

There's no time to teach *that*: Integrating the immune system, autoimmunity, literacy, and research into an over-crowded curriculum.

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Abstract:

Because of various curricular mandates, teachers are faced with covering an ever-expanding range of topics with little room for study of more interesting aspects of biology. Adding to this problem is the need for many teachers to incorporate literacy strategies to remediate student deficits. In addition, assigning independent research often results in plagiarized reports based on unreliable sources. To manage these issues, I have developed a curriculum framework that utilizes autoimmunity, while simultaneously fostering increased literacy and improved research methods. After a general introduction to the immune system, students will explore the specifics of autoimmunity. Experimental Autoimmune Encephalomyelitis (EAE), the mouse model of Multiple Sclerosis currently being researched by Dr. Stephen D. Miller of Northwestern University, will be used as the basis. Students will read, summarize, and formulate questions about current immune-related news articles. Then they will engage in independent research about an autoimmune disease, utilizing relevant and appropriate web sites. Students' website searches will not only focus on the disease, but will also require them to identify resources available for patients. Steering them in this direction will also provide them with a model for any type of future disease research. The unit is designed for flexibility in its implementation, and can successfully be transferred to a wide variety of topics.

Teacher Guide

I. Overview

Because of various curricular mandates, teachers are faced with covering an ever-expanding range of topics with little room for more interesting aspects of biology. Adding to this problem is the need for many teachers to incorporate literacy strategies to remediate student deficits. In addition, assigning independent research often results in plagiarized reports based on unreliable sources. Consequently, teachers do not always have the flexibility or the time to teach topics not directly covered by the standards, and independent student research into these “extra” topics can often be frustrating. This unit serves as a framework, utilizing autoimmunity, while simultaneously fostering increased literacy and improved research methods. It is designed for flexibility in its implementation, and can successfully be transferred to a wide variety of topics.

Science Concepts: This framework incorporates the following topics:

- The basic functioning of the immune system
- The nature of autoimmunity
- Multiple Sclerosis as an example of an autoimmune disease
- On-going research involving Experimental Autoimmune Encephalomyelitis (EAE), the mouse model of MS
- Current immune-related news articles
- Independent autoimmune disease research

Literacy/Research Exercises: This framework does not include a hands-on laboratory component; however, it incorporates the following “Best Practice” literacy and research strategies:

- YouTube Graphic Organizers
- Two-Column and 2-Column note taking templates
- Synthesis Journals
- News article summarizing strategies
- Standardized Test Practice – ACT format
- Guided search strategies for effective internet usage
- Note-taking methods for internet research
- Medical pamphlet design and rubric
- Oral Presentation Graphic Organizer

Introduction

Essential Question - What is the immune system and what does it do for you?

Background Information

Immune System Basics

Building Connections

Autoimmunity

In-Depth Study

Individual Autoimmune Research and Presentation

Assessment

Making Connections

Curriculum Integration: This unit is probably best placed into pre-existing units on viruses or on the immune system. The unit is designed to be implemented in either pieces or as a whole. The literacy/research strategies can be applied to many other topics.

Student Activities: Students will learn about the basics of the immune system and specifics about autoimmunity. Utilizing Internet resources, such as YouTube, news sites, and organizational websites, students will engage in a variety of literacy and research activities.

Relevance for Students: The functioning of the immune system, and especially autoimmunity, are often overlooked by teachers because of curricular mandates and complexity, yet many students have direct experience with various autoimmune conditions – diabetes, multiple sclerosis, arthritis, etc. Using “Best Practices” to explore these topics will not only provide students with background information about a specific disease but will also let them improve their literacy skills and give them a framework for relevant disease research in the future.

II. Science and Literacy Background

Science Background:

Teachers should review the basic functioning of the immune system for themselves before implementing this unit. Depending on the class level, this review could be quite specific. Using any general biology text book, such as Holt *Biology* or a college-level text such as *Biology – 8th Ed.* Campbell and Reece should suffice. For teachers with access to on-line resources, the brochure *Understanding the Immune System: How it Works* – published by the National Institute of Allergy and Infectious Diseases of the National Institute of Health will be very useful. This can be found at

<http://www.niaid.nih.gov/topics/immunesystem/documents/theimmunesystem.pdf>

In terms of autoimmunity, excellent background information and an extensive list of autoimmune diseases can be found on the American Autoimmune Related Diseases Organization (AARDA) website. <http://www.aarda.org>

Literacy Background:

Although science teachers are not reading or literacy specialists, it is becoming more imperative for them to incorporate literacy strategies into the curriculum in an effort to remediate substantial deficits or to support already strong skills. The amount of information available on the Internet is overwhelming and often unreliable. Consequently, science teachers need to make sure that students have guidance in vetting the quality of a website and are especially careful in avoiding outright plagiarism when collecting information. To achieve both of these goals, teachers need to incorporate literacy and research skills into their curricula and must model them for the students. There are many excellent resources available in print and on-line for non-reading teachers. Science teachers should strive to work collaboratively with literacy specialists, reading teachers, or members of the English, Media/Library, or ESL/ELL/Bilingual departments to meet district-specific initiatives or to foster specific goals, as these people are the best resource for content area literacy. In addition, the list below suggests several books that provide teachers with a brief theoretical and practical introduction to literacy research and practice and methods of incorporating these into a science curriculum.

Daniels, H. and S. Zemelman. *Subjects Matter: Every Teacher's Guide to Content-Area Reading*. Heinemann. Portsmouth, NH. 2004.

Daniels, H., S. Zemelman, and A. Hyde. *Best Practice: Today's Standards for Teaching and Learning in America's Schools*. Third Edition. Heinemann, Portsmouth, NH. 2005.

Ivey, G. and D. Fisher. *Creating Literacy-Rich Schools for Adolescents*. ASCD. Alexandria, VA. 2006.

Specific Literacy Skills:

Following is a brief description of each of the specific literacy skills utilized in this unit. The descriptions are meant to be illustrative in nature and include paraphrases from a wide variety of published and non-published sources, as well as original material. Citations are not directly provided for all of the material, but some specific journal references are included as a guide for further reading.

KWL

A KWL (Know/Want to Know/Learned) is an organizational chart used to access students' prior information about a topic, develop questions, and then synthesize information. It can successfully be utilized as a qualitative pre/post assessment tool.

Students can either be given the KWL chart prior to a full-class review, or it can be used with the entire class at once. In the "K" column, students generate a list of what they know about a topic. Teachers should record this list, even if it contains faulty information or misconceptions. Once the list is complete, the teacher should guide the students into completing the "W" column – what they students want/need to know about the topic. It is here that the teacher can bring up any inconsistencies or misconceptions from the "K" column and formulate questions based on them. Often times, the class will continue to add questions to this section throughout the

discussions. As the unit progresses, students and teachers should fill out the “L” column with correct concepts that they have learned. By regularly referring back to the KWL, students are able to verify that they are engaged in mastering new concepts.

Teachers should provide students with their own copies of KWL charts and should allow for flexibility between different class sections. Teachers should also feel free to guide the students, especially in the “W” section to ensure that specific content will be explored.

Ogle, D.M. (1986). K-W-L: A teaching model that develops active reading of expository text. *Reading Teacher*, 39, 564-57

Graphic Organizers

A variety of graphic organizers are used throughout the curriculum to allow students to interact with the material, whether presented through text, video, or orally. These can be customized in endless ways, but they keep the students engaged in the lecture/video/discussion and provide them with a way to record both information and reactions to the material.

2-Column Notes – also known as Cornell Notes

There are many different literacy strategies involving note-taking. One of the most researched is that of 2-Column notes, also known as Cornell notes. Teachers should explore the various note-taking formats utilized in their own schools and should collaborate with colleagues to develop a consistent strategy. The more times that students are exposed to and practice note-taking, the more successful they become at extracting information from text and websites. Various on-line tools such as Diigo, allow students to utilize electronic “sticky notes” to annotate a website and save it for later reference.

Summarizing information from the text is also a difficult skill for students at all levels. Encourage students to follow a “Rule of 7” – use no more than 7 words in a summary. This allows them to eliminate extraneous information and provides them with a more succinct framework from which to study the material.

“Rule of 7” Example:

Passage: “The compound is an environmental toxin found in air pollutants including tobacco smoke and auto exhaust. Acrolein also is produced within the body after nerve cells are damaged. Previous studies by this research team found that neuronal death caused by acrolein can be prevented by administering the drug hydralazine, an FDA-approved medication used to treat hypertension.” Findings suggest new cause, possible treatment for multiple sclerosis – EurekAlert 11.23.2010

Ex. Acrolein – toxin; produced-nerve damage; hydralazine blocks

While 7 words may be too few (or too many) in some cases, the goal is for the students to fully interact with the text and only record what is important. This task becomes easier, especially if students have annotated the text first.

Rationale

- Note-taking is an essential study strategy that should be explicitly taught to students as it allows students to generate understandings and reflect on ideas.
- Students who take brief notes of the most essential details outperform students who take detailed notes of the same materials.
- Short, efficient notes reflect deeper understanding of the information.
- It is essential that students organize and reflect on their notes. Notes should only reflect the significant components of the text. The act of separating main ideas from details strengthens the understanding and memory of the content area.

Implementation

Though some students may need scaffolds (writing notes in the left-hand column, filling in portions of the details for students prior to reading, chunking text, and so on), these scaffolds should be removed over time so that students can complete the strategy independently.

1. When teaching 2-Column Notes to students, first explain the purpose of the notes:
 - 2-Column Notes help students record the significant details of the text, and this helps students generate a deeper understanding.
 - 2-Column Notes help students understand the relationship between ideas when they summarize and meta-cognitively reflect on their learning.
 - 2-Column Notes serve as a study aid.
2. Guide students through 2-Column notes by modeling the strategy. It is helpful for students to see you complete the entire 2-Column Note process:
 - Review notes from the previous lecture [reading, demonstration, chapter, etc.].
 - Record important ideas in the right-hand column.
 - Review/reread the notes.
 - Determine the main idea of the notes.
 - Record the main ideas in the left-hand column.
 - Summarize the notes on the bottom of each page.

Modifications/Variations

- Teachers put questions for students to answer in the left-hand column.
- Teachers complete sections of the text or insert visuals for students.
- Teachers or students create a “look for” in the left column and use the right to include the information. Some examples are attached.

Berthoff, A. E. (1987). Dialectical notebooks and the audit of meaning. In T. Fulwiler (Ed.), the Journal Book (pp. 11-18). Portsmouth, NH: Boynton/Cook.

General Template:

<p><u>Main Ideas:</u> Review the notes in the right column. Label the main ideas.</p> <p>Use headings and subheadings as a scaffold.</p> <p><u>Questions:</u> Do you have any questions about what you read?</p> <p>Create a possible study/discussion question.</p> <p><u>Clarification Tools:</u> Diagrams Charts Symbols Pictures</p>	<p><u>Organization:</u></p> <ul style="list-style-type: none"> - Underline - Indent - Use bullets - Use color if needed - Skip lines between ideas <p><u>Technique:</u></p> <ul style="list-style-type: none"> - Paraphrase - Use abbreviations - Be concise <p><u>Content:</u></p> <ul style="list-style-type: none"> - Use arrows, circles, underlining, etc to show relationships between ideas.
<p><u>Summary:</u> Provide a summary here. Remind students that when writing a summary:</p> <ol style="list-style-type: none"> 1. Highlight the most important ideas. 2. Delete unnecessary details. 3. Combine ideas using more general terms. 4. Create a main idea statement and place it appropriately in the summary. 	

Synthesis Journal

A Synthesis Journal is another type of graphic organizer which allows the students to put together information from disparate sources. It can be structured in a variety of formats, but generally relies on developing an answer to a “Guiding Question” – in this case, “What is the immune system, and what does it do for you?” Having students reorganize their information is an additional strategy that forces them to interact with the information and improve their cognition of the material.

Burrell, K.I., & McAlexander, P.J. (1998). Ideas in practice: The synthesis journal. *Journal of Developmental Education*, 22 (1), 20-22, 24, 26, 28, 30.

Think/Pair/Share

Think/Pair/Share is a cooperative learning strategy that allows the students to both individually and in small groups work with content. Students are given a question, a section of a worksheet/graphic organizer, or other format which requires them to access prior information. Students should be instructed to “think” about the answer for a few minutes and individually record their thoughts. Then, students should “pair” with another student and compare their answers with their partner. Both students should be encouraged to discuss the information, correct any misconceptions, and add additional information to their own answer. Then, students should “share” the information with the class in a structured format, again adding/highlighting specific details at the teacher’s direction.

Lyman, F. T. (1981). The responsive classroom discussion: The inclusion of all students. In A. Anderson (Ed.), *Mainstreaming digest* (pp. 109-113). College Park: University of Maryland Press.

News Article / Text Annotation

Text annotation is a **meta-cognitive literacy strategy** that involves noting important ideas and examples in the margins and is a widely practiced writing-to-learn strategy. The purpose of annotation is to isolate key ideas in the text to study them later, but the ultimate goal is for students to be able to synthesize and rephrase ideas as this is the only way a teacher can ensure the student understands the text. Annotation provides students with an opportunity to **hold their thinking** while engaging with a **text** and facilitates their learning of the **content**. The thought of annotating a text might conjure up images of coloring a **text** to eradicate white space. To circumvent the coloring concept, researchers suggest teachers should tell students to avoid using a highlighter for the following reasons:

- Kids have to own their annotations; it’s just too easy to highlight an entire page without being thoughtful.
- It’s cumbersome to move between highlighter and pen when working with a **text**.
- Pens are just as easy to underline with as a highlighter!
- Prevents “over-marking” of a text (aka meaningless marking of said **text**!).

Rationale for teaching annotating skills:

- If you don't teach students how to annotate in a manner that is specific to the **processes** in your discipline, who will?
- When a reader isolates information, he or she is more likely to remember it and add it to his or her **schema** for the discipline.
- Students utilize cognitive strategies and skills when they are underlining, including: activating prior knowledge, making connections, asking questions, summarizing a chunk of a text, making predictions, analyzing the author's craft, making inferences, and so on. These are some of the **best practices in literacy** instruction.
- Annotation is **transparent** through teacher **modeling** and can be easily **transported** to other disciplines and **texts**.

Steps to teach annotation:

1. The teacher must **model** and provide direct instruction as he or she would any other strategy.
2. Provide the students with a purpose for reading and annotating the text.
3. **Model** annotating a text using the purpose you would like the student to use.
4. Allow students practice.
5. Provide students with both oral and written feedback.
6. Re-teach and remodel as necessary.
7. Have students use their annotations through extending activities: studying, summarizing, discussion, and writing.

Suggested annotation steps for students:

1. Check off information you understand.
2. Underline only the most important information necessary for understanding the paragraph.
3. Put a "?" by terms that are not familiar, and then find out their meanings.
4. Mark off any information that is not necessary for understanding the article.
5. Write brief summaries in the margins, explaining the key points.
6. At the end of the article, write a 2-sentence summary in your own words, that utilizes the following framework:

Researchers have discovered that.....

This is important because.....

Simpson, M. L., & Nist, S. L. (1990). Textbook annotation: An effective and efficient study strategy for college students. *Journal of Reading*, 34, 122-12

Standardized Test Practice – ACT Format

Standardized testing is a “necessary evil” in the field of education. While there are many different tests and formats, one of the most challenging for students seems to be the Science Reasoning section of the ACT (American College Test). During this test, students are presented with 7 passages, involving a variety of text, graphs, figures, and tables. Students are not expected to be familiar with the content. In fact, many of the passages are designed to be unfamiliar, have highly technical terms, and much extraneous information in the data. Students need to practice these types of passages with unfamiliar and highly technical information in order to increase their scientific reasoning ability and to perform better on these types of assessments.

Evaluating Internet Websites

Few things are more frustrating when assigning students to engage in Internet research than when students refer solely to Wikipedia or to the first link that comes up after a Google search. With the vast amounts of information available, students need to be able to assess the validity of specific websites and ascertain whether or not the website can serve as reputable source of information. Completing an Internet Evaluation Sheet, encourages students to look critically at the sites that they are exploring and provides them with a framework for both in- and out-of-class searches.

Alexander, Jan and Marsha Ann Tate. “Evaluating Web Resources.” July 25, 2001. [last update]. Online. Wolfgram Memorial Library. Available: <http://www2.widener.edu/Wolfgram-Memorial-Library/webevaluation/webeval.htm>. 26 October 2001.

Northrup, Mary. “Web Site Evaluation Checklist.” The Book Report September/October, 2001: 48.

University of Wisconsin, InternetWorkshop Working Group. “Checklist for Evaluating Web Sites.” September 5, 2001 [last update]. Online. University of Wisconsin. Available: <http://www.library.wisc.edu/libraries/Instruction/instmat/webeval.htm>. 26 October 2001.

Educational Pamphlet Creation/Patient Consultation

One of the most frustrating aspects of assigning students to access information from on-line resources is the high amount of information and the difficulty that students have with summarizing, paraphrasing, avoiding plagiarism, and being able to internalize the information. Instead of having students write a report, create a PowerPoint, and do a presentation to the class, creating a pamphlet and simulating a Patient Consultation is an effective method to have students engage in disease research and present their findings to others in a more “private” setting. A pamphlet format necessitates using short phrases, which helps to eliminate the wholesale “cutting and pasting” of information. Structuring the pamphlet so that the information must come from a variety of sources also discourages the students from finding the information in one-place and merely copying it into another format. Many computer applications, such as Microsoft Office Publisher, have templates that make it easy to create a professional looking pamphlet.

Engaging in a role-playing exercise allows students to practice being both physician and patient and provides them with a direct peer-feedback format of sharing information in a less-threatening method than a whole-class presentation.

III. Student Outcomes and Learning Objectives

Students will be able to:

- Assess what they know about the functioning of the immune system.
- Develop questions about what they need to learn about the immune system.
- Take notes and summarize information from a variety of sources, including text, video, websites, lecture, etc.
- Collaboratively synthesize scientific information.
- Hypothesize what happens when the immune system does not function properly.
- Annotate and summarize current news articles.
- Practice standardized test questions on an autoimmune topic.
- Analyze the appropriateness of web resources.
- Synthesize web-based information into a creative format.
- Present research information to peers.
- Assess the effectiveness of their own and other's work.

IV. Time Requirements

1-14 Days (45 minute class periods) – depending on level of implementation

Introduction – 1 day

Background Information – 2-3 days

Building Connections – 1-4 days

In-Depth Study – 3-5 days

Assessment – 1 day

V. Advance Preparation

Equipment and Materials

- Access to the Internet for multiple class periods
- Copies of Student Worksheets:
 - KWL – The Immune System
 - YouTube Graphic Organizer – Immune System Animation
 - 2-Column Notes - Understanding the Immune System
 - Immune System – Synthesis Journal
 - YouTube Graphic Organizer – Autoimmune Disease
 - “Findings Suggest...” Current Event News Article
 - “Findings Suggest ...” – Annotation Example
 - Standardized Test Practice – EAE

- Standardized Test Practice – EAE – Answers (optional)
- Autoimmune Disease Project
- Evaluating Internet Websites
- 2-Column Notes – Autoimmune Disease
- Autoimmune Disease Pamphlet – Grading Rubric
- Patient Consultation Graphic Organizer
- Patient Consultation Evaluation
- Pre-downloaded/saved YouTube videos, NIAID Science Education Brochure, NobelPrize.org Animation,

Materials Preparation Time – 1 - 45-minute period

VI. Student Prior Knowledge and Skills

Expected Content Knowledge

This unit is designed to be implemented with a variety of students at a variety of levels. Ideally, students should have a basic understanding of the immune system and/or the body's response to viruses and bacteria; however, this is not a pre-requisite. More advanced students may be able to skip the "Introduction" and "Background Information" sections and go directly to "Building Connections." Teachers should be aware that accessing various websites and news articles may present the students and the teacher with unfamiliar subjects. A basic Biology text should be available for a reference.

Expected Literacy Knowledge

Teachers need to model and practice the literacy skills in order to be most effective. This is especially true with 2-Column note taking using the "Rule of 7," and annotating news articles/readings. Modeling a completed "Disease Pamphlet" and demonstrating an appropriate "Patient Consultation" will also improve the activities.

VII. Assessment

Because of the flexibility of the unit, a variety of assessment methods may be employed. Teachers should integrate these activities into their own current assessment strategies.

Student Section

I. Overview

The following pages contain teacher master copies of the student worksheets. Each worksheet contains applicable instructions.

KWL: The Immune System

Follow your teacher's instructions to fill out the "K" and "W" sections of the KWL chart about the Immune System.

<u>K</u>now: This is what I know.	<u>W</u>ant: This is what I want to know.	<u>L</u>earn: This is what I learned.

YouTube Graphic Organizer – *Immune System Animation*

<http://www.youtube.com/watch?v=bm4YS293qh4>

Name _____

Per. _____

After watching the YouTube video above, fill out the following:

<p>Facts I learned about the immune system...</p> <p>1.</p> <p>2.</p> <p>3.</p> <p>4.</p> <p>5.</p>	<table border="1"><thead><tr><th data-bbox="968 217 1297 256">Characters/Creatures:</th><th data-bbox="1297 217 1984 256">What they represented?</th></tr></thead><tbody><tr><td data-bbox="968 256 1297 391">→</td><td data-bbox="1297 256 1984 391"></td></tr><tr><td data-bbox="968 391 1297 526">→</td><td data-bbox="1297 391 1984 526"></td></tr><tr><td data-bbox="968 526 1297 660">→</td><td data-bbox="1297 526 1984 660"></td></tr></tbody></table>	Characters/Creatures:	What they represented?	→		→		→	
Characters/Creatures:	What they represented?								
→									
→									
→									
<p>Watching this helped me understand (be specific):</p>	<p>Questions I have about how the immune system works.</p> <p>?</p> <p>?</p> <p>?</p> <p>?</p>								
<p>What I liked/disliked about this clip the most was:</p>									

Understanding the Immune System – NIAID Science Education Brochure

<http://www.niaid.nih.gov/topics/immunesystem/documents/theimmunesystem.pdf>

As you read the brochure, take notes (in your own words) about each of the sections. Be concise!

Topic	Notes – Rule of 7 (no more than 7 words per section)
Introduction (p. 1)	Summary:
Self and Non-self (pp.2-3) antigen	Difference:
Structure of the Immune System (pp.3-7) lymphoid organs lymphocytes lymph nodes lymphatic vessels	Function and 2 examples

Understanding the Immune System – NIAID Science Education Brochure

<http://www.niaid.nih.gov/topics/immunesystem/documents/theimmunesystem.pdf>

As you read the brochure, take notes (in your own words) about each of the sections. Be concise!

<p>lymph</p> <p>Immune Cells and Their Products (pp. 7-19)</p> <p>B cells</p> <p>T cells</p>	<p>Summary:</p>
<p>Phagocytes and Their Relatives</p> <p>T cell Receptors</p> <p>Cytokines</p>	<p>Summary:</p>

Immune System – Synthesis Journal

Fill in each of the sections using information from each of the sources.
Then, summarize the information in your own words to answer the central question.

What is the prior knowledge of the class?

What is the immune system, and what does it do for you?

What does the teacher say?

What does you-tube say?

What does the text say?

YouTube Graphic Organizer – *What is an Autoimmune Disease*

Name _____

<http://www.youtube.com/watch?v=0mz33fLJGwQ>

After watching the YouTube video above, fill out the following:

P. _____

<p>Facts I learned about autoimmune diseases...</p> <ol style="list-style-type: none">1.2.3.4.5.	<table border="1"><thead><tr><th data-bbox="970 219 1297 261">Personal Stories:</th><th data-bbox="1297 219 1982 261">What was the problem?</th></tr></thead><tbody><tr><td data-bbox="970 261 1297 813">→</td><td data-bbox="1297 261 1982 813"></td></tr><tr><td data-bbox="970 813 1297 813">→</td><td data-bbox="1297 813 1982 813"></td></tr></tbody></table>	Personal Stories:	What was the problem?	→		→	
Personal Stories:	What was the problem?						
→							
→							
<p>Watching this made me feel:</p>	<p>Questions I have about autoimmune diseases.</p> <p>?</p> <p>?</p> <p>?</p> <p>?</p>						
<p>I can go here for more information:</p>							

As you read about Multiple Sclerosis, annotate the article. For each paragraph:

1. Check off information that you understand.
2. Underline only the most important information necessary for understanding the paragraph.
3. Put a “?” by terms that are not familiar, and then find out their meanings.
4. Mark off any information that is not necessary for understanding the article.
5. Write brief summaries in the margins, explaining the key points.
6. At the end of the article, write a 2-sentence summary in your own words, that utilizes the following framework:

Researchers have discovered that.....
This is important because.....

Findings suggest new cause, possible treatment for multiple sclerosis – EurekAlert 11.23.2010

WEST LAFAYETTE, Ind. - Researchers have found evidence that an environmental pollutant may play an important role in causing multiple sclerosis and that a hypertension drug might be used to treat the disease.

The toxin acrolein was elevated by about 60 percent in the spinal cord tissues of mice with a disease similar to multiple sclerosis, said Riyi Shi, a medical doctor and a professor of neuroscience and biomedical engineering in Purdue University's Department of Basic Medical Sciences, School of Veterinary Medicine, Center for Paralysis Research and Weldon School of Biomedical Engineering.

The research results represent the first concrete laboratory evidence for a link between acrolein (pronounced a-KRO-le-an) and multiple sclerosis, he said.

"Only recently have researchers started to understand the details about what acrolein does to the human body," Shi said. "We are studying its effects on the central nervous system, both in trauma and degenerative diseases such as multiple sclerosis."

The compound is an environmental toxin found in air pollutants including tobacco smoke and auto exhaust. Acrolein also is produced within the body after nerve cells are damaged. Previous studies by this research team found that neuronal death caused by acrolein can be prevented by administering the drug hydralazine, an FDA-approved medication used to treat hypertension.

The new findings show that hydralazine also delays onset of multiple sclerosis in mice and reduces the severity of symptoms by neutralizing acrolein.

"The treatment did not cause any serious side effects in the mice," Shi said. "The dosage we used for hydralazine in animals is several times lower than the standard dosing for oral hydralazine in human pediatric patients. Therefore, considering the effectiveness of hydralazine at binding acrolein at such low concentrations, we expect that our study will lead to the development of new neuroprotective therapies for MS that could be rapidly translated into the clinic."

The researchers also learned the specific chemical signature of the drug that binds to acrolein and neutralizes it, potentially making it possible to create synthetic alternatives with reduced side effects. The studies are detailed in a paper appearing online this month in the journal *Neuroscience*. The paper

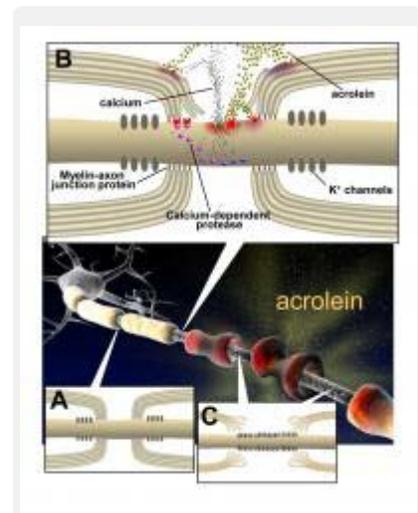


IMAGE: This drawing depicts how the environmental pollutant acrolein may damage nerve insulation called myelin in multiple sclerosis. "A" represents the normal structure of nerve fibers and myelin; "B" represents how...

[Click here for more information.](#)

was written by doctoral students Gary Leung, Wenjing Sun and Lingxing Zheng; graduate research assistant Melissa Tully, who is an MD-Ph.D. student at Purdue and the Indiana University School of Medicine; postdoctoral researcher Sarah Brookes; and Shi.

In multiple sclerosis, the myelin insulation surrounding nerve cells is destroyed and the nerve fibers themselves are damaged.

"We think that acrolein is what degrades myelin, so if we can block that effect then we can delay the onset of MS and lessen the symptoms," Shi said.

Acrolein induces the production of free radicals, compounds that cause additional injury to tissues after disease or physical trauma.

"We've discovered that acrolein may play a very important role in free radical injury, particularly in multiple sclerosis," Shi said.

The elevated acrolein levels in the MS mice were cut in half when treated with hydralazine. The drug represents a potential long-term therapy to slow the disease's progress.

"To our knowledge, this is the first evidence that acrolein acts as a neurotoxin in MS and also the first time anyone has demonstrated hydralazine to be a neuroprotective drug," Shi said.

Other researchers had previously shown that acrolein damages liver cells and that the damage can be alleviated by hydralazine, leading the Purdue researchers to study its possible effects on spinal cord tissues.

Further research will be conducted, and Shi's group has identified other potential compounds for binding acrolein. The research team, in a possible future collaboration with the Indiana University School of Medicine, also is working to improve the sensitivity of detection methods to measure acrolein levels in people with multiple sclerosis.

Findings suggest new cause, possible treatment for multiple sclerosis – EurekAlert 11.23.2010

WEST LAFAYETTE, Ind. - Researchers have found evidence that an environmental pollutant may play an important role in causing multiple sclerosis and that a hypertension drug might be used to treat the disease.

The toxin acrolein was elevated by about 60 percent in the spinal cord tissues of mice with a disease similar to multiple sclerosis, said Riya Shi, a medical doctor and a professor of neuroscience and biomedical engineering in Purdue University's Department of Basic Medical Sciences, School of Veterinary Medicine, Center for Paralysis Research and Weldon School of Biomedical Engineering.

The research results represent the first concrete laboratory evidence for a link between acrolein (pronounced a-KRO-le-an) and multiple sclerosis, he said.

"Only recently have researchers started to understand the details about what acrolein does to the human body," Shi said. "We are studying its effects on the central nervous system, both in trauma and degenerative diseases such as multiple sclerosis."

The compound is an environmental toxin found in air pollutants including tobacco smoke and auto exhaust. Acrolein also is produced within the body after nerve cells are damaged. Previous studies by this research team found that neuronal death caused by acrolein can be prevented by administering the drug hydralazine, an FDA-approved medication used to treat hypertension.

The new findings show that hydralazine also delays onset of multiple sclerosis in mice and reduces the severity of symptoms by neutralizing acrolein.

"The treatment did not cause any serious side effects in the mice," Shi said. "The dosage we used for hydralazine in animals is several times lower than the standard dosing for oral hydralazine in human pediatric patients. Therefore, considering the effectiveness of hydralazine at binding acrolein at such low concentrations, we expect that our study will lead to the development of new neuroprotective therapies for MS that could be rapidly translated into the clinic."

The researchers also learned the specific chemical signature of the drug that binds to acrolein and neutralizes it, potentially making it possible to create synthetic alternatives with reduced side effects.

The studies are detailed in a paper appearing online this month in the journal Neuroscience. The paper was written by doctoral students Gary Leung, Wenjing Sun and Lingxing Zheng; graduate research assistant Melissa Tully, who is an MD-Ph.D. student at Purdue and the Indiana University School of Medicine; postdoctoral researcher Sarah Brookes; and Shi.

In multiple sclerosis, the myelin insulation surrounding nerve cells is destroyed and the nerve fibers themselves are damaged.

"We think that acrolein is what degrades myelin, so if we can block that effect then we can delay the onset of MS and lessen the symptoms," Shi said.

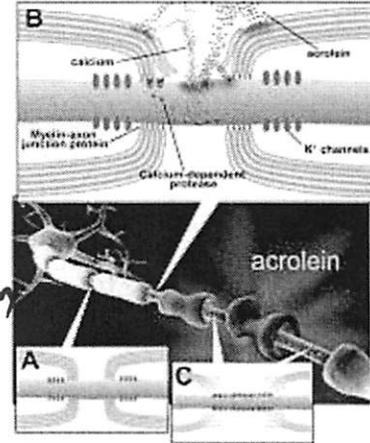


IMAGE: This drawing depicts how the environmental pollutant acrolein may damage nerve insulation called myelin in multiple sclerosis. "A" represents the normal structure of nerve fibers and myelin; "B" represents how...

[Click here for more information.](#)

↑ 60% in MS

found in air pollution

drug neutralizes toxin

no side effects

can create new forms

? (high blood pressure)

not necessary

? (breaking down)

? (name of drug)

? (start)

? (protects nerves)

not necessary

? fatty tissue

blocking acrolein → blocking myelin damage → slowing MS

✓ Acrolein [?] induces ^(starts) the production of free radicals, compounds that cause additional injury to tissues after disease or physical trauma.

✓ "We've discovered that acrolein may play a very important role in free radical injury, particularly in multiple sclerosis," Shi said.

What are free radicals?

↓ 50% ✓ The elevated acrolein levels in the MS mice were cut in half when treated with hydralazine. The drug represents a potential long-term therapy to slow the disease's progress.

✓ "To our knowledge, this is the first ^{*} evidence that acrolein acts as a neurotoxin in MS and also the first time anyone has demonstrated hydralazine to be a neuroprotective drug," Shi said.

acrolein damages liver ✓ Other researchers had previously shown that acrolein damages liver cells and that the damage can be alleviated by hydralazine, leading the Purdue researchers to study its possible effects on spinal cord tissues. (made better)

✓ Further research will be conducted, and Shi's group has identified other potential compounds for binding acrolein. The research team, in a possible future collaboration with the Indiana University School of Medicine, also is working to improve the sensitivity of detection methods to measure acrolein levels in people with multiple sclerosis.] not necessary

Summary

Researchers have discovered that acrolein, a poison found in air pollution and automobile exhaust, may damage nerve cells and be responsible for causing multiple sclerosis. This is important because drugs that treat high blood pressure can block acrolein and may be effective in MS patients.

EAE – The Mouse Model of Multiple Sclerosis

Standardized Test Practice

EAE (Experimental Autoimmune Encephalomyelitis) is the animal model of the disease multiple sclerosis. In EAE, mice are given central nervous system proteins (from the brain and spinal cord) to stimulate an autoimmune response. The foreign proteins (antigens) cause the immune system to break down the myelin sheath (fatty covering) around the nerve cells. This may happen in one of several ways: B cells (a type of white blood cells) may be producing antibodies (proteins that attack foreign proteins) to its own central nervous system. Or, T cells (a different type of white blood cells) may be attacking the spinal cord directly. The result is that the spinal cord is damaged and that the mice have trouble walking, and may even become completely paralyzed. To complicate the subject, other T cells (T regulator cells) may be effective in stopping the autoimmune response of either B or T cells.

Experiment 1

Two strains of mice, SJL and C57BL, were given separate injections of two specific central nervous system protein, PLP and MOG. The progression of the disease was measured by rating the mouse's gait (walking movement) on an EAE scale of 0-5 over the course of 50 days.

- 0 – normal gait
- 1 – waddling gait
- 2 – severe waddling gait
- 3 – impaired righting reflex- ability to turn over when placed on back
- 4 – hind limb paralysis
- 5 - death

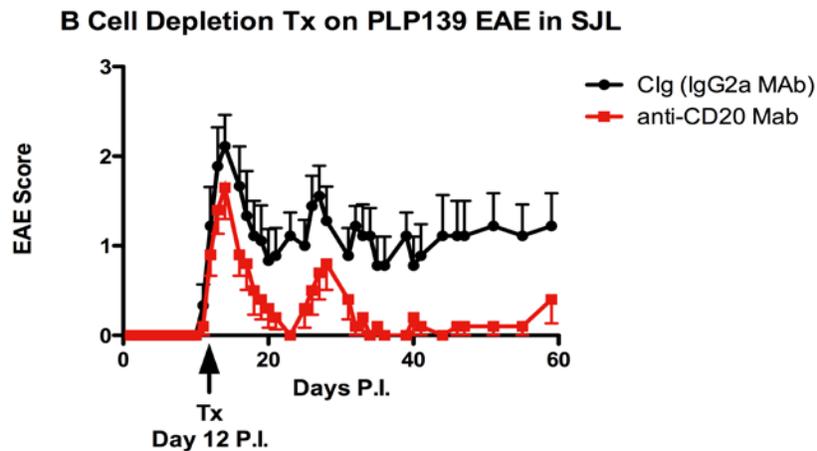
Average EAE Score		
Mouse Strain + Protein		
Day	SJL + PLP	SJL + MOG
0	0	0
10	0.7	0.2
20	4.2	0.1
30	1.2	0.1
40	3.1	0.2
50	1.4	0.1
C57BL + PLP		
0	0	0
10	1	0.9
20	4.2	3.6
30	1.2	4.4
40	0.5	4.5
50	0.3	4.6

Table 1

Experiment 2

On Day 0, two groups of mice were injected with PLP139 antigen and their disability was measured. 12 days following injection of the PLP139 antigen, one of the groups was given an injection of a protein (anti-CD20 Mab) that depletes the B cells and prevents them from producing antibodies to the spinal cord. The other group was given an injection of a protein (CIg-IgG2aMAB) that has no effect on the immune system. The EAE scores were measured in both groups for 60 days following initial injection. The results are displayed in Figure 1.

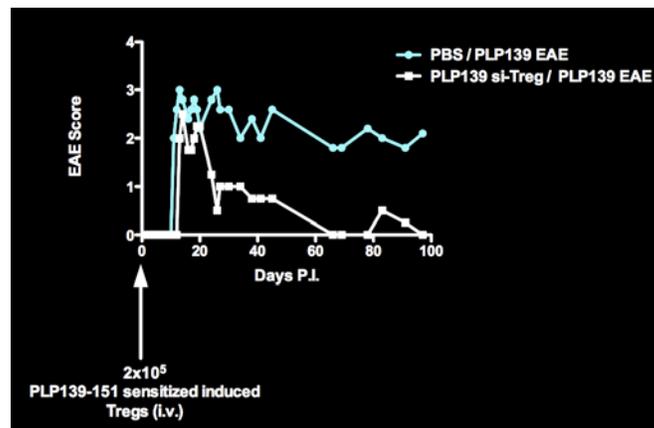
Figure 1



Experiment 3

On Day 0, one group of mice was injected with PLP139 antigen and a neutral buffer solution (PBS/PLP139 EAE), while the other group was injected with the PLP139 antigen and T regulator cells that had been sensitized to any immune system response against this antigen (PLP139 si-Treg/PLP139 EAE). The EAE scores were measured in both groups for 60 days following initial injection. The results are displayed in Figure 2.

Figure 2



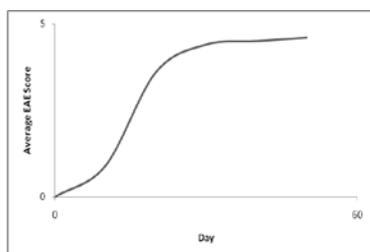
1. Which of the following changes in Experiment 2 would permit a test of the hypothesis that depleting T cells with a protein (called Anti-CD8) would reduce the effects of the disease?
 - A. Repeat the experiment using the same concentration of Anti-CD8 protein that depletes the T cells.
 - B. Repeat the experiment without injecting the mice at Day 0.
 - C. Repeat the experiment using both Anti-CD8 and Anti-CD20 proteins.
 - D. Repeat the experiment without using additional proteins.

2. The results in Experiments 2 and 3 demonstrate that blocking the actions of specific immune cells
 - F. has an immediate effect on EAE scores.
 - G. has a delayed effect on EAE scores.
 - H. has no effect on EAE scores.
 - J. has a negative effect on EAE scores.

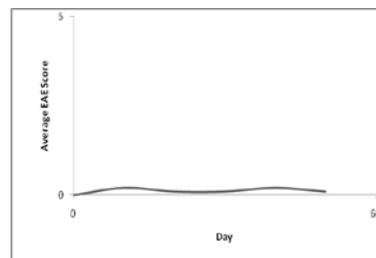
3. Based on the information in Table 1, which statement is correct?
 - A. The mice with an EAE score of 0 received no injections.
 - B. The average score of C57BL + PLP mice is lower on Day 40 than the SJL + MOG mice on Day 40.
 - C. The MOG protein has a significant effect on SJL mice.
 - D. C57BL + PLP mice become paralyzed and then recover.

4. Which of the following graphs best represents the data presented in Table 1 for SJL mice injected with PLP protein?

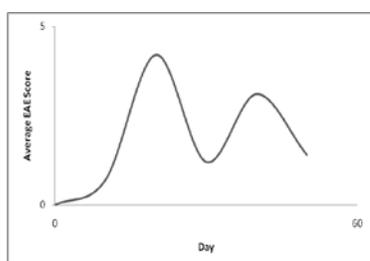
F.



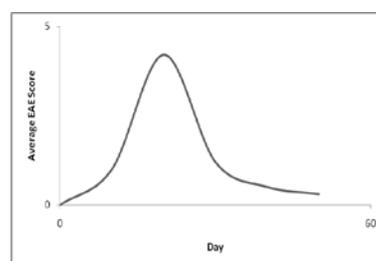
G.



H.



J.



5. Based on the results of Experiment 3, what strain of mice was most likely used?
- A. C57BL only
 - B. SJL only
 - C. Both C57 and SJL
 - D. Neither C57 nor SJL
6. Multiple Sclerosis and EAE diseases come in two forms: a. relapsing/remitting - the disease symptoms get worse, then better, then worse, etc. and b. chronic – the symptoms get worse and do not get better. Rituximab is a drug developed to control the relapsing/remitting form of the disease and has shown to be most effective in mice at 50 days after initially being exposed to nervous system antigens. What is the most likely effect of Rituximab?
- F. Depletes B cells
 - G. Blocks MOG proteins
 - H. Increases T regulator cells
 - J. Removes PLP proteins from the body

EAE – The Mouse Model of Multiple Sclerosis

Standardized Test Practice - Answers

Note: This passage is modeled after the ACT test, the college entrance exam. The Science section of the test consists of several passages on a topic, followed by question sets. The passages include descriptions of experiments, graphs, and data tables. There is always a large amount of unfamiliar, technical vocabulary that is designed to confuse the less able student. The test measures scientific reasoning, not scientific content knowledge, so students do not need to be familiar with the topics to do well. Have students focus on the main ideas and reasoning behind the answers, not on the details.

1. Which of the following changes in Experiment 2 would permit a test of the hypothesis that depleting T cells with a protein (called Anti-CD8) would reduce the effects of the disease?
 - A. Repeat the experiment using the same concentration of Anti-CD8 protein as Anti-CD20 protein.
 - B. Repeat the experiment without injecting the mice at Day 0.
 - C. Repeat the experiment using both Anti-CD8 and Anti-CD20 proteins.
 - D. Repeat the experiment without using additional proteins.

Correct: A Anti-CD8 will deplete T cells and would let the researcher know if these cells had any effect on the disease

Wrong: B. EAE disease will not start without the initial injection at Day 0. **C.** Using both Anti-CD8 and Anti-CD20 adds a second variable and does not let the scientist determine which cells are playing a role. **D.** This will not affect the T cells.

2. The results in Experiments 2 and 3 demonstrate that blocking the actions of specific immune cells
 - F. has an immediate effect on EAE scores.
 - G. has a delayed effect on EAE scores.
 - H. has no effect on EAE scores.
 - J. has a negative effect on EAE scores.

Correct: G The EAE scores do not drop until after at least Day 15

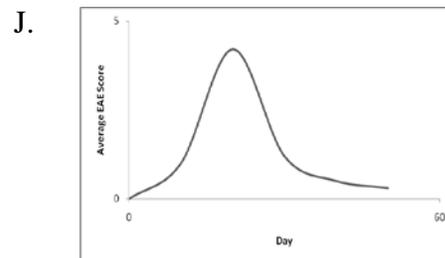
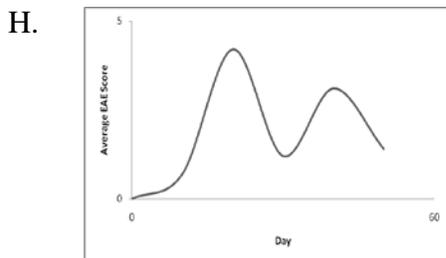
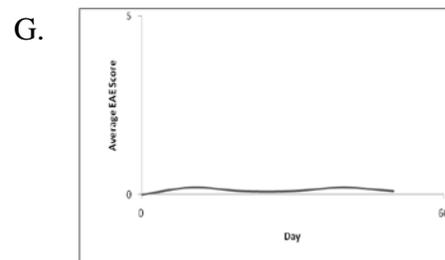
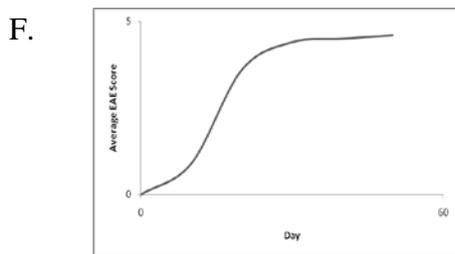
Wrong: F. EAE scores initially rise. **H.** The mean EAE score for the treated groups is lower than for the control group. **D.** Although the EAE scores decrease, the lower the EAE score, the more positive the results

3. Based on the information in Table 1, which statement is correct?
- A. The mice with an EAE score of 0 received no injections.
 - B. The average score of C57BL + PLP mice is lower on Day 40 than the SJL + MOG mice on Day 40.
 - C. The MOG protein has a significant effect on SJL mice.
 - D. C57BL + PLP mice become paralyzed and then recover.

Correct: D On Day 20, these mice show paralysis and then return to an almost normal gait

Wrong: A. All mice received injections. **B.** C57BL + PLP – Day 40 = 0.5; SJL + MOG – Day 40 = 0.2. **C.** SJL mice injected with MOG showed few signs of EAE

4. Which of the following graphs best represents the data presented in Table 1 for SJL mice injected with PLP protein?



Correct: H This matches the increase, decrease, and increase of the data.

Wrong: F. This would be the graph for C57BL + MOG mice. **G.** This would be the graph for SJL + MOG mice. **J.** This would be the graph for C57BL + PLP mice.

5. Based on the results of Experiment 3, what strain of mice was most likely used?
- A. C57BL only
 - B. SJL only
 - C. Both C57 and SJL
 - D. Neither C57 nor SJL

Correct: D The data for PBS/PLP139 (the top line) needs to be compared to the data in Table 1. In Figure 2, the EAE scores peak, then stay elevated. In Table 1, neither group of mice shows this pattern in the same time period.

Wrong: A. C57BL + PLP mice EAE scores increase and then decrease almost to normal. This looks like C57BL + MOG results, but the experiment used the PLP protein, not the MOG protein. **B.** SJL mice EAE scores show a different pattern over the same time period **C.** Contradicts the results.

Note: This is a very difficult question. It is the type that most students on standardized tests would miss, due to the complexity and the “trickiness” of the answer.

6. Multiple Sclerosis and EAE diseases come in two forms: a. relapsing/remitting - the disease symptoms get worse, then better, then worse, etc. and b. chronic – the symptoms get worse and do not get better. Rituximab is a drug developed to control the relapsing/remitting form of the disease and has shown to be most effective in mice at 50 days after initially being exposed to nervous system antigens. What is the most likely effect of Rituximab?
- | | |
|------------------------|---------------------------------------|
| F. Depletes B cells | H. Increases T regulator cells |
| G. Blocks MOG proteins | J. Removes PLP proteins from the body |

Correct: F MS and EAE are diseases caused by the immune system “overreacting” to the body’s normal proteins, so the drug must work to block the immune system, not the proteins. Figure 1 shows data most representing the relapsing/remitting form of the disease, so Rituximab would most likely deplete the B cells.

Wrong: G. MOG is a protein and not the target of the drug. **H.** In Figure 2, the data resembles a more chronic form of the disease. By Day 50, the drug is not at its most effective point. **J.** PLP is a protein and is not the target of the drug.

Autoimmune Disease Project

Your assignment will be to help understand the question:

“What happens when your own immune system attacks you?”

Hypothesis: If my own immune system attacks me, then _____

Assignment:

1. Research an autoimmune disease – go to the American Autoimmune Related Disease Association - www.aarda.org. Click on “Autoimmune Information,” then “Patient Information.”
 - a. Click on the specific disease you are researching to find out some brief background information – ex. Multiple Sclerosis.
 - b. Once you have a general idea of the disease, search for a national organizational website for that disease – ex. National Multiple Sclerosis Society www.nationalmssociety.org
 - c. Analyze the website, using the “Evaluating Internet Websites” worksheet
 - d. Take notes about your disease using the “2-Column Notes – Autoimmune Disease” packet.
2. Prepare an educational, full-color pamphlet about your disease.
 - a. Use a Microsoft Publisher (or similar template). Your pamphlet must include the information from your notes, be in your own words, and be understandable by someone not familiar with the disease.
 - b. Use the “Autoimmune Disease Grading Pamphlet Rubric” worksheet as a guide to help you prepare the best pamphlet.

3. Engage in a Patient Consultation – you will role-play the job of a doctor who needs to explain a recently diagnosed autoimmune disease to your patient.

- a. Plan your consultation using the “Patient Consultation Graphic Organizer” worksheet.
- b. Pair up with a partner and use your Disease Pamphlet and your notes to help your “patient” understand his/her disease. Remember to role-play in a serious manner.
- c. Have your “patient” fill out the “Patient Consultation Evaluation” worksheet.

4. Revisit your original hypothesis, and revise it below:

Hypothesis: If my own immune system attacks me, then _____

Evaluating Internet Websites

Before doing research, use the Chart below to analyze an Internet Website and to make sure that the website provides a reliable source of information.

Authority	Is there an <u>author(s)</u> or sponsor(s)? What are their <u>qualifications</u> ? Can you verify? • Address • Phone number • E-mail <i>Check the header (top) or footer (bottom) of the page.</i>
Accuracy	Are <u>sources</u> listed? Who is responsible? Any <u>errors</u> ? • Grammatical • Technical Can you <u>verify the information</u> ?
Objectivity	What is the <u>purpose</u> of the site? • Is there a bias? • Are they selling? • Are they trying to persuade? • Look for “About us/Mission/ Purpose” links.
Currency	Is the website <u>dated</u> ? • When was it put on the web? • When was it <u>updated</u> ? • Is the information current?
Coverage	What is the depth of the information? • Summary • Outline • In-depth How much is covered? • Is it a specific topic? (i.e. Civil War)? • Is it a broad subject (i.e. U.S. History)?

Name of Author or sponsor _____

Their Qualifications _____

Sources-Errors-Verified Information _____

Explain the purpose of the site _____

When was the site published & updated? _____

Compare your site to an encyclopedia article. Compare the amount of information provided. Are there any differences in information between the two sources? Explain why there might be differences. _____

Sources cited:

Alexander, Jan and Marsha Ann Tate. "Evaluating Web Resources." July 25, 2001. [last update]. Online. Wolfgram Memorial Library. Available: <http://www2.widener.edu/Wolfgram-Memorial-Library/webevaluation/webeval.htm>. 26 October 2001.
 Northrup, Mary. "Web Site Evaluation Checklist." The Book Report September/October, 2001: 48.
 University of Wisconsin, InternetWorkshop Working Group. "Checklist for Evaluating Web Sites." September 5, 2001 [last update]. Online. University of Wisconsin. Available: <http://www.library.wisc.edu/libraries/Instruction/instmat/webeval.htm>. 26 October 2001.

2 Column Notes - Autoimmune Disease

As you read information, take notes (in your own words) about each of the sections. Be concise!

Disease:

Topic	Summary – Recommended 5-7 words (your own)
<p>General Info Explain autoimmunity</p> <p>Explain your specific disease:</p> <p>Causes Role of Immune System:</p>	
<p>Questions I need answered:</p>	

2 Column Notes - Autoimmune Disease

As you read information, take notes (in your own words) about each of the sections. Be concise!

Topic	Summary – Recommended 5-7 words (your own)
<p>Major Symptoms (How do you know you have it?)</p> <p>What body parts does it affect? How?</p> <p>Are there preventions? (tests, early treatments,...)</p>	
<p>Questions I need answered:</p>	

2 Column Notes - Autoimmune Disease

As you read information, take notes (in your own words) about each of the sections. Be concise!

Topic	Summary – Recommended 5-7 words (your own)
<p>Treatments/Cures Is the disease curable, (goes away completely), treatable (live with it), or uncurable?</p> <p>What treatments are available?</p> <p>Is treatment effective? Use data here. (cure rates, life expectancies,...)</p>	
<p>Questions I need answered:</p>	

2 Column Notes - Autoimmune Disease

As you read information, take notes (in your own words) about each of the sections. Be concise!

Topic	Summary – Recommended 5-7 words (your own)
<p>Resources: Organizational Web Page (Title and URL)</p> <p>Closest Support Group Location</p> <p>Current Research Study (Topic, Institution, and Location)</p> <p>Current Patient On-line Blog/Journal (Title and URL)</p>	
<p>Questions I need answered:</p>	

Assignment: Create a pamphlet that clearly explains the disease. The pamphlet should include the components presented below and should be in your own words. It is designed to be used during a consultation with a patient who has just been diagnosed with the disease.

Name _____

Autoimmune Disease Pamphlet Grading Rubric

Excellent = clearly explained in your own words; correct information; appropriate scientific vocabulary
Good = clearly explained in your own words; correct information; some appropriate scientific vocabulary
Average = primarily clear explanation in your own words; primarily correct information; some appropriate scientific vocabulary
Fair = somewhat clear explanation; lacking your own words, correctness, and/or appropriate scientific vocabulary
Poor = unclear explanation; copied or incorrect information; little/no scientific vocabulary

	Excellent 5	Good 4	Average 3	Fair 2	Poor 1
Pamphlet Components					
1. General autoimmunity	_____	_____	_____	_____	_____
2. Specific disease	_____	_____	_____	_____	_____
3. Role of immune system	_____	_____	_____	_____	_____
4. Causes (if known)	_____	_____	_____	_____	_____
5. Risk factors	_____	_____	_____	_____	_____
6. Symptoms	_____	_____	_____	_____	_____
7. Preventions	_____	_____	_____	_____	_____
8. Treatments/Cures	_____	_____	_____	_____	_____
9. Treatment effectiveness	_____	_____	_____	_____	_____
10. Resources - organization	_____	_____	_____	_____	_____
11. Support group location	_____	_____	_____	_____	_____
12. Research study	_____	_____	_____	_____	_____
13. Current patient blog	_____	_____	_____	_____	_____
Pamphlet Quality					
1. Organized	_____	_____	_____	_____	_____
2. User-friendly	_____	_____	_____	_____	_____
3. Graphics	_____	_____	_____	_____	_____
Patient Consultation (attached)					
1. Completion	Yes _____	No _____	_____	_____	_____
2. Partner evaluation	_____	_____	_____	_____	_____

Deductions _____ **Total** _____ **Comments** _____

Patient Consultation Graphic Organizer

Use the information collected during research to create some “talking points” to be used when explaining the disease to a patient.

Disease: _____

Big Picture: What is this disease (in my own words), how does the diseases relate to the immune system and autoimmunity.

Details: What is the disease? How will it affect the patient? What can be done?

Illustration/Graph: To help the patient understand

Vocabulary: What I need to know to explain this concept to a patient (define words that are unfamiliar):

Resources: Recommendations for the patient:

Patient Consultation Evaluation

The purpose of this activity is for the patient to evaluate the experience of a consultation. The student (patient) who is evaluating should use the following form to critique the doctor (another student) and the pamphlet.

Pamphlet & Consultation	Your comments
<p>1. Based on the information in the pamphlet and from your doctor, do you understand the following:</p> <ul style="list-style-type: none">• symptoms• causes• treatments• resources for help	
<p>2. Based on your conversation with your doctor, rate the quality of the consultation. Consider word choice, time, “bedside manner,” and the ability to answer questions.</p>	