APPENDIX B

STSE

Science-Technology-Society and the Environment

Important Note

These STSE modules are intended for teacher reference. Each is designed to target specific outcomes within Biology 3201.

Drugs and Homeostasis

Outcomes:

1. Explain how the nervous system helps maintain homeostasis. (317-1)
2. Describe disorders linked to the nervous system and their effect on the homeostasis of the system and the organism as a whole. (317-4)
3. Analyse how and why technologies related to the treatment of nervous system disorders were developed and improved over time. (115-5)
4. Describe how the use of prescription and nonprescription drugs can have a role in maintaining or disrupting homeostasis. (317-7)
5. Distinguish between questions that can be answered by science and those that cannot, and between problems that can be solved by technology and those that cannot. (118-8)
   - Debate the merits of using drugs for treatments of nervous disorders against the long-term side effects.

6 Propose courses of action on social issues related to science and technology, taking into an array of perspectives, including that of sustainability. (118-10)
   - Debate the legalization of certain drugs such as marijuana for medicinal purposes.

Introduction

Drugs have been considered invaluable to society as an instrument in the treatment of disease. Insulin is a hormone used to control diabetes. Chemotherapy uses drugs to destroy cancer cells. The use of painkillers such as Tylenol and antibiotics are prevalent in society. Prozac is a well-known drug used in the treatment of depression. Drugs have also been considered a danger to society in because of their inappropriate use and addictive nature. Many high profile actors have admitted to drug and alcohol abuse such as Ben Affleck, Wimona Rider and Robert Downey Jr. and have sought rehabilitation for their addictions. This module will examine the medical use of drugs in the treatment of disease, as well as, their abuse in society. It will also examine the long-term affects of drugs on the health of the human body.

Neurotransmitters and the Nervous Response

Many drugs affect neurotransmitters. Neurotransmitters are chemicals secreted by neurons which stimulate motor neurons or neurons of the central nervous system. If you recall, a wave of depolarization is carried across a presynaptic neuron until it reaches the bulb-like ends of the axon. The end of the axon contains the neurotransmitter in its vesicles. Depolarization causes the calcium gates to open and trigger the release of the neurotransmitter through exocytosis. The neurotransmitter diffuses between the synapse of the terminal end of the axon of the presynaptic neuron and the dendrites of the postsynaptic neuron. The dendrites of the postsynaptic neuron have specialized receptor sites to which the neurotransmitter will attach. The neurotransmitter will then either excite or inhibit the neuron. Once a neurotransmitter has attached to the receptor site of the postsynaptic neuron, an enzyme is released from the presynaptic neuron to break down the neurotransmitter.

Some neurotransmitters are excitory and include acetylcholine, norepinephrine (noradrenaline), **serotonin** and dopamine. Other neurotransmitters are associated with relaxation such as dopamine and serotonin. Many neurotransmitters can have multiple functions.

The drugs abused in society are typically stimulants or depressants thought to block or enhance certain neurotransmitters. Diseases of the nervous system are often associated with the improper functioning of a neurotransmitter or improper functioning of the enzyme used to break them down once they have been released and attached to the receptor site of the postsynaptic neuron. Drugs can be developed to mimic the effects of the affected neurotransmitter or enzyme to treat these diseases.

Drugs in the Treatment of Disease

As just discussed, imbalances in neurotransmitters can contribute to certain diseases. Several well known examples are Parkinson's disease and Huntington's disease. Parkinson's disease is believed to be caused by a dopamine deficiency due to the gradual death of the neurons that produce dopamine. A dopamine deficiency can result in tremors and rigidity in the limbs since messages can not be sent between areas of the brain controlling body movement.

Huntington's disease is believed to be caused by a malfunctioning of an inhibitory neurotransmitter. Huntington's is a genetic disorder characterized by jerky movements and loss of mental and emotional abilities due to the destruction of neurons in certain areas of the brain.

Potential treatment is aimed at replacing the damaged neurons in both of these cases through the experimental use of stem cell transplants. At present, other treatments involve targeting the defective neurotransmitters such as increasing dopamine levels in Parkinson's patients.

More and more research has shown that mental illness is also a result of imbalances of neurotransmitters. Mental illnesses were once considered to have no biological basis but rather be due to factors in an individual's environment such as experiencing stress or forms of mental and physical abuse. At one time, sufferers of mental illness were deemed as "weak minded" and lacking the skills to cope with life.

As science has progressed, genetic connections were made with individuals in the same family suffering from mental illness. This lead to the exploration of a biological basis for mental disorders and resulted in a greater understanding by society regarding the causes of mental illness. Mental illness has now become discussed more openly in society and appreciated as a medical condition.

Debate still continues regarding the issue of nature versus nurture in the onset of mental illness but all must agree that the biological basis of mental disorders exists. The effective treatment of mental disorders with drugs also adds support to the biological basis of these disorders. This next section will explore the biological basis of certain **mental illnesses** and the use of drugs in their treatment.

Clinical Depression

Clinical depression is the most frequently encountered mental illness. Clinical depression is now considered a physical condition in which there is a fault in the brain chemistry. It may afflict up to 5% or more of the population. Symptoms of depression include a distinct change in mood accompanied with an extreme feeling of hopelessness. Other symptoms include: loss of appetite; weight loss; headaches; sleeplessness; loss of energy; and tiredness. Symptoms of anxiety are also quite common. Suicide is common in about 15% of depressed patients.

Serotonin, dopamine, and noradrenaline are neurotransmitters linked to clinical depression. Those suffering from depression either secrete too little of a particular neurotransmitter or too much of the neurotransmitter is broken down by enzymes (*monoamine oxidases*) when it is reabsorbed into nerve endings.

Three major classes of drugs are used in the treatment of depression. They are *monoamine oxidase inhibitors* (MAOI's) , *selective* ***serotonin*** *re-uptake inhibitors* (SSRI's), and *tricyclic compounds*. Drug treatment is difficult because some drugs may have no effect and the patient may spend a period of time searching for the proper drug and dosage that

may help to alleviate the depression. It also takes several weeks for the drugs to take effect, if they are to work. In this time period, the patient could go into remission or the condition may worsen. The result can be unrelated to the drug. These factors may make the treatment with drugs difficult and the process of finding a successful drug very lengthy. It is unknown why the effect of drugs take such a length of time. It is also unknown why some drug treatments are successful and others are not. More research into the causes of depression is needed in order to obtain more successful treatment.

Tricyclic inhibitors appear to slow the re-uptake of **serotonin** and noradrenaline. MAOI's are believed to inhibit monoamine oxidase (MAO). MAO is an enzyme that is believed to break down **serotonin** and noradrenaline. It has been shown that enhancement of these neurotransmitter systems leads to the elevation of mood. A danger of MAOI's and tricyclic compounds is the increased risk of heart failure. MAO inhibitors can not be taken with certain foods such as cheese, avocado, and wine because this interaction will raise blood pressure that can cause heart failure and death. Usually, doctors will avoid prescribing MAOI's for these reasons. These drugs can also be lethal at relatively low dosages which is a concern for suicidal patients.

Serotonin re-uptake inhibitors are the most widely prescribed antidepressant. It appears to have fewer dangerous side-effects. A well known example is Prozac. It functions by blocking **serotonin** uptake and therefore increasing the levels of **serotonin** at the synapse. Side effects include nausea, headache, insomnia and anxiety.

Bipolar Disorder

Bipolar disorder is also known as *manic depression*. It affects about 5 in 1000 people. It is characterized by severe mood swings ranging from mania to depression, with normal periods in between. During a manic phase, the individual may think that they are invincible, behave recklessly or believe in delusions such as ones of fame. During the depressive phase, the individual loses interest in their usual activities, may sleep excessively or suffer from insomnia. They may also be at risk of suicide during the depressive stage.

At one time, sufferers from manic depression were unable to function in life normally. Fortunately, manic depression can now be treated with both medication and psychotherapy. The most common medication is lithium carbonate. It functions by maintaining the chemical balances in the brain to prevent mood swings. Lithium appears to work in the treatment of both mania and depression. This is because it is believed that the depressive phase is a result of the preceding manic phase. If the manic phase can be controlled, then the depressive phase can be controlled indirectly. Other drugs may be used to treat the symptoms of depression.

Unfortunately, the long term use of lithium can affect the kidney and thyroid gland since lithium interferes with water and salt balance. There must be regular check ups to ensure that the lithium levels do not rise to a toxic level. Other side-effects of lithium treatment include: diarrhea; nausea; hand tremor; blurred vision; confusion; and swelling in the legs and feet. The side effects of this medication are why some manic depressives are reluctant to continue use of lithium. Researchers and drug companies are working to find better medications with less side-effects. In the meantime, patients are left with the dilemma of taking a medication that provides the benefit of treating their mental disorder but can also create grave concerns over some of its very serious side-effects.

The causes of manic depression are still uncertain. There appears to be a genetic link and episodes can also be triggered by stress. Chemical changes are also being studied. Manic behaviour is believed due to a high level of noradrenergic activity. This activity continues until the neurotransmitter systems are depleted. It is believed that lithium may prevent mania by preventing noradrenaline depletion.

Schizophrenia

A greater understanding in society of schizophrenia as a mental illness was created by the award winning movie, *A Beautiful Mind*. The movie focuses on the life of John Forbes Nash Jr. and his struggle to cope with his mental illness. Nash was a mathematical genius who later received a Nobel Prize in Economics. Actor, Russell Crowe, plays Nash and portrays the symptoms of the disorder, as well as Nash's struggle. The primary symptoms of schizophrenia include disturbance of thought

patterns, disturbance of **affective reactions** and autism or withdrawal. Secondary symptoms include hallucinations, delusions and paranoia. These symptoms all represent a loss of contact with reality. This disorder appears at a rate of 1 to 2 percent in the population.

There is a biological basis that predisposes individuals to the development of schizophrenia. A form of dopamine dysfunction, such as excessive dopamine activity, is believed to cause schizophrenia. Schizophrenic patients seem to have an excess number of dopamine receptors.

Chlorpromazine and related drugs have been used in the treatment of schizophrenia and functions in blocking the dopamine receptors. Unfortunately, the side effects are similar to Parkinson's disease. Other side-effects include abnormal body and face movements and extreme pacing. If this occurs, either the dosage is adjusted or a new medication is prescribed. Other side-effects include dry mouth, constipation, blurred vision and low blood pressure. Unfortunately, patients with schizophrenia are faced with a similar dilemma as those with bipolar disorder. They must rely on a drug to treat their disorder and enable normal functioning in life that has difficult side-effects.

Commonly Abused Drugs

Alcohol

Alcohol is probably the most commonly abused drug in society. Of all abused drugs, it is presently the only one considered legal upon reaching of age. It has been a large part of our culture for many years and is often associated with social functions and celebrations. However, alcohol use definitely has its dark side. It is known to alter personalities and cause people to behave in manner outside their normal personalities. A night of abusing alcohol can lead embarrassment and regret once the effects have worn off. Poor judgment while drinking alcohol can lead to making deadly decisions such as drunk driving. Also, people have abused alcohol to the extent they vomit in their sleep and choke to death. Groups such as MADD (Mothers Against Drunk Driving) are advocating for the responsible use of alcohol.

Alcohol is usually considered to be a depressant but can act as a stimulant in small doses. Alcohol affects the nervous system by increasing the inhibitory neurotransmitter GABA (Gamma Amici Biotypic Acid). It also modifies the effects of another excitory neurotransmitter called glutamate. A blood alcohol content of 0.10 can induce blurred vision, slurred speech, poor muscle coordination, and lack of rational judgment. A blood alcohol content of 0.40 to 0.50 will induce coma and a level of 0.60 will result in death. If a driver is found to have a Blood Alcohol Concentrate of 0.05, they receive a fine and a 24 hours suspension of the licence. If the driver is found to have a BAC (?) That 08 there is a fine and a car suspense. Alcohol abuse can lead to short-term memory loss and blackouts. It can irritate the gastrointestinal tract and increase hydrochloric acid production. Its long-term use can also cause liver disorders such as cirrhosis of the liver and heart disease.

Alcoholism is considered to be a genetic and environmental disease that can lead to death. Alcoholism is associated with addictive personalities and may be a secondary result of depression. Severe alcoholics often appear jaundiced due to cirrhosis of the liver. Their immune systems are impaired and they are more prone to disease. There are organizations such as Alcoholics Anonymous that enable sufferers of alcoholism and their families to cope with this disease.

Marijuana

A Canadian Senate committee has proposal the legalization of marijuana for non-medical use, citing that it is less harmful than alcohol. They believe that marijuana should be governed by the same laws as alcohol. They believe legalization would allow for better regulation and taxation of the drug. Many argue that prohibition of drugs like marijuana supports organized crime. It would also save money in law enforcement. This means that it could potentially be sold in corner stores. Others raise

concerns about addiction and health concerns. There also concern that it may be the "gateway" to abuse of more dangerous drugs. It is believed that if marijuana is legalized , more teens will abuse the drugs because access would be easier. As a result of this the Court of Canada has drafted legislation that would decriminalize marijuana usage. Individuals possessing a small amount of the drug would be fined much like the a speeding ticket. It is quite possible that within the lifetime of this module marijuana will be decriminalized.

Marijuana is derived from the Indian hemp plant *Cannabis sativa.* The active compound in marijuana is tetrahydrocannabinol (THC) works by binding to CB1 receptors found on presynaptic membranes in the brain. These receptors function in blunting pain. THC also causes the release of the neurotransmitter dopamine which elevates mood and controls muscle movements. The biochemical pathways can explain the how the drug affects its users and how it may also be used for medicinal purposes.

In low concentrations, THC causes euphoria. It has the ability of enabling the user to block out pain, frustration or confusion. There are also some serious health concerns regarding the use of marijuana. In high concentrations can cause hallucinations, anxiety, depression, and psychotic symptoms. Smoking marijuana can cause lung cancer, sinusitis, and bronchitis. It increases the level of carbon monoxide in the blood which, in turn, reduces the amount of oxygen reaching the heart. Repeated use tends to lead to the inability to deal with everyday challenges. Long term use can result in: impaired speech; memory loss; difficulty in understanding complex ideas; insomnia; impaired visual perception; and infertility. Marijuana use has also been linked to reducing immunity towards disease.

Marijuana has been demonstrated to have some positive effects in the treatment of disease. It has been used to treat medical conditions such as nausea in chemotherapy patients and to stimulate appetite in AIDS patients. It may also offer relief from pain and reduce spasticity due to multiple sclerosis. It has been shown to help sufferers of severe arthritis. It can be used as an anti-epileptic and anti-depressant. It is believed to be far less addictive than many prescribed painkillers. Furthermore, it is believed that marijuana could be manufactured in other forms so that it does not have to be smoked and harm the lungs.

Regulations are now in place that permit sufferers from terminal illnesses and chronic conditions to grow and smoke their own marijuana. They may also designate someone to grow it for them. At present, the Canadian Medical Society opposes marijuana use for medicinal purposes because of the lack of clinical research. Debate continues among the medical community about prescribing the use of marijuana. The legal system, however, supports the use of marijuana for medicinal purposes since denying an individual treatment that they believe helps their medical problem would be infringing on their human rights.

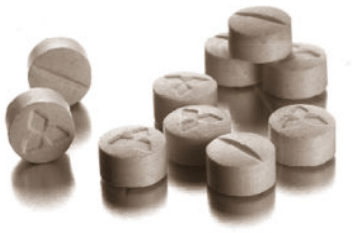
Cocaine

Cocaine is derived from the plant *Erthoxylon coca* and can be inhaled, smoked or injected. It results in a feeling of euphoria followed by depression. Cocaine acts by first stimulating the release of norepinephrine and dopamine and in higher doses the release of **serotonin**. Cocaine then interferes with the re-uptake of these neurotransmitters and these neurotransmitters build up in the synapse. Prolonged use will cause the body to produce less dopamine and the user will need more cocaine. Side effects include mental impairment, convulsions, hallucinations, stroke, heart attack and death.

Heroin
Heroin is a highly addictive derivative of morphine and comes from the opium poppy, *Papaver somniferum*. Heroin is normally injected but can also be snorted or smoked. It operates by binding to ophioid receptors in the brain in which natural chemical endorphins are involved in the relief of pain. Heroin mimics the action of endorphins. After initial exposure users experience a surge of cuphonia "Rush" followed by a drowsy trance-like slate. Prolonged use can cause less endorphin production. Side effects include: depressed respiration; impaired coordination; and decreased tolerance to pain; long term effects can include: collapsed veins; infections of heart valves and liver disease. Death can result from overdose.

Rohypnol
Rohypnol is a drug associated with rave parties and comes from the benzodiazepine family. It is considered to be the "date rape" drug and has become famous for its use in committing sexual assault. It is often given to an unsuspecting victim by dissolving it in beverage while they are unaware. It is similar to Valium™ but has ten times its strength. In combination with alcohol, it can be deadly. Rohypnol is highly addictive and has severe withdrawal symptoms. Its use can cause deep sedation, respiratory distress, blackouts for up 24 hours, and amnesia.

Ecstasy
Ecstasy is known as Methylene Dioxy Meth Amphetamine (MDMA) and has street names such as X, Rolls, E, Adam, Beans and Buddies. It is one of the designer drugs associated with rave parties. When Ecstasy first became popular, it was believed to be a "safe" drug with no side-effects. It was soon discovered, like many drugs, to have deadly consequences with its abuse.



The initial use of ecstasy results in: increased heart rate; increased blood pressure; dilation of pupils and bronchi; brain stimulation; increased motor activity; tightening of jaw muscles; grinding of jaws; overheating; sweating; heat stroke; and dehydration. Complications can result in renal failure, depression, liver failure, cardiovascular collapse and respiratory failure to name a few. The long-term use of ecstasy can result in irreparable brain damage. Its use is known to damage the brain cells that produce **serotonin**. In fact, long after ecstasy use, the nerve fibres in the brain that were destroyed by its use have grown back abnormally or not at all.

Designer Drugs

Designer drugs are associated with underground high school and college parties called *raves*. They are called designer drugs because they are created by altering the molecular structure of existing drugs to enhance their effects. They are prepared by underground chemists known as "cookers". "Cookers" are untrained and unlicensed chemists that work in poorly constructed laboratories. Of course, these conditions offer little quality control and makes abuse of these drugs even more dangerous.

Designer drugs are derived from three different types of drugs. These drugs are known as *PCP*, *fentanyl*, and *amphetamine/methamphetamine*. The street drugs created from these drugs are known as XTC, Ecstasy, Adam, Eve, Lover's Speed, GHB, Special K, Fantasy and Nature's Quaalude. Fentanyl derivatives are known to be up to 1000 times more potent than heroin. Ecstasy is derived from amphetamine/methamphetamine in higher doses can result in paranoia, depression and violent irrational behaviour. In general, designer drugs can create a wide range of physical problems such as: hypertension; uncontrolled tremors; total paralysis; seizures; permanent brain damage; and death.

Prescription Drugs

In recent years, concern has arisen over the abuse of prescription drugs. Some prescription drugs are easily addictive and patients can experience difficulty with withdrawal along with

dangerous side effects. Adolescents are becoming frequent abusers of prescription drugs due to the effects of euphoria that can be produced by these drugs. Crimes of breaking and entering pharmacies for the purpose of stealing prescription drugs is on the rise. There are three main prescription drugs that are most commonly abused: *Opioids, CNS depressants* and *stimulants*.

Opioids

Opioids are typically used to treat pain. These medications fall into a class of narcotics and include morphine, codeine and Demerol™. Opioids function by attaching to specific proteins called opioid receptors. These receptors are found in the brain, spinal cord and gastrointestinal tract. When opioids attach to the opioid receptors they are able to block the transmission of pain messages to the brain. Opioids can produce a feeling of euphoria by affecting regions of the brain that enable us to perceive pleasure. However, they can result in physical dependence and addiction. Tolerance of opioids can result in the need to take higher doses to achieve the same effect. Withdrawal will cause: restlessness; muscle and bone pain; insomnia; diarrhea; vomiting; cold flashes; goose bumps; and involuntary leg movements. A large dose can lead to respiratory depression resulting in death.

CNS Depressants

CNS depressants are often used to treat anxiety and sleep disorders by slowing normal brain function. Common CNS depressants include barbiturates and Valium™. Most CNS depressants act on the brain by affecting the neurotransmitter gamma-aminobutryic acid (GABA). The function of GABA in the human body is to decrease brain activity. Therefore, increased doses will create the drowsy effect required to treat anxiety and sleep disorders. Individuals can build a tolerance to CNS depressants over time and require larger doses. Withdrawals can cause the opposite effects of the drug. The mind can race out of control, possibly resulting in seizures and other problems.

Stimulants

Stimulants are used to treat narcolepsy, obesity, depression, and attention-deficit hyperactivity disorder (ADHD). These drugs enhance brain activity and result in increased alertness, energy, elevated blood pressure, increased heart rate and respiration. Examples of stimulants include Ritalin™ and Dexandrine™. The chemical structure of stimulants is similar to the chemical structure of the neurotransmitters norepinephrine and dopamine. Stimulants work by increasing the amount of these neurotransmitters to the brain. An increase in dopamine results in an increase in blood pressure, increase in heart rate, constriction of blood vessels, increase in blood glucose and it opens the pathways of the respiratory system. Stimulants do not result in physical dependence or withdrawal. However, they can be used compulsively and high doses repeatedly can lead to feelings of hostility and paranoia. High doses can cause body temperatures to rise to a dangerously high level. They can also create an irregular heartbeat leading to the risk of cardiovascular failure. There is also the potential of lethal seizures.

Conclusion

Drugs can play a role in both maintaining and disrupting homeostasis. When problems in the neurotransmitter balance occur, such as in the case of mental illness, drugs can play a role in restoring the balance. However, further study into the effects of different neurotransmitters is essential to achieve a better understanding of diseases caused by neurotransmitter imbalance. This can lead to better drug treatments that have less serious side-effects. Drug abuse can also disrupt homeostasis. Understanding the effects of drug abuse on neural pathways and the overall health of an individual can aid in the education of individuals considering drug abuse. It can also aid in the treatment of those suffering from addiction. Understanding the seriousness of drug abuse on long-term health may make one think twice about engaging in the legal and illegal use of drugs.

Questions

Understanding Concepts

1. For each mental illness, (*clinical depression, bipolar disorder and schizophrenia*) list the neurotransmitters involved, the nature of the imbalance of the neurotranmitter, the drugs used in their treatment, and side-effects of each

of these drugs. This may be done in the form of a chart.

2. For each street drug, (*alcohol, marijuana, cocaine, heroin, Rohypnol™ and ecstasy*) list the effects on neural pathways, the short-term effects of the drug and the long-term effects of the drug.

3. What are the dangers of using designer drugs?

4. For each of the prescription drugs, (*opioids, CNS depressants and stimulants)* list the effects on neural pathways, the short-term effects of the drug and the long-term effects of the drug.

Extensions

1. Debate the pros and cons of the use of marijuana in the treatment of chronic pain.

2. Debate the merits of whether or not to use drugs for treatments of nervous such as mental illness disorders against the side effects of these drugs.

3. Debate the merits of legalizing marijuana. Research the present legislation regarding the legalization of marijuana.

4. Using the knowledge that you have gained about the causes of mental illness, respond to the following statement; "Mental illness is a figment of one's imagination and one can chose whether or not to control their thoughts."

5. Choose a drug of interest to research. Report your findings in the form of a magazine article.

6. Write a letter to a friend who you know is abusing drugs. In this letter, use what you know about the dangers of drug use to persuade them quit and seek help.

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Stem Cell Research

Outcomes:

1. Identify examples of technologies that were developed based on understanding of cell division. (116-3)
2. Describe disorders linked to the nervous system and their effect on the homeostasis of the system and the organisms as a whole. (317-4)
3. Analyse why and how technologies related to the treatment of nervous system disorders were developed and improved over time. (115-5)
4. Select and integrate information on the application of technologies based on cell division. (213-7)
5. Construct arguments to support a decision, using examples and evidence and recognizing various perspectives. (118-6)
6. Debate the merits of funding specific scientific or technological endeavors and not others. (117-4)

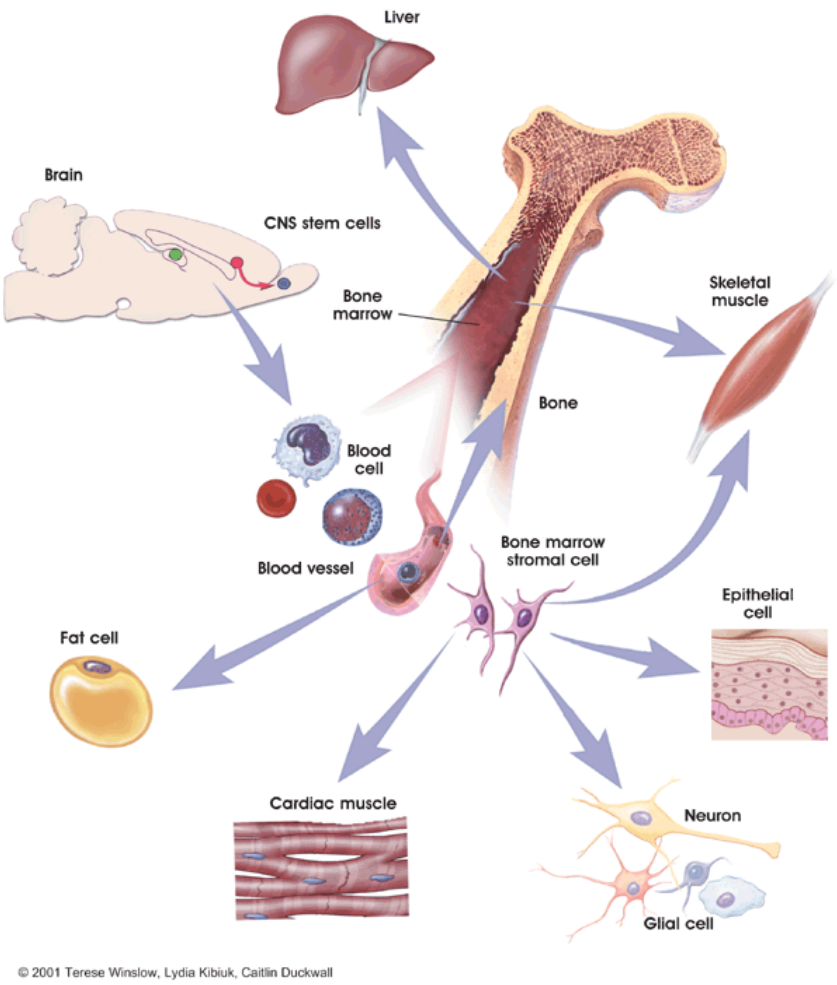
Introduction

Imagine that your father has been diagnosed with Parkinson's disease and you begin to watch his condition deteriorate. Tremors become more evident and his movement more rigid. He is unable to enjoy his normal day to day activities. You fear how the debilitation of this disease will affect his human spirit and you know the condition can only get worse. You hear of countries in Europe who are transplanting embryonic stem cells in the brains of Parkinson's patients. It is a relatively new treatment that is considered unethical in North America due to the lack of research and the use of embryonic stem cells. You begin to ask yourself questions about the ethical use of an embryos' stem cells to treat your father. If you pursue this treatment, will you be sacrificing the life of an unborn child for your father's quality of life?

When does human life begin? The scientific community, the pro-life movement and the pro-choice movement have debated this question for a number of years. The onset of stem cell research has added another dimension to this debate. Is it morally acceptable to cultivate cells from a human embryo to cure a terminal disease? From where do scientists obtain these embryos? Should the therapeutic cloning of an individual be permitted in order to cure a disease of this individual? What happens to the embryo from which the stem cells were retrieved? As these questions are being debated, scientists are considering such scientific endeavors as how stem cells can be used to understand and treat cancer, researching how stem cells can be used to treat spinal cord injuries and how stem cells can provide a cure for Parkinson's disease.

What are Stem Cells?

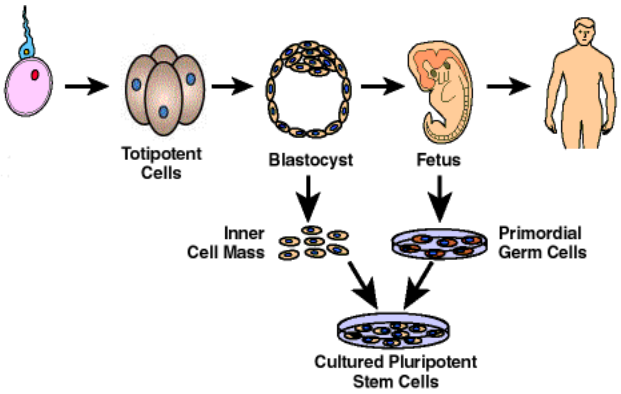
When the human egg is fertilized with sperm, all the genetic information is in place to begin development. Scientists are beginning to understand how a single fertilized egg cell can divide into a multicellular organism with cells that have differentiated to perform a variety of purposes. Each of these differentiated cells has been derived from a single cell and, despite performing different functions, contains identical genetic information. These undifferentiated cells are known as *stem cells* and have the ability to form any type of cell in our bodies. The inner cell mass of the blastocyst contains stem cells that later differentiate into the hundreds of specialized cells that make up the human organism. In adults, stem cells can be found in tissue such as: the bone marrow; skin; liver; peripheral blood; blood vessels; muscle; and brain. The stem cells in adults are used to replace cells that need to be replaced through normal wear and tear, cells that have been damaged through injury, and cells that have been damaged through disease.



Stem cells have three unique properties. First, they have the ability to divide and renew themselves for a long period of time. Secondly, they are unspecialized. Thirdly, they have the ability to differentiate into specialized cells.

Types of Stem Cells

There are two main types of stem cells that scientists are interested in studying: *embryonic stem cells* and *adult stem cells*. Embryonic stem cells can be obtained from the inner cell mass of the blastocyst four or five days after fertilization. Embryonic stem cells can be also derived from a five to ten week old fetus. It is more common to use stem cells from the blastocyst rather than the fetus. Embryonic stem cells are considered to be *pluripotent* which means they may eventually give rise to any type of cell in the human body. Ethical issues arise from the use of embryonic stem cells since the embryos are destroyed and the debate continues to rage about when life begins.



Initially, adult stem cells were believed to mainly give rise to the types of cells of the tissue for which they were found. However, recent research has been exploring the possibility that adult stem cells from one tissue may be able to differentiate into cells of another tissue type. This is known as

transdifferentiation or *plasticity*. This is an area of research that is rapidly advancing, especially since it avoids the ethical issue of using stem cells from embryos. For example, hematopoietic stem cells normally give rise to all the types of blood cells. Recently, they have shown the ability to differentiate into brain cells, skeletal muscle cells, cardiac muscle cells and liver cells. Bone marrow stromal cells normally give rise to bone cells, cartilage cells, fat cells, and other types of connective tissue cells. However recent research is showing that they may differentiate into cardiac muscle cells and skeletal muscle cells. Brain stem cells can be shown to differentiate into blood cells and skeletal muscle cells.

If adult stem cells are able to demonstrate plasticity then it is believed that liposuction could potentially provide a source of stem cell since they have been known to reside in fat tissues. Discarded human umbilical cords and human placentas could also provide valuable sources of stem cells. In the future, a person could also be asked to donate their stem cells to be used later in life, if the need arises.

Present Research

Stem cell research began over 20 years ago when scientists isolated stem cells from mouse embryos. Human stem cells were first isolated from human embryos in 1998. These human embryos were obtained through embryos that were produced for the purpose of *in vitro* fertilization and were no longer required by the donor for fertility purposes. In this case, the donor was required to provide informed consent for their embryos to be used in stem cell research.

Scientists are presently trying to understand two main properties of stem cells. First, they would like to understand how stem cells can remain unspecialized for a period of time and renew themselves for a period of years. Secondly, scientists would also like to understand the signals that eventually cause cells to differentiate into specialized cells. Scientists believe that certain genes within a cell must be "turned on" and other genes must be "turned off" to become these specialized cells. This fundamental knowledge would enable scientists to develop treatment for diseases in which cells have been damaged beyond the means of the body to normally repair themselves.

Scientists have found that embryonic stem cells that divide within the laboratory, renew themselves without differentiating for a year or more. The same can not be said for adult stem cells at present. Scientists are hoping to understand the processes that regulate stem cells division to remain unspecialized and proliferate compared to the processes that lead to the differentiation of cells. This knowledge can enable scientists to grow embryonic adult stem cells in the laboratory more effectively. It has actually taken twenty years for scientists to learn how to grow embryonic stem cells without them spontaneously differentiating into specialized cells. The ability to grow large numbers of unspecialized cells in the laboratory is critical to continued research.

Scientists believe that certain genes are found within stem cells that produce internal signals that guide cell differentiation. They also believe that there are external signals that guide cell differentiation. These signals include chemicals secreted by other cells, physical contact with neighbouring cells and the presence of certain molecules. Understanding these signals can better enable scientists to learn how to control the differentiation into the desired cell type.

Scientists are also learning to direct the differentiation of stem cells through a variety of techniques. Such techniques include changing the chemical composition of the medium, altering the surface of the culture dish or modifying the cells by inserting specific genes. The development and refinement of techniques that control differentiation will eventually lead to cells that can be transplanted to cure diseases such as heart disease, muscular dystrophy and diabetes.

Finally, scientists are developing methods of *therapeutic cloning*. (Also known as *somatic cell transfer*.). Stem cells are created by transferring genetic material from a transplant recipient into an egg cell. This egg cell is stimulated to divide and produce stem cells that contain identical genetic information as the patient. However, this process has resulted in several ethical debates. Does the production of these stem cells result in the

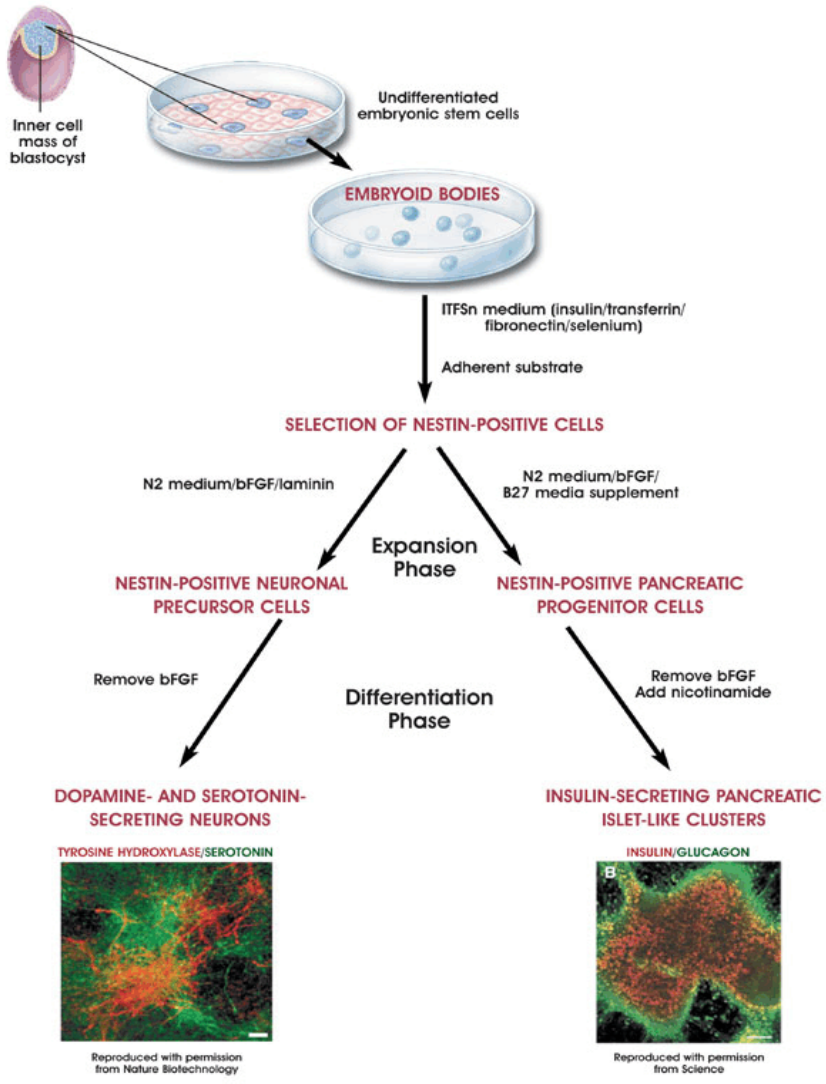
production of an embryo that is later destroyed? Is this process essentially the cloning of an individual?

The Technique of Culturing Embryonic Stem Cells

Millions of stem cells can be cultured from approximately 30 cells taken from the inner cell mass of the blastocyst in about six months.

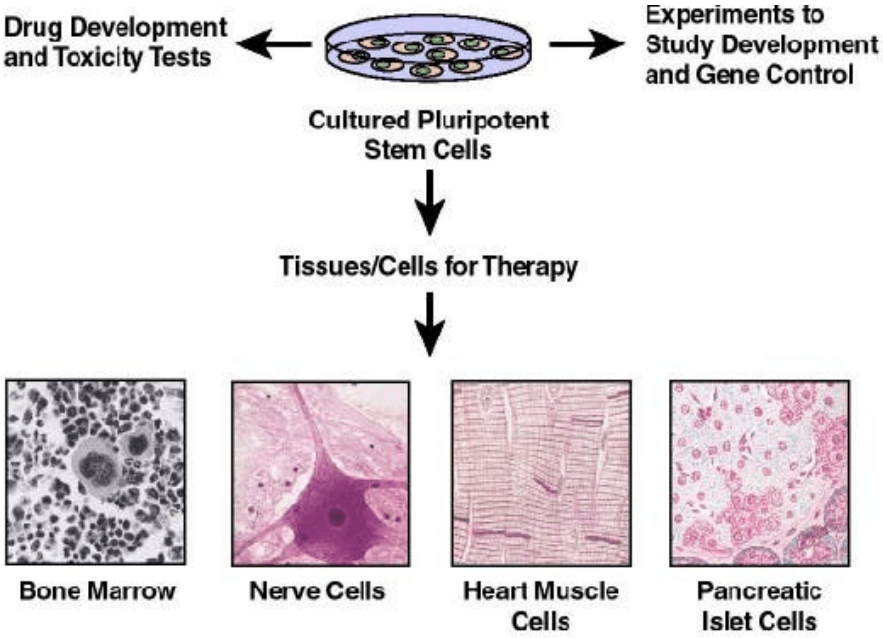
When the cells from the inner cell mass are removed, they are transferred to a plastic laboratory culture dish. This culture dish contains a *nutrient broth*. The inner surface of the culture dish is coated with a *feeder layer*. This layer contains mouse embryonic skin cells that are treated so that they will not divide. The feeder layer is important because it provides the inner cells mass with a sticky layer to which they may adhere. It also releases nutrients into the culture medium. The feeder layer of mouse embryonic stem cells does pose some problems in that viruses and other macromolecules could be transmitted to human cells. Scientists are presently developing methods of culturing human stem cells that do not require the mouse feeder cells.

The stem cells will divide very quickly and overcrowd the culture dish. They will then be plated to other culture dishes. This process of *replating* will continue for about six months. Stem cells can be frozen and used later for experimentation.



The Potential use of Stem Cells in the Treatment of Disease

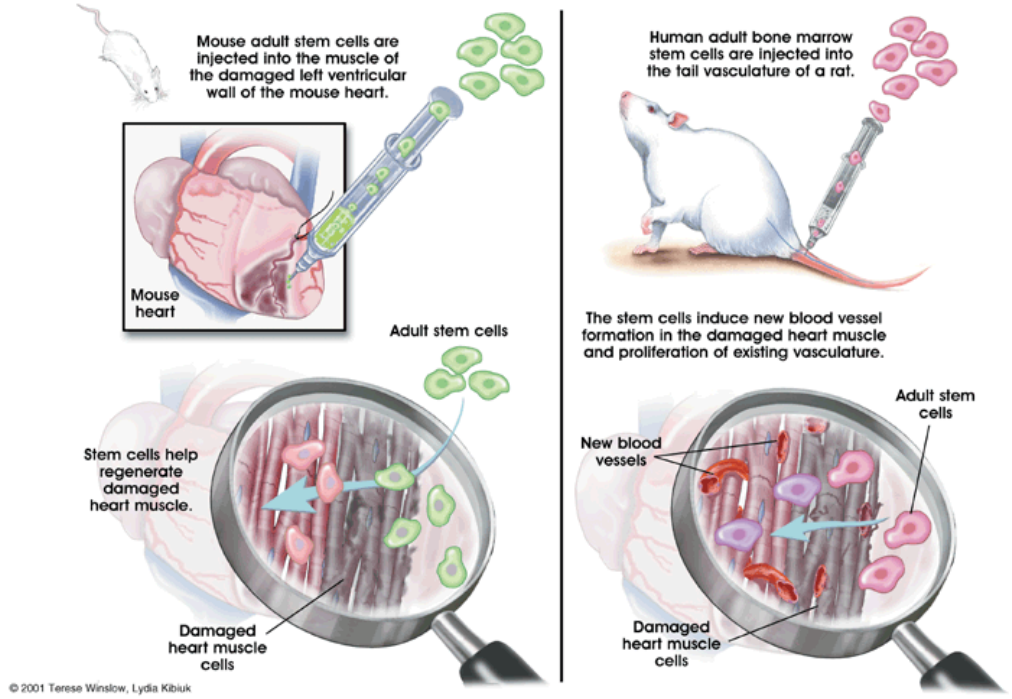
As discussed earlier, stem cells are useful in research because they are unspecialized cells that have the potential to differentiate into specialized cells.



Specialized cells in the human body that have been damaged through injury or disease could be replaced by stem cells if these stem cells can be induced to differentiate into the cell type that has been damaged. This is known as *cell-based therapies*. For example, this means that stem cells can potentially be used to replace damaged cells of the pancreas that no longer produce insulin. Stem cells could potentially replace the nervous cells that have deteriorated in an individual with Parkinson's disease. There are a great many other diseases and conditions that may be treated through the success of stem cell research. They include: spinal cord injury; stroke; Alzheimer's disease; burns; osteoarthritis; rheumatoid arthritis; cancer; Purkinje cell degeneration; Duchenne's muscular dystrophy; heart disease; vision loss; and hearing loss. Scientists are specifically working on the directed differentiation of adult stem cells in the treatment of Parkinson's disease, diabetes and heart disease. These specific cell types include dopamine producing neurons, insulin-producing cells and cardiac muscle cells.

In Parkinson's disease, a particular nerve cell or neuron called the dopamine (DA) producing neuron have been degenerated or destroyed. Loss of the DA neuron leads to the tremor, rigidity and loss of mobility observed in Parkinson's patients. Studies on mice with Parkinson's disease indicate that when dopamine producing neurons were transplanted into the brains of mice the symptoms of Parkinson's were alleviated. Scientists are now trying to produce dopamine producing neurons from human stem cells for *neurotransplantation* of Parkinson's patients. It is quite possible that within the lifetime of this module, a cure for Parkinson's disease could be found.

As the knowledge of how stem cells differentiate unfolds, a better understanding of diseases caused by abnormal cells division and differentiation such as cancer can be obtained and ultimately lead to a cure. Understanding these processes can also lead to the prevention of birth defects.



The use of stem cells in cancer treatment can have a wide range of applications. Cancer cells and stem cells both have the ability to renew themselves. Understanding these processes can help scientists understand why cancer cells resist aggressive treatments and continue to proliferate. As well, cancer treatments such as chemotherapy can cause a high degree of damage to healthy cells and tissues in the body. Stem cells can be used to restore the immune system for aggressive cancer treatments. Embryonic stem cells could also be used to restore the immune system of patients undergoing bone marrow transplants.

Stem cells may eventually be produced that are resistant to chemotherapy and therefore better enable patients to deal with the effects of chemotherapy. In addition, stem cells could be used to create cancer vaccines by providing antibodies against cancer cells.

The Benefits and Risks of Embryological Stem Cells and Adult Stem Cells

Most of the debate around stem cell research centers around the use of embryological stem cells as opposed to adult stem cells. Embryonic stem cells can differentiate into any type of specialized cells. The plasticity of adult stem cells is only presently being investigated and more research is needed to determine how adult stem cells can differentiate into other types of cells. Researchers have learned how to culture embryonic stem cells in large numbers for the past twenty years. Adult stem cells are difficult to find in mature tissues and researchers have not developed techniques to culture them in large numbers.

The use of adult stem cells from a patient offers a distinct advantage in that this patient will not reject their own stem cells after transplantation. Not only is the risk of rejection eliminated from the patient's immune system but also immunosuppressant drugs will not be necessary. It has not been determined whether a patient would reject stem cells from a donor such as in the case of the use of embryonic stem cells.

There is the potential that stem cells derived from an embryo could contain viruses or diseases that could be transmitted to the patient. There is also a concern that these stem cells lead to the development of tumors after transplantation.

Conclusion

Research on the use of stem cells is advancing fast. Stem cells research has also gained momentum through the involvement of such celebrities as Michael J. Fox and Christopher Reeves. Stem cells could be used to replace the damaged neurons in the brain of Parkinson's patients such as Michael J. Fox. They could also be used to repair the damaged spinal cord tissue such as in the case of Christopher Reeves. Some however, will argue that one should not devalue human life from the moment of conception until death and that it would be immoral to use embryonic stem cells in the treatment of disease. At present, the Canadian Institute of Health Research has developed guidelines that prohibit cloning and the production of embryos strictly for research purposes. Research on embryos is only permitted if those embryos were developed for reproductive purposes and they are obtained with full informed consent.

The debate about the ethical use of stem cells rages on in society. In the meantime, researchers continue their work with stem cells from the existing embryos produced through *in vitro* fertilization and are developing the possibilities from adult stem cells. They must do this in the hope of finding successful treatments for disease and damaged tissue while respecting the ethical issues surrounding the debate of stem cell research.

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Questions

Understanding Concepts

1. Construct a table that outlines the benefits and risks of using embryological stem cells compared to adult stem cells.
2. What are the potential sources of embryological stem cells? What are the potential sources of adult stem cells?
3. What are three properties possessed by stem cells that scientists find valuable in their research to use stem cells to treat disease?
4. Describe what scientists know about the factors that cause the differentiation of cells.
5. What techniques have scientists begun to develop that direct the differentiation of stem cells?
6. What is meant by cell-based therapies?
7. Describe the process of therapeutic cloning.
8. Briefly outline the steps used to culture large numbers of embryonic stem cells.

Extensions

1. Scientific research in the use of stem cells is fast advancing. This is an opportunity for students to update this module in regards to the latest research. Research the most current research in any of the following areas:
   - **The use of embryological stem cells**. Are scientists still using embryological stem cells? From where are these stem cells obtained? What are the present advantages offered by the use of these stem cells? What are the present disadvantages offered by the use of these stem cells? If these types of stem are not being used, why not.
   - **The use of adult stem cells.** Are scientists still using adult stem cells? From where are these stem cells obtained? What are the present advantages offered by the use of these stem cells? What are the present disadvantages offered by the use of these stem cells? If these types of stem are not being used, why not.
   - **The use of stem cells in cell based therapies.** What disorders are presently being explored as disorders that may benefit from stem cell research? Are there any disorders that are being successfully treated through the use of stem cells? Are these therapies using embryological or adult stem cells? What are some possible/potential problems with these treatments?
   - **The use of stem cells in developing drugs.** What type of research is taking place in regard to developing drugs to treat disease? Are stem cells being used successfully in the development of drugs to treat disease? If so, what types of diseases?

This research may be done individually or by student groups. Presentations may be a valuable way for students to share what they have learned.

2 Explore the latest stem cell research in regard to the treatment of a particular disease or disorder. Examples may include Parkinson's Disease, diabetes, spinal cord injury, stroke, Alzheimer's Disease, burns, osteoarthritis, rheumatoid arthritis, cancer, Purkinje cell degeneration, Duchenne's muscular dystrophy, heart disease, vision loss and hearing loss. This may be presented in the form of a paper or class presentation.

3. Read each of the following articles. Each article presents views on the ethical use of stem cells in research. Using the background knowledge that you have obtained in this module and the arguments presented in these articles, develop your own arguments for or against the use of stem cell research.

Actor Christopher Reeve believes that embryonic stem cell research will allow him to walk again one day.

Stem cells are blank human cells that scientists think might be turned into any type of tissue, specifically tissue that might be used to repair -- in Reeve's case, for example -- damaged spinal cord cells.

Some scientists believe that stem cells from fertilized human eggs, known as embryos, hold the most promise for success.

"If you had the FDA (Food and Drug Administration) involved and everybody working together, I am positive in 10 years I'd be on my feet ... I would not be sitting here in a wheelchair," Reeve said.

Reeve, who was paralyzed in a May 1995 horse-riding accident, has joined the debate in the United States over whether the federal government should fund research on stem cells from human embryos created by in-vitro fertilization. Many abortion opponents -- including Pope John Paul II -- also oppose using human embryos for research.

The decision is up to U.S. President George W. Bush, who met Monday with the pontiff in Italy.

There, the pope compared embryo research to euthanasia and infanticide. "A free and virtuous society, which America aspires to be, must reject practices that devalue and violate human life at any stage from conception until natural dead," the Pope said.

It was only recently that scientists began creating embryos specifically for stem cell research. Before that, most embryos for such experiments were fertilized eggs that parents decided not to use for pregnancy and otherwise would have been discarded.

While not directly responding to John Paul's comments, Reeve said that the issue is not about ethics. "You really don't have an ethical problem because you're actually saving lives by using cells that are going to the garbage," Reeve said. "I just don't see how that's immoral or unethical. I really don't."

In the near future, there is a chance that scientists might be able to obtain stem cells from less-controversial sources, such as umbilical cords. But some researchers say those kinds of cells might never be as medically useful as stem cells from human embryos.

CNN Medical Correspondent Elizabeth Cohen contributed to this report.

Subject: Text of Bush Speech on Embryonic Stem Cell Research
Source: Reuters; August 9, 2001

Text of Bush Speech on Embryonic Stem Cell Research

Following is the text of U.S. President George W. Bush's speech on Thursday announcing his decision to prohibit any federal funding for new embryonic stem cell research:

Good evening. I appreciate you giving me a few minutes of your time tonight so I can discuss with you a complex and difficult issue, an issue that is one of the most profound of our time.

The issue of research involving stem cells derived from human embryos is increasingly the subject of a national debate and dinner table discussions. The issue is confronted every day in laboratories as scientists ponder the ethical ramifications of their work. It is agonized over by parents and many couples as they try to have children or to save children already born.

The issue is debated within the church, with people of different faiths, even many of the same faith, coming to different conclusions.

Many people are finding that the more they know about stem-cell research, the less certain they are about the right ethical and moral conclusions.

My administration must decide whether to allow federal funds, your tax dollars, to be used for scientific research on stem cells derived from human embryos.

A large number of these embryos already exist. They are the product of a process called in vitro fertilization which helps so many couples conceive children. When doctors match sperm and egg to create life outside the womb, they usually produce more embryos than are implanted in the mother. Once a couple successfully has children or if they are unsuccessful, the additional embryos remain frozen in laboratories. Some will not survive during long storage, others are destroyed. A number have been donated to science and used to create privately funded stem-cell lines. And a few have been implanted in an adoptive mother and born and are today healthy children.

Based on preliminary work that has been privately funded, scientists believe further research using stem cells offers great promise that could help improve the lives of those who suffer from many terrible diseases, from juvenile diabetes to Alzheimer, from Parkinsons to spinal cord injuries. And while scientists admit they are not yet certain, they believe stem cells derived from embryos have unique potential.

You should also know that stem cells can be derived from sources other than embryos: from adult cells, from umbilical cords that are discarded after babies are born, from human placentas. And many scientists feel research on these types of stem cells is also promising. Many patients suffering from a range of diseases are already being helped with treatments developed from adult stem cells.

However, most scientists, at least today, believe that research on embryonic stem cells offers the most promise because these cells have the potential to develop in all of the tissues in the body.

Scientists further believe that rapid progress in this research will come only with federal funds. Federal dollars help attract the best and brightest scientists. They ensure new discoveries are widely shared at the largest number of research facilities, and that the research is directed toward the greatest public good.

The United States has a long and proud record of leading the world toward advances in science and medicine that improve human life, and the United States has a long and proud record of upholding the highest standards of ethics as we expand the limits of science and knowledge.

Research on embryonic stem cells raises profound ethical questions, because extracting the stem cell destroys the embryo, and thus destroys its potential for life.

Like a snowflake, each of these embryos is unique, with the unique genetic potential of an individual human being.

As I thought through this issue I kept returning to two fundamental questions. First, are these frozen embryos human life and therefore something precious to be protected? And second, if they're going to be destroyed anyway, shouldn't they be used for a greater good, for research that has the potential to save and improve other lives?

I've asked those questions and others of scientists, scholars, bioethicists, religious leaders, doctors, researchers, members of Congress, my Cabinet and my friends. I have read heartfelt letters from many Americans. I have given this issue a great deal of thought, prayer, and considerable reflection, and I have found widespread disagreement.

On the first issue, are these embryos human life? Well, one researcher told me he believes this five-day-old cluster of cells is not an embryo, not yet an individual but a pre-embryo. He argued that it has the potential for life, but it is not a life because it cannot develop on its own.

And while we must devote enormous energy to conquering disease, it is equally important that we pay attention to the moral concerns raised by the new frontier of human embryo stem cell research. Even the most noble ends do not justify any means.

My position on these issues is shaped by deeply held beliefs. I'm a strong supporter of science and technology, and believe they have the potential for incredible good -- to improve lives, to save life, to conquer disease. Research offers hope that millions of our loved ones may be cured of a disease and rid of their suffering. I have friends whose children suffer from juvenile diabetes. Nancy Reagan has written me about President Reagan's struggle with Alzheimer's. My own family has confronted the tragedy of childhood leukemia. And like all Americans, I have great hope for cures.

I also believe human life is a sacred gift from our creator. I worry about a culture that devalues life, and believe as your president I have an important obligation to foster and encourage respect for life in America and throughout the world.

And while we're all hopeful about the potential of this research, no one can be certain that the science will live up to the hope it has generated.

Eight years ago, scientists believed fetal tissue research offered great hope for cures and treatments, yet the progress to date has not lived up to its initial expectations. Embryonic stem cell research offers both great promise and great peril, so I have decided we must proceed with great care.

As a result of private research, more than 60 genetically diverse stem cell lines already exist. They were created from embryos that have already been destroyed, and they have the ability to regenerate themselves indefinitely, creating ongoing opportunities for research.

I have concluded that we should allow federal funds to be used for research on these existing stem-cell lines, where the life-and- death decision has already been made.

Leading scientists tell me research on these 60 lines has great promise that could lead to breakthrough therapies and cures. This allows us to explore the promise and potential of stem cell research without crossing a fundamental moral line by providing taxpayer funding that would sanction or encourage further destruction of human embryos that have at least the potential for life.
I also believe that great scientific progress can be made through aggressive federal funding of research on

umbilical cord, placenta, adult and animal stem cells, which do not involve the same moral dilemma. This year your government will spent $250 million on this important research.

I will also name a president's council to monitor stem-cell research, to recommend appropriate guidelines and regulations and to consider all of the medical and ethical ramifications of biomedical innovation.

This council will consist of leading scientists, doctors, ethicists, lawyers, theologians and others, and will be chaired by Dr. Leon Cass, a leading biomedical ethicist from the University of Chicago.

This council will keep us apprised of new developments and give our nation a forum to continue to discuss and evaluate these important issues.

As we go forward, I hope we will always be guided by both intellect and heart, by both our capabilities and our conscience. I have made this decision with great care, and I pray it is the right one.

Thank you for listening. Good night, and God bless America.

Genetics Research in Newfoundland and Labrador

Outcomes:

1. Predict the effects of mutations on protein synthesis, phenotypes, and heredity. (315-7)
2. Describe factors that may lead to mutations in cell's genetic information. (315-6)
3. Explain the circumstances that lead to genetic disease. (315-8)
4. Demonstrate an understanding of genetic engineering, using knowledge of DNA. (315-9)
5. Describe and evaluate the design of technological solutions and the way they function, using genetic principles. (116-6)
6. Construct arguments to support a decision or judgment concerning the use of genetic engineering, using examples and evidence and recognizing various perspectives. (118-6)
7. Analyze and describe examples where genetics based technologies were developed and based on scientific understanding. (116-4)
8. Analyze from a variety of perspectives the risks and benefits to society and the environment of applying the scientific knowledge gained through the genetic research. (118-2)
9. Identify and describe science and technology-based careers related to the field of biotechnology. (117-7)

Introduction

If you had the opportunity to help scientists cure a particular disease, would you do so? Most people would likely say, yes. There are many people across Newfoundland and Labrador who are doing exactly that. They are giving consent to a local company called Newfound Genomics to use their DNA in genetic research.

Newfoundland and Labrador has become the focus of some exciting research in the field of genetics in recent years. Newfound Genomics Incorporated is a biotechnology company that was established in Newfoundland and Labrador in June 2000 to study how genes affect human health and disease. *Genomics* is the study of how genes apply to health and disease.

Founder Populations

Newfoundland's current inhabitants arose from about 20,000 to 30,000 immigrants from Ireland, Scotland and Southwest England in the late 1600's to the 1840's making those early immigrants Newfoundland's *founding population*. The population grew largely from expansion rather than through immigration, which limited genetic diversity. Certain genetic traits became more prevalent in the new population while other traits were eradicated. This explains why, compared to other populations, there is a higher incidence of some diseases in Newfoundland while some other diseases are rare or non-existent.

Newfound Genomics and their Research

Scientists at Newfound Genomics are presently studying some common diseases in Newfoundland

and Labrador. These diseases include obesity, type 2 diabetes, inflammatory bowel disease and osteoarthritis. Their research includes clinical, environmental and genetic factors of these diseases. They will also examine relationships between different diseases. Other diseases are also being examined through partnerships with other academic institutions. Future studies may include inflammatory arthritis and, respiratory, infectious and dermatological diseases.

Genes and Disease

DNA in our cells is used to make proteins. When genes in our DNA are altered, the proteins produced by them are altered as well, and we become more susceptible to disease. Some of these variations in the genetic code are referred to as *Single Nucleotide Polymorphisms (SNPs).* In the case of SNPs, a nucleotide *substitution* has taken place in the genome. Other variants in the genome include *insertions* and *deletions* in the nucleotide sequence.

Some SNPs have already been identified as associated with some diseases. The Affymetrix® and MassARRAY genotyping systems are two types of technology discussed later that scientists are using to determine if an individual possesses the genetic make-up (SNP) that contributes to a particular disease. Imagine that you can now provide a genetics company with a swab of your cheek cells and they can use this technology to determine the presence of variation in your genome that can either diagnose a particular disease or predict the onset of a disease.

Other SNPs have not been identified with any disease. These SNPs may have no effect on the health of the individual or the SNP may have yet to be connected to a particular disease. This is largely the work that researchers at Newfound Genomics are performing. They can examine the genome for SNPs and are hoping to make connections between individuals with a particular SNP and a disease. Researchers can then examine the sequences of nucleotides in these SNPs in more detail to understand their effect on disease.

A better understanding of the sequences of these genes can lead to a better understanding of the physiological effects of their variations. This may, in turn, lead to the development of drugs that may restore the normal functioning of the affected protein. This is a more revolutionary way of treating disease. Instead of treating the symptoms of a disease, scientists are discovering the exact cause of a disease in regard to the genetic variation. Determining the precise genetic cause and the affected protein, will likely greater enable scientists to treat the cause of a disease as opposed to the symptoms.

Laboratory Technology

Scientists at Newfound Genomics obtain DNA samples and supporting medical information from patient donors. The DNA samples taken from patient volunteers are either in the form of blood samples or *buccal* cells. Buccal cells are epithelial cells taken from the inside of the cheek. DNA is then extracted from either the blood samples or the buccal cells.

DNA Extraction

Laboratory technologists extract DNA using blood cells or buccal cells. The DNA can be extracted using a kit from a scientific supply company.

In the case of blood samples, DNA extraction begins with lysing the red blood cells and collecting the white blood cells. A solution (enzyme) is then used to break down the lipid membranes of the cells and the nuclei of the cells to release DNA. Another solution is used to remove protein from the DNA sample. The DNA is precipitated in alcohol. After drying, the DNA is dissolved in a solution used to protect the DNA from enzymes that cause shearing. In the case of buccal cells, the same procedure is used but does not include the red cell lysis step.

After DNA extraction has taken place, freezers are used to store DNA at -86˚ C for an indefinite period of time for analysis and further study.

DNA Genotyping

Scientists will use the DNA samples to carry out a process called *genotyping*. This is considered to be analysis using *genetic markers*. Researchers at Newfound Genomics are presently looking at gene

markers that could indicate the presence of a gene sequence contributing to a particular disease. A gene marker is a specific portion of a chromosome that lies near a particular gene or is part of a particular gene that is being studied. Once the gene marker is identified, a probe can be developed to search for the gene marker in other DNA samples. This probe consists of a DNA sequence that is complementary to the sequence of the gene marker. Sometimes this probe also contains a radioactive or fluorescent chemical tag so it can easily be determined if it bonds to the gene marker.

Newfound Genomics uses three methods of genotyping:

Basic Molecular Genotyping
This involves a PCR reaction to amplify DNA. A review of PCR amplification is found in Figure 1. Specific primers have been developed for the variant to be examined in the genome.

Gel electrophoresis is then used to determine if the variant is present. In gel electrophoresis, a 2% agarose gel is used with ethidium bromide (EtBr) stain to adhere to the DNA. The EtBr will illuminate with UV light. If the variant is present in the DNA sample, then the primer would have enabled the DNA to amplify and the EtBr would bind to the DNA and would be evident in UV light.

This is a more time consuming method of genotyping and tends to be used with small projects. With the new MassARRAY technology recently implemented at Newfound Genomics, it will likely be used less often.

Affymetrix® Genotyping
The Affymetrix technology will perform a general scan of the genome. It contains a gene chip that has the capability of scanning for the presence of SNPs. The Affymetrix System at Newfound Genomics has a gene chip that can search for 1500 SNPs. A chip is presently being developed that can scan for 10, 000 SNPs. As discussed earlier, it can be used to determine if a SNP known to contribute to disease is present or to make connections between the presence of SNPs and the appearance of a disease.

The Affymetrix technology can also be used in *gene expression* studies. In gene expression studies, scientists are examining particular genes that may be "turned on" or "turned off" during the different stages of a disease.

The Affymetrix technology incorporates PCR into its technology. It will use probes in its technology to search for genetic markers. It also uses fluorescent chemical tags in other aspects of its technology to detect the presence of genetic markers.

MassARRAY Genotyping
The MassARRAY technology is more specific than the Affymetrix and can compare a greater number of parameters for experimental work. The MassARRAY will analyse genetic samples for a particular SNP or a number of SNPs. It is capable of examining from either the entire genome, several areas of the genome or one specific area of the genome for a SNP. It can examine the genetic information for one individual or many individuals for one or many SNPs. In addition, it can examine and compare a large number of individuals for SNPs. Like the Affymetrix, it is useful is making the connection between the presence of a SNP and a disease. It can also examine the genome for the presence of SNPs that are known to be related to disease.

The MassARRAY also incorporates PCR into it technology in addition to the use of primers. Sequenom Inc, a partner of Newfound Genomics, developed this technology.

Ethics

All studies at Newfound Genomics are approved by the HIC (Human Investigations Committee) at the Faculty of Medicine. Donor volunteers are required to give their full informed consent. This consent allows researchers to use the donor volunteers' DNA for one particular study, or it may allow researchers to use a donor volunteers DNA for similar studies later. All participants must be volunteers since it is considered unethical to purchase body fluids in Canada. Newfound Genomics does not provide individual feedback to participating volunteers regarding their specific genetic makeup. The genetic

information obtained is pooled with information from all participating volunteers with a similar medical condition.

The main ethical issue concerning the use of donor volunteers' DNA deals with privacy. Newfound Genomics does not provide insurance companies nor employers' access to DNA information to protect the privacy of their volunteers. It is expected that the type of research done by Newfound Genomics can determine the presence of genes that may contribute to certain diseases. If insurance companies were able to access this kind of information, would it likely influence decisions regarding the issuing of life insurance policies? If employers were aware that an employee or a potential employee had the genetic make-up that would likely lead to the development of a debilitating disease, would they make an unfavorable decision regarding the future or continued employment based on this information? As scientists continue to uncover the connection between genes and disease in the hope of better medical treatment, it is conceivable that there are other agencies such as businesses that may use this knowledge to further their own interests. This is why genomics companies are careful to ensure the confidentiality of those who volunteer the use of their DNA to further the interest of science and will develop their own codes of ethical conduct to reassure volunteers and the public about the nature of their research.

The Business Community

Newfound Genomics must act as an instrument of science but also must operate in the business world. It is important that their research is properly financed. The company is focusing on 3 lines of business; novel gene discovery, validation studies, and laboratory services. It is also important that Newfound Genomics does not work in isolation from other genetic research companies and academic institutions. For example, Newfound Genomics has developed a partnership with Memorial University working to build research capacity and joint research initiatives.

Once Newfound Genomics discovers genes that are responsible for the development of certain diseases they will patent the use of this information for the development of drugs and diagnostic applications. It is predicted that drugs developed from genomics research will represent between 30-50% of global drug revenues by the year 2020.

Genetic companies are cautious regarding the ownership of genetic information. If you are patenting DNA, is it then the property of the individual who volunteered the use of their DNA that is being patented? Do genetic companies have the right to patent DNA if it can be argued the property of the donor? If DNA is patented, then do those who volunteered their DNA have a right to reap the economic benefits of the research? Imagine how difficult it could be for genetic companies to exist as business institutions if all those who donated their DNA were provided royalties based on the success of the research. Furthermore, is it ethical for one to sell their DNA for research or for companies to buy it?

Careers in Biotechnology

At present, Newfound Genomics is located in St. John's and on the west coast of the province employing about 10 people. Newfound Genomics collaborates with Memorial University in the training of scientists, students and health care professionals for research. Their intention is to advance the academic, intellectual, social and economic benefits for this province. It is expected that genetics research will be a fast growing industry due to the unique genetic make-up of this province and therefore offer employment opportunities to people in this province.

Conclusion

Newfound Genomics is an established and well-recognized biotechnology research company with a number of research projects underway. Although it is too early for major results, any findings at present are kept within the domain of the company. In fact, the company will not release any findings until it is published and undergone a peer review. This is because this information is considered "intellectual property" and it must remain private so that Newfound Genomics can reap the academic and

financial benefits of their work. It will be interesting to see the extent of the development of biotechnology and genetics research in our province and to anticipate the benefits for Newfoundland and Labrador both economically and medically.

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Special thanks to Lynette Peddle, BSc who explained the technological aspects of Newfound Genomics.

Questions

Understanding Concepts

1. Outline the benefits, both medical and economic, of genetics research in this province.

2. What is a founder population? How does it lend itself to genetics research?

3. Why are researchers looking for genetic markers?

4. What are some of the long term goals of Newfound Genomics?

5. Why is it important to study genes in relation to disease?

6. What are some of the benefits offered to Newfound Genomics by their partnership with other biotechnology companies?

7. What are the benefits of using Affymetrix and MassARRAY technology ?

8. Give two reasons why Newfound Genomics does not release the results of their research until it is published.

Extensions

1. Go to the website for Newfound Genomics (www.newfound-genomics.com) and follow the links to "**about us**" and "**Our Team**". Examine the educational background and work experience of the Newfound Genomics team members. Make a list of 15 items that describe the qualifications and work experience required to work in the field of biotechnology. What conclusions can you make about this list?

2. Why is it important that Newfound Genomics assure their patient volunteers that access to their DNA from outside groups will be protected?

3. Consider the following issues:
    1. Do you want to know if you will suffer from a genetic condition later in life?
    2. Do employers have the right to know your genetic status? Insurance companies?
    3. Who should have ownership of genetic information?

4. Research how you may carry out a DNA extraction using a DNA source such as onion cells, a blender, salt, detergent, meat tenderizer and ethanol. What is the reasoning behind the use of each of the materials used in this type of DNA extraction?

Extraterrestrial Life: Myth or Reality

Outcomes:

1. Outline evidence and arguments pertaining to the origin, development, and diversity of living organisms on Earth. (316-4)
2. Explain the role of evidence, theories and paradigms in the development of evolutionary knowledge. (114-2)
3. Explain how knowledge of evolution evolves as new evidence comes to light and as laws and theories are tested and subsequently restricted, revised or replaced. (115-7)
4. Construct arguments to support a decision or judgment, using examples and evidence and recognizing various perspectives. (118-6)
5. Identify new questions that arise from what was learned. (214-17)
6. Use library and electronic research tools to collect information on a given topic. (213-6)

Introduction

Imagine if somewhere in our galaxy, or beyond, organisms resembling intelligent life existed. What if extraterrestrial beings, such as Vulcans and Klingon Warriors of Star Trek, actually roamed around outer space? Many scientists believe that life could possibly exist on other planets. *Exobiology*, or *Astrobiology*, is a branch of biology that studies the possibility of life beyond Earth. Support for Exobiology can actually be found using our knowledge of how life has formed and evolved on Earth. Since the last century, numerous expeditions have been made and probes have been sent throughout our solar system in search of extraterrestrial life. On Earth, radio-communication is used to send signals into outer space in the hopes of reaching intelligent life. Radio-telescopes are used to detect signals from extraterrestrials. This module uses what is known about the origin and evolution of life on Earth to examine the possibility of extraterrestrial life.

The Origin of Life on Earth

The Big Bang Theory attempts to explain how the sun and planets in our universe were formed. It states that at one time our entire universe was compressed into one atomic nucleus. Between 10-12 billion years ago an extraordinary explosion, trillions of degrees in temperature, blew apart the universe and it has been expanding ever since. Swirling clouds of dust condensed in the center of our solar system to form the sun and swirling clouds of dust and ice that orbited the sun came together, through gravity, to form the planets.

Earth probably formed about 4.5 billion years ago. At first, the atmosphere probably contained hydrogen gas. Later, volcanoes likely created an atmosphere that was made up of carbon monoxide, carbon dioxide, nitrogen, water vapour and possibly methane and ammonia. Oxygen was not present in

this atmosphere. It is important to consider this because oxygen is considered to be an oxidizing agent that would disrupt chemical bonds. This would prevent the formation of organic molecules and, therefore, life as we know it.

In the 1920's Haldane-Oparin hypothesized that inorganic molecules can be used to make organic molecules. They predicted that the components of Earth's early atmosphere could spontaneously develop into organic compounds in the presence of an energy source. Gases containing hydrogen, ammonia, methane and water vapour condensed to form pools on Earth's surface known as primordial soup. This mixture spontaneously produced organic compounds when it was exposed to lightning and ultraviolet radiation. These organic compounds evolved over a long period of time to produce early life forms.

Further support for the Haldane-Oparin hypothesis, was provided by experiments of Miller and Urey in 1953. Miller and Urey designed an apparatus that combined methane, ammonia, water vapour and hydrogen. They exposed these gases to an energy source that simulated lightning. They discovered that urea, amino acids and other organic compounds were produced.

As a result of the work done by these scientists, it was believed that the atmosphere is composed of gases that could produce organic compounds. These gases are carbon dioxide, nitrogen, water vapour, and small amounts of hydrogen and carbon monoxide. It was also believed that submerged volcanoes and deep sea vents played a greater role in chemical reactions than lightning and UV radiation. In fact, one of the earliest life forms on earth are Archae bacteria found in hot springs, nourished by the thermal vents of the Earth's molten core.

Scientists believe that early life forms originated from small organic molecules called monomers. Organic molecules then advanced to polymers such as nucleic acids and proteins. It has been found that clay can be used to polymerize reactions in which monomers can be joined into polymers. Scientists suggest that monomers may have splashed from the oceans onto lava or other hot rocks, bonded electrically to the rocks and then polymerized through catalysts such as iron and zinc in the rocks. Monomers and polymers may have formed aggregates and developed forms of heredity and reproduction.

The first organisms probably came into being about 4.1 billion years ago when Earth's crust first solidified. Evidence of ancient prokaryotic fossils called stromatolites dates back to 3.5 billion years ago. The stromatolites were likely photosynthetic but heterotrophic life forms probably existed 4 billion years ago. Earth would have required a reducing atmosphere as opposed to an oxidizing atmosphere (which would have had existed at the time of the photosynthetic stromatolites). A reducing atmosphere would add electrons to molecules, thereby enabling simple molecules to form more complex molecules. Eventually, these complex molecules became enclosed in membranes and the first organisms appeared.

Another theory, the Panspermia theory, explained that life originated elsewhere in the universe and somehow found its way to Earth by intelligent beings or by chance, such as by meteorites. The fact that rocks have traveled from Mars to Earth lends support to this theory. It is also known that microorganisms can remain dormant for a long period of time and survive under space conditions. Therefore, it seems possible that microorganisms from Mars or from meteors could have reached Earth and survived.

Based on these theories, scientists have been exploring space for possible clues to the existence of life. They have been looking for an atmosphere similar to Earth's early atmosphere. They are also looking for water, organic molecules, and an energy source such as the sun or volcanoes.

Extreme Environments on Earth

Life was not believed to have existed in extreme environments until recent years. These extreme environments include temperatures below zero and temperatures of near boiling. They include miles above in the atmosphere and miles beneath Earth's surface. Spores can hibernate for centuries and flourish when water reenters the environment. Organisms can live in extremes of pressure, salinity,

acidity and radiation. Organisms that live in extreme environments are known as *extremophiles*.

The presence of extremophiles on Earth indicates that life can exist on the icy planets and hot planets. Extremophiles have been found under thousands of meters of ice in Antarctica in conditions believed to the similar to Jupiter's moon Europa. Extremophiles are common in hot ocean vents and it is believed that these bacteria may be the first life forms on Earth. Scientists believe that planets undergoing volcanic activity in the presence of water could foster similar life forms as those found on Earth near the hot ocean vents. Extremophiles have also been found living in pockets of water several kilometers below Earth's surface. They use hydrogen gas to survive, formed by the splitting of water in the presence of uranium. Scientists believe that it is possible to find this kind of life form on Mars since water and uranium are present on this planet.

Scientists hope to better understand the origin of life on Earth and how life might originate on other planets. They have been exploring places on Earth that resemble the conditions of Early earth when life began. These environments include the ocean floor, the surface of hot volcanic springs and tidal pools. If these conditions that are believed to have produced life on earth exist elsewhere in the universe, then life may exist elsewhere in the universe. Scientists are looking for planets and moons that may have molten cores and oceans. Sunlight is not always considered essential since it is not necessary for chemical reactions (chemosynthesis) if geologic activity is present.

The Search for Life Beyond Earth

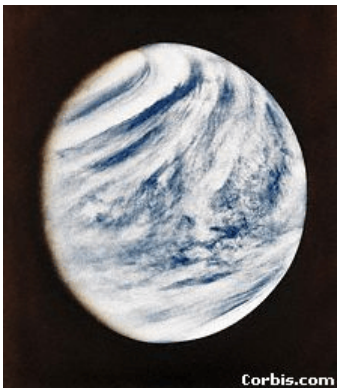
Scientists are aware that the elements found on Earth are the same that exist throughout the universe. These elements are believed to have been formed by exploding stars. Therefore, it is reasonable to assume that the carbon in our bodies, the iron in our blood, and the calcium in our bones came from processes that took place in space.

As mentioned earlier, scientists haven been exploring the universe for evidence of life by looking for three main components that could support life: an energy source, water and organic molecules. Organic molecules have been found on other planets. Comets have been shown to contain water and organic matter. Volcanoes on Earth and other planets can provide energy for life, as well as, water vapour and organic compounds. The icy surfaces of moons and planets also suggests that liquid water could have existed or presently exists to sustain life.

Life from Earth has been shown to survive under the conditions of the moon. Bacteria that were accidently transported to the moon by a spacecraft survived on the moon. This suggests that if life from Earth could survive on the moon, then perhaps it could have evolved and survived elsewhere in the universe.

The habitable zone in our solar system is the region in which scientists believe life may be supported. It was once believed to be between the planets of Venus and Mars. This is because they are close enough to the Sun for the solar energy to drive chemical reactions but not so close that the energy of the Sun would destroy organic molecules or evaporate water from the surface of these planets. Scientists have expanded the habitable zone since the gravitational pull of larger planets can create enough energy to heat the cores of orbiting moons. As a result, there are several planets and moons that could be habitable.

***Venus*:** Numerous space missions have been sent over the years to Venus from the US and the former Soviet Union. The Venera probes from the Soviets in 1966 to 1982 found that Venus was dry and hot with very little oxygen. The heat was so intense that the probes were destroyed after a half hour of collecting data. It is believed that Venus was more temperate at one time but that some kind of catastrophe created a greenhouse effect that trapped heat within the atmosphere. Venus's terrain consists of gently rolling plains with some broad depressions and low rising mountains. Much of Venus is covered by lava flows and some active



volcanoes still exist. It is believed that Venus once had large amounts of water. Now, rain falls as carbon dioxide and sulfur. The atmosphere is made up of mainly carbon dioxide and thick layers of sulfuric acid. Lightning strikes at a rate of more that 10 times per second. There are low amounts of water vapor and oxygen.

Mars: There have been numerous expeditions to Mars in search of life. NASA Viking probes in 1976 examined soil from the surface of Mars to look for signs of life. No life was found but some chemical reactions were evident in the soil. Dry river beds were also found to indicate that there was once water on the surface. This means that the atmosphere was more dense at one time and may have supported life. Polar ice caps on Mars grow and recede with the seasons. The landscape of Mars consists of plains, canyons, mountains, volcanoes, craters and dry river beds. There is presently a thin atmosphere composed of carbon dioxide, nitrogen, argon and small amounts of oxygen and water. It is believed that a catastrophic event must have occurred about 3.5 billion years ago. The atmosphere thinned out and the ozone layer that may have existed collapsed. The planet was exposed to harmful UV rays and the river beds either evaporated or froze into the ground.

Mars meteorites found in Antarctica may contain possible fossils. This has created serious debate among scientists. Some believe that life once existed on Mars and that we may one day find a rich fossil.

Europa: Europa is one the moons that orbit Jupiter. Scientists are considering the possibility that life may exist on Europa because they have found evidence to support the existence of oceans beneath its icy surface. The Galileo space probe found the icy landscape was fractured and suggests that something must be constantly fracturing and replacing the ice such as an ocean beneath. The lack of craters also indicates that the icy surface must constantly be replaced. Scientists are speculating that life could exist in this ocean. The ocean may be warmed by Europa's molten core and may contain deep sea vents that support life similar to Earth. The surface of Europa is relatively smooth with very few craters. The gravitational pull of Jupiter could create enough heat to maintain liquid water underneath Europa'a icy surface. The atmosphere is composed solely of oxygen. It is believed that this oxygen is not produced biologically.

Titan: Titan is Saturn's largest moon and is characterized by an impenetrably disease, thick, clouded atmosphere. Its lower atmosphere is composed primarily of nitrogen, with low amounts of argon and methane. Its upper atmosphere contains high amounts of methane formed from the trace amounts of organic compounds, known as liquid hydrocarbon, in the lower atmosphere. It is believed that there are large lakes on the surface of Titan containing these liquid hydrocarbons and that these conditions are similar to those of the primordial Earth when terrestrial life originated. Pictures from the Hubble telescope indicate that there may be land masses similar to continents. Probes should reach Titan in 2004 to determine the accuracy of these pictures. In 1979, the Pioneer 11 spacecraft determined that the temperature was too cold to support life. Since then the discovery of extremophiles on Earth suggest that this may not be the case.

In 1998, the European Space Agency's Infrared Space Observatory (ISO) discovered water vapor in the atmosphere of Titan. The distance from the sun would indicate that the surface would be too cold to support liquid water but scientists speculate that it is possible that comets or asteroids striking the surface could maintain water in its liquid state for up to 1000 years.

Tagish Lake Meteorite:
Fragments of a meteorite fell to Earth in 1999 in Tagish Lake of the Yukon territory. These fragments contained organic blobs similar to those created in laboratories attempting to simulate life. It is possible that Earth was provided with these organic globules from meteorites throughout history, including when life first began to form. This meteorite originated from the outer asteroid belt and could have easily landed on Jupiter and Europa.

This discovery has added to the debate over the Panspermia theory.

Conclusion

Many scientists believe that intelligent life forms do not exist beyond Earth. More scientists are likely to agree that microscopic life is common in our galaxy. However, many feel that our search among the stars for signs of life is much like the voyage of Columbus. We will never know whether life exists elsewhere unless we continue our exploration of the universe. "...Our mission is to explore strange new worlds; to seek out new life and new civilizations; to boldly go where no man has gone before..."

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Questions

Understanding Concepts

1 Discuss the significance of the work done by Haldane, Oparin, Miller, and Urey regarding the beginning of life on Earth.

2. What features are scientists exploring on other planets that may lead to the formation and existence of life?

3. What types of evidence have been found by scientists to suggest life can exist beyond Earth?

4. Describe five types of extremophiles found on Earth. Explain why scientists believe they may be found elsewhere in the universe.

5. What evidence suggests that life could exist on Venus, Mars, Europa, and Titan?

Extensions:

1. Enter the following website: www.pbs.org/lifebeyondearth/resources/teacher.html. Do the activity entiltled *Alien Creatures: Extra terrestrial and Terrestrial Oddities*. Use what you know about evolution and adaptation to create your own alien creature suited to live according to the conditions on another planet.

2. Enter the following website: www.pbs.org/lifebeyondearth/resources/teacher.html. Do the activity entiltled *The Habitable Zone: A Europa Probe.* Design a probe to travel to Europa that would have to consider the conditions of the planet. This probe would search for signs of life which means that you would have to consider how to identify life outside of Earth.

3. Determine the signs of life that researchers should be exploring when looking for life beyond Earth. Consider if these signs of life should be the same as organisms on Earth.

4. Enter the following website: www.pbs.org/lifebeyondearth/listening/drake.html. Use the Drake Equation to calculate the possibility that life exists beyond Earth. Discuss how you feel about the accuracy of this formula.

5. *Cassini Saturn Orbiter* and *Huygens Titan Probe* will reach Titan in the summer of 2004. Research their findings and explore if these results could support the existence of life on Titan.

6. Debate whether or not you feel life could exist beyond Earth.