

英 語

医学部医学科・応用生物学部共同獣医学科

問 題 冊 子

注意事項

- (1) 試験開始の合図があるまで、問題冊子を開かないこと。
- (2) 問題冊子は23ページで、解答用紙は4枚である。問題冊子や解答用紙に、落丁、乱丁、印刷不鮮明のものがあつた場合は、ただちに試験監督者に申し出ること。
- (3) 受験番号は、4枚の解答用紙のそれぞれの指定箇所に丁寧に記入すること。
- (4) 問題は、**1** および **2** の2つの大問よりなる。
- (5) 解答は解答用紙の指定箇所に丁寧に記入すること。
- (6) 解答用紙は、持ち帰らないこと。
- (7) 問題冊子は、持ち帰ること。
- (8) 各大問の満点に対する配点の比率(%)を次のとおりとする。
1 は39%、**2** は61%
- (9) 設問は英文で書かれている。

Part 1

Questions 1–8 :

Read the following text on sniffer dogs and fill in the blanks (1)–(8) to complete the sentences. For each blank, you have four choices given below. Choose the best word and write A, B, C, or D in boxes 1–8 on your answer sheet.

People noticed long ago that illness had a particular smell. Hippocrates, the ancient Greek ⁽¹⁾_____, famously sniffed his patients. In the last several decades, medical research found that dogs could smell ⁽²⁾_____ such as hypertension and malaria.

The smells of disease come mostly from volatile organic compounds (VOCs). We excrete hundreds of VOCs in our sweat, breath, urine and other bodily fluids, ⁽³⁾_____ a signature smell. If we're sick, it stands to reason that our cells' metabolism changes, and so ⁽⁴⁾_____ our odor signature.

Scientists first identified cancer VOCs in 1971. But it wasn't until 1989 that someone put dogs and cancer VOCs ⁽⁵⁾_____ in an essay in *The Lancet* titled "Sniffer Dogs in the Melanoma Clinic?"

Evidence was slow to build, ⁽⁶⁾_____. Finally, in 2004, a research team in the United Kingdom conducted a study to ⁽⁷⁾_____ if dogs could detect bladder cancer from urine. After seven months of training, the dogs got it right 40 percent of the time. That may not seem amazing today, but it was statistically ⁽⁸⁾_____ and inspired others to conduct similar research.

(Adapted from Heather Millar, "The Nose Knows: Can Dogs Be Trained to Sniff Out Cancer?," *Cure*, April 18, 2017, <https://www.curetoday.com/publications/cure/2017/spring-2017/the-nose-knows-can-dogs-be-trained-to-sniff-out-cancer>)

- | | | | |
|------------------|---------------|------------------|----------------|
| 1. A. accountant | B. architect | C. skipper | D. physician |
| 2. A. methods | B. diseases | C. prescriptions | D. tissues |
| 3. A. creating | B. diagnosing | C. impairing | D. shortening |
| 4. A. is | B. has | C. does | D. should |
| 5. A. under | B. together | C. with | D. apart |
| 6. A. neither | B. seemingly | C. however | D. thus |
| 7. A. see | B. wonder | C. presuppose | D. argue |
| 8. A. immaterial | B. reversal | C. irrelevant | D. significant |

Part 2-A

Questions 9–15 :

Read the following text on teens with phones and choose from A–I the phrase which fits each blank (9)–(15). Write the correct letter in boxes 9–15 on your answer sheet. There are two extra phrases that are not necessary.

Four out of five teenagers with mobile devices keep them in their rooms overnight — and nearly a third of those bring them into their beds while sleeping — according to a study that offered new evidence that mobile devices _____ necessary for peak health. The study, _____ of 1,000 children and parents by consumer advocacy group Common Sense, _____ offered the most comprehensive picture yet of the impact of mobile devices on teen sleep patterns, which researchers have long warned can undermine cognitive functioning and mental health _____ rates. The poll also found smartphones caused _____ as many parents fear the devices are causing their teens to become “addicted.” But _____, according to researchers, concerned the round-the-clock nature of how teens use mobile devices. Many reported using their phones moments before bedtime, almost _____ and at least occasionally during the night; the main activities included _____, playing games and watching videos.

(Adapted from Craig Timberg, “Many Teens Sleep With Their Phones, Survey Finds—Just Like Their Parents,” *The Washington Post*, May 29, 2019, https://www.washingtonpost.com/business/technology/mimicking-their-parents-many-teens-sleep-with-their-phones-survey-finds/2019/05/28/1bf2ee68-8188-11e9-9a67-a687ca99fb3d_story.html)

- A. the most striking findings
- B. checking social media
- C. deadly flight accidents
- D. undermine the rest
- E. conflict within homes
- F. create unreasonable children
- G. based on a poll
- H. immediately upon rising
- I. while increasing obesity

Part 2-B

Questions 16–23 :

Read the following text on therapy animals and choose from A–J the phrase which fits each blank (16)–(23). Write the correct letter in boxes 16–23 on your answer sheet. There are two extra phrases that are not necessary.

Animals have helped humans in lots of different ways over the years. Some animals are (16) _____ who are anxious to feel calmer. They're called emotional support animals. Some animals can even become therapy animals, who are specially trained to help people in (17) _____.

An emotional support animal is an animal which provides its owner with comfort and support during stressful situations. Some people can struggle to do things like flying on a plane, or taking an exam because of (18) _____. Support animals can reassure and comfort these people, and help ease their stress.

According to Dr Christine Rhodes, a lecturer in health and social care at the University of Derby, having emotional support animals around is linked to “decreased depression” and (19) _____. Dr Rhodes said recent studies have shown that owning an animal can help relieve stress and boost (20) _____. She said: “Studies also show that interacting with animals can increase the stress-reducing hormone oxytocin and lower cortisol (stress hormone) levels, which helps us to (21) _____ and feel more relaxed.”

Despite being allowed in most places in the US, emotional support animals are not given the same (22) _____ in the UK. Some UK airlines will allow some dogs on board for emotional support, but not other animals like cats or rabbits.

Between 2017-18 United Airlines in the US saw an increase of 75 % in people (23) _____ with emotional support animals. Animals such as a turkey, miniature horse, cats and dogs have all travelled with their owners. However, some places in the US have recently started cracking down on what kinds of animals are allowed to board planes and enter public places, after someone tried to bring a peacock onto a plane, and a kangaroo into a restaurant.

(Adapted from “Therapy Animals: From Dogs to Pigs – What Are Emotional Support Animals?,” *BBC Newsround*, November 13, 2019, <https://www.bbc.co.uk/newsround/50389274>)

- A. calm down
- B. helping people
- C. legal recognition
- D. powerful engine
- E. positive emotions
- F. reduced blood pressure
- G. requesting to travel
- H. requesting to pay
- I. severe anxiety
- J. stressful situations

Part 3

Questions 24–27 :

Read sentence A, then rearrange the words and phrases in the round brackets in B to make a sentence with a similar meaning to A. In each question, there is ONE word or phrase which is not used. Then, in boxes 24–27 on your answer sheet, write the word or phrase which is not necessary to complete the sentence.

Example:

0. A : Last night Peter declared his love for Emily.

B : Peter (that / very / Emily / told / loved / he / last night) her.

The completed sentence B is “Peter told Emily last night that he loved her,” and the word “very” in the round brackets is unnecessary. So you write:

0
very

Write ONLY the unnecessary word or phrase in the boxes on your answer sheet.

24. A : There is still one week to go before we finish putting this bike together.
 B : We still (whole / assembling / week / to / have / the / since / complete) this bike.
25. A : John was very close to catching the last train for Nagoya last night.
 B : John (last / caught / mostly / train / nearly / for / the / bound) Nagoya last night.
26. A : Can you watch these bags until I finish washing my hands?
 B : Can you (my / the restroom / in / eye / on / I / am / bags / while / keep / an / seeing) ?
27. A : The day will soon come when smartphones can help us communicate with each other in English.
 B : It will (ourselves / in English / take / long / can / understood / not / we / be / make / before) with smartphones.

The examination continues on the next page.

Part 1

Questions 28–35 :

Read the following text and choose from A–I the sentence or phrase which fits each blank (28)–(35). Write the correct letter in boxes 28–35 on your answer sheet. There is one extra sentence or phrase that is not necessary.

**The Art of Medicine:
The Reflections of a Very Junior Doctor in Breaking Bad News**

Being a clinician, I appreciate that in this fast paced and ever evolving medical interface where time is of the essence, it has become unfortunately less common to witness situations that remind us that medicine is, in fact, an art. Breaking bad news is an example of this. I witnessed the art of compassion during a heart wrenching moment in this family's life and it is a memory that will stay with me throughout my career.

It was almost Christmas and I had been a qualified doctor for approximately five months. I remember being pleased that it was Friday but annoyed that ward rounds would start late as the consultant had not yet appeared. _____⁽²⁸⁾ I was to join my consultant, a specialist in Acute Stroke Medicine, in the post-anaesthetic care unit (PACU). I found my way to the PACU which often acted as a surrogate intensive care unit (ICU) in the absence of ICU beds. Being a medical rather than surgical doctor, this was unfamiliar territory and as I navigated my way around the beds full of moribund-looking patients with lines and tubes and breathing apparatuses in tow, I tried my best not to look like a lost medical student all over again. In hindsight, I doubt this newly qualified doctor was fooling anybody. The familiar face of my consultant deep in conversation with nursing staff put me back at my ease.

The patient was an elderly — woman with a large right-sided intra-cerebral haemorrhage who had come to hospital during on-call hours the preceding night. Her past medical history was significant for multiple myeloma, hypertension and ischaemic heart disease. _____⁽²⁹⁾ In stark contrast to her peri-operative neighbours, a sense of “home” had invaded the clinically white and blue surroundings. Her family had brought her a seamless beige quilt, tucked in at all sides with painful precision, and a candle flickered at her bedside. This was no longer a hospital bed. The relative darkness of the room stood at stark contrast to the sunlight

outside, and yet the sombre lighting reflected the mood perfectly.

Having listened to a detailed collateral history by way of the nursing staff, as well as painstakingly trawling through the chart for past medical information, the stroke consultant made his way towards the bedside to perform his examination. At this point in my career, I had performed examinations on live patients and had also examined patients that I would subsequently pronounce as deceased. But this was different. She was entirely unresponsive with a Glasgow Coma Score of 3, signifying the lowest possible state of consciousness and as such carrying a very poor prognosis. _____ He began by speaking to her. He squeezed her hand and introduced himself to the ears that arguably could not hear. He approached the exam with an intense tenderness that cannot be learned, as though it were his own mother who lay on the bed, and he did so despite his lack of audience. Following a number of basic yet crucial tests, he performed the doll's eye manoeuvre. This simple yet devastating bedside test involves passively rotating the patient's head from side to side in the horizontal plane, and failure of the eyes' gaze to deviate with the moving of the head, signifies brain stem damage. This lady in her 90s had indeed suffered brain stem death.

The patient's family was gathered in a nearby meeting room. They consisted of many offspring, all adult, their respective partners and the guest of honour: the patient's husband. I had been introduced as an integral part of the medical team but I felt like a fraud. Like my consultant, I had just met the patient for the first time that morning, _____ I had contributed nothing of worth. Was it for that reason that I wanted to distance myself from the "team" or did I not want to associate myself with the breaking of bad news that would come next? Had the news been good, I wonder would I have been more keen to shake their hands.

One of the daughters, I surmised she may have been the eldest, took us aside and whispered "he has moderate dementia you know, so please if you could explain things... simply...". She trailed off and looked down at the floor. She also knew we would be the bearers of bad news. My consultant, careful to make eye contact with everyone in the room in turn, made sure to make the patient's husband and next of kin his number one focus. He introduced himself and his role, slowly, and paused. A clock on the wall ticked loudly. _____ Time was of no consequence. But the husband needed no such pause to intervene, as he swiftly recounted a tale of how he and his wife had been walking, him supporting her with his arm wrapped around her side, and about how she suddenly gave way.

“She slipped through my fingers”, he cried, “I have to accept responsibility for this, before God, this was my fault!”

The stroke consultant listened. He listened to the whole thing in painstaking detail. When it was his turn again, he reassured the husband that this bleed was spontaneous and had simply happened,⁽³³⁾_____ The man would not let go of his blame and the sons and daughters all joined the crusade to put an end to his misguided perceptions. “She just went from under me and I tried to catch her but I just couldn’t get to her in time”, he sobbed, and it took every fibre in my body not to sob with him. I remember not being able to look at him, and my gaze was transfixed on the mahogany table in front of me. And I was embarrassed to have tears clouding my vision. This went on and on and on, in circles, over and over again for almost one hour. The man’s children joined in, attempting to reassure, repeating the words of the doctor, telling their aged father that it was okay, and that no blame rested with him. Each one of them carrying the weight of this bad news pertaining to their mother yet trying to show a brave face. Each one of them reassuring their father, as he had no doubt done for them countless times when they were young. He needed somebody to blame, he needed a reason that this had happened, because as we all want to believe “bad things don’t happen to good people”. My consultant listened patiently at every turn and, once the sobbing began again,⁽³⁴⁾_____ Never before had I witnessed such incredible patience from a senior doctor. “Mr. X, I am telling you now, man to man, and as a doctor, that NOTHING you did caused this. There was NOTHING you could have done. Now I want you to repeat that back to me”. The man, finally, through his tears, acknowledged that the doctor was looking him in the eye, “man to man”, and saying that it was not his fault.

I’ll never know whether the man with moderate dementia was able to retain that this was a primary spontaneous intra-cerebral haemorrhage in a patient who was already receiving palliative care for end stage multiple myeloma. But what I do know is that I witnessed a particular kind of art that day,⁽³⁵⁾_____

(Adapted from Toni Anderson, “The Art of Medicine: The Reflections of a Very Junior Doctor in Breaking Bad News,” *Patient Education and Counseling* 103 (2020): 670-671.)

- A. She was intubated and ventilated and looked tiny amongst all the machinery that kept her ticking.
- B. he would grasp the man's hand and start from the beginning.
- C. only I had merely witnessed the clinical examination.
- D. and that it was not secondary to a traumatic fall.
- E. No sooner had these thoughts reached my consciousness, did the call arrive.
- F. and I know for a fact that it will stay with me forever.
- G. Nevertheless, he approached the patient in the exact same manner I had seen him do so many times before.
- H. I should have been more informed when I had gone to see the patient's family.
- I. He then explained, in non-medical jargon, that the patient had suffered a large and unexpected bleed on the brain, and paused.

Part 2

Questions 36–45 :

Read this text below and fill in the blanks (36)–(45) to match the responses. For the blanks, you have 12 choices given below. For each question (Q), choose the best answer (A) by writing A to L in boxes 36–45 on your answer sheet. There are two extra answers that are not necessary.

Interview with a Veterinarian

Dr Joanna Paul is a small animal veterinarian from Melbourne, Australia. After graduating with honours from the University of Melbourne in 2006, she began her veterinary career in an animal shelter. This valuable experience gave her not only strong foundations in medicine and surgery, but a determination to work in partnership with pet owners to ensure their pets stay as happy and healthy as possible, so that they can always be much loved members of the family. Over several years in private practice she has seen countless examples of the beautiful bond that can be shared between a pet and its person, and has had the privilege of being involved in keeping that bond strong. Joanna divides her time between two gorgeous dogs of her own, a toddler, a baby, work, study, and her own website for pet parents.

- Q : What made you want to become a veterinarian? A : (36) _____
- Q : How would you describe what you do? A : (37) _____
- Q : What is a typical day for Joanna as a veterinarian? A : (38) _____
- Q : What do you like about what you do? A : (39) _____
- Q : What do you dislike? A : (40) _____
- Q : What is most challenging about what you do? A : (41) _____
- Q : What advice would you offer someone considering this career? A : (42) _____
- Q : What is a common misconception people have about being a veterinarian? A : (43) _____
- Q : Who was the biggest influence on your career choice? A : (44) _____
- Q : What is the most preventable problem you have seen in your career? A : (45) _____

- A. Although I'm lucky enough not to see it often, the thing I do not like most is neglect. Most people who bring their pet into a vet clinic have their best interests at heart, but occasionally I see things that make me feel very sad. In these cases I will do everything in my power to advocate for the animal.
- B. As most people know, our healthcare system in this country is a mess. I face many areas of red tape that affects the delivery of patient care. In addition, patients taking responsibility for their own health is a problem. Many patients feel they do not have to make lifestyle changes (example: lose weight, quit smoking, or using drugs) to get better. They keep doing these things, which makes their disease worse. It can be frustrating at times.
- C. Certainly, my wonderful, supportive parents always had faith in my abilities and encouraged me to follow my dreams. Then there was my uncle Doug, the country vet who showed me what it was really like. Funnily enough, and I guess this may speak volumes about my stubborn character, one of the influences I'll never forget was a GP (general practitioner). I was probably about 20 at the time and had been pretty unwell for some time with a viral infection, and in his words, had 'lost my spark'. He looked at me kindly and said, 'Getting into veterinary science is hard. I don't think I could get into medical school if I had to these days, it's just so much harder now. Maybe you should consider something else...' He truly was just suggesting that I was putting too much pressure on myself and should stop and regroup. But those words lit a fire in my belly and I knew I had to prove him wrong. And I did.
- D. Do your research, because you need to know what you're getting yourself into. Do it for the right reasons. Just loving animals isn't enough. You need to have an interest in science (vets even have to do maths!), a desire to continually learn new knowledge and skills throughout your career, and a strong work ethic. To start with, it's a hard road just to become a vet. Veterinary science is one of the most expensive courses to study in Australia and it's pretty difficult to get into (it took me three years of university to get accepted). Then you find yourself in a job with huge responsibility, long hours, and pretty average financial compensation. According to the Australian Veterinary Association, a vet who has just graduated will earn around \$45,000 per year, and most can expect to earn around \$76,000 at the peak of their career. You really have to be passionate about it.

- E. I can't tell you how many times someone has said to me, 'Oh I wanted to be a vet growing up, but I really love animals and couldn't stand putting them to sleep...' Euthanasia is certainly part and parcel of being a vet. The thing is, gently and quietly ending the suffering of an old and unwell pet as he or she lays peacefully in their owner's arms is not something I feel any guilt about, and in fact I see it as a privilege to be able to offer them this one final act of kindness. But that doesn't mean it's easy or that I'm made of stone. I'm sure a keen observer would be able to see the slight tremble of my hands as I deliver the drug into a vein, or hear the sadness in my voice as I offer my genuine, heartfelt condolences for what may be the third or fourth time that day. Protecting myself from this isn't something I've entirely perfected, and I suspect neither have the many, many vets out there who suffer from compassion fatigue and burn out, and this leads into my answer to the next question.
- F. I see obesity day in and day out. Admittedly some dogs are much greedier than others, but it's up to us as owners to be responsible and ensure they get great nutrition and the right amount to eat. Some pets have a legitimate medical reason for an inability to lose weight, such as an under-active thyroid, but there are usually other symptoms, and these cases are by far the minority. Just as with people, obesity in pets predisposes to many other diseases, such as diabetes, cardiovascular disease, and osteoarthritis. It also decreases quality of life and shortens the lifespan, and let's be honest, we all want our pets to be with us, happy and healthy, for as long as possible.
- G. New acquaintances would usually be fairly predictable in their response to my admission of being a vet. The most common thing people would say was 'Oh, so you put your arm up cows' bums'. Well, no. I mean, only if it's a really cold day.

- H.** One of the great (and challenging) things about being a vet is that there really is no typical day. Sure, we see some things more commonly than others, but when we walk into that consulting room, the possibilities are almost endless. A typical day usually includes a large variety of furry (and sometimes feathery or scaly) patients with their owners. Some are sick and some are hurt. Some bound in with a big goofy grin on their face, anticipating pats and treats, while others are a bit more cautious or downright scared. With some patience and a gentle touch the frightened ones usually manage ok. I do a few hours of surgery most days. Some days I eat lunch. Some days I don't. I get to spend my time at work practicing medicine, surgery, radiology, dentistry, laboratory work, nutrition, animal behaviour, and a whole lot more. One thing I can say about being a vet is that it's not boring!
- I.** Thankfully I often see healthy pets for routine vaccinations and annual health checks. This is fantastic, as good preventative care catches things early when they do go wrong, leading to a much better outcome for pet and owner. I think this has improved a lot over the years, as people have begun to realise how important regular check-ups are for monitoring a pet's health. At every health check, pets get a full, nose-to-tail examination, sometimes picking up things that the owner hasn't noticed yet. In appropriate cases we do blood tests as well, as they are our best indicator of what's going on inside the pet.
- J.** Veterinary science, as the name suggests, is a science. The nerd in me loves that I get to know all sorts of really interesting sciencey things, but not only that, I have the privilege and honour of being able to use that knowledge to help pets and their people. And this is the part I really like. The human-animal bond. I love the special relationships people have with their pets. I love being involved in preserving those relationships and keeping them strong, by maintaining the pet's health or helping with their behaviour. Pets enrich our lives in so many ways, being there for us through the good times and the bad. They don't judge us when we're having a bad day. We can just be ourselves with them, share our secrets with them, and love them without ever fearing not being loved back. It's for these reasons and many more that I find my job incredibly rewarding every day.

K. Well, oddly, when I was a kid I wanted to fly planes... I was totally fascinated about how those huge, heavy things lifted up into the sky, and I thought it would be awesome to spend my work days travelling around the world. Yup, that's right, not exactly animal related! I was never a particularly organised student, and in year 9 when it came time to do my required two weeks of 'work experience' I discovered I had nothing planned. During a quick brainstorming session with my mum she said, 'How about your uncle Doug? You could stay up there with them and do your work experience in the vet clinic.' In retrospect I think maybe she had the ulterior motive of getting rid of my teenage self for a couple of weeks, but at the time I thought, 'Yeah, mum, that's a great idea!' So off I went, gumboots packed, into the countryside to experience rural veterinary practice first hand. I had no idea what I was in for! I remember one moment vividly, as I was standing next to a cow who was having some surgery for 'cancer eye'. I was concentrating intently on the fascinating procedure when I felt a fine warm spray on my face. I must have recoiled a bit, because Doug glanced over momentarily, and with a wry grin said, 'You've been christened', handing me a towel. Yep, got a little too close to the surgical field and got more than I'd bargained for from a tiny nicked blood vessel. We drove around in his car full of veterinary paraphernalia from cow to dog to bunny to horse, occasionally stopping for a bite to eat or to chat with a farmer — and I loved every minute. This was when I knew I would be a vet.

L. Well, the Oxford dictionary defines a veterinarian as a 'person qualified to treat diseased or injured animals'. I'd like to respectfully tell them they're wrong. Or at least they're not telling the full story. Veterinary medicine is just as much about prevention as treatment, and I see preventing disease or injury as just as important a part of my job as treatment. Also, we don't walk into a consulting room to find just a dog or a cat sitting alone, maybe reading a magazine and waiting for their appointment. Our job involves working with pet owners just as much (or maybe more so) as it involves their furry friends.

(Adapted from Joanna Paul, "Interview with a Veterinarian," *My Pet Warehouse*, May 19, 2014, <https://www.mypetwarehouse.com.au/my-pet-blog/expert-pet-advice/interview-with-a-veterinarian>)

Part 3

Questions 46–60 :

Read the following text and answer the questions that follow. Write the correct letter (for example, A, B, C, ...) in boxes 46–60 on your answer sheet.

Researchers Develop ‘Poisoned Arrow’ to Defeat Antibiotic-resistant Bacteria

Poison is lethal all on its own — as are arrows — but their combination is greater than the sum of their parts. A weapon that simultaneously attacks from within and without can take down even the strongest opponents, from E. coli to MRSA (methicillin resistant *Staphylococcus aureus*).

A team of Princeton researchers reported today in the journal *Cell* that they have found a compound, SCH-79797, that can simultaneously puncture bacterial walls and destroy folate within their cells — while being immune to antibiotic resistance.

- (A) Bacterial infections come in two flavors — Gram-positive and Gram-negative — named for the scientist who discovered how to distinguish them. The key difference is that Gram-negative bacteria are armored with an outer layer that shrugs off most antibiotics. _____ no new classes of Gram-negative-killing drugs have come to market in nearly 30 years.
- (B) “This is the first antibiotic that can target Gram-positives and Gram-negatives without resistance,” said Zemer Gitai, Princeton’s Edwin Grant Conklin Professor of Biology and the senior author on the paper. “From a ‘Why it’s useful’ perspective, that’s the crux. _____ what we’re most excited about as scientists is something we’ve discovered about how this antibiotic works — attacking via two different mechanisms within one molecule — that we are hoping is generalizable, leading to better antibiotics — and new types of antibiotics — in the future.”

(C) The greatest weakness of antibiotics is that bacteria evolve quickly to resist them, but the Princeton team found that even with extraordinary effort, they were unable to generate any resistance to this compound. “This is really promising, which is why we call the compound’s derivatives ‘Irresistin,’” Gitai said.

(D) It’s the holy grail of antibiotics research: an antibiotic that is effective against diseases and immune to resistance ⁽⁵²⁾ _____ being safe in humans (unlike rubbing alcohol or bleach, which are irresistibly fatal to human cells and bacterial cells alike). ⁽⁴⁸⁾

(E) For an antibiotics researcher, this is like discovering the formula to convert lead to gold, or riding a unicorn — something everyone wants but no one really believes exists, said James Martin, a 2019 Ph.D. graduate who spent most of his graduate career working on this compound. “My first challenge was convincing the lab that it was true,” he said.

But irresistibility is a double-edged sword. Typical antibiotics research involves finding a molecule that can kill bacteria, breeding multiple generations ⁽⁵⁶⁾ _____ the bacteria evolve resistance to it, looking at how exactly that resistance operates, and using that to reverse-engineer how the molecule works in the first place. ⁽⁴⁹⁾

But since SCH-79797 is irresistible, the researchers had nothing to reverse engineer from.

“This was a real technical feat,” said Gitai. “No resistance is a plus from the usage side, but a challenge from the scientific side.”

The research team had two huge technical challenges: Trying to prove the negative — that nothing can resist SCH-79797 — and then figuring out how the compound works.

To prove its resistance to resistance, Martin tried endless different assays and methods, none of which revealed a particle of resistance to the SCH compound. Finally, he tried brute force: for 25 days, he “serially passaged” it, meaning that he exposed bacteria to the drug over and over and over again. Since bacteria take about 20 minutes per generation, the germs had millions of chances to evolve resistance — but they didn’t. To check their methods, the team also serially passaged other antibiotics (novobiocin, trimethoprim, nisin and gentamicin) and quickly bred resistance to them.

Proving a negative is technically impossible so the researchers use phrases like ⁽⁵⁷⁾ “undetectably-low resistance frequencies” and “no detectable resistance,” but the upshot is that SCH-79797 is irresistible — hence the name they gave to its derivative compounds, Irresistin.

They also tried using it against bacterial species that are known for their antibiotic resistance, including *Neisseria gonorrhoeae*, which is on the top 5 list of urgent threats published by the Center for Disease Control and Prevention.

“Gonorrhea poses a huge problem with respect to multidrug resistance,” said Gitai. “We’ve run out of drugs for gonorrhea. With most common infections, the old-school generic drugs still work. When I got strep throat two years ago, I was given penicillin-G — the penicillin discovered in 1928! But for *Neisseria gonorrhoeae*, the standard strains that are circulating on college campuses are super drug resistant. What used to be the last line of defense, the break-glass-in-case-of-emergency drug for ⁽⁵⁸⁾ *Neisseria*, is now the front-line standard of care, and there really is no break-glass backup anymore. That’s why this one is a particularly important and exciting one that we could cure.”

The researchers even got a sample of the most resistant strain of *Neisseria gonorrhoeae* from the vaults of the World Health Organization — a strain that is resistant to every known antibiotic — and “Joe showed that our guy still killed this strain,” Gitai said, referring to Joseph Sheehan, a co-first-author on the paper and the lab manager for the Gitai Lab. “We’re pretty excited about that.”

The poison-tipped arrow

(F) Without resistance to reverse engineer from, the researchers spent years trying to determine how the molecule kills bacteria, using a huge array of approaches, from classical techniques that have been around since the discovery of penicillin through to cutting-edge technology.

Martin called it the “everything but the kitchen sink” approach, and it eventually revealed that SCH-79797 uses two distinct mechanisms within one molecule, like an arrow coated in ⁽⁵⁹⁾ poison.

(G) “The arrow has to be sharp to get the poison in, but the poison has to kill on its own, too,” said Benjamin Bratton, an associate research scholar in molecular biology and a lecturer in the Lewis Sigler Institute for Integrative Genomics, who is the other co-first-author.

(H) The arrow targets the outer membrane — piercing through even the thick armor of Gram-negative bacteria — while the poison shreds folate, a fundamental building block of RNA and DNA. The researchers were surprised to discover that the two mechanisms operate synergistically, combining into more than a sum of their parts.

(I) “⁽⁵⁰⁾_____ you just take those two halves — there are commercially available drugs that can attack either of those two pathways — and you just dump them into the same pot, that doesn’t kill as effectively as our molecule, which has them joined together on the same body,” Bratton said.

(J) There was one problem: The original SCH-79797 killed human cells and bacterial cells at roughly similar levels, meaning that as a medicine, it ran the risk of killing the patient before it killed the infection. The derivative Irresistin-16 fixed that. It is nearly 1,000 times more potent against bacteria than human cells, making it a promising antibiotic. As a final confirmation, the researchers demonstrated that they could use Irresistin-16 to cure mice infected with *Neisseria gonorrhoeae*.

New hope

⁽⁶⁰⁾This poisoned arrow paradigm could revolutionize antibiotic development, said K.C. Huang, a professor of bioengineering and of microbiology and immunology at Stanford University who was not involved in this research.

“The thing that can’t be overstated is that antibiotic research has stalled over a period of many decades,” Huang said. “It’s rare to find a scientific field which is so well studied and yet so in need of a jolt of new energy.”

The poisoned arrow, the synergy between two mechanisms of attacking bacteria, “can provide exactly that,” said Huang, who was a postdoctoral researcher at Princeton from 2004 to 2008. “This compound is already so useful by itself, but also, people can start designing

new compounds that are inspired by this. That's what has made this work so exciting."

In particular, each of the two mechanisms—the arrow and the poison—targets processes that are present in both bacteria and in mammalian cells. Folate is vital to mammals (which is why pregnant women are told to take folic acid), and of course both bacteria and mammalian cells have membranes. "This gives us a lot of hope, because there's a whole class of targets that people have largely neglected because they thought, 'Oh, I can't target that, because then I would just kill the human as well,'" Gitai said.

"A study like this says that we can go back and revisit what we thought were the limitations on our development of new antibiotics," Huang said. "From a societal point of view, it's fantastic to have new hope for the future."

(Adapted from Princeton University, "Researchers develop 'poisoned arrow' to defeat antibiotic-resistant bacteria," *Phys.org*, June 3, 2020, <https://phys.org/news/2020-06-poisoned-arrow-defeat-antibiotic-resistant-bacteria.html>)

Questions 46–50 :

From the list of words, select the best expression to complete (46)–(50). Write the correct letter A–G in boxes 46–50 on your answer sheet. Each expression can only be used once. There are two extra words.

- A. while
- B. In fact,
- C. Because
- D. until
- E. If
- F. during
- G. But

Questions 51–53 :

Based on the context clues provided in the sentence or the paragraph, choose the definition that is closest in meaning to the underlined words.

(51) **lethal**

- A. serious
- B. dangerous
- C. deadly
- D. rare

(52) **holy grail**

- A. a gift from heaven
- B. a goal that is sought after for its great significance
- C. a religious path to enlightenment
- D. something you come across by accident

(53) **cutting-edge**

- A. sharp
- B. risky
- C. urgent
- D. advanced

Question 54 :

What does the author want to explain by using the phrase their combination is ⁽⁵⁴⁾ greater than the sum of their parts?

- A. A poisoned arrow is more than twice as effective as a non-poisoned arrow.
- B. SCH-79797 is even more effective than a combination of two different drugs, one that punctures bacterial walls and the other that destroys folate, separately used.
- C. Irresistin is made from two effective drugs, resulting in a more powerful medicine than the two original drugs.
- D. Scientists can produce a drug that is more effective than other drugs by combining poison and arrows.

Question 55 :

Choose from paragraphs (A) – (E) the paragraph that best explains the meaning of being immune to antibiotic resistance.

(55)

Question 56 :

The phrase irresistibility is a double-edged sword means that

(56)

- A. If antibiotics do not become resistant, the researchers cannot reverse-engineer them to see how they work.
- B. Irresistibility is desired because it defeats bacteria on two different levels, piercing the outer membrane and shredding folate.
- C. Antibiotics research involves finding a molecule that can kill bacteria, but also breeding it until it becomes resistant.
- D. To find irresistible antibiotics, researchers need to solve two challenges at the same time, find out how resistance operates and find a drug that does not become resistant.

Question 57 :

Proving a negative is technically impossible means in this context,

(57)

- A. that so far it has not been possible to prove that SCH-79797 has negative effects.
- B. that the technology is not advanced enough yet to prove its negative effects.
- C. that even though resistance has not been detected so far, it does not mean that resistance will never occur.
- D. that resistance is at such a low level that it cannot be detected.

Question 58 :

What does the underlined sentence below say about the drugs for *Neisseria gonorrhoeae*?

⁽⁵⁸⁾ “What used to be the last line of defense, the break-glass-in-case-of-emergency drug for *Neisseria*, is now the front-line standard of care, and there really is no break-glass backup anymore.”

- A. What used to be the least effective drug to treat this disease is now the most used one.
- B. There is only one drug that can successfully treat this disease, but in the past doctors thought it was not safe.
- C. There used to be a drug that was only used for the most serious cases, but now it is the only drug that is effective.
- D. There is a drug that treats this disease more effectively than other drugs, which caused all the other drugs to become obsolete.

Question 59 :

Choose from the paragraphs starting with (F) – (J) the paragraph in which the meaning of the “everything but the kitchen sink” approach is best explained.

⁽⁵⁹⁾

Question 60 :

K.C. Huang thinks “This poisoned arrow paradigm could revolutionize antibiotic development.”

⁽⁶⁰⁾

Choose the sentence that does NOT reflect his opinion.

- A. Antibiotic research has not seen any successes for a very long time, and this discovery will give this field of research a boost.
- B. The successful idea of combining methods to attack bacteria gives inspiration to researchers to look for new areas for synergy.
- C. Researchers thought they had reached the limitations on the development of antibiotics, but this research has reset the boundaries.
- D. The synergy between two mechanisms of attacking bacteria will inspire new interest in a scientific field that has not been studied for decades.