USAMRIID

Biological Warfare and Bioterrorism:

Recognition, Protection, and Treatment

Robert G. Darling, MD, FACEP

CDR, MC, USN

U.S. Army Medical Research Institute of Infectious Diseases

Intro Slide:

Emergency physicians are likely to play a major role in dealing with the aftermath of a BW attack. We will likely provide the first line of defense and if we understand the threat well enough we may even be the first to identify it.

Briefly introduce the nature of the threat through historical examples. Give a brief overview of which BW agents you will discuss, their clinical effects and the various countermeasures that are already in place as well as some that are on the horizon.

Unlike chemical weapons, which generally act within minutes (and the patient either dies or the combat medic gives him antidote and saves him), biological agents have incubation periods on the order of days, and they progress more gradually, so the first sign of a biological attack is likely to be sick patients showing up at your doorstep.

So, rather than the combat medic, it's likely to be the primary care provider that is the first responder in a biological attack.

Biological Warfare

The intentional use of microorganisms or toxins derived from living organisms to produce death or disease in humans, animals, or plants

Biological Terrorism

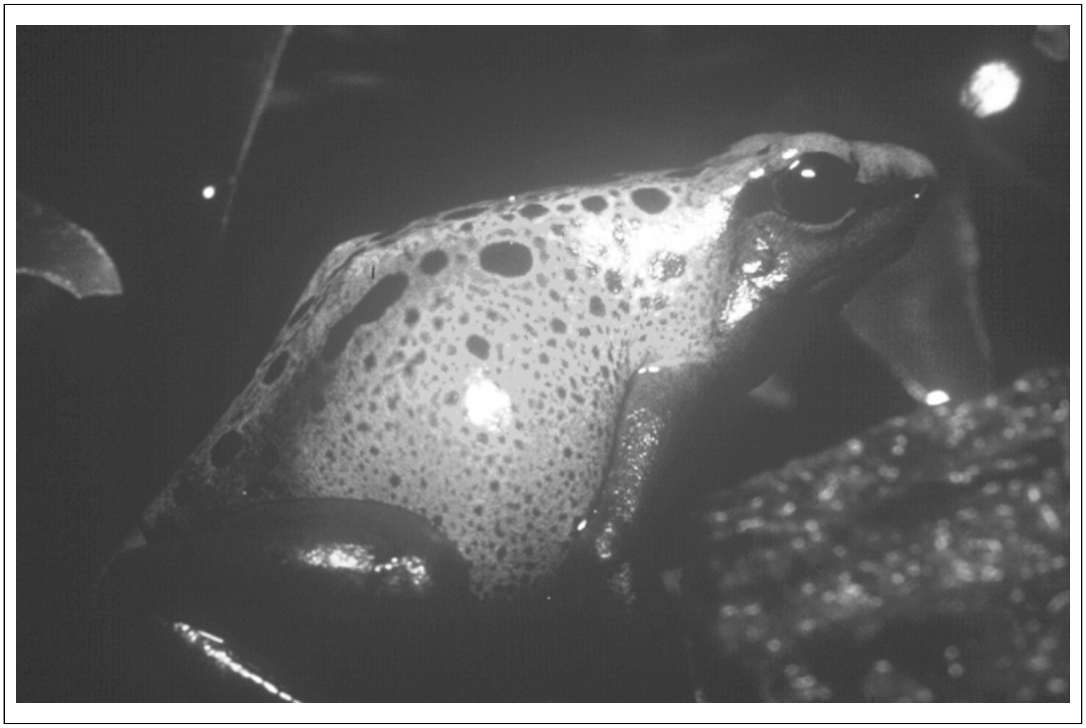
The threat or use of biological agents by individuals or groups motivated by political, religious, ecological or other idealogical objective.*

*** W. Seth Carus, 1998. Bioterrorism and Biocrimes, Center for Counterproliferation Research, National Defense University**

Quite simply, biological warfare and biological terrorism are similar events along a continuum from highly focused, assassin-style actions to the massive destruction of a population or it's economic viability. Many of the same agents are used along this continuum, although some are clearly better employed for certain types of targets than others. Mature, state-sponsored bioweapons programs of the past recognized this tailoring of agent to event and thus incorporated a spectrum of viral, bacterial and toxin agents in their armamentarium.

BT - The premeditated, unlawful use or threat of use of biological agents which is intended to create fear and/or intimidate governments or societies in the pursuit of political, religious, or ideological goals

Ancient aboriginal people such as the forefathers of these South American tribesman used poison darts to subdue the enemy. Some poisons were obtained from plants, others came from animals such as (next slide)



This frog from South America. The poison arrow frog secretes a toxin from its skin and this was used by the native population to coat their arrows or the tips of their spears prior to battle. This toxin was a very effective at subduing the enemy.

The Tartars attacked the well fortified Genoese- controlled city of Kaffa (modern Feodosiya, Ukraine) in 1346 by catapulting the plague infected corpses of their dead comrades into the city thinking this would created an epidemic of Plague in the enemy.

The British, under the leadership of Sir Jeffrey Amherst, gave blankets infected with the scabs and secretions of the victims of small pox to to native American Indians during the French and Indian War. The Indians had never been exposed to this dreaded disease and hundreds of thousands died.

The Japanese experimented on and killed at least 3,000 Chinese POWS during WWII while conducting BW weapons research in the infamous Unit 731 located in occupied Manchuria on mainland China. New research by Japanese and Chinese scholars suggest that as many as 270,000 Chinese civilians may have been killed in BW weapons experiments during WWII.

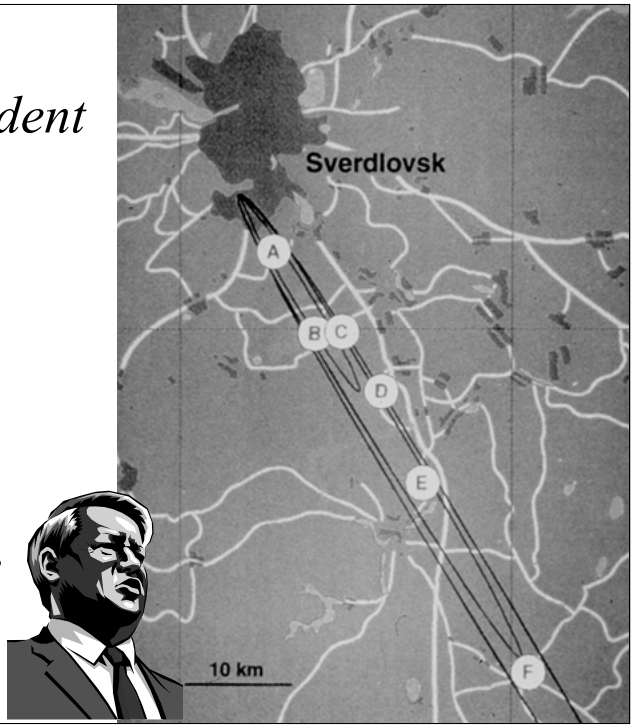
The BW Weapons convention was signed by 140 countries in 1972. At the time only 4 countries were know to have BW capability. Today some 20 countries have an offensive BW weapons capability. Nearly all of these additional countries had signed the original treaty in 1972. 5 of these countries are know to support international terrorism.

Small scale assassinations using the castor bean toxin Ricin - Bulgarian dissident Georgi Markov, 1978, London.

The largest ever epidemic of inhalation anthrax occurred in 1979 in the town of Sverdlosk (now Yekaterinberg) in Russia, when a bioweapons plant inadvertently released a small amount of weapons grade anthrax spores upwind of a populated area.

Sverdlovsk Incident

- April 1979
  - ≥ 66 Anthrax fatalities
- 1988
  - Soviets present data:
    - 96 cases
    - 79 gastrointestinal
- May 1992
  - Yeltsin admits due to "military developments"



The largest ever epidemic of inhalational anthrax occurred in 1979 in the town of Sverdlovsk in Russia.

The Soviets denied, at the time, that it was due to an accidental release of anthrax spores from a military BW research / production facility.

They even went so far as to present a paper at an American convention in 1988, claiming the anthrax came from contaminated meat.

However subsequent information revealed all the deaths occurred in a nice tight cluster emanating from the BW plant.

Meteorological data from the local airport revealed the wind happened to be blowing in this direction all day.

In 1992, Yeltzin admitted to the accident…. He ought to know, he was the Communist Party Kommisar for the Sverdlovsk oblosk at the time.

International Biological Weapons Programs

Known
- Iraq
- Russia

Probable
- China
- Iran
- North Korea
- Libya
- Syria
- Taiwan

Possible
- Cuba
- Egypt
- Israel

Source: Committee on Armed Services, House of Representatives. Special Inquiry into the Chemical and Biological Threat. Countering the Chemical and Biological Weapons Threat in the Post-Soviet World. Washington, D.C.: U.S. Government Printing Office; 23 Feb 1993. Report to the Congress.

In 1972 (the year the Biological Weapons Convention was signed), there were 4 countries with known BW capability. Within 20 years, that number had more than tripled.

Today, 17 countries are suspected of either including or developing bio agents in their offensive weapons programs.

Nearly all these countries are signatories to the '72 BWC, yet they have maintained offensive programs.

This list, by the way, is unclassified, and is included in the new FM 3-101-6 (Draft).

Offensive BW Program: Iraq

1995 disclosures to UNSCOM:

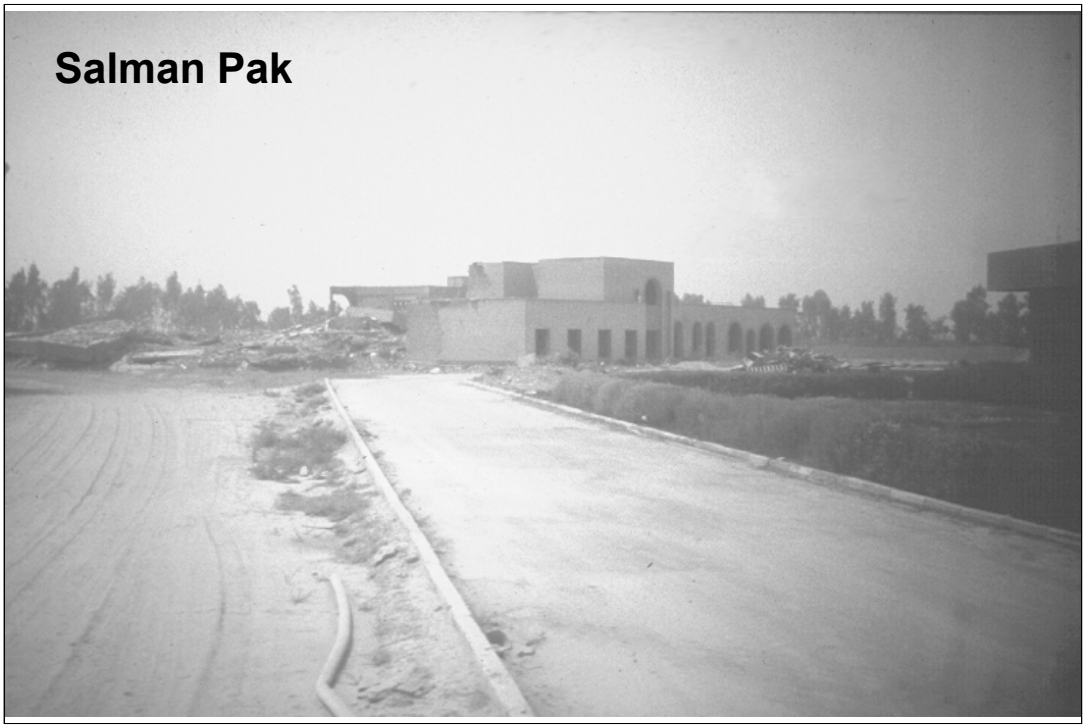
	Produced	Weaponized
Botulinum toxin	**19,000 Liters**	**10,000 L**
Anthrax spores	**8,500 L**	**6,500 L**
Aflatoxin	**2,200 L**	**1,580 L**

UN Doc S/1995/864, 11 OCT 1995

GSACEP © 2001

In August of 1991, when the 1st UNSCOM team went into Iraq, we knew that they were working on BW agents. During that inspection, they admitted to working on anthrax, botulinum toxins, and aflatoxin.

It was not until 1995, after the defection of Kamal Hassan, that we learned that, at the time of the Gulf War, the Iraqis had extensive amounts of anthrax and botulinum weaponized and ready to use.

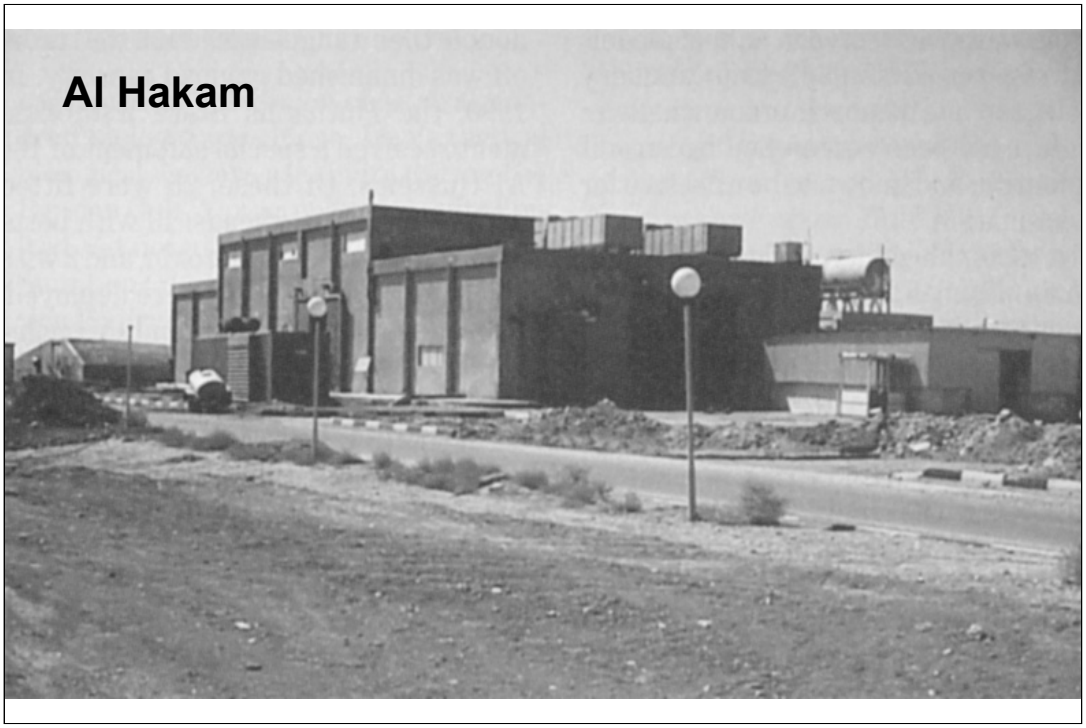


1 hr S. of Baghdad. Primary Iraqi BW **research lab.**

Began work in the 1980's. This was a state of the art biosafety level 4 type lab with a wall within a wall construction and other features consistent with a maximum biocontainment facility.

Partially destroyed during the air war in Jan 1991. The Iraqui's destroyed it further prior to the first UNSCOM inspections in Aug 1991.

There were at least 6 other research labs throughout Iraq.



Al Hakam Single-Cell Protein Plant - Iraq's major facility for **production** of BW agents. It began mass-producing anthrax in 1989, and of the >8000 L produced, 6000 L was used to fill weapons, and the remainder was stored here.

This plant was destroyed in JUN 96.

We also know that the former Soviet Union had (and still has) a tremendous BW program that employed up to 55,000 people, in its heyday, at no fewer than 18 facilities under an agency known as Biopreparat.

Biopreparat still exists today, as a network of nominally civilian research institutes, created in 1973 as a cover for the existing military program.

In 1992, President Yeltsin promised to terminate the program, but this remains to be seen. It has certainly down-sized (now ~15,000 employees), but is still quite active.

In the 1995 Ebola epidemic in Zaire, Russia offered to send Ebola Immune Globulin to the stricken area. Clearly they have a very advanced BW program.

GSACEP © 2001

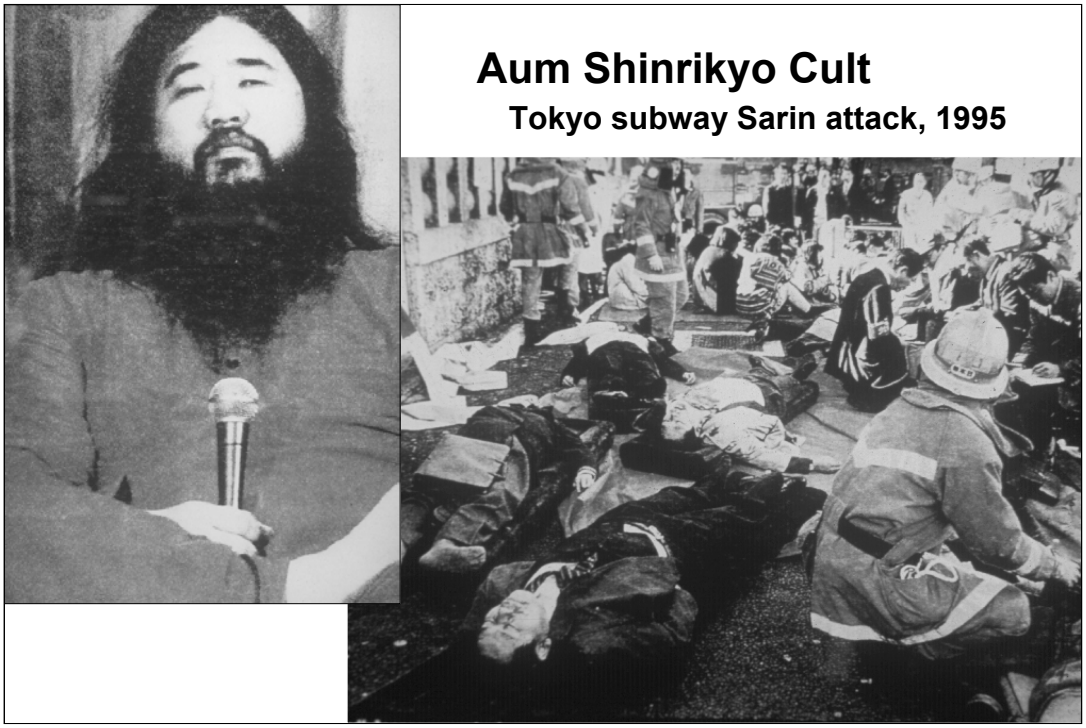
This facility at Obolensk in Russia was one of 6 research centers devoted exclusively to the study of plague. At its peak the US had a maximum of 3 scientists who focused their efforts on *Yersinia Pestis,* the bacterium that causes plague. Clearly the Soviets had a well developed BW weapons capability and had a major interest in Plague.

The former commander of USAMRIID, COL Franz, visited Russia several times in 96-97, and came back with pictures of a production facility that had 40 of these 64,000-liter fermenters that were dedicated only to the production of anthrax. They literally had ton quantities (reportedly ~30 metric tons) of dried anthrax spores stored and weaponized.

The concern today is, "what happened to that program and to many of the thousands of scientists who worked in that program?" With the economic situation in Russia today, there is certainly a concern that many of these people are going to work for countries that may support international terrorism.

Our awareness of this threat has increased, and although a lot is being done to prepare to respond to this threat, more needs to be done.

This is another Russian BW facility located in the city of Stepnogorsk and we could continue. All told at its peak the Soviets had as many as 40 separate facilities and 50,000 people devoted to BW weapons research and production. The big question is since the dissolution of the Soviet Union what happened to the left over weapons and where have all the scientists gone. We know that many of them have gone unpaid for months and the fear is they have left Russia and have gone to places such as Iraq, Iran, North Korea and other countries interested in developing this capability.

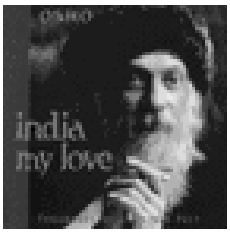


Switch gears from state- sponsored BW programs to self- financed terrorist organizations such as the Aum which was led by Shoko Asahara. The Tokyo sarin attack in 1995 is well known. It resulted in 11 deaths and over 5,000 injuries both physical and psychological. Hospitals and doctor's offices were overwhelmed with casualties. Due to the relative incompetence of the Aum Japan was lucky because the quantity of Sarin deployed could have resulted in hundreds of thousands of dead.

What is not well known is that on 8 prior occasions the Aum had attempted to disperse various quantities of either anthrax or bot toxin but in each attempt they were unsuccessful due to technical difficulties.

Rajneeshee Cult

- **Oregon, 1984**
- **Contaminated salad bars - *S. typhimurium***
- **751 cases of enteritis**



GSACEP © 2001

In the U.S., in 1984, the Rajneeshee Cult, in the Dalles, Oregon, contaminated local salad bars with Salmonella in an attempt to sway a local election by keeping voters at home.

Over 750 cases of enteritis resulted from this attack.

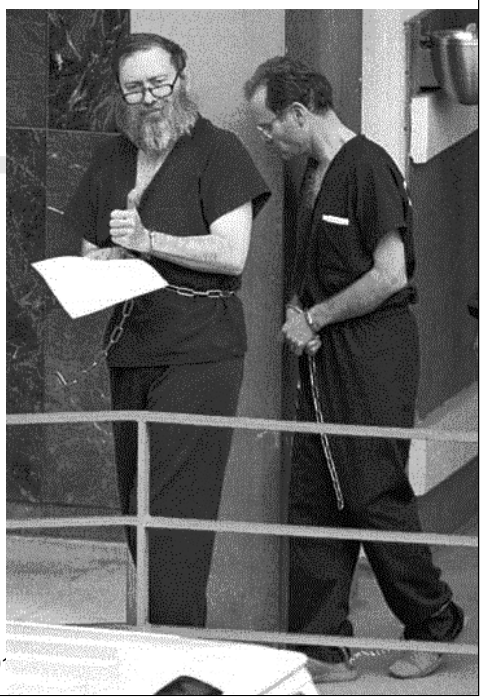
It's important to note that we did not even suspect a biologic attack until a cult member confessed the following year.

(They also imported over 2000 homeless people to vote in the election.)

Larry Wayne Harris

1995 possession of plague

1998 possession of anthrax



GSACEP © 200

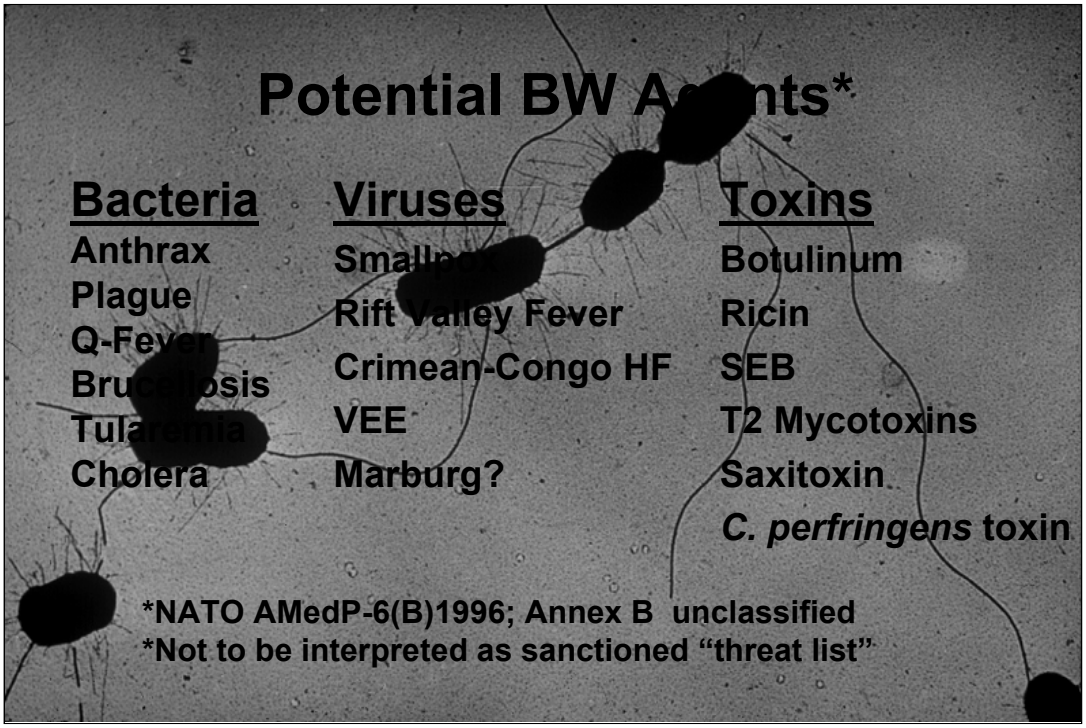
Most of the recent BW threats have turned out to be hoaxes, but there is always the possibility that someone is going to carry this out and do it right.

In 1995, this man, Larry Wayne Harris, was arrested and detained in OH for possessing plague bacteria (*Y. pestis*), but he was only convicted of mail fraud, because at the time there was no law that prohibited the possession of these types of organisms.

He was arrested again in '98 in Las Vegas, as he was thought to have possession of anthrax bacilli (it turned out that all he had was the vaccine strain).

Since the media coverage surrounding that incident, there have been a number of other hoaxes, and our FBI colleagues tell us that, in numerical terms, BW threats far exceed chemical threats in the recent past.

.



This list shows the most likely agents to be used in BW or BT. However, only a few of these would be useful as LARGE SCALE bioweapons. They need to be:

1. Inexpensive to acquire and produce in large quantities.
2. Stable in the environment and capable of aerosolization.
3. Reliably cause infection after exposure and infection must produce severe disease. Asymptomatic carriers are not useful to the bioweaponeer or terrorist.

Terrorists have a much larger list of agents to choose from. For example, we have documented attacks where salmonella or shigella has been used during terrorist incidents in the past 15 years right here in the US. However, these agents are unlikely to be of high value in a battle field scenario. Other agents with high fatality or great ability to incapacitate the enemy would probably be more useful to the battlefield commander.

Lethal vs. Incapacitating Agents

Lethal	**Incapacitating**
– Anthrax	**– Q fever**
– Tularemia	**– SEB**
– Plague	**– VEE**

Incapacitating agents may be more effective –

- **Unit unable to perform mission**
- **Casualties consume scarce medical and evacuation assets**

GSACEP © 2001

Some of these agents such as anthrax and plague, are lethal (high CFR), while some are only incapacitating, such as Q fever and SEB.

Incapacitating agents may be more effective in some situations, due to the demand on the medical and evacuation infrastructure, or due to the panic in the civilian population.

For these reasons, the old U.S. offensive program focused on incapacitating agents.

Destroyed U.S. Biological Warfare Agents

Lethal

- ***B. anthracis***
- **Botulinum toxins**
- ***F. tularensis***

Anticrop

- **wheat stem rust**
- **rye stem rust**
- **rice blast**

Incapacitating

- ***Brucella suis***
- **VEE virus**
- **SEB**
- **Q fever agent**

GSAC

This is the list of agents the US was most interested in when we had an offensive BW weapons program in place from 1943-1969. Note we also had an interest in anti-crop weapons.

Soviet BW Priorities

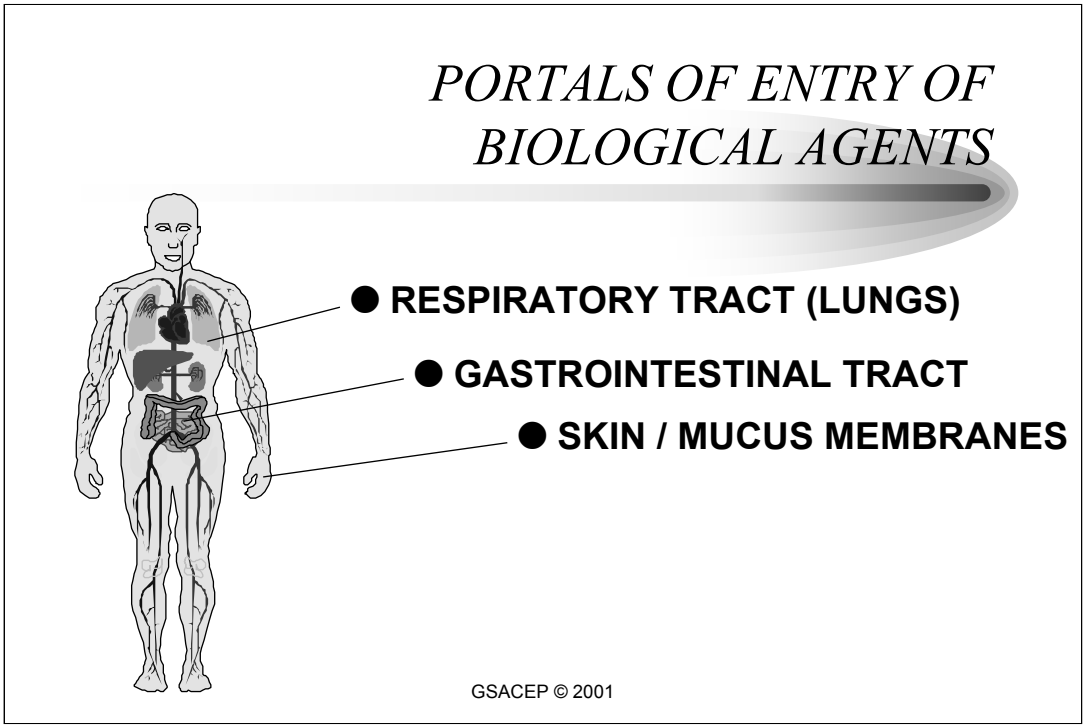
"Agents Likely to be Used"

Smallpox	**26**
Plague	**23**
Anthrax	**21**
Botulism	**21**
VEE	**20**
Tularemia	**20**
Q Fever	**20**
Marburg	**18**
Influenza	**17**
Melioidosis	**17**
Typhus	**15**

Vorobjev, A., et.al., "Criterion Rating" as a Measure of Probable Use of Bioagents as Biological Weapons, International Symposium, Severe Infection Diseases, Kirov, June 1997

GSACEP © 2001

This is the Soviet list of best candidates for BW weapons. They preferred the lethal agents and developed an elaborate point scoring system for determining what made a good biological weapon. As you can see the first 2 weapons were small pox and plague, both of which are highly lethal as well as contagious.



There are various routes of exposure, but inhalation is the primary one we worry about with BW agents.

Intact skin is an excellent barrier against nearly all BW agents, but mucous membranes, the eyes and mouth, and breaks in the skin provide other portals of entry.

Of course, a terrorist could use the percutaneous route by injecting an agent.

Delivery Systems

- **Aerosol delivery: Optimal**
  - **Generation of particles 1-5 microns**
    - **Settle in lower respiratory tract**
    - **Not detectable by our senses**
  - **Larger - mucocilliary clearance**
  - **Smaller - exhaled**

- **Explosive munitions: Poor delivery**
  - **Heat, light from explosion inactivate agent**
  - **Inefficient production of particles of 1-5 u size**

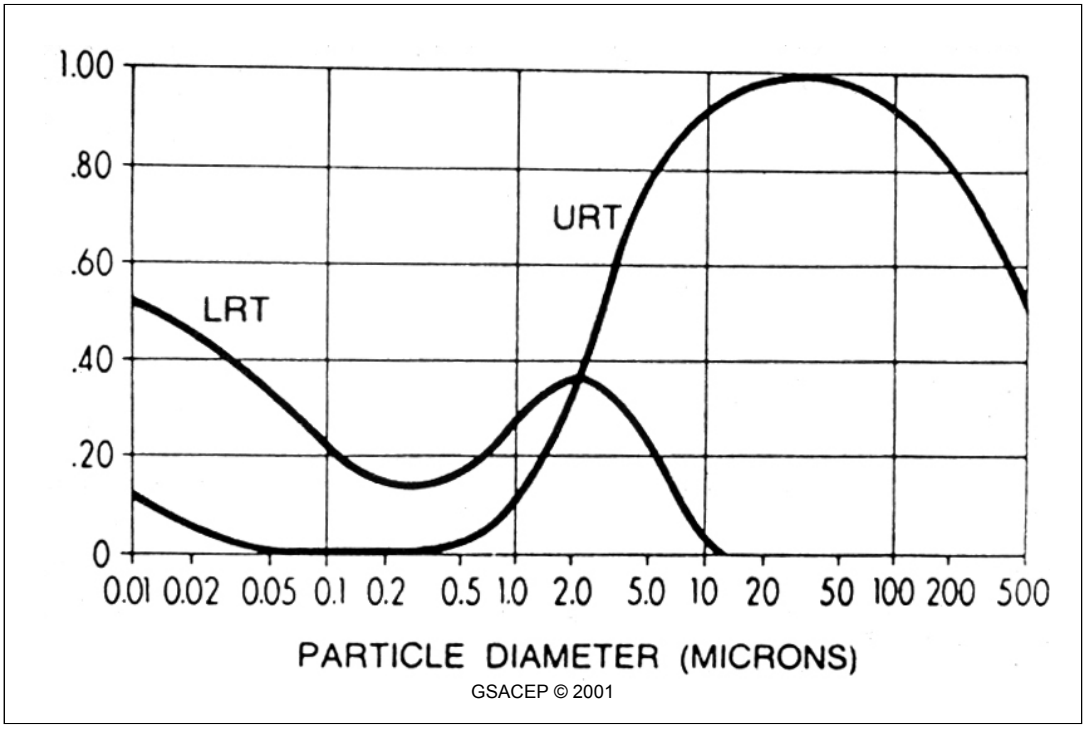
GSACEP © 2001

So to provide this inhalational exposure, the most effective means is by a respirable aerosol, and this means an aerosol with particles (or droplets) of about 1-5 microns in diameter.

- Particles larger than this tend to either settle-out rapidly in the environment or are trapped in the upper airways and subjected to mucocilliary clearance.
- Particles smaller than 1 micron tend to remain in the air, and, although they do reach the lower respiratory tree, they come right back out with the next exhalation.

These aerosols are invisible and odorless (unlike the chemical agents); they are not detectable by the human senses.

Explosive munitions are not a very effective delivery method because they don't produce many particles in this size range. Also, the explosion inactivates much of the agent.


1.00
.80
.60
.40
.20
0
URT
LRT
0.01 0.02 0.05 0.1 0.2 0.5 1.0 2.0 5.0 10 20 50 100 200 500
PARTICLE DIAMETER (MICRONS)
GSACEP © 2001

The Ag Pilatus Porter

Any Pilatus Porter can be converted to an Ag version and re-standardized by the operator within a few hours. Two versions are available:

Integral Tank

installed in the cabin-compartment. Capacity 1125 liters (305 US Gal) stainless steel.

Pump SIMPLEX with impellers.

Spray boom for 62 nozzles or 2 to 6 MICRONAIRS.

Operation ranges from ULV to HV depending on equipment.

Self-contained

Underwing spray pod MICRONAIR.

2 pods fixed on underwing-hard points. Capacity 189 liters (50 US Gal) each.

The atomizers MICRONAIR AU 4000 have a variable output of 0–30 liters/min. (0–8 US Gal) each.

EP © 2001

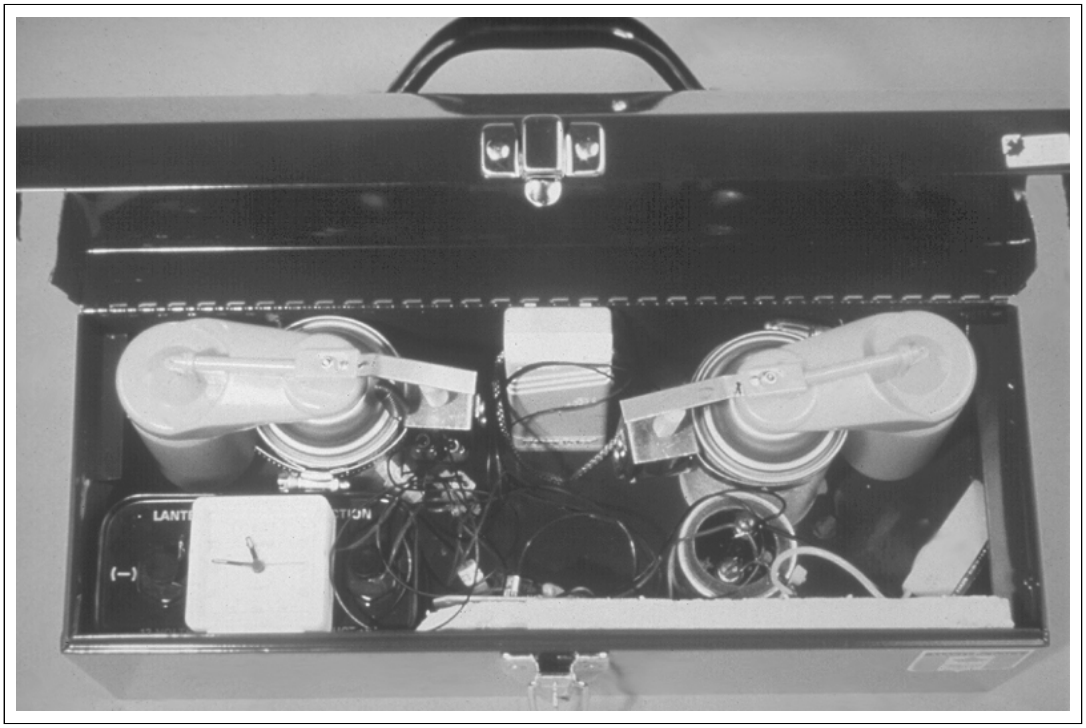
Example of a commercially available agricultural sprayer capable of delivering a respirable aerosol in the 1-5 micron range. This device would require few modifications to effectively deliver a biological weapon.

Another example is this truck-mounted insecticide sprayer, which can be easily modified to produce a biologic aerosol.

This is similar to truck-mounted devices that the Iraqis bought from the Italians just prior to the Gulf War.

Using a device like this in the right weather conditions...

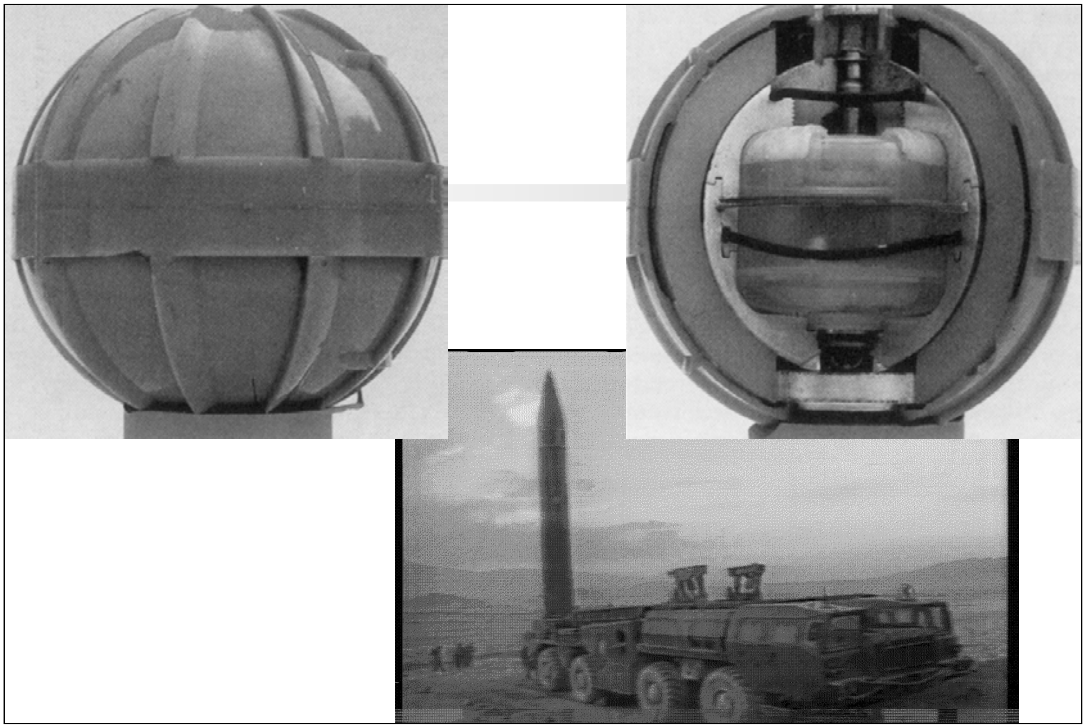
...(inversion-type air layer, where the clouds stay close to the ground), someone could create a big invisible aerosol cloud (unlike this smoke cloud, which is highly visible), that would hug the ground and spread out 20-30 km or more for a point source, even further if the device is vehicle–mounted and run along a road, creating a line source.



Biologic agents can also be put in smaller devices, such as this modified toolbox with a battery powered sprayer.

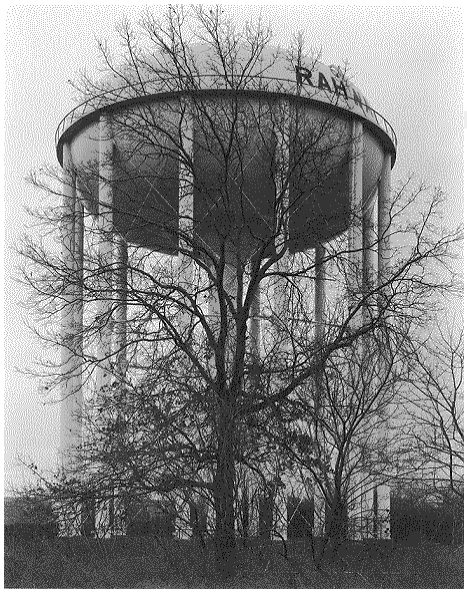
This could be carried just about anywhere. It could be placed at the air intake of a building, or in a shopping mall or subway, and release the aerosol covertly, without creating any signature or general alarm.

This device, by the way, was built by one of our Technical Escort Unit soldiers for a recent exercise. (I'm glad he's on our side.)



Biologic agents can also be disseminated using aerosols contained in bomblets that can be released from missiles, such as this SCUD-D, which can carry 2-3000 bomblets.

These would be released at altitude and drop on the target area, creating multiple point sources for biologic agent release.



GSACEP © 2001

Exposure to biologic agents can also occur through ingestion, from food or water supplies.

It's often said that it would be possible for a terrorist group to put a biologic agent into the water supply of a city or military compound and cause death or disease in the people drinking that water.

This is possible, but it is not as easy as it might sound.

The water supply to a city is usually large enough that the dilution effect alone would be substantial, and literally **ton** quantities of the agent would have to be dumped into the water supply for it to have any effect downstream.

Water Purification Methods

- **Coagulation / Flocculation not effective for ricin, T-2 mycotoxins or saxitoxin**
- **Chlorine (5 mg/l; 5 ppm) for 30 min inactivates botulinum, but not ricin, T-2 mycotoxins or saxitoxin**
- **Reverse osmosis systems effective vs. ricin, 2 mycotoxins, saxitoxin. (Probably effective vs. botulinum toxin and SEB but not tested)**

GSACEP © 2001

Also, because of the chlorination of industrial and municipal water supplies, many of the agents would be inactivated.

Chlorine, for instance, at 5ppm, destroys bacterial agents and can also destroy botulinum toxins.

Reverse osmosis is effective against all agents tested. Tested agents did not include Bot or SEB, but these are larger molecules (than Saxitoxin, for ex, which is ~300 MW), and would certainly remove these.

Ingestion of BW agents in **food** can also be a risk.

In a field situation, access to food supplies should be controlled and food sources should be known, not only to reduce the chances of **BW**–caused disease, but also to reduce the risk of **endemic** disease.

Dermal Exposure

- **Intact skin provides excellent barrier vs. BW agents (exception: mycotoxins)**
- **Mucous membranes, abrasions or other lesions can provide portal of entry**
- **Vector-borne delivery (unlikely)**
- **Injection (assassination)**

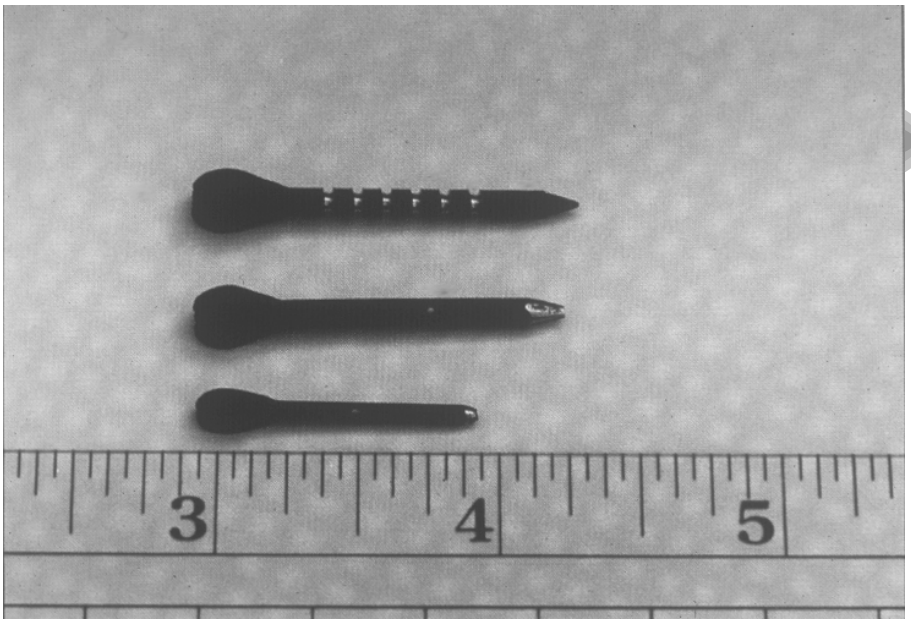
GSACEP © 2001

Dermal exposure to BW agents is another potential route of entry, but intact skin protects against most of the BW agents (T-2 mycotoxin is one exception).

Some parts of the body, however, such as the mucous membranes of the mouth and the conjunctiva, need to be protected because certain BW agents can be absorbed at these sites (and cause disease as readily as if they were ingested or inhaled).

A good example is a hemorrhagic fever virus such as Ebola, which, if present on the conjunctival sac of primates, will kill them just as rapidly as if it had been injected or ingested.

Its important to remember that, if there's an intact integument, and the airway and mucous membranes are protected, then we're pretty well protected against nearly all of the BW agents.



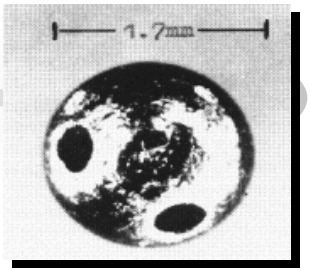
GSACEP © 2001

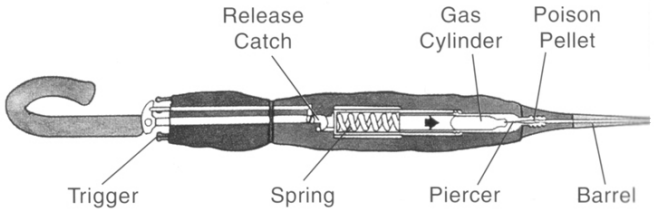
These flechettes were designed to be used with either chemical or biologic agent, (either wet or dry) which would fill the grooves or drill-holes.

Although outlawed by the BWC, an adversary might ignore such restrictions, as has occurred in the past.

Markov Assasination

- **London, 1978**
- **Developed by Soviet KGB**
- **Ricin (castor bean toxin)**
- **Used in at least 6 other assassinations**





GSACEP © 2001

This is the delivery device used in the 1978 assassination of the Bulgarian exile Gorgi Markov in London.

It was developed by the KGB, and deployed by the Bulgarian Secret Service, who covertly injected Mr. Markov with a tiny pellet (the size of the head of a pin) which had two reservoirs drilled into it containing ricin, the castor bean toxin.

The reservoirs were covered with a wax designed to melt at body temperature, and the pellet was injected into the back of his thigh as he was waiting for a bus.

Ricin inhibits protein synthesis, and 3 days later, he died from multiple organ failure.

This technique was apparently used in at least 6 other assassinations in the late 70's.

Acquisition of Etiologic Agents

- **Field samples or clinical specimens**
- **Commercial biological supply houses**
- **Multiple culture collections**
- **Universities**
- **Foreign laboratories**

GSACEP © 2(

Unfortunately, it's not difficult for terrorists to get their hands on these agents.

Many are available from commercial supply houses or can be harvested from field samples, or even clinical samples.

Anthrax, for example, occurs naturally in animal populations throughout the world (incl SW U.S.).

It would not be difficult to harvest Bacillus anthracis from a dead animal in areas where this disease is endemic.

Sources of Agents for Terrorism Use

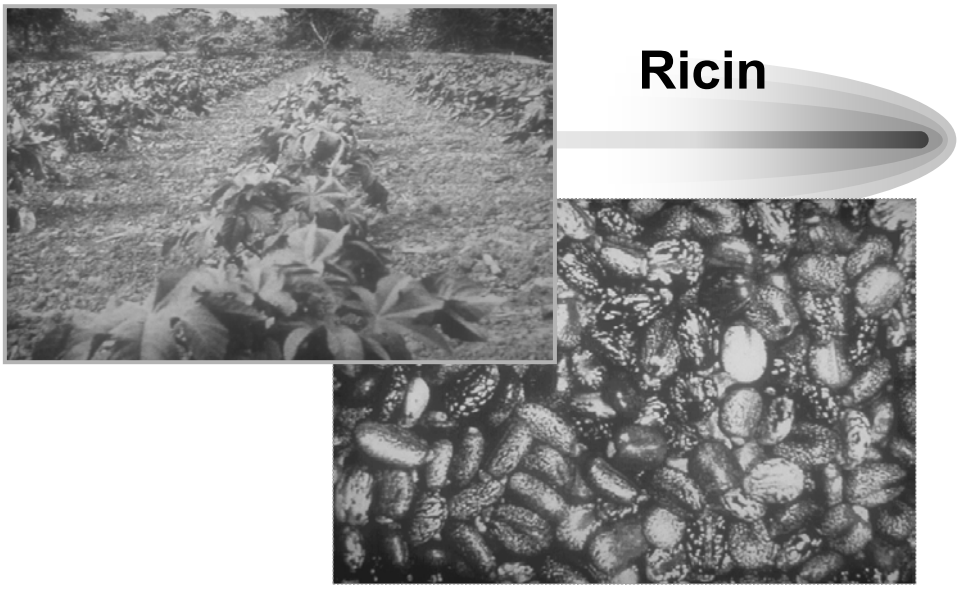
- **World Directory of Collections of Cultures and Microorganisms**
  - 453 worldwide repositories in 67 nations
  - 54 ship/sell anthrax
  - 18 ship/sell plague
- **International black-market sales associated with governmental programs**

GSACEP © 2001

And ATCC is not the only culture collection supply house out there.

There are over 450 similar enterprises throughout the world, and 54 of them sell anthrax.

Black-market sales of BW agents is another major concern.



Over a million tons of castor beans are processed annually worldwide.

The waste mash from this is 5% RICIN.

Although this is not an extremely toxic agent, its so ubiquitous that it's a significant risk.

This slide shows two 1,450 liter fermenters at the Al Hakam Single-Cell Protein Plant in Iraq.

They were used to produce botulinum toxin prior to the war.

These same fermenters could be used to make vaccines, Antibiotics, even beer; and this illustrates the concept of "dual use" technology.

Ex - Tetanus toxoid vaccine - to produce the vaccine:

•lg fermenter (like this),

•fill w/ culture media,

•allow the bacteria to produce toxin,

•then chemically inactivate the toxin to produce toxoid vaccine.

Take away the last step, and rather than a vaccine, you have a biologic weapon.

Clearly, the technology needed to produce BW agents is quite simple - easily within the grasp of almost any country or terrorist organization.

This also illustrates the difficulty we have with enforcement of the BWC.

Low Cost

Costs* of producing mass casualties per square kilometer:

Conventional	**$2000**
Nuclear	**800**
Chemical	**600**
Biological	**1**

*** Chemical-Biological Expert Panel, UN, 1969**

GSACEP © 2001

Biologic weapons are sometimes called the poor man's nuclear bomb, and this chart demonstrates this.

A U.N. panel estimated the relative cost of these WMD's, and showed that biologic weapons are far cheaper than any other class of wpn in terms of producing mass casualties per square km: 1$ compared to $600 for CW, $800 for Nuclear, and $2000/km for Conventional weapons.

These figures are in 1960's dollars, but the relative ratio probably remains about the same today.

Impact of BW on Healthcare System

- **Terror in the affected population and in the medical care system**
- **Overwhelming numbers, ICU demands, or special medication needs**
- **Need for personal protection in medical care, clinical lab, autopsy suites**
- **Problems with handling remains**

GSACEP © 2001

These weapons could easily overwhelm our medical care capabilities. We might need large numbers of beds, a lot of intensive care capability, special medications, and proper protective equipment for medical personnel. We might also have problems handling the remains of people who have died from these agents.

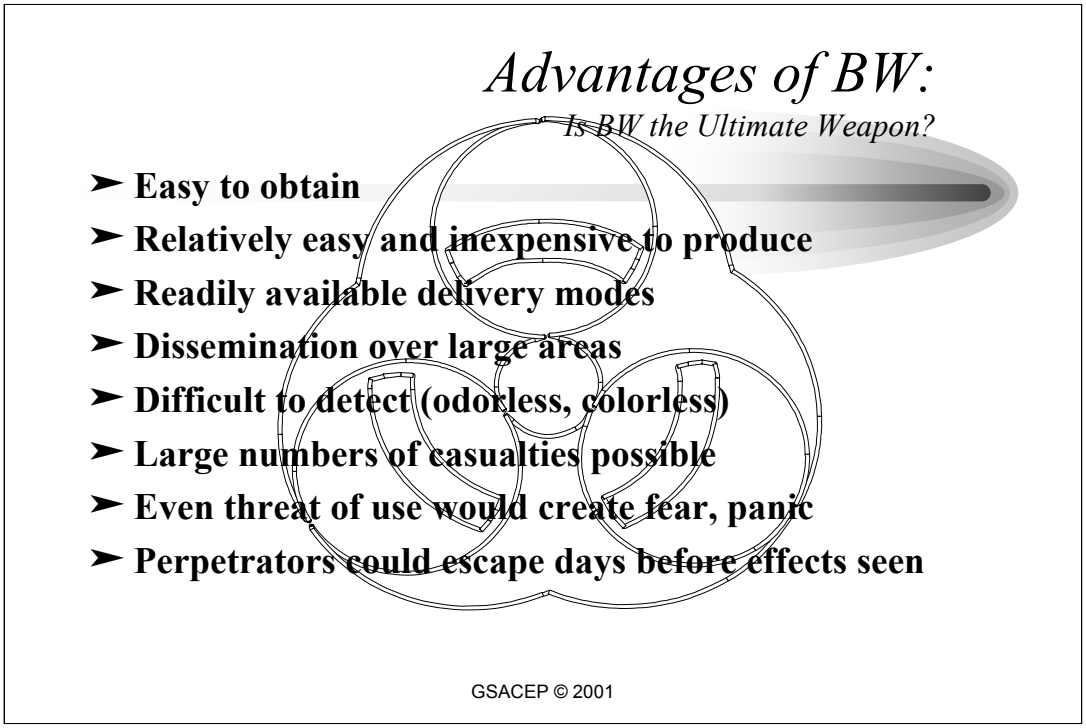
To highlight how these things can overwhelm our response capability, USAMRIID simulated a terrorist attack scenario in Denver in 1997, where anthrax was aerosolized into a shopping mall ventilation system.

We assumed 9k out of the 10k people in the mall were exposed and infected with the organism. We also assumed that the terrorists told us at 24 hrs what they had done, so it gave us a jump on treating some of these people.

(Remember that these agents can be very hard to detect.) If we were able to start 90% of the exposed population on Antibiotics by the end of day 2, we would still have about half of the exposed people being hospitalized.

We would need ~3k ICU beds and 2,600 ventilators.

In a large city like Denver, we would have only 200-300 ICU beds available. Clearly, even a small-scale attack could overwhelm the medical care capability of a large city.



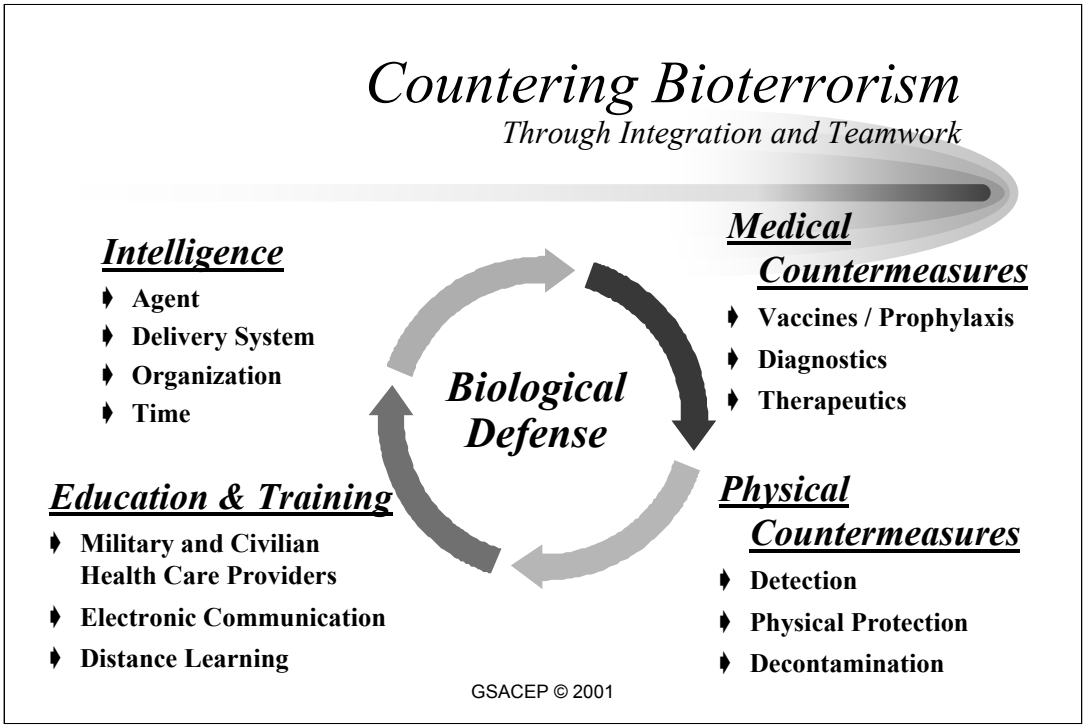
So, is a biologic agent the ultimate weapon? Well, I've touched on most of these points... (easy to get hold of, inexpensive, hard to detect, can be disseminated over long distances, and even the threat of its use can create fear and panic. It can rapidly overwhelm medical resources)

It's also worth noting that, since all these agents have incubation times (of hours to days), the perpetrators could escape maybe days before effects are seen.

For all these reasons, it is an ideal terrorist weapon, and could be an ideal weapon in some military scenarios as well.

Use of endemic agent may cause confusion (BW vs. natural epidemic?)

Potential for secondary/tertiary transmission



Biolologic defense is a layered defense system, consisting of accurate threat **intelligence**, **physical countermeasures** (such as detection, personal protection, decontamination procedures), **medical countermeasures** (such as vaccines, oral chemoprophylaxis, diagnostics & therapeutics), and **education & training** (like what we're doing here today).

And I'll touch on each of these briefly.

Portal Shield

Portal Shield

This is one of several detection systems available to the US military. None are perfect and we have a lot of work to do in this area before we will reach a high level of confidence in these systems.

The Portal Shield works by continuously sampling ambient air at a rate of over 900 liters a minute. Particles in the 1-10 micron size are concentrated and once a certain threshold level is reached the particles are subjected to a series of 8 different “smart tickets” that can give a presumptive identification of a possible BW agent.

BIDS

GSACEP © 2001

Detection of biologic agents is significantly more problematic than detection of chemical agents.

This is the Biol Integrated Detection System, or BIDS. It was fielded in DS/DS, and it works by continuously sampling the air (through these stacks) and concentrating particles of the 1-5 micron range.

It then subjects them to analytical & Ab-based assays (which take about 30 minutes to run).

The original model could detect 4 different agents (anthrax, plague, Bot A, & SEB),…the improved version adds 3 more (brucellosis, tularemia, & ricin).

Since it takes about 30 min to run the assays, this needs to be placed at least a half hour up-wind of the troops you're trying to protect.

LRBSDS

The Long Range Biological Standoff Detection System (LRBSDS) uses **laser-induced fluorescence** to detect aerosol clouds w/ particles of the right size range, up to 30 km away - the improved version will be able to reach out to 100km. It can differentiate smoke, pollen, and pollution from BW aerosols.

Physical Protection

- **Currently fielded chemical masks protective only if properly fitted and in use at the time of exposure**
- **Surgical masks ineffective due to difficulty obtaining seal**
- **Add BDO for T-2 Mycotoxin**

GSACEP © 2001

✓ The standard chemical protective gear will protect against all BW threats. In fact for most BW agents standard hospital based precautions will probably be sufficient to protect against infection. There are a few exceptions which will be discussed.

Improvised Airways Protection for Toxin Aerosols

Airways Protection	*Time to Death*
➢**Ricin (large protein)**	
– Control Animals	48-72 hr (n-6)
– 1 Layer T-shirt	55, 70 hr and 6 days
– 1 Layer Cravat	72 & 72 hr; One Survived
– 2 Layer T-shirt	All Survived (n=3)
– 2 Layer Cravat	All Survived (n=3)
➢**Saxitoxin (low molecular weight)**	
– Control Animals	6-10 min (n=4)
– 2 Layer T-shirt	All Survived (n=4)
– 2 Layer Cravat	All Survived (n=4)

Creasia, Donald A., Personal Communication, 1995.

GSACEP © 2001

USAMRIID

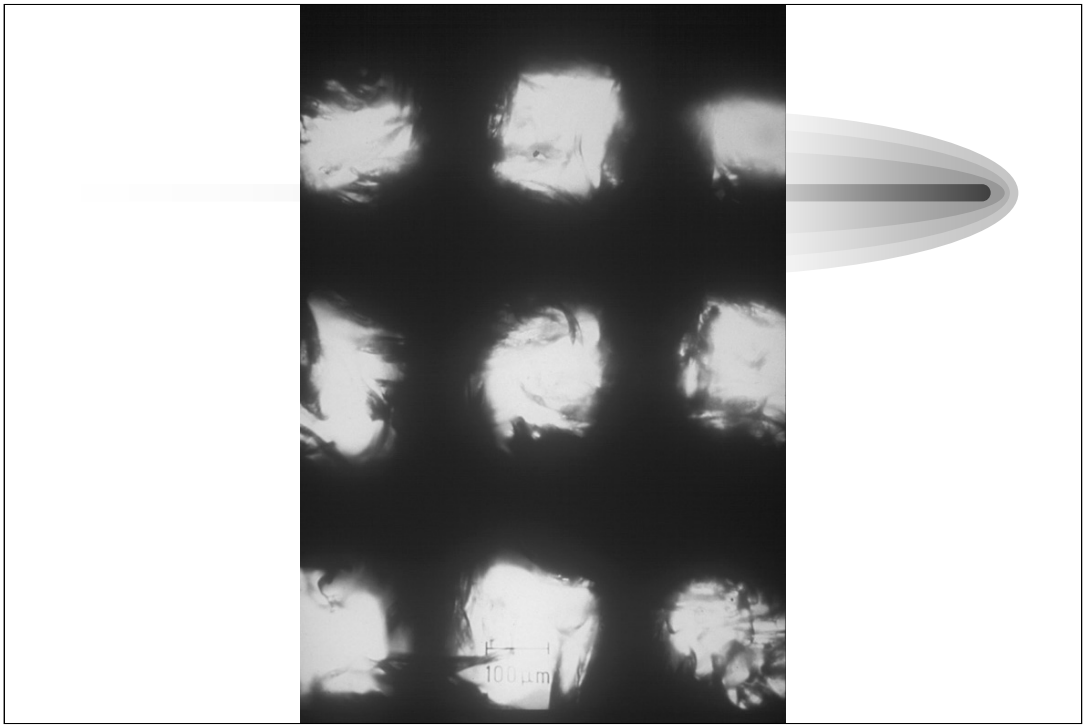
This study was done back in '95 at USAMRIID, to demonstrate the effectiveness of improvised methods of protecting airways from biological aerosols.

Mice were exposed to 5-10 LD_{50}s of aerosolized toxin over a period of 10 minutes.

Note that a double-layer T-shirt or cravat protected the animals completely.

We're not advocating throwing away your gas mask and depending on your T-shirt, but, for short periods, you might be able to use something like this in an emergency if you don't have your mask (perhaps to get out of an area that's under attack)

Note that this technique even protected against a very small particle such as saxitoxin which is far smaller than the optimally sized 1-5 micron particle seen in respirable BW weapon aerosols.



Micrograph of a T-shirt, showing the pores.

Note the 10 micron scale in the lower center pore; it shows that the pores are larger than 10 microns, but still filter out some portion of the aerosol.

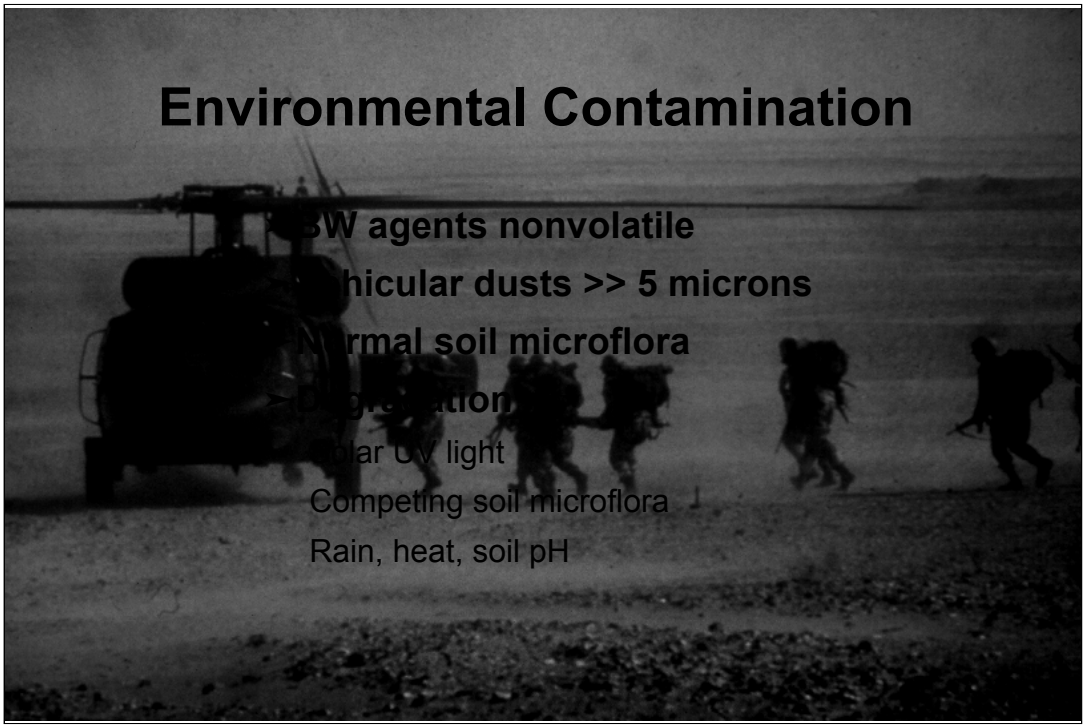
And when you combine 2 layers, you can filter out a significant portion of an aerosol.

Patient Decontamination

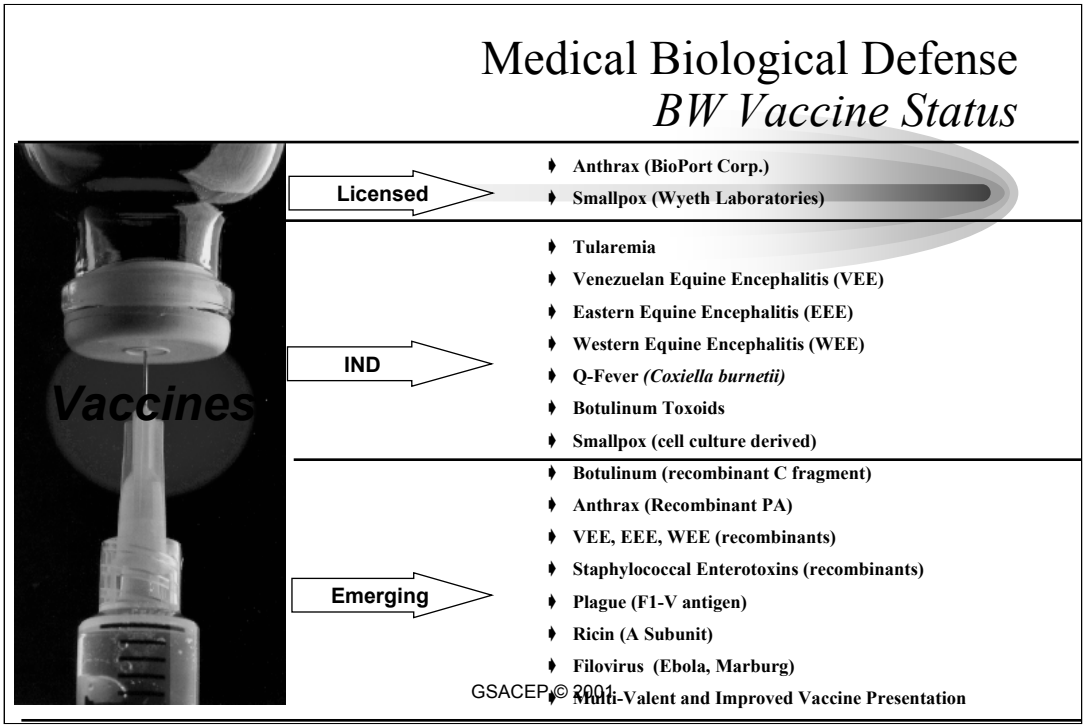
- Intact skin is an effective barrier for BW agents (except mycotoxins)
- Soap and water decontamination adequate for BW agents
- If skin grossly contaminated, wash contaminated areas with a 1:10 dilution household bleach solution (contact time 10-15 minutes)

GSACEP © 2001

Exposure to biological weapons does not generally require the same sort of vigorous decontamination procedures employed with chemical weapons exposure. Most BW's are not dermally active and have incubation periods of at least 12 hours or more likely several days. During this period most patients will have removed their clothes and have showered several times removing most of any gross contaminant even if it was ever present. In addition even the hardy anthrax spore will rapidly degrade to harmless state when exposed to direct sunlight and air.



Again, in contrast to chemical agents the BW agents are much more likely to degrade rapidly in the environment than the more resistant chemical compounds. The problem of reaerosolization of BW particles is probably of only minor concern. These particles possess an electrostatic charge and rapidly combine with dust and other small particles causing them to settle out onto the ground.



Immunization is the preventive method of choice for many diseases. It's generally the most cost-effective, and most of the research at USAMRIID is directed toward vaccine development.

This slide shows some of the vaccines we have available, either licensed, or investigational, as well as some that are in the pipeline.

Note that the Greer Plague vaccine (no longer availalble) was never really a BW vaccine, because it didn't protect against an inhalational exposure. A new recombinant subunit vaccine (containing F1 & V antigens) protected mice for a year against an inhalational challenge, but its still in the pre-clinical phase.

Also, a human cell culture derived smallpox vaccine is about to start clinical trials at USAMRIID. This is important, since no one is making any more vaccinia, and the current stores are very limited (6-7,000 doses at CDC)

Also, there are several recombinant vaccines listed here, that are being developed to reduce the side effect rates seen with the current vaccines.

Multi-Agent Vaccine for Biological Threat Agents

- Naked DNA Vaccines
- Replicon Vaccines

- **Fewer Immunizations**
- **Lower Cost**
- **Can Custom Design**
- **Enhanced Operational Readiness**

GSACEP © 2001

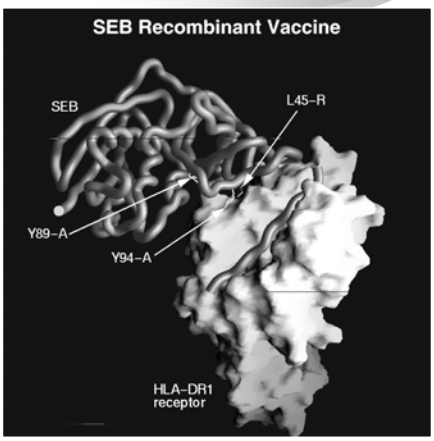
Two other areas of intensive research at USAMRIID are in replicons and DNA vaccines.

Replicons are attenuated viral particles with the genes from some target antigen inserted. They replicate within the host cells, elaborate the antigen, and induce immunity.

DNA vaccines are hoped to combine genes from several different antigens into one naked DNA genome, and they elicit an immune response against those target antigens. The hope is that one day we will be able to give many immunizations with one DNA vaccine.

USAMRIID
Bioengineered Vaccine Candidates

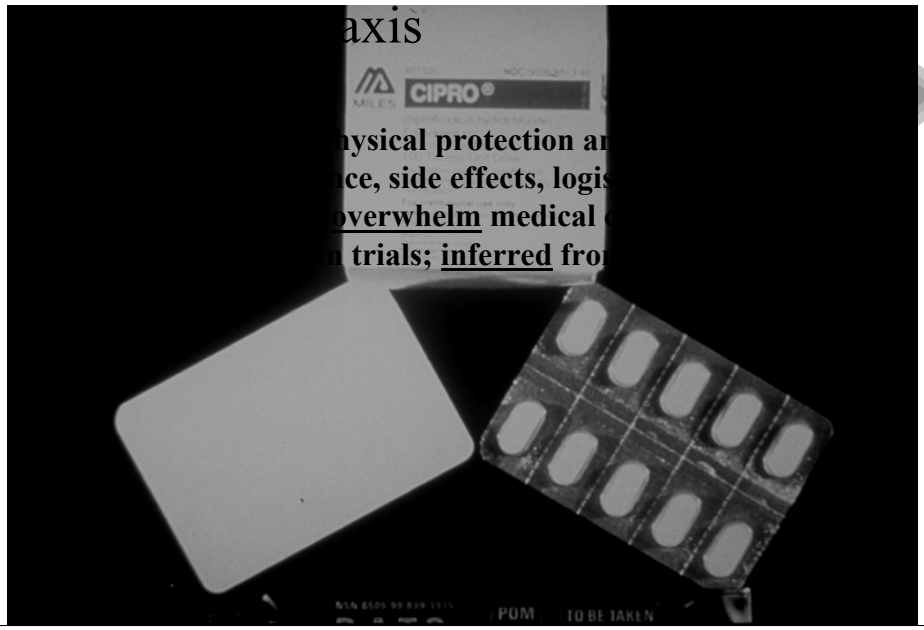
- **Staphylococcal enterotoxins**
- **Botulinum toxins**
- **Anthrax**
- **Plague**
- **Alphaviruses**
  - **–VEE, WEE, and EEE**



GSACEP © 2001

At USAMRIID, we're also using molecular modeling to engineer conformationally- correct recombinant antigens.

This model of the SEB recombinant vaccine was designed with the least amount of structural alteration to maximize **conformation-dependent antigenicity**. It is scheduled for product transition in 4QFY99.



We can also provide prophylaxis some of these agents, such as anthrax, post-exposure. Anthrax-exposed individuals can be given Antibiotics and immunized over the course of the next 4 weeks, and they will be protected.

In Desert Storm, U.S. forces stockpiled 30 million doses of Cipro (ciprofloxacin) for this purpose.

Prophylaxis, however, is not without problems: compliance, side effects of the medications, and logistics on the battlefield.

Also, agent exposures could overwhelm medical countermeasures (if the exposure is of great enough magnitude),

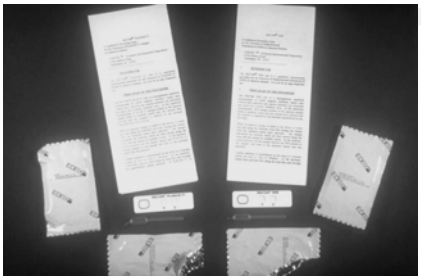
so, prophylaxis should only be considered a secondary adjunct to physical protection and vaccination.

[Chemoprophylaxis means giving Antibiotics to prevent an incubating infection from becoming a full-blown disease.]

[and these CM's are not evaluated in humans; they're inferred from animal data, since we can't ethically expose humans to live agents]

Diagnostics

Rapid and Confirmatory



- **Development and evaluation of diagnostic assays**
- **Technologies field-tested with Theater Area Medical Laboratory (TAML)**
- **DOD Reference laboratory for biological agent confirmation**

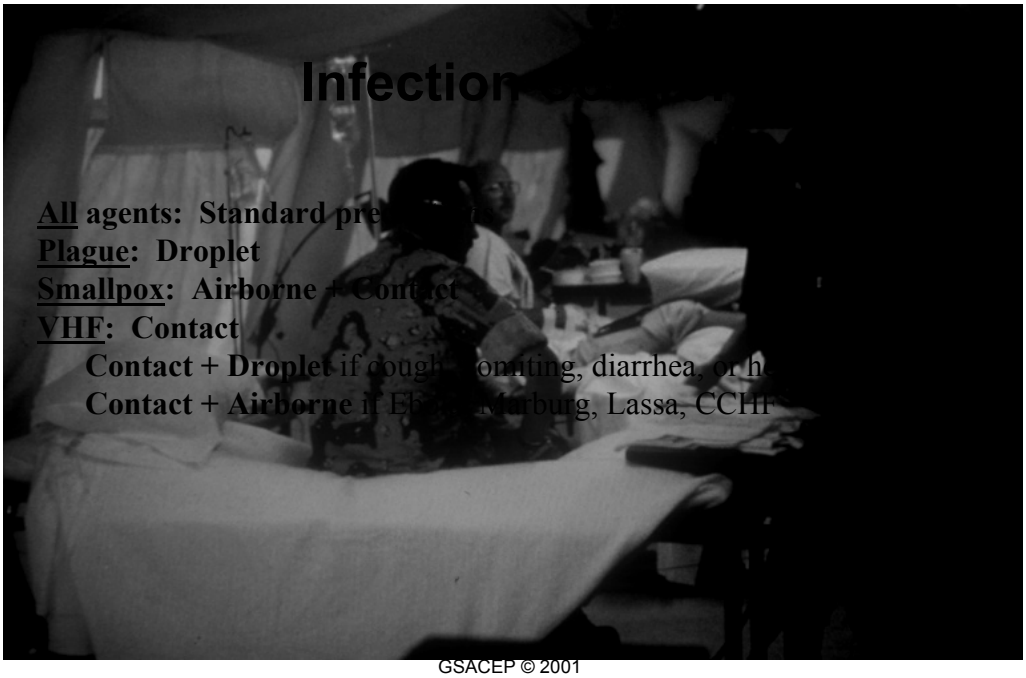
GSACEP © 2001

Clinical Diagnosis is often difficult for BW agents, especially during the prodrome or early illness, as many of these disease's present w/ nonspecific Symptoms (F/C/malaise/N/V).

Deployable diagnostic kits have been developed for BW threat agents as well as endemic pathogens. Antibody-based assays were deployed during Desert Storm, which can identify agents in 30 min.

A gene amplification (PCR) assay was developed at RIID that can fit in a briefcase (shown here on the left); the largest part of it is the notebook computer, so we expect to have a smaller device very soon.

In fact, the device on the right is a prototype hand-held PCR device that is in advanced development at USAMRIID.



Risks to other patients, or to healthcare providers caring for pts who have been exposed to a BW agent is agent-dependent.

In general, the standard precautions we use in the normal everyday medical care environment will provide adequate protection against most of the BW agents.

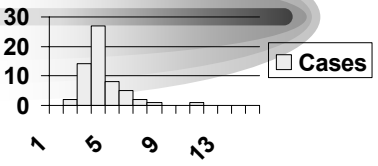
Fortunately, only a few agents can spread person-to-person, and would require personal protection over and above the standard precautions.

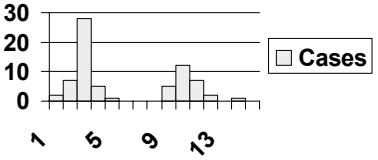
These are: smallpox, pneumonic plague, and possibly the VHFs (depending on the clinical syndrome). For the remainder, simple barrier protection is all you need.

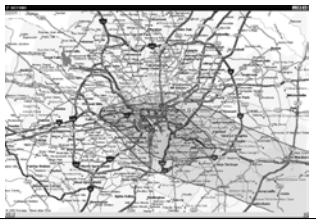
For an agent like smallpox, you may have to upgrade your protection to a filtered respirator, or set up a “smallpox” tent for quarantine of these patients away from the rest of the MTF.

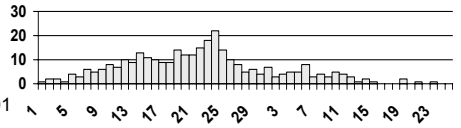
BW Attack or Naturally Occurring Disease?

- **Higher morbidity & mortality than normally expected for a disease**
- **High attack rates among exposed**
- **Disease outside normal geographic area**
- **Distinctive downwind pattern - plume**









GSACEP © 2001

In order to diagnose a BW exposure, you have to remember a few important points.

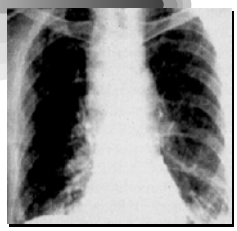
Environmental detectors may not be sufficient to alert you, and the early symptoms of BW agents (are nonspecific and) can look like symptoms of normal endemic diseases.

However, there are some factors that may lead you to believe that you've been attacked with a BW agent,

and these include: the occurrence of large numbers of acutely ill pts (you'd see a very steep epidemic curve), a high attack rate, or an illness far outside of its normal geographic distribution.

Also look for an unusual local distribution of disease, such as a distinctive downwind pattern reflecting a cloud plume, or …

BW Attack or Naturally Occurring Disease?



- **Multiple simultaneous epidemics**
- **Unusual presentation of a disease**
  - **respiratory instead of cutaneous**
- **Dead animals**
  - **multiple species; reverse spread**
- **Direct evidence - discovery of a potential delivery device, suspicious activity, munitions**

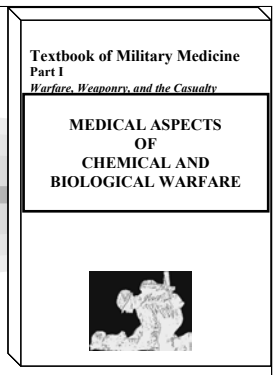
GSACEP © 2001

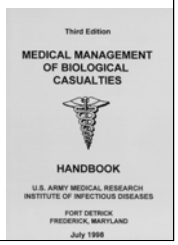
…multiple simultaneous epidemics, or an unexplained number of dead or sick animals.

Of course, there could be direct evidence, such as finding a spray device or bomblet, and in the terrorist scenario, they announce their attack 50% of the time (according to our FBI colleagues).

BW Resources

- **Internet:**
  - **www.usamriid.army.mil**
  - **www.nbc-med.org**
- **Toll-free number: 1-888-USA-RIID**
- **MCBC, FCBC Courses (in-house, exportable)**
- **Texts (TMM, "Blue Book," JAMA, 6 Aug 97)**
- **CD ROM**





GSACEP © 2001

I would like to mention some of the other resources available for further information (or to answer your questions) regarding this subject.

Two excellent inter-net sites are: the USAMRIID home-page (www.usamriid.army.mil.), and the Surgeon General's NBC home-page (www.nbc-med.org).

Also, for more urgent questions, USAMRIID has a toll-free number : 1-888-USA-RIID (888-872-7443) [remember this is 888, not 800 We host several different courses (geared toward different audiences from the field medic to the physician) [call Rosalee Holland at 410-436-2230, D-584]

And our interactive satellite course will occur again this SEP; videos of last year's show are still available.

Our "Blue Books" are available upon request, and our CD-ROM will hit the streets this year (that should be very soon).

Operational Medicine Division

Distance Learning Program

3rd annual "Medical Response to Biological Warfare and Terrorism" broadcast:

- **➢18,716 participants**
- **➢$4.29/CME credit hour**

GSACEP © 2001

I would like to mention before closing that we are working on a number of ways to bring this information to you in the field.

Last year, USAMRIID held its 3rd satellite distance learning pgm, which was broadcast from the FDA studio in Rockville, MD.

This SEP, we are going to do this again. This is a 12-hr, 3-afternoon, interactive pgm in which we broadcast live scenario-based training for education of BW defense.

Last year, we were able to reach over 18,000 healthcare providers in one 3-day period. That's more than we've reached in the entire history of our in-house course. This year we hope to reach more than twice that number of healthcare providers from both the military and civilian healthcare communities.

This is a very cost-effective program, as it cost only about $66 per student, and only about $5.50 per CME credit hour to produce.

595 sites with 18,167 participants worldwide

$66 per student

$5.50/CME credit hour (12)

$4.50/CNE credit hour(14.4)

Trained triservice and civilian healthcare providers, public health practitioners, first responders, and allied health professionals

Distributed 500+ videotape sets of 1997 broadcast to military medical facilities

Finalizing an educational CD-ROM for 2nd quarter FY99

Resource Telephone numbers

Summary

- **Biological warfare and terrorism are very real threats**
- **Mass casualties could result**
- **Medical defenses are available against several threat agents**
- **Suspect a biological attack in setting of mass casualties with a similar clinical syndrome**

GSACEP © 2001

USAMRIID

Emergency physicians are likely to see the first wave of casualties in a BW attack. Many patients will present with what looks like a non-specific respiratory infection or flu-like illness. You need to keep BW in the back of your mind, and have an increased index of suspicion that such an attack can occur.

If you think BW in your differential Dx, then you've bought time - and time may be critical in the response cycle.