The Journal of Toxicological Education **1:** 31-53 (2013)
http://www.jtoxed.org

JToxEd
The Journal of Toxicological Education

Agents of Bioterrorism: Curriculum and Pedagogy in an Online Masters Course

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Abstract

The Agents of Bioterrorism course (BSBD 640, University of Maryland University College) is a graduate level course created in response to an elevated need for scientists working in the field of medical countermeasures to biological and chemical weapons in the years following 9/11. Students read and evaluate assigned current primary literature articles investigating medical countermeasures at each stage of development. In addition, students learn concepts of risk assessment, comparing and ranking several agents of terror. Student learning is assessed through a variety of assignments. A term paper focuses on a lesser known weapon of terror, with students recommending the best countermeasure in development and delivering a risk assessment comparing their agent to other major weapons of terror discussed throughout the semester. Similarly, a group project on an assigned major weapon of terror (anthrax, plague, smallpox, vesicants, or nerve agent) focuses more heavily on evaluating primary literature and concluding which countermeasure(s) in development are the best. Students complete the course with a fundamental understanding of the mechanism of action of many biological agents, information literacy for the medical literature available at PubMed and the primary scientific literature, and a basic understanding of the role of the government in biodefense research. This paper describes the pedagogical approaches used to teach this course and how they might be adopted for other courses.

Keywords

toxicology, graduate, bioterrorism, countermeasures, chemical threats, biological warfare, chemical warfare

Introduction

Agents of Bioterrorism is a graduate-level course designed to educate students on the biology and threat of the most important chemical and biological weapons of terror. The course is part of the Masters of Science in Biotechnology: Biosecurity and Biodefense Specialization at the University of Maryland University College. An online course, created in 2007 by Joshua Gray and Lee Pierce, Agents of Bioterrorism is the first in the Biosecurity and Biodefense Specialization series. The course provides fundamental information on the biology and mechanism of action of the most important potential agents of terror and an introduction to the role of government. It also develops student skills in scientific literacy and writing.

The threat of biological and chemical terrorism has received increased attention since the 9/11 World Trade Center and Pentagon attacks and the subsequent anthrax letter attack. Prior to this time, most research on medical countermeasures was performed by military laboratories (such as the United States Army Medical Research Institute for Infectious Diseases (USAMRIID) and the United States Army Medical Research Institute for Chemical Defense (USAMRICD)) and focused on prophylactic protection of the warfighter, and not on the civilian population. However, in the time since 2001, the biodefense landscape has dramatically changed focus from prophylactic protection of warfighters to post-exposure treatment of exposed civilians. There is now an increased role of civilian research laboratories in biodefense research due to NIH-funding of biodefense and an effort by the government to facilitate the development of these countermeasures[1].

In July of 2004, President George W. Bush initiated Project Bioshield[2], a White House initiative designed to quickly develop medical countermeasures for the treatment of agents of terror, including biological, chemical, and radiological weapons. This important legislation gave the National Institutes of Health the power to oversee new grant money specifically designated for this purpose, the FDA was given special fast-tracking authority for medical countermeasures. The Biomedical Advanced Research and Development Authority (BARDA) was created under the Department of Health and Human Services to facilitate the FDA approval of medical countermeasures. The Strategic National Stockpile, managed by the Centers for Diseases Control, was created to provide medical countermeasures in the event of a national emergency involving bioterrorism or a national pandemic. The Project Bioshield program continues to produce medical countermeasures, including medicines for smallpox, anthrax, and botulinum toxin, for example[3].

The Agents of Bioterrorism course covers the agents of bioterrorism from the perspective of medical countermeasure development over a twelve week semester (Syllabus, Appendix 1). Students learn the mechanism of action of each agent through the reading of review articles and book chapters from "Medical Aspects of Biological Warfare," published by the Borden Institute and freely available online[4]. Students summarize selected articles from the primary literature on medical countermeasures combatting those agents at a variety of stages of development, from screening of chemical libraries to clinical trials. Through risk assessment assignments, students compare and contrast the agents of terror, focusing on the features that make them more or less threatening. In a group project, students research novel medical countermeasures for a major weapon of terror, such as anthrax, plague, smallpox, or nerve agent. Finally, the term paper

includes a detailed risk analysis and analysis of medical countermeasures for a minor weapon of terror. Each of the assignments will be covered in detail throughout the rest of the paper.

Target Audience and the Online Classroom

Students in the course come from a variety of backgrounds; while many students are currently serving in the military, others include recent graduates and those attempting to reenter the workforce. Almost all students are participating part-time and are currently employed in a full time position which may or may not be related to biosecurity. Approximately half of the students have Bachelor of Arts of Science degrees in biology and/or chemistry. Class size is typically 10-20. Given the writing-intensive focus of the course, increased course size would be difficult to achieve without changing aspects of grading and professor feedback. For more information, visit the UMUC webpage for the program[5]. Although this course is taught online, the authors anticipate that it may be adapted to face-to-face classrooms. This paper does not focus on the mechanics of online teaching.

Course Structure

The learning objectives for the course (Table 1) are centered on developing an understanding of the science of agents of biological and chemical terrorism and medical countermeasures against them. These objectives are met through the use of five types of assignments: conference participation, paper reviews, risk assessment rubric design, a term paper, and a group project, each of which are described in detail below.

Table 1. Course Objectives for Agents of Bioterrorism. Course Objectives are mapped against Student Learning Expectations of the University of Maryland University College[6]. Student Learning Expectations include: Written Communications (COMM), Technology Fluency (TECH), Information Literacy (INFO), Program Content Knowledge (KNOW), and Critical Thinking (THIN). Course objectives are also linked to their relevant assignment(s): conference participation (CP), paper reviews (PR), risk assessment rubric design (RARD), a term paper (TP) , and a group project (GP).

Course Objective:	COMM	TECH	INFO	KNOW	THIN	Linked Assignments
Comprehend the chemical and biological effects of the biological, chemical, and nuclear weapons most likely to be employed in bioterrorism.	X			X		CP, PR, TP, RARD, GP
Predict the impact of these weapons on various human organ systems.	X				X	TP, GP
Evaluate possible strategies for defense against attack by such weapons.					X	CP
Analyze the methods and challenges of detecting attacks by such weapons.		X				CP, RARD
Examine the bioethical challenges of anti-bioterror research and its implications for society.				X	X	CP
Develop an understanding of the epidemiology of bioterror agents and the application of risk assessment to its analysis.				X		CP, RARD
Competently navigate the scientific literature and evaluate the scientific issues, including novel bioterror threats and potential therapies.	X	X	X		X	PR, TP, GP

Table 2. Grade Distribution for Agents of Bioterrorism.

Assignment Type	Percent of Grade
Participation – weekly participation in online discussion forums	15
Writing assignments – five assigned	20
Group project	25
Term paper	15
Revised term paper	15
Risk assessment rubric – three assigned	12
Reference assignment (pass/fail)	3

Assignment Details

Paper Reviews:

Five paper reviews are completed throughout the semester: anthrax (*Bacillus anthracis*), plague (*Yersinia pestis*), smallpox (*Variola major*), nerve agents (sarin, VX, tabun, etc.), and vesicants (mustard gas, nitrogen mustard). Students are provided a chapter from "Medical Aspects of Biological Warfare" or a current review article together with an assigned article from the primary literature discussing a countermeasure in development for that agent.

Paper reviews are broken down into five sections: a one-two sentence concise summary of the findings of the paper, 2-3 paragraphs discussing the molecular mechanism of action of the agent, a paper review discussing the findings of key experiments in 3-4 paragraphs, a future directions section discussing the next experiments required to push the countermeasure closer to approval, and a references section with at least three citations. Note that the signs and symptoms resulting from exposure to the agent are not discussed - these are discussed in the classroom. Examples are provided for the paper, "*Yersinia pestis* with delayed attenuation as a vaccine candidate to induce protective immunity against plague," which is one of the assigned papers for week three[7].

1-2 sentence summary: The student must carefully and concisely discuss the findings of the paper. Careful crafting of a two sentence summary allows evaluation of whether the student comprehended the reviewed article and provides good practice for scientific writing. Example: "The authors generated an attenuated strain of *Yersinia pestis* with a key transcription factor for virulence factors (crp) under the control of an arabinose-driven promoter. Infection of mice with this strain allowed colonization of tissues followed by rapid attenuation and a dramatically improved immune response than that of a standard crp knockout strain."

Molecular mechanism of action: In this section students discuss how the agent works at the molecular level. For *Yersinia pestis*, this would include a description of the virulence factors and how they target the cells of the body. In the final paragraph, students provide special attention to the particular molecular mechanism being targeted by the medical countermeasure. For example, in the referenced article, the authors generate an attenuated strain of *Yersinia pestis* by targeting the crp transcription factor which drives the production of many virulence factors

important for infection of mammals including the Yops. Students should describe what crp is, how it works, and why it is important for the virulence of *Yersinia pestis*.

Paper review: In this section, students provide a narrative for the key experiments of the paper. Students focus on why experiments were done, what was found, and what the outcomes mean. The desired level of writing is equivalent to "Scientific American", such that another student reader can follow the key experiments without having to read the actual scientific article. Ideally, students reviewing other papers will read, understand, and ask questions about the paper reviews of other students. As there are typically three papers assigned at random to the class, students also self-assess by reading the reviews of their classmates, asking questions, and offering criticism.

Future directions: Students are asked to describe future experiments that would allow the medical countermeasure to proceed toward development. This can include experiments directly discussed and proposed by the authors of the article, but must also include some experiments designed by the students themselves.

The grading rubric can be found in the syllabus in Appendix 2. Extensive feedback is provided after each review, and the repetitive nature of the assignment allows improvement across the five reviews. Turnitin is used for all major assignments in the course as a plagiarism detection tool.

Risk Assessment Rubric

The risk assessment rubric is a matrix of agents comparing different agents of terror in order to generate a relative risk for each agent. As a starting point, students are exposed to the Centers for Disease Control rubric for ranking of biological agents of terror[8]. Next, students in the classroom are asked to propose features that make an effective weapon of terror. Some examples include: ease of manufacture, availability of treatment, ability to survive outside of the host, financial cost or economic outcome, lethality, and ease of acquisition. The merits and relative importance of their developed categories are then peer reviewed and discussed in an online conference.

The following week, students are asked to create a rubric comparing the tularemia against cholera as potential agents of terror. Students choose their own categories and scoring metrics for those categories and back up their scores with rationale based on the agent. The rubrics are then posted online and the students are asked to criticize each other's rubric, making arguments for which scores might be changed. Students must then either concede the argument or make a case for why their scores were accurate to begin with. Typically students begin with a rubric such as the one below (Table 3). Each category is equally weighted and little or no explanation is provided with the table. Feedback to the student for this assignment was, *"You have a good number of categories, but you need to consider weighting the categories. For example, is "availability" as important as "infectious dose"? If not, use a multiplier to give more weight to one or the other category. Also, use some descriptions as needed for the categories, because not all of them are clear. For example, "public perception" and "special preparation" are a little vague. You can use a description underneath the table to describe these things*." Care is taken to

not give too much advice, as the students will learn from one another and begin to reach consensus. Within the online discussion forums, students challenge one another on the scores given in particular categories, providing rationale for why they disagree. This develops information literacy as the students must find the information to make their claim.

	Tularemia	Cholera
Availability	5	2
Death if untreated	3	5
Disease (symptoms)	4	3
Easily disseminated	5	3
Infectious Dose	5	1
Incubation Period	3	0
Persistence of organism	3	1
Person to person transmission	0	2
Public Perception	2	5
Special Preparation	5	2
Medical Treatment	2	1
Vaccine Status	5	3
Total Points (60)	42	28

Table 3. Example of the first risk assessment that a student produced. Students are asked to compare tularemia and cholera using categories of their choice and to generate scores for those categories. The total score indicates the relative threat of one agent versus the other. As expected, cholera, an unlikely weapon of terror, scored lower than tularemia.

In subsequent weeks, students are asked to add agents to their rubrics, beginning with two viral hemorrhagic fever viruses (Appendix 3). The challenge is to tweak the scores and categories to fit an ever-increasing diversity of agents, while simultaneously making sure the scores are reasonable. Dramatic improvement can be seen since the previous assignment, as the student has added better descriptions, altered potential point maximums (weighted the scores), and consolidated categories that may have been redundant.

After an additional round of faculty grading and peer review, the students are asked to add two nerve agents to the rubric. These are chemical, not biological, agents. This requires further modification of the rubric so that the relative risks of chemical and biological agents are

directly compared. Although this kind of comparison may not be typically done, the act of putting the table together greatly facilitates learning by comparison of agents that are quite different. Furthermore, the assignment of selecting two nerve agents is difficult, as there are very few differences between them. It is expected that their scores will be similar. Key differences I look for are for acetylcholinesterase aging and volatility, both of which can moderately affect the score.

The third rubric is accompanied by a writing assignment (Appendix 4). In this assignment, the students write about their rubric, providing rationale for the scores. In this particular write-up, the student discussed their difficulty with several features. For example, he explained that dosage of agent was a problem, because the scores would vary based on the dose of agent. Justification of the scores by the student in these paragraphs is a good indicator of understanding of the agents. Through three cycles of feedback with professor comments, the rubrics are continually improved and prepared for placement within the term paper.

Term Paper and Term Paper Revision

The term paper utilizes skills learned from assignments completed earlier in the semester, paper reviews and risk assessment rubrics, to evaluate an unfamiliar weapon of terror. Students find research articles discussing medical countermeasures for their agent and summarize and categorize them. They then evaluate which of the medical countermeasures is the best, based on whatever criteria they can make a case for, such as: stage in drug development, efficacy, ability to be used post-exposure, lack of side effects, cost. Students include their conclusion in the abstract and conclusion of the paper.

The students then write a risk analysis discussing the relative risk of their agent (using their risk assessment rubric) compared with other, better known agents of terror. Attention is paid to the particular categories of the rubric that make the most difference and the problems that might occur due to difficulties in deciding scores. In many ways, the risk assessment rubric helps guide their discussion to make a case about the relative risk of their agent. The term paper is written in the style of a report to the Defense Threat Reduction Agency (DTRA) and the Biomedical Advanced Research and Development Authority (BARDA), with the main focus being on the relative risk of the agent (important to DTRA) and the state of medical countermeasure development (important to BARDA).

A second version of the term paper is then assigned with questions and comments given individually for each student. An attempt is made to provide a similar amount of work for each student, regardless of the grade given on the assignment. If the student excels at all aspects of the paper, earning an A, they are typically assigned to find and include 5-6 additional medical countermeasures and to change their conclusions as necessary. For example, if the student focused too much on vaccines, they might be assigned to investigate small molecules or neutralizing antibodies and to reevaluate their conclusion based on the new medical countermeasures. Struggling students are told which additional papers to add rather than relied upon to pick their own articles.

Typically students have difficulty with writing the abstract, which is often written to state what is in the paper, as an introduction might be written, rather than having the actual findings of the paper. They also have difficulty with writing introductions and conclusions for each of the individual sections, failing to compare and contrast countermeasures of a particular type. Students with little preparation in finding scientific articles are directly assigned particular papers to aid them in their research. These errors are pointed out and asked to be correct in the revision.

The grade of the revision is based entirely on their ability to address the concerns raised by the first draft: no attention is paid to the first grade given on the paper. This kind of treatment is very similar to that which occurs between a graduate student and their mentor when revising papers. Needless to say, some students experience great difficulty in accepting criticism. Instructions for the revised term paper can be found in the syllabus (Appendix 5).

20% of the value of the revision is based on making sure the "track changes" feature is enabled in Microsoft Word as the students write the revision. Most students have not used this function and begin their revision without selecting it. Providing a heavy penalty for not using it seems to work well - only 1-2 students per semester ignore this. Despite many efforts and endless announcements, I have never reached complete compliance with this issue.

Group Paper

In addition to a term paper, students participate in a group paper focusing on one of the major potential weapons of terror: anthrax, plague, nerve agent, vesicants, or smallpox. Because the risk of these agents is well established, the risk assessment is not included in this paper. Instead, students perform an analysis of the current medical countermeasures available, discussing their benefits and problems. They also provide a more in-depth analysis of countermeasures in development focusing on the many approaches to countermeasure design. As with the term paper, students are asked to provide their informed opinion on the best medical countermeasure(s) in development for their assigned agent.

Course Discussions

In addition to discussing the science of how the agents and their countermeasures work, course discussions focus on the current regulatory environment for medical countermeasure development in the United States, primarily regulatory issues and governmental strategy for medical countermeasure development after 2001. Project Bioshield, signed by President George W. Bush in 2004, designated $1.7 billion to the Department of Health and Human Services (DHHS) in 2003. This funding was significantly more than the Department of Defense, which had only $267 million budgeted for 2003[9]. Ongoing financial support since this time has dramatically altered medical countermeasure research in the U.S., with a dramatic shift toward the funding of civilian non-military based research laboratories awarded via competitive grant applications. Today, programs such as the National Institutes of Health (NIH) Countermeasures against chemical threats (CounterACT) program fund a wide diversity of laboratories for medical countermeasure development. Current funding from the NIH for biodefense is approximately $1.5 billion. The role of BARDA and DTRA are covered. The NIH CounterACT program is used as an example of how the NIH provides funding to research investigators.

Weekly discussions include the following topics:

- Risks associated with vaccination of civilians against potential biological agents such as smallpox, anthrax, and ricin.
- Costs of medicines purchased by BARDA for the National Stockpile.
- The use of primates in research as a result of the FDA's two animal rule.
- Forced vaccination and the CDC's ability to enforce quarantine.
- Fritz Haber and the ethics of the use of chemical weapons: then and now.
- Recent activities performed by BARDA.
- Dirty bombs – bombs using conventional explosives to spread radiological material.
- Toxic industrial chemicals (TICs) and toxic industrial materials (TIMs).
- Epidemiology: differentiating a natural outbreak from an attack.
- Defensive versus offensive biodefense research: can they be separated?
- Agricultural bioterrorism and the USDA.

Discussions occur in message board-format: posts are made by students over the course of a week. Typically there are two or three equally-weighted discussions per week. To receive full credit, students should make original responses, exhibit high interactivity with classmates, indicate that they've read other students' posts in their own responses, indicate that they've read the course material in their responses, and participate on a regular basis (not make posts all at once at the end of the week). Ideally students draw in ideas from their own research to contribute to an active discussion forum in which students teach each other. The professor plays a role in facilitating discussion, asking questions that spur additional thought and research, and policing discussions to make sure they are civil and appropriate. Examples of rubrics used at UMUC are provided in a document by Wilke[10].

Conclusions and Recommendations for Implementation

This course provides students with a fundamental understanding of the mechanism of action of the most important potential biological and chemical weapons including anthrax (*Bacillus anthracis*), plague (*Yersinia pestis*), smallpox (*Variola major*), vesicants, and nerve agent. Other less-likely agents are covered as well, including toxins (such as ricin (*Ricinus communis*) and botulinum (*Clostridium botulinum*)), toxic industrial chemicals (TICs) (such as chlorine and phosgene), natural diseases that might be weaponized (such as influenza and tularemia (*Francisella tularensis*)), and many other agents. By focusing on medical countermeasures in development, students are exposed to the primary literature and review a number of recent papers on each of the agents. Through composition of a risk assessment rubric, students learn about how different features of each agent can contribute to its weaponization potential. Finally, by analyzing a number of medical countermeasures and recommending the best for further development, students communicate their understanding of the bioterrorism agent, ability to read scientific articles, and scientific writing.

Parts of the course might be used in a course focused on early stage drug development; the process for drug development is somewhat different for medical countermeasures[11]. One key difference is the FDA's two animal rule, which allows approval without human efficacy data[12].

For example, because there are no human cases of smallpox, new drugs for smallpox must be developed proving efficacy in animal models. Also, most development of medical countermeasures is avoided by the largest pharmaceutical companies, instead occurring synergistically between small companies supported by federal grants and government agencies, such as USAMRIID and USAMRICD, DTRA, and BARDA. The current system is a model of how drug development can occur for an alternative market: the federal government's National Stockpile.

The writing assignments, in which students summarize scientific articles for their peers at a level equivalent to a Scientific American style, could be adapted to any type of article. This kind of assignment has been shown to work well even with students who have not had experience reading scientific articles before. Key to their success, however, is multiple iterations of grading and correction and timely feedback. I also found that having multiple students review the same paper and then reading and commenting upon each other's' reviews is extremely helpful in having them improve. Using an online system in a message board format works best, giving them time to read multiple reviews and respond to questions. It also provides the opportunity for students to become proficient at searching for answers, helping their scientific information literacy development.

The rubric assignments in which students compare different biological and chemical weapons of terror could be adopted into a face-to-face classroom format. One example activity is having students produce ideas for "what makes an effective weapon of terror", compiling these ideas on a whiteboard, and then having the students rank the categories by overall importance. Over subsequent weeks, as the students learn about different agents of terror, scores could be generated for each agent. Students could be challenged to develop scores and justify them using facts that they've found on their own, again developing their informational literacy skills. This activity could be adapted for a traditional course focused on diseases; the categories in the original rubric would be different. They could also be challenged to investigate a novel agent on their own, filling in their scores, and then summarizing in paragraph form the rationale for the scores used.

Online message board-style discussions have been very helpful for this course and might be adopted in a face-to-face setting as an adjunct to in-class discussion. The development of the risk assessment rubric is much easier when done online. Students can add new categories or comment upon existing ones throughout the week, but also refer back to the rubric after the week has been completed. They have access to each other's risk assessments and can adapt ideas from one another in the development of their own rubric. Collaboration is strongly encouraged.

Student preparedness for the course varies widely. It is very helpful if the students have taken upper level Biochemistry, Molecular Biology, Immunology, and Microbiology. Students with such a background develop a greater ability to read and discuss scientific articles. The graduate program in Biosecurity and Biodefense does not have prerequisites in these areas, and therefore some students are at a disadvantage. Because the reports in the course are targeted at a general audience, summarizing articles and their findings, with training and feedback even

students without much background in biology can succeed. As a graduate course, a letter grade of C is considered failing. Approximately one third of the students earn an A in the course.

Acknowledgements

The authors thank Nary Kim for providing samples of his writing for use in this paper. The authors also thank Dr. Lee Pierce for help with original course design. Finally, the authors thank Dr. Rana Khan, director of the UMUC program in Biosecurity and Biodefense for her help with editing the manuscript. The contents and opinions in the work presented here do not necessarily represent those of the United States Coast Guard or the federal government.

Appendix 1: Sample Course Syllabus

Week	Themes	Readings/Assignments
1	**Introduction** Sep 9 - Sep 15	Introduction to the Course. History of biological and chemical weapons. Risk Assessment by the government Who Regulates Bioterrorism? Brief History of Regulation Assignment (Due Sep 15): References and Resources/Plagiarism (post in conference, not assignment folder) Student Introductions
2	**Anthrax** Sep 14 - Sep 22	Introduction to Anthrax Pulmonary Function Review Anthrax Vaccine Anthrax paper review (Due Wednesday, Sep 18th) The first of a track of discussions on risk assessment (RA) starts this week RA: What makes an effective biological or chemical weapon? Term paper topic selection (respond to main topic with your choice of topic as the subject. No duplicates allowed!)
3	**Plague** Sep 21 - Sep 29	Introduction to Plague Plague paper review (Due Wednesday, Sep 25th) Study groups assigned. Get to know your classmates, choose a group leader, and begin preliminary work on data collection for your paper, which is due Nov 3rd.
4	**Tularemia and Cholera** Sep 28 - Oct 6	Introduction to Tularemia and Cholera Homeland Security Presidential Directives RA1: Use your risk assessment knowledge to design a rubric to help compare Tularemia and Cholera (due Oct 2nd in conference and assignment folder)
5	S**mallpox** Oct 5 - Oct 13	Introduction to Smallpox The dark side of Personalized Medicine Smallpox review (due Oct 9th) Continue Group Project work
6	**Hemorrhagic Fever** Oct 12 - Oct 20	Continue working on group projects and term papers Hemorrhagic fever discussion. If you were a terrorist... RA: Test your rubric on hemorrhagic fevers (due Oct 16th)
7	**Toxins** Oct 19 - Oct 27	Introduction to Toxins Paper review assignment on toxins (due Oct 23rd) If you were a terrorist... RA discussion: Compare four toxins using your rubric.

8	**Nerve Agents** Oct 26 - Nov 3	Physiology review of the nervous system Sarin, soman, VX, and many more! **Term paper due Nov 3rd** RA: Apply your rubric to nerve agents and their therapies. (due Oct 30th)
9	**Vesicants** Nov 2 - Nov 10	Introduction to vesicating agents. Paper review on vesicants (Due Nov 6th)
10	**Other Chemical Weapons** Nov 9 - Nov 17	Dirty bombs and nuclear devices Discussion on other chemical weapons **Study Group assignment due Nov 13th** *Discussions this week are worth 2% of your final grade - 1% for chemical weapon discussion and 1% for everything else.*
11	**Epidemiology** Nov 16 - Nov 24	Introduction to Statistics and Epidemiology Epidemiology case study If you were a terrorist... Group Project discussions RA: Agricultural Bioterrorism discussion **Second version of term papers (due Nov 24th)** Post term papers in public forum for others to read and comment upon *Discussions this week are worth 2% of your final grade - 1% for group discussion, 1% for everything else.*
12	**Wrap-up** Nov 23 - Dec 1	Bioethics of Biodefense Research Continue Group Project discussion First response - getting science to people in the field The military and the IRB *Discussion grade is worth 2% this week: 1% for term paper discussions, and 1% for everything else.*

Appendix 2 - Rubric for Writing Assignments

	Excellent	Good	Acceptable	Needs Improvement	Poor	Missing
Summary of the **Findings** of the paper. (1-2 Sentences)	10 pts Summary of the findings concisely states all of the important findings of the article. Contains what was done and what was found.	8 pts Summary of the findings states most of the important findings of the article. Contains what was done and what was found.	6 pts Summary misses one key finding of the article. Contains what was done and what was found.	4 pts Summary misses two key findings of the article. Contains what was done and what was found.	2 pts Summary misses more than two key findings or states only what was done, not what was found.	0 pts No description of findings
Show understanding of how the agent works (2-3 paragraphs)	25 pts Section explains molecular mechanism of the agent and explains the molecular target of the medical countermeasure in adequate detail, preparing the reader for the subsequent paper review.	20 pts As in Excellent, but missing one key molecular mechanism or molecular target of the medical countermeasure.	15 pts As in Excellent, but missing two key molecular mechanisms and/or molecular targets of the medical countermeasure.	10 pts Section is missing multiple explanations of mechanism and does not anticipate what the reader needs to know to understand the subsequent paper review.	5 pts Section is present, but does not cover what is asked for. For example, it may discuss history, pathology, or some other aspect of the agent.	0 pts Shows no understanding of how the agent works
Paper review – explain experiments and significance (2-3 paragraphs)	25 pts Explanation is 2-3 paragraphs and shows mastery of understanding of the experiments and significance of the paper. Explanation includes what was done, what was found, and what it means.	20 pts As in Excellent, but missing one key experiment of significance or is overly focused on an incorrect aspect of the paper.	15 pts As in Excellent, but missing two key experiments of significance or is overly focused on an incorrect aspect of the paper.	10 pts As in Excellent, but missing three key experiments of significance or is overly focused on an incorrect aspect of the paper.	5 pts Explanation is present, but shows a lack of understanding of what was done in the paper.	0 pts Does not describe the experiments and significance
Future Directions – unanswered questions, what can be done in the future? (1 paragraph)	10 pts Explanation is one paragraph and describes at least three strong future directions for possible research.	8 pts Explanation is one paragraph and describes at least two strong future directions for possible research.	6 pts Explanation is one paragraph and describes at least one strong future direction for possible research.	4 pts Explanation includes at least one direction for possible research, which was taken directly from the paper.	2 pts Explanation is present and includes at least one direction for possible research, but this direction is incorrect.	0 pts Future directions are not present in the report
Structure, style and organization	10 pts Structure, style and organization (SSO) are impeccable and consistent throughout.	8 pts SSO is strong with only a few minor errors.	6 pts SSO contains many minor errors or a few major errors.	4 pts SSO is inconsistent with many major errors.	2 pts SSO is quite weak with many errors and little support for conventions.	0 pts SSO is completely unorganized and/or style is completely inconsistence
Spelling and Grammar	10 pts Spelling and grammar are impeccable and consistent throughout.	8 pts Spelling and grammar are strong with only a few minor errors.	6 pts Spelling and grammar contains many minor errors or a few major errors.	4 pts Spelling and grammar are inconsistent with many major errors.	2 pts Spelling and grammar contain many errors and little support for conventions.	0 pts Spelling and grammar are unacceptable.
References	10 pts At least three references are present and are of good quality, APA format is used.	8 pts Three references are present, APA format is not followed.	6 pts Less than three references are present or three references are present but are not of good quality.	4 pts Less than three references are present and APA format is not followed.	2 pts Although references are present, they are not of good quality and the formatting is inconsistent.	0 pts References are not present.

Appendix 3 - Student Rubric Assignment 2 - Example

Characteristic	0%	25%	50%	75%	100%	**Point Value**	**Tularemia**	**Cholera**	**Yellow Fever**	**Ebola**
Availability of agent	Unavailable	Low	Moderate	High	Very High	4	4	2	2	1
Death if untreated	0-20%	21-40%	41-60%	61-80%	81-100%	10	8	10	4	10
Disease (severity of symptoms)	Minor	Moderate	High	Debilitating	Lethal	10	8	6	4	10
Easy Dissemination	Not Transmissible	Difficult	Moderate	Easy	Very easy and can co	10	10	6	5	10
Ease of Production	Very Difficult	Diffifcult	Moderate	Easy	Available in excess	6	4	1	3	2
Infectious Dose	Non-Lethal	High	Moderate	Low	Very Low/Unknown	8	8	1	8	8
Incubation Period	Not Applicable	1 month or more	2-4 weeks	5-14 days	0-5 days	4	3	4	4	3
Persistence of Organism	Cannot survive outs	Low survival outs	Survival possibl	Can Survive outside	Can survive outside o	6	4	1	2	2
Person to Person Transmission	Not Transmissible	Fluids	Close Contact	Contact	Indirect	8	0	2	0	8
Public Perception/Social Disruption	Little to none	Minor	Moderate	High	Severe	8	4	8	2	7
Special Preparation (Preparedness Response)	None required	Easy	Moderate	Difficult	Extreme/Unknown	8	8	3	4	8
Medical Treatment (Countermeasures)	Readily Available	Available with mi	Mostly Availabl	Limited availabity a	Little to no availabilit	10	5	2	2	8
Vaccine Status	Readily Available	Available with mi	Mostly Availabl	Limited availabity a	Little to no availabilit	10	10	6	2	10
					Total Points	102	76	52	42	87

Appendix 4 - Student Rubric Assignment 3 - Example

Characteristic	0%	25%	50%	75%	100%	Point Value	Tularemia	Cholera	Yellow Fever	Ebola	Sarin (GB)	Tabun (GA)
Availability of agent	Unavailable	Low	Moderate	High	Very High	4	4	2	2	1	3	4
Death if untreated	0-20%	21-40%	41-60%	61-80%	81-100%	10	8	10	4	10	N/A	N/A
Disease (severity of symptoms)	Minor	Moderate	High	Debilitating	Lethal	10	8	6	4	10	10	10
Easy Dissemination	Not Transmissible	Difficult	Moderate	Easy	Very easy and can cover large area	10	10	6	5	10	10	10
Ease of Production	Very Difficult	Difficult	Moderate	Easy	Available in excess	6	4	1	3	2	4	6
Infectious Dose	Non-Lethal	High	Moderate	Low	Very Low/Unknown	8	8	1	8	8	8	7
Incubation Period	Not Applicable	1 month or more	2-4 weeks	5-14 days	0-5 days	4	3	4	4	3	4	4
Persistence of Organism	Cannot survive outside of host	Low survival outside of host	Survival possible outside of host in specific conditions	Can Survive outside for limited time of host in most conditions	Can survive outside of host regardless of conditions for a significant amount of time	6	4	1	2	2	1	4
Person to Person Transmission	Not Transmissible	Fluids	Close Contact	Contact	Indirect	8	0	2	0	8	3	5
Public Perception/Social Disruption	Little to none	Minor	Moderate	High	Severe	8	4	8	2	7	6	3
Special Preparation (Preparedness Response)	None required	Easy	Moderate	Difficult	Extreme/Unknown	8	8	3	4	8	8	8
Medical Treatment (Countermeasures)	Readily Available	Available with minor to moderate cost	Mostly Available with moderate cost	Limited availabity at high cost	Little to no availability	10	5	2	2	8	8	8
Vaccine Status	Readily Available	Available with minor to moderate cost	Mostly Available with moderate cost	Limited availabity at high cost	Little to no availability	10	10	6	2	10	10	10
Period of Time from Exposure to Death	Survives	30 days or more	14-30 days	5-14 days	0-5 days	10	N/A	N/A	N/A	N/A	10	10
Color/Odor	Colored/Smells	N/A	N/A	N/A	Colorless/Oderless	4	N/A	N/A	N/A	N/A	4	1
					Total Points		76	52	42	87	89	90

Tabun (GA) is an extremely toxic man-made chemical substance (CDC, 2013). It is the easiest to manufacture and can be disseminated through many routes, such as aerosol, contamination of water/food sources, and can be absorbed through the skin or eyes (CDC, 2013). Depending on the amount of tabun absorbed in the body, symptoms can occur within second to hours after exposure (CDC, 2013). The primary mechanism is the inhibition of acetylcholinesterase enzyme by phosphorylation of the catalytic serine (Carletti et al., 2013). Since the enzyme is critical in the function of glands and muscles, tabun prevents the proper operation, causing symptoms such as drooling, excessive sweating, nausea, convulsions, and much more, it can even lead to death (Martin & Lobert, 2009). There are antidotes available; however they are most effective if given immediately after exposure (CDC, 2013). Removing chemicals from the body right after exposure is also critical and treatment would require supportive medical care (CDC, 2013).

Sarin (GB) is a man-made extremely volatile chemical toxin that is easy to manufacture and can be spread through various routes including inhalational, ingestion, and sometimes through skin contact (CDC, 2013). The mechanism of action is through the inhibition of acetylcholinesterase causing the muscle and gland functions to continually keep going, which can tire them out and cause blurred vision, vomiting, airway obstruction, convulsions, and much more, it can also lead to death (Abu-Qare & Donia, 2002). The symptoms can occur within seconds or hours depending on the amount of sarin exposure (CDC, 2013). Treatments soon after exposure consist of antidotes, decontamination, and supportive medical care in a hospital environment (CDC, 2013).

Nerve agents can be easily produced by chemical techniques, inexpensive to manufacture, and readily available (OPCW, n.d.). They are also the most potent and quickest acting chemical weapon, making nerve agents a prime choice for use in warfare (CDC, 2013). Both nerve agents are organophosohourous compounds and are categorized in the "G" agents, which tend to be non-persistent volatile liquids (OPCW, n.d). As seen above, they are very similar in how they are disseminated, symptoms, and their mechanism of action. Although sarin and tabun are both immediate health threats, sarin is short-lived due its high volatility; it evaporates quickly, while tabun which is less volatile can persist on exposed surfaces for a longer period of time (CDC, 2013). Tabun is also more effective than sarin through penetration of skin route because it is readily soluble in organic solvents (Martin & Lobert, 2009). However, tabun has a fruity odor, so the smell can be a sign for tabun exposure while sarin is odorless, so there is no indicator for sarin exposure (CDC, 2013). Also, tabun would be more likely used in developing countries because some consider it to be outdated (OPCW, n.d). Production and stockpiling of both nerve agents is prohibited (OPCW, n.d). These are very similar nerve agents, and although sarin is more deadly, tabun may have a slight risk over sarin due to its increased persistence, its variable effective routes of exposure, and the ease of production, even developing countries can use this as a weapon.

Some of the categories were hard to fill in because it all depended on the dosage of the nerve agents, for example, death if untreated, if it is a high amount of nerve agent then it can occur in minutes, and if it's a moderate amount, most people completely recover from it, so I added period of time from exposure to death on it. Also, I added color and odor because that might be important for indication or signs of nerve agent exposure. Other categories I thought were important were solubility and volatility, but that seemed to fit in other ones such as persistence, infectious dose, easy dissemination and such.

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Appendix 5 – Term paper rubric and revised term paper rubric

The term paper is the culmination of everything you have learned in the class, most importantly **risk assessment and countermeasure options** on a potential chemical, biological, or radiation weapon that might be used in a terroristic manner.

There are two major agencies in the United States that deal directly with the development of medical countermeasures: the Defense Threat Reduction Agency (DTRA) and the Biomedical Advanced Research and Development Authority (BARDA). Their main job is to provide funding to academic, commercial, and government research laboratories and clinics to support the development of these countermeasures. DTRA and BARDA rely on administrators and ad hoc reviewers to determine the merit of various proposals for research. They also come up with a secret list of important chemical agents and use that list to help decide which agents get funded. Obviously, no single person can really do a comprehensive literature review on all of the potential agents out there. This is where you come in.

As a graduate of the Biotechnology program at UMUC, you've been hired as an ad hoc reviewer by DTRA and BARDA to investigate the current risk and state of research for countermeasures for your assigned agent. Your report will be used to determine the relative importance of your agent versus all of the other potential agents. To aid in this determination, you will include a **risk assessment** (the one that you did in class, with your term paper agent added to it) and provide rationale in paragraph form for the scores given for each attribute on the risk assessment. You will include scores for anthrax and other agents that you provided scores for in the class for comparison purposes (but no write-up on those scores). This will enable your boss at those agencies (me) to have a good idea of the relative importance of that agent. Do not include the numerical scores in the paragraphs of the paper.

The other important contribution that DTRA and BARDA expect is a report on the state of **countermeasures** for your agent. Countermeasures can be anything that protects against the agent, including many things we covered in class, such as vaccines, antivirals (if you are dealing with a virus), antibiotics (if you are dealing with a bacteria or fungus), small molecule drugs, inhibitors, and anything else.

- What are the current available countermeasures (not the focus of your paper, but necessary)
- What are the countermeasures in development?

Start with a short analysis of the current countermeasures available and where they fail - do they require too many boosters? Are they short-lived? Can they be given to immunocompromised people? Etc. To search for countermeasures for your agent, you might start by trying to find a review article for your drug, use the textbook, and Pubmed. Since BARDA and DTRA are concerned with the CURRENT state of research, you will be sure to include the most recent publications on these topics, which is where Pubmed comes in. Of course, DTRA and BARDA aren't interested in citations from newspapers, magazines, or trade websites, so you won't include too many of these in your citation list. Wikipedia citations would probably get you fired, so you won't even think about using that as a source.

These agencies will then expect a determination as to which of these countermeasures in development represents the best (ie, most fundable) option in terms of delivering a countermeasure to the American people. You will perform a critical analysis of the various countermeasures, and using your scientific expertise, provide a strong recommendation as to which countermeasure you think should be focused on. You can expect that any given reader will want to find all of the information for the paper in the abstract, including your recommendation on countermeasures and determination of risk, so you'll be sure to include that.

Ultimately, the goal of BARDA is to develop a stockpile of countermeasures for potential weapons of terror. Because your supervisor doesn't have enough time to do his own research on your agent, you should describe the agent in enough detail so that he understands how the countermeasures work. (Rely on your Writing Assignment skills from earlier in the semester to help.)

You can expect that your supervisor will not be happy with your first draft, and will have questions that result from his reading of your report, so you can expect to have to produce a second version (i.e., resubmit your term paper) to address these issues. Your supervisor will want you to address ALL of his concerns (this is why we do the revised term paper.)

To summarize, here's what you should include:

Your paper may be from 6000-8000 words or so, not including references, tables, or figures.

Post your assignment in your assignment folder on the due date. Post in Microsoft Word format. Also upload your assignment to Turnitin prior to the deadline.

Use the following headings in your report:

- Table of contents
- Abstract, summarizing your position statement about which countermeasures to move forward with and how much of a risk this biological or chemical weapon is.
- Molecular mechanism of action of the agent - enough to understand how the countermeasures you describe work.
- History, pathogenesis, and symptoms, if you want to add these. However, these are NOT a critical part of the term paper.
- Brief History of weaponization of this agent, if any, and weaponization potential.
- Countermeasures: include vaccines (if applicable), drugs, and therapies. Do NOT include information on environmental cleanup, first response, or personal protective equipment such as respirators or gear - these are not medical countermeasures. Include a critical analysis to find the best countermeasure approach.
- Risk assessment: include normal geographic area, reservoirs, ability to spread, and anything else we covered in class that can be used to characterize the relative risk of this agent. Consider the CDC scale as a guidance as well. Do consider the availability and effectiveness of countermeasures when performing your assessment. A copy of your risk assessment rubric should be entered into your report in table form, including comparisons

with the other agents you rated in class. A description should follow that table describing your rationale behind each of the scores given for your agent.
- Conclusion
- References in APA format. You should have enough primary citations to convince me that you have actively searched the literature for good sources. Your sources should be as current as possible.

Description	**Percentage**
Molecular mechanism – convince me that you understand how the agent works	25%
Risk assessment	20%
Countermeasure evaluation	25%
Structure, style, and organization	10%
Spelling and grammar (feel free to have the writing center or colleagues read your paper for these errors)	10%
References - proper citation format and a healthy collection of quality peer reviewed publications	10%

Submission checklist

Did you submit your paper to Turnitin? This is required, or the paper is considered late.

Did you complete all of the items listed above?

5 points are automatically deducted from your assignment if you use Wikipedia as a reference (and you are fired).

Does your paper meet the word limit? 5 points deducted for each thousand words you are under this limit.

Some ideas for topics: influenza, swine flu, avian influenza, ebola, salmonella, white phosphorous, lewisite, chlorine, chloropicrin, ricin, dioxin, saxitoxin, other toxins, cholera, tularemia, botulinum, tetrodotoxin, Brucella suis, Coxiella burnetti, HIV, yellow fever. You may choose something not on this list with approval.

Term paper revision details

In each of your papers I will have used the rubric described for the original assignment to determine which areas you have done well in, and which areas you were deficient in. I will also post specific ‘assignments’ based on these deficiencies for you to complete for your second version. The second paper is graded **solely** on your ability to include these changes and address my concerns - in other words, the grade you got on the first paper is irrelevant - I am now grading your ability to respond to criticism.

There is no page or word limit for the revision. I do not want you to cut out sections unless I specifically ask you to do so. This will allow you to add the necessary work without having to edit and remove other information from your paper, and therefore should be easier on you.

As you complete this revision, give me details using the comment ability in word to show me where you modified the paper, including which sections were added. Leave my original comments in place so I can easily see where you made changes. This is important! Submit this version to the assignment folder.

Then, save it as a second file, and remove all grading and comment information. This is the version you should post in the Class Discussion area. This second version is also the version you should submit to turnitin.com.

Grading rubric:

Description	Percentage
Incorporation of changes I've asked for into the second version	70%
Leaving on the 'Track Changes' option so that I can see what you've changed.	20%
Annotate major changes you've made where you think I would want to see them. Use the comment function to tell me that you added 6 papers, or changed a major area, etc.	10%

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