Activity II: Travel and the Spread of Disease

lesson overview

Materials: Internet access and computers for small student groups; worksheets; biology text and medical guides

Time for set-up: minimal (verify web site availability); if teacher intends on doing sequence comparison with Genbank and PAUP, it is recommended that (s)he attempts it before assigning, so (s)he can trouble shoot any problems for students (about 2 hours).

Time for lesson: About 10 hours. 3 hours for group research (with little or no at-home work), 2 hours for discussion and presentations, 3 hours for sequence analysis (with at-home work for final analysis), 1 hour for transposon/ genetic engineering-related topic research, 1 final hour for presentations / discussion.

Student Prerequisites: Ability to navigate the Internet, cut and paste in a word processing document, work in groups. Basic science and health knowledge.

Icons for recommended subject areas where activities could be used:
PRE, STAT, BIO, Health, SS, ENG

Objectives / Link to Standards Matrix:

Students will learn about the causes, methods of transmission, effects of, and preventative measures for several epidemics.
Students will understand how the spread of epidemics is related to travel.
Students will learn about the historical evolution of air travel and its relatedness to other historical events, such as epidemics.
Students will use the Internet and other sources to obtain information.
Students with create multimedia presentations.
Students will understand how simple preventative strategies can significantly reduce spread of illness, and understand one historical model of this.
Students will design an original model and/or equation to determine the influence of travel on spread of epidemics.
Students will summarize data and analyze it, using charts, graphs, and equations.
Students will understand how illnesses perpetuate themselves through mutation within species and across major taxonomic groups.
Students will obtain and compare DNA or protein sequences, using internet resources, to determine genetic relatedness between "strains."
Students will discuss and learn the social and scientific significance of mutation, gene jumping, and genetic engineering.

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Student Assessments: This handout, charts and graphs, 2 presentations, original scientific and/or mathematic model, math (polynomial) work and prose explanations, tree of relatedness, trees or sequence alignment, 2 discussions

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Travel has been linked to the spread of disease for centuries. With the increased development of transportation, including highways and airports, the road is being paved for the speedy transport of diseases from one place to another.

You will be assigned one epidemic to research as a group, using the prompts and questions below. Use the following websites to answer these questions and begin your group work.

Thinkquest (**Start here**!): http://library.thinkquest.org/11170/
CDC: http://www.cdc.gov/
CDC Traveler's Health: http://www.cdc.gov/travel/
(check out "destinations" and "diseases")
National Center for Infectious Diseases: http://www.cdc.gov/ncidod
Pan American Health Organization: http://www.paho.org/
World Health Organization: http://www.who.org
Division of Global Migration and Quarantine:
http://www.cdc.gov/ncidod/dq/index.html (for list of Communicable Diseases of current concern)
FluNet for data after 1999: http://oms2.b3e.jussieu.fr/flunet/activity.html
20 Years of AIDS Research at NIH "In Their Own Words":
http://www.niaid.nih.gov

Also consider online resources from medical journals such as the Emerging Infectious Diseases Journal at http://www.cdc.gov/ncidod/eid/index.htm. The following articles are a nice start:

Dr. Mary E. Wilson's "Travel and Emergence of Infectious Diseases" from April-June 1995: http:///www.cdc.gov/ncidod/eid/vol1no2/wilson.htm

Dr Stephen S. Morse's "Factors In the Emergence of Infectious Diseases" at http:///www.cdc.gov/ncidod/eid/vol1no1/morse.htm

Pim Martens and Lisbeth Hall's "Malaria on the Move: Human Population Movement and Malaria Transmission":
http:///www.cdc.gov/ncidod/eid/vol6no2/martens.htm

In this activity, students will use multiple web sites to obtain information about the spread of epidemics.

Students will start at the thinkquest site lited above. It contains brief overviews of several viral, parasitic, and bacterial epidemics, including an animated map for each epidemic, to show a sequence of events in its spread. The site also has links to other Internet pages like those listed above, including prevention and AIDS-related sites.

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It should be noted that because the thinkquest site is created by many people, some of which are young adults, the information is not necessarily reliable and accurate.

This activity mainly focuses on use of maps and general reading to explain spread of different epidemics. There are numerous extensions of this work, especially in biology courses with emphasis on evolution, generation of mutant strains, cross-species jumping of strains, anatomical effects of illness, prions, genetic engineering, and use of genetic analysis and pedigrees to understand transmission of genetically-related illness (like Mad-Cow-Associated illness).

The following worksheet should be used to initiate exploration about these illnesses; it is not recommended to leave education on this subject after worksheets are completed. Further research should be encouraged, as this is probably material that will intrigue many students.

1. What are the four ways in which epidemics are spread? After listing each, provide one example of a situation where transmission could occur. *(Be sure your examples are appropriate!)*
   1. through air (or droplets of water in air)
   example: sneezing and coughing
   2. through bites of infected animals and insects
   example: mosquito bites, rat bites
   3. through direct personal contact
   example: shaking hands, hugging, exchanging body fluids
   4. through consumption of contaminated food or water
   example: drinking water with a parasite in it

2. What are the three kinds of epidemics listed?
   a) parasites
   b) bacteria
   c) viruses
   Bonus: What is the fourth?
   d) prions - most students wont know this one, which is relevant to Mad Cow Disease

Activity II: Travel and the Spread of Disease

3. Group Work: Your teacher will assign you one of the following epidemics.
   - Mad Cow-related human diseases
   - Ebola
   - AIDS
   - Black Death and Bubonic Plague
   - Smallpox
   - Typhoid
   - Influenza

Research this epidemic using the web sites listed or other information. Also answer the questions below. You will be giving a ten minute presentation on your epidemic, so be prepared to present your information in a polished form.

For a challenge, teacher could assign students to research one of the epidemics of current concern, which may NOT be addressed at the thinkquest site.

Communicable diseases of the most concern for the Division of Global Migration and Quarantine as of August 2001 were (1) Tuberculosis, (2) HIV, (3) Syphilis, (4) Charcroid, (5) Gonorrhea, (6) Granuloma Inguinale, (7) Lymphogranuloma Venereum, and (8) Leprosy

a) How could your epidemic be spread through travel (on airplanes or ships)? Describe each situation completely in a paragraph. Your situations should be appropriate for the mode of travel and should be feasible as likely situations.

b) Did any of these situations occur? Use a map and/or historical account to determine if spread of the epidemic can be accounted for, in part, due to ship or airplane travel.

As examples, have students look at AIDS spread with the map from the thinkquest site. Note that the maps at this site are not entirely sufficient to document spread of epidemics - some maps are of current events only (Herpes is "sporadic worldwide" to start with), while others only show certain strains / events (Influenza) or certain time periods (Cholera).

You can use this AIDS discussion to present options of using newspaper articles (that are online). NYTimes has many articles and associated activities, one specifically about "AIDS and Travel."

http://www.nytimes.com/Learning/teachers/lessons/981028wednesday.html.

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Tuberculosis spread is also a hot current topic and has been presented on popular TV shows such as "60 minutes" (2000). Tubercuosis is also prevalent in popular films (like "Tombstone" or "Moulin Rouge"). Students might also find interesting information at hospitals, clinics, and even blood donor centers. For instance, recently the Red Cross began a policy whereby people are not allowed to donate blood if they have spent six weeks or more in the United Kingdom over the last few years, for fear of spreading foot & mouth disease or CJD (associated with Mad Cow disease).

c) What are general details about the disease? List:

- basic symptoms
- required gestation times
- where it originated
- what it does to its host

d) What was the speed of spread of one of the epidemics?

- Create a timeline to show the sequence of number of victims (and location, if this is available) by this epidemic.
- Find the number of cases per year over the period of time that is documented for this epidemic and plot them on a scatterplot.

Teacher can create a very large historical scatterplot with years on the x-axis and number of victims / cases on y-axis, so students can get a sense of time. This will become important in the next question.

Here are some anticipated "eras" for some diseases:

Mad Cow-related = Late 1980s - present
Ebola = 1990s - present
AIDS = Early 1980s - present

For Influenza, Smallpox, Black Death/Bubonic Plague, Typhoid, have students pick a specific strain or a historical occurrence for which there is sufficient documentation to collect information. These vary tremendously.

e) Indicate the following in a chart covering up to 30 years.

- Number of cases/victims
- # Victims this year - # victims last year.
  Answers will be positive or negative, depending on growth or decreases.
- % change (positive or negative)
  Plot percent change versus time on a new graph for your epidemic over this time (up to 30 years).

f) When were effective treatments imposed or sanitation / preventative measures imposed? Can you identify main factors contributing to the demise of the epidemic? Mark these on your graph.

Note that although health measures may be imposed in America, they may not necessarily be imposed elsewhere. Note Diphtheria map on thinkquest site - America has a low occurrence due to stringent immunization standards, but for the rest of the world, Diphtheria remains a problem.

4. Share your information with the class in a 10-minute multimedia presentation. Include plenty of visuals including your charts and graphs.

What follows are three examples of some of the information students may find from the web sites mentioned on the first page of this activity.

Example 1: Influenza

Influenza is a virus with an incubation period of about 1-5 days. Symptoms include high fever, headaches, weakness, extreme exhaustion, stuffy nose, sore throat, chills, body aches, and dry cough.

There are three types of influenza, A, B and C. Type A is the most feared type because it can be the most deadly. Type A is spread from animals to humans. Type B and C are spread from human to human. Type A and B are those associated with epidemics.

Epidemics of Type B occur every year around the world, but mortality rates tend to be low. In the United States alone, there are 10,000 hospitalizations and 20,000 deaths per year due to Influenza or a combination of Influenza and other illnesses (like pneumonia). Epidemics of more sizable proportions with significantly higher mortality rates include 1918-19 Spanish Flu (over 20 million dead), 1957-8 Asian Flu (Type A), 1968-9 Hong Kong Flu (Type A). There were also two Type A flu epidemic "scares" in Hong Kong in 1976, 1997, and 1999, although all were limited to a few cases.

Type B Influenza is spread through the air (coughing and sneezing) and through touching contaminated surfaces (like doorknobs and telephones) then touching the mouth, nose, or eyes. For Type B, animal strains mutate to become virulent in human hosts. Animal strains are thought to be spread through fecal matter. Animal workers may come in contact with this and unwillingly transmit the virus by not washing hands or equipment used to handle the animal and prepare it for consumption.

Flu could be spread through travel when infected animals are transported (Type A only) or through human-to-human contact such as sneezing, coughing, shaking hands (Type B or C). Although flu-like symptoms were recorded in 412 BC and 1580 AD, the thinkquest site indicates that Influenza originated in Africa, then came to America with soldiers in 1918.

International cases of the flu have been reported to the CDC from some countries since 1994. Countries have only consistently reported cases since 1999, when 179,539 cases were reported. In 2000, 186,789 cases were reported. In the first half of 2001 131,165 cases were reported.

As previously mentioned, there are approximately 10,000 hospitalizations and 20,000 deaths each year in the United States, alone. According to the Centers for Disease Control and Prevention (CDC), the US flu season is heaviest from October through May, although cases occur year round.

Example 2: AIDS

Note to teachers: The thinkquest site names some specific at-risk groups. However, there is nothing inherent to the disease that targets just the groups indicated. Students need to be made aware that a behavior like unprotected sex or intravenous needle sharing puts a person at risk, not the group to which he or she identifies.

Acquired Immune Deficiency Syndrome is a virus with an incubation period of 8 to 10 years. It is transmitted through bodily fluids other than saliva. It is preceded by HIV. Patients experience immune system collapse, allowing other infections to persist and become possibly deadly. It is common for and AIDS patient to die of pneumonia or influenza.

AIDS is thought to have originated in African Monkeys in Zaire, where it infected its first human hosts. It then appears to have migrated to New York (probably via airplane). It then spread throughout the East Coast of America and the West Coast (perhaps another airline event), before becoming pandemic. AIDS is spread through travel when people visit foreign places and engage in at-risk behaviors (needle sharing, unprotected sex, or blood infusions from unchecked blood supplies), then return with the disease to their home, where they may engage in more at risk-behaviors.

A timeline of NIH-reported cases:

- June 1981: 1st US patient identified
- August 1981: 108 cases (US only)
- July 1982: 413 cases (155 of them are deaths) (US only)
- September 1982: 593 cases (243 deaths) (US only)
- June 1983: 1,641 cases (644 deaths) (US only)
- August 1983: 1,972 cases (759 deaths) (US only)
- September 1983: 2,259 cases (917 deaths) (US only)
- January 1984: 3,000 cases (1,283 deaths) (US only)
- June 1984: 4,918 cases (2,221 deaths) (US only)
- November 1984: 6,993 cases (3,342 deaths) (US only)
- May 1985: 10,000 cases (4,942 deaths) (US only)
- January 1986: 16,458 cases (8,361 deaths) (US only)
- December 1986: 28,098 cases (15,757 deaths) (US only)

August 1987: 40,051 cases (23,165 deaths) (US only)
March 1988: 136 countries report 84,256 cases (through World Health Organization)
August 1988: 72,024 cases (US only) estimated that 1 to 1.5 million have HIV
September 1988: 111,000 cases documented worldwide by World Health Organization. It is estimated that 250,000 cases actually exist.

AIDS Cases Worldwide, According to the World Health Organization (WHO)

Population	1981-1996	1992	1993	1994	1995	1996
Male	488,300	40,330	87,945	64,730	59,285	54,653
Female	85,500	6,307	16,671	13,830	13,682	13,820
White	267,487	22,320	47,468	32,677	29,402	26,229
Black	198,780	15,576	37,523	30,373	28,729	28,346
Hispanic	101,253	8,223	18,410	14,612	13,961	12,966
Asian/ Pacific Islander	4,090	334	761	573	558	561
Ameican Indian / Alaskan	1,544	121	369	246	237	207

Example 3: Mad Cow Disease / Creutzfeldt-Jakob Disease

Mad Cow Disease, otherwise known as Bovine Spongiform Encephalopathy (BSE), is a prion epidemic that produces holes in the brain and affects the spinal cord. Incubation periods last for 4 to 5 years. Symptomatic cattle are unusually nervous and aggressive, exhibit abnormal posture and gait, appear uncoordinated, have difficulty rising from a prone position, have low milk production, and lose weight while maintaining a healthy appetite. It is related to similar diseases in other animals, including sheep, mice, goats, cats, mink, mule deer, and elk. The disease is thought to have "jumped" hosts when sheep waste including brain tissue was included in cattle feed, as a means to increase milk production.

The first reported cases occured in November of 1986. Between Novem-

ber of 1986 and April of 2001, 180,900 cases of BSE were confirmed in the United Kingdom. In 1990, about 300 cases per week were being reported. In 1993, about 800 cases per week were being reported. To prevent new cases from emerging, United Kingdom National Health officials recommended that animal waste not be fed to animals in 1989. Because of incubation times, the effect of this recommendation would not be seen for many years.

Reported Cases of Mad Cow Disease Worldwide in December 2000

Country	Native	Imported
UK	180,376	0
Ireland	487	12
Portugal	446	7
Switzerland	363	0
France	150	1
Belgium	18	0
Netherlands	6	0
Liechtenstein	2	0
Denmark	1	1
Luxembourg	1	0
Germany	3	6
Oman	0	2
Italy	0	2
Spain	0	2
Canada	0	1
Falklands	0	1

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Creutzfeldt-Jakob Disease (CJD) is a prion disease that occurs at a very low incidence in older people all over the world. CJD has a variant, abreviated as CJDv, that appears to be derived from BSE. This was affirmed due to the similarity between bovine and human infected brains, remarkably early onset of the disease, higher incidence of the disease (particularly for people with no at-risk genetic makeup), and the proximity of the victims to the dramatic amount of BSE cases. People are thought to acquire CJDv by eating ground beef that may contain of brain, skull, or spine tissue. In December of 1996, ten cases of CJDv were reported in the United Kingdom. From October 1996 to June 2001, 101 cases of CJDv were reported, with all victims occuring in the United Kingdom except for 3 in France and 1 in Ireland.

Incidences of Variant Creutzfeldt-Jakob Disease

Year	UK	France	Ireland
1994	8	1	0
1995	10	0	0
1996	11	0	0
1997	14	0	0
1998	17	0	0
1999	24	2	1
2000	3	0	0

People can avoid the disease by avoiding ground beef that may contain at-risk tissues. Solid muscle (steak) has not been shown to be a risk. Freezing, drying, and heating disease-laden beef has not been proven to kill disease-causing agents.

An interesting timeline with interventions to assist in prevention occurs at: http://www.cdc.gov/ncidod/EID/vol7no1/brown.htm

5. As a class, compare graphs, charts, the aviation timeline, and the passenger miles chart to help you answer the following questions.

Aviation Timeline :

1903: Wright Brothers' "Flyer" makes first controlled flight of a powered, heavier-than-air aircraft.
1909: Monoplanes developed and used for relatively short-distance flights.
1911: First practical seaplane built.
1913: Airplanes used by French and British during WW1 as bombers and surveillance craft.
1918: Fighter planes developed (and used in battle).
1927: Long-distance passenger craft developed that had constant radio contact with the ground.
1930s: The "Air Age" begins with pioneers like Amelia Earhart, Howard Hughes, and Charles Lindbergh.
1933: First of the modern airliners (Boeing 247) developed. It could carry 13 passengers and travel at 155 mph.
1936: Spitfires (fast maneuverable fighter airplanes) developed for use in WWII.
1943: Helicopters are mass-produced for WWII.
1943: Jet-powered fighters are developed and used in WWII.
1947: Airplanes fly faster than the speed of sound.
1947: Radar is developed to keep track of aircraft from the ground.
1950s: The airliner begins to replace other means of transportation as the primary means of long-distance travel.
1968: Aircraft are developed that can take off and land vertically, without the use of a runway (Harrier "Jump Jet.").
1969: The Concorde is developed and used as the first supersonic airliner. (It crosses the Atlantic Ocean in less than 3 hours.)
1981: Space Shuttle is developed as a reusable space ship that can land after reentry into Earth's atmosphere.
1981: The Lockhead F-117A is developed, which is virtually invisible to radar.

Passenger Miles for US Intercity Air Traffic

Year	Miles (billions)
1945	3
1950	10
1955	23
1960	32
1965	54
1970	109
1975	136
1976	150
1978	189
1979	210
1980	204
1981	201
1982	214
1983	232
1985	263
1986	293
1987	322

Note: This does not apply to international travel.

5a) Is spread of epidemics linked to increased air travel?
- Defend your answer.
- Determine statistically.
- Provide examples of epidemics that are directly linked to air travel.

b) How might air travel change to restrict epidemic spread, if it is to be held accountable for it? Are there things done now, that you know of?

This may require some research to answer.

c) We have not considered some important characteristics of epidemics, when accounting for number of cases in a year. For instance, AIDS and Influenza are very different, and some researchers say they should not be evaluated in the same way. Why not? What can we include in our analysis to account for this?

Some epidemics infect a host for many years, and some for only a short period of time. Because of this, numbers of AIDS patients may far surpass the numbers of Influenza patients, even though the same number of people may die from these epidemics.

So that information is not biased in this way, number of deaths might be a better means of counting victims.

Students may also come up with differences like the way a disease is spread, its effect on a population, if treatments are available, etc.

d) Design a model to further research the influence of air travel on the spread of epidemics. Your test must follow these restrictions:
- It must be of a small-scale, as it will be modeled in a classroom.
- It must be harmless.
- It must be easy to measure.
- One must be able to do it in less than one hour.

Use the handshaking model to inspire your students. Remind them that the model must involve air travel. Some may consider the contact that different airport / airplane personnel will have with one passenger. The film "12 Monkeys" provides chilling insight into this. The film is not recommended for use in entirety, but the last few minutes show the actual disease transmission from airport (customs check), to customs agents and passenger, to plane, to passengers all around the world.

e) Bonus Question (Extra Credit): Why did passenger miles decrease in 1980 and 1981?

Air Traffic Controllers' Strike and Resulting Firing (Reagan Era)

6. Handshaking has been known to be linked to the spread of illness.

The following polynomial serves as a great model for linking human behavior to consequences (illness). Due to studies of communicable disease transmission in daycare facilities in Finland in the 1980s, there occurred a great deal of education regarding the importance of hand washing. As a result, disease spread decreased dramatically.

The number "N" of possible handshakes within a group of "n" people is approximated by the polynomial $N = (1/2)n^2 - (1/2)n$

a) Compare the number of handshakes
- at a political rally (n = 500),
  124,750 handshakes
- at an investment banking meeting (n = 50),
  1225 handshakes
- or a business department meeting (n = 10).
  45 handshakes

b) In the United States, the amount of colds you catch can be approximated as $(1/100)((1/2)n^2 - (1/2)n)$. In Finland, the amount of colds can be approximated as $(1/200)((1/2)n^2 - (1/2)n)$. In which country was there a lot of advertisement about the benefits of washing your hands? Prove this by showing the respective number of cold-exposure in a room of 100 people in Finland or the United States.
  45 - USA
  22.5 - Finland

c) Of course, being exposed to a cold does not mean you will "get" the cold. What can people do to help prevent common illness (like Influenza, colds, and infections) in their every day lives, without the help of a doctor?
  There are different levels of this. Students may mention those below and others.
  1) Prevent illness by preventing exposure to illness.
     Wash hands; avoid touching hands to mucous membranes (eyes, nose, mouth); cover and treat wounds; clean foods / filter water
  2) Prevent illness while being exposed to illness.
     Get plenty of sleep and exercise so immune system is at its best; Vitamins & Minerals may help (for example, many people take Vitamin C and Zinc supplements); keep your environment clean
  3) Decrease longevity of illness once it is acquired.
     Same as #2; Eat Chicken Soup (maybe not a myth!); Use vaporizers (to assist in breathing); Use over-the-counter drugs to decrease symptoms.

7. Discussion of the perpetuance of illness:

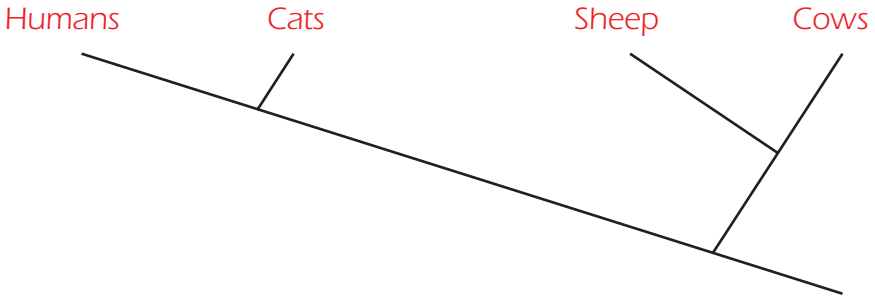
a) People can be immunized for many kinds of diseases. Similarly, there are treatments available for many diseases. If you are treated for an illness, why might you still get sick?

There are multiple strains of illness, which are variants or mutants of the same thing. Colds and Influenza mutate all of the time, explaining why people may get sick every year or multiple times in a year, with the same "bug."

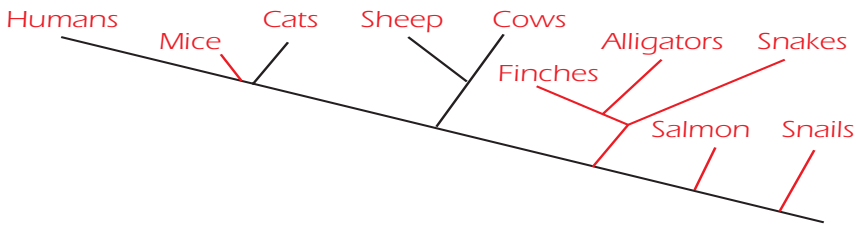
b) Why does the journal "Nature" tell readers to be cautious in believing people that say we have nothing to worry about regarding epidemic strains in chickens, pigs, or cows?

Although it is rare, strains may jump major taxonomic groups! For instance, for Mad-Cow-related diseases, all affected are in the same class (Mammalia), but span many different orders! This may have much to do with the epidemic type (prion), but it nevertheless provides a notable example. In cases like Type A Influenza, infection is only animal-to-human.

c) There are Mad Cow -Related Diseases in cows, cats, sheep, and humans. Create a tree of relatedness that shows these 4 groups and how they are related.



d) Where would the following be on your tree (draw them in)? Mouse, Salmon, Snail, Finch, Python, Alligator



The given lines are the branches of the tree you filled in for section c. Place the other branches where you think they belong.

e) Obtain sequences of DNA, RNA, or protein that are related to an illness that apparently spans across several animal groups (at least 4 groups is ideal).

Some examples of illnesses with some animal groups they affect:

- Mad Cow Disease-related illness (sheep, cat, mouse, mink, cow, goat, human)
- Influenza (birds, pig, human)
- AIDS (African monkey, human)
- Smallpox (dog, cow, human)
- Tuberculosis (cow, birds, human)
- Hemorrhagic Fever (rodents, monkeys, human)

Genbank (c/o the National Institute of Health) provides sequences in their databases. Swissprot (primarily a protein database) also provides sequences. Genbank is at
http://www.ncbi.nlm.nih.gov/Genbank/GenbankSearch.html

To use Genbank, students must simply pick the type of sequence they desire (nucleotide, protein, etc.), then enter in key words to look for it, using an Entrez search (Blast is the other recommended method). Once they have found a sequence, they should note the type (DNA, RNA, or protein), the length of it, and its implications / related information (for example, the title of the article it was submitted in and features including association with other genes or diseases).

i) The keywords for my search will be _prion, scrapie, mad-cow disease, Creutzfeldt-Jakob disease (CJD), sheep, cow, cat, human and (circle one) nucleotide / protein.

ii) Fill in the chart below. Ideally, all of your sequences will be from **different organisms** BUT will be of **similar types** (for instance, all DNA), **size** (for instance, all about 795 base pairs), and have **similar significance** (for instance, all are sequence for WW gene and all are related to SS disease).

Note: Often researchers will list sequences that are related to each other in their notes. Pay special attention to this, as it will help you determine what other sequences to look for.

LOCUS #	Organism	DNA or protein	Length (bp)	Implications/ significance/ title of article	Sequences it is related to
HUMPRION D00015	*Homo sapiens* (human)	DNA (mRNA w/ translation)	245	*Science* article about link to Scrapie, Down's Syndrome, Alzheimers	cat, sheep, hamster (LOCI should be noted here)
AF003087	*Felix catus* (cat)	DNA (w/ translation)	795		several variations
S55629	*Bos taurus* (cow)	DNA (w/ translation)	795	*J Inf Dis*: "... prion proteins in bovine spongiform encephalopathy"	
AJ00073	*Avis aries* (sheep)	DNA (w/ translation)	960	*Proc. Natl. Acad. Sci* "2 alleles linked to scrapie..." & other article	

Students might also note publications that a sequence is linked to (there are icons for this next to sequences, if publications are available). Students should be able to read abstracts from the articles on the web site. There may also be available 3D graphics of proteins.

iii) Cut and paste your sequences into a word processing document. Label and place quotations around each sequence.

cow

"MVKSHIGSWILVLFVAMWSDVGLCKKRPKPGGGWNTGGSRYPGQGS
PGGNRYPPQGGGGWGQPHGGGWGQPHGGGWGQPHGGGWGQ
PHGGGWGQPHGGGGWGQGGTHGQWNKPSKPKTNMKHVAGAAA
AGAVVGGLGGYMLGSAMSRPLIHFGSDYEDRYYRENMHRYPNQVYYR
PVDQYSNQNNFVHDCVNITVKEHTVTTTTKGENFTETDIKMMERVVEQ
MCITQYQRESQAYYQRGASVILFSSPPVILLISFLIFLIVG"

sheep

"MVKSHIGSWILVLFVAMWSDVGLCKKRPKPGGGWNTGGSRYPGQ
GSPGGNRYPPQGGGGWGQPHGGGWGQPHGGGWGQPHGGGW
GQPHGGGGWGQGGSHSQWNKPSKPKTNMKHVAGAAAAGAVVG
GLGGYMLGSAMSRPLIHFGNDYEDRYYRENMYRYPNQVYYRPVDQYSN
QNNFVHDCVNITVKQHTVTTTTKGENFTETDIKIMERVVEQMCITQYQR
ESQAYYQRGASVILFSSPPVILLISFLIFLIVG"

cat

"MVKSHIGSWILVLFVAMWSDVGLCKKRPKPGGGWNTGGSRYPGQG
SPGGNRYPPQGGGGWGQPHGGGWGQPHGGGWGQPHGGGW
GQPHGGGGWGQGGSHSQWNKPSKPKTNMKHVAGAAAAGAVVG
GLGGYMLGSAMSRPLIHFGNDYEDRYYRENMYRYPNQVYYRPVDQYS
NQNNFVHDCVNITVKQHTVTTTTKGENFTETDIKIMERVVEQMCITQ
YQRESEAYYQRGASVILFSSPPVILLISFLIFLIVG"

human

"MLVLFVATWSDLGLCKKRPKPGGWNTGGSRYPGQGSPGGNRYPPQ
GGGGWGQPHGGGWGQPHGGGWGQPHGGGWGQPHGGGW
GQGGGTHSQWNKPSKPKTNMKHMAGAAAGAVVGGLGGYMLGSA
MSRPIIHFGSDYEDRYYRENMHRYPNQVYYRPMDEYSNQNNFVHDC
VNITIKQHTVTTTTKGENFTETDVKMMERVVEQMCITQYERESQAYYQ
RGSSMVLFSSPPVILLISFLIFLIVG"

iv) Analyze your sequences either by computer or by comparing sequences visually. Visual analysis works best with short sequences. Cut and paste long sequences into a sequence analysis site / software. Clustalw, Phylip, and PAUP are 3 popular sequencing programs. They are free (a beta version at least), well documented, and offer support upon request.

Teachers should practice with the software before students use it. Sometimes the analysis is very technical (the web sites are written at a college level).

Clustalw can be used directly on-line at either of these two sites:
http://www.clustalw.genome.ad.jp/
http://dot.imgen.bcm.tmc.edu:9331/multi-align/Options/clustalw.html
Phylip can be read about and dowloaded from either of these two sites:
http://evolution.genetics.washington.edu/phylip.html
http://www.ibb.waw.pl/docs/PHYLIPdoc/mail.html
PAUP can be read about and downloaded from:
http://paup.csit.fsu.edu/

The sites are each very sensitive concerning what they will accept. Students should be careful not to include irrelevant information as their inputs - only sequences and labels. Do not use any special formatting.

The sites each offer forms of analysis including sequence alignment, trees, bootstrapping values, and other statistics values, for detailed analysis.

Proteins may be easier to work with, as they tend to be very short. If DNA is worked with, remind students:

* *there is redundancy, in terms of which codons produce which amino acids. This means that even if a codon were to change by one or two nucleotides, a congruent amino acid could be produced.*
* *DNA is made up of exons and introns - some information codes for amino acids, while other information is non-coding and simply provides navigation information or no known purpose.*
* *insertion mutations in a sequence may not necessarily change the protein product it can produce, if the sequence folds upon itself at the insertion. (There are plenty of other exceptional circumstances like this, as well.)*

Answer / Example:

cow (266 char)

"MVKSHIGSWILVLFVAMWSDVGLCKKRPKPGGGWNTGGSRYPGQGSPGGN
RYPPQGGGGWGQPHGGGWGQPHGGGWGQPHGGGWGQPH*GGGW
GQPHGGGGWGQGGTHGQWNKPSKPKTNMKHVAGAAAAGAVVGGLGGY
MLGSAMSRPLIHFGSDYEDRYYRENMHRYPNQVYYRPVDQYSNQNNFVHD
CVNITVKEHTVTTTTKGENFTETDIKMMERVVEQMCITQYQRESQAYYQRG
AS*VILFSSPPVILLISFLIFLIVG"

sheep (257 char)

"MVKSHIGSWILVLFVAMWSDVGLCKKRPKPGGGWNTGGSRYPGQGSPGGN
RYPPQGGGGWGQPHGGGWGQPHGGGWGQPHGGGWGQPHGGGW
GQGGSHSQWNKPSKPKTNMKHVAGAAAAGAVVGGLGGY
MLGSAMSRPLIHFGNDYEDRYYRENMYRYPNQVYYRPVDQYSNQNNFVHD
CVNITVKQHTVTTTTKGENFTETDIKIMERVVEQMCITQYQRESQAYYQRG
AS*VILFSSPPVILLISFLIFLIVG"

cat (257 char)

"MVKSHIGSWILVLFVAMWSDVGLCKKRPKPGGGWNTGGSRYPGQGS
PGGNRYPPQGGGGWGQPHGGGWGQPHGGGWGQPHGGGWGQPH
GGGGWGQGGSHSQWNKPSKPKTNMKHVAGAAAAGAVVGGLGG
YMLGSAMSRPLIHFGNDYEDRYYRENMYRYPNQVYYRPVDQYSNQNNF
VHDCVNITVKQHTVTTTTKGENFTETDIKIMERVVEQMCITQYQRESEA
YYQRGAS*VILFSSPPVILLISFLIFLIVG"

human (250 char)

"M*LVLFVATWSDLGLCKKRPKP*GGWNTGGSRYPGQGSPGGNRYPPQ
GGGGWGQPHGGGWGQPHGGGWGQPHGGGWGQPH*GGGWGQ
GGGTHSQWNKPSKPKTNMKHMAG*AAAGAVVGGLGGYMLGSAMSRP
IIHFGSDYEDRYYRENMHRYPNQVYYRPMDEYSNQNNFVHDCVNITIKQHT
VTTTTKGENFTETDVKMMERVVEQMCITQYERESQAYYQRGSSMV*LFS
SPPVILLISFLIFLIVG"

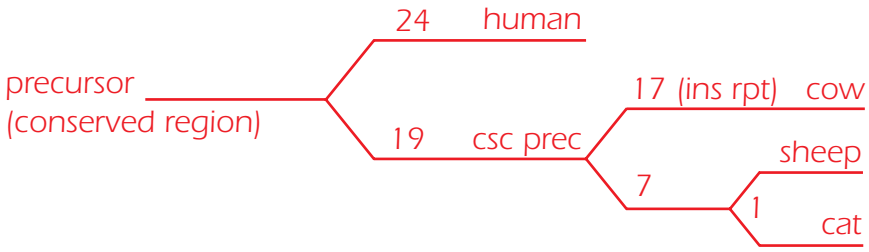
KEY:

* homologous region in blue (conserved region)
* homologous regions across cow, sheep, and cat (but not human) in green (csc precursor region) (19 char)
* heterogenous regions in red

Activity II: Travel and the Spread of Disease

As soon as the number of similarities and differences have been determined, a chart can be constructed. Students can construct a tree using the data from this chart. They should keep in mind differences from the homologous region (conserved region) and differences in terms of each pairwise comparison. They can also comment on the type of changes they observe - insertions, deletions, or substitutions.

Students might notice repeating patterns in their sequences and comment about how repeats can help in the folding of nucleotides and proteins! This redundancy may also be the first step in the evolution of a disease. In the example above, the long red region in the cow is simply part of an extra repeat.



v) Using the comparison information, students can establish percent similarity and relatedness in terms of years and number of mutations since divergence. They can compare these values with traditionally upheld values of relatedness and divergence between the organisms. The goal is to get a feel for the likelihood of a strain "jumping" from one organism to another through mutation or an organism spontaneously evolving.

Comparison	# Similiarities	# Differences	% Different	Type of change
cow & conserved	230	36	15.65	
sheep & conserved	230	27	11.74	
cat & conserved	230	27	11.74	
human & conserved	230	24	10.43	
cow & csc	249	17	6.83	
sheep & csc	249	8	3.21	
cat & csc	249	8	3.21	
cow & sheep	249	8	3.21	2 del (repeating sequence)/ 1 ins, 6 sub
cow & cat	248	9	3.63	2 del (rep seq)/ 1 ins, 7 sub
cow & human	228	22	9.65	4 del/ins, 18 sub
sheep & cat	256	1	3.91	1 sub
sheep & human	225	25	11.11	5 del / ins, 20 sub
cat & human	225	25	11.11	5 del / ins, 20 sub

8. Assign each student or student group to take one topic and return to class with information about that topic, ready to share in a 2 minute presentation about how the topic is related to this unit.

- naturally-occurring transposons or jumping genes in corn
- transposons or jumping genes in bacteria or humans
- human-induced genetic recombination and cloning
- human-induced genetic recombination and gene therapy
- human-induced genetic recombination and improving plant stocks (genetic engineering)
- human-induced genetic recombination and improving animal stocks (genetic engineering)
- geneticly engineered organisms for cleaning up oil spills
- human-induced genetic recombination such as stem cell research

In summary, why are genetically manipulated food and animals so controversial? How is this related to mutation in strains of disease and their effects on new hosts?

Teachers may choose to extend this question, which is currently designed as a very short homework / discussion activity. These topics are of great current interest and may cause much debate. Be sure to remind students about appropriate behavior during a discussion / debate.