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**ENHANCING TRANSPARENCY IN
BIOLOGICAL AND TOXIN RESEARCH:
MONITORING RESEARCH ACTIVITIES
USING THE INTERNET**

VOLUME 1



SEPTEMBER 1996

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VOLUME 1



Dept. of Foreign Affairs
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S U M M A R Y

The Internet has emerged as a global medium for information exchange. Previous studies related to enhancing transparency of biological research used the method of collateral analysis of scientific publications. Drawing on commercial on-line services, these studies documented the types of research carried on with certain materials in specific countries. This study examines the potential contribution of the Internet for enhancing transparency of information related to biological pathogens and toxins. The objectives of the study are to develop a map of biological and toxin resources on the Internet, and to assess this information using three case studies. These case studies include:

- cell collections of microorganisms on the Internet;
- research on Bacillus anthracis (the bacterium which causes anthrax);
- research on the Venezuelan equine encephalomyelitis virus.

The following Internet sites create indices of information. They were used extensively and found to be the most useful for finding information:

- AltaVista (located at <http://www.altavista.com>);
- Lycos (located at <http://www.lycos.com>); and,
- Yahoo (located at <http://www.yahoo.com>).

As well, other search tools were tested such as WebCrawler, InfoSeek and Excite. These were found not to be as useful for biological and toxin information. Approximately half of the time connected to the Internet made use of the WebCompass Resource Discovery Agent (registered trademark of

Quarterdeck Software). This is an intelligent software agent which searches the Internet on the basis of key words and creates databases of relevant information. The various Internet sites retrieved by this method are provided in annexes to this report.

In order to examine the extent of biological and toxin information resources on the Internet, over 120 hours were spent connected to the Internet searching by key-words and downloading information during April and May 1996. Over 3,000 files containing more than 35 megabytes of information were downloaded from over 1000 Internet sites related to biological and toxin information.

The following sites on the Internet were the largest organized centres of biological and toxin information with links to hundreds of other Internet sites:

- The World-Wide Web Virtual Library Biosciences (the searchable index is located at <http://golgi.harvard.edu/htbin/biopages>);
- The World-Wide Web Virtual Library Microbiology and Virology (located at <http://golgi.harvard.edu/biopages/micro.html>);
- The World-Wide Web Virtual Library Epidemiology (located at <http://www.epibiostat.ucsf.edu/epidem/epidem.html>);
- The World-Wide Web Virtual Library Biotechnology (located at <http://www.cato.com/interweb/cato/biotech/>; and,
- Martindale's Bioscience Guide (located at <http://www-sci.lib.uci.edu/~martindale/MedicalPath.html>).

As well, this study sought to identify culture collections which make bacteria, fungi and viruses available for research and commercial purposes. The following are the major repositories:

- American Type Culture Collection (located at <http://www.atcc.org/>);
- Microbial Strain Data Network (MSDN located at <http://www.bdt.org.br/msdn/msdn.html>);
- All Russian Collection of Microorganisms (VKM located at <http://www.stack.serpukhov.su:70/1s/db/vkm>);
- Microbial Information Network of China (located at <http://sun.im.ac.cn/>); and,
- WFCC World Data Center for Microorganisms RIKEN, Japan (located at <http://www.wdcm.riken.go.jp/wdcm/STRAIN.html>).

More importantly, a total of 484 separate centres around the world are listed on the Internet that make microorganisms available for free, exchange or for a fee. Of these centres, over 30 have established their own Internet sites. There are 286 culture collections that provide various bacteria, 244 that provide fungi and 38 that provide virus samples. For example, 56 culture collections provide samples of Bacillus anthracis. These culture collections are listed in the annexes to this report. Many fewer collections make viruses available. In the case of the Venezuelan equine encephalomyelitis virus, only two collections provide samples of this virus.

This study also examined the sources of information and sites of research related to the two microorganisms, B. anthracis (the causative bacterium of the disease anthrax) and the Venezuelan equine encephalomyelitis (VEE) virus

which causes Venezuelan equine encephalomyelitis. For B. anthracis, 49 Internet sites are listed in the report which detail research, disease outbreaks and medical diagnosis. For the VEE virus, 38 sites are listed in the report.

Access to the Internet provides an anonymous, universally-accessible system for gathering biological and toxin information. At the present time, the Internet is well suited for specific inquiries such as the location of particular cultures of bacteria. While there is a tremendous amount of information related to biological research, the quality and reliability of that information varies greatly. The accuracy of the information that is available must be assessed carefully in each case. Since there is no centralized control, the onus is on the user of the information to verify its accuracy.

The Internet provides much broader categories of information. The accessibility of this information has greatly increased. Previously, this scientific information was available in journals and on-line databases. Both required a certain level of scientific expertise to access and their use could be monitored. This has changed with the Internet. Through the Internet, access to this information is essentially anonymous. The threshold for acquiring information about biological pathogens and toxins has been lowered by its accessibility on the Internet.

There are some important limitations that this study identifies. Since the development of the World Wide Web hypertext system is recent, only current information is available (that is, from 1995 to 1996). If, for example, research is needed from 1980, it is unlikely that it will be directly accessible on the Internet. However, this is changing since more information sources including scientific databases are becoming accessible through the Internet.

GLOSSARY

These definitions are adapted in part from the Internet glossary located at <http://wfn-ship.princeton.edu/>

FTP File Transfer Protocol allows a user on one computer to transfer files to and from another computer over a TCP/IP network.

HTML Hypertext Markup Language is a hypertext document format used by the World-Wide Web. Built on top of SGML. "Tags" are embedded in the text. A tag consists of a "<", a "directive", zero or more parameters and a ">". Matched pairs of directives, like "<title>" and "</title>" are used to delimit text which is to appear in a special place or style. HTML over the WWW has made it possible for any connected computer, with the suitable software, to share information.

HTTP Hypertext Transfer Protocol is the client-server TCP/IP protocol used on the World-Wide Web for the exchange of HTML documents.

Hypertext A term coined by Ted Nelson around 1965 for a collection of documents (or "nodes") containing cross-references or "links" which, with the aid of an interactive browser program, allow the reader to move easily from one document to another. The WWW is the hypertext-based client server system based within the Internet.

Internet (Note: capital "I"). The Internet is the largest computer network accessible to the public in the world. It is a three level hierarchy composed of backbone networks, mid-level networks, and stub networks. These include

commercial (.com or .co), university (.ac or .edu) and other research networks (.org, .net) and military (.mil) networks and span many different physical networks around the world with various protocols including the Internet Protocol.

There are several bodies associated with the running of the Internet, including the Internet Architecture Board, the Internet Assigned Numbers Authority, the Internet Engineering and Planning Group, Internet Engineering Steering Group and the Internet Society.

Network Hardware and software data communication systems linked together are called networks. They are often also classified according to their geographical extent: local area network (LAN), metropolitan area network (MAN), wide area network (WAN) and also according to the protocols used.

Protocol A set of formal rules describing how to transmit data, especially across a network. Low level protocols define the electrical and physical standards to be observed, bit- and byte-ordering and the transmission and error detection and correction of the bit stream. High level protocols deal with the data formatting, including the syntax of messages, character sets, and sequencing of messages.

Server A computer which provides some service for other computers connected to it via a network.

SGML Standard Generalized Markup Language is a generic markup language for representing documents. SGML aims to separate information from its presentation and thus facilitate different presentations of the same information.

TCP/IP Transmission Control Protocol/Internet Protocol is the most common protocol used on Ethernet and the Internet. It was developed by DARPA.

TCP is built on top of Internet Protocol (IP) and is nearly always seen in the combination TCP/IP (TCP over IP). It adds reliable communication, flow-control, multiplexing and connection-oriented communication. It provides full-duplex, process-to-process connections.

URI Uniform Resource Locator is a standard for specifying an object on the Internet, such as a file or newsgroup. URLs are used extensively on the World-Wide Web. They are used in HTML documents to specify the target of a hyperlink.

Here are some example URLs:

`ftp://wuarchive.wustl.edu/mirrors/msdos/graphics/gifkit.zip`

`http://www.w3.org/default.html`

`news:alt.hypertext`

`telnet://dra.com`

`mailto:dbh@doc.ic.ac.uk`

`http://www.w3.org/default.html#Introduction`

The part before the first colon specifies the access scheme or protocol. The part after the colon is interpreted according to the access scheme. In general, two slashes after the colon indicate a hostname (host:port is also valid). Schemes include: ftp and http (World-Wide Web).

Usenet A collection of discussion groups on the Internet where people may post messages on selected topics.

Web browsers NCSA Mosaic, Netscape and Microsoft Internet Explorer are examples of commonly used software programs used to access the WWW and other resources on the Internet.

WWW World-Wide Web (WWW, W3, The Web) An Internet client-server hypertext distributed information retrieval system which originated from the CERN High-Energy Physics laboratories in Geneva, Switzerland.

The WWW has been the fastest growing part of the Internet since its public introduction in 1991. In the early 1990s, the developers at CERN spread word of the Web's capabilities to scientific audiences worldwide..

On the WWW everything (documents, menus, indices) is represented to the user as a hypertext object in HTML format. Hypertext links refer to other documents by their URLs. These can refer to local or remote resources accessible via FTP, or news, as well as those available via the http protocol used to transfer hypertext documents.

The client program (known as a browser), e.g. Mosaic, Netscape, runs on the user's computer and provides two basic navigation operations: to follow a link or to send a query to a server. A variety of client and server software is freely available.

Chapter 1

INTRODUCTION

The parties to the Biological and Toxin Weapons Convention (BTWC) have come to recognize that transparency or openness in research related to biological and toxin agents can be useful in maintaining the prohibitions against biological weapons and warfare. Towards this end, previous studies used the method of collateral analysis of scientific publications drawing on commercial on-line services, to document the types of research carried on with certain materials in specific countries. Three such reports were submitted to the BTWC/VEREX study conducted in 1992-93. It is worth repeating that these reports did not try to suggest that these activities were suspicious or in any way related to proscribed activities. Their purpose was to gather and present in a systematic way the information that is freely available, with a view to assessing its utility in developing a "snapshot" of biotechnological development in each of the countries.

Since 1993, there has been a dramatic growth in the information resources that comprise the Internet. Even seasoned computer watchers were surprised by the extent of the growth and the accessibility of the information resources. This is especially true for the information resources of the World Wide Web (WWW). The WWW is an Internet service based on hypertext technology. There is no centralized control over the Internet. There is a major difference between looking at finished scientific publications and the types of information available on the Internet. The information on the Internet can be more

fragmentary; such as scientific speculation, experiments that did not work, and other technical information. This includes information that rarely gets into the finished product. If we can apply the 'iceberg' metaphor to information (i.e. only ten per cent is visible), it is possible that, with these new technologies of information gathering, significantly more information can be obtained. To pursue the iceberg metaphor, it may also be possible to see below the waterline. Again, the purpose is to assess whether our understanding of information availability might also help in developing a clearer understanding of technological development in various countries.

This study proposes to examine how these new information sources can enhance the transparency of information related to biological pathogens and toxins. It should be pointed out that in examining the research and information available on the Internet, these are likely to be perfectly legitimate research and development activities. It is not the aim of the study to suggest that these activities are not in accord with the provisions of the BTWC. However, it is recognized that knowledge gained from research can be used for detrimental purposes.

At the present time the Internet is the broadest-based computer information system in existence. It will give unprecedented access to information and, the positive aspects of this development are numerous. Some of these developments could also impact on the arms control landscape, both positively and negatively.

Objectives of this Study

1. Develop a map or guide to the biological and toxin resources on the WWW and Internet including indices of research, biological discussion groups, biological how-to guides and company advertisements. Given the diversity of

sources and sheer amount of information, it is not possible, within the scope of this study, to refer to every individual web site related to biological research. However, many are described in the text.

2. Assess this information using three case studies:

- Cell collections listed on the Internet.
- Research on Bacillus anthracis (the causative bacterium of anthrax) available on the Internet.
- Research on the Venezuelan equine encephalomyelitis virus available on the Internet.

3. Compare the type and quality of information available on the Internet to that reviewed in previous studies mentioned above.

4. Identify relevant conclusions concerning the utility of using the Internet to monitor biological and toxin research.

Chapter 2

INTERNET RESOURCES AND METHODOLOGY

The advent of the WWW hypertext system on the Internet has caused tremendous growth and interest in the global system of networked computers. Having its origin in the US Department of Defense ARPANET, the number of host computers containing information on the Internet has grown from 235 in May 1982 to over five million computers that are networked together in 1996. Estimates suggest that over thirty million people have access and use the Internet. The growth of the WWW has been especially dramatic. Therefore, any attempt to make a comprehensive survey of biological resources available will need several different approaches.

This study used a three-part approach. First, this study surveyed the central subject-orientated guide to the Internet, called the WWW Virtual Library. Second, the study used the search engines which contain regularly up-dated indexes of the WWW. Third, a software agent, called WebCompass, was used to automatically search the Internet.

Search engines or programs for the Internet and WWW include Open Text, Alta Vista, WebCrawler, Yahoo, Deja News and Lycos. Search engines can be used with the appropriate key words to search sites on the WWW or specific documents. What follows is a brief description of one of the largest indexes of the Internet, the Lycos Catalog.

Lycos

The Lycos catalog (at the WWW at <http://lycos.com>) has been called 'the Catalog of the Internet'. As of January 1996, the following resources can be searched and accessed by key word searches:

- 4,385,944 web documents with extended abstracts;
- 6,743,409 binary objects (sounds, images, programs, archives);
- 6,924,411 abstracts of other web documents; and,
- 18,053,764 unique URLs (Uniform Resources Locators specify WWW sites), and by May 1996 Lycos stated that over 30,000,000 URLs are indexed.

The Lycos catalog has indexed 29,374,956,768 bytes of web documents (that is 2,093,191,313 words). As well there are 56,249,191 links between documents. By using key words, the Lycos catalog and other indexes listed below were used to create a map of sites related to biological and toxin research.

AltaVista	http://altavista.digital.com
Excite	http://www.excite.com
Lycos	http://www.lycos.com
OpenText	http://www.opentext.com:8080/omw/f-omw.html
Webcrawler	http://www.webcrawler.com/
What's New	http://newtoo.manifest.com/search.html
Yahoo	http://www.yahoo.com

AltaVista

AltaVista started service on the Internet in Decemeber 1995. It provides access to one of the largest Web indexes: 30 million pages found on 225,000

servers, and 3 million articles from 14,000 Usenet news groups. It is accessed over 10 million times daily. There is no charge to use the service.

The following table shows a sample search comparing the two top Internet search engines; AltaVista and Lycos. The sample search terms are the words toxin, neurotoxin, mycotoxin and aflatoxin (singular or plural). In each case, AltaVista has ten to twenty times as many hits as Lycos.

<u>Search term</u>	<u>AltaVista</u>	<u>Lycos</u>
toxin(s)	47,890	2148
neurotoxin(s)	2935	386
mycotoxin(s)	3184	250
aflatoxin(s)	4016	247

WebCompass Resource Discovery Agent

WebCompass is a World Wide Web and Internet information access and discovery tool that can build and update custom indexes of the Internet automatically. Using multiple search resources simultaneously provides comprehensive coverage of the Internet.

Studies have shown that no single Internet search resource can find all the relevant documents. Simultaneous use of many Web search resources is the only way to guarantee comprehensive searching. The use of WebCompass lets one simultaneously use all of the search resources such as AltaVista, Yahoo, and Lycos, that are now available on the Web..

In order to examine the extent of biological and toxin information resources on the Internet, over 120 hours were spent connected to the Internet searching by key-words and downloading information during April and May 1996. Over 3,000 files containing more than 35 megabytes of information were downloaded from over 1000 Internet sites related to biological and toxin information.

Chapter 3

BIOLOGICAL AND TOXIN INTERNET RESOURCES

The following sections give overviews of the Internet resources related to bioscience research. The WWW Virtual Library is the starting point for examining biological and toxin resources on the Internet. It is located at [http://www.w3.org/hypertext /DataSources/bySubject/](http://www.w3.org/hypertext/DataSources/bySubject/). There are separate sections on Biosciences, Biotechnology, Microbiology and Virology.

Each of the Web Virtual Library Section home pages is a hub, or a hyperlinked card catalog, from which one can find information pertinent to that Section. Many of the Sections have intentional (or accidental) redundancies so that pertinent information is not missed.

It is useful to begin a search using the Section's list of URLs. Many of the Sections will also link with redundant Sections, or with search engines. Annex A explains the form of the information in the subsequent annexes.

The World-Wide Web Virtual Library: Biosciences

This Virtual Library site contains an index of bioscience resources available on the Internet. Information is categorized first by provider followed by specific subject references. Annex B lists the Internet sites related to bioscience research. It is located at <http://golgi.harvard.edu/htbin/biopages.html>.

The Biosciences Virtual Library contains an updated listing of laboratories that have WWW home pages on the Internet which describes their research.

Annex C lists the WebCompass Resource Discovery Agent-generated database of bioscience Internet sites. There are 156 sites listed and of these 122 are summarized.

The World-Wide Web Virtual Library: Biotechnology

The World Wide Web Virtual Library's biotechnology page lists links to Web, FTP and gopher sites containing biotechnology resources. This site covers biotechnology, pharmaceutical development, genetic engineering, medical device development, and related fields such as pharmacology and toxicology. It differs from Biosciences in that Biotechnology places more emphasis on product development and the delivery of products and services.

It is located at <http://www.cato.com/interweb/cato/biotech/>.

Annex D lists the Internet sites related to biotechnology. Annex E lists the WebCompass Resource Discovery Agent-generated database of bioscience Internet sites. There are 538 sites listed and of these 422 are summarized.

**The World-Wide Web Virtual Library: Microbiology and Virology
(Biosciences)**

The World Wide Web Virtual Library's microbiology and virology page has lists of protocols and databases. It is provided in a format geared toward academic researchers.

It is located at <http://golgi.harvard.edu/biopages/micro.html>. Annex F lists the microbiology and virology Internet sites. Annex G and Annex H list the microbiology and virology sites generated from WebCompass.

Virtual Library: Bioscience Journals, Conferences and Current Awareness Service

The World-Wide Web Virtual Library's home page on Bioscience Journals, Conferences and Current Awareness Services lists bioscience Web sites, biology Internet resources, electronic news, biologists' addresses and links to search engines for bioscience information.

Its address is <http://golgi.harvard.edu/journals.html>.

The World-Wide Web Virtual Library: Epidemiology

The Epidemiology Page is maintained by the Department of Epidemiology and Biostatistics at the University of California, San Francisco. It has links to a wide variety of medical and bioscience resources, including governmental and academic. It is located at <http://chanane.ucsf.edu/epidem/epidem.html>. Annex I lists the Internet sites related to epidemiology.

The World-Wide Web Virtual Library: Pharmacy

The World-Wide Web Virtual Library: Pharmacy is located at <http://www.cpb.uokhsc.edu/pharmacy/pharmint.html>.

Annex J lists toxin and neurotoxin research sites. Annex K lists the WebCompass derived sites.

Martindales Bioscience Guide

It is located at <http://www-sci.lib.uci.edu/~martindale/HSGuide.html>. This site includes on-line courses in bacteriology and virology as well laboratory guidelines. It has links to over 500 other Internet sites.

CHAPTER 4

CULTURE COLLECTIONS ON THE INTERNET

The following lists all Internet sites where animal and microbial strains can be obtained for research and commercial purposes.

ATCC: American Type Culture Collection

The American Type Culture Collection (<http://www.atcc.org/>) is a private, non-profit organization located in Rockville, Maryland. Presently the following selections are searchable: cell cultures (3,000 lines); bacteria and bacteriophages (15,000 strains); protozoa and algae (1,200); animal and plant viruses (2,500); and recombinant material. Many of the media formulations for bacterial growth are also available.

Microbial Strain Data Network (MSDN)

MSDN (<http://www.bdt.org.br/msdn/msdn.html>) and Base de Dados Tropical (Brazil) provide access to numerous smaller collections, including:

- AVIS Animal Virus Information System;
- Brazilian Catalogues (available in Portuguese and English);
- CCALA Czech Algae and Cyanobacteria;
- CCM Czech Bacteria;
- DSM Deutsche Sammlung von Mikroorganismen;
- IBSO Siberian Luminous Bacteria;

- KMMGU Russia Bacteria;
- IMI International Mycological Institute Fungi;
- IPPAS Russia Algae;
- MSU Russia Yeasts;
- NCYC UK National Collection Yeasts;
- LEBIN Russia Basidiomycetes;
- RIAM Russia Fungi;
- Slovenia Filamentous Fungi;
- VKM Russia of Bacteria, Fungi and Yeasts;
- VKM Russia Genetically Modified Organisms; and,
- VKPM Russia of Industrial Organisms (Bacteria, Fungi, Yeasts).

ARS Culture Collection (Agricultural Research Service, USDA)

This repository, also known as the NRRL Culture Collection, is a major source of microbial strains. It is located in Peoria, Illinois, USA, and maintains about 80,000 strains (URL <http://www.mpr.ncaur.gov/arsmgr.html>).

All of their collections will soon be available over the Internet. At the present, however, only one catalog is available. This is the Actinomycetales Culture Collection (URL <http://www.mpr.ncaur.gov/src/actino.html>).

WDC: World Data Center on Microorganism Database

The World Directory of Culture Collections is maintained by the World Data Center for Collection of Microorganisms (WDCM). The WDCM was originally located in Australia and is now based at RIKEN (Institute of Physical and

Chemical Research), Saitama, Japan. The World Directory is a catalogue of 484 culture collections from over 55 countries. It does not collect or provide cultures; it describes the culture collections and lists the materials that they provide. Annex L lists the culture collections broken down in the categories for viral, bacterial and fungal specimens. It is located at <http://www.wdcm.riken.go.jp/wdcm/STRAIN.html>.

Centraalbureau voor Schimmelcultures (CBS)

The CBS was established in 1905 and is presently a scientific institute of the Royal Netherlands Academy of Arts and Sciences. Cultures from the CBS are available to both commercial and non-profit organizations.

The CBS (<http://www.cbs.knaw.nl/www/CBSHOME.HTML>) contains a vast collection of:

- Filamentous fungi (28,000 strains from CBS);
- Yeasts (over 4,500 strains); and
- Bacteria (8,000 strains from various organizations in the Netherlands).

Culture Collection of Algae and Protozoa (CCAP)

The CCAP currently maintains approximately 2,000 strains of algae and protozoa and supplies these cultures to the research community and industry. This is a very useful web site. For example, the instructions for preparing dozens of culture media are available. The collection was first established at the German University in Prague and is now located in the United Kingdom. It is located at <http://wiua.nwi.ac.uk/ccap/ccaphome.html>.

**DSM: Deutsche Sammlung von Mikroorganismen und Zellkulturen
(German Collection of Microorganisms and Cell Cultures)**

This Internet site has a searchable index of the DSM collections. Further information about DSM is available via FTP. It is located at <ftp://ftp.gbf-braunschweig.de/pub/DSM/plvirdos.exe>.

E. coli Genetic Stock Center (CGSC)

The E. coli Genetic Stock Center (CGSC) at Yale includes information about several thousand strains, mutations, genes, and references. Access is also provided via direct telnet to <cgsc.biology.yale.edu>.

Fresh Water Cultured Algae Collection

Several hundred fresh water algae cultures are available from Loras College, Dubuque, Iowa, USA. This site provides an alphabetical list of species that are available. It is located at <http://www.bgsu.edu/departments/biology/algae/html/LorasColl.html>.

Fungal Genetics Stock Center (FGSC)(Kansas)

FGSC contains databases for *Aspergillus*, *Fusarium*, *Neurospora crassa*, *Neurospora sitophila*, *Neurospora tetrasperma* as well as other species of *Neurospora* and related genera. Also present are individual plasmids (*N. crassa* and *A. nidulans*), *A. nidulans* gene libraries and *N. crassa* gene libraries. The site also contains a list of genes isolated from *Aspergillus* and *Neurospora*. It is located at <http://www.kumc.edu/research/fgsc/main.html>.

Rockefeller University - Lancefield Collection

Important streptococcal strains from the Lancefield collection are located in the Lancefield Collection. Each listing contains pertinent information about the strain. It is located at <http://www.rockefeller.edu/vaf/vaf.home.html>.

Salmonella Genetic Stock Center

This center provides access to thousands of strains of Salmonella. These strains are provided without charge to researchers at non-profit institutions; a small charge for strains is made for researchers at commercial laboratories. It is located at [gopher://acs6.acs.ucalgary.ca/11 /facdep/biol/sgsc/](http://gopher://acs6.acs.ucalgary.ca/11/facdep/biol/sgsc/).

Fungal Culture Collections, Uppsala University, Sweden

About 3,000 strains of fungi are available through this database, known as "Mycoteket". It is located at <http://ups.fyto.uu.se/mykotek/index.html>.

VKM: All-Russian Collection of Microorganisms

Access to this site provides information to over 6,000 strains of bacteria, fungi, yeasts, and genetically-modified organisms. Repeated attempts to access this site failed. It is located at <http://www.stack.serpukhov.su:70/1s/db/vkm>.

Microbial Information Network of China

Presently the China Directory of Microorganisms is available for searching. Organisms that are covered include bacteria, actinomycetes, yeast, fungi, and viruses. Retrieved entries provide a few words on the use of the organisms, as well as the media and temperature used for culture. It is located at <http://sun.im.ac.cn/>.

JFCC: Japanese Federation of Culture Collections

These databases include cultures of algae, bacteriophages, protozoa, and viruses, but are especially strong in fungi (18,000 strains) and bacteria (9,500 strains). It is located at <http://www.wdcm.riken.go.jp/wdcm/JFCC.html>.

Availability of B. anthracis and the VEE virus

In order to assess bacterial and viral availability, the number of culture collections which provide samples of B. anthracis and the VEE virus were

determined. The World Directory of Culture Collections is maintained by the World Data Center for Collection of Microorganisms, at the following URL:

<http://www.wdcm.riken.go.jp/htbin/CCINFO.pl>.

Searching by the keyword “anthracis”, 56 culture collections were identified that provide B. anthracis samples for free, exchange or for a fee. Annex M lists the culture collections which can provide B. anthracis samples. Only two culture collections provide samples of the VEE virus. They are also listed in Annex M.

Chapter 5

RESEARCH ON BACILLUS ANTHRACIS

The following sections summarize research related to B. anthracis obtained from various Internet sites. The information gathered has been placed into the following sections:

Section 1. Molecular research related to B. anthracis;

Section 2. Research on diagnosis, pathology and biohazard;

Section 3. Research on disease outbreaks; and,

Section 4. Research related to arms control.

Annex O lists the WebCompass Resource Discovery Agent-generated database of Internet sites related to B. anthracis.

Section 1. Molecular research related to B. anthracis

NIDR/DIR Laboratory of Microbial Ecology

This Internet site describes research in the Laboratory of Microbial Ecology, National Institutes of Health, Bethesda Maryland (Henning Birkedal-Hansen, D.D.S., Ph.D., Acting Chief). The crystal structure of the protective antigen protein from B. anthracis is detailed. The following four references detail researchers who study anthrax toxin at National Institute of Dental Research. The summaries are from the same Internet site but they represent different information sections.

http://128.231.106.172/DIRweb/LME/LMEhome/lme_homepage.htm (the reference to size indicates the amount of information and the date when the information was accessed)
size 2K - 18 Apr 96

NIDR/DIR/LME Vaccine and Therapeutic Development Section

This site describes the research of Jerry M. Keith, Ph.D at the Laboratory of Microbial Ecology Vaccine and Therapeutic Development Section. The research program studies the structure and mechanism of action of bacterial protein toxins by using biochemical and genetic methods to analyze and alter protein structure and cultured eukaryotic cells to analyze the mechanisms of anthrax toxin action. It is located at National Institute Of Dental Research, NIH Bldg. 30, Room 316-30 Convent Drive, Bethesda MD 20892-4350.

http://128.231.106.172/DIRweb/LME/LMEhome/vaccine.htm - size 3K - 18 Apr 96

NIDR/DIR/LME Kurt Klimpel

This site describes the research on anthrax toxin of Kurt R. Klimpel, Senior Staff Fellow. National Institute of Dental Research, NIH Bldg. 30, Rm. 316 30 Convent Drive Bethesda MD, 20892-4305.

http://128.231.106.172/DIRweb/LME/LMEhome/Klimpel/klimpel.htm - size 5K - 18 Apr 96

NIDR/DIR/LME Valery Gordon

Valery M. Gordon is the Senior Staff Fellow. The address is National Institute of Dental Research Building 30, Room 316 30 Convent Drive Bethesda MD 20892-4305.

http://128.231.106.172/DIRweb/LME/LMEhome/Gordon/gordon.htm - size 5K - 18 Apr 96

NIDR/DIR/LME Stephen Leppla

This site details the anthrax toxin research by Stephen H. Leppla, Ph.D. Research Chemist. National Institute of Dental Research, NIH Building 30, Room 316 Bethesda MD.

http://128.231.106.172/DIRweb/LME/LMEhome/leppla/leppla.htm - size 3K - 18 Apr 96

VTPB Faculty

This site describes research at the Department of Veterinary Pathobiology Faculty in Texas. Faculty names and photos are linked to individual home pages including biographic information. With emphasis on experimental brucellosis and anthrax, controlled infections were evaluated to improve diagnostics and vaccines suitable for delivery to wildlife. Development of handling and restraint facilities appropriate for captive wildlife, and natural (genetic) disease resistance in wildlife are discussed.

http://cvm.tamu.edu/~vtpb/faculty.html - size 41K - 21 Apr 96

University of Szeged

This Internet site describes the research program on anthrax toxin and other peptide toxins at University of Szeged, Hungary. This site also provides a detailed description of research and experimental facilities.

http://www.mdche.u-szeged.hu/edu/phdb2.html - size 12K - 28 Mar 96

Centre for Biochemical Technology, India

This site details the research at the Centre for Biochemical Technology (CBT). Address: Delhi - 110 007 Telephone: 91-11-7257471. It describes genetic fusion and expression of the S1 subunit of pertussis toxin and A-subunit of cholera toxin to B-subunit of anthrax toxin. A comparison of B-subunits to deliver antigens was described. Expertise for synthesis of biologically active peptides exists at the Centre; the facility for custom-made synthesis of small peptides for research is also available.

<http://sunsite.sut.ac.jp/asia/india/jitnet/india/csir/cbt.html> - size 7K - 21 Apr 96

Medicine Research

This site describes research on anthrax toxin at the Department of Medicine - Faculty Research; researcher Shu Man Fu. (Professor of Medicine and Microbiology, Ph.D., Rockefeller University).

<http://www.med.virginia.edu/som-cl/internal/research.html> - size 15K - 17 Apr 96

University of Massachusetts Amherst

This site describes past research on the disease anthrax at the University of Massachusetts, Amherst, Department of Microbiology.

<http://www.petersons.com/sites/gradinc/78819009.html> - size 12K - 27 Apr 9

Outline: Stephen L. Morgan

This site describes the use of analytical techniques on anthrax toxin in the laboratory of Stephen L. Morgan in the Department of Chemistry and Biochemistry at University of South Carolina.

<http://www.cosm.sc.edu/chem/morgan.html> (5K)

Bacillus anthracis

This site describes the molecular studies and the comparative analysis of 23S ribosomal RNA gene sequences of B. anthracis and Bacillus cereus determined by PCR-direct sequencing.

<http://rrna.uia.ac.be/pub/lsu/Bacant.BGL>

Characterization of the Bacillus anthracis S-layer

This site describes French research at the Pasteur Institute dealing with the outer surface of B. anthracis. The gene coding for the S-layer protein (sap) was cloned on two contiguous fragments in *Escherichia coli*, and the complete sequence of the structural gene was determined. The protein, Sap, is composed of 814 residues, including a classical prokaryotic 29-amino-acid signal peptide.

<http://www.pasteur.fr/Bio/pub/Etienne-Toumelin1.html>

Anthrax toxin

This site describes anthrax toxin research at the Pasteur Institute in France. (Published as Pezard C., Weber M., Sirard J.C., Berche P., Mock M. *Laboratoire de Genetique Moleculaire des Toxines Infection & Immunity*, 63(4):1369-72, 1995.) The two toxins secreted by *Bacillus anthracis* are composed of binary combinations of three components. Six mutant strains that are deficient in the production of one or two of these toxin components were previously constructed and characterized. This work examined the antibody response to the in vivo production of toxin components in mice immunized with spores of strains producing these proteins.

<http://web.pasteur.fr/Bio/pub/Pezard1.html>

Anthrax Images

This US government site assesses experiments of mass aerogenic vaccination of humans against anthrax and recent advances in the development of an improved, human anthrax vaccine. It is reported that pathogenicity in the Genus *Bacillus* is associated with the induction of the enzyme superoxide dismutase in *B. anthracis* and related *Bacillus* species.

http://www.dtic.mil/gulfink/nbrv_bib/anthrax.html

STC Biological Research Activities

This site provides information on the mission, background, and experience of the STC team engaged in biological research activities. Their mission is to support immunological testing and technical evaluation of toxin and pathogen agents relevant to the U.S Army's Bio-Chemical Mission Area, and to provide expertise in the detection of biological agents. The U.S. Army Chemical and Biological Defense Command (CBDCOM) required state-of-the-art capability in conducting biological monitoring, testing and evaluation.

<http://www.stcnet.com/projects/biores.html> (4k)

Prokaryotic SSU rRNA Taxonomic List

This site contains molecular research concerning the relatedness of bacteria including *B. anthracis*.

http://geta.life.uiuc.edu/RDP/data/SSU_tax.html

Section 2. Research On Diagnosis, Pathology And Biohazard

JHMI-InfoNet: Pathfinder Laboratory

This site describes procedures for diagnostic testing for anthrax as well as laboratory summaries in the Department Of Pathology.

http://infonet.welch.jhu.edu/clinical/pathfind/lab_summaries.html - size 39K - 27 Feb 96

Diagnostic Lab at NYSCVM

The Diagnostic Laboratory at the New York State College of Veterinary Medicine describes in this site the historical development of anthrax vaccine pre-World War II and the present day diagnostic testing for anthrax.

<http://zoo.vet.cornell.edu/DL/dl.html> - size 11K - 13 Apr 95

Husbandary And Research Uses Of "Other" Species

David W. Brammer, DVM, describes laboratory experience with the disease anthrax and the susceptibility of various animals to the disease.

<http://netvet.wustl.edu/species/NEW/OTHER/MINK.HTM> - size 39K - 13 Jul 95

Office of Biosafety

The Office of Biosafety, Laboratory Centre for Disease Control, Health and Welfare Canada, has undertaken the preparation of Material Safety Data Sheets for infectious substances. These MSDSs provide pertinent information on biohazards and the safe handling of specific microorganisms in the laboratory including B. anthracis.

<http://hpb1.hwc.ca:8300/E221T51> - size 5K - 27 Apr 9

McGill Laboratory Biosafety Manual - Biohazards Associated With Exposure

This site provides details from the McGill Laboratory Biosafety Manual - First edition, 1995, 'Biohazards Associated With Exposure to Animals'. Over 150 diseases have been classified as zoonoses including B. anthracis. Zoonoses are diseases that can be transmitted from animals to humans. Information is provided on every species of animal handled at McGill.

More information is available on specific zoonoses, proper work and animal handling procedures, and personal hygiene and protective equipment for work with animals. McGill University has developed an occupational health program which includes medical monitoring of people who contact zoonoses.

<http://blizzard.cc.mcgill.ca/eso/biosafe/7.htm> - size 8K - 29 Nov 95

South Dakota Animal Disease Research

This site describes research at the South Dakota animal disease research and diagnostic laboratory. It includes a list of reportable diseases July 1, 1993 - June 30, 1994. It describes the incidence of anthrax in South Dakota.

<http://www.sdstate.edu/~wbmd/http/vet/report/diseases.txt> - size 1K - 19 Apr 96

Pathology Handbook, Clinical Microbiology/Virology

The Clinical Microbiology/Virology Laboratory offers a wide range of services for the serology, isolation and identification of bacteria, including B. anthracis. It describes techniques for collecting specimens B. anthracis.

<http://pathweb.pds.med.umich.edu/handbook/micro.htm> - size 24K - 19 Apr 96

GIDEON update

This site describes the software program called GIDEON (update # 95.4 December 1, 1995). It is used to diagnose unusual diseases, including anthrax. This is based on exposure history as well as basic signs and symptoms.

<http://www-leland.stanford.edu/~blackman/gideon/whatsnew/wn9504.txt> - size 7K - 15 Nov 95

Bacillus spores

This site reviews research and history of B. anthracis spores. Spores released from animal exudates contaminate soil in an area for many years. Pathogenesis: Spores enter body through abrasions in skin or oral/intestinal mucosa (localized, or may enter blood for systemic infection) germinate and multiply. Wool Sorter's Disease pulmonary disease is seen in persons sorting infected sheeps' wool or goats' hair. It is reported that biological warfare material in the form of aerosolized anthrax spores caused 50 deaths in Soviet Union due to an explosion at a bio-warfare research facility.

<http://salk.utmem.edu/classes/micro/Bacillus.html>

UV Decontamination

This site details research about the amount of UV energy needed to kill bacteria. Ultraviolet energy levels in microwatts at wavelength of 254 nanometers required for 99.9% destruction of various microorganisms were measured. The UV energy in microwatt-seconds per square centimeter for cell death were 8500 for Agrobacterium tumefaciens and 8700 for B. anthracis.

<http://www.pura.com/bacteria.htm>

Inbred Strains

Outbred KM mice from Shanghai Institute of Biological Products in 1972 and inbred since 1974 by Lou Zhenmei, Laboratory Animals Centre, Beijing are described at this site. These mice are sensitive to attenuated B. anthracis and are used in anthrax research.

<http://www.informatics.jax.org/strains/docs/AMMS.html>

ADDL Microbiology Service

This site at Purdue University describes the ADDL Microbiology Service. The Microbiology Service of the Animal Disease Diagnostic Laboratory provides cultural examinations for a wide variety of bacteria including B. anthracis.

<http://www.vet.purdue.edu/depts/newaddl/bacteriology/> - size 13K - 1 Aug 95

Isolation of B. anthracis

This site described isolation and biosafety issues related to B. anthracis. It describes how to isolate and store specimens. It describes septicemic infection in cattle, sheep, elk, bison, horses, swine and mink.

http://hazard.com/vtsiri/library/cdc_biosafety/section_7 - size 114K - 29 Mar 96

US Department of Agriculture

This U.S. government site contains information about occurrence of anthrax in swine. It compares the rates of anthrax over the past three years and calculates economic lossess.

<http://www.oklaosf.state.ok.us/osfdocs/budget/bb960401.html> - size 21K - 26 Jul 95

Minnesota Department of Health

This site of the Minnesota Department of Health, Communicable Diseases describes diagnostic and identification procedures for B. anthracis.

<http://www.health.state.mn.us/Health-docs/dpc/rules.html> - size 21K - 18 Dec 95

Statement of Scope & Collecting Levels

This site describes the Collection Development Policy of the National Agricultural Library (U.S. Department of Agriculture National Agricultural Library Beltsville MD 20705). It contains information about B. anthracis.

<http://www.nal.usda.gov/acq/scopqtoz.htm> - size 51K - 10 Apr 96

Bacillus cereus and other Bacillus spp.

This site describes research at the U.S. Food & Drug Administration Center for Food Safety & Applied Nutrition Foodborne Pathogenic Microorganisms and Natural Toxins. It describes procedures for isolating B. anthracis.

<http://www-micro.msb.le.ac.uk/FDA/chap12.html> - size 12K - 3 Mar 96

Fort Detrick

This site describes development work on anthrax vaccine in the 1995 Annual Report (U.S. Army Medical Materiel Development Activity, Fort Detrick, Frederick, Maryland 21702-5009). U.S. Army Medical Materiel Development Anthrax Vaccine was produced in pilot lots by the USAMRIID.

<http://www.medcom.amedd.army.mil/usammda/95ann.htm> - size 120K - 26 Mar 96

ASTMP Vol. II: Annex A Chapter III Pt. 6/9

This site describes US government research (ASTMP Vol. II: Annex A Chapter III Pt.3/10. IIIJ.19) entitled 'Medical Countermeasures for Anthrax.'

The objective is to develop and assess medical countermeasures against the disease.

<http://204.7.227.67/infonet/per-log/astmp/vol2/annex-a/chap3-4b.html> - size 12K - 25 Oct 95

Sharing Technologies

The site of Sharing Technologies describes research and development related to medical research intended to protect military personnel from battlefield hazards, including anthrax.

http://mrmc-www.army.mil/shartech_t.html - size 7K - 15 Feb 96

United States Army Medical Materiel Development

This site describes the United States Army Medical Materiel Development Activity at Fort Detrick, Maryland 21702-5009, Biological Systems Project Management Division. It describes work on anthrax vaccines.

<http://www.medcom.amedd.army.mil/usammda/bspmd.htm> - size 4K - 29 Jan 96

Section 3. Research On Disease Outbreaks

Research Priorities for Improvement of Animal Health in Africa

This site describes research priorities for improvement of animal health in Africa. It discusses the anthrax situation. It states that good vaccines exist against soil-borne diseases, for instance anthrax and although eradication is not a realistic possibility, there is no technical excuse for their wide-spread occurrence in domestic livestock in certain tropical countries. (Gerrit Uilenberg, located at Institut d'Elevage et de Medicine Veterinaire des Pays Tropicaux).

<http://ifs.plants.ox.ac.uk/ifs/uganda/gerrit.htm> - size 32K - 21 Apr 96

Observations From Anthrax Outbreak in Sheridan County Herd

This site describes an anthrax outbreak from the veterinary viewpoint (NF94-128. Observations From Anthrax Outbreak in Sheridan County Herd by Dr. John Gamby, Veterinarian Dr. Roger Sahara, NE Dept. of Agriculture, Field Veterinarian).

Anthrax killed 23 head of cows and calves on a Sheridan county Nebraska ranch in June 1994. *Bacillus anthracis* was confirmed on culture by the Panhandle Veterinary Diagnostic Laboratory.

The predominant clinical sign in affected cattle was a progression from normal appearing to dead in a matter of hours.

<http://ianrwww.unl.edu/ianr/pubs/nebfacts/nf94-128.htm> - size 5K - 20 Apr 96

Zoonotic Diseases

This site describes research and analysis on zoonotic diseases at the University of California, Office of Research. It states that *B. anthracis* is a gram-positive spore-forming aerobic rod. Occurrence is worldwide. Most mammals are susceptible; but it is most commonly seen in cattle, sheep, horses, swine, goats (guinea pigs, rabbits, mice, experimentally). Recent outbreaks have been related to prospective military use of the organism.

<http://research.ucsb.edu/pro/policy.html> - size 27K - 19 Jan 96

GramStain Tutor

Naturally and experimentally infected animals pose a potential risk to laboratory and animal care personnel. Direct and indirect contact of the intact and broken skin with cultures and contaminated laboratory surfaces, accidental

parenteral inoculation, and rarely, exposure to infectious aerosols are the primary hazards to laboratory personnel. A licensed vaccine is available through the Centers for Disease Control and Prevention; however, immunization of laboratory personnel is not recommended unless frequent work with clinical specimens or diagnostic cultures is anticipated .

<http://www.labmed.washington.edu/Tutors/GS/GST.Demo/altspecies.html>

Recombinant DNA

This site describes guidelines for recombinant DNA work with microorganisms such as B. anthracis. Recombinant DNA molecules are defined as molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell.

<http://www.med.virginia.edu/research/UVA-Guidelines.html>

Aerobic & Facultative Gram-Positive Rods

This site describes the properties of different classes of bacteria including B. anthracis. Topics include Bacillus anthracis, Bacillus cereus and other Gram positive aerobic rods.

<http://salk.utmem.edu/classes/micro/AerobeIndex.html>

IWF-Datenblatt

This site describes research on B. anthracis. It details the bacterial morphology and behaviour under different culture conditions.

<http://www.iwf.gwdg.de/iwfger/alldaten/E327.html>

Antec International Ltd.

This site describes studies in which bactericidal solutions were tested against various bacteria including B. anthracis.

<http://www.gate.net/~antecint/bacteact.html>

Graduate Student's Page

This site describes field studies on B. anthracis, the causative agent of anthrax, an often fatal disease of animals. Once completed, the assay will be used to study anthrax spore ecology in Wood Buffalo National Park and the Mackenzie Bison Sanctuary, where sporadic epidemics of anthrax have killed hundreds of northern bison. Despite the prevalence of C. jejuni infections, very little is known about the interactions of these organisms with intestinal cells.

<http://gpu.srv.ualberta.ca/~mmid/grads.html>

Threonyl Muramyl Dipeptide

This site describes studies on the immunization against anthrax with B. anthracis protective antigen combined with adjuvants. Immunological adjuvants have desirable properties and sometimes side-effects. Adjuvants enhance the immune response.

<http://gopher.hivnet.org:70/newsgroups/drugs/398>

Anthrax - Russia Images

This site and the following four listings are from the World Health Organization's Internet site. They describe anthrax outbreaks in the respective countries.

<http://www.healthnet.org/old/promed1995-hma/0641.html>

Anthrax - Republic of Georgia

*<http://www.healthnet.org/old/0970.html> *promed1995-hma/**

Anthrax - Rep. of Georgia Images

<http://www.healthnet.org/old/promed1995-hma/0966.html>

Anthrax & botox - Iraq Images

<http://www.healthnet.org/old/promed1995-hma/0720.html>

Association for Veterinary Informatics

This web site contains the Association for Veterinary Informatics Newsletter from January-February, 1996. Noell Moseley writes about an anthrax outbreak.

“The Internet forms a readily available global resource of experience available to be asked. Similarly the non-medical professionals, especially journalists, form a key component as they tell us of new events below the medical or veterinary horizon. For example, I lately received a key series of reports of anthrax in Azerbaijan from journalists in Baku but which was not being reported by the relevant Ministries.”

Also reviewed at this Internet site was the proposal for disease monitoring to deal with unusual disease outbreaks such as anthrax. In order to expand the animal and zoonotic disease components of ProMED, a separate sublist, PROMED-AHEAD, was set up through a grant to the Federation of American Scientists (FAS) from the Geraldine R. Dodge Foundation. It is to accommodate subscribers who prefer to receive only animal and zoonotic disease postings. The name reflects its intended content, i.e. AHEAD = Animal Health/Emerging Animal Diseases.

<http://www.cvm.uiuc.edu/avi/janfeb96.html> - size 54K - 25 Feb 96

Section 4. Research Related To Arms Control

DRES Documents

This site contains research summaries related to anthrax from the Defence Research Establishment Suffield Publications.

<http://www.dsis.dnd.ca/shared/uudres.htm> - size 96K - 8 Jan 96

Lawrence Livermore National Laboratory

This site summarizes work on verification of production of potential biological warfare agents such as B. anthracis. This work was done at Lawrence Livermore National Laboratory Public Affairs, November 9, 1995 David Schwoegler, Phone: (510) 422-6900.

<http://www.llnl.gov/PAO/NewsReleases/Older/November95/NR-95-11> - size 3K - 21 Mar 96

Los Alamos

This site details work on B. anthracis spore detection equipment called Quadnet, Cell4-1lanl. The report is titled 'Biological Weapons Detector Developed With Applications For Biomedical Industry'. The work was done at Los Alamos, N. M

Los Alamos National Laboratory has developed a lightweight, compact version of an instrument that can rapidly analyze single cells and is expected to find widespread applications in the pharmaceutical industry and in clinical microbiology.

Their instruments collect air samples and measure the size and quantity of particles. If the volume of airborne particles suddenly increases, an alarm

sounds and soldiers test samples in a flow cytometer and other devices to determine quickly if the particles are biological.

The newly developed flow cytometer is laser-activated and computer controlled. It can detect toxins, viruses, and bacteria including B. anthracis spores.

Los Alamos received \$5.5 million from the U.S. Army Chemical and Biological Defense Command at Aberdeen Proving Ground, Md, for the project. Three prototypes will be delivered to the Army in July. The Army wants 150 cytometers over three years

<http://www.vyne.com/qnetwww/archives/CELLA-1LANL> - size 4K - 1 Apr 96

Chapter 6

RESEARCH ON THE VEE VIRUS

The following sections summarize research on the VEE virus. Annex O lists the WebCompass-generated database of sites related to research on this virus. The information gathered has been placed into the following sections:

Section 1. Molecular Research Related To The VEE Virus;

Section 2. Research On Diagnosis, Pathology And Biohazard;

Section 3. Research On Disease Outbreaks; and,

Section 4. Research Related To Arms Control.

Section 1. Molecular Research Related To The VEE Virus

Franziska B. Grieder, Microbiology & Immunology

This site describes research related to the molecular basis of VEE pathogenesis. The research was carried out at the Uniformed Services University, Department Of Biochemistry, Washington D.C.

The Uniformed Services University of the Health Sciences is part of the national center for biomedical education, which includes the F. Edward Hébertflag School of Medicine, the Graduate School of Nursing, and the Graduate Program. The Armed Forces Radiobiology Research Institute recently became part of the University. It conducts a wide variety of experiments on radiation effects on cellular and molecular processes.

The following are references to published papers that are described at this site:

Grieder, F.B., Davis, N.L. and Johnston, R.E. Specific restrictions in Venezuelan equine encephalitis virus pathogenic process result from single amino acid changes in the glycoproteins. *J. Virol.*, accepted for publication, 1994.

Davis, N.L., Grieder, F.B., Smith, J.F., Greenwald, G.F., Valenski, M.L., Sellon, D.C., Charles, P.C., and Johnston, R.E. A molecular genetic approach to the study of Venezuelan equine encephalitis virus pathogenesis. *Arch. Virol.*, 9:99-109, 1994.

Grieder, F.B., Davis, N.L., Sellon, D.C., Aronson, J.F., and Johnston, R.E. Molecular genetics of Venezuelan equine encephalitis virus pathogenesis in mice. Keystone Symposium on Molecular Immunology of Virus Infections. *J. Cell. Biochem.*, (Suppl. 17d, pg. 65), Taos, NM, March, 1993.

<http://bob.usuf2.usuhs.mil/mcb/faculty/node29.html> - size 2K - 13 Mar 96

Microbiology Seminar

This site describes research related to the UAB Microbiology Seminar "The Molecular Genetics of Venezuelan Equine Encephalitis Virus Pathogenesis" presented by Robert Johnston, Ph.D.

<http://www.microbio.uab.edu/events/Johnston.html> - size 932 bytes - 19 Mar 96

Sergey A. Dryga

This site describes research done on the VEE virus by Sergey A. Dryga. Research Associate Phone, office: (314)-362-2745 FAX: (314)-362-1232 email: dryga@borcim.wustl.edu.

<http://www.microbiology.wustl.edu/dept/postdoc/sdryga.html> - size 7K

Division of Vector-Borne Infectious Diseases

This site describes research at the Division of Vector-Borne Infectious Diseases. The Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases is a major centre for viral research specializing in VEE virus. The Division of Vector-Borne Infectious Diseases (DVBID) is the focus for information, surveillance, prevention, and control of vector-borne infectious diseases for the Public Health Service, state and local health departments, educational institutions, and professional organizations in the United States and around the world.

<http://www.cdc.gov/ncidod/publications/brochures/dvbid.htm> - size 10K - 28 Mar 95

University of North Carolina at Chapel Hill

This site describes research related to VEE virus at the University Of North Carolina At Chapel Hill, School of Medicine, Department of Microbiology and Immunology. The Department of Microbiology and Immunology is housed in a modern research building. Spacious research laboratories are supplemented by special tissue-culture facilities, several special-purpose darkrooms, animal-care facilities, computer facilities, and more than 600 square feet of space designed specifically as a BL-3 physical containment facility for research on pathogenic organisms.

Robert E. Johnston, Professor (Ph.D., Texas at Austin, 1973) conducted research on the molecular genetics of viral pathogenesis and the design of recombinant vaccines for the alphaviruses Sindbis and VEE virus.

<http://www.petersons.com/sites/gradinc/80145009.html> - size 13K - 28 Apr 96

Alan Jackson

This site describes research related to VEE virus. This work was done in Canada by Alan C. Jackson, B.A., M.D., FRCPC, FACP, Assistant Professor, Associate Professor of Medicine (Neurology) at Queen' University in Kingston.

Jackson AC, SenGupta SK, Smith JF: Pathogenesis of Venezuelan equine encephalitis virus infection in mice and hamsters. *Veterinary Pathology* 28:410-418, 1991.

<http://www.queensu.ca/micr/jackson.htm> - size 3K - 5 May 95

GSDB Manual for ASCII AWB2: A.8 Sequence Definitions: Complete Genome

This site describes research related to gene structure of the VEE virus.

http://www.ncgr.org/doc/ascii/ascii_96.html - size 1K - 28 Mar 96

Family Togaviridae

This site describes research related to gene structure of the VEE virus.

http://life.anu.edu.au/viruses/Ictv/fs_togav.htm - size 6K - 20 Feb 96

VEE virus

This site describes research related to the VEE virus. It is titled 'Nucleocapsid and Glycoprotein Organization in an Enveloped Virus. The researchers were R. Holland Cheng, Richard J. Kuhn, Norman H. Olson, Michael G. Rossmann, Hok-Kin Choi.

<http://trout.csb.ki.se/users/rhc/RRCELL-2.html> - size 54K - 22 Mar 96

PICO

This site describes research related to the interaction of the VEE virus to poliovirus.

<http://hs1304silver1.cpmc.columbia.edu/PICO/Refs/Capsid.html> - size 75K - 19 Apr 96

Russian State Research Center of Virology and Biotechnology

This site describes the Russian State Research Center of Virology and Biotechnology "Vector" Main Research & Development Branches. It conducts fundamental research in the field of molecular virology.

The Center conducts studies of the following agents causing viral infections: Eastern and Venezuelan equine encephalomyelitis, tick-borne encephalitis, Congo-Crimean hemorrhagic fever, Marburg, HIV-1, HIV-2, vaccinia, variola, measles, mumps, rubella viruses, cytomegalovirus, hepatitis A, B, C, D, E and other viruses.

It also works on a contract basis as the Republican Research Scientific-Consulting Center For Expertise, St. Petersburg, Russian Federation. It has the following areas of expertise; large-scale production of therapeutic, diagnostic, and prophylactic preparations for medicine and veterinary, as well as different biochemical and immunochemical reagents, nutrient media, sera, for research and practical purposes.

<http://www.extech.msk.su/gnc-re/nprav/nd-58e.htm> - size 1K - 7 Dec 95

Zoonotic Diseases

This site describes research related to the diagnosis of infections with the VEE virus. (UCSB Office of Research. ZOONOTIC DISEASES). (Text Modified from Document Created by Michael S. Rand, DVM, ACLAM).

<http://research.ucsb.edu/pro/policy.html> - size 27K - 19 Jan 96

Section 2. Research On Diagnosis, Pathology And Biohazard

Venezuelan Equine Encephalitis Antibody

This site describes research related to identifying the presence of Venezuelan Equine Encephalitis Antibody.

It details the need to establish the presence of antibodies to the VEE virus and that the significance of titer is dependent on epidemiologic history.

<http://pathweb.pds.med.umich.edu/HANDBOOK/Venezuel.htm> - size 2K - 19 Apr 96

Encephalitis

This site describes research related to the disease caused by viruses. Encephalitis is an infection of the central nervous system that may be caused by one of several mosquito-borne viruses.

<http://www.r09.tdh.state.tx.us/zoonosis/encephal.html> - size 1K - 17 Apr 96

BMBL-Section VII-Viral Agents

This site describes safety procedure for working with the VEE virus.

<http://biosafety.ihe.be/GB/USA/CDCManual/secti7f1.html> - size 15K - 26 Feb 96

Live Virus Vaccines

This site describes research related to the requirements of live virus vaccines including the VEE virus.

<http://aphisweb.aphis.usda.gov/BBEP/vb/9cfrs/300332.html> - size 169K - 5 Jan 96

World-Wide Incidence of Alphavirus

This site describes research related to the world-wide incidence of Alphavirus. It includes information on Alphavirus pathogenesis and incidence.

<http://www.microbiology.wustl.edu/sindbis/bib/geoBib> - size 191K - 5 Apr 9

Arboviruses

This site describes research related to arboviruses. These viruses are spread by blood sucking insects. In the U.S. the tick and the mosquito are the vectors.

There are four virus families that harbor arboviruses: Togaviridae, Flaviviridae, Bunyaviridae and Reoviridae. Although 63 arboviruses have been isolated within the U.S. and Canada, only six cause significant illness - St. Louis encephalitis (SLE), Eastern Equine encephalitis (EEE), Western Equine encephalitis (WEE), Powassan encephalitis (POW), California encephalitis (Lacrosse virus) and Colorado tick fever (CTF).

There are three major alphaviruses which are arthropod borne: EEE, WEE and VEE (Venezuelan equine encephalitis).

<http://fiona.umsmmed.edu/%7Eeyar/arbo.html> - size 17K - 20 Mar 96

APHIS Web—APHIS Publications

This site describes research related to USDA Animal and Plant Health Inspection Service. The research from programs of the U.S. Department of Agriculture are available to anyone. It discusses the dangers posed by importation of animals with VEE.

<http://www.aphis.usda.gov/oa/pubs.html> - size 75K - 15 Apr 96

Summary Of Classification Of Biological Agents According To Risk

This site describes research related to biosafety when working with the VEE virus. It includes a classification of biological agents according to risk.

<http://www.oehs.upenn.edu/bio/bsm/appendixa.html> - size 17K - 20 Jul 95

1994-1995 Annual Report: Industrial Hygiene Section

This site describes research done by to the Industrial Hygiene Section at the University of North Carolina.

The University of North Carolina at Chapel Hill has three active biosafety level 3 (BL-3) laboratories.

One of the BL-3 laboratories handles Venezuelan Equine Encephalitis virus (VEE), a virus that causes encephalitis in horses but also is pathogenic for humans. The VEE containment facility was successfully decontaminated with formaldehyde gas so that maintenance, including replacement of HEPA filters serving the facility, could be performed.

<http://www.adp.unc.edu/hs/bs95p15.html> - size 18K - 25 Jan 96

BMBL-Section I

This site describes research related to the precautions necessary to work with the VEE virus. Microbiology laboratories are special work environments that may pose identifiable infectious disease risks to the researchers.

<http://biosafety.ibe.be/GB/USA/CDCManual/section1.html> - size 10K - 29 Feb 96

Medical Chemical and Biological Defense

This site describes research related to Medical Chemical and Biological Defense - Biological. Developing medical defenses for biological pathogens and toxins is the objective of this research and development. Vaccines have been fielded recently against the virus that causes Western, Eastern, and Venezuelan equine encephalitis. Vaccines against Q fever and tularemia are in advanced development. Advanced studies promise to improve substantially upon the existing anthrax vaccine which was developed in the 1950's. Researchers have isolated and characterized a stable non-spore forming variant of the anthrax bacillus for production of protective antigen, leading to an improved vaccine which is less reactogenic and safer to produce.

http://mrmc-www.army.mil/biodef_t.html - size 7K - 14 Feb 96

Virus/Disease Index, 1995

This site describes research related to VEE virus outbreaks. It is the CRC Press Home Page Virus/Disease Index, 1995.

<http://www.crcpress.com/PRODS/3206.htm> - size 15K - 16 Aug 95

ADDL Serology Tests

This site describes research related to serology tests run at ADDL. This includes tests for the VEE virus.

<http://www.vet.purdue.edu/depts/newaddl/serology/tests.html> - size 46K - 1 Aug 95

Section 3. Research On Disease Outbreaks

CHAART Venezuelan Equine Encephalitis

This site describes research titled 'Characterization of Venezuelan Equine Encephalitis Emergence Sites Using GIS'. The project institution is the University of Texas Medical Branch and its principal investigator is Dr. Robert Tesh.

This proposal is a pilot study to develop remote sensing and geographic information systems (GIS) to identify locations of potential VEE emergence.

Center for Health Applications of Aerospace Related Technologies (CHAART) is part of the Ecosystem Science and Technology (ECOSAT) Branch of the Earth Science Division at the NASA Ames Research Center.

<http://geo.arc.nasa.gov/esdstaff/health/mou/nih/vee.html> - size 4K - 27 Mar 96

HIC infoDate

An outbreak of Venezuelan equine encephalitis (VEE) that began in northwestern Venezuela in April 1995 has spread westward to the Guajira peninsula and to Colombia resulting in a minimum of 13,000 cases in humans and an undetermined number of equine deaths.

The current epidemic is the largest in the region since 1962-1971, when outbreaks affected Colombia, Ecuador, Peru, Venezuela, all the countries of Central America (except Panama), Mexico, and Texas.

No major outbreaks had been recognized since 1973, suggesting that epizootic viral strains (subtypes IAB and IC) had become extinct. However, based on recent molecular phylogenetic studies, these strains may have evolved from strains maintained in silent cycles of rodent-mosquito transmission.

Partial nucleotide sequencing and antigenic analysis of three human isolates from the current epidemic indicates they are related to the IC epizootic strain of VEE virus isolated during a large outbreak in Venezuela and Colombia during 1962-1964.

http://ch.nus.sg/MEDNEWS/oct95/hicn8374_8.html - size 9K - 30 Dec 95

Infectious Diseases in Latin America

This site describes research related to changing disease patterns in Central America. It is titled 'Infectious Diseases in Latin America and the Caribbean: Are They Really Emerging and Increasing?' Author: A. David Brandling-Bennett, Francisco Pinheiro.

<http://www.medscape.com/Medscape/External/EID/EID.9601.v02.n01/e2108.brandling/e2108.brandling.html> - size 14K - 22 Apr 96

FAS ProMED Proposal

This site describes research related to the FAS Promed Proposal. Its title is 'A Demonstration Program For Global Monitoring Of Emerging Diseases'.

The FAS ProMED project is proposing to the world health community that a demonstration program be set up to test the feasibility of a global system of monitoring emerging infectious diseases. The demonstration program would concentrate on a small number of strategically located medical facilities, and would give these facilities top priority on training and other assistance.

Encephalitis/meningitis, similarly, includes some infections with a history of rapid epidemic spread (e.g. *Neisseria meningitidis* [meningococcus]), and many that are significant regional threats, such as the meningococcus in parts of Africa and Asia, Japanese encephalitis in Asia, and a number of encephalitides in the Americas, including Venezuelan equine encephalomyelitis.

<http://www.fas.org/promed/proposal.html> - size 64K - 5 Apr 96

EquineCare Watch—January 1996

This site describes research related to VEE pathology. It is summarized from EquineCare Watch, January 1996. The EquineCare Watch monthly bulletin is provided as a service of Thoroughbred Racing Communications, Inc., New York, NY. In horses, clinical signs occur approximately five days after infection and include fever, impaired vision, irregular gait, wandering, reduced reflexes, circling, incoordination, yawning, grinding of teeth, drowsiness, pendulous lower lip, inability to swallow, photophobia, head-pressing, inability to rise, paralysis, occasional convulsions and death. Mildly affected animals may slowly recover in a few weeks but may have residual brain damage. Mortality for horses diagnosed with VEE is 50 to 75 percent.

<http://bloodhorse.com/health/ecwatch.html> - size 27K - 21 Feb 96

Disease Outbreak

This site describes what actions are taken by the U.S. Government when an infectious disease outbreak occurs. It states that U.S. Government response to international epidemics occurs on an ad hoc basis. During 1994 and early 1995, the U. S. Naval Medical Research Institute Detachment (NAMRID) in Lima, Peru, detected several cases of dengue fever, oropouche, and Venezuelan

equine encephalitis (VEE) in northern Peru. These diseases are caused by arboviruses, which are carried by insect vectors, and vaccines against several arboviral illnesses are available. CDC followed up on the NAMRID reports and determined that VEE had occurred among Peruvian soldiers stationed in the area of the border dispute with Ecuador.

<http://www.whitehouse.gov/WH/EOP/OSTP/CISET/html/2-plain.html> - size 18K - 7 Nov 95

Travelers Guide To Avoiding Infectious Diseases

This site is a travelers guide to avoiding infectious diseases. It also lists areas where diseases such as VEE are known to occur or where outbreaks have happened.

<http://www.familyinternet.com/peds/top/001925.htm> - size 15K - 19 Apr 96

Bulletins Around the World

This site contains bulletins detailing disease outbreaks from around the world. The countries include - Australia, Canada, European Union, France, Hungary, Mexico, United Kingdom and the United States as well as the World Health Organization.

<http://www.cdc.gov/epo/mmwr/international/world.html> - size 7K - 10 Apr 96

Divisional Group Symposium

This site describes research related to Emergence of Epidemic/Epizootic Venezuelan Equine Encephalitis from Enzootic Transmission Cycles in RNA Viruses.

<http://www.asmtusa.org/mtgsrvc/gm96dvt.htm> - size 4K - 9 Apr 96

Health Department - Mosquitoes found in Brownsville

This site discusses potential VEE virus vectors in the United States. Mosquitoes found in Brownsville are the Anopheles species, breed primarily in permanent bodies of fresh water and may be vectors of VEE.

<http://www.brownsville.lib.tx.us/HEALTH/mesq.html> - size 4K - 5 Feb 96

VEE outbreak rampant in Venezuela, Columbia

This site describes a VEE outbreak rampant in Venezuela and Columbia. American horse owners, especially those in the southern United States are at risk.

<http://www.wsmith.com/ride/news/vee.htm> - size 2K - 8 Jan 94

Handbook of Zoonoses, Section B: Viral Zoonoses, Second Edition

This site describes research about the potential vectors of the VEE virus and their role in disease outbreaks.

<http://www.colostate.edu/Depts/IPM/natparks/mosquito.html> - size 26K - 18 Apr 96

Section 4. Research Related to Arms Control

Battlefield of the Future

This site has the text of a US army conference speculating on future trends. In it, Chapter 9 deals with the topic Twenty-First Century Germ Warfare. In it, the VEE virus is discussed. It was written by Lt Col Robert P. Kadlec, USAF.

<http://www.cdsar.af.mil/battle/chp9.html> - size 51K - 8 Mar 96

Chapter 7

PRINCIPAL FINDINGS AND CONCLUSIONS

- The Internet provides an anonymous, universally-accessible system for acquiring information about current biological and toxin research. Although it is the most extensive system available, the information cannot be considered to be comprehensive since it is lacking reference to scientific research before 1995. The older on-line services such as DIALOG provide better historical coverage of research. However, this study clearly shows that the Internet provides a significant enhancement in transparency of research and information related to biological pathogens and toxins.
- Using the WWW virtual library for Bioscience and Search engines such as AltaVista, a map was developed of biological and toxin resources.
- There are over 480 culture collections in the world that are listed on the Internet that provide samples of bacteria, viruses and fungi.
- Fifty-six culture collections provide B. anthracis samples for free or a nominal charge. Two collections provide samples of the VEE virus.
- The review of information from Internet sites related to B. anthracis and the VEE virus show that important information can be obtained. These sites detail the types of research and which research centres are involved. Other types of information include reports about disease outbreaks and vaccine development.

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