# Civilian Biodefense

January 2000

JSR-99-105

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# REPORT DOCUMENTATION PAGE

Form Approved
OMB No 0704-0188



| 1. AGENCY USE ONLY (Leave blank) | 2. REPORT DATE | 3 REPORT TYPE AND DATES COVERED |
|---|---|---|
| | January 17, 2000 | |

**4. TITLE AND SUBTITLE**

Civilian Biodefense

**5. FUNDING NUMBERS**

13-988534-A4

**6. AUTHOR(S)**

S. Koon, et al.

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**

The MITRE Corporation
JASON Program Office
1820 Dolley Madison Blvd
McLean, Virginia 22102

**8. PERFORMING ORGANIZATION REPORT NUMBER**

JSR-99-105

**9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)**

Defense Advanced Research Projects Agency
3701 North Fairfax Drive
Arlington, Va. 22203-1714

**10 SPONSORING/MONITORING AGENCY REPORT NUMBER**

JSR-99-105

**11. SUPPLEMENTARY NOTES**

**12a. DISTRIBUTION/AVAILABILITY STATEMENT**

Distribution limited to US Government ~~Organizations~~ Agencies Only
PROPRIETARY INFORMATION APR 2000

**12b. DISTRIBUTION CODE**

Distribution Statement B

**13. ABSTRACT** *(Maximum 200 words)*

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In addition to the DARPA sponsorship, a part of this study was chartered by the CIA, whose organizations are interested in the signatures and collection possibilities of BW production facilities.

Our study focused on technical and organizational issues throught the entire civilian timeline.

| 14. SUBJECT TERMS | | | 15. NUMBER OF PAGES |
|---|---|---|---|
| | | | 16. PRICE CODE |
| 17. SECURITY CLASSIFICATION OF REPORT | 18. SECURITY CLASSIFICATION OF THIS PAGE | 19. SECURITY CLASSIFICATION OF ABSTRACT | 20 LIMITATION OF ABSTRACT |
| Unclassified | Unclassified | Unclassified | SAR |



17. SECURITY CLASSIFICATION OF REPORT | 18. SECURITY CLASSIFICATION OF THIS PAGE | 19. SECURITY CLASSIFICATION OF ABSTRACT

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# Civilian Biodefense

- Report Summary
- Annotations
- Appendices

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This document summarizes the results of a JASON study during the summer of 1999. It contains material in three forms:

1) The charts used to deliver the briefing summarizing the study

2) Annotations to the charts (such as this one) that capture, where required, the spoken words that go along with the chart.

3) Text appendices, referenced in the annotations, that offer supplementary or explanatory material.

# Briefing outline

- Study definition
- Technical topics
- Investment priorities and recommendations



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# Briefing outline

- Study definition
  - Study origin and scope
  - Four notional scenarios
  - Agricultural vulnerabilities
  - Framing the problem
- Technical topics
- Investment priorities and recommendations

*Civilian Biodefense*

The briefing is divided into three major sections.

I'll first talk about the definition of the study. Reviewing the origin and scope of the study. I'll then walk you through four notional scenarios that were useful in guiding our thinking While our observations and recommendations do not directly address these scenarios, they do vividly portray the threat and point out some common problems in biodefense. I also want to spend some time on agricultural vulnerabilities that became apparent to us in the course of the study, and then tell you how we've framed the biodefense problem.

The second section is a list of technical topics on which we have comments and recommendations.

Finally, I'll discuss what JASON believes to be priorities for the investment of government resources and offer some recommendations, primarily about government organization.

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# Study origin and scope

- DARPA Director asked for studies by JASON, DSRC, and ISAT on defense of *civilians* against bioweapons/bioterrorism
- CIA's Non-Proliferation Center and Clandestine MASINT Operations Center are interested in BW intelligence collection and signatures
- Scope from intelligence through preparations through event to response and attribution
- Focus on technical and organizational issues
- Four notional scenarios to focus thinking

*Civilian Biodefense*

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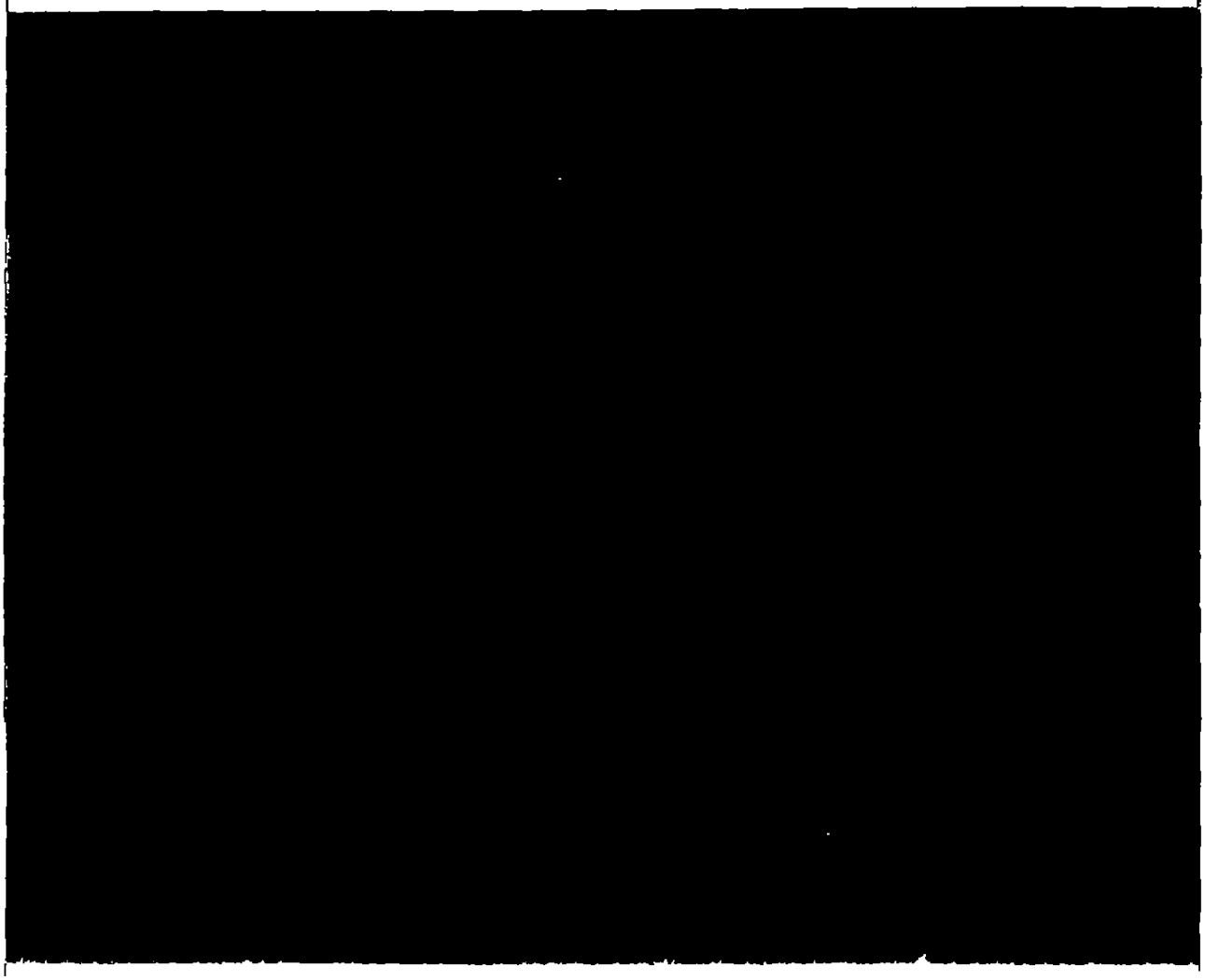
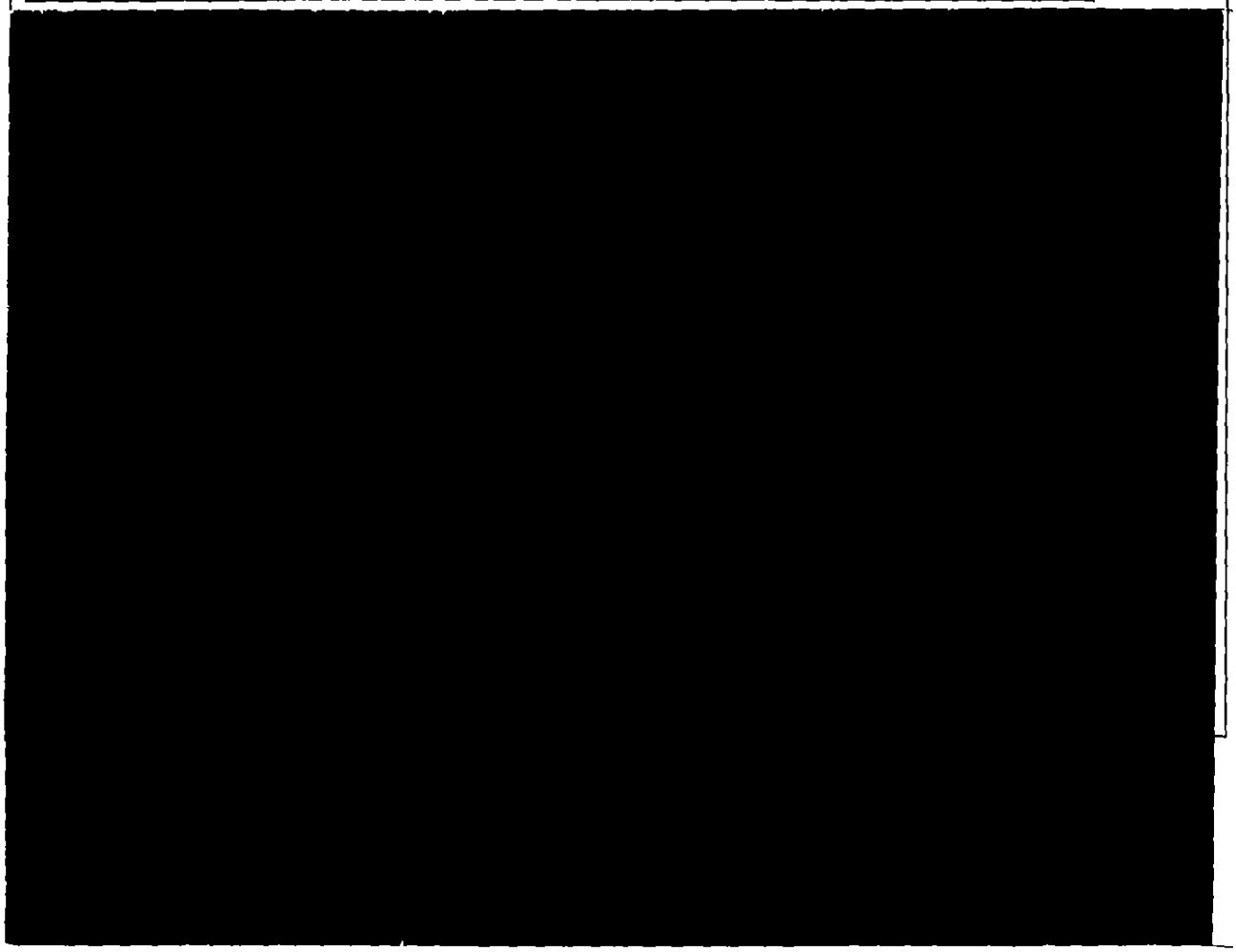
In addition to the DARPA sponsorship, a part of this study was chartered by the CIA, whose organizations are interested in the signatures and collection possibilities of BW production facilities.

Our study focused on technical and organizational issues throughout the entire civilian timeline. As noted before, four scenarios guided our thinking, and I would like to take you through them in turn.

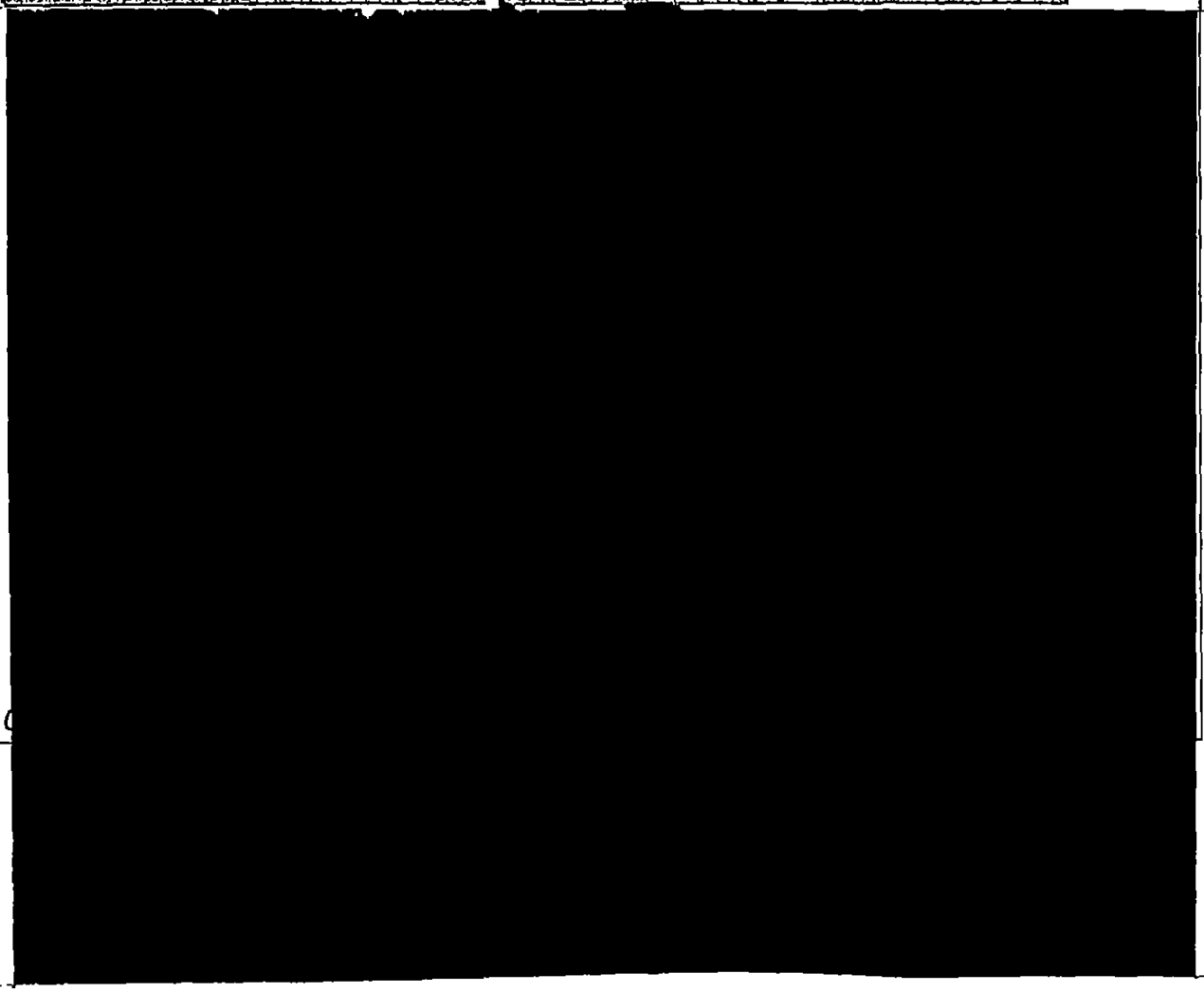
# BW scenario #1



# BW scenario #1



# BW scenario #2



# 1947 smallpox incident

- March 1: Man arrives NYC from Mexico
- March 5: Hospitalized with fever; dies March 10
- April 4: Smallpox diagnosed

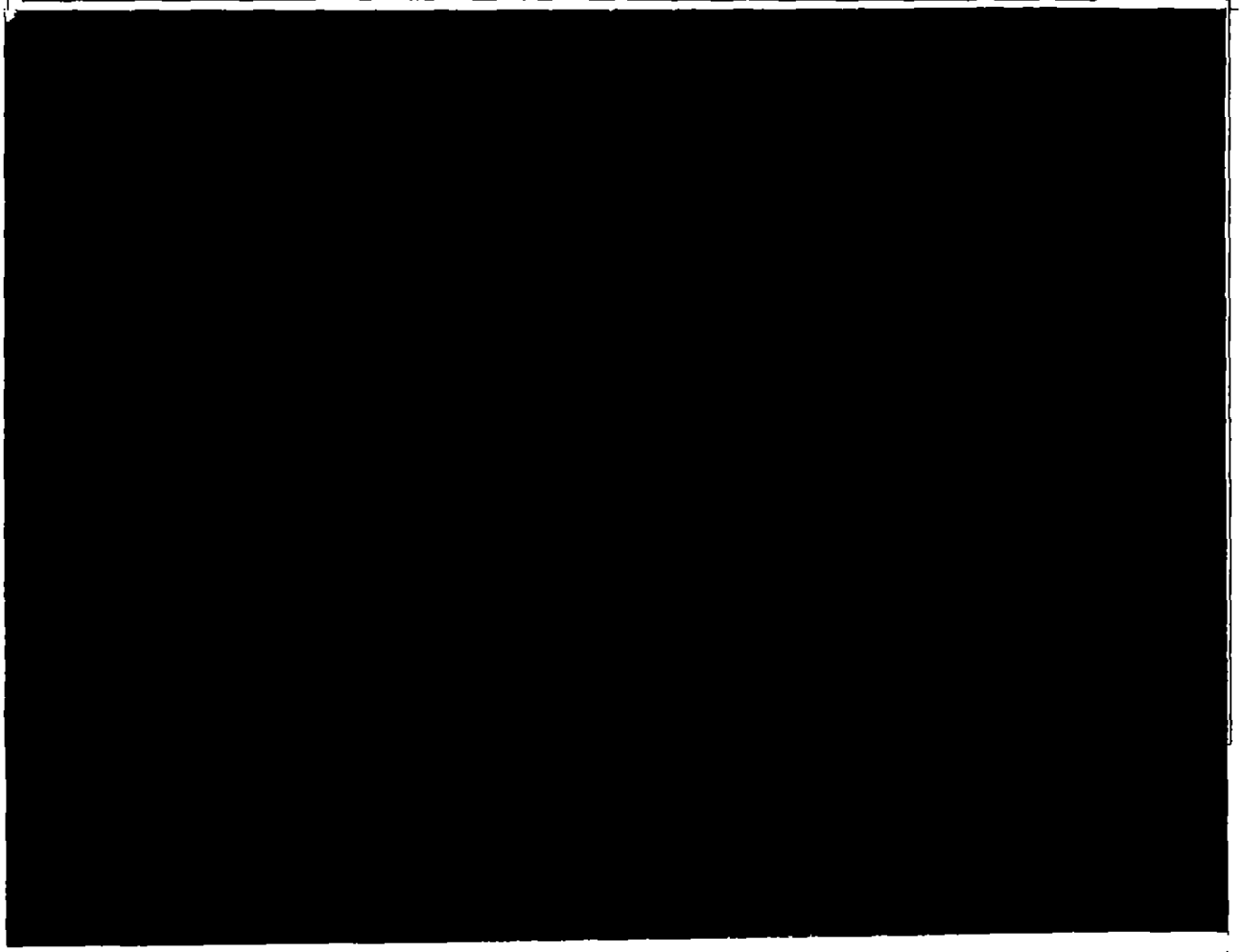
- 3 secondary and 12 tertiary infections; 3 deaths
- 6,350,000 immunizations deplete US supply



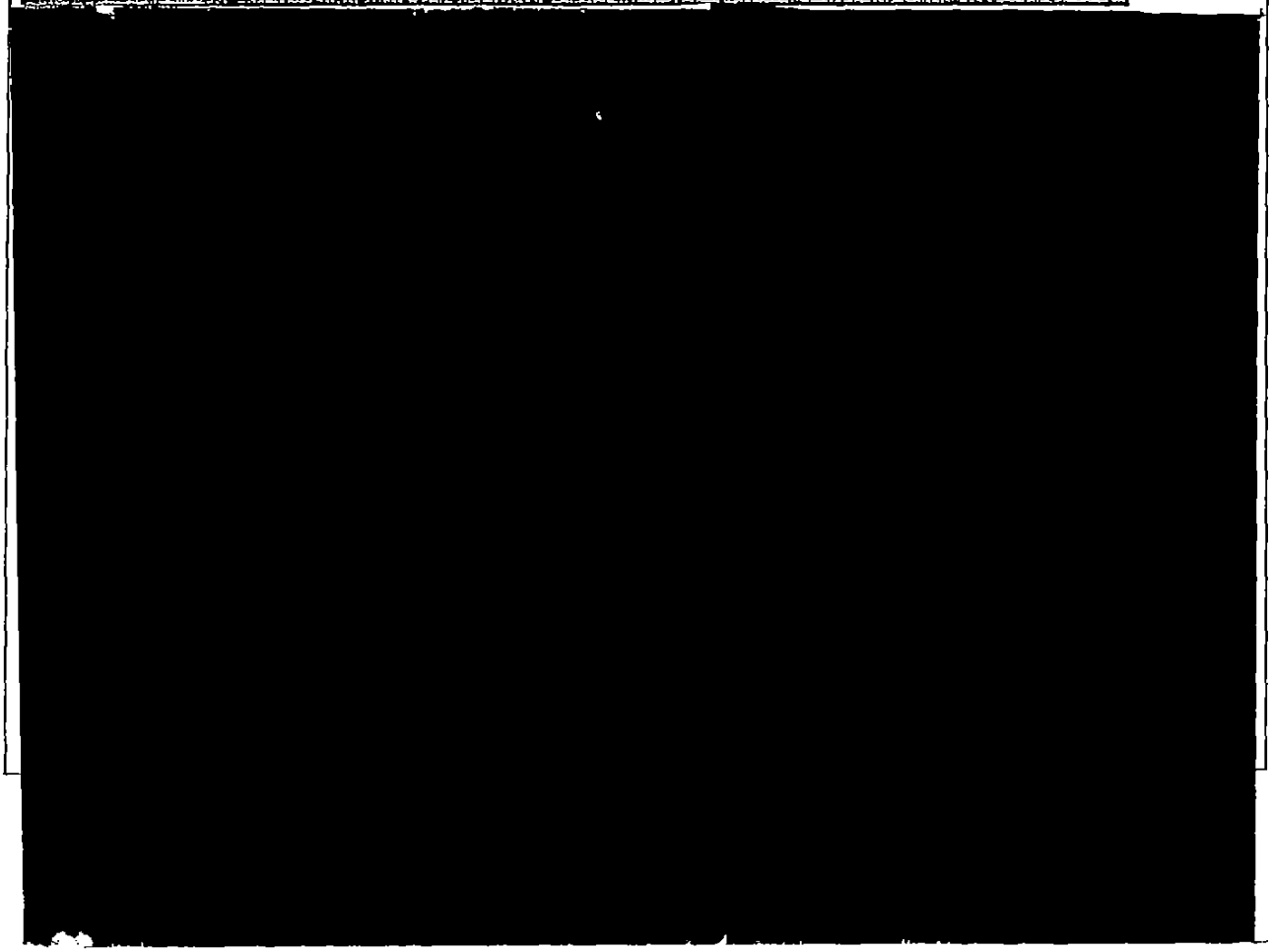
A useful reference point is an incident that occurred in 1947, when an infected man arrived by bus in New York City. Although he died within 10 days of arriving, it took a month to diagnose the disease. He induced 3 secondary and 12 tertiary infections, resulting in 3 additional deaths.

This infection caused the prompt immunization of a large fraction of the New York metropolitan area and depleted the national supply of vaccine.

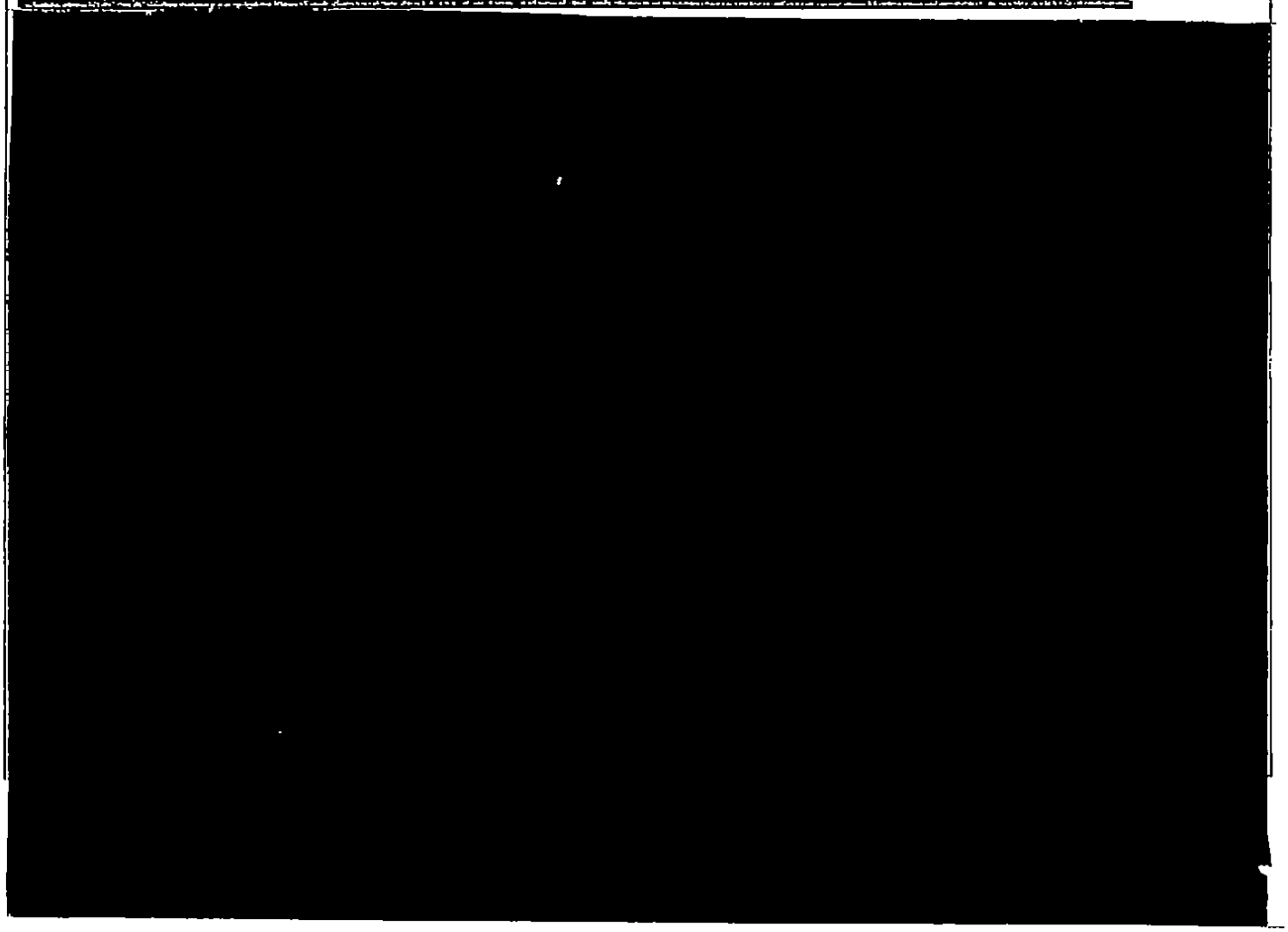
# BW scenario #2



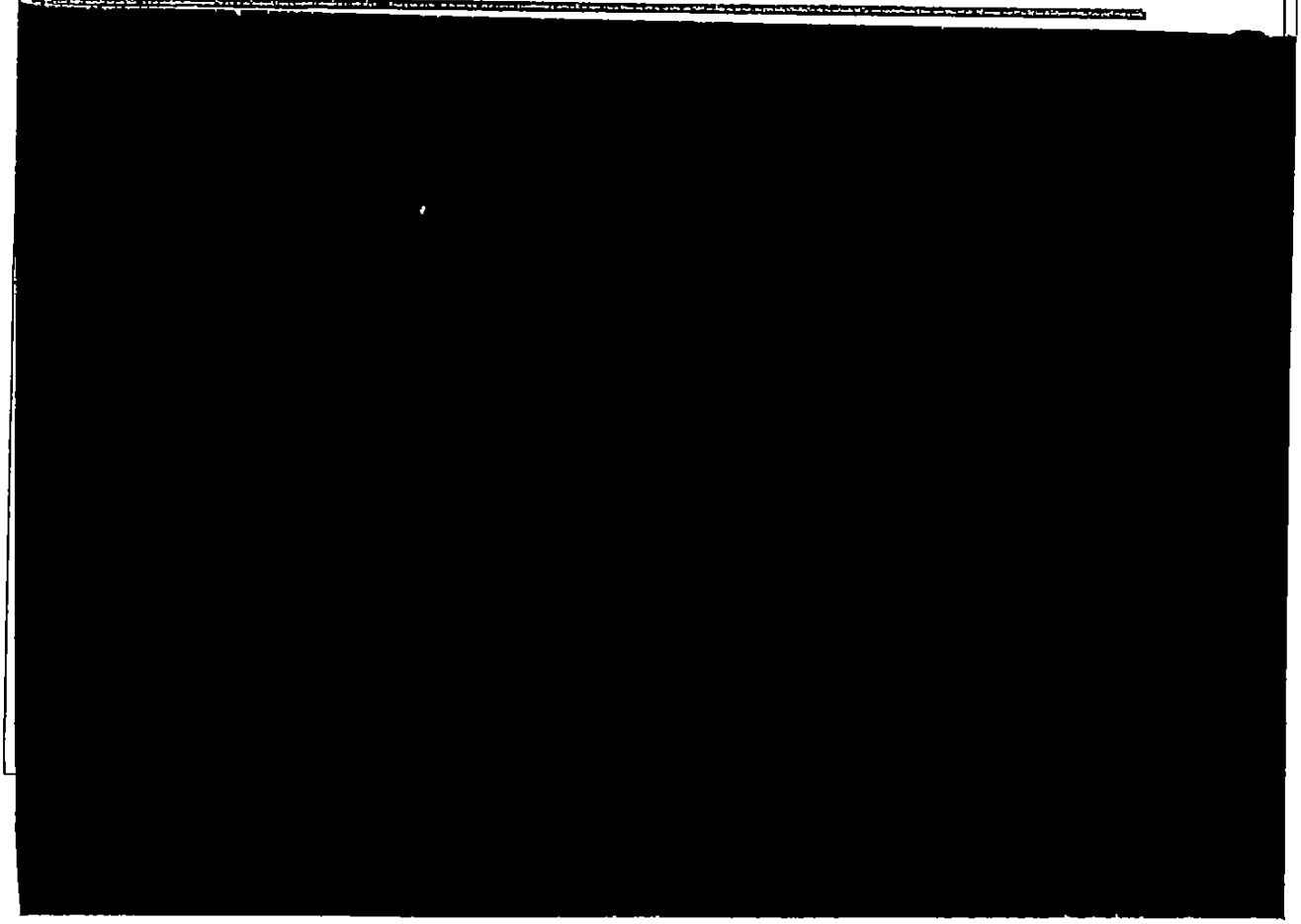
# BW scenario #3



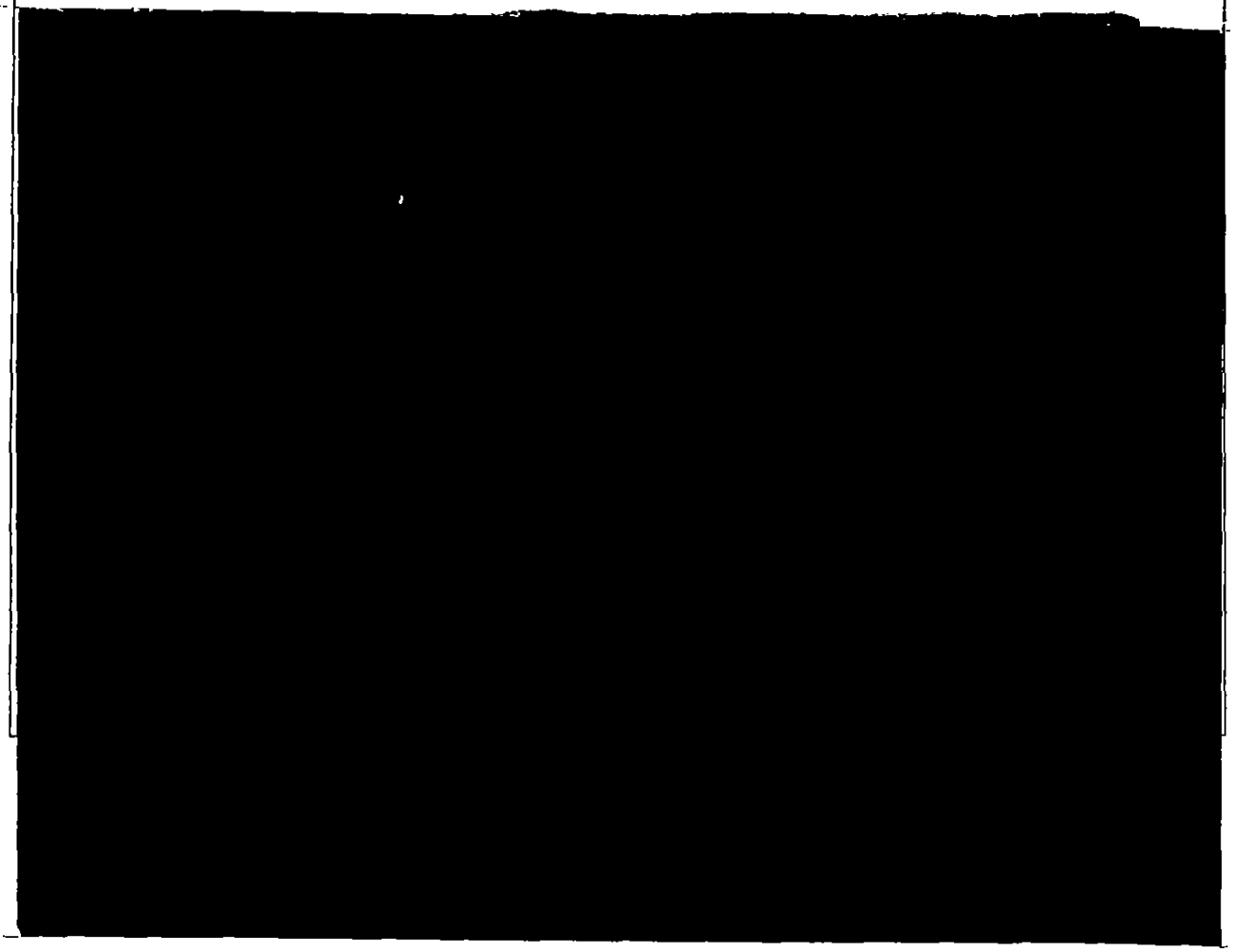
# BW scenario #3



# BW scenario #4



# BW scenario #4



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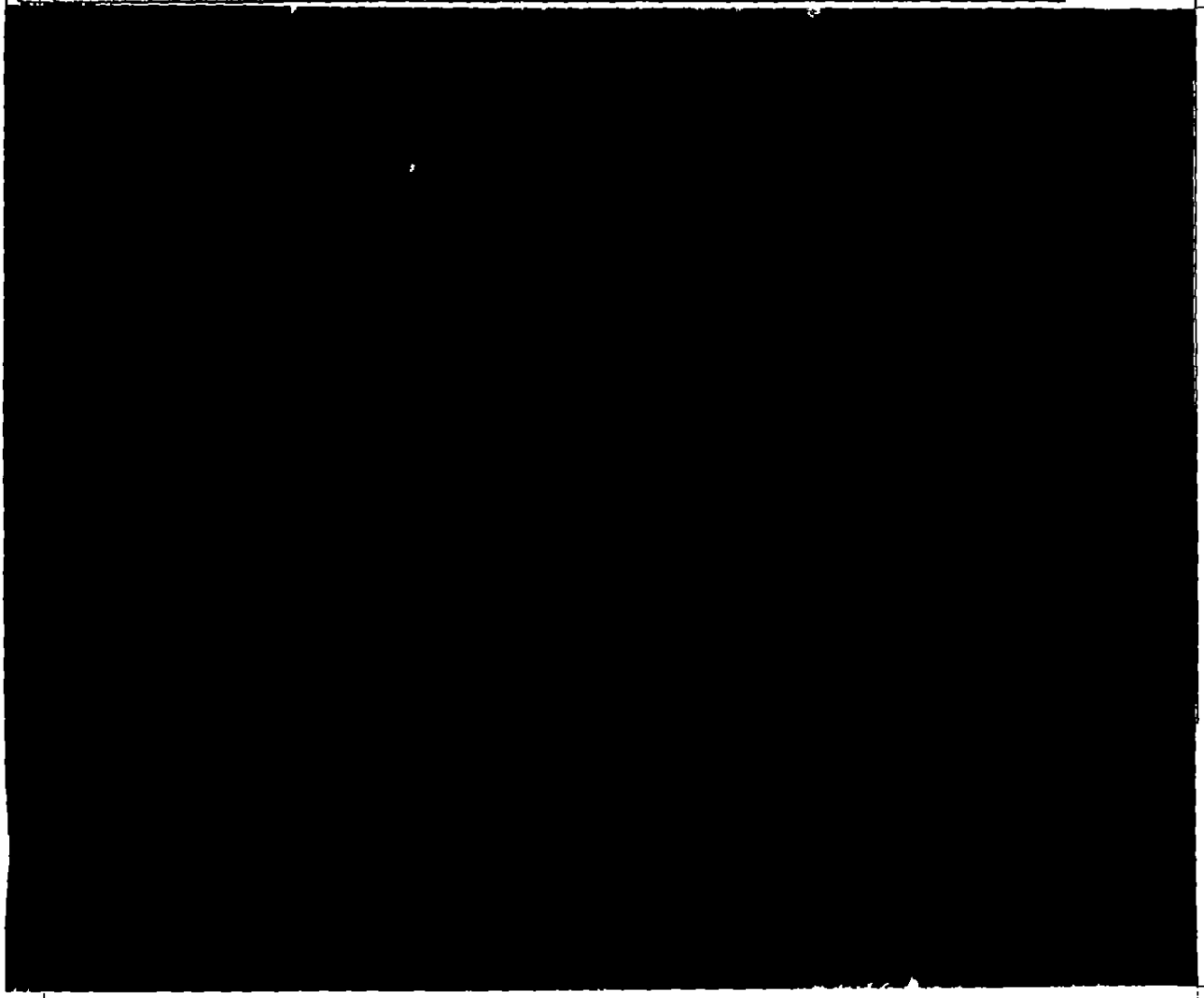
# Agricultural vulnerabilities



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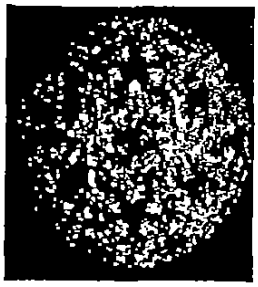
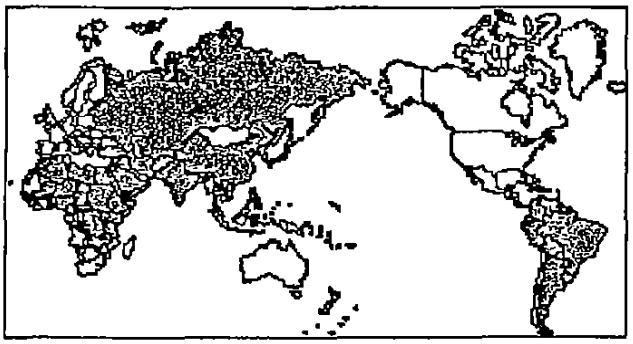
# Foot and Mouth Disease (FMD)

- Most infectious of all animal diseases
- Virus affects all cloven-hoofed animals
  - Produces vesicles in the mouth, on the teats, and on the skin between and above the hoofs.
- Rarely kills adult animals; young and weak may die.
- Production losses can be dramatic; cost of eradication high
- One case of FMD jeopardizes exports from a country





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Foot and mouth disease (FMD) is a virus that affects all cloven-hoofed animals; it is the most infectious of all animal diseases. Although it rarely kills adult animals, the young and weak may die.

FMD can cause dramatic production losses and imply great expense to eradicate. International trade rules are such that one case of FMD in a country can jeopardize all animal exports from that country.

The map shows as gray areas all countries where FMD is present. North America, Australia, and Western Europe are notable FMD-free areas, and are hence vulnerable to FMD attack.

# Taiwan FMD incident

- March, 1997 outbreak induced indefinite ban on pork exports
- 900,000 animals destroyed; maybe 1.6 million finally; 15% of total herd.
- Vaccine available; not seen as cost effective as routine preventive measure
- 41% of pork to Japan was from Taiwan
- Cost to Taiwan just over $1 billion annually until imports can be reinstated
- Suspect smugglers of bringing disease

[redacted]



A good example of what FMD can do is an outbreak that occurred in Taiwan in March, 1997. While smugglers were suspected of causing the disease by importing infected animals, [redacted]

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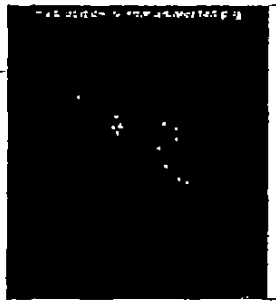
# African Swine Fever (ASF)

- DNA virus; sole member of *asfarviridae*
  - Non-virulent in well-adapted hosts (ticks and warthogs in Africa)
  - 3 virions will cause death in domestic swine; hemorrhagic disease="pig ebola"
  - Clinical symptoms in 3-4 days; 100% mortality in in 7-10 days; intracelluar symptoms much earlier; how to diagnose?
  - Endemic in southern Africa, Sardinia (no ticks, but pig to pig infection); flares elsewhere

[redacted]



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A different agricultural vulnerability is African Swine Fever (ASF). This is caused by a DNA virus. The virus coexists well in, and is passed back and forth between, two hosts in Africa, ticks and warthogs. However, it is virulent in domestic swine; as few as 3 virions will cause ASF, a hemorrhagic disease with symptoms similar to those of Ebola in humans.

ASF is endemic in southern Africa. It also infects domestic swine in, for example, Sardinia, where it is thought to be transmitted by pig-to-pig infection. Irregular outbreaks occur elsewhere.

[redacted]

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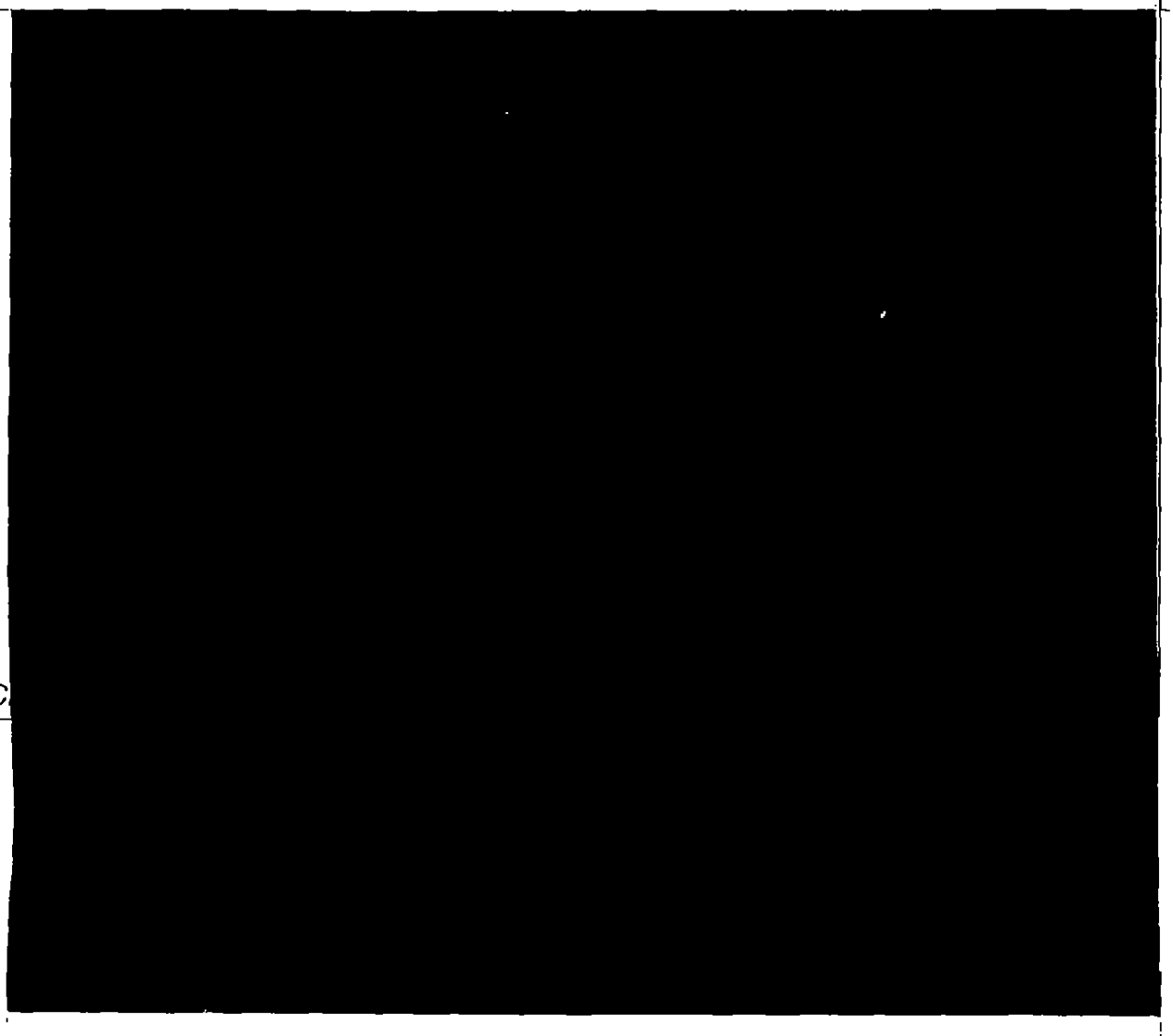
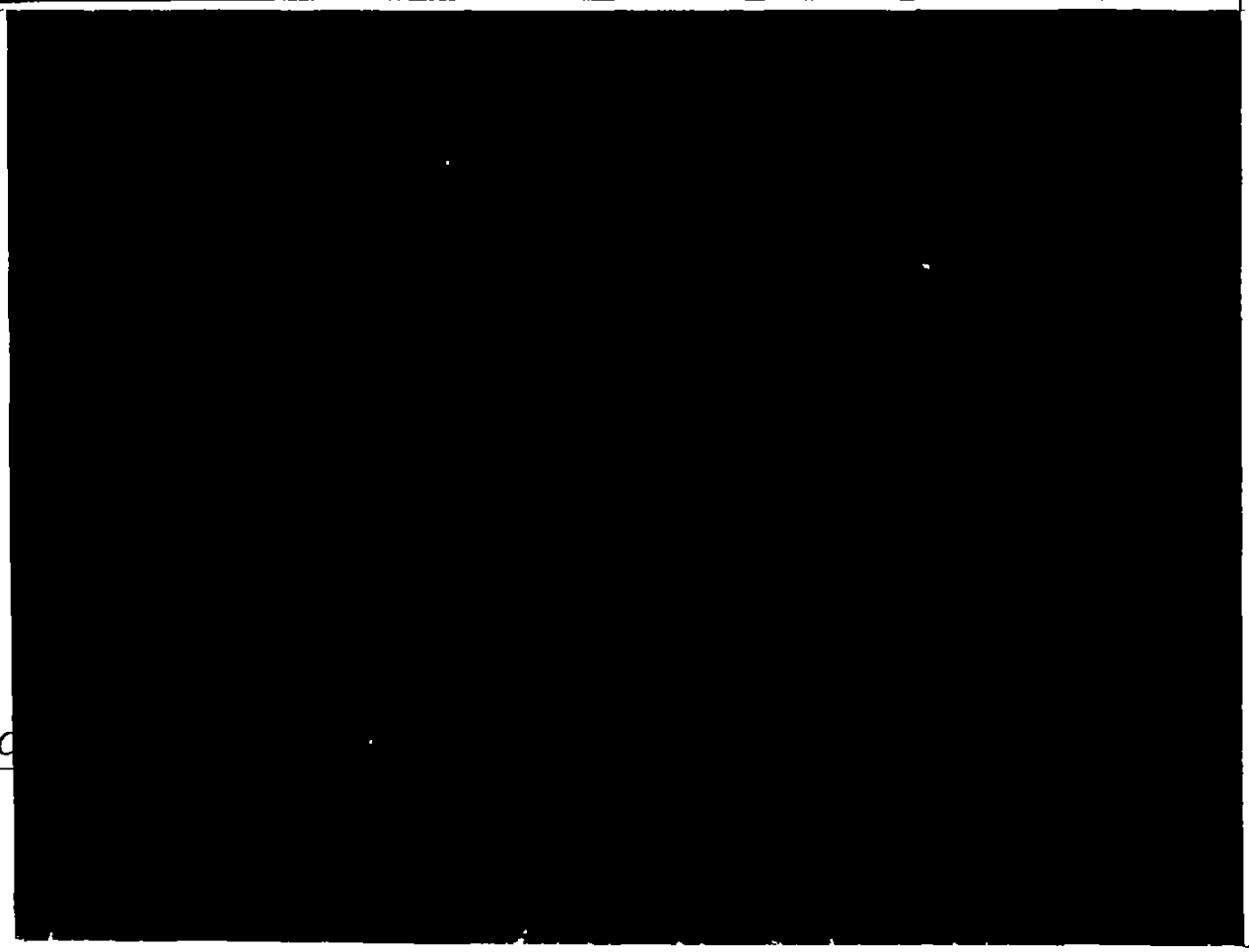
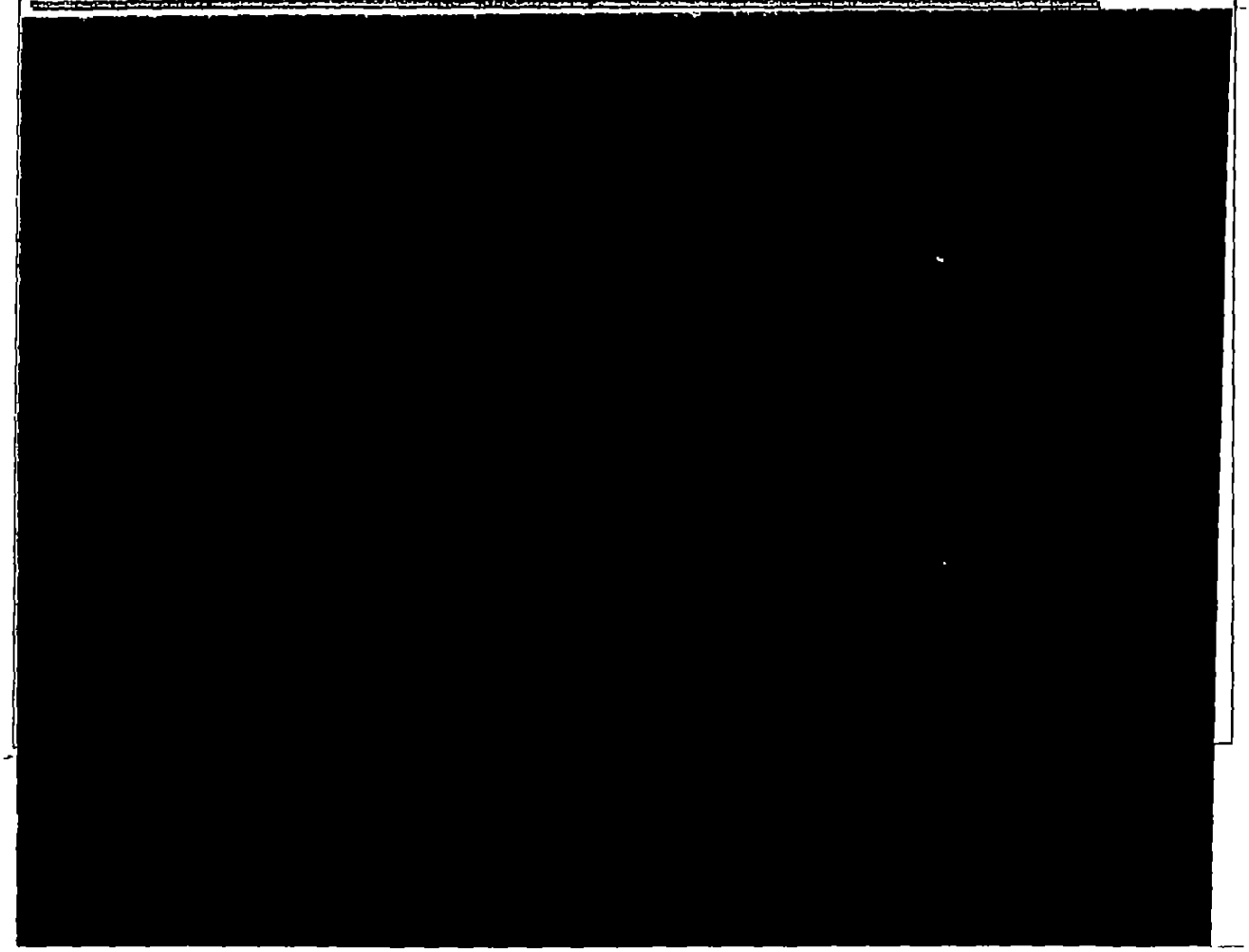
# Framing the problem



# BW timeline



# Managing civil response



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# Briefers

| Briefer | Company | TalkTitle |
|---|---|---|
| [redacted] | | |

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As input to our study, we heard a number of briefings on a variety of topics.

# Briefing outline

- Study definition
- Technical topics
  - Intelligence
  - Sensors, concentrators, and sensor arrays
  - Instrumenting the biome
  - Presymptomatic triage
  - Medicinal programs
  - Building and personal protection
- Investment priorities and recommendations



Let me now turn to a variety of technical topics, speaking to each one in turn

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# Briefing outline

- Study definition
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  - Intelligence
    - Vaccine surveillance
    - Strain analysis
    - Pathogen isotopics
    - Domestic intelligence
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With respect to intelligence matters, there are four suggestions we'd like to make.

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# Vaccine surveillance

- Vaccines exist for some agents (smallpox, anthrax, ...) and could be developed for others (ebola, marburg, ...)
  - Most likely requires worker vaccination to produce/distribute/deliver
  - Mass vaccination would prevent national self-infection

Smallpox virus

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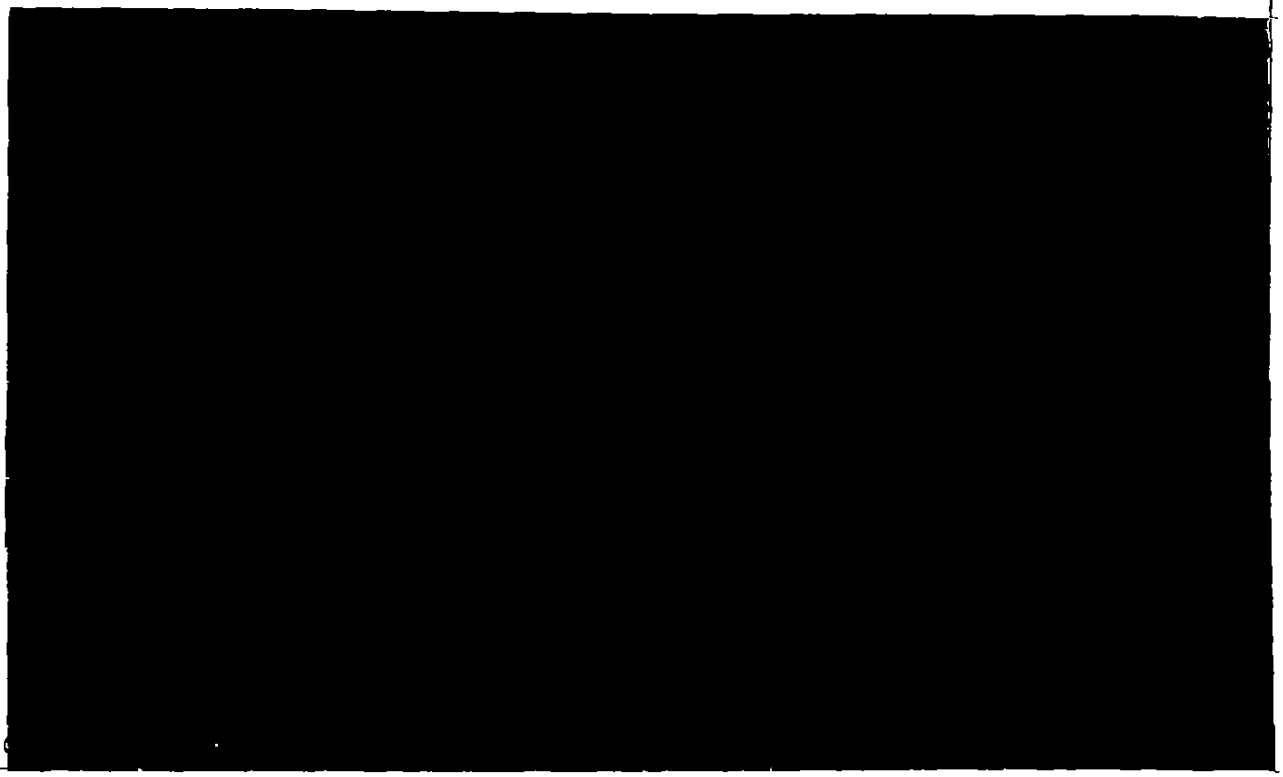
The first suggestion has to do with using vaccines and vaccination programs as indicators of BW intentions.

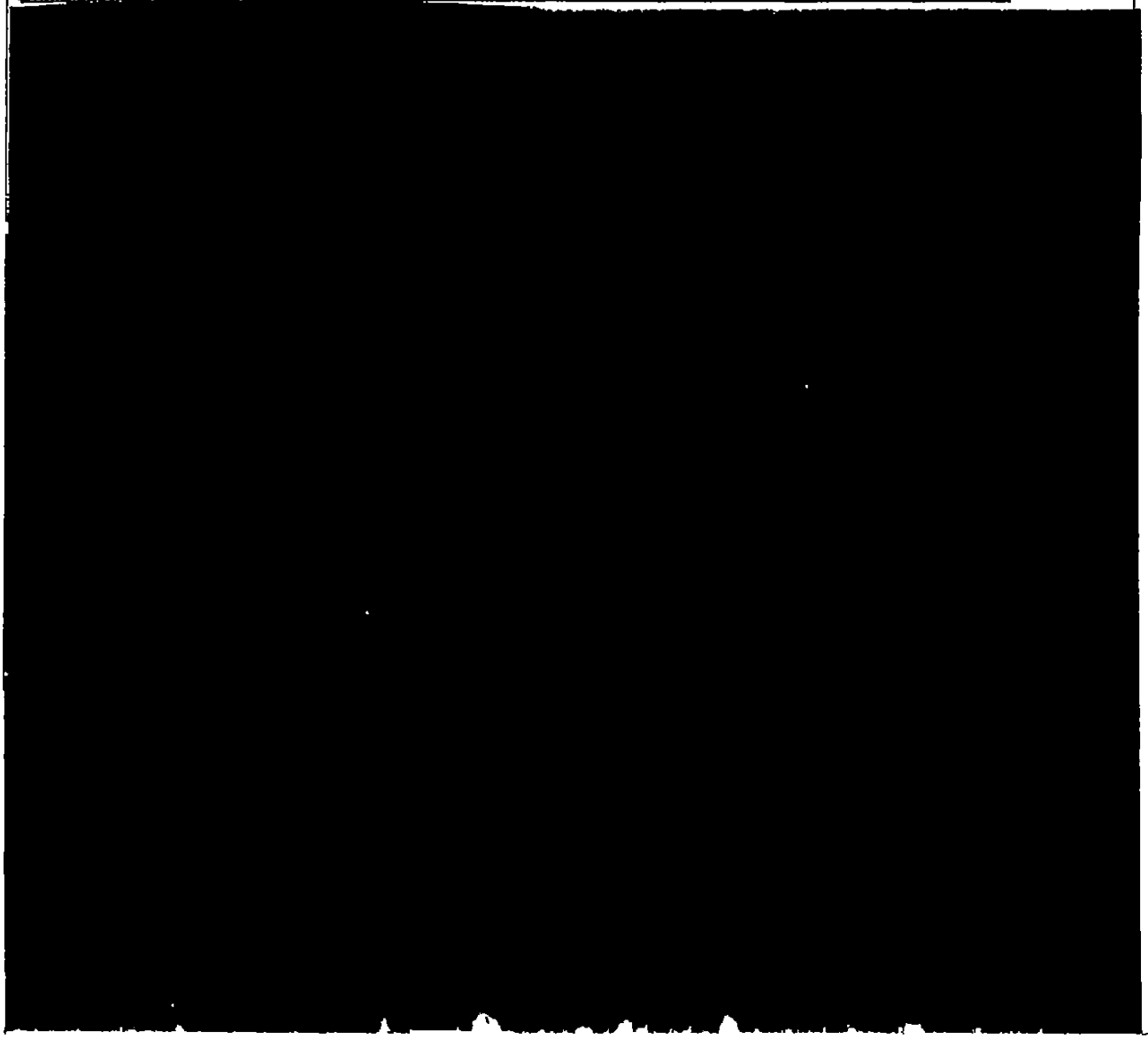
# Strain analysis

# VNTR analysis varies with locale

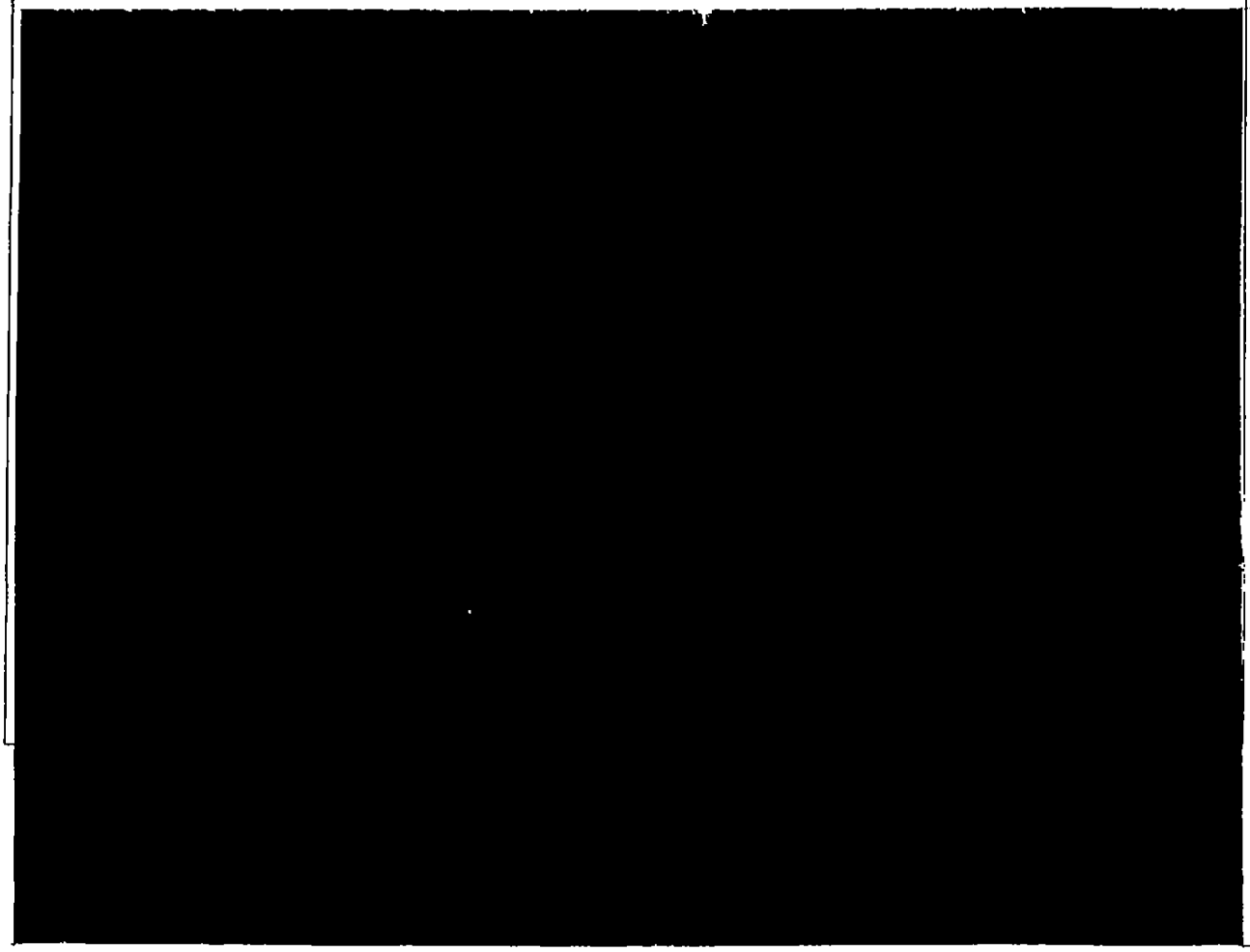


Work by Paul Keim on anthrax illustrates the potential of the method. The VNTRs of a variety of anthrax isolates from around the world have been quantified and the results used to organize the isolates into a phylogenetic tree Samples from a given region can then be placed on this tree and "foreign" strains identified.

# Strain analysis allows localization



# Program of strain analysis



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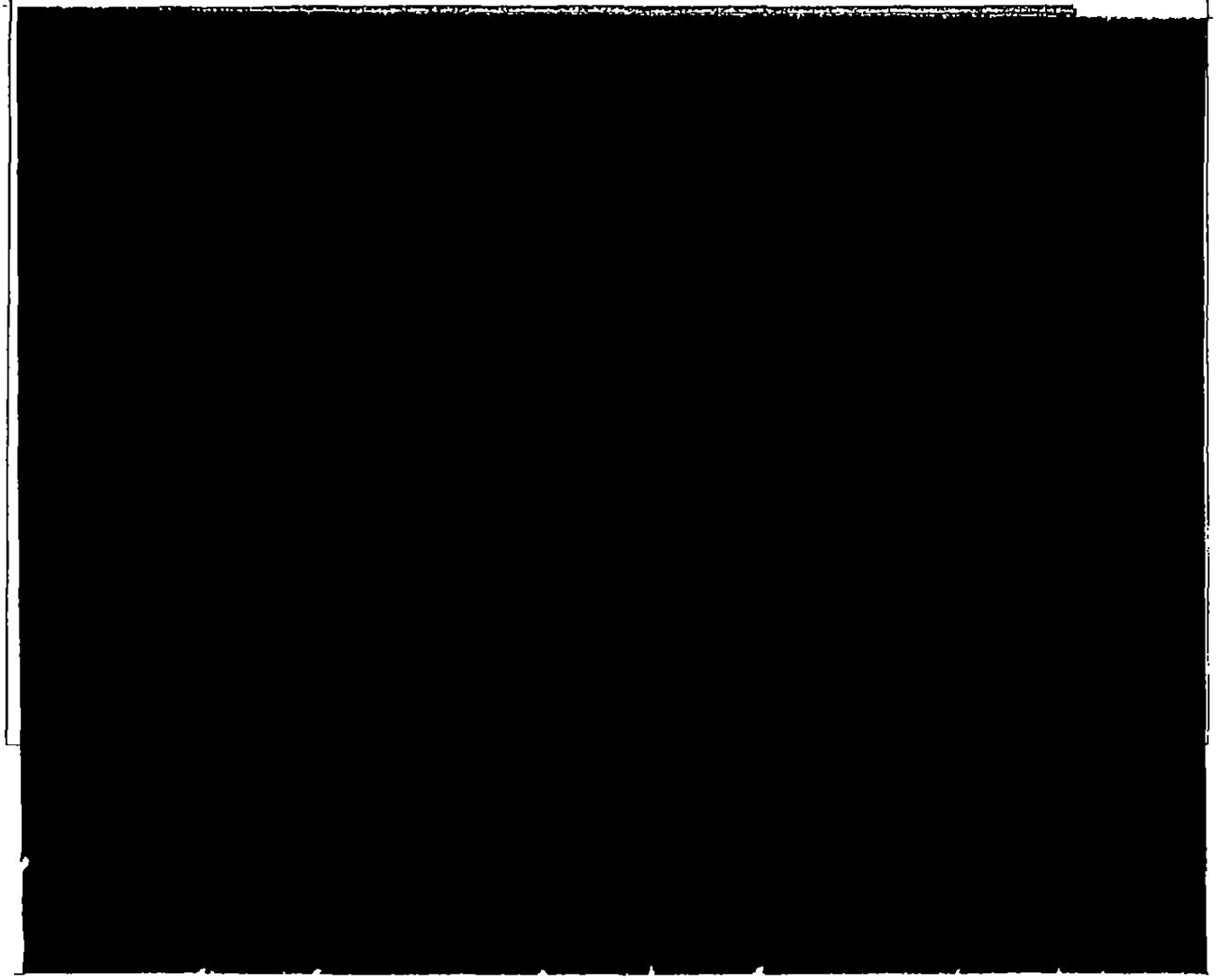
# Pathogen isotopics



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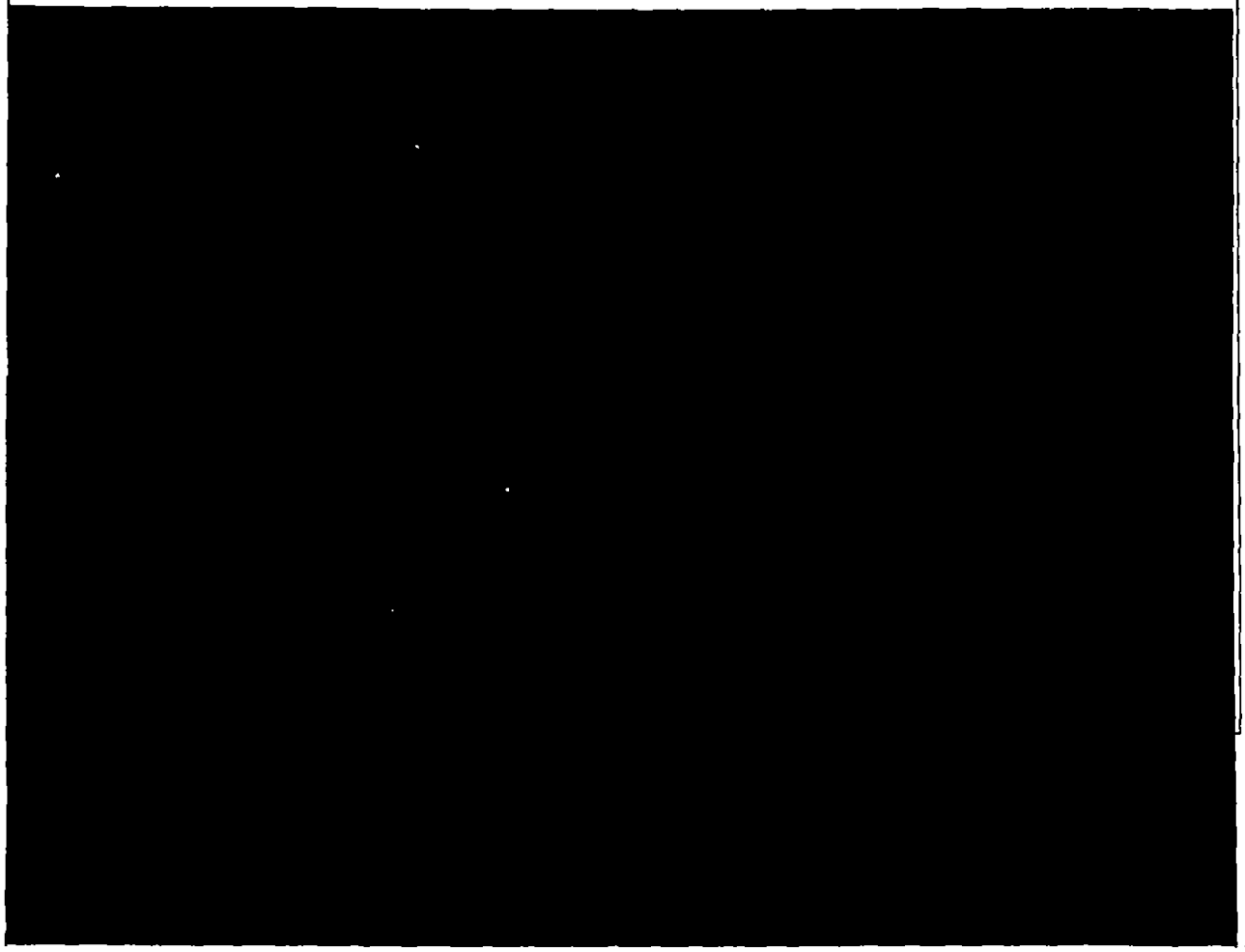
# Research program in pathogen isotopics

A research program in isotopic analysis of pathogens would couple into the academic expertise that exists in mass spectrometry. Forefront instrumentation such as ion microprobes and Accelerator Mass Spectrometry would allow the analysis of small samples. Studies to determine analysis protocols and the variation in isotopic composition would then follow.

# Domestic intelligence



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We'll now turn to some observations and recommendations on sensors and sensor arrays. [Supplementary material on this topic is contained in Appendix I.]

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# Guiding principles for sensors

- Track the population
  - Put sensors where people are!
- Detect as early as possible
- Capitalize on the selectivity and sensitivity of biochemical systems
- Maximize overlap with existing systems and infrastructure
- Maximize impact of dollars and effort
  - Simple things first!
- Venues: threats, special events, buildings, fixed and mobile arrays

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These are the principles that we believe should guide thinking about sensors. Note that there are a variety of venues in which sensors might be deployed, and that there are differing needs in differing venues.

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# Sensor for anthrax threat discrimination

- The mere *threat* of a BW attack is being exploited
- These events extract a price!
  - Psychological BW warfare
  - Real economic costs
  - Confidence in our ability to respond is eroded
  - "Cry Wolf" effect: one day it won't be a hoax....
- Anthrax discrimination [redacted] and the technology exists



One clear need we see is a sensor to simply but reliably deal with anthrax threats, both hoaxes and real events.

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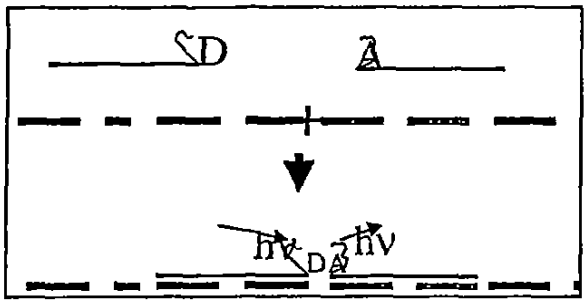
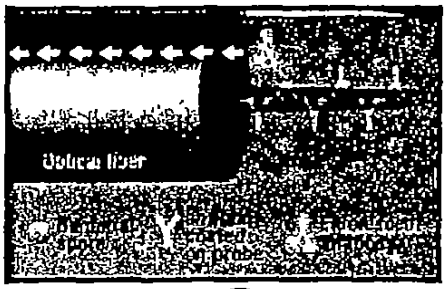
# Anthraxometer

- A variety of technologies are possible

FRET




"tickets"


[redacted]

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A variety of technologies would permit construction of an "anthraxometer", a simple field device that could reliably identify anthrax spores. Among the possibilities are Fluorescence Resonance Energy Transfer (FRET) applied directly to DNA probes [see Appendix II], immunoassays using fiber sensors, or even the simple "ticket"-type sensors that are fielded for some agents. [redacted]

# Sensors for special events

- Historically targets of value
  - Atlanta and Munich Olympics
  - 1984 UK Conservative Convention

[redacted]

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# Concentrators

- Overall system sensitivity is

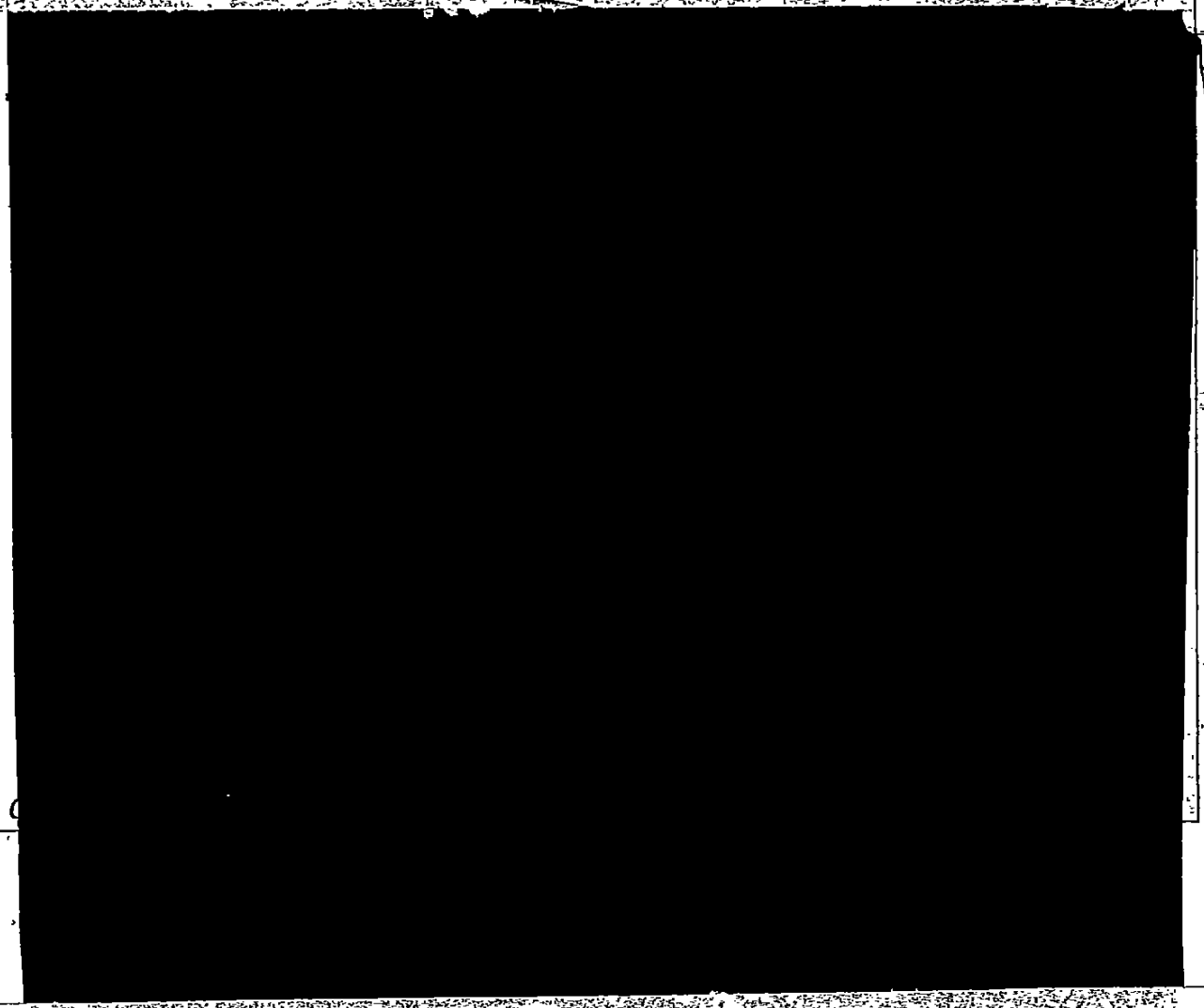
  (Concentrator gain) × (PCR gain) × (sensor SNR)

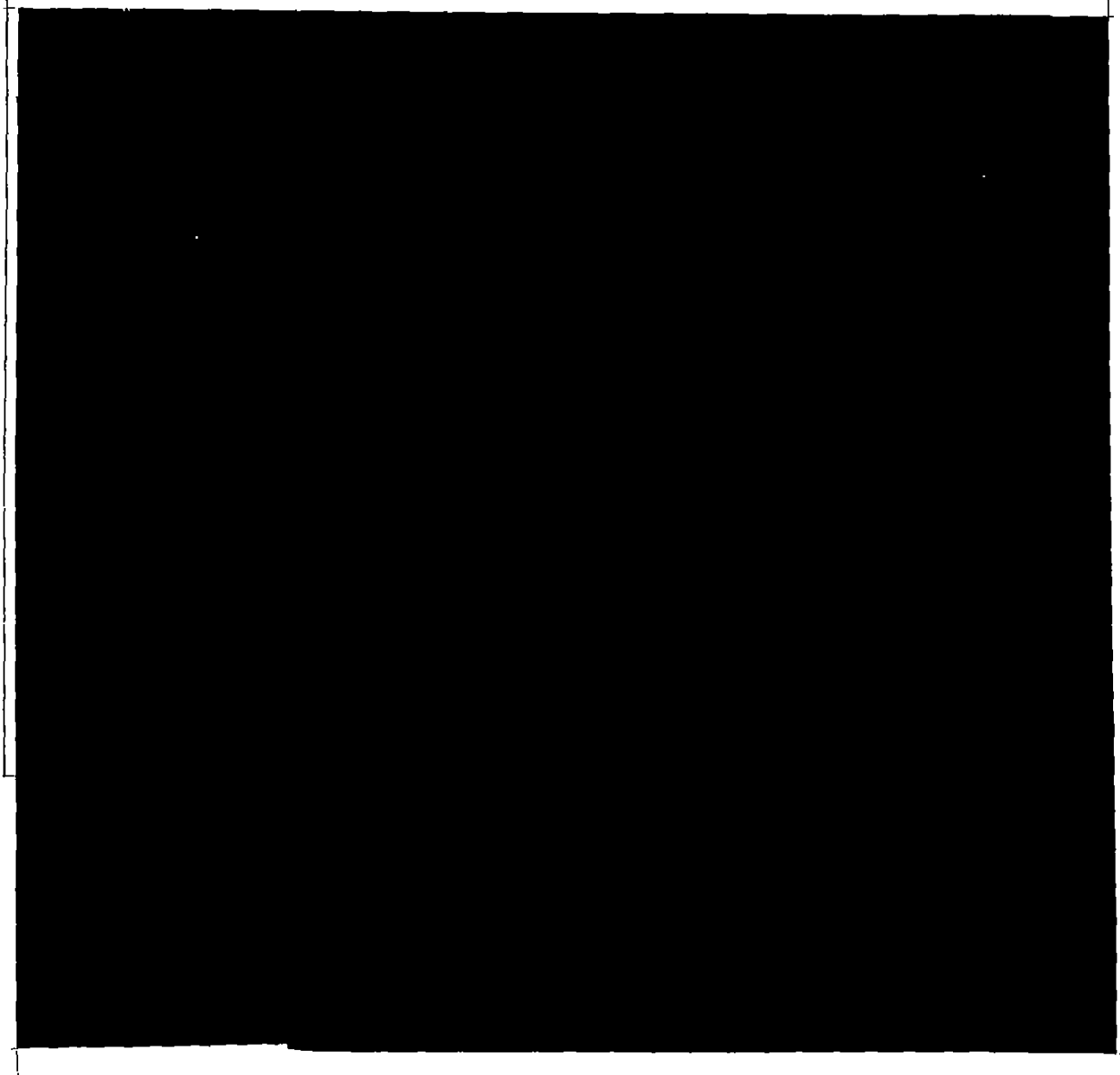
- Concentrators will not be driven by the commercial biotech sector
  - **Interests are sensitivity, selectivity, SNR**
- Big factors to be gained here, modest technology needs, potentially large leverage per dollar

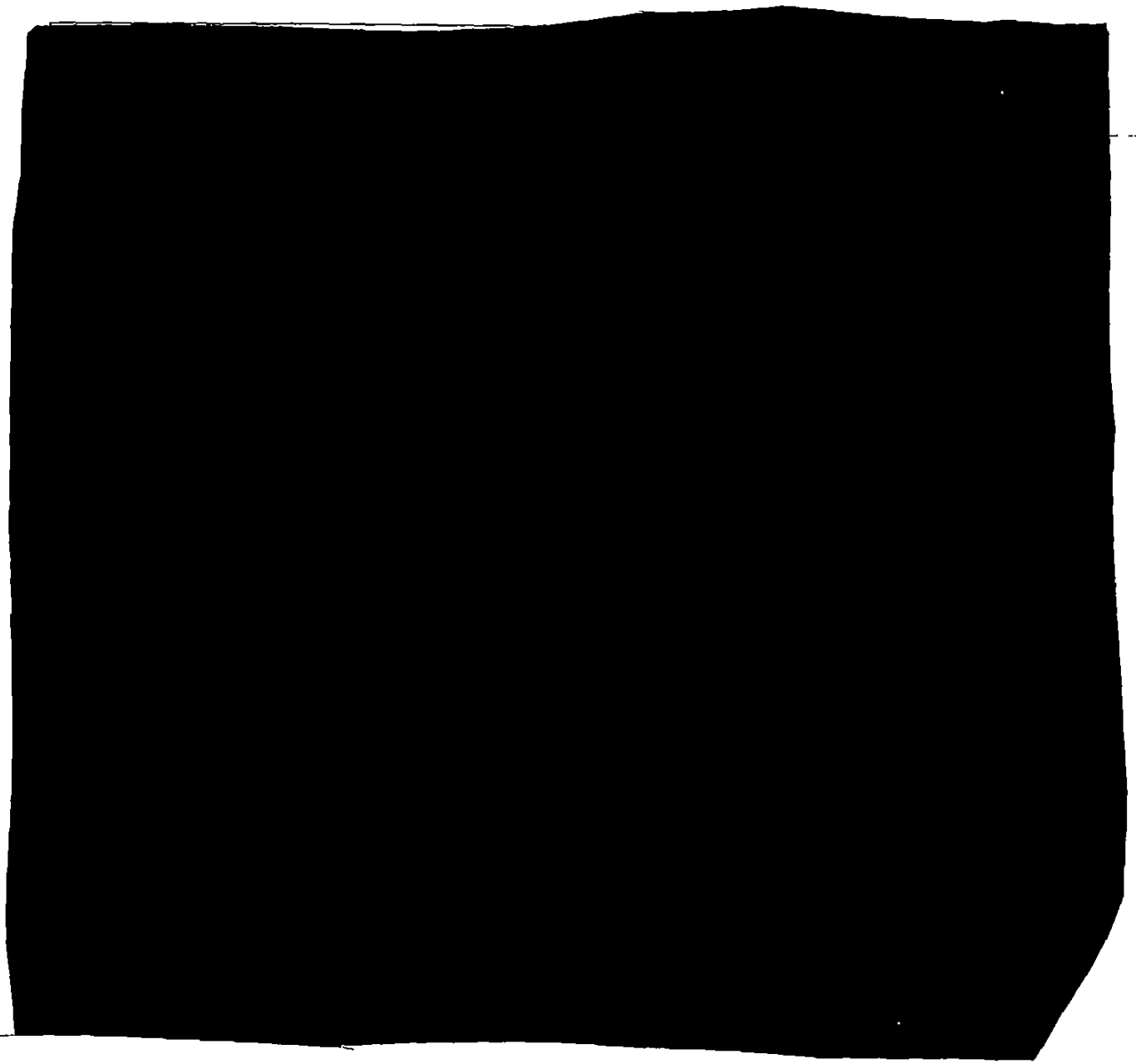


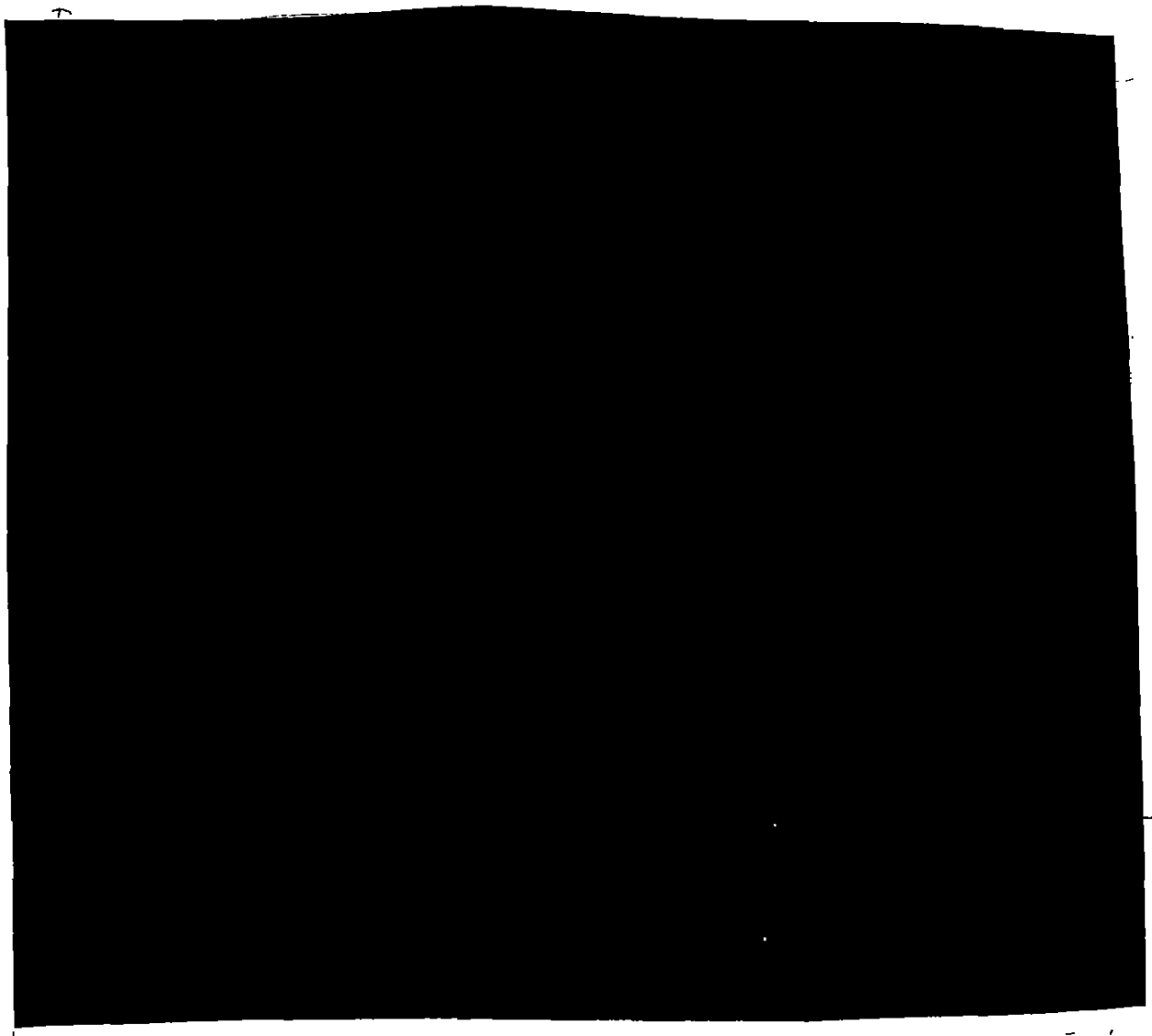
The capability of a given sensor will depend upon the efficiency of the concentrator (how much air can be sampled), gain due to PCR amplification (available only for sensors detecting nucleic acid sequences) and the biochemical sensor itself.

While commercial biotech interests might drive the latter two technologies, concentrator technologies are likely not high on the commercial agenda. We think that there may be technical advances possible here that are of unique DOD interest.









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# Instrumenting the biome

- Organisms are effective integrators/concentrators
  - Continuously sample the environment
  - Respond in a biologically meaningful way
  - Plants, animals, BITSISE example
- People
  - Above advantages *and* "Self-report" above a threshold
  - And are what we really care about!
- Public health Grand Challenge

  *Know the health-state of the population with high spatial, demographic, and temporal resolution and low latency*
- Move epidemiology toward a realtime activity
  - Data mining
  - Facilities sampling
  - Widespread health-state telemetry

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I now want to discuss the general idea of instrumenting the biome (i.e., living organisms). Organisms are effective integrators and concentrators of BW agents. Plants and animals have shown responses to intentional and unintentional releases, and could well be modified to enhance their sensitivity.

Humans offer similar advantages, as well as "self reporting", and they are what we really care about protecting. People as sensors thus necessarily links civilian biodefense to public health. Indeed, steps to move epidemiology from its traditional retrospective character toward a realtime activity would have clear benefits from both public health and biodefense perspectives.

# Outbreak of West Nile-Like Viral Encephalitis -- New York, 1999

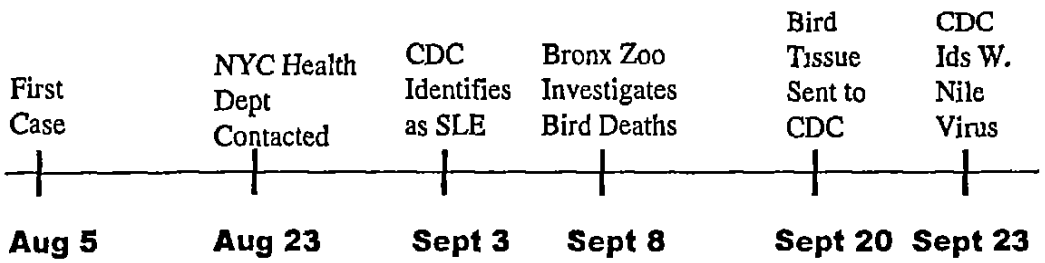
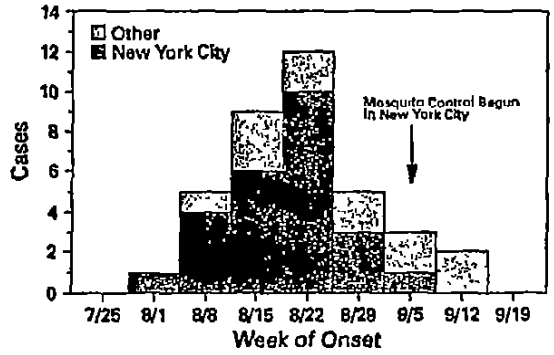



FIGURE 1. Seropositive cases of West Nile-like virus, by week of onset — New York, 1998

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The recent outbreak of West Nile viral encephalitis in New York City provided a good demonstration of the strengths and weaknesses of the present system for detecting disease outbreaks. Note that mosquito control measures only began after the peak in the number of cases. The drop in new cases in the week of 8/29 may have been due to the die-off of the primary carrier of the virus – birds.

# NYTimes 10/11/99 on West Nile

- "We've learned about the need for, and benefits of, improvements in laboratory coordination," said Scott Lillibridge, who leads the CDC's Bioterrorism Preparedness and Response Program. "We've also learned how helpful surveillance can be, particularly in beginning to track the beginning, extent or progress of an infectious disease outbreak."

- Dr. Stephen Ostroff, the acting deputy director for science and public health at the CDC, said that confusion is a normal part of an investigation of emerging disease. "Anyone who continues to maintain that there was some mistake here doesn't understand the way science proceeds in outbreak investigations," Ostroff said. "You won't hear any apologies from me."

- "We're spending hundreds of millions on questionable stockpiles of vaccines and antibiotics," said Zelicoff, the scientist at the Sandia Laboratory. "We should be improving the ability of local public health officials to recognize and report strange illnesses to a central authority that can quickly tell them what to do about it."

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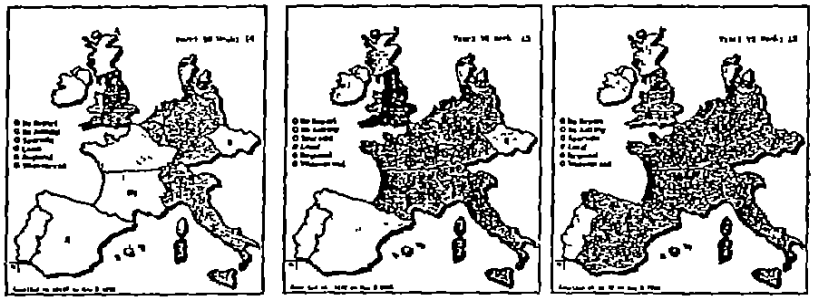
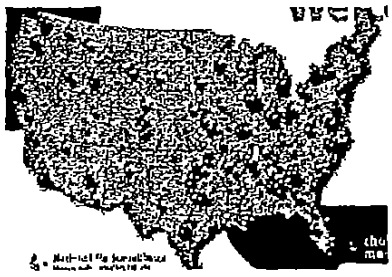
Several others have recognized the need to signifcantly improve monitoring of the population's health state.

# Opportunities for data mining

- The health system produces, with varying detail, completeness, and timeliness, health-state information
  - Billing and insurance records
  - ER admissions/symptoms, lab results
  - HMOs, pharmacies
- Collect and analyze to determine natural spatio-temporal patterns, variability; look for anomalies



http://www.eiss.org/public/index.htm



http://www.fluwatch.com/

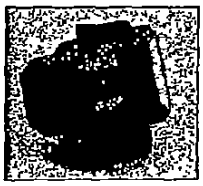


The health system produces data that could be used to improve civilian biodefense. Efforts must be made to standardize, collect, and analyze such data on shorter timescales. The figure at left, documenting flu in Europe during three successive weeks this Spring, shows one example of what might be achieved. A network of physicians provides the primary data. Similarly, the figure on the right shows a commercial network of physicians in the US that monitors flu in nearly realtime. The website even allows one to sign up for regular e-mail notification of flu activity in one's state. [Appendix III contains further material on data mining.]

# Facilities sampling

# Widespread health-state telemetry

- Wearable, non-invasive instrumentation for various physiological parameters
  - Pulse, pressure, respiration, temperature, blood sugar, ...



- Combine with averaging, geolocation, and cellular telemetry for realtime monitoring
- Disperse among *some* of the population
  - Patients would volunteer; could require for emergency responders
  - Obvious privacy issues
- Datamining for release detection, epidemiology, science, ...

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DARPA and others have sponsored the development of portable and rugged noninvasive monitors of vital signs. Deployment of such devices among even a fraction of the population, combined with geolocation and telemetry, would be a very interesting resource for a number of different applications.

# Briefing outline

- Study definition
- Technical topics
  - Intelligence
  - Sensors, concentrators, and sensor arrays
  - Instrumenting the biome
  - Presymptomatic triage
  - Medicinal programs
  - Building and personal protection
- Investment priorities and recommendations



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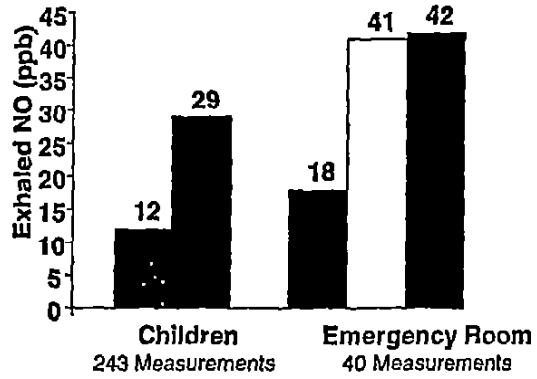
# Presymptomatic triage

- Determine who's been infected *before* symptoms
  - Stem an epidemic for contagious agents
  - Quell public fear
  - Efficiently deploy medicines
  - Efficient quarantine and hospital allocation
- Obvious dual use
- Research and engineering needed
  - A layered system of increasingly specific sensors
- Sampling through
  - Nasal swabs, urine/feces, breath, blood, saliva, ...
- Technologies include
  - Simple molecules (NO), immunoassays, expression analysis





Gene expression array

*Civilian Biodefense*

Knowing who has not been infected (and who has before symptoms become evident) would be of clear use in dealing with a bioevent. Exactly what to look for (both for warning and differential diagnosis) is very much a research topic. Possibilities include simple metabolites, immunoassays, and expression analysis. An example of the first is shown in the upper figure, where exhaled NO is shown to be a good presymptomatic indicator of respiratory infection. The lower figure shows a gene chip, where the expression levels of several tens of thousands of genes can be monitored and changes highlighted.

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# Gene expression patterns

Numbers of genes perturbed >2-fold


Confounding effect of stress?

Roland Somogy briefing 7 July 1999

*Civilian Biodefense*

One way in which a gene expression array might be used for presymptomatic triage is shown in the lefthand figure, deriving from experiments at Incyte. Expression in a cell line is compared with an unperturbed reference state under three different chemical stimuli. Genes that respond in both common and stimulus-specific mode are identified.

One can imagine doing similar studies in various disease states to identify both warning and discriminating genes. Of course, one would have to investigate the confounding effects of stress.

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## Research in presymptomatic triage

- What's the best sampling protocol?
  - Studies of school children, …
- Study gene expression using patients with a wide range of health states to determine both warning and discriminatory genes
- Study expression of similar genes in people under emotional and/or physical stress to explore confounding effects
- Engineer a fieldable system

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A research program in presymptomatic triage, as outlined above, is recommended.

Appendix V contains additional material on presymptomatic triage.

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# Briefing outline

- Study definition
- Technical topics
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  - Presymptomatic triage
  - Medicinal programs
  - Building and personal protection
- Investment priorities and recommendations



There are two programs having to do with medicines that we would like to highlight.

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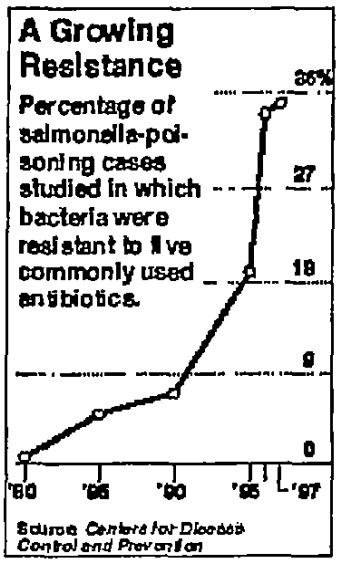
# "Silver bullet" antibiotics

- Bacteria evolve resistance to specific antibiotics
- Slowing rate of development of new antibiotics, but new drug targets developing
- Government to fund development and stockpiling of one or a few new antibiotics
  - Likely to cost ~ $0.5B each
- Withhold their use until a Bio event (e.g., via patent)
  - Prohibit livestock use
  - Medical use only as "drug of last resort"




Civilian Biodefense

"Reserved" antibiotics as described in this chart clearly raise ethical and policy issues, but could be an effective part of civilian biodefense.

**JASON** *1999*

# Smallpox preparation

- Smallpox among the most dangerous threats
  - Virulent, communicable
  - We have had mass protection through immunization programs
  - But risk magnified now by a non-immunized population
  - Protection is manageable at reasonable cost
- Upon winning the Cold War, a nuclear Stockpile Stewardship program began. But upon winning the "Smallpox War", there is no analogous effort
- Begin a smallpox preparation program
  - Stockpile sufficient medicines and diagnostic reagents
  - Create mechanisms for their distribution and administration
  - Develop/test/stockpile passive protection devices

*Civilian Biodefense* 

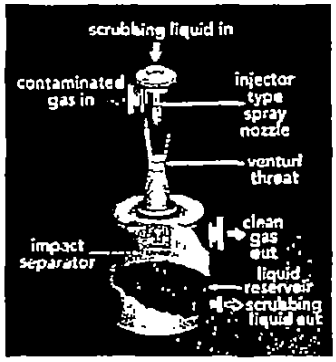
Appendix VI contains a further discussion of smallpox

# Briefing outline

- Study definition
- Technical topics
  - Intelligence
  - Sensors, concentrators, and sensor arrays
  - Instrumenting the biome
  - Presymptomatic triage
  - Medicinal programs
  - Building and personal protection
- Investment priorities and recommendations

# Building protection

- Piggyback on existing systems
  - HVAC
  - Fire suppression system for decontamination
  - Water system
- Dual use for "sick building" syndrome, public health
- Modest technologies can be very effective
  - HEPA filters
  - Retrofit "scrubbing"/monitoring systems
  - Positive pressure



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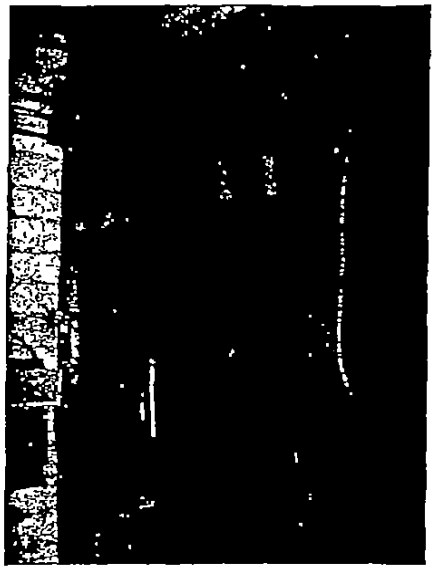
# Protecting JASON's building against BW

HVAC installation
at north end of building 29

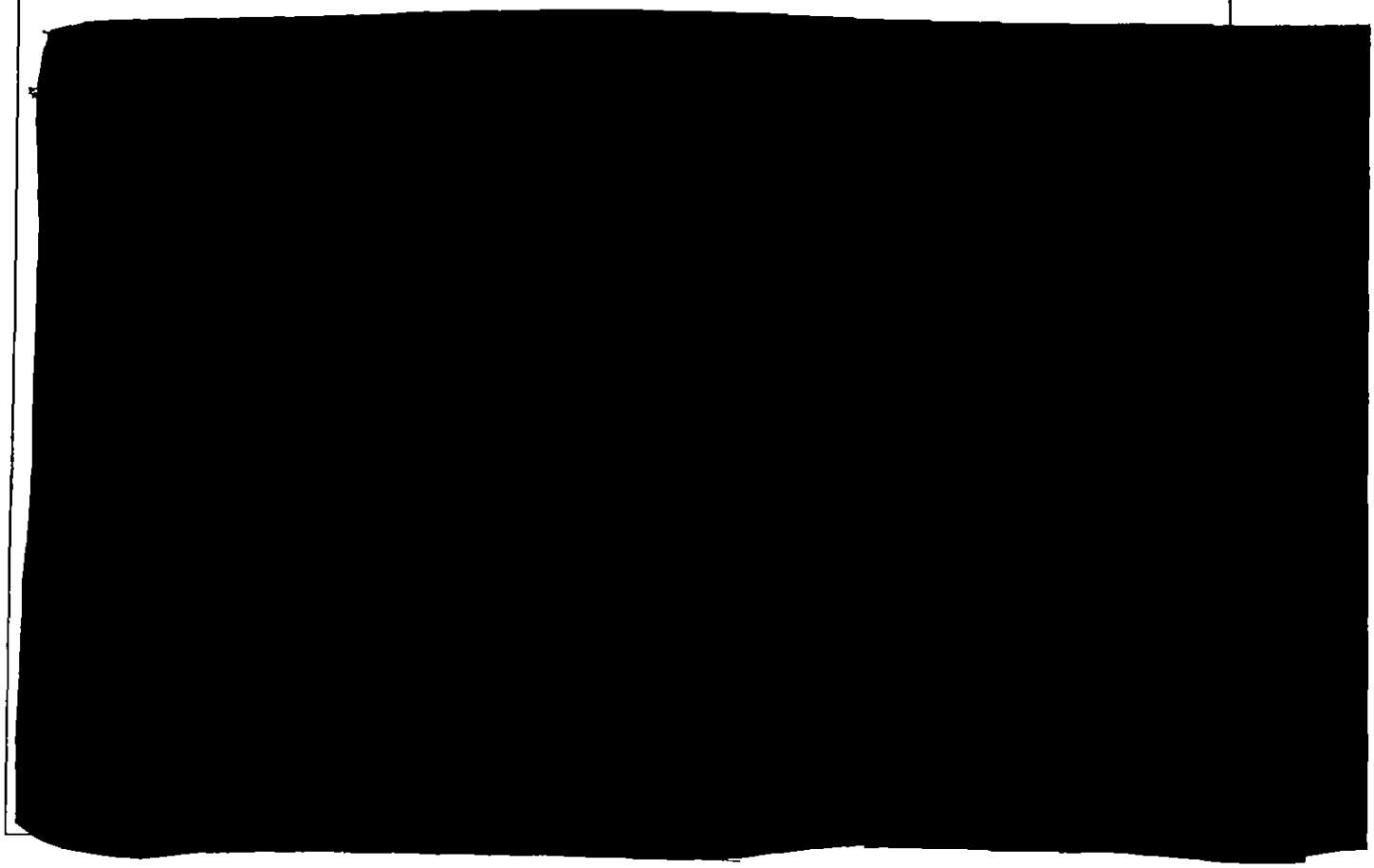


Modest air intake

*Civilian Biodefense*

Here is an example of what it would take to protect JASON's building Although the HVAC installation is large (left photo), the air intake is modest (right photo shows interior view).

[redacted]



Building protection raises the issue of dispersal and models of the atmospheric boundary layer. While we did not do an extensive survey, our sense is that this field would benefit from a modern set of experiments.

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# Personal protection devices

- US hospital system ill-equipped for large numbers
  - HMOs act to minimize empty beds
  - Runs out of beds in times of flu
- In natural disasters, food, shelter, routine care in large open spaces
  - A bioevent brings incapacitation, contagion
- Personal "smart tent" for high-tech home care
  - Isolate the sick after decontaminate
  - Provide life support and feedback to family
  - Monitor and communicate patient status
- Engineer, produce, stockpile, distribute

*Home is where the bed is!*

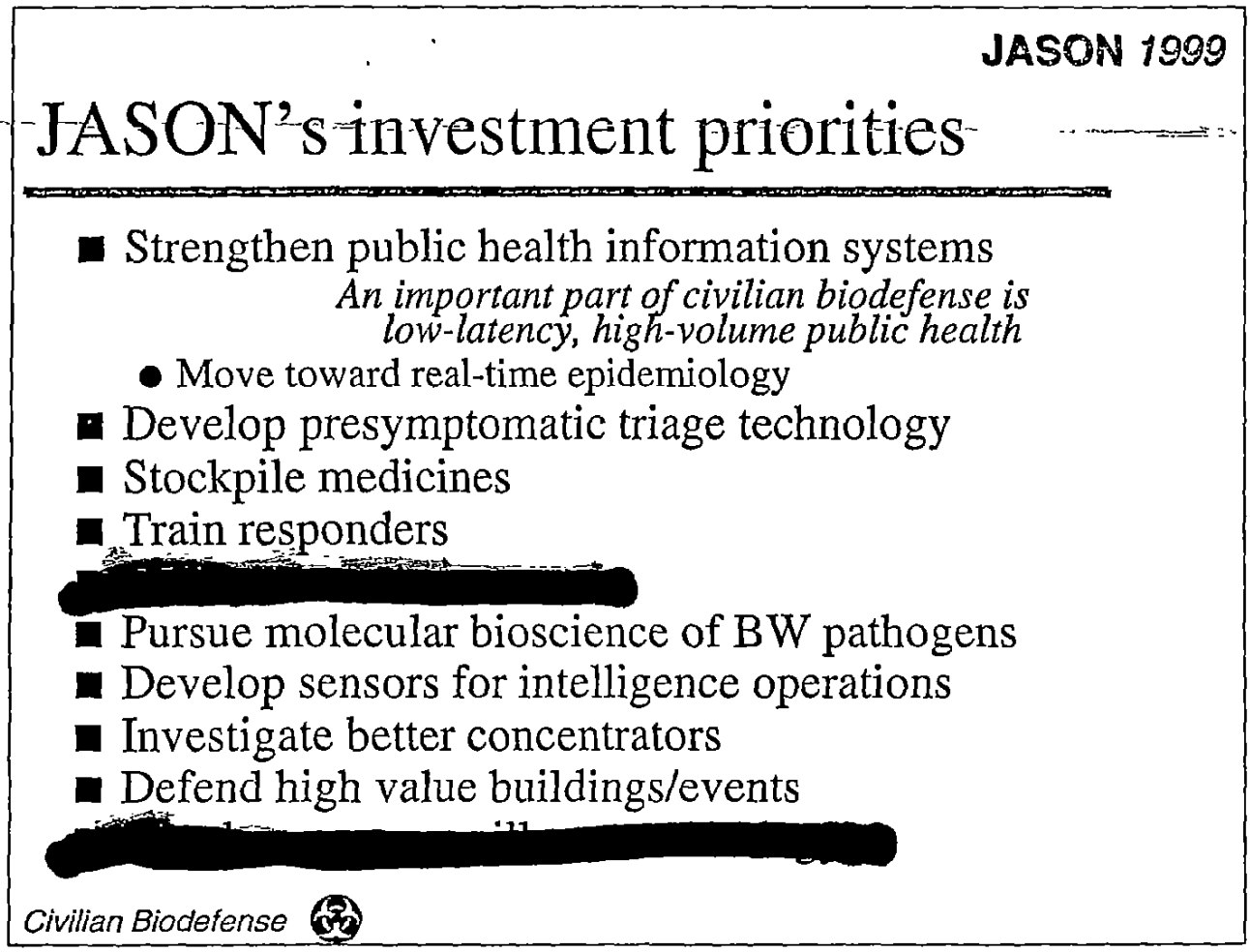
*Civilian Biodefense*

The "smart tent" described in this chart might be useful in civilian response to a bioevent Appendix VIII elaborates on personal protection devices.

# Briefing outline

- Study definition
- Technical topics
- Investment priorities and recommendations






This chart lists our priorities for investment toward civilian biodefense. The first item bears some expanding, while the balance of the items are in no particular order.

A key goal of the Civilian Biodefense program must be to detect, differentiate, and manage the consequences of a BW release in the presence of a natural background of other human disease. Thus, ***civilian biodefense necessarily involves low-latency, high-volume public health.*** This public health connection is perhaps self-evident in a post-event phase. But detecting and characterizing the release of bioagent would be greatly facilitated by improvements in public health capabilities, particularly if delays in monitoring can be reduced.

The public health nature of civilian biodefense challenges the DOD to work effectively with HHS and other "non-traditional" governmental partners. This connection between public health and national security is unprecedented, in our view, and offers many opportunities for dual use capabilities and technologies. There is a useful analogy between a program to improve public health for the purposes of BW surveillance and the 1950's effort to construct the nation's interstate highway system. Both address national security needs but also have much larger "dual use" benefits to the nation.

capabilities and technologies. There is a useful analogy between a program to improve public

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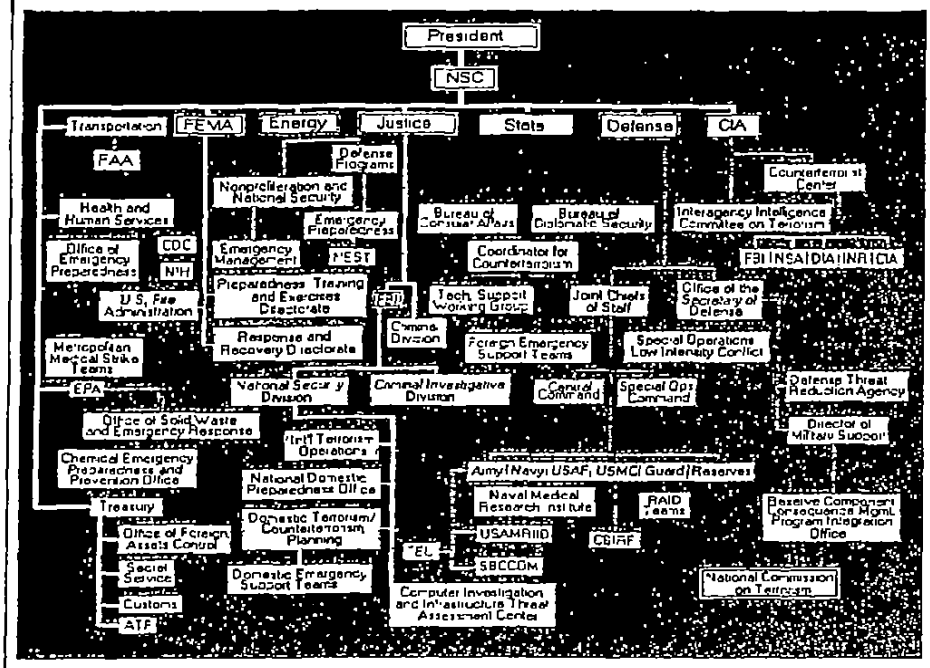
# A different aspect of the threat




- Many players, complementary and overlapping capabilities, responsibilities
- Contrast with nuclear situation
- NDPO is currently "lead" agency
- USDA is late to the table

*Civilian Biodefense*

Civilian biodefense embraces agencies across the government, as well as involving state and local authorities This is in contrast with nuclear weapons, where responsibility is concentrated within a few organizations. Coordinating and adjudicating among these multiple interests is no mean task.

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# Agency recommendations

- Foster a national *scientific* infrastructure for biodefense
  - Assign a lead Federal agency for biodefense science
  - Build linkages between national labs, academia, commercial biotech
  - Fund BW-specific molecular bioscience
  - Insure lab to field coupling and tech transfer
- Foster an operational infrastructure for biodefense
  - Clarify/adjust roles and responsibilities of the various players
  - Clarify operational issues
    - Forcible decon, quarantine, use of stockpiled medicines
  - Training of frontline responders
    - Develop and distribute curriculum
    - Exercises

*Civilian Biodefense*

Appendix IX contains further programmatic recommendations.

# "Take home" points

- Civilian biodefense implies detection, differentiation, and consequence management of a BW release against the natural background
- Necessarily involves low-latency, high-volume public health
  - Obvious in post-release phase, but detection/differentiation greatly facilitated by improved public health capabilities



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# "Take home" points (II)

- DARPA/DOD can best complement and enhance the existing public health infrastructure by
  - Improving collection, mining, and monitoring of existing public health data
  - [redacted]
  - Determining the optimal mix of sensor, epidemiological, and correlative data for timely warnings and discrimination
  - Developing technologies for pre-symptomatic triage and forensics
- Must work with HHS and other non-traditional partners
- There are many dual-use opportunities

*Remember the interstate highway system*



There is a useful analogy between a program to improve public health for the purposes of BW surveillance and the 1950's effort to construct the nation's interstate highway system. Both address national security needs but also have much larger "dual use" benefits to the nation.

# A Appendix: BW Sensors

Sensors would be one element of an early warning system for BW defense. Strategic sensor deployment could be very important given the time lag for an in vivo identification of a virus/bacteria and a potential latency involved in an infectious spread The problem is as much "what to sense" as it is "where to sense it". Given the range of potential BW weapons, and the plethora of attractive targets, they must be selectively developed and strategically deployed. We heard a briefing on animal viruses which could be genetically engineered to affect humans, in addition to a variety of existing bacteria/viruses which could wreak havoc on the general human population

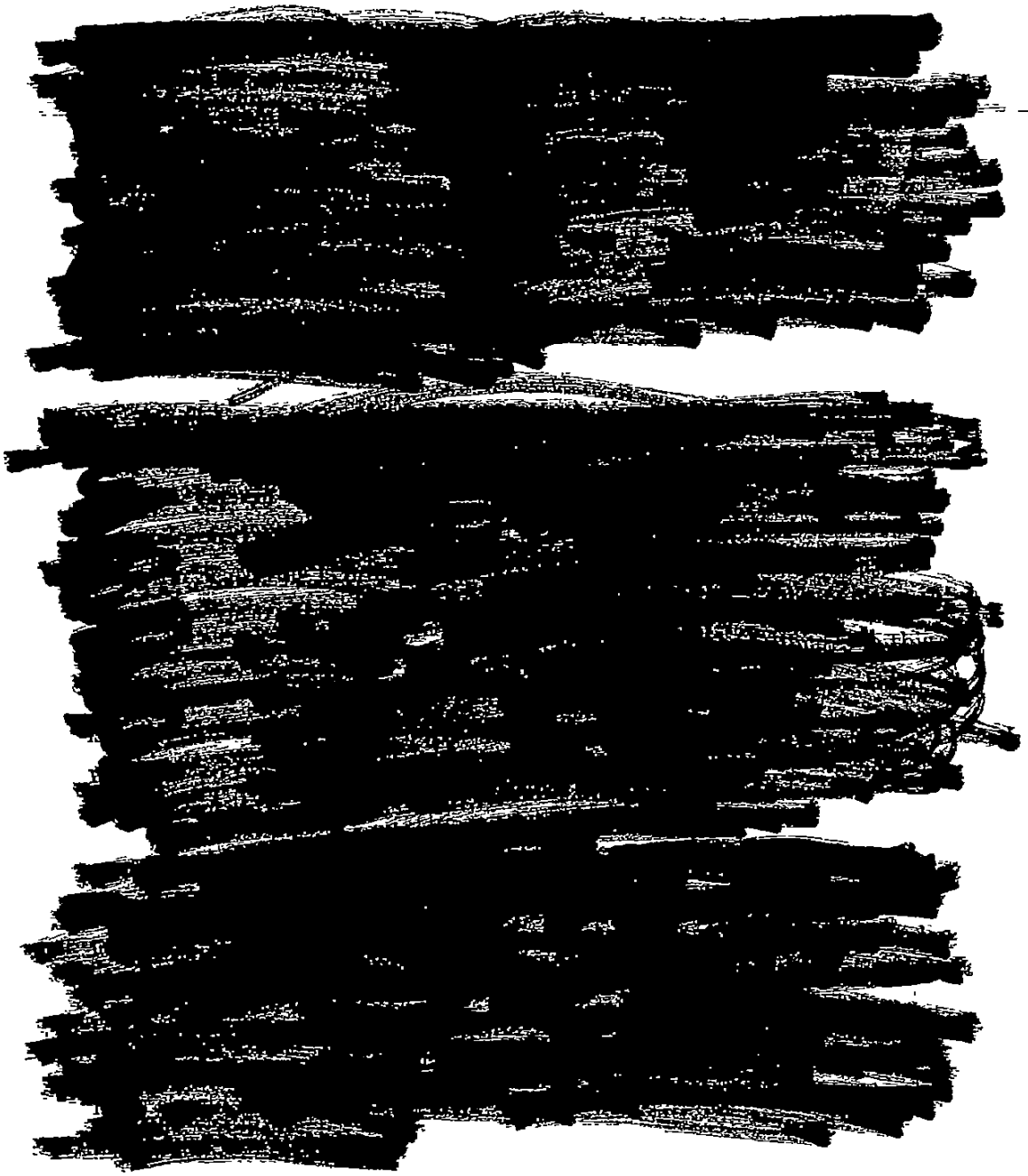
Sensors developed to provide warning against such BW agents should focus on responding to existing agents. In the example of modifying animal viruses to affect humans, we were told that although technically feasible, the task is still non-trivial. The problem then is to determine the subset of agents that represent the most likely threats. Many people in the field agree that anthrax is a likely candidate for tactical military usage due to its durability, infectiousness, and lethality It also appears to be the substance of choice for hoaxes, judging from the number received by the FBI per year on a national basis.

Other likely agents have been identified, and their relative probability for usage by criminals and/or terrorists will not be discussed here. Rather, we wish to emphasize that only this basic subset of agents should be used as the predicate for a focused sensor development program. We heard a briefing on the role of primers in the Polymerase Chain Reaction (PCR), and such primers could be used as part of a sensor package to recognize specific base pairs in the toxic agent genome [redacted]

[redacted]

[redacted]lowever, whatever the scheme, any sensor package must be robust from the elements as well as from unauthorized tampering

[redacted]



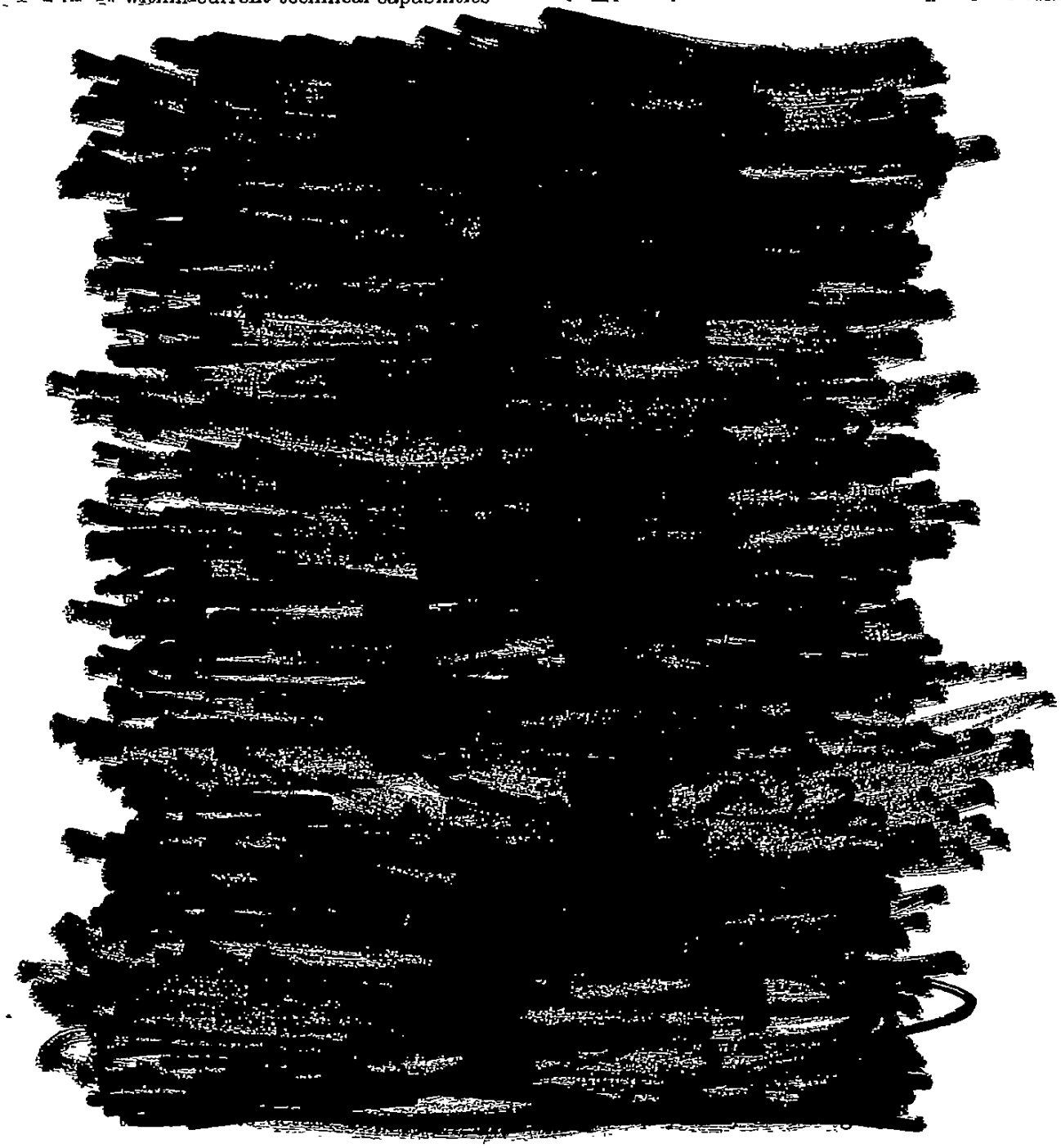
# B Appendix: FRET Technology

Molecular biology methods involving dual primers monitored with FRET (Fluorsecence Resonant Energy Transfer) seems in principle to be a reliable method for identifying the genus, species, and even the strain of a bacterium. In this approach, two primers are required Specificity is gained because a positive signal is only obtained if each primer hybridizes with the target DNA, since each primer is typically a 20-mer, a very low false positive rate is achieved

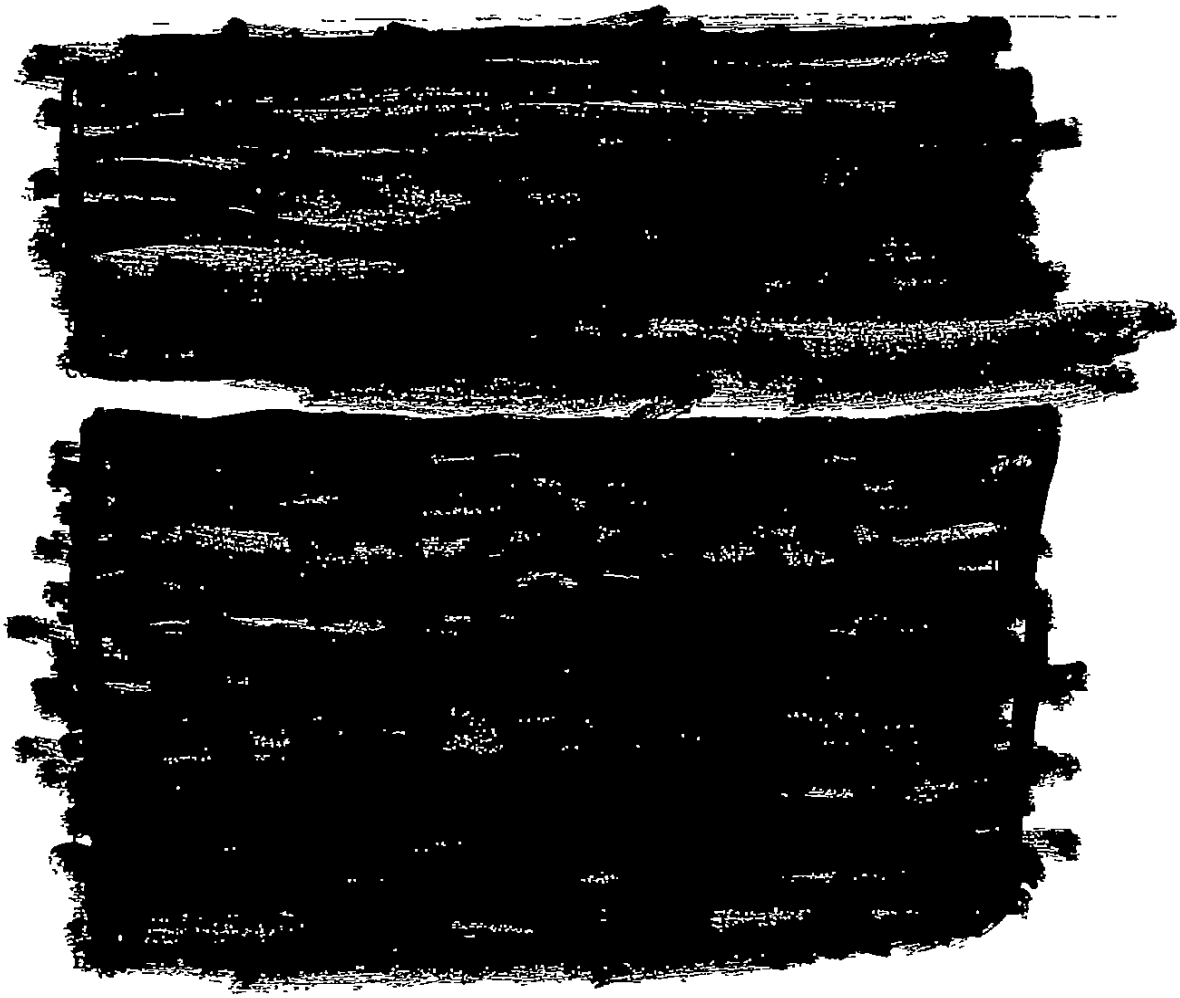
When the target DNA strand is present, then both primers hybridize at their targeted locations Each of the two different primer types is labelled with a dye molecule that is chosen such that energy transfer can occur from one dye molecule to the other. FRET is a probabilistic process based on dipole-dipole interaction between suitable donor and acceptor molecules. Energy transfer between the donor and acceptor molecules results in increase of the fluorescence intensity of the acceptor The donor and acceptor are chosen such that excitation of the donor occurs at a different wavelength than excitation of the acceptor. A typical donor/acceptor pair might be fluorescein isothyocyanate (FITC) as the donor and tetramethyl rhodamine isothyocyanate (TRITC) as the acceptor. If the donor and acceptor species are separated, then excitation of the donor only produces fluorescence of the donor species. Alternatively, if the donor and acceptor are in close contact, then excitation of the donor results in energy transfer and subsequent fluorescence of the acceptor. This signal is only present when the species are in close proximity, which in the present case is when the desired hybridization of both primers to the target DNA has occurred.

Each strain of a bacterium, and every different type of bacterium, must be different at some level in its genetic code. At present, primers for such purposes are available in the public domain for bacteria of importance to public health, such as candida However it seems to be only a matter of time and resource allocation before such primer targets are available for any known bacterium or virus of interest, including those of concern for a BW

attack Array methods can enable detection of hundreds of different bacteria in parallel, so that detection schemes for the highest ranked threat are likely within current technical capabilities



corresponding new primer material to the units and would involve significant logistical time and expense



Another virtue of this approach is that as new primers become available to detect new BW threats, the sequence of concern need only be transmitted to the existing units and the new primer would then be made on cue from reagents on hand.

[redacted]

With respect to development of such a system, it should be noted that the needs of the commercial sector and the defense sector diverge with respect to primer synthesis [redacted]

Additional technical details on FRET can be found at: http://www.visi.com/soft-flow/fcap/FRET.htm

# C Appendix: Mining Medical Reporting and Billing Data

In a BW attack, a commonly-quoted scenario is that people exposed to a BW agent such as anthrax would go along their business after the event (subway dispersal for example), eventually develop symptoms, then report for medical care, and would be sent home because the symptoms would likely be mistakenly diagnosed as influenza By the time humans are symptomatic their prognosis for survival is low, so these early symptomatic cases would mostly eventually die of the attack-induced anthrax infection However, there is a distribution of incubation times of anthrax in humans, depending on individual metabolism properties, the dose of spores received, stress factors, and other variables If there were a way to recognize these early "flu symptom" reports as characteristic of a BW attack before the majority of the people subjected to the BW agent were symptomatic, it might be possible to take action to identify the event location and administer effective treatment to the people who were exposed but who are not yet symptomatic and therefore to obtain an earlier warning on the timeline after an event has occurred.

Other factors to consider are that influenza is not a "reportable" disease, and that the medical records transmission from individual physician to the state health authorities or the CDC is currently very slow. Thus, any data flowing through the infectious disease reporting channels currently would appear far too late to allow action to be taken in a timely fashion to save the lives of the people exposed to the agent in the BW attack

An alternative option is to consider use of the medical billing records data and its associated infrastructure Almost every visit and telephone call to a health care provider is logged into a data system and identified generically according to its topic· "broken leg", "flu-like symptoms", "fainting", etc. The data are available both rapidly and also are available historically The question is: *Can one use and mine this data to obtain early warning that an outbreak has occurred?*

To do this, one needs to know the natural background, and its fluctuation characteristics, against which the signal is to be detected. The billing and associated medical records are, of course, available for many of the past- years and in the future as well, and can be used to establish this background Diseases like influenza presumably propagate in predictable, and qualitatively known spatiotemporal patterns; for instance Asian swine influenza initiates in Asia, spreads eastward around the globe, at a known rate on average, propagates spatially in a characteristic fashion, etc The averaging statistics for humans traveling globally, becoming infected, etc. will smooth out many fine-grain fluctuations due to the variability in any individual year or infection type.

Cooperation would be needed from a large HMO in order to gain access to their medical/billing records for statistical analysis. These medical/billing data records should be examined to explore the baseline, and statistical variation therein of the spatiotemporal characteristics of past diseases. From an analysis of these data it should be possible to determine statistically what spatiotemporal characteristics would be required in order to, with 4-sigma confidence (for example), detect an "outbreak", based on comparison to the historical record and reporting pattern of disease Significant signals would be produced from temporally and/or spatially collocated cases in "influenza symptoms" for example that are anomalous relative to the expected past history of naturally-propagating diseases.

This approach does not require any significant improvement in the current billing/medical record reporting structure, just data mining and analysis in order to determine statistically significant anomalies and to use these anomalies as a warning that an improbable deviation from historical trends in health state has occurred. This fits the definition of an "outbreak" in its classical sense, except that data mining in this fashion might well expose such events early enough to allow identification that an event has occurred and to allow action at an earlier stage than would otherwise be done. Of course, it has implications not only for monitoring BW events but also general public health concerns.

In addition to the technical issues associated with data mining, there are potentially significant concerns regarding confidentiality of medical records and other privacy rights that would need to be resolved before the method could be tested or applied.

# D Appendix: Wide-Scale Sampling of Human Pathogens and Indicators

## D.1 Introduction

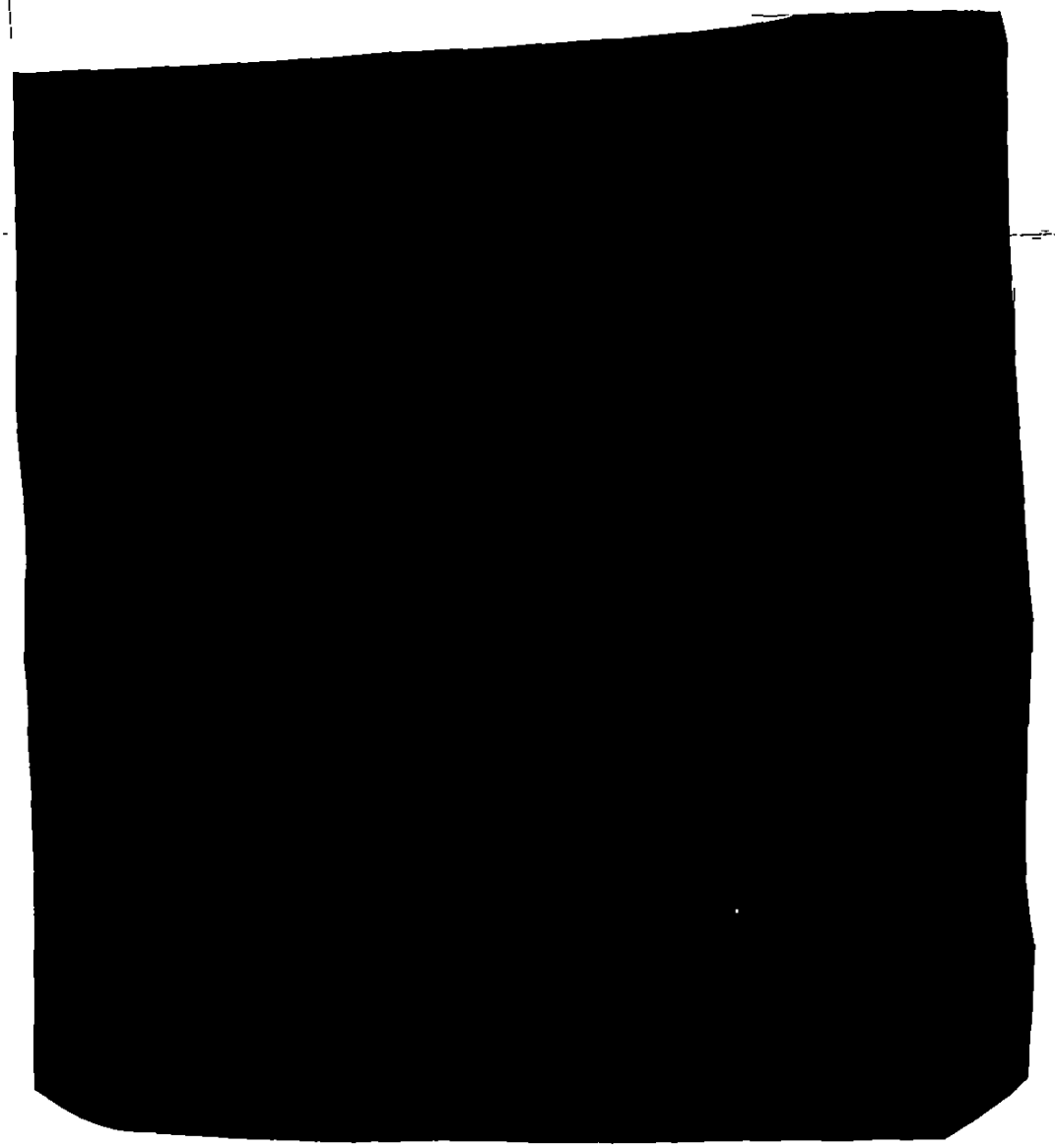
[redacted]

[1]David Koplow has agreed that "No treaty could empower inspectors to conduct random intrusive body searches for possible telltale evidence of radiation or biological weapons" [Arms Control Inspection Constitutional Restrictions on Treaty Verification in the United States", *New York University Law Review* 66, 355 (1988)]

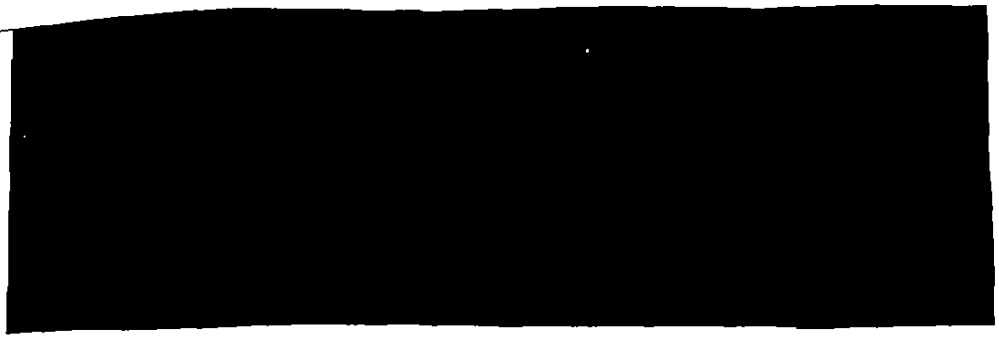
[2]Of course, women also urinate, but not in devices as convenient for sample-talking as urinals.

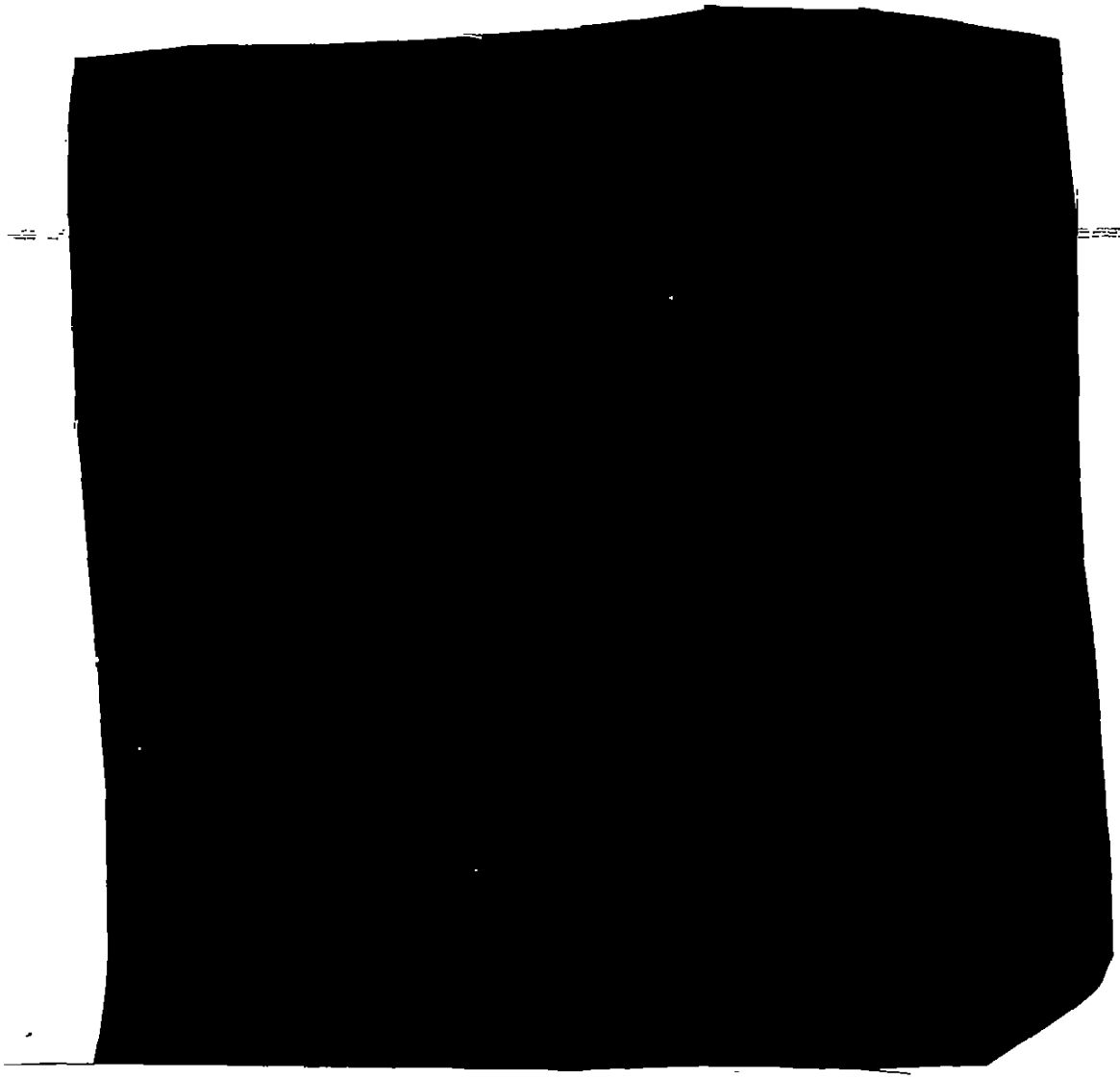


Of course, women also urinate, but not in devices as convenient for sample-talking as urinals.



## D.2 What Information could be Gathered?



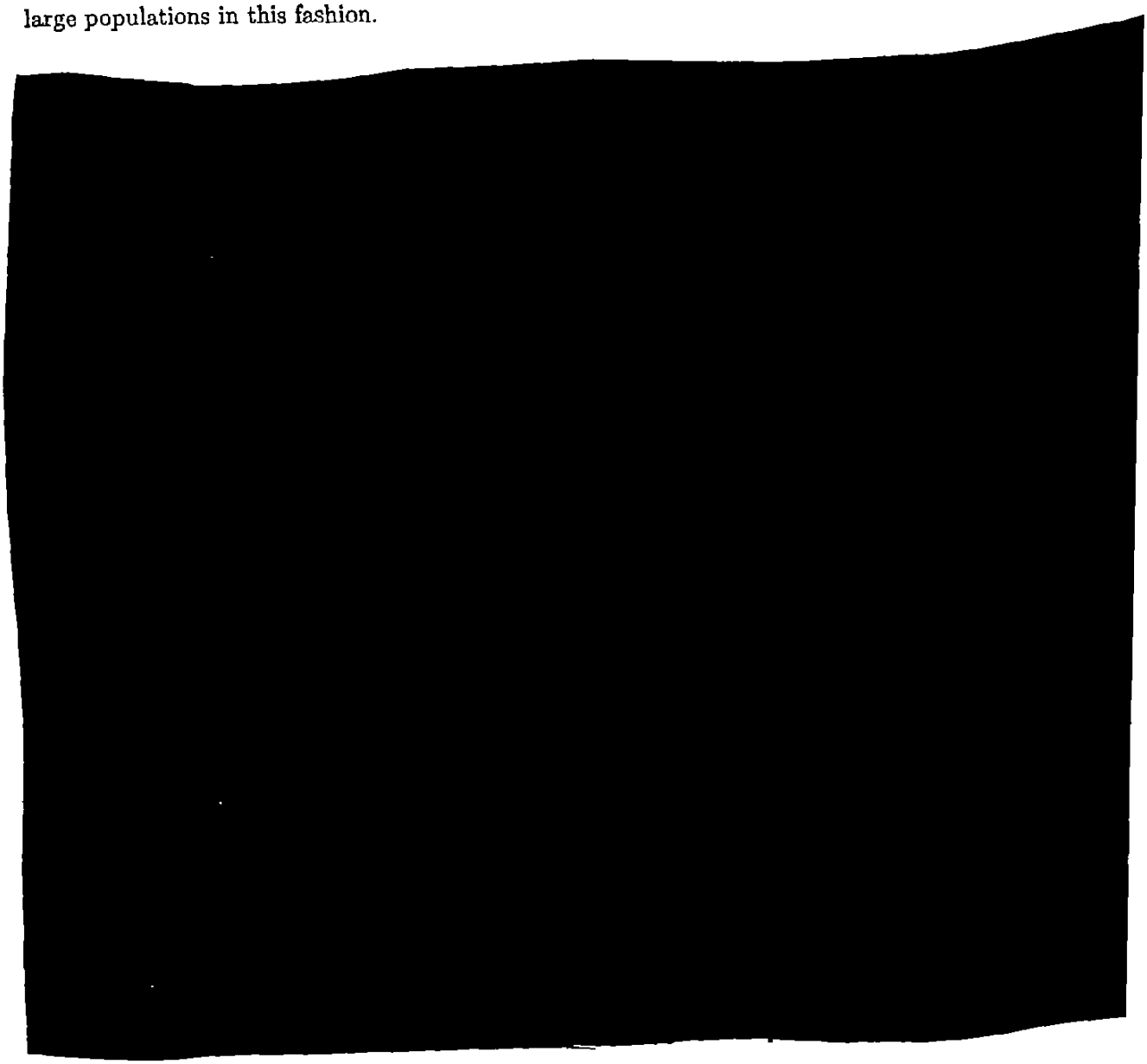


## D.3 Where will the Samples be Gathered?

## D.4 How is the Sampling Done?

# E Appendix: Presymptomatic Triage

Identification of who has, and who has not, been exposed to a BW attack is clearly a critical component of the response to such an incident There are several important reasons to be able to perform rapid diagnosis/screens of large populations in this fashion.



[redacted]

A major key to addressing this situation is to realize that the term "symptoms" refers to external physical observables that are readily monitored by medical practitioners. These include pulse, temperature, blood pressure, medical state (coughing, pains, etc.), and the like.

[redacted]

An alternative approach would exploit, and attempt to detect in as noninvasive a fashion as possible, the biochemical reactions that the body is undertaking in response to a viral or bacterial infection in response to the introduction of disease. These are also "symptoms" but are biochemical as opposed to physical observables. Such biochemical reactions must clearly occur while a virus is multiplying in the body but before external physical symptoms are displayed; similarly, when an anthrax infection is progressing, internal biochemical changes must be occuring in the patient that ought to be detectable well before external physical symptoms are displayed.

Two generic methods are now becoming available that can in principle be exploited for this purpose. The first is gene expression chips, in the general area of proteonomics, and the second is antibody-based chips that in principle can perform identification and quantification of proteins. We discuss each of these concepts below.

Conventional DNA chip-based arrays, used widely in genomics, are designed to identify and react with specific DNA sequences in the samples of concern. Such methods would be useful in forensic aspects of a BW attack in order to identify the strain and perhaps geolocate the origin of the agent, however they are not particularly useful for the rapid screen that we desire herein. In proteomics, the gene expression patterns, as opposed to the genes themselves, are probed, again using chip-based arrays However,



the genes themselves, are probed, again using [redacted]

in this instance, hybridization is performed against long (perhaps 1000 base pair) sequences of oligonucleotides chosen to be specific for c-DNAs that are related to protein expression. The quantity and type of c-DNA levels in a cell then serves as a biochemical indicator of that cell state as well as of the cell type.

A specific chip-based proteomics implementation, taken from the work of Pat Brown at Stanford (http://cmgm stanford.edu/pbrown/yeastchip.html), is depicted in Figure 1 below.

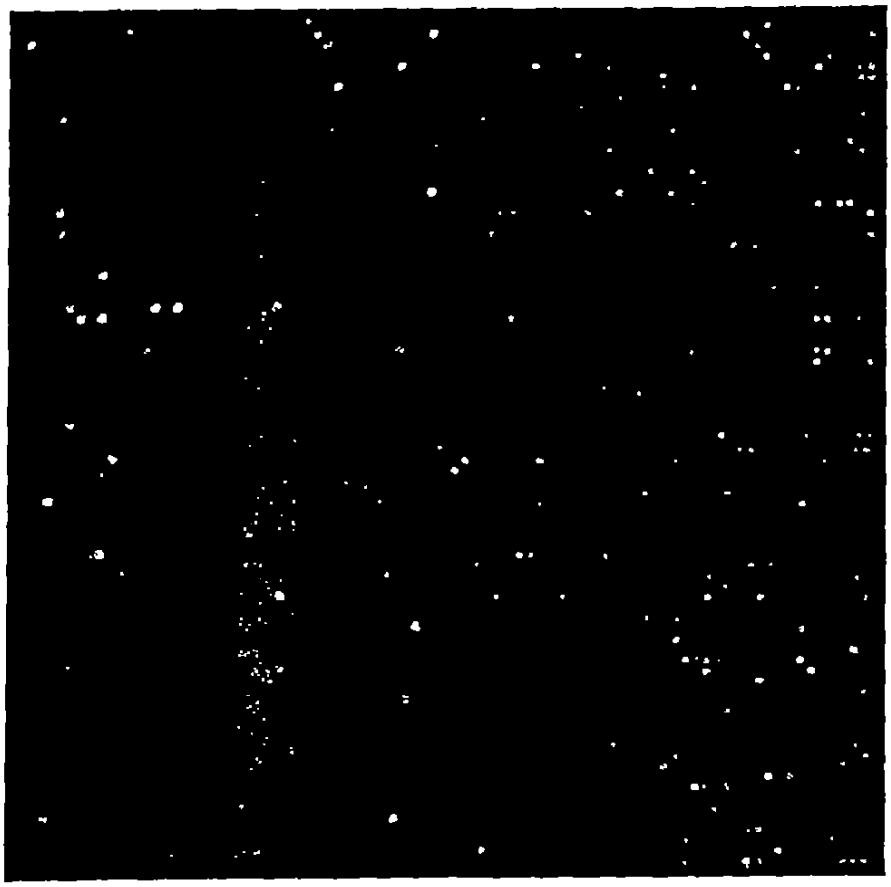


Figure 1: This chip has 6116 Yeast Genes, 96 Intergenic regions, and numerous control samples, with a total of 707,520 spots printed altogether. The chips are made using a a microarrayer, which is a high-capacity system developed to monitor the expression of many genes in parallel.

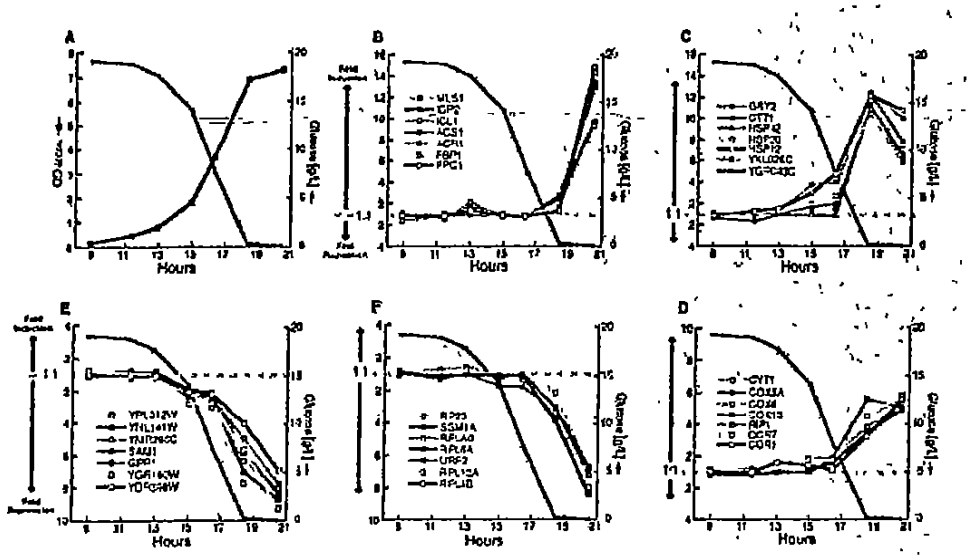


Figure 2: .

The power of the method is that different states of stress, infection, or other states in the biochemical/metabolic cycles will produce different patterns of gene expression that can be detected by the array. For example, the figure above, again taken from Pat Browns lab (http://cmgm.stanford.edu/pbrown/explore/Graphs.jpg), shows: (A) a temporal profile of the cell density, as measured by optical density at 600nm, and glucose concentration in the media. (B) Seven genes exhibited a strong induction (9 fold) only at the last time point (20.5 hours). With the exception of IDP2, each of these genes has a carbon source response element (CSRE) UAS. There were no additional genes observed to match this profile. (C) Seven members of a class of genes marked by early induction with a peak in mRNA levels at 18.5 hours. Each of these genes contain stress response element (STRE) motif repeats in their upstream promoter regions. (D) Cytochrome-c oxidase and ubiquinol cytochrome-c reductase genes. Marked by an induction coincident with the diauxic shift, each of these genes contain a consensus binding motif for the HAP2,3,4 protein complex. At least 17 genes shared a similar expression profile. (E) SAM1, GPP1, and several genes of unknown function are repressed prior to the diauxic shift, and continue to be repressed upon entry into stationary phase. (F) Ribosomal protein genes comprise a large class

of genes which are repressed upon depletion of glucose Each of the genes profiled here contains one or more RAP1 binding motif upstream of its promoter. RAP1 is a transcriptional regulator of most ribosomal proteins. The main point is that the various different stress/metabolic states all display their own gene expression characteristics, which can be monitored by their signatures on the array.

The concept should be extendable to humans as well once the proteomics chips are developed for this purpose The concept to be exploited is that characteristic disease states, such as upper respiratory infections for example, would display characteristic patterns of gene expression, and that these patterns would be diagnostic of the body's response to the infection prior to the display of classical externally monitored physical symptoms such as fever, coughing, etc. Epithelial cells contained in the urine or in sputum would be excellent targets for use in exploitation of this technological capability both in the BW defense arena as well of course as in general applications to public health

The other approach is to, instead of detecting the c-DNAs that accompany gene expression, to detect the proteins directly. In this instance, an antibody-based array, with the antibodies selected to bind the various proteins of interest, would need to be developed. It is not necessary that each antibody is highly selective towards the specific protein of concern; provided that the array is of high enough dimensionality, then the unique patterns produced on the array can be used to probe the various levels of protein expression that are desirable to serve as indicators of the health state of the patient. These types of arrays are in their infancy, but there is no obvious technological reason why they could not be developed for this purpose

The research project that needs to be launched to assess the promise of this method involves two components.

1. determine the time-dependence of gene expression patterns in sputum, urine, blood, etc initially in test animals and then in humans, in response to various infections, and



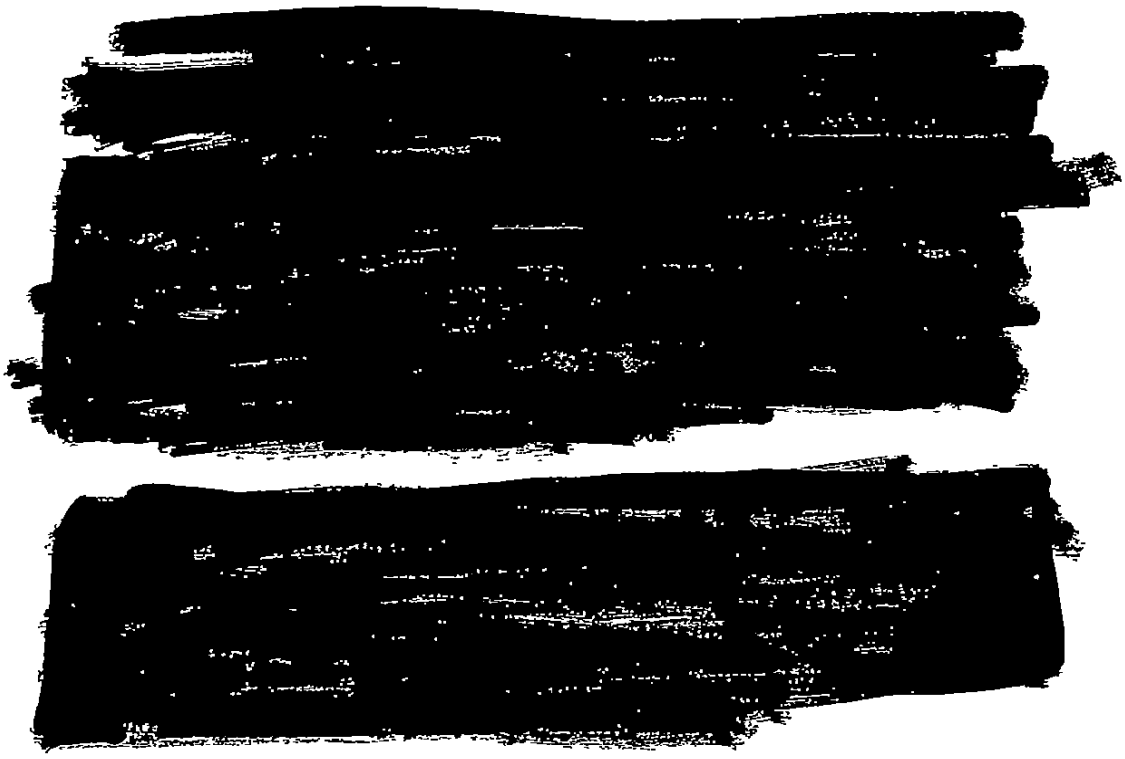
response to various infections, and

2. develop suitable proteonomic chips and transition them into a low-cost manufacturing environment, to make them available for use in the event of a BW attack.

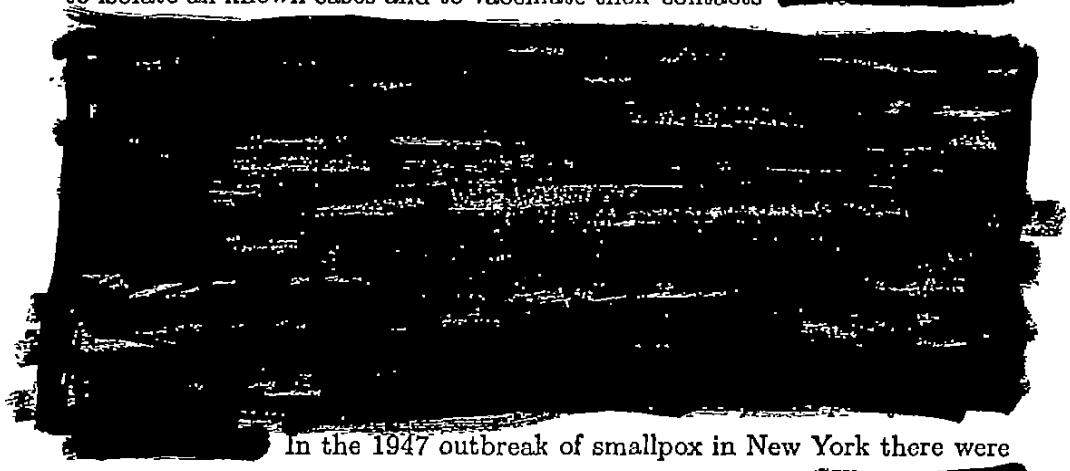
Note that clearly this is a dual-use technology development program, because the obvious enabling capability that would be presented due to the development of a noninvasive or minimally invasive, low cost, presymptomatic diagnostic test for influenza, tuberculosis, and other diseases would clearly impact the public sector's capabilities for non BW monitoring, diagnosis, and treatment of disease.

# F Appendix: Small Pox – A Program for Action

Smallpox (variola) is widely considered one of the most serious threats for biological warfare or bioterrorism. Because of its long incubation period (usually 10–14 days) it is of no tactical utility. However, if not checked, a smallpox epidemic would disable an army or a civilian population. Fatality rates in unimmunized populations are typically 30%, even with modern medical care. [Much lower death rates have sometimes been reported, and are probably attributable to cases in previously vaccinated individuals whose immunity has not completely faded and to infection by the milder strain variola minor (alastrim).] Smallpox has received comparatively little attention in the recent medical literature because no cases have occurred for more than 20 years. For reviews see Dixon (1962), Fenner, et al. (1988) or, more briefly, Baxby (1981).

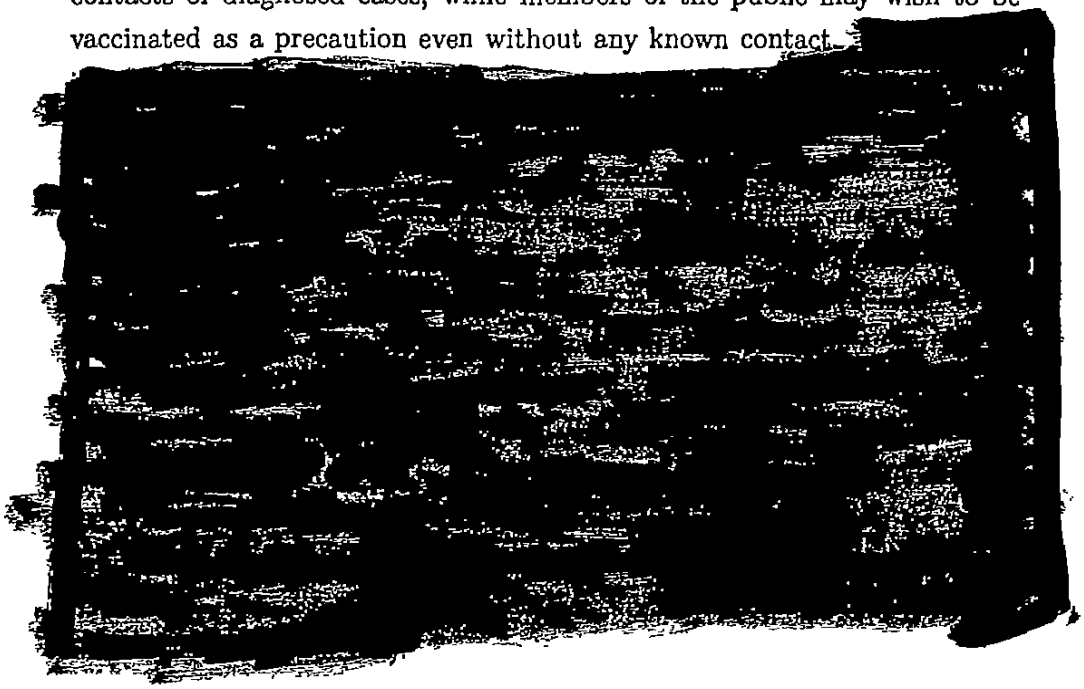


The traditional, and effective, means of checking a smallpox outbreak is to isolate all known cases and to vaccinate their contacts [redacted]



In the 1947 outbreak of smallpox in New York there were three rounds of cases, for a total of 12, three of whom died [redacted]

Public health authorities may wish to restrict vaccination to known contacts of diagnosed cases, while members of the public may wish to be vaccinated as a precaution even without any known contact [redacted]



An unknown number of members of the general public will, knowingly or unknowingly, contact an infected individual before the outbreak ends, and it is only natural to wish to be vaccinated as soon as possible. Further, if vaccination is attempted before exposure there is the opportunity for re-vaccination if the initial attempt fails. There will also be (reasonable) fears that the stock of vaccine will be exhausted.

At present the CDC holds about 7,500,000 aging doses of vaccine [redacted] Severe complications occur in roughly $10^{-5}$ of vaccinations, and the death rate from vaccination has been estimated as $5 \times 10^{-7}$ (Fenner, *et al.* 1988, p. 309), the latter may be reduced by use of methisazone (see below) and modern supportive medical care.

It is sometimes considered that the existing vaccine (even if fresh) is unsatisfactory because it is contraindicated in immunosuppressed and eczematous individuals and in pregnant women (fetal vaccinia is rare and its risk may be further reduced by the simultaneous administration of VIG so that only routine vaccination is contraindicated, for a pregnant contact of a diagnosed case the risk of vaccination is very much less than the risk of smallpox). This is only a minor drawback because if most of the population is vaccinated then the unvaccinated will be protected by "herd immunity"—the inability of the disease to propagate in a population with a high level of immunity. Herd immunity also protects individuals whose vaccination did not "take", a well known and comparatively common problem.

An additional prophylaxis against smallpox was developed in the 195s's (Bauer 1985). It consists of the drug methisazone (Marboran· 1-methylisatin, 3-thiosemicarbazone). An extensive field trial (Bauer, *et al* 1969) found that it reduces the risk of smallpox six-fold in contacts of known cases, and deaths



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by a similar factor. During this trial the contacts were generally (as ethically required) vaccinated; methisazone was effective both in those whose vaccinations "took" and in those in whom it did not. It appears that the effects of methisazone and vaccination are synergistic; methisazone is a supplement to post-contact vaccination, not a replacement for it. Methisazone has also been effective as a treatment in a small number of cases of eczema vaccinatum and vaccinia gangrenosa (Bauer 1985), complications of smallpox vaccination. The end of endemic smallpox has largely eliminated demand for methisazone.

[redacted]

Methisazone was the first anti-viral compound to be licensed by the FDA (in 1960). Its only known toxicity is nausea and vomiting, "only rarely severe", in approximately one quarter of those receiving it (Bauer, *et al.* 1969). A host of new broad spectrum anti-virals exist or are under development.

[redacted]

Smallpox is believed to be acquired through the upper respiratory tract by inhalation of particles containing virus. This suggests that a useful degree of protection against infection may be obtained from simple face masks (Lowe, Pearson and Utgoff 1995), goggles, and similar low-technology sealing and air filtering devices.

[redacted]

"Excretions from the nose and mouth [are] the most important source of infectious virus" (Fenner *et al* 1988, p.123), implying that masks should be applied to patients as well as to the uninfected. However, because the patient is a source of infection which must be contained, a patient's mask should provide air at slightly less than atmospheric pressure, filtered before it returns to the atmosphere (rather than before it is breathed).

[redacted]

[redacted]

Much simpler masks, consisting only of a layer of gauze or similar fibrous substance, without an air blower or airtight seal to the face, are nearly ubiquitous in hospitals (and were widely worn during the 1918–19 influenza epidemic).

[redacted]

It is likely that the reappearance of smallpox would lead to widespread panic.

[redacted]

In order to manage this situation it would be necessary to ensure, and to convince the public, that sufficient vaccine and protective devices are available for the entire population, even if expert opinion holds that they are only necessary for contacts of known cases. To build confidence it will be necessary to make vaccine and VIG available on demand to any licensed physician Ordinary commercial channels should be adequate for supplying masks, which should be freely available to the public

It is interesting to contrast the response of the medical community to the end of endemic smallpox to that of the national security establishment to the end of the Cold War The medical community disarmed unilaterally by



the end of the Cold War The medical community disarmed unilaterally by

letting vaccine stockpile shrink and production facilities be dismantled, while the national security establishment continued an ambitious ballistic missile defense program, designed to ensure the effectiveness of the nuclear deterrent against hypothetical future threats.

1. Stockpiling of enough doses of smallpox vaccine to protect the entire US population This should not wait for the development of a new vaccine. In the past, vaccine has cost only a few cents per dose (Fenner, *et al.* p. 541) The technology is old, several decades ago there were dozens of vaccine manufacturers in the world. A simple RFP for production of one of the standard strains of vaccine to WHO specifications would likely produce bids from numerous generic drug companies, in the US and abroad Vaccine should be made available to physicians as freely as other prescription drugs, perhaps through the usual commercial channels in addition to the national stockpile maintained by CDC.

2. Stockpiling of enough VIG to meet the expected level of adverse reactions (estimates range from $3 \times 10^3$ to $10^5$ cases, depending on severity and the source cited) produced by vaccinating the entire US population. If most pregnant women (about $3 \times 10^6$ at any time) choose to be vaccinated they should be provided with VIG, increasing the demand to $3 \times 10^6$ doses. Production of VIG requires either the development of recombinant DNA methods or the vaccination of sufficient individuals to serve as plasma donors.

3. Stockpiling of enough [redacted]-molecule antiviral agents [redacted] to treat all contacts if smallpox appears suddenly and all cases of generalized vac-



tacts if smallpox appears suddenly and all cases of generalized vac-

cinia if the entire population is vaccinated.

[redacted]

4. Stockpiling reagents for the diagnosis of smallpox.

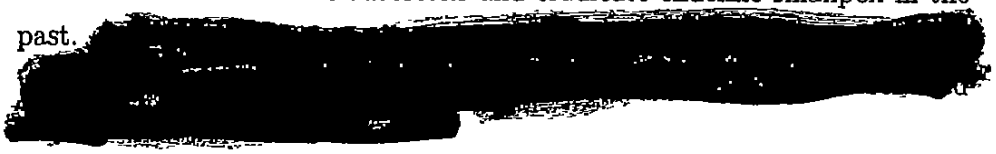
[redacted]

5. There should be a program to test (and develop if necessary) passive protective devices such as masks and goggles to prevent the transmission of contagious viral diseases Once useful protective devices are identified they should be stockpiled in sufficient quantity to protect the entire population

   We make another recommendation concerning future research on smallpox:

6. It has been standard practice (Dixon 1962; Fenner, *et al* 1988) that all laboratory personnel working with smallpox virus must be successfully vaccinated at three year intervals. This rule should continue in force, and no research with or manipulation of viable virus should be undertaken except by vaccinated workers An accidental escape of virus would not just endanger the laboratory staff but would threaten a world-wide pandemic. For this reason no level of containment should be considered adequate protection in itself; people err and systems fail

Modern advances in biotechnology may lead to better vaccines, drugs and reagents However, the time required for development and licensing may be long, and these efforts are not reason to neglect proven technologies which were sufficient to contain outbreaks and eradicate endemic smallpox in the past.



We thank D. A. Henderson for discussions.

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# G Appendix: Building Protection

The easiest protection to implement is positive pressure of filtered air in buildings or vehicles This means that the normal air change rate of two per hour, which ensures that the integrated dose of micron-size particles within a building is equal to the time integrated dose outside the by a level of contamination in the building that is almost zero All one needs to do this is to ensure that the pressure in the building exceeds the dynamic pressure of the wind outside, so that there is no place on the building where air and its accompanying load of particulate are brought in

The positive pressure can be implemented in office suites or in the entire building, as is desired. It depends to some extent upon the HVAC (Heating Ventilation and Air Conditioning) system. Consider a truly collective protection, so that every inlet of air into the building is replaced by a in the external atmosphere, feeding a plenum from which any leak is to the outside, with the building plenum separated from the positive-pressure plenum by a HEPA (High Efficiency Particulate Airfilter).

Options other than HEPA filters are wetted rotating blades, wetted multiple turning vanes, electrostatic precipitation, and even efficient ways of heating the gas (above the sterilization or decomposition temperature of the agent) and then cooling it via regenerators, in order to avoid an excessive heat input in warm weather or cold

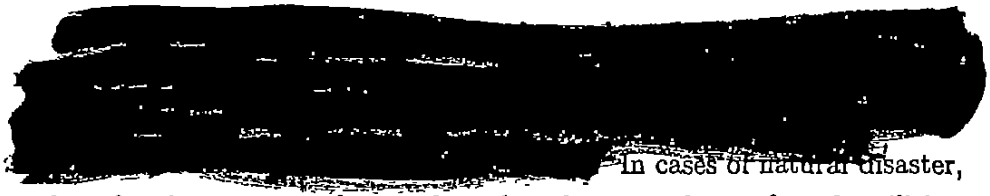
An increased requirement for heat or power would be imposed by faster than normal airflow through a building, with outside air heated to the comfortable temperature in the winter time, and cooled to the internal temperature in the summer time. This burden may be eased by the use of "regenerators" that allow efficient exchange of heat (and moisture) from air to a solid bed, and that then give back the air and moisture, as required, if the flow path is periodically reversed and exhausted through the filters.

The above schemes may be used as well on vehicles as on buildings, and with the exception that fast-moving vehicles need more internal pressure in order to compensate the frontal dynamic pressure in moving against still air or against the breeze. On the other hand, this "ram air pressure" is automatically available, as needed.

# H Appendix: Personal Protection

## H.1 Tents

In almost every briefing we've heard on the subject of BW terrorism, the problem of systematic medical care for victims after an attack is mentioned and quickly dismissed as being impossible, overwhelming We know from our own experience, news reports, and briefings from experts that the US health system, in particular hospitals and emergency rooms, are not equipped to deal with large numbers of sick, infectious people as might be expected from an attack. Indeed, we have heard that major metropolitan areas literally run out of hospital beds in times of flu outbreaks, making it difficult to find ER space for even automobile accident victims. If anything, the direction in "managed" health care is to reduce the number of "unused" hospital beds, much as the airline industry tries to fill every available seat



In cases of natural disaster, such as hurricanes, tornadoes and earthquakes, or refugees from hostilities, public services of various kinds are able to mobilize quickly to provide shelter, food and routine medical assistance, often making use of large open fields or unoccupied space in buildings to house and care for people in the early stages of crisis management. As has been emphasized, BW attacks create new problems related to timing and understanding of the attack, the debilitating effects of the infection on the affected individual and the likely need to isolate infected people from others Are there technical developments that might help this [redacted] situation?

One that comes to mind is based on a paraphrase of Willy Sutton's famous line on robbing banks homes are where the beds are. We imagine a "smart" personal "tent" that quarantines a person, monitors his or her

state of health, and provides guidance and information to the victim and support persons. Victims would be placed in the tent (maintained at negative pressure by a small blower exhausting through a filter), decontaminated, and cared for at home or in small groups by untrained relatives, friends, or volunteers Monitoring and information services are provided by a sensor-information package that uses ordinary telephone lines to communicate with emergency services to provide them with data on the overall attack and to relay information to the victims and their support group

Personal protection systems certainly exist, civilian use of gas masks in Israel is an example Should a reasonable isolation/monitoring tent be developed successfully, one can imagine stockpiling moderate numbers and distributing them to actual or potential victims when an event is identified The timescales involved are likely to be long enough (unfortunately) so the systems could be transported almost anywhere in the US from a central repository without materially affecting their usefulness.

The two general areas for development are the tent itself and the monitoring/information package The tent must provide isolation, decontamination, and life-support The monitoring package involves instrumentation, information processing and networking. It should be capable of monitoring the individuals vital signs, assisting with diagnosis, providing feedback and assistance to the victim and local supporters and providing data for evaluation of the scope and course of the attack.

The successful development of such a package would have wide application in general areas of health care, for example, facilitating home care for routine illnesses Indeed, such a development may help to eliminate the need to enter hospitals for certain routine illnesses, thus reducing the chances that an individual will contract some much more serious disease.

## H.2 Gas Masks

One can improve on the typical gas mask, which have difficulty fitting tightly around the neck, especially for people with beards The suggested approach will not compensate for a thick beard, but it can be useful.

Assume that the user breathes through the mouthinto a mask, which can house an efficient canister effective against BW and also against CW. When the wearer exhales through the mask itself, most of the air is intended to go out through a flapper valve, but may not, depending on how well the mask was applied and fitted in the first place

But the expulsion of air through the mask can be used to advantage by having a kind of rolled internal cuff around the neck and face, so that the positive pressure in the mask from exhaling in order to exhaust air into the atmosphere, holds the cuff more tightly against the skin than would otherwise be the case.

# I Appendix: Programmatic Issues

Operational components must be coupled with appropriate technical entities in the BW arena. [redacted] This includes, but is not limited to the recognition that a BW agent has been released, rapid identification of the biological agent itself, information management relative to patient care and disease containment, vaccine retention and dissemination (which subsumes the notion of triage), and coordination of the law enforcement response in the face of extreme public safety issues

There are a number of agencies with responsibilities for pieces of this problem, and what is required is a relatively seamless operational plan, backed-up by a focused, goal-oriented biological research program [redacted]. The resultant fine-tuning of this balance will affect survival rates in the event of an actual BW incident.

Because the problem is so comprehensive, indeterminate, and exacerbated by the use of contagions with latent symptomatology, the associated issues are unlike those associated with other potential weapons of mass destruction. [redacted] demands that there be a well-coordinated inter-agency technical/operational effort. This includes identifying the most important and promising areas of research, as well as establishing who should conduct that research. Such an inter-agency effort should heavily favor pre- and post-incident strategies that focus on a distribution of realistic scenarios as judged by expert analyses, rather than addressing those unlikely to occur in the near term.

An effective strategy applied to the BW problem also demands a highly synergistic relationship between law enforcement, the medical community, and pharmaceutical companies Much of the required technical expertise resides with the latter, and [redacted] the case with nuclear weapons of mass destruction, where nearly all the expertise resides within the U. S National Laboratory system, the expertise required to address the biological weapons problem is more diffuse. Although certain elements of the nuclear problem can be used as a model, BW defense poses its own unique bureaucratic challenges.

Therefore, an effective strategy should comprise five key elements:

1. focused research on the development of anti-BW technology such as sensors, information sharing tools, etc ,
2. examining the viability of mass inoculations for emergency response and/or for prophylactic implementation (it might pay to examine the polio vaccine distribution program of the sixties as a model),
3. the assignment of responsibilities for reporting on local, state, and national levels in order to coordinate the emergency medical/law enforcement response for the most probable scenarios,
4. inter-agency training to insure adequate preparedness, and

[redacted]