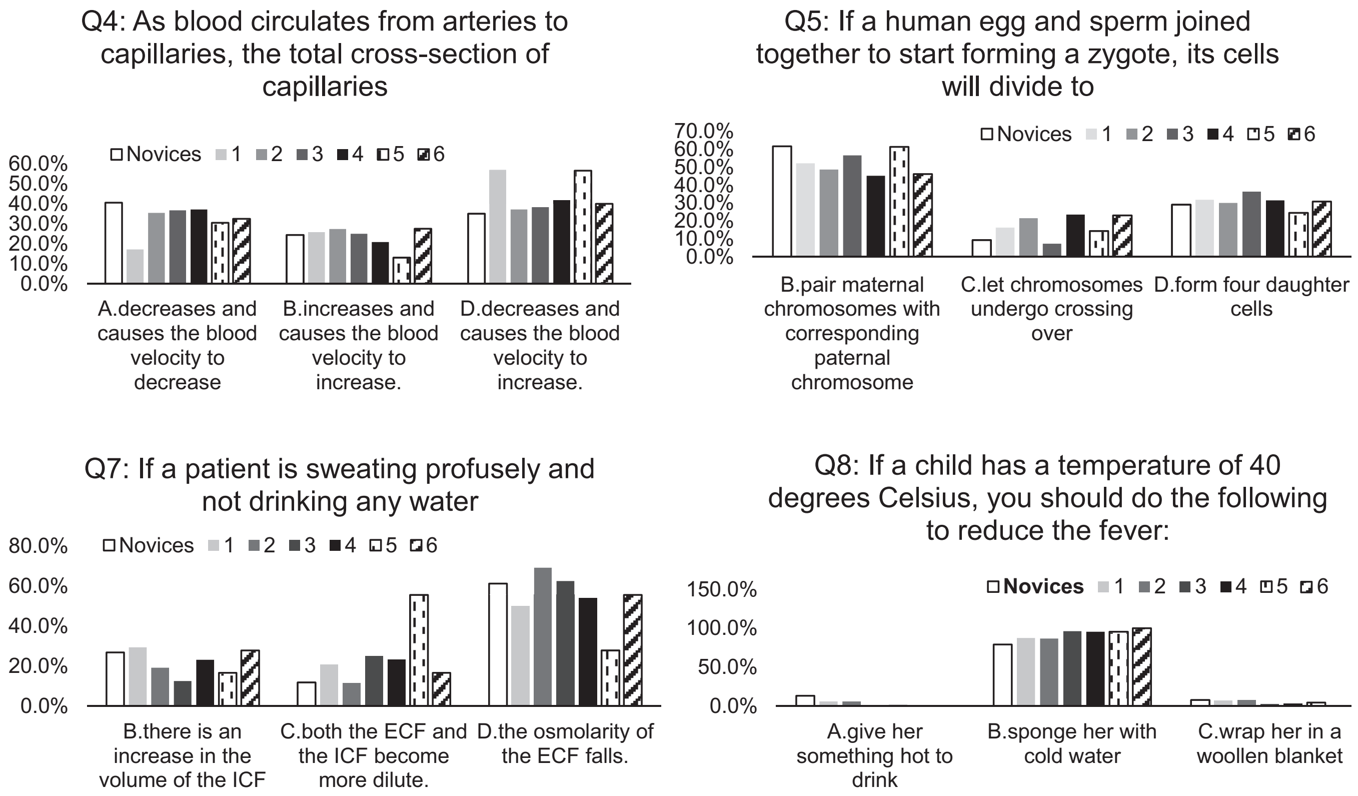

Figure 4. Percentages of incorrect options chosen per question across training years. ECF, extracellular fluid; ICF, intracellular fluid.

their everyday reality sufficed. Educators could thus continuously probe whether students do indeed acquire a scientific understanding of these concepts.

Regarding the cardiovascular system, findings from our study for the single loop misconceptions (the only question where the majority of participants chose the correct option) did not support evidence from similar studies (8, 17). However, two questions, namely how blood leaves the arterial system to enter the venous system and what happens to blood velocity when blood circulates from arteries into capillaries, showed no significant disappearance of misunderstandings between second years and the two final years. This supports findings that some naïve understandings about the cardiovascular system are not always resolved through teaching in the senior years and that the cardiovascular system poses particular conceptual difficulties with integrating foundational knowledge into a functional understanding of how the circulatory system works (17, 22). Specifically in the question where students had to draw on underlying physics principles (for example that the cross-sectional area of capillaries increases as blood from the arterial system enters it, therefore velocity will decrease, as flow is constant), our findings corroborate misconceptions found in similar studies (23, 33).

Although we did not find evidence in the literature of medical students' misconceptions about cell division (mitosis and meiosis), we found that a significant number of senior medical students in our study could not differentiate between the nature, sequence, and significance of mitosis and meiosis. From our questions about fluid balance and thermoregulation, high proportions of senior students gave incorrect responses. Elsewhere, educators identify homeostasis as an area where students demonstrate an oversimplistic understanding of complex processes (13, 34, 35). Unsurprisingly, in this study, participants displayed similar misunderstandings, for example, that water moves to replenish lost volume as part of fluid balance. Students disregarded the osmolarity gradient and solute concentration changes that result from volume changes. In some cases, students, regardless of their training, did not apply causal reasoning.

Our findings regarding the fine-grained qualitative analysis helped clarify why these misunderstandings persist. The core observations from the study were, first, that in all four questions there was one misunderstanding that was more dominant across years of training, and second, that there appears to be common themes underlying these incorrect understandings of the domains that were tested. In the question pertaining to the cardiovascular system, the majority of participants thought that the total cross-sectional area of capillaries will decrease as blood circulates from arteries into capillaries, thus causing blood velocity to increase. Responses further showed that participants confused the cross section of a vessel with total cross section of the area. They therefore reasoned that as blood flows from an artery to capillaries, the vessel gets smaller and narrower, with a smaller cross section, hence reasoning that the smaller the diameter of the vessel, the higher the pressure of flow. This indicated that they do not have a fundamental understanding that total cross-sectional area increases and that velocity of blood flow is therefore inversely proportional to the total cross-sectional area. They seem to misunderstand the relationship between vessel diameter and flow, where increased surface area results in decreased resistance. Students potentially visualize these structures

Table 3. *Examples from the questionnaire's raw data of categories of misunderstandings clustered per question*

Question 4

1.1. Velocity and cross-sectional surface area confusion

Participants confused the relationship between cross-sectional area and velocity. First, they do not understand that the rate/velocity of blood flow is inversely proportional to the total cross-sectional area. Second, they do not understand that while individual vessel diameter decreases, the total cross-sectional area increases in the progression from arteries to arterioles to capillaries. The capillaries widen as the increase in blood volume passes through it, causing an increase in the velocity of the blood.

- *As capillaries are smaller the area decreases and therefore an increase in the blood's velocity.*

1.2. Resistance-pressure-flow misunderstanding

Participants were confusing the relationship between vessel radius, pressure, and flow. They reason that it is the radius of the vessel that is causing the pressure, rather than that for a given pressure differential, the radius influences the flow rate.

- *The smaller the diameter of the vessel, the higher the pressure of flow or flow rate.*
- *Decreased cross sectional area means that blood has to flow through a narrower channel, and this applies greater pressure onto the blood thus making it flow faster.*

1.3. Misunderstanding about vessel wall thickness, constriction, and velocity.

Participants reasoned that velocity is determined by the thickness of the vessel wall. Participants further reasoned that muscles actively contribute to propelling blood, rather than the fact that for a given state of muscular contraction, arteries are passive conduits. While capillaries are narrower than arteries and they do not have muscular components to dilate or constrict, the total cross-sectional area of capillaries increase, and that is why velocity decreases.

- *Arteries are thick and muscular while capillaries are one cell wall thick. The muscular walls of the arteries help push the blood through the circulatory system thus increasing the blood velocity. The absence of these muscles in capillaries decreases the blood velocity.*
- *Blood capillaries are thinner than arteries, and therefore doesn't allow blood to flow as freely so the velocity will increase.*

1.4. Teleological understanding about the purpose of blood flow

Participants reasoned that the purpose of blood flow is to provide organs with nutrients and to allow gaseous exchange and that blood flow should slow to allow this, rather than understanding that blood flow decreases as the total cross-sectional area of capillaries increases, based on principles of physics, which is advantageous for nutrient and gaseous exchange.

- *Blood capillaries need to slow down for effective exchange*
- *The blood leaving the arterial system carries oxygenated and nutrient rich blood from the heart to organs that need it, after which veins take the deoxygenated blood back to the heart so blood must slow down.*

Question 5

2.1. Confusing the stages of cell division

Participants confused mitosis with meiosis. They do not understand that meiosis occurs only during formation of the gametes and does not occur once the zygote is formed and that replication of cells occurs via mitosis.

- *In the steps of meiosis a zygote is a cell that contains both parents information. Maternal and paternal chromosomes align in the zygote and after that it undergoes mitosis.*
- *A zygote needs to divide now so meiosis needs to first take place to ensure everything is copied from the mother and the father and then copied again and again and so on.*

2.2. Misunderstanding that maternal and paternal chromosomes pair during mitosis

Here, participants misunderstand that whilst pairing does take place as a normal sequence in mitosis, it is not the pairing of maternal with paternal chromosomes.

- *When a zygote divides it allow for maternal and paternal chromosomes to pair up so that it could form a complete set in its body*
- *The zygote will have maternal and paternal genes crossing over in a way in which genetic material mixes.*

2.3. Confusion about genetic variation during mitosis

Here participants mistakenly reasoned that genetic variation occurs during mitosis.

- *Exchange of genes occurs in a zygote when maternal and paternal chromosomes pair. This is to allow crossing over for genetic variation of both the mother and the father so that all children will not look the same.*
- *Cross over is required for genetic variation, this occurs after the zygote is formed.*

Question 7

3.1 Confusion about osmolarity

In this question participants do not conceptually understand that the osmolarity of a solution increases if more water than solutes are removed.

- *The ICF will decrease as it* [fluid] *is moving to the ECF and not being replenished due to the patient not drinking any water. As a result of the sweating the osmolarity of the ECF will fall*
- *The osmolarity of the ECF would fall because it will be concentrated with salts since the patient is not drinking water in order to dilute the salt in the sweat.*

3.2 Misunderstanding about osmosis to move water from ICF to ECF

Here participants do not understand that during osmosis water moves from area of low solute concentration to area of higher solute concentration. Therefore, water will move from ICF to ECF.

- *Sweating removes water from the body. If there is a lack of water in the body, cells are prioritized. Thus extracellular fluid will be moved into cells. This is from high concentration to low concentration which is with the diffusion gradient and thus osmosis, and increases the volume of ICF.*
- *Water is traveling down a concentration gradient via osmosis because water concentration is low in the ICF because no water is coming into the body. So water moves from ECF to ICF.*

3.3 Confusion about water in ICF and role of sweating

Here participants reason that sweating regulates the water in the ICF.

- *In order to maintain the volume of the ICF, the sweat glands secrete more sweat to regulate the volume of water in the ICF.*
- *When the patient sweats, the body realizes that there is a loss in water in the body. The body responds in such a way to help retain water so that it is not all lost through sweating to keep the water in the ICF.*

Question 8

4.1 Confusion about heat loss mechanics and shivering thermogenesis

In this question participants show an understanding that cooling is required when a child has a fever, but they do not recognise possible negative effects of cold water. While cold water could be an acceptable method to reduce the temperature in an adult, the possible negative effects of hypothermia are not considered. Biomedical causal reasoning is therefore not applied.

- *The child's temperature is above the normal core body temperature of 37 degrees Celsius. This means that mechanisms need to be initiated or put into place in order to promote heat loss. One such mechanism includes behavioural actions such as sponging with cold water, which will allow heat to be lost from the body to the water via conduction.*
- *Sponging the child with cold water will drastically reduce the temperature of the child. Doing this will also prevent further problems arising.*

4.2 Thinking that hot drinks will cool down body temperature during a fever.

Here participants do not take into account that temperature homeostasis mechanisms are dysregulated in fever; therefore, hot drinks may not trigger appropriate response to cool the body.

- *A hot drink will allow the child to sweat more, hence there will be decrease in temperature*
- *The hot drink will heat up the body causing a process in homeostasis to occur whereby the body will cool down the body by making it excrete sweat and cool down the body.*

4.3 Folklore

Participants draw on unscientific and everyday explanations to explain thermoregulation and thermogenesis.

- *Sponging with cold water is what my mother used to do when I had fevers. It also makes sense, because cold water would cool down the child and warm water would just make it worse.*
- *I have no idea, but from experience, after having had a hot drink that aids flu, whilst having a fever, I would then break out in sweats then feel cooler.*

4.4 Confusion about heat loss mechanics and evaporation

Here participants do not understand that covering the body will promote sweating but prevent/minimize evaporation, so the temperature will in fact increase.

- *Wrapping the child in a woollen blanket will increase in temperature and would stimulate the temperature control center to regulate and normalize her body temperature. The sweat glands will be stimulated to become more active so in that way she will sweat and cool down.*
- *A warm blanket will allow the child to sweat and thus lose heat in the body.*

Example participant responses are in italics. ECF, extracellular fluid; ICF, intracellular fluid.

incorrectly and/or struggle to move cognitively between static entities (the walls of the vessels) and processes (blood flow). Finding from this study corroborated empirical evidence that potential misconceptions can arise when students are applying causal reasoning in conceptualizing physiological systems (20, 23, 44). Regarding cell division, the majority of participants thought that when a zygote divides, maternal chromosomes and corresponding paternal chromosome pair. Participants thus confused meiosis with mitosis, resulting in a sequential misconception, as replication occurs via mitosis after fertilization. Although not pertaining to medical students, studies have shown conceptual difficulties with regards to mitotic and meiotic division (27–30). Findings from this study support the notion that students struggle with the complexity of bringing together a large number of subordinate concepts to arrive at a coherent understanding of cell division. Regarding homeostatic balance when a person is sweating and not drinking water, the majority of participants thought that the osmolarity of the extracellular fluid will fall. Participants did not understand that osmolarity of a fluid increases if more water than solutes are removed indicating that participants have a deep-seated incorrect understanding of osmolarity. In this question, results show that participants apply causal reasoning incorrectly, potentially based on an unscientific understanding of osmosis. Pertaining to homeostasis in temperature regulation, the majority of participants reasoned that a child with a fever should be sponged down with cold water. Although there is contention whether sponging with cold water will indeed be detrimental to a child with fever, the qualitative analysis of participant's free text rationale indicated that they disregarded the possible negative effects of cold water on the skin of a child with a fever. Participants provided clinical explanations to treat the fever but did not apply causal reasoning to address underlying biomedical processes related to cold water. Medical students at our faculty are trained to exercise problem-solving skills, as many will work in resource-poor settings in South

Table 4. *Percentages of misunderstandings identified from the open-ended responses per question*

Misunderstandings	Percentages	Interrater Reliability
Question 4		82%
Velocity and cross section surface misconception	63%	
Resistance and pressure misconception	21%	
Teleological misunderstanding about the purpose of blood flow	13%	
Misconception about vessel wall thickness, constriction, and velocity	3%	
Question 5		82%
Misunderstandings about stages of cell division	42%	
Misunderstanding that maternal and paternal chromosomes pair during mitosis.	38%	
Misunderstanding about genetic variation during mitosis	20%	
Question 7		72%
Misunderstanding about osmolarity	71%	
Misunderstanding about osmosis to move water from ICF to ECF	16%	
Misunderstanding about water in ICF and role of sweating	13%	
Question 8		86%
Misunderstanding about heat loss mechanics and shivering thermogenesis	86%	
Misunderstanding that hot drinks will cool down body temperature during a fever.	8%	
Folklore	3%	
Misunderstanding about heat loss mechanics and evaporation	3%	

ECF, extracellular fluid; ICF, intracellular fluid.

Africa. They need to be able to reason through safety precautions, as well as what is doable. To drop body temperature, these doctors need to advocate/educate what is available to people in remote areas, as well as what is the safest option. A tepid bath, and therefore not a cold bath, is both doable and safe. Results further indicate that heat loss mechanics and shivering thermogenesis are not understood (34). Participants resorted to instinctive reasoning and in the process disregarded the complexity of thermoregulation, thermogenesis, and heat regulation mechanics. Educators could thus explore whether medical students do have a coherent understanding of these concepts. Research has indicated that homeostatic physiological processes are particularly difficult for students to grasp, resulting in a breeding ground for misconceptions, as students have an oversimplistic understanding of the processes involved (35). Our findings with both questions probing homeostasis confirmed that, in applying causal reasoning, students focus on a particular component and disregard the complexity of the overall processes contributing to homeostatic balance. Results further showed that physiological processes, such as blood circulation, were described by their results (blood needs to slow down for effective exchange), and in doing so, participants have an unscientific understanding of the process. This potentially indicate that students resort to teleological reasoning in physiology. We take the view that if educators understand what lies behind an incorrect answer, teaching can be adjusted to ensure that misconception do not arise and survive instruction.

In this study, we have identified a range of discipline specific misunderstandings held by a substantive number of students across an entire medical program. We further explored what underlies incorrect answers to gain insight into the nature of these misunderstandings.

The empirical evidence from this study can be used to alert educators that certain common misunderstandings remain in medical education and that some students across all years hold on to specific unscientific understandings in the medical domains we have identified.

Our study has limitations. First, it is a cross-sectional study rather than a longitudinal study. The latter would have enabled us to check the persistence of particular misconceptions at the level of individual students over time. In a cross-sectional design there is the possibility, however, unlikely, that specific misconceptions disappear in individual students in 1 yr and reemerge in the next, and vice versa without being detected. Another limitation is that the eight questions from questionnaire only probed misconceptions in a limited set of domains and in itself cannot evaluate a comprehensive understanding of medical students' knowledge or lack thereof. We therefore plan to adapt and extend our questionnaire. A further limitation of the questionnaire was that it was not vetted, for example, to include a discrimination index or point biserial. We recommend that future studies should use a more comprehensive approach. We acknowledge that the wording of our questions could have led to a range of interpretations from participants, and plan to apply more rigor to ensure questions are indeed probing students' biomedical understanding without leaving room for misinterpretations.

We used a mixed methods approach and multiple raters, the latter possibly helping to overcome researcher bias in qualitative analysis. Nevertheless, other limitations of our study are *1*) that we could have missed categories of misconceptions in the data, and *2*) that the categories could in fact be further broken down into more specific groupings. Although we applied rigor to identify the common themes underlying the incorrect answers, these themes remain the interpretation of a small set of experts and can thus only serve as a guideline to begin to understand students' incorrect reasoning.

Conclusions

While the use of eight questions in a cross-sectional study cannot claim persistent and surviving misconceptions, our findings suggest that there are certain fundamental concepts that medical training falls short in teaching effectively. An important take away from this study was to identify concepts that medical students struggle to master. If these concepts are not addressed, they could potentially survive training and become robust misconceptions. Our results could inform curricular innovations to help develop better approaches to teaching these concepts to prevent biomedical misconceptions.

We encourage researchers to repeat our study in different settings to ascertain whether similar results can be found. We further recommend that educators be alerted to designing teaching and learning opportunities that actively facilitate the development of causal mental networks enabling students to understand disease in terms of general underlying biomedical structures and processes. There is a need to explore which educational methods will best address misunderstandings to prevent surviving biomedical misconceptions.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

E.B., S.M., A.A., K.B., F.C., G.G., and H.G.S. conceived and designed research; E.B., A.A,. and K.B. performed experiments; E.B., S.M., A.A., K.B., F.C., C.G., G.G., V.Z., and H.G.S. analyzed data; E.B., S.M., A.A., K.B., F.C., C.G., G.G., V.Z., and H.G.S. interpreted results of experiments; E.S.B., and S.M. prepared figures; E.B. drafted manuscript; E.B., S.M., A.A., K.B., C.G., G.G., V.Z., and H.G.S. edited and revised manuscript; E.B., S.M., A.A., K.B., F.C., C.G., G.G., V.Z., and H.G.S. approved final version of manuscript.

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