ANGLAIS

2007

1. Unseen reading comprehension : /30

Read the article, *Bubbling under, The Economist 10th April 2007* and choose the answer that **best** completes each sentence according to the information given in the text.
There is only **ONE** answer for each question.

1. Hoelscher's research aim is...

a) to improve understanding of how blood clots form.
b) to develop a drug that eliminates air bubbles.
c) to use gas bubbles to break down blood clots.
d) to track blood circulation in the brain.

2. In this technique ultrasound is used...

a) to identify the precise location of a stroke.
b) to help gas bubbles to reduce the effect of a blood clot.
c) to stop gas bubbles from absorbing a blood clot.
d) to measure the gas bubbles in the blood vessels.

3. This technique...

a) will soon be tested in San Diego.
b) will soon be available for use by paramedics.
c) is the first medical use of gas bubbles.
d) Is the first time gas bubbles have been used with ultrasound.

4. Microbubbles...

a) are composed of air.
b) are smaller than five microns.
c) have a shell-like surface.
d) All of the above.

5. The tiniest micro-bubbles can...

a) become trapped in the lining of blood vessels.
b) move through the blood-brain barrier.
c) protect the brain from dangerous substances.
d) All of the above.

6. Micro-bubble drugs would be able to reach specific organ targets because ...

a) antibodies can be placed on their surface.
b) they have a fatty surface containing target-specific molecules.
c) Antibodies on the bubbles can be made to link only with specific proteins.
d) All of the above.

7. Borden and Dayton are working on using gas bubbles...

a) to deliver drugs.
b) to treat stroke.
c) to attach antibodies to fatty surfaces.
d) to develop a new drug called biotin.

8. In the rat experiments ultrasound was used to...

a) monitor the progression of bubbles in the rats.
b) to modify the surface of the bubble once it reached a specific location.
c) to prevent the bubbles from sticking to a precise location.
d) to keep biotin hidden from the immune system.

9. The researchers were also able to...

a) control the speed of the bubbles.
b) direct the bubbles towards a target.
c) make the bubbles adhere firmly to specific targets.
d) All of the above.

10. The main therapeutic application from this technology will be...

a) new types of antibody stimulating drugs for treating cancer.
b) a means of delivering small drug doses precisely with fewer side-effects.
c) safe gene therapy using small pieces of DNA.
d) preventing the radiation damage in cancer patients.

11. Research in this field...

a) has only been of interest to university laboratories.
b) will perhaps attract interest from the private sector.
c) has already attracted interest in the private sector.
d) has only been carried out by the private sector.

12. Nanotrope and Targeson are interested in ...

a) developing bubbles for a clotbusting drug.
b) devising a high speed drug manufacturing process.
c) making a bubble which can be adapted to deliver any type of drug.
d) All of the above.

13. What problems which need to be solved before bubble therapy can be used?

a) drug dosage, level of ultrasound used, bubble size.
b) bubble size, brain haemorrhage, drug dosage.
c) level of ultrasound used, bubble size, blood vessel damage.
d) drug dosage, ultrasound dose, type of gas in bubble.

14. What is the main advantage of bubble therapy?

a) It is not an invasive treatment.
b) It is a safe combination of ultrasound and drugs.
c) It allows the drug to be directed and confined to a specific location.
d) It allows you to treat the whole body without side-effects.

15. In general, the aim of this article is to...

a) show that bubble therapy will replace commonly used drugs.
b) present research that could lead to new types of drugs.
c) give results of a trial of a new blood-clot treatment protocol.
d) explain how bubbles can be injected into the body.

Bubbling under

Apr 10th 2007,From Economist.com
Microbubbles: how to treat disease by putting bubbles in the bloodstream

THILO HOELSCHER, a neurologist at the University of California, San Diego, is a man with a plan. His plan is to deal with strokes by blowing bubbles at them. The bubbles in question would be small enough to inject into blood vessels leading to the affected part of the brain. When they got to the blood clot that caused the stroke, they would be jiggled into action by the application of ultrasound. The result would be a zillion tiny jackhammers chipping away at the clot before it had had a chance to cause too much permanent damage.

Whether Dr Hoelscher's plan will work remains to be seen. But it should not take long to find out. A feasibility study, in which some of San Diego's ambulances will be equipped with vials of pre-generated bubbles and special ultrasonic zappers will start before the end of the year. Whether it works or not, though, it is but one example of a new idea in medicine. This is to use tiny bubbles of gas not merely to highlight organs during ultrasonic scanning, as has been done for several years already, but also as a form of treatment.

Microbubbles are not any old bubbles. They contain not air but a chemically stable gas such as perfluoropropane. This gas is encapsulated in a fatty shell—the result being somewhat like a small balloon. A very small one. Even the largest microbubbles under investigation for medical use are only five microns across, less than the diameter of a red blood cell. More advanced bubbles are only a few hundred nanometres across and can move easily through the lining of a blood vessel. They may also, crucially, be able to cross the blood-brain barrier, a tightly sealed layer of cells that protects the brain from dangerous chemicals, including many drugs. Put such a drug in the surface layer of a microbubble and you might be able to smuggle it into the brain.

Having got itself into the brain (or anywhere else), the structure of a microbubble can also be employed to allow it to find a specific target within the organ in question. That is because the fatty layer can have target-specific molecules, such as antibodies that link up with proteins found in only one type of cell, included in it.

This kind of approach is being tested by Mark Borden and Paul Dayton, who work at another of the University of California's campuses, in Davis. They have demonstrated in rats that bubbles which have an appropriate outer layer can be equipped with molecules of biotin (a harmless chemical that likes to stick to proteins) hidden under the surface. Although biotin is not a target-specific molecule, the fact it is hidden means it cannot stick to anything inappropriate. However, by using an ultrasonic technique similar to the one employed routinely to look at bubbles in human patients during scanning, Dr Borden and Dr Dayton are able to tweak the coatings of their experimental bubbles when they arrive at the target. That reveals the biotin and makes the bubbles stick.

Indeed, the two researchers can do more. They can use their sound waves to steer bubbles towards a target as though those bubbles were surfing a wave in the sea. Moreover, they can slow the bubbles down when they arrive where they are wanted. Once the bubbles have stuck good and fast to their targets, the researchers can then turn up the ultrasound and burst them, releasing their payloads precisely where they can do most good. The result is smaller, better-aimed doses that should bring fewer risks of side effects.

In principle, such payloads could be traditional small-molecule drugs such as those used for cancer chemotherapy. They could be therapeutic proteins such as antibodies. They could be radioactive isotopes designed for highly local radiotherapy. They could even be pieces of DNA intended as gene therapy.

Such work, of course, is not confined to the academy. ImaRx Therapeutics of Tucson, Arizona, has just begun a trial of its own bubble-based stroke therapy, which it is branding as SonoLysis. The bubbles are being tested in conjunction with an established clot-buster called tPA. Meanwhile, two other American firms, Nanotrope and Targeson, are working on ways of making customised bubbles to order by forcing an emulsion of water and oil combined with whatever therapeutic agent is desired through a narrow plastic nozzle at high speed.

Bubble therapy is certainly not yet reliable. Safe doses of sound waves, the best size for the bubbles and the amount of drug each should carry have all to be worked out. At least one trial, run by Michael Daffertshofer of the University of Mannheim, in Germany, had to be stopped because the researchers found out that the ultrasound they were using actually caused brain haemorrhages. Nevertheless, if safe combinations of bubbles and ultrasound can be worked out, blowing bubbles at diseases could be a clever way to tackle local problems without subjecting the whole of a patient's body to treatment it does not need.

2. Written Expression (/30). Create a paragraph from the material below. Make necessary changes: verbs (tense + active/passive form), other grammatical changes (i.e. pronouns—object/possessive pronoun). Add articles, prepositions, punctuation, etc. when necessary. The first sentence has been done for you.

Percy Lavon Julian: The Treatment of Glaucoma

1. Millions/people/owe/they/eyesight/Percy Julian/African-American chemist/who/transcend/racial/ bias/revolutionize/treatment/glaucoma
2. Born/Alabama/1899/Julian/bar/from/college preparatory program/because/he/race.
3. Nonetheless/he/excel/academically/gain/admittance/DePauw University/Indiana.
4. After/earn/he/doctorate//University/Vienna/Austria/Julian/return/DePauw.
5. 1935/he/synthesize/physostigmine/natural/substance/use/reduce/pressure/eyeball/cause/by/glaucoma/which/can/ lead/blindness.
6. Breakthrough/cut/cost/drug/from/hundreds/dollars/to/few/cents/drop.
7. Treatment/become/widely/available/earn/Julian/worldwide/acclaim.
8. When/DePauw/decline/appoint/he/to/its/faculty/Julian/leave/academia/join/Glidden Company.
9. There/he/use/he/knowledge/chemistry/make/variety/products/from/soybeans/fire-fighting/foams/use/during/World War II.
10. 1948/he/developed/new/way/synthesize/hydrocortisone/which/still/use/treat/rheumatoid/arthritis.
11. 1953/he/establish/Julian/Laboratories/successful/ enterprise/that/he/sell/for/more/2 million dollars/1961.
12. Julian/continue/he/private/research/studies/until/he/death/April 19/1975.

Millions of people owe their eyesight to Percy Julian, the African-American chemist who transcended racial bias to revolutionize the treatment of glaucoma.

TSVP

3. Gap fill text. Complete each blank with an appropriate word. Write your answers in the space provided below. (/15)

National Institute of Neurological Disorders and Stroke
What is Chronic Pain?

While acute pain is a normal __1__ triggered in the nervous system to alert you to possible injury and the need to take care of yourself, chronic pain is different. Chronic pain persists. Pain signals keep firing in the nervous system for weeks, months, even years. There may have been an initial mishap -- sprained back, serious infection, or there may be an ongoing cause of pain -- arthritis, cancer, ear infection, but some people suffer chronic pain in the __2__ of any past injury or evidence of body damage. Many chronic pain conditions __3__ older adults. Common chronic pain complaints include headache, low back pain, cancer pain, arthritis pain, neurogenic pain (pain resulting from damage to the peripheral nerves or to the __4__ nervous system itself), psychogenic pain (pain not due to past disease or injury or any visible sign of damage inside or outside the nervous system).

Is there any treatment?
Medications, acupuncture, local electrical stimulation, and brain stimulation, as well as surgery, are __5__ treatments for chronic pain. Some physicians use placebos, which in some cases has resulted in a __6__ or elimination of pain. Psychotherapy, relaxation and medication therapies, biofeedback, and behavior modification may also be __7__ to treat chronic pain.

What is the prognosis?
Many people with chronic pain can be __8__ if they understand all the __9__ of pain and the many and varied steps that can be taken to undo what chronic pain has done. Scientists believe that advances in neuroscience will __10__ to more and better treatments for chronic pain in the years to come.

What research is being done?
Clinical investigators have __11__ chronic pain patients and found that they often have lower-than-normal levels of endorphins in their spinal fluid. Investigations of acupuncture include wiring the needles to stimulate __12__ endings electrically (electroacupuncture), which some researchers believe activates endorphin systems. Other experiments with acupuncture have __13__ that there are higher levels of endorphins in cerebrospinal fluid following acupuncture. Investigators are __14__ the effect of stress on the experience of chronic pain. Chemists are synthesizing new analgesics and discovering painkilling virtues in drugs not normally __15__ for pain.

1.	4.	7.	10.	13.
2.	5.	8.	11.	14.
3.	6.	9.	12.	15.

Heparin Scare: Deaths from Tainted Blood-Thinner Spur Race for Safe Replacement

As health inspectors probe nearly 100 deaths tied to contaminated heparin, researchers develop safer version in the lab

Blood thinners made from the complex carbohydrate heparin have been routinely used in the U.S. since the 1930s to keep veins, arteries and lungs clear of potentially fatal clots and to reduce the amount of time that kidney failure patients spend on dialysis machines. These drugs are so popular that there is not enough heparin—the active pharmaceutical ingredient (primarily derived from pig intestines) that enables these blood thinners to stop or prevent blood from clotting during medical procedures and treatments—to meet the daily U.S. demand of 300,000-plus doses. To make up the difference, U.S. drug makers purchase the majority of the heparin used in their products from China.

It's unlikely that many patients considered the source of the drug until earlier this year, when doctors began reporting hundreds cases of severe side effects (including dangerously low blood pressure) attributed to contaminated batches at U.S. hospitals and clinics around the country. The U.S. Food and Drug Administration (FDA) has cited 81 deaths as a result of the contamination and continues to investigate whether the tainted meds were responsible for others.

In the wake of the deaths, the FDA launched an investigation to pinpoint the source of contamination, which it traced to Changzhou SPL Company, Ltd., based in China that supplied Wisconsin-based Scientific Protein Laboratories, LLC, (SPL) with the heparin it sold to companies such as Baxter International, Inc., in Deerfield, Ill., for that company to use in its blood-thinner products.

The incident added to fear about the safety of products made in China first raised last year when the industrial poison melamine was found in pet food that sickened and killed hundreds of U.S. cats and dogs. Melamine was also later found in dairy products, including baby formula made in China, blamed for sickening thousands of infants and killing four.

The heparin contamination was particularly disturbing, because the contaminated blood thinners passed through several layers of supposed screening. When the tainted drugs were discovered, Baxter, the supplier of 50 percent of heparin in the U.S. market, recalled nearly all of its doses (purchased from SPL). The FDA, which had since December been investigating complaints related to heparin products, tapped the expertise of several groups of scientists to find the nature and the source of the contamination by March and has since been working to tighten its screening of heparin imports from China, which supplies 70 percent of the heparin used in blood thinners worldwide. (The European Union, the U.S., Canada and Brazil supply nearly all of the rest.) The agency's investigation and efforts to find more effective ways of detecting contaminants is ongoing.

In an effort to prevent future scares, scientists are trying to develop a safer, more effective synthetic form of heparin that could be made in U.S. labs, thereby negating the need for purchasing possibly contaminated ingredients from China or other countries lacking stiff safety regs. Robert Linhardt, a professor of biology, chemistry and chemical engineering at Rensselaer Polytechnic Institute in Troy, N.Y., in February received a phone call that validated his five-year quest to develop heparin in the lab.

The crisis begins

The Missouri Department of Health and Senior Services first notified the U.S. Centers for Disease Control and Prevention (CDC) of a potential heparin problem in early January. Alexis Elward, an internist specializing in infectious disease at Saint Louis Children's Hospital, had alerted the department that some of her pediatric dialysis patients had suffered serious allergic reactions (including angioedema, shortness of breath, nausea, vomiting, diarrhea and abdominal pain) and, in some cases, dangerously low blood pressure after they took heparin-based blood thinners (used to prevent clots when waste is being filtered from the blood of patients whose own kidneys are too damaged to perform the function).

On January 9, CDC investigators notified the FDA, which sent investigators to inspect Baxter's manufacturing plant in Cherry Hill, N.J., where they found contaminated doses of blood thinners containing heparin. Baxter then voluntarily recalled nine lots of heparin—about 10 percent of the company's annual production of the blood thinner—and the FDA warned health care providers to stop administering the drug. U.S. health care facilities had been purchasing more than one million multiple-dose vials of heparin-based blood thinners monthly, half of which were made by Baxter.

Most of the problems involved dialysis patients who had received high intravenous doses of a type of heparin (high molecular weight heparin) that thins the blood for about an hour while they are

undergoing treatment. Another type—low molecular weight heparin—thins the blood for hours longer than the high molecular weight variety and is more likely to be used on patients staying in the hospital (to prevent clots while bedridden). There are some synthetic forms of low molecular weight heparin, such as sanofi–aventis's Lovenox, but currently there is no synthetic high molecular weight alternative on the market.

Baxter had called Linhardt to tap his expertise and to help track down the source of contamination. He agreed to share his findings with FDA officials, who soon began calling him for daily updates and to get his take on what they found. "Often the FDA suggested experiments that I should try in my lab," he says. "Apparently, the FDA was using my lab to confirm and validate results that other laboratories were reporting."

On the trail of a killer

Within weeks, the FDA had narrowed the list of suspected contaminants to oversulfated chondroitin sulfate (OSCS), because it mimics heparin's capabilities and appears to be heparin when tested in the lab. Although OSCS is based on chondroitin sulfate (prepared from animal cartilage or beef trachea) that many people take as an anti-inflammatory to treat osteoarthritis, OSCS has the opposite effect, activating immune system enzymes that cause inflammation as well as a drastic drops in blood pressure. The question: What was it doing in batches of heparin, where it would have no purpose other than to increase the volume, driving up sales of an artificially pumped up product, Linhardt says.

Baxter tracked the contaminant to SPL, which has a facility in China that manufactures the heparin that companies such as Baxter bought and used in their blood-thinner products. The Chinese facility, known as Changzhou SPL, used a supply chain for the ingredients to make its heparin that included unregulated labs and farms in rural China. The FDA ultimately traced the poisoned heparin back to 12 Chinese companies that had added OSCS to their products.

Chinese officials initially disputed charges that the contaminants came from their country but have since acquiesced to the FDA's demand that Chinese companies test all ingredients used in U.S. drugs for contamination. The FDA, which says it has developed improved tests for screening heparin for contamination, is also planning to participate in an international summit at an undetermined location next year where international scientists and regulators will discuss ways to improve and enforce drug safety rules. This case—like those involving melamine in baby formula and pet food—illustrates the danger of U.S. dependence on products, including drugs, from other countries where safety standards are lower than those enforced by the FDA.

Searching for a synthetic alternative

The threat has given a new sense of urgency to Linhardt's effort to develop a synthetic version of the heparin use in short-term blood thinners, but he still faces some major obstacles. Although it is possible to bioengineer heparin in the lab, the drug's complex structure makes it difficult to mass produce: It takes at least 100 metric tons of heparin to meet the world's needs for a single year. Through trial and error, it took Linhardt and his team a year to make just 100 milligrams of his synthetic version. "The challenge is there are multiple enzymatic steps involved," Liu says. "These enzymes are very sensitive to temperature and not very stable," which means the fermentation process is not always successful.

Even if the enzymes survive the fermentation process and produce heparin, making that much of the drug synthetically (without the use of swine) could require using a 264,172-gallon (one-million-liter) fermenter 100 times. The largest fermenter on RPI's campus has a capacity of 10.6 gallons (40 liters) and would be able to produce only one gram of synthetic heparin at a time with each successful fermentation.

Linhardt hopes to be able to make a gram of synthetic heparin within a year, which would be enough to administer 100 doses in mice and allow the researchers to at least move forward with animal trials. He believes that one kilogram of synthetic heparin would provide the 10,000 doses needed to get through clinical testing on as many as 1,000 patients, although he says he is not able to give a timeline for when he would be able to make that much heparin. Success would mean that U.S. pharmaceutical companies could make the heparin they use in their blood-thinner products rather than importing it from China.

A key factor in the success of synthetic heparin, at least initially: whether hospitals, clinics and insurance providers would be willing to pay a premium for it if it costs more than heparin coming from swine (which is about 20 cents per dose). Given how difficult it has been to produce small amounts today, it would take years and a "staggering" investment to make synthetic heparin a feasible business, says Erin Gardiner, a Baxter spokesperson, who adds that her company is not planning to get into the synthetic heparin business.

Scientific American- November 4, 2008, By Larry Greenemeier

PHARMA 4EME ANNEE
EXAMEN D'ANGLAIS AVRIL 2009

NOM PRENOM_____
N° TABLE_____

FEUILLE DE REPONSE
DETACHER SOIGNEUSEMENT CETTE FEUILLE DU SUJET ET Y REPORTER LES REPONSES
Seuls les dictionnaires unilingues anglais sont autorisés

1. Reading comprehension

1.	4.	7.	10.	13.
2.	5.	8.	11.	14.
3.	6.	9.	12.	15.

2. Written expression

Reading Comprehension:

Read the article entitled ***Heparin Scare : deaths from tainted blood-thinner spur race for safe replacement*** (Scientific American, 04/11/09).

Choose the best answer for each question.

1. The drug heparin...

   a) has been prescribed for a century in the USA.
   b) was developed for kidney dialysis patients.
   c) is a commonly used anti-coagulant extracted from pig intestines .
   d) all of the above.

2. In 2008, the US Food and Drug Administration...

   a) withdrew all heparin products from the US market.
   b) announced that 81 patients had died as a result of taking heparin.
   c) decided to ban Chinese-produced heparin from the USA.
   d) asked patients to check the source of the heparin products they were taking.

3. The heparin problem was alarming because...

   a) the supply of drugs from China to the USA is carefully monitored.
   b) contamination had previously been restricted to dairy products.
   c) melamine is known to cause fatal side-effects in dogs and cats.
   d) all of the above.

4. When the problem was discovered Baxter International INC....

   a) bought back all the doses it had sold to SPL.
   b) called back all of the heparin sourced in China.
   c) called back all its heparin products.
   d) there was a shortage of heparin products in the US market.

5. The FDA asked various teams of scientists...

   a) to find out exactly what contaminants had caused the problem.
   b) to find other suppliers for the drug in Europe, Canada and Brazil.
   c) to develop a detection test to screen patients for contaminants.
   d) all of the above.

6. Robert Linhardt was approached by the FDA because...

   a) he had been working on Chinese pharmaceuticals.
   b) they needed to implement new screening procedures.
   c) he is a renowned professor of biology and chemistry.
   d) he had been working on a synthetic version of heparin.

7. The crisis first came to light when...

   a) investigators found contaminated heparin at Baxter's manufacturing plant.
   b) severe symptoms in children in kidney dialysis were observed.
   c) patients reported allergic reactions after taking heparin.
   d) heparin-based blood thinners were given to hypertensive patients.

8. The patients who were particularly affected were taking...

a) high molecular weight heparin for long periods of time.
b) high molecular weight heparin for short periods of time.
c) low molecular weight heparin for long periods of time.
d) synthetic forms of low molecular weight heparin.

9. Oversulfated chondroitin sulfate (OSCS)...

a) can easily be distinguished from heparin in the lab.
b) is a commonly prescribed treatment for osteoarthritis.
c) can cause blood pressure to fall dramatically.
d) all of the above.

10. OSCS was added to heparin products in China ...

a) to generate greater quantities of saleable product.
b) because there was confusion between Chinese and US drug labelling.
c) because SPL had difficulty finding heparin sources in China.
d) all of the above.

11. What steps will be taken to prevent further contamination problems?

a) Chinese companies will test all pharmaceutical products before export.
b) new FDA tests will make it easier to screen drug products.
c) new safety rules will come into effect next year.
d) The USA has reduced the importation of drugs from developing countries.

12. What is the problem with Linhardt's synthetic version of heparin?

a) producing just a small amount takes a year.
b) the method does not produce guaranteed results.
c) he has not yet managed to control the enzymatic steps in the process.
d) all of the above.

13. If Linhardt was able to perfect the fermentation process...

a) it would still be difficult to scale up the production process.
b) he would be able to build a fermentation plant for his product.
c) the production process would be less expensive.
d) he would attract investment from pharmaceutical companies.

14. What is the next step for Linhardt's synthetic heparin?

a) to produce cheap heparin which can compete with pig-derived heparin.
b) convince US companies to invest in US synthetic heparin.
c) to make enough heparin to set up animal trials of synthetic heparin.
d) to reduce the time it takes to produce heparin.

15. In general, this article...

a) argues that all heparin must now be sourced in pigs from the USA.
b) describes how new synthetic drugs will remove the risk of contamination.
c) describes how drug imports are being closely monitored.
d) implies that the USA will probably remain dependant on imported heparin.

2. Written expression. Create a paragraph from the material below. Make neceessary changes : verbs (tense+active/passive form), other grammatical changes (i.e. pronouns,-object/possessive pronouns). Add articles, prepositions, punctuation, etc., when necessary. Verbs are in **bold type**. The first sentence has been done for you.

The Mouse Man

One hundred years ago in a lab at Harvard University, a young zoology student was busily overseeing the breeding of pair after pair of brother and sister mice. The "Mouse Man", as he was known on campus, was trying to create the first inbred lab animal - a strain of mouse whose genes would be stable and identical. Such a mouse would allow biologists to reliably replicate their experiments for the first time. His professor said it couldn't be done, but the Mouse Man proved him wrong. We are all indebted to those inbred mice and their descendants, which have helped researchers develop treatments for a wide range of human diseases.

Example : Clarence Little/**is**/student/Harvard University/when/he/zoology professor/**give**/he/live mouse
Clarence Little **was** a student at Harvard University when his zoology professor **gave** him a live mouse.

1. Professor/**tell**/he/to learn/everything/he/**can**/about it
2. In 1909/he/**create**/first in-bred strain/of mouse
3. He/finding/**provide**/researchers/with/homogenous genetic background/for/they/experiments
4. In 1929/Clarence Little/**found**/Jackson Laboratory/which/**be** considered/be/important center/for research/into/mouse genetics
5. Since/laboratory's creation/original lab mouse/**join**/by thousands/strains
6. About/25 million/mouse/**use**/labs/around/world/each year
7. Tiny/*mus musculus*/**be**/most common/research model
8. It/**help**/clarify/nature/many human illnesses/cancer/diabetes/Alzheimer's disease
9. Most importantly/lab mouse/**replace**/humans/in trials
10. These tests/**lead** to/development/many drugs/including/treatments/rheumatoid arthritis/arthritis/osteoporosis
11. While/Clarence Little/**be**/man/behind/modern lab mouse
12. Researchers/nineteenth century/**recognise**/that/mouse/**share**/many physiological traits/with humans
13. Gregor Mendel/**begin**/he invesigation/inheritence/by/**study**/colour traits/mouse
14. However/he/**change**/to/study of peas
15. Following/he/bishop's disapproval/his study/with/mouse

. Reading comprehension.

Read the article, *Are tumours our oldest ancestors?* (New Scientist, March 12th, 2011) and choose the **best** answer for each item.

NB. There is only **one** answer for each question.

1. A new and controversial hypothesis about cancer suggests that...

a) cancers can develop resistance strategies to all modern treatments.

b) humans originally evolved from cancers.

c) in the last 40 years many new therapies have reduced mortality from cancer.

d) all of the above.

2. It is thought that some cancers become resistant to therapy over time...

a) because cells in a tumour work together to counter the action of drugs.

b) because cancer cells have evolved from bacterial cells.

c) because natural selection pushes cells to compete to develop strategies to survive therapy.

d) because cells work together to avoid natural selection.

3. What new hypothesis is proposed by Lineweaver and Davies?

a) Tumour cells cooperate with each other because they are relics of ancient animals.

b) Tumour cells can resist drugs because they have the survival tactics of ancient animals.

c) The ability of tumour cells to resist therapy is limited.

d) All of the above.

4. What happened over 600 million years ago?

a) single-celled animals began to replicate without any control.

b) controlled replication evolved with the emergence of multicellular organisms.

c) cancer cells developed the ability to proliferate within organisms.

d) single-celled animals stopped replicating.

5. Current scientific opinion suggests that...

a) cancer occurs when there is a problem with the genetic control of replication.

b) cancer results from an excessive control of replication within the body.

c) cancer is a "living fossil" of early gene regulation.

d) All of the above.

6. What is new and different in the Lineweaver and Davies hypothesis?

a) They suggest that cancer is not connected to evolution.

b) They suggest that cancers are able to strictly control cell proliferation.

c) They suggest that cancer was originally an early animal.

d) All of the above.

7. Why do the processes of angiogenesis and metastasis add support to this new hypothesis?

a) because they show that cancer cells compete against each other.

b) because they imply that cancer cells work together to ensure the tumour's survival.

c) because they correspond to the behaviour of ancient multicellular organisms.

d) because they are not really understood well by cancer researchers.

8. For Lineweaver and Davies...

a) tumours are hidden within each and every one of us.

b) cancers occur when the ancient genes stop functioning.

c) we all have the genetic trace of these early animals in our bodies.

d) tumours occur when cells succeed in escaping genetic controls.

9. One consequence of this hypothesis is that tumours...

a) can be thought of as a colony of competing bacteria.

b) have an almost limitless number of strategies for resisting therapy.

c) are dependent on natural selection for their survival.

d) can only defend themselves with the tactics they evolved half a billion years ago.

10. Lineweaver and Davies' hypothesis ...

a) has been received with enthusiasm by the scientific community.

b) has been rejected by most researchers in this field.

c) has received a mixed response from researchers in the field.

d) brings support to the results of other researchers working in this field.

11. For Mansri Srivastava, ...

a) the hypothesis fails to explain the evolution of cancer genes.

b) the hypothesis fails to explains the role of metastasis in ancient animals.

c) the hypothesis is wrong to suggest that angiogenesis existed in early animals.

d) the notion of cancer as a "living fossil" is too restrictive to be useful.

12. For Lineweaver...

a) a certain type of angiogenesis must have developed in early animals.

b) proto-angiogenesis should not be restricted to early animals.

c) angiogenesis did not have to play a role in early animals for it to emerge later.

d) angiogenesis emerged in cancers because it had to.

13. Genetic profiling could be a way of testing this hypothesis if it shows...

a) that different people have evolved different ways of resisting treatment.

b) that toxins from early animals make effective anti-cancer drugs.

c) that response to therapy is the same in different patients with a specific tumour.

d) that response to therapy varies according to the toxins used.

14. For Maley, this research...

a) does not change the fact that finding an effective treatment for cancer is difficult.

b) implies that cancers have a wide range of strategies for resisting treatment.

c) suggests that treating predictable cancers will become easier.

d) All of the above.

15. In general this article...

a) discusses the problems with existing cancer therapies.

b) presents a new way of looking at the way cancers function in the body.

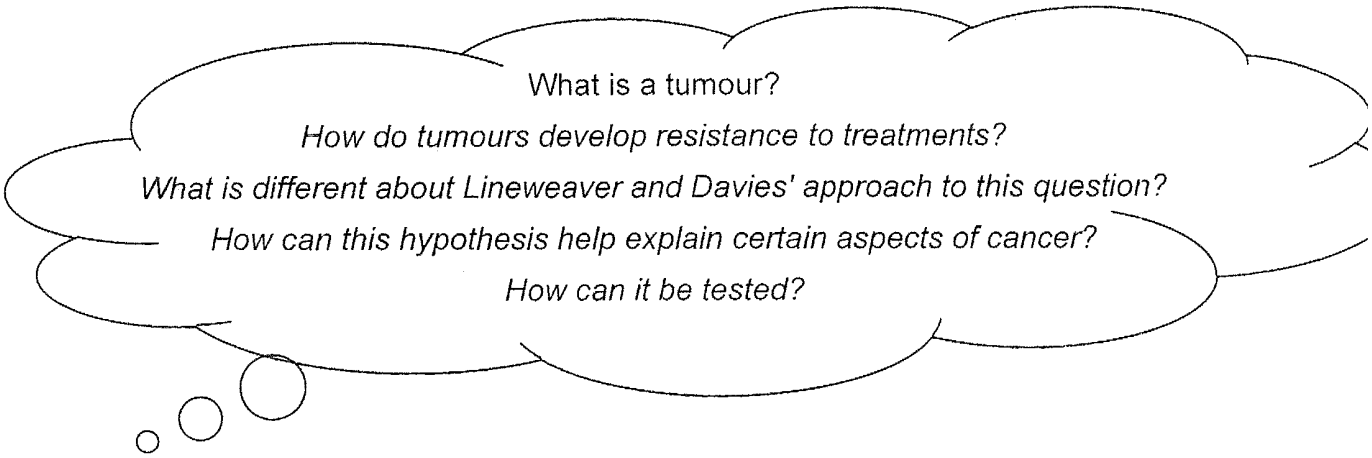
c) argues that cancer specialists need to change the way they think about cancer.

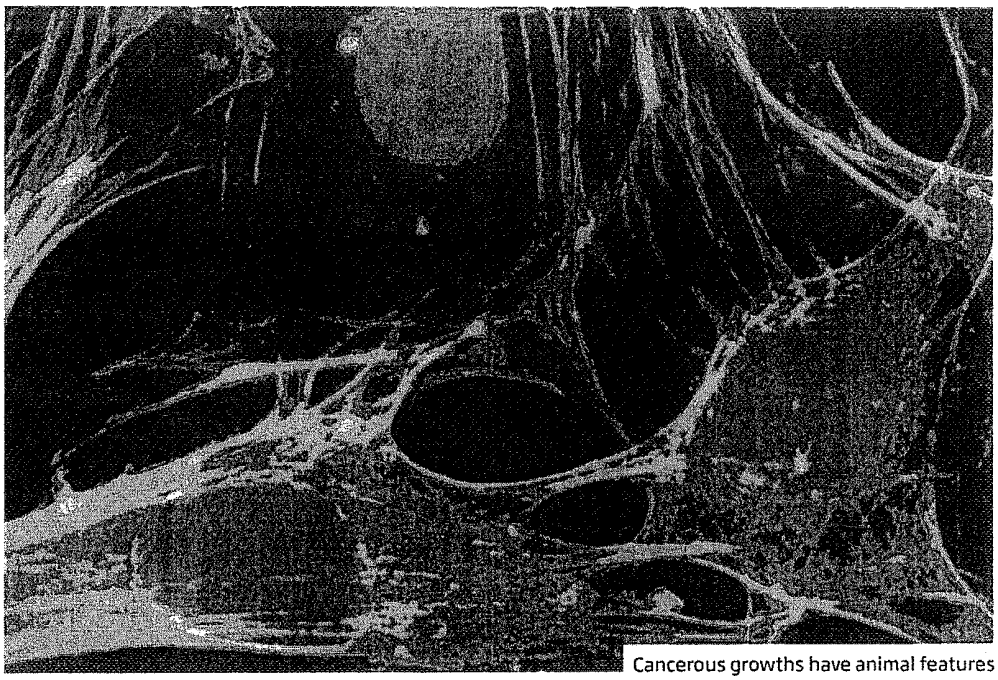
d) describes the way in which new approaches to cancer are changing therapy.

Q2. Are tumours our oldest ancestors? Open questions

Using information that you have carefully selected from the article, *Are tumours our oldest ancestors?*, Answer the following questions, using your own words.

Please **make your handwriting as easy to read as possible**.





Cancerous growths have animal features

Are tumours our oldest ancestors?

Colin Barras

CANCER remains a formidable foe even 40 years after Richard Nixon officially declared war on it. A new and controversial hypothesis now offers hope that the war can ultimately be won. It suggests tumours have a limited ability to evade modern therapies – a consequence of the idea that cancer is our most distant animal ancestor, a "living fossil" from over 600 million years ago.

Some cancers evolve resistance to a treatment within a few years. One possible explanation for this is that the cells within a tumour act independently, competing with one another via natural selection to evolve therapy-dodging innovations.

Astrobiologists Charles Lineweaver at the Australian National University in Canberra and Paul Davies at Arizona State University in Tempe have an alternative explanation. They say that evidence of basic cellular cooperation within tumours suggests cancers are a throwback from the origin of the animal kingdom – and that any ability to resist modern drugs relies on an ancient and ultimately limited array of survival tactics.

Their hypothesis builds on an old idea that suggests a link between cancer and the origin of multicellular animals, sometime before 600 million years ago. For billions of years before that point, the animals' single-celled ancestors replicated with reckless abandon. Once organisms contained multiple cells, however, replication had to become more restrained, to avoid adverse effects on the organism.

Cancer is thought to be triggered by a malfunction of the genes that try to hold back this uncontrolled replication. But Lineweaver and Davies go further: cancer is not simply linked to the evolution of animals – it was the earliest animals. They believe these organisms had cracked the problem of runaway replication but they still lacked total control over cell growth and proliferation.

The hypothesis helps to explain some of the more unusual features of tumours, says Lineweaver. Some cancer cells build a network of blood vessels, a process known as angiogenesis, to bring nutrients into the tumour – evidence of tumour-wide cooperation. Other cells gain the ability to spread to other tissues, or metastasise, which is difficult to explain if all cancer cells act independently.

> **"Cancer is not simply linked to the evolution of animals – it was the earliest animals"**

Lineweaver and Davies think the genetic toolkit at work in these first animals is buried within all of us. The genes that came later might have tinkered with it, but whenever those later additions malfunction the ancient genes can revert to their initial function.

Consequently, a tumour is not a collection of independently evolving cells, like bacteria, with almost infinite potential to evolve resistance to therapy. It is a group of largely cooperating cells relying on a finite collection of survival strategies that were locked in place over half a billion years ago (*Physical Biology*, DOI: 10.1088/1478-3975/8/1/015001).

Reactions to Lineweaver and Davies's idea vary from cautious enthusiasm to outright scepticism. Carlo Maley at the University of California in San Francisco, who studies the evolutionary processes at work in cancer, is receptive: "They make a bunch of interesting predictions," he says.

Others are more guarded. It is an "imaginative metaphor", says Mansi Srivastava at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, who studies the evolution of genes including those involved with cancer. However, she thinks the idea of cancer as a living fossil from the dawn of animal life is a step too far. "There is no evidence to believe that the ability to develop blood vessels is an ancient feature of animals."

Lineweaver disagrees: "Fully developed angiogenesis had to have evolved from proto-angiogenesis," he says. "I think it's clear that some form of proto-angiogenesis was very important for the earliest animals."

Genetic profiling may soon help to test the hypothesis, says Lineweaver. The ways a particular cancer responds to treatment in different people should correlate with each other, he says, because they should share strategies for dealing with toxins that were developed in the earliest animals.

Even if cancer does have a limited ability to resist treatment, though, Maley has a reality check. If the war on cancer has taught us anything, it is that battling even a predictable cancer will remain "plenty hard" in the short term. ■

Nom :
Prénom :
N°table :

PHARMACIE 4ème ANNEE

EXAMEN

ANGLAIS SCIENTIFIQUE

18 avril 2012

Dureé : 1 heure

2 sections :

1) Compréhension écrite

2) Rédaction

(6pages)

aucun dictionnaire, même unilingue, n'est autorisé

Antibiotics may make you fat

Newscientist 28 March 2012 by Jessica Hamzelou

THE trillions of bacteria that colonise our guts are in jeopardy. Overusing antibiotics has not only led to the development of dangerous superbugs, but has changed the bacteria that live inside us. Now evidence suggests that new gut floras may be responsible for our expanding waistlines.

Antibiotic use has been rising for the past 70 years. They are now often prescribed as a precaution for illnesses when the cause has not been confirmed as a bacterial infection. Martin Blaser, a microbiologist at New York University, fears that over-prescribing antibiotics could be harming some communities of "good" bacteria that line your intestines.

The effects could be long-lasting, too. For example, some antibiotics seem to permanently oust *Helicobacter pylori* from their home in our stomachs. Widespread use of antibiotics has been correlated with a fall in the number of people playing host to *H. pylori*. That might seem like good news since the bug has been linked to stomach cancer and gastric ulcers, both of which have become less common. However, these positive outcomes coincide with a surge in cancers of the oesophagus, attributed to the more acidic environment *H. pylori* leaves behind when it vacates the stomach (*Nature Reviews Microbiology*,

To investigate whether overusing antibiotics could also play a part in the rise of obesity, Blaser's team fed infant mice low doses of penicillin to mimic doses given to farm animals. After 30 weeks, penicillin-fed mice were between 10 and 15 per cent bigger and twice as fat as drug-free mice.

When the team looked at the mice's gut bacteria, they found that the antibiotic-fed mice had a different complement of bugs to the untreated mice. Low doses of antibiotics had seemingly shifted the balance of certain gut microbes, reducing the numbers of *Lactobacillus*, which is a "good" bacterium linked to a .lower risk of cancer recurrence

To confirm that the mice owed their supersize to an altered gut microbiome, the group turned to germ-free mice, which are bred in a sterile environment and have no gut bacteria. Within five weeks of being given gut bacteria from the mice fed antibiotics, the once germ-free mice were 35 per cent larger than mice with a regular microbiota.

In the initial experiment, the biggest mice were those that had started antibiotic treatment from birth. Even mice that were only given drugs for four weeks ended up as large as mice on antibiotics for the full 30 weeks. This suggests that gut flora may be most vulnerable to disruption in the earliest moments of life, says Blaser.

Antibiotics used to treat children may also have a detrimental effect on their immune systems, says Blaser. In a separate study in mice, his team mimicked the short courses of higher dose antibiotics that young children tend to receive for infections. The group then investigated whether these pulsed doses were having any effect on helper T-cells - a group of immune cells that secrete chemicals to direct the immune response. They found that the levels of these chemicals were significantly lower in antibiotic-fed mice, suggesting that their immune systems may have become compromised. Blaser presented his findings at the in Paris, France, last week.International Human Microbiome Congress

Although no one yet knows why certain groups of bacteria may affect weight, Blaser says that we might expect young children exposed to antibiotics to gain weight like the mice. Indeed, similar effects have already been spotted in humans: when Teresa Ajslev and her colleagues at Copenhagen University Hospital in Denmark followed the development of 28,000 babies, they found that those given antibiotics within the first six months of life were more likely to be overweight at age 7, even if their mother had a healthy weight (*International Journal of Obesity*,).DOI: 10.1038/ijo.2011.27

What's more, the problem could get even worse for future generations, Blaser says. We think babies first acquire bacteria during birth, when they travel through their mother's vaginal canal or are exposed to hospital environments. A newborn girl treated with antibiotics could grow up with an altered microbiome, and be unable to provide her own children with the missing bacteria.

Blaser is not the only one to be concerned. Kristine Wylie at the University of Washington in St Louis, Missouri, says it could well be true that antibiotics are contributing to soaring obesity rates. "The pulses of antibiotics really reflect what children are given [in real life]," she says.

A recent study of 3000-year-old human faeces suggests that the make-up of our microbiomes has changed. To protect ourselves from disease, we may want to repopulate our guts with the bacteria we evolved with, says Blaser. The best places to investigate the role of bacteria are poorer countries with limited access to antibiotics, he adds. "You'd have to go to developing countries and start hoovering up faeces," says Brett Finlay at the University of British Columbia in Vancouver, Canada.

"Microbes are not accidental - we have co-evolved with them," says Blaser. "They are useful, but they are changing as a result of lifestyle, and this is changing our disease risk." The answer isn't to stop giving antibiotics, he says. "A lot of what we have to do is research. We need to narrowly treat infections. We need better diagnostics and better therapeutics."

1.Reading Comprehension. Read the article entitled, *Antibiotics may make you fat* (Newscientist March 28, 2012). For each question choose **one** answer. Write your answers in the table provided.

1. The overprescription of antibiotics has resulted in :
   a) antibiotic-resistant bacteria.
   b) altered intestinal bacteria.
   c) an increased risk of obesity.
   d) all of the above.

2. *Helicobacter pylori* :
   a) is often changed due to antibiotic use.
   b) is increasingly absent in the human gut flora.
   c) is no longer a major cause of stomach cancer.
   d) both b & c.

3. When *Helicobacter pylori* is not present in people's gut flora :
   a) the stomach becomes more acidic.
   b) the risk of oesophageal cancer increases.
   c) gastric ulcers disappear.
   d) both a & b

4. The aim of Martin Blaser's team :
   a) was to investigate whether low doses of penicillin leads to weight gain.
   b) was to make a comparison between infant mice and farm animals.
   c) was to see if there is a correlation between the overuse of antibiotics and obesity.
   d) both b & c.

5. The team found :
   a) that mice fed antibiotics became obese.
   b) that their gut flora changed.
   c) that all « good » bacteria was eradicated.
   d) that only infant mice responded to treatment.

6. The team concluded :
   a) that a change in gut flora led to weight gain in the infant mice.
   b) that germ-free mice who were given antibiotics also increased in size.
   c) that the 30-week treatment of penicllin resulted in the biggest mice.
   d) all of the above.

7. In another study, Blaser's team :
   a) investigated the effects of high doses of antibiotics on the immune system.
   b) wanted to simulate in mice the real doses that young children receive.
   c) looked at how helper T-cells trigger an immune response.
   d) both a & b.

8. The antibiotic-fed mice :
   a) presented fewer helper T-cells.
   b) presented a decrease in chemicals involved in the immune response.
   c) presented compromised immune systems.
   d) all of the above.

9. Teresa Ajslev and her team :
   a) followed 28,000 babies who had been given antibiotics in the first 6 months of life.
   b) found that overweight children generally have overweight mothers.
   c) found that overweight children had been given antibiotics as babies.
   d) found that babies given antibiotics in the first 6 months of life were at a greater risk of being overweight as children.

10. It is thought that :
   a) bacteria are first acquired at birth.
   b) newborns treated with antibiotics have altered gut flora.
   c) an altered microbiome could affect future generations.
   d) all of the above.

11. Blaser suggests that :
   a) man's ancient ancestors were better protected from disease.
   b) populations from poorer countries have more microbial flora.
   c) reintroducing certain bacteria into our guts could help fight disease.
   d) people with limited access to antibiotics are generally healthier.

12. It is Blaser's opinion that :
   a) further studies and more efficient diagnostic techniques are needed.
   b) certain microbes are becoming more virulent.
   c) antibiotics need to be replaced with other treatments.
   d) lifestyles should be changed.

Answers to M-Choice questions

1	4	7	10
2	5	8	11
3	6	9	12

Give a synonym, explain or translate the following words or expressions <u>underlined</u> in the text.

1. In jeopardy	
2. oust	
3. make-up	

2. Writing. (20pts) **In your own words**, write a structured paragraph (50 words minimum) to answer each of the following questions using information from the text. Write your answer in the space provided.

1. Discuss Martin Blaser's work regarding antibiotics and weight gain.

2. Discuss how young children are affected by the overuse of antibiotics and the long-term consequences.