To: Barbara RING <ring@fas.harvard.edu>
Subject: Anthrax Doses: Lesions from History (fwd)

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---------- Forwarded message ----------
Date: Thu, 1 Nov 2001 01:15:27 EST
From: Martinfurmanski@aol.com
To: cbw-sipri@sipri.se
Subject: Anthrax Doses: Lesions from History

Dear SIPRI Group:

I appreciate Dr. Messelson's note on Anthrax doses. For those interested in historical narratives, some of the previous "unexpected" anthrax cases may be of interest. Also some background on inhalation Anthrax dose determinations and how that relates to the current outbreak.

Some previous inhalation anthrax cases have presented with only tenuous connections to anthrax sources. In these cases the sources of the anthrax were geographically close, but how and why the particular individual developed inhalation anthrax while many (perhaps dozens or hundreds) of other individuals who presumably were exposed to similar doses did not is the problem. Several such cases were associated with goat hair processing mills in New Hampshire and Philadelphia that were known to process anthrax contaminated material. Among workers at these plants cutaneous anthrax occurred with some regularity, and there was one epidemic of 5 cases of inhalation anthrax among employees in 1957. There were, however, sporadic cases in the surrounding population that were not "occupational."

One case was in a 29 year old male whose only connection with the mill was that he walked by the mill on his way to his work (which was not at the mill). He had a preexisting lung disease which may have made him more susceptible (there is evidence from monkeys that such is the case). But his exposure must have been similar, at least statistically, to many others walking along the same sidewalk. There is always the problem of a high-dose "killer puff" however, which complicates the epidemiology.

Another case was in a 46 year old worker at an auto body shop who developed and died of inhalation anthrax. His autobody shop was across the alley from the goat hair mill, and the exhaust fans (that exhaust the anthrax-contaminated dust) discharged into the alley. The alley was 60 feet (20 meters) wide--which is big for an alley in my neighborhood. Again, presumably several other workers would have had the opportunity for a similar exposure. And anthrax was found in the autobody shop dust as well as the goat

hair mill. It would seem others at the autobody shop must have been exposed, but again, a time-limited "killer puff" might have occurred.

Two other cases were not well investigated but seem similar: both were housewives (37 and 50 years old) who lived near to (one 1 1/2 blocks, the other 1 1/2 mile away) from a tannery that was known to be anthrax contaminated. If they walked by or visited the tannery is unknown, but they lived close to it.

Two cases were more directly associated with known sources, but still had "token" exposures. One was a 51 year old secretary at a goat hair mill who was only in the "dirty" part of the mill for a few minutes, yet developed inhalation anthrax. Another was a 53 year old electrician at Ft. Detrick in the days when the offensive BW pilot plant there produced anthrax agent. Although he did not work in a "dirty" area, he developed and died of inhalation anthrax, and his tool kit was found to be contaminated.

Incubation times?

There is a "randomness" in these cases that may be due to random localized "killer puffs" of spores, or, alternatively (or concomitantly) , to a randomness in the dose-response curve of anthrax spores.

Heterogeneity

The transient "killer puff" scenario is reasonable, because clouds of spores are rather time-and-space limited, because they travel rather like smoke, traveling downwind and dispersing outward and upward if they are in the open air with a wind, and become dilute rather quickly if released in modern buildings where there are high rates of air exchange and modern air handling systems. They can make a persistent "danger zone" only where they are being continuously generated (a discharging weapon or perhaps from disturbing a deposited powder in a mail sorting machine??) , or where there is minimal ventilation, or where the ventilation is heavily re-circulated (which may include some buildings, but is NOT the case with aircraft).

This being said, there are some strange things about the dose-response curve of inhalation anthrax that make it behave strangely. Normally most infectious agents are like drugs and poisons in that the larger the dose, the more people become ill. At low doses nobody gets sick, at medium doses some people get sick, and with high doses almost everyone gets sick. Epidemiologists say that the dose that causes 50% of people (or animals, if it is an experiment) to get sick is the ID50, for "Infectious Dose 50%." The dose that kills 50% is the LD50. for "lethal dose 50%." For nasty diseases like anthrax which are essentially 100% fatal without treatment, most workers use LD50 for both measures, though with milder diseases these numbers are often significantly different.

?

Most diseases have a relatively straight forward and "steep" relationship between the dose and the numbers of people (or animals) they make sick (or kill). For instance, if it takes 50% of people are made ill if exposed to, say, 10,000 organisms of disease X, then about 5% might be made sick from 1,000 organisms, and 95% by 100,000 organisms.

Inhalation anthrax doesn't seem to work that way. In the offensive BW days at Ft Detrick they ran a series of 1,236 monkeys (that is a LOT of monkeys!!!) , killing them with graded doses of inhaled anthrax spores, but they got a very "flat" dose-response curve. They found that 8,000 to 10,000 spores was indeed the mathematical LD50, but the curve just stayed flat. At 1,000 spores 33% still died, and at only 100 spores 14% still died. At high doses it was the same, with only 80% dying (i.e. 20% still surviving) when

Data?

exposed to 100,000 spores.

If you extrapolate the curve (which of course is dangerous--I only do it to make a point---the curve has to have a "knee" in it somewhere, I hope) you still have 5% fatalities with a dose of 10 spores, and a 1% fatality rate with a dose of a single spore. ?

So, do single spores kill 1% of the people who inhale them? Scary thought, considering that 1 milligram of anthrax spores (a cube 1 millimeter on a side) contains 10*8 (100,000,000) spores. But this first monkey data is not the whole story. In the goat hair mills there was anthrax in the dusty air. You could culture it out, and if you piped it into monkey cages the monkeys died of inhalation anthrax once they got to a dose of around 1000 spores. The curve in these industrial monkey exposures was more straight forward, and would calculate out to a higher LD50. Only about 3% of monkeys died at 1000 spores total dose, and at 18,000 spores it was only 22%, but the line was reasonably straight, and pointed upward. So this is where the higher 50,000 spore LD50 comes from. or $10^{9}/mg$?

What about humans? There were people working in the goat hair mills, and they got cutaneous anthrax fairly regularly, but it was easily dealt with using Penicillin. There were only a handful of occupational inhalation anthrax cases, most in a single cluster of five cases in 1957. The workers routinely had anthrax spores in their nasal swabs, and tolerated inhalation doses calculated to range from 72 to 690 of the dangerous under 5 micron particles PER DAY. Unimmunized employees tolerated 510 such small particles per 8 hour shift, and none developed inhalation anthrax. And these workers did 40 hours a week, week after week. Although the anthrax in the air varied considerably, both in amount and in the size distribution of the particles, the cumulative doses must have been considerable. And the monkey data suggests cumulative dose is important. But the Ft Detrick workers who did the investigations at the mills were surprised that so very few workers ever got inhalation anthrax. Seroconversion tested?

I should note that the workers all got anthrax vaccine in the late 1950s/early 1960s so that all this data is in my Historical bailiwick: to my knowledge there is essentially no occupational anthrax in the mills (if they still exist) today. At any rate the vaccine stopped the disease in the early 1960s (except for that secretary mentioned above, who was not vaccinated).

Why the difference between the 1236 monkeys at Ft Detrick, and the monkeys and people at the goat hair mills? Hard to say. Maybe the Ft Detrick spores were biologically "weaponized" (one imagines so--that part of the Ft Detrick work was not an industrial hygiene project, after all) so maybe the "natural" spores in the goat hair dust didn't germinate so regularly, or cause disease reliably, even if you could get them to grow on culture plates (here is that viability--infectivity disassociation again: I mentioned in the Crop-duster e-mail). In other words, maybe "natural" spores that sporulate in the "natural" conditions on a goat dead of anthrax might only become truly virulent to cause human disease only a fraction of a percentage of the time. If by technical manipulations the Bioweaponeers can get that "yield" of highly virulent spores up to as little as a few % or so, then you may well get into that flat curve where even small 10-100 spore doses will statistically cause some disease. Yes.

The flat HIGH end of the 1236 monkey anthrax dose-response curve is a conundrum indeed. If a single (or a few) "virulent" spore can kill, why

don't 1,000 virulent spores kill every time???? Is some subset of hosts considerably more resistant? In the human outbreaks as well (Occupational, Sverdlovsk, 2001 East Coast) we have data that seems to indicate that young humans are more resistant: just about all inhalation anthrax cases are in people over 40 years old. Smoking has been suggested as a risk factor, particularly with heavy drinking, in the Sverdlovsk outbreak. I haven't heard about smoking in the current cases, and the old occupational cases don't mention it. Monkeys don't smoke (but I bet there would be a campaign to get them to start if they had disposable income), but they do have a pulmonary mite infection that predisposed them to inhalation anthrax. I do not know how lung mite infestation (or their ages) affected the 1236 monkey data (were all the high-dose survivors young or mite-free?) because the full data has not been published in the open literature. The human data on "youth resistance" is made less compelling because the human outbreaks all seem to be low-dose exposures, so it is not really clear that high-dose survivors would be young. Tragically, we know the resistance of youth is not absolute, nor is there some resistant human sub-population: the Japanese in their WWII BW War Crimes could kill 100% of young men (under 30 years old) with a high inhaled dose of a very crude non-weaponized anthrax preparation.

yes

not smoking

not Semiskis.

CK. not all alveolar

If the above "increased virulent spore yield" scenario is valid it becomes very important to determine if the current East Coast Anthrax is to some degree biologically "weaponized" in the sense of having a high germination and infection rate (as well as the physical weaponization of a small, milled particle size and ??electrostatic additives??). If it is, we perhaps need to worry more about that 10 or 100 spore dose causing disease. I would hope that USAMRID knows what the germination and infectivity rates are by now: I hope they tell the CDC and everyone gets a handle on it. Certainly things like nasal swabs, which did not predict disease in the mills, are surely a good predictor of risk now--no question about that--but if we start worrying about 10 or 100 one micron spores being an effective dose, a negative nasal swab may be no reassurance that you haven't received a dangerous dose. That is why geographic/temporal exposure should be the indication for antibiotics, not a positive nasal swab.

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Sure?

Further note: there is evidence from monkey studies and some from the Sverdlovsk outbreak that very low doses may result in very long incubation periods--hence the 60 day regimen of antibiotics. It will make plotting exposures, especially low-dose exposures difficult but not impossible, as Dr. Messelson and his group demonstrated in Sverdlovsk.

CK trend antibiotic?

Another very important thing is that when we are talking about 1% or even 0.1% attack rates at very low doses, we must remember the denominator of the equation. A residual exposure that has a 0.1% attack rate in a mailroom with 10 workers produces a risk of only 1% that there will be even a single illness. Enough in my book to give antibiotics, but not a public health threat. The same risk in a major office building with 10,000 exposures would produce 10 cases, and an exposure in a metropolitan subway system with 400,000 riders would produce 400 cases, probably enough to strain the ICU capacity of many cities.

I hope all this history is not too boring for those of you who do not concern yourself with what happened long, long ago, in the first half of the 20th century, "before there were spaceships or even plastic!"

Martin Furmanski MD
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To: Barbara RING <ring@fas.harvard.edu>
Subject: Re: B. anthracis dose response (fwd)

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---------- Forwarded message ----------
Date: Mon, 26 Nov 2001 08:38:52 EST
From: Martinfurmanski@aol.com
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Subject: Re: B. anthracis dose response

Drs Nass & Meselson:

Comments on Dr. Nass posting Nov 23 & Dr. Meselson's comments Nov 24:

DR NASS'S COMMENTS:

1. Day locn. outliers exposed in plume footprint but would arise of
2. Smudging.

1. Were late Sverdlovsk Cases due to re-aerosolization?:
It appears from all published accounts that all of the identified victims in Sverdlovsk were in the area of the primary plume on the day of the release. There were not any "outliers" that I recall reading about. Although one can theorize that some of these victims, who frequented the "downwind plume" area might have been exposed weeks later by disturbing anthrax agent that that had settled during the primary release, the case for this postulation would be much stronger if the late cases contained one or more "outliers" who were known NOT to have been in the primary plume. I do not think this is the case. And windborne "secondary plumes" would have smudged the case-location map sideways, as the wind on the day of the release was from a rather atypical direction.

2. Was the Connecticut woman immunologically impaired?
I agree that advancing age will probably reduce overall immune function (whatever that means) and is a risk factor for inhalation anthrax. She may be a very sensitive "indicator host," but she still had to get anthrax from somewhere. I think it is easier to defend a single airborne spore than any other scenario.

3. Sheep & anthrax
Clearly Dr Meselson speaks with authority on the subject. Sheep are very sensitive to anthrax. If I were in charge of the National Monuments in Washington DC I'd take a page out of Andrew Jackson's presidency and get a flock to graze on the Capitol Mall and the White House Lawn.

CK

4. Butchering & anthrax risk.

Dr. Meselson is absolutely right again. Animals freshly dead of anthrax have massive numbers of vegetative anthrax bacilli in their blood, but no spores. Sporulation begins only slowly, and is highly dependent on temperature, not occurring at all below 70 degrees F. April in Sverdlovsk is cooler than that, I think. Even at 90 degrees F sporulation takes about 8 hours to begin, and abundant spores are not produced for 24 hours. Sporulation is absolutely dependent on exposure to atmospheric oxygen and requires considerable (over 60%) humidity. Therefore it needs a carcass that has been opened and/or skinned. Hence the veterinary directive to bury or burn the carcasses as soon as possible WITHOUT autopsy. The tropical anthrax/butchering outbreaks are rather interesting in this regard: if meat is dried and aged (thus letting spores form in abundance), the outbreak is the classical (if very rare) intestinal anthrax with enteritis, hemorrhagic ascities and massive mesenteric lymphadenitis, much like inhalation anthrax, but abdominal. But if the meat is eaten raw or partially cooked from animals freshly dead of anthrax (and in the tropics you better act fast if you are going to sell raw meat from a dead animal!) you do not get sporulation, and the outbreaks are limited to anthrax tonsillitis and cutaneous anthrax, presumably from vegetative anthrax bacilli, which cannot survive the gastric acidity to cause enteritis or mesenteric lymphadenitis. And there is a really fascinating outbreak related to butchering freshly dead animals where tonsillitis and anthrax Bronchopneumonia rather than anthrax mediastinitis occurred. To a pathologist like me that's a big deal, but the paper is under submission & therefore embargo so I'd better shut up.

Also oropharyngeal in humans (?)

Were inhalation anthrax case missed in African epidemics? Well, I don't particularly look for them there, because the rate of single-spore inhalation anthrax takes a VERY large indicator population that is VERY closely monitored for inhalation anthrax. (see my posting on Caveman Meteorology). And in the context of the very large anthrax epidemic in Zimbabwe in 1978-80 very few western trained medical personnel were looking at the population at risk, as there was a civil war going on. (and those who read the PSR journal know there is more controversy about that anthrax outbreak than I have time & space to go into here).

5. The "1300 Monkeys"

I picked the number 1300 because I like to give rounded estimates with specific numbers if I can't check them, and I was away from my study for a few days. Dr. Meselson is once again correct: it is really 1,236 monkeys, and the citation I have is by Glassman. My reference if from the "Discussion" portion (pages 657-659) following the paper Brachman, Kaufmann & Dalldorf, "Industrial Inhalation Anthrax"(pgs 646-657) published in Bacteriological Reviews Sept 1966 Vol 30, No. 3. Glassman ascribes the 1236 monkey series to Joseph V. Jemski. It definitely was an aerosol experiment, and I imagine it used "state of the art" weaponized anthrax (c. mid 1950s?) as it was probably trying to determine standardized effective doses for weapons deployment and defense. In my mind I thought there were firm data points for the 100 spore exposure, but looking again at the paper I see there are no data points plotted, and so the 100 spore end of the graph may itself be an extrapolation from larger dose data points. I yield to Dr. Meselson's more detailed account of the raw data on that series.

6. Papers with serial autopsies and definition of anthrax strains.

The references are three papers by Young, Selle and Lincoln, "Respiratory Pathogenicity of Bacillus Anthracis Spores" parts I, II, and III. All are in Journal Infectious Diseases Nov-Dec 1946 Vol 79 (pgs 234-246, 247-253, 254-271). Yes, it is 1946 and it was the work done during WWII. Back then they wanted to publish what they did and get back to peacetime work. And,

yes, the strain definitions, etc. were different then than now, but if you want to look at anthrax work, you have to look at the historical literature and gleen what you can. (Goodness, Eppinger in 1894 could give us all a good run for our money as far as understanding anthrax pathophysiology!) They did know what they were doing, even if they didn't know DNA carried the genetic code. And they could infect mice and culture anthrax. The strain variants were colonial morphological variants of varying degrees of "roughness" or "smoothness" but I'm not sure what they would correspond to today. But they were pragmatists and they determined their strains by pretty solid things like "breeding true" and characterized them with pretty solid parameters like LD50s.

7. No comment.

8. ID/ LD

I am sloppy and lump everything as LD because without treatment they are essentially the same, and I have read so much old, pre-antibiotic literature that I still think of it that way. I should be better, but for human inhalation anthrax I don't think there has been an untreated survivor. In a really big release, though, you are right, and the difference between treatable and untreatable exposures will, alas, become a point of importance, I fear. God forbid.

9. Age & Susceptibility:

Children get cutaneous anthrax, but there may be different host factors for cutaneous versus inhalation anthrax. The 1946 papers cited above find very significance differences in their "colony morphology" strains in inhalation challenges, but they all seemed to be the same for cutaneous challenges.

Regarding age and susceptibility to inhalation anthrax. I agree that there is a clear bias toward persons over 40 in the industrial and Sverdlovsk series, where exposures were probably rather low, arguably below one LD50 average dose. At these low levels of exposure, variations in host susceptibility would be most evident. But it is not to say that the resistance of youth is absolute. I have under submission a paper written with Sheldon Harris regarding a series of inhalation anthrax cases that came from the Japanese BW program's crimes against humanity. With doses that were obviously considerably over one LD50, they reported 100% infections in a group of 22 male victims with an average age of 29.4 years (range 25-37).

The old 19th century Austrian literature lists several 23 year olds, and refers to a report of a 19 year old. Although Eppinger is really quite sophisticated, some of his cases may not stand up to modern scrutiny, and his cited cases are even harder to authenticate. And 19th century nutrition and overall health was not comparable to today's population. Also the circumstances of the exposures may mean that they are not completely applicable to the modern "militarized spore" problem.

Thank you for your comments.

Martin Furmanski MD
Newport Beach, CA.

To: Barbara RING <ring@fas.harvard.edu>
Subject: Improvised Exposure Calculations & Outliers (fwd)

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---------- Forwarded message ----------
Date: Mon, 26 Nov 2001 08:41:27 EST
From: Martinfurmanski@aol.com
To: cbw-sipri@sipri.se
Subject: Improvised Exposure Calculations & Outliers

Drs Meselson, Nass, SIPRI DG:

I have run some very rough approximations regarding the Oct 8-9-10 "Trenton mailbox" release and the NYC and Connecticut outliers. I apologize for the lack of sophistication of these calculations, but I command residual mathematical abilities at only about a high school algebra level. But maybe this oversimplified approach may be of value to those less scientific types on the SIPRI DG. It also may stimulate workers (dare I say modern major generals?) with a "command of the integral and differential calculus" to do this problem properly. If I make a blunder, please point it out--and anyone offering a more sophisticated treatment would be most welcome. I am looking for Dr. Meselson's ASA newsletter article, but I am having trouble finding it out here in the provinces. I'm sure it would have helped me, but please bear with this very approximate approach. It is only meant as a rough estimate of possibilities, rather than a quantitative model.

I will run through a narrative scenario with examples of actual numbers. This scenario is a little "non standard" because it is a very small "instantaneous point source release" rather than a large prolonged point source release or a military line source release. So many of the existing models I have access to don't apply very well.

I admit I have run this problem a couple of times to find a set of numbers and circumstances that would demonstrate that the Single Spore Lethal Event (SSLE) Hypothesis is POSSIBLE under POSSIBLE circumstances for the Oct 8-9-10 Trenton mailbox release scenario. Once better meteorological models are applied to Oct 8-9-10 we may have a fairly rigorous test for my hypothesis. Specifically it would appear that there probably would need to have been temperature inversion conditions existing for at least several hours during the period of SW winds during Oct 8-9-10 to allow for delivery of enough single spores over the Coastal New Jersey-New York City-Western Connecticut metropolitan area. Another source of uncertainty in my calculations is in the total amount of agent released and of that agent's LD50. These last two numbers have been estimated below, but could quite

reasonably differ substantially in either direction.

I will use several "rules of thumb" that come from an old, never classified US Army Chemical Warfare Service technical manual on deployment of "screening smokes." I think it is not unreasonable to apply them.

1) The leading edge of the cloud advances at the wind speed.

2) The lateral edges of the cloud diffuse outwardly at a 10% rate: i.e. 2 meters in total width for each 10 meters of travel downwind.

3) The top of the cloud diffuses upward differently under three different atmospheric conditions:

A) Under "lapse" (normal, daytime, turbulent) conditions the cloud is rapidly drawn upward by thermal forces and it's concentration on the ground is rapidly dissipated. This condition is provides little downwind surface delivery of a biological agent.

B) under "neutral" conditions, typical of cloudy nights, no temperature gradient exists, and cloud tops diffuse upward indefinitely at about the lateral 10% rate. The surface delivery of biological agents under this condition decreases with the square of the downwind distance (the longitudinal lengthening cancels out see #4 below), and so such agents can be delivered under this condition, but with limited downwind range and with a marked gradient effect of falling dose trailing away from the source.

C) under "inversion" conditions, the cloud top diffused upward until it reaches a temperature inversion layer, which acts as a meteorological "ceiling." Such conditions are common on clear nights (and in Southern California on sunny days, where it causes our prominent, quite visible photochemical smog layer). Under inversion conditions downwind concentration of aerosols decreases only because of lateral diffusion of the advancing front (see #4 below) , and hence ~~concentration~~ decreases only linearly with downwind distance. Under these conditions surface delivery of significant biological doses is possible over quite prolonged distances. Indeed, if such a plume is progressing though a wide, uniformly populated area, the special case of single-spore delivery may experience little or no overall downwind degradation of agent delivery (as far as total number of cases is concerned), because the decrease in agent concentration is compensated for by the increase in overall population exposed due to the widening area "at risk." (someone check this reasoning--there might be a fallacy in it--I think it holds because my high school "cancel out the units" check is OK, but I could be wrong.).

4) The trailing edge of the cloud is retarded because of "ground effect friction" resulting in a progressive lengthening of the cloud. The rule of thumb is that the cloud lengthens to 20-50% of the downwind distance traveled. This factor is of little importance in calculations of downwind biological dose delivery, because the dilutional factor of the lengthening of the cloud is exactly compensated for by the prolongation of the time of exposure to the cloud for persons who remain stationary and are exposed to the entire length of the cloud as it passes. I will address only this stationary host situation.

I will assume uniform distribution of agent throughout the cloud, and zero concentration outside the nominal limits. Because we are addressing single-spore "single hit" delivery, I think this is a fair simplification to make. As long as we are worried only about very dilute clouds causing single spore inhalations, local imbalances in agent concentrations probably don't matter.

I need to set some estimate on the amount of spores released at the mailbox. The news accounts of the isolation bag that contained the Leahy

letter contained "24,000 spores" but appears this meant 24,000 spores on the swab they stuck through a hole into the bag to test for contamination. Sen. Leahy said the letter contained enough agent to kill 100,000 people. If this assumes an LD50 of 10,000 spores, it would mean 20,000,000,000 spores, or about 200 mg. This would mean a "lump" of powder 10 mm x 20 mm x 1 mm (in everyday terms 1/5 of a 1 gm artificial coffee sweetener packet) or a layer 100 mm x 200 mm x 0.01 mm which seems quite reasonable for an envelope's contents. An envelope could have held quite a bit more.

0.9

The perpetrator had the problem of filling and transporting the envelopes, using the highly dangerous "militarized" anthrax agent. It would seem that this would require biological containment, for instance a glove box, with resultant decrease in manual dexterity due to the use of the captive heavy-duty gloves. The agent had to be transferred from its storage container into the envelopes, and then the envelopes transferred into a sealable transportation container, perhaps a heavy duty Ziplock bag, a mason jar, or a gasketed military ammunition-type container. This would involve substantial direct contamination of the outside of the envelopes and the inside of the transportation container. After sealing the transport container, the outside of the transport container could be sterilized inside the glovebox, and safely removed for transportation. When this previously unopened transport container was opened and the letters removed most of the contaminating agent would be released (remember it is easily aerosolized). This total contaminating dose consists of the agent contaminating the surface of the envelopes, the inner surface of the transport container, as well as spores that had transversed the wall of the (at least two) envelopes during transportation and handling. For the present set of calculations I will assume this inadvertent "spillage contamination" in the "Trenton mailbox" release to be 1 mg, (1 cubic mm of powder). This amounts to 0.25 % of the total of 400 mg transferred to the two known letters. It seems to be a reasonable physical amount of inadvertent contamination deposited during envelope filling.

I will assume because the agent in the Oct 9 letters was processed in a sophisticated manner, that it would likely be somewhat more virulent than the 1950s "1236 monkey" preparation, and so I assign it an inhalation LD50 of 5,000 spores. Again, I think this is not unreasonable and falls within the confidence limits of the 1236 monkey data.

or maybe up to 10^5 if 1 mg.

Such a release would release 100,000,000 spores. Although this may appear to represent "thousands of LD50 doses", it would likely produce no "case cluster" in the vicinity of the release. The 10-second 75 meter downwind exposure to this release would be 25 spores per exposed person. 25 spores amounts to 0.005 LD50, or about 5 cases per thousand persons (1 person in 200). (and this value is only if you believe the SSLE hypothesis that very low doses can cause disease: conventional wisdom might well consider 25 spores to be incapable of causing any disease at all). The clandestine maildrop was likely chosen for its lack of witnesses, so it is unlikely there was more than a handful of people, if any, in the vicinity. The concentration of such instantaneous point source releases drops with the square of the distance from the source until the cloud top reaches the inversion layer ceiling, so even these very low exposures drop rapidly to the "random" single-spore dose. For instance, for this 1 mg release, the average exposure drops to a single spore after only approximately 35 seconds and 250 meters of downwind travel. And the risk of a single spore causing disease would be 0.2 per 1,000, if you believe in SSLE. Exposures to such "instantaneous point sources" are also very limited temporally: at the 75

See Screen '94

meter point the cloud passes in 5 seconds, and at the 250 meter point in 17 seconds. So the 1 mg mailbox release would not be expected to produce a "telltale outbreak" localized in the immediate vicinity of the Trenton mailbox.

What is the Oct 9 release cloud like, using these rules of thumb, after it has traveled 100 km? Such a distance would have taken about 5 hours in the 20 kph wind of Oct 9. It would be at that point over New York City. I assume a temperature inversion at 1,000 feet (300 meters). The cloud is at that point is 20 km wide, 300 meters high, and (for the sake of argument, although it cancels out, as in #4 above) 20 km long. Therefore it occupies a total volume of 300 x 20,000 x 20,000 meters, or 120 billion (12 x 10*10) cubic meters. If assuming the 100,000,000 spore release upwind, there is one spore per 1,200 cubic meters. What is the chance that such a dilute cloud would produce disease in the population at risk?

Well, humans at rest breathe at about 10 l/minute. The cloud above will take one hour to pass, being 20 km long, driven by a 20 kph wind. So each human will breathe 600 liters, or 0.6 cubic meters of air during its passage. Therefore each person has a 0.6 / 1,200 risk of inhaling a single spore during the passage of the cloud. This amounts to 0.5 per 1,000 persons exposed. But even if you inhale that single spore, you only have a 1 in 5,000 chance (0.2 per 1,000) of developing inhalation anthrax if the SSLE theory holds. So the overall risk of developing inhalation anthrax is 1 in 10,000,000.

The cloud passed over the region that includes Newark, Jersey City, Brooklyn, Manhattan, Queens and the Bronx, and on toward White Plains, Stamford and Bridgeport before reaching Oxford CN. In the "worst case" dusk-to-dawn" scenario, it will travel 12 X 20 kph= 240 kms before sunrise dissolves the nocturnal temperature inversion, and the cloud disperses. Thus Hartford and New Haven might also have been in the at-risk area, but probably not cities of central Massachusetts or Boston. What is the total population in these areas that were at risk of inhaling a single spore? 10 million people? (can you see I ran these numbers a couple of times?) So with a cloud of the above description, we can expect, statistically, at least one case of inhalation anthrax from the release of 1 mg of spores containing with a LD50 of 5,000 if the SSLE theory holds. We observed two cases, so there is some statistical robustness to the observation.

IMPORTANT PUBLIC HEALTH COMMENT FOR THE MEDIA:

I know media people monitor this DG (Hi, Judy Miller!) So before we see headlines in the NY Times "entire NYC metropolitan area at risk for anthrax" some perspective must be put on exactly what risk was involved. Obviously from the two cases the risk is about 1 in 10 million or so, and the only intervention that might have prevented these "random downwind" deaths was to put all 10 million people on antibiotics for 60 days. (and who would have thought that Oxford, CN was a place at risk?). In addition to the pharmacoeconomics of this intervention (which must be horrifically bad----after all a 94 year old woman has overstayed her 84 year old life expectancy by 10 years-----does her estate have to pay us back $200,000 for those 10 Years?) From a purely public health viewpoint, though, I would think that putting all 10 million people on antibiotics would have caused more than two deaths from pregnant women getting doxycycline, or from severe penicillin allergies in people who did not know they were allergic, or who

were so scared of anthrax they took penicillin anyway.

The public health importance of theorizing the SSLE mechanism is that it explains these two deaths in the context of the very extensive but negative environmental contamination studies. After all, these two cases do not seem to share any other common factor of exposure risk factors except being downwind from Trenton NJ on Oct 8-9-10. They also, of course, share the common risk factor of age.

SCIENTIFIC VALUE OF THE DOWNWIND OUTLIERS

I feel that the downwind outliers were caused by anthrax demonstrating the SSLE pathogenesis. This theory would be essentially impossible to prove experimentally, and indeed would require another such release in a large metropolitan area to be replicated.

The experimental framework to demonstrate SSLE pathogenesis is easy to design, but not possible to perform. Simply expose an experimental group of animals to single spores, and see how many die. Compare this number with predictions based upon the large-dose LD50 to see if the SSLE hypothesis predictions are met.

But to reliably expose animals to a single spore, but not to multiple spores, you have to expose a population to an average of considerably less than a single spore, and deal with the distribution of "zero spore" and "1 spore" animals. This increases the number of animals you need, by perhaps 4 fold? (My quantitative statistics is lame, I'm afraid, but I'm just making a point that doesn't require much quantitation). If you consider that the threshold of causing 1 unexpected death by SSLE pathogenesis for an anthrax agent preparation with an LD50 of 10,000 is 10,000 1-spore animals, then we quickly get to obviously impractical numbers of animals. How many "SSLE deaths" do we need to reach statistical significance? 10? So we need 10,000 x 4 x 10 = 400,000 experimental animals, and that doesn't count the controls. Clearly not possible, even if one could find the SSLE deaths among the "natural mortality" of such a huge experimental animal colony.

Because of the very low level of disease caused by single spores, it looks as if only large metropolitan areas contain enough potential hosts (humans, in this case) to detect the effect of such 1 mg "accidental" discharges. And, indeed, one wonders that if these two cases would have been recognized as such, had there not been a preexisting very high level of suspicion for inhalation anthrax cases because of the concurrent anthrax outbreak.

The above study is obviously just a crude demonstration of possibility and a very rough estimate of the magnitude of the expected effect. I think it shows the SSLE hypothesis is a viable explanation for the NYC and Connecticut outliers.

As before, comments are most welcome.

Martin Furmanski MD
Newport Beach CA.

To: Barbara RING <ring@fas.harvard.edu>
Subject: New Weather Data on Outliers & Correction (fwd)

Matthew Meselson
Department of Molecular and Cellular Biology
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7 Divinity Avenue
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telephone: (617) 495-2264
telefax: (617) 496-2444

---------- Forwarded message ----------
Date: Thu, 29 Nov 2001 03:05:53 EST
From: Martinfurmanski@aol.com
To: cbw-sipri@sipri.se
Subject: New Weather Data on Outliers & Correction

Dear SIPRI DG:

I am beginning and assemble some real meteorology data to evaluate the actual conditions on Oct 8-9-10 to test if the far downwind, single-spore lethal event scenario can explain the NYC and Connecticut outliers. I had previously stated that I felt that temperature inversion conditions were probably necessary to allow the long, 200 km transit of the aerosol from Trenton, through NYC, to Oxford, CT.

Thanks to a brilliant young meteorology graduate student at U of Washington (who happens to be my niece) it looks like there is preliminary hard data that confirms my prediction, at least on the first examination. The radiosonde soundings that are done twice daily from Brookhaven NY show that up until 7 AM on Oct 9 the conditions were unfavorable for my Trenton-NYC-CT transit. There was no inversion and the wind was from the north. But by 7PM on Oct 9 conditions had changed dramatically. The wind was brisk at 20 knots from the required SW direction, and a temperature inversion had formed. These winds remained essentially constant and favorable, and the inversions remained for the next several days.

We still need to get more detailed hourly wind data, to find out just when on Oct 9 the wind changed. We will also try and do some more sophisticated modeling, but so far so good.

Also a Correction/Modification on my "improvised calculations" regarding the Trenton Mailbox Release Scenario. Thanks to the graciousness of Mark Wheelis I have gotten a copy of Dr. Meselson's ASA Newsletter article on downwind dose calculations. It is invaluable, and I am still digesting it. But I find that I may have used an inaccurate conversion factor in my calculations. Dr Meselson used a conversion of 10*9 spores per milligram, while I had used 10*8 per milligram. I had used a conversion factor established for very crude anthrax preparations used by the Japanese during WWII, while Dr Meselson's number was derived for dry spore sophisticated material, and applied to the Sverdlovsk release. Clearly Dr Meselson's

number is the appropriate one to apply to the Daschle/Leahy agent. This does not materially change my "downwind" calculations, because I based them on numbers of spores. The result of changing the conversion factor is probably best made by reducing the weight of contaminating agent released when the isolation container was opened to allow the letters to be mailed. I had set this amount at 1 mg, but with a conversion factor of 10*9, this need only be 0.1 mg. If anything, this makes the scenario even more plausible, as this amount is probably invisible.

I will share additional data as it becomes available.

Martin Furmanski MD
Newport Beach, CA.

To: Barbara RING <ring@fas.harvard.edu>
Subject: Meteorology on Outliers (fwd)

Matthew Meselson
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---------- Forwarded message ----------
Date: Fri, 7 Dec 2001 19:16:07 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: Meteorology on Outliers

Dr Meselson:

Thank you for your kind thoughts about my postings on the SIPRI DG site regarding downwind single-spore exposures. I greatly appreciate them. In thinking about the problem, I must agree with you that spore heterogeneity, at least in the extreme degree of my previously articulated scenario of "1 live bullet and 9,999 blanks" is unlikely. For instance, I have too much faith in the parsimonious nature of selective pressures in natural selection to think that such waste of spores would continue under even the rather special case of anthrax evolution. Those 9,999 unlucky spores must have evolutionary benefit. Again I go back to the sperm/fertilization analogy. It may only take a single spore to initiate a fatal infection, but that initiation likely has a probability of only 10*-4 (for a strain with an LD50 of c 10,000) or so.

Although the news has made a lot about contaminated letters found in Oxford CT, one must still start believing in very low dose or single-spore lethality if one is to believe that secondarily contaminated mail is a possible vehicle.

NOTE ADDED JUST BEFORE I EMAILED THIS: I wrote this email and just now saw the NY Times article from today that states that the Leahy letter was processed at 5:27 PM on Oct 9. It fits very well indeed. Read on:

I have been pursuing the specifics of the weather in the NJ-NYC-CT area during the period in question with Courtney Schumacher (my niece), who is a graduate student in meteorology at U of Washington. She has turned up some very interesting data that I'd like to share with you and get your opinion, if I may.

Firstly, I should say that if you take the "downwind bearing" of a 227 degree (SW) wind and go 100 kms NE from Trenton NJ, you pass directly over Manhattan (where the hospital worker worked) and the Bronx (where she lived). If you continue another 100 kms on exactly the same bearing you cross over

Oxford, CT, where the 94 year old retired legal secretary lived. As I said to my niece, it is such a straight line that if it were experimental data it would look faked. Get out a road map: it is really quite remarkable.

Ms (a MS but no PhD until this spring) Schumacher has compiled the hourly surface wind data from the NJ-NYC Island-CT area (drawn from the regions airports, mainly). For the period of Oct 8-9-10 to cover the period of the mailing of the Daschel/Leahy letters (Oct 9). Winds had been blowing from the North steadily on Oct 8, but dropped to essentially dead calm conditions throughout the morning of Oct 9. Beginning at noon winds throughout the region shifted to blow from the Southwest, though Trenton itself was essentially becalmed until 3PM, when a SSW wind began, shifting to SW at the 4PM 5PM and 6PM readings, and dropping in velocity but maintaining a SW direction after 7PM. This 4PM to 7PM SW wind was brisk, peaking at 9 knots (17 kph) at the 5 meter "surface" measurement. As I said, this SW wind was similarly brisk throughout the Northern New Jersey and NYC area throughout the afternoon of Oct 9, dropping in velocity as night fell.

Ms Schumacher has also provided balloon sounding data ("Skwert charts") from the region (Long Island is the closest she could get) for this period of time, and it appears likely that there were temperature inversions both locally (over Long Island) at low (under 500 foot) altitudes, and generally (over the region as a whole) at about 3500 ft (1,000 m). The prevailing SW wind measured at 7PM on Oct 9 was a brisk 20 knots (37 km per hour) at the 500 foot altitude determination.

Did the inversion exist at 5pm Oct 9? or earlier?

We know that the letters mailed on Oct 9 "leaked" spores quite freely, and that the automated mail sorting machines produced sufficient aerosols to infect and kill two postal workers at the Trenton mail sorting facility. This "sorting" aerosol (and perhaps other aerosols associated with the actual mailing of the letters, or even their preparation) must have escaped into the air of Trenton sometime on Oct 9. If one or all of these possible aerosols were released during the 4PM to 7PM "meteorological window" then we have a clear "downwind" path to NYC and Oxford CT. Even if driven at the surface wind velocities such a cloud would have traveled to NYC by midnight, where SW winds were still brisk. Because it is likely that such a cloud would have been driven by the faster (37 kph) 500-foot level winds, the entire 200 km Trenton-to-NYC-to-Oxford CT transit could have taken place in under 5 1/2 hours, well within the duration of that day's strong SW winds. I am reminded of the similar "meteorological window" you determined at Sverdlovsk.

I have done some rough calculations about what lies in this "downwind" path, and it is also quite remarkable. I used the 2000 census data, and assumed that the downwind area at risk is a roughly 4 km wide path "downwind," using as a model your large-scale Sverdlovsk dose plots that go out to 50 kms. Such a 4 km wide path covers the following major cities:

New Brunswick NJ
Highland Park NJ
Edison NJ
Piscataway NHJ
Woodbridge NJ
Elizabeth NJ
Newark NJ
Jersey City NJ
Hoboken NJ

Union City NJ
West New York, NJ

Manhattan (North 1/2) NYC
Bronx NYC
Yonkers NY
White Plains NY
New Rochelle NY
Wilton NY
New Caanon NY

Stamford CT (1/2)
Nagatuck CT
Waterbury CT (1/4)
Sothington CT
New Britain CT
Hartford CT

The total population of these cities (correcting for the fractional coverage of some cities, as indicated above) is 3,607,049 by 2000 census data. This is probably an underestimate, as I was picking cities off a Auto Club road map, and I am unfamiliar with the East Coast. There may be considerable population in unincorporated and rural areas, or in cities that I missed. But even with this presumed "undercount," this is a considerably larger population of potentially exposed "downwinders" than was present in Sverdlovsk. And these are just those within the 4 km wide downwind path.

I have done some very rough calculations, assuming a 1,000 meter temperature inversion limiting upward spread of the cloud, and limiting the lateral mixing to the 4 km wide path. Assuming that a single spore will cause an infection with a 1 in 10,000 probability, and that 3,600,000 persons were exposed to the 1 km high, x 4 km wide front, my calculations indicate that a total release in the order of 1 to 2 mg would result in about 2 predicted cases. Since the Daschle/Leahy letters apparently contained approximately 4 grams of agent each, and the sorting machines were violent enough to produce aerosols of sufficient concentration to cause two proximal deaths, this estimate does not seem unreasonable.

Ms Schumacher has posted her data for me on a private web site, including the hourly surface wind maps of the region and a really impressive animation of these surface wind maps. If you are interested in viewing this data directly, I can give you directions and a key. I will try and attach three of the surface wind maps with this email. I use AOL, and I often have problems with attached files because AOL compresses them with ZIP, and they need to be UNZIPPED to be opened. A second 'Unzipped" folder is then created, and it can be opened, hopefully. If they won't open for you and you are interested, I can fax them directly to you or give you directions to Ms Schumacher's data on the internet. Please note the maps are designated as MONTH-DAY-HOUR with the HOUR being Universal (GMT) Time. In Oct EDT was UT - 4 hours. So file 100920 is Oct 9 at 4PM EDT, 100921 is Oct 9 at 5 PM EDT, and 100922 is Oct 9 at 6PM EDT.

Ms Schumacher is trying to get some more sophisticated computer modeling of the afternoon of Oct 9 done, but these have not yet become available to us.

I would appreciate your views on the above scenario, as your experience at Sverdlovsk seems to be quite applicable.

Yours truly,

Martin Furmanski MD
Newport Beach, cA


100920.gif+.sit

To: Barbara RING <ring@fas.harvard.edu>
Subject: Additional Meteorological Data (fwd)

Matthew Meselson
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---------- Forwarded message ----------
Date: Sat, 8 Dec 2001 09:18:06 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: Additional Meteorological Data

Dr Meselson:

Ms Schumacher has provided some additional, independent data which is quite interesting. It is a computer reconstruction done by a friend of her's at NOAA. It uses the data in NOAA's records to trace the predicted path of a mass of air beginning in Trenton NJ at an altitude of 500 feet (we wanted ground level, but apparently the model only goes down to 500 feet minimum altitude), released at 8 PM on Oct 9 (when we requested the reconstruction, we were unaware that the Leahy/Daschel letters had been processed at 5:27 PM). Winds were falling by 8 PM, but the directions were about the same. At any rate, the reconstruction parameters are reasonably close, at least for a first approximation.

I attach the file as an attachment (folder Trajectoriescsh.pdf). The important one is labeled Trajectories from CSH (40.21N, 74.77W) 10/10/2001 As before, it is in UT, so the OO UT plot is really 8 PM on Oct 9. The Solid Line is the 00 UT plot, and it goes from Trenton over NYC, and then along Long Island Sound and Cape Cod, before reaching a point midway between Cape Cod and Western Nova Scotia after 24 hours. Winds were dropping by 8 PM, but this is still a 24 hour transit of about 560 km (350 miles), giving an average speed of about 23 kph. This would place the cloud over NYC in about 4 hours, or 9:30 PM. The higher winds of earlier that day might well have speeded the process. Oxford CT is a little north of the predicted path, but the scale of the map is large, and detail of that scale is hard to determine. And the earlier (8AM) plot from Oct 9 (Trajectories 10/9/2001, 12 UT) is significantly more northerly in its path across Connecticut. At any rate, some inaccuracies of the reconstruction and/or lateral scatter of cases is to be expected after 200 km downwind transit..

The reconstruction also has an altitude plot which indicates that the stability conditions were very stable. Over the first 24 hours the mass does not rise at all above its 500 foot initial altitude, and indeed only very slow ly settles to the surface. Little vertical mixing appears to have been occurring, so a ground-release may well have kept close to the earth. I had

Ah.

chosen 1,000 meters (3,300 feet) as my ceiling in calculating the release requirements, but I may have been overly cautious. If the release remained confined by very stable atmospheric conditions, the release amount might be considerably less than the 1-2 mg I calculated, for 2 downwind deaths among 3.6 million exposed persons. If a ground release only dissipated upward at the same rate that the 500 foot parcel of air migrated downward, it would not have significantly dissipated upward during the first 12 hours, and only reached 500 feet at 24 hours. If the "dispersal ceiling" of the aerosol cloud is taken at 100 meters (330 feet) rather than 1,000 meters, then the release necessary for the 2 deaths would be an order of magnitude less, or 0.1-0.2 mg.

Yes

This is all pretty good confirmation of our previous data, and has the benefit of being a computer-generated model produced by an operator who was unaware of the specific reason for our request. Certainly it could stand some fine adjustments for release altitude and time of release, but don't you think it is worth pursuing? Ms Schumacher and I are running out of resources and expertise (her field is really tropical weather).

Any guidance you might be able to offer would be most appreciated.

Yours truly,

Martin Furmanski MD
Newport Beach, CA

Trajectoriescsh.pdf

To: Barbara RING <ring@fas.harvard.edu>
Subject: Downwind Outliers (fwd)

Matthew Meselson
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---------- Forwarded message ----------
Date: Thu, 13 Dec 2001 18:02:12 EST
From: Martinfurmanski@aol.com
To: cbw-sipri@sipri.se
Subject: Downwind Outliers

DOWNWIND SINGLE-SPORE EXPOSURE TO AIRBORNE ANTHRAX AGENT IN NYC AND
CONNECTICUT â ˜OUTLIERâ ™ CASES.

Dec 13, 2001

To be published?

Martin Furmanski
Newport Beach CA

The assistance of Courtney Schumacher, U of Washington Dept of Atmospheric Sciences, is gratefully acknowledged for her guidance in obtaining, decoding and interpreting the archival meteorological data. Any errors in the application of the meteorological data to the Oct 9 release are entirely my own, however.

ABSTRACT

The recent series of human anthrax cases contains two conspicuous â œoutliersâ in New York City and rural Connecticut whose association with the remaining cases is obscure. All other cases have been closely and directly associated with readily identifiable exposures to letters containing 2 gram quantities of anthrax spores. Although exposure to letters secondarily contaminated with anthrax in the mail processing process has been theorized, extensive investigation has thus far failed to identify any plausible specific focus of such contamination that might have been the source of the inhalation exposure of these two cases.

The home and work locations of the NYC case, and the home of the Connecticut case lie on a line with ~~of a~~ compass bearing of 227 degrees. The fact that this line also passes directly through Trenton, NJ led us to investigate the possibility that these cases were airborne downwind exposures.

(1)

We conclude these cases may well be the result of ~~an~~ extremely low-dose inhalation exposures to the far downwind tail of an inadvertent very dilute aerosol produced when the letters destined for Senators Daschel and Leahy were processed on Oct 9 at the Trenton NJ postal facility.

SINGLE SPORE LETHALITY

It is almost certain that such far downwind exposures would be limited to inhalation of a single spore. Although it is often stated that â œthousands of sporesâ are needed to cause inhalation disease, this number represents the LD50, and lesser doses can be expected to produce disease, but with a lower probability (at lower frequency). Large series of non-human primate exposures indicate that the inhalation dose-response curve of anthrax spores that have been processes for bioweapon purposes demonstrates an extremely â œflatâ curve, with a slope of only 0.67 probits per log. In this series the LD50 was 4,000 spores, but published mortality curves remained 34% at 1000 spores, and 14% at 100 spores. This curve is based upon the log-normal model of lethality which takes into account variations of susceptibility of the exposed population. If extrapolated, it would predict approximately a 0.6 %(6 per 1,000, 1 in 167) mortality from a single spore. An alternative model, perhaps more appropriate to apply to a single-spore lethal event, is the independent action model, and for an LD50 of 8,000 it predicts a 0.01% (1 in 10,000) fatality rate at exposure of 1 spore.

Despite the apparent rashness of such an extrapolation, there is good experimental evidence for the contention that a single inhaled anthrax spore is fully capable of causing fatal disease, and indeed frequently does so. Although the probability of such an occurrence is admittedly small, it is finite, and if a large enough population is exposed to very dilute anthrax aerosols, occasional â œsporadicâ inhalation anthrax cases can be expected to occur after exposure to even highly dilute anthrax aerosols.

Experiments in the 1940s using laboratory rodents revealed single spores could and did frequently cause fatal infections in both inhalation and subcutaneous challenges. This was investigated in some detail to investigate why the LD50 for inhalation was so much higher than for subcutaneous challenge in this system.

Subcutaneous injection of spores required only a very few spores to cause fatal systemic infection. The subcutaneous LD50 for mice for example, using the Vollum strain (reportedly less virulent than the Ames strain) was only 5 spores. With such a low LD50, it is reasonable to assume that single spores could initiate infection in occasional exposures. Inhalation anthrax LD50s were several orders of magnitude greater.

The WWII Ft Detrick workers concluded that the inhalation exposure required a much greater challenge because of barriers to â œinvasionâ compared to the subcutaneous route, and that individual spores were still capable of initiation fatal infection. When mixtures of Vollum anthrax strains with identifiably different colonial morphologies were inhaled by laboratory rodents, the systemic infections that followed were initiated by only a very few spores, with the average number of spores being 2 (two spores). Clearly single spore lethal events contributed to this mortality.

Similar mixed inhalation exposures occurred in humans during the Sverdlovsk event. The Sverdlovsk release contained a mixture spores demonstrating at least 4 distinct genotypes, and mixed infections demonstrating simultaneous

infection by at least 3 types were identified in 4 of 11 cases. But the majority of cases studied (7 of 11) demonstrated only monotypic infection, and this preponderance of monotypic over oligotypic cases strongly suggested infection was often mediated by single spores. The monotypic cases did not appear to have a particular propensity for advanced age nor downwind position of victim in this admittedly small series.

Careful

Bacillus anthracis is extraordinarily genetically homogeneous, particularly for a disease well known from historical accounts in antiquity. Such homogeneity in the face of known long-term existence implies a â œgenetic bottleneckâ that restricts the development of genetic diversity over time. Single-spore initiation of veterinary infections would be such a genetic bottleneck, having the effect of a monoclonal â œsubcultureâ at each veterinary infection. Individual veterinary cases are important in maintaining areas of endemic infection, and in the introduction of the infection into new areas. The genetic homogeneity of anthrax supports the contention that single spores can and indeed usually are responsible for the establishment of systemic infection in the ingestion/veterinary system.

Unclear if diverse sites — Also dormancy

TRENTON RELEASE OCT 9

It is known that about 5:30 PM on Oct 9, 2001, two letters containing finely divided anthrax agent that had been specially treated to be easily aerosolized were processed at a Trenton NJ postal facility in automated machines that produced a significant aerosol of the anthrax agent. Two fatal cases of inhalation anthrax developed in the postal workers from this exposure. This aerosol was dispersed into the air of Trenton NJ during the evening of Oct 9.

The distance from Trenton NJ to New York City is 100 kms, and to Oxford CN it is 200 kms. Under favorable conditions this distance can be traversed by small-particle biological aerosols. In a large-scale US army test, simulants were tracked over 725 kms (450 mles) downwind. Surface-level release of simulants in the San Francisco test of 1950 showed delivery of viable biological simulants at the most distant surface sampling station, 34 km downwind. Outside the Sverdlovsk metropolitan area, no â œfar downwindâ human cases have been reported, but the rigor of surveillance for such cases is uncertain, and the rural population was probably too sparse to detect the low level of downwind risk. Veterinary cases, however, occurred at least 50 km downwind from the Sverdlovsk release.

METEOROLOGY OF OCT 9

We have investigated the downwind path of this residual anthrax aerosol using meteorological archival data and computer models.

The surface winds throughout the region during the evening of Oct 9 were brisk, measuring 9 knots (17 km/hr) at 5PM and 6 knots (11.5 km/hr) at 6PM in Trenton, and 11 knots (21 km/hr) at 5PM and 9 knots (17 km/hr) at 6PM in Newark. The direction of these winds was from the SW, with bearings between 220 and 230 degrees. Examination of hourly plots of the wind speed and direction from stations throughout the New Jersey-New York City-Connecticut region indicate that New York City and Western Connecticut remained directly downwind of Trenton throughout the evening of Oct 9.

(2)

It appears from balloon sounding data of OCT 9 that this aerosol was released

(3) during a period of very stable lower atmospheric conditions, that would have greatly limited an aerosol's dilution by mixing with overlying air masses. Independently we obtained a computer simulation that plotted the trajectory of a mass of air released at 500-meter altitude at 8 PM on Oct 9 from Trenton. Driven by winds not slowed by surface friction, this mass traveled at an average speed of 20 km/hr (12 knots) and passed over New York City within 6 hours and southern Connecticut within 12 hours. It demonstrated no tendency to mix with surrounding air masses during the first 12 hours, indicating very stable, non-turbulent lower atmosphere conditions.

dT/dz lapse?

POPULATION AT RISK

Although the likelihood of a single inhaled spore causing disease may be quite small (possibly 0.01% (1/10,000)), if millions of persons are in the path of a very dilute aerosol of anthrax spores, thousands may inhale such a dose, and from these an occasional active infection may be expected.

The population placed at risk from the passage of such a residual â œOct 9 Trentonâ aerosol was calculated from 2000 US Census data by totally the population of cities or portions of cities that fell within a 4 km wide path running along the line connecting Trenton, the Bronx, and Oxford, CT. The 4km width was chosen because the relatively stable atmospheric conditions probably resulted in limited lateral dispersion of the aerosol, and similar long-range plots of the Sverdlovsk release, using more sophisticated computer models, resulted in a long-distance maximum width of this magnitude. The population in this path included major centers in Northern New Jersey, portions of New York City, and cities in Connecticut. The aggregate population totaled 3.6 million.

no but ok

RELEASE CALCULATIONS

If the risk of developing inhalation anthrax from inhalation of a single spore is taken as 0.01% (1 in 10,000) as predicted from the independent action model, and two cases of inhalation anthrax have been identified, then 20,000 persons would be predicted to have inhaled a single spore. This amounts to 5.5 per 1,000, or I in 180 persons of the 3.6 million at risk.

Calculations were made using an aerosol cloud with a 4 km width, and an average wind speed of 20 km/hr. Calculations based on two different height constraints were made: one for a â œceilingâ of 1,000 meters, taking an area-wide temperature inversion as a maximum limit, and one for a â œceilingâ of 100 meters, assuming very stable conditions, and recognizing strong local temperature inversions occurred that evening at this altitude. For a predicted incidence of 2 cases of systemic anthrax in the 3.6 million exposed population, the release at Trenton were predicted to be 1 mg and 0.1 mg, respectively. These amounts appear consistent with possible releases caused by the mechanical sorting machines.

CLINICAL CORRELATION WITH OUTLIER CASES

+/−

The incubation periods of the two-outlier cases fall within the known limits if the exposure was on Oct 9-10. The NYC hospital worker fell ill on Oct 25, 16 days later, and the Connecticut woman on Nov. 15, 36 days later. Of the Sverdlovsk victims, 20 had incubations periods longer than 16 days, and 5 longer than 36 days. Both outliers were older than 60 years of age, and

advanced age appears to be an independent risk factor for susceptibility to inhalation anthrax.

NEED FOR FURTHER INVESTIGATION

More sophisticated meteorological investigation of the Oct 9 release is required: this work was done using predominantly public-domain NOAA archival data, "eyeball" analysis and educated guesses. Such help is requested from the general academic and scientific community. A more detailed analysis using standard meteorological models such as the MM5 may be a logical next step, but we have limited access to the meteorological resources available for such analysis, and several weeks would be necessary to produce this next phase. There are doubtless workers with more expertise and an ongoing interest in the field of aerosol propagation and that geographic area.

I have seen no mention of this hypothesis in any CDC news release (or anywhere else except my postings on SIPRI), and I am unaware of any official investigation along these lines. If there is, please someone tell me and I will stop trying to re-invent the wheel.

Detailed meteorological examination has not yet been done for Sept 18 (when the first set of letters were processed at Trenton), and Oct 12 (when the second set of letters were re-processed at the Washington DC postal facility, and when infectious aerosols were again generated). Such studies might produce other â œdownwindâ at-risk areas where intensive retrospective case searches might be indicated to identify other â œoutlierâ cases.

It is unlikely that the risk of single-spore lethality from inhalation exposure can be experimentally investigated, due to the very large number of experimental animals that would be necessary to reach statistical significance with predicted attack rates of 1 in 10,000. Indeed, if the Oct 9 exposure had not exposed so many humans in a large metropolitan area, during a period of intense surveillance for inhalation anthrax, it is likely that it would not have been detected.

REFERENCE DATA

The hourly surface wind plots for NJ-NYC-CT for the evening of Oct 9 are quite interesting visually. For those who want to see them, I can send them individually as an attachment to individual emails on request. Be advised I use AOL, and such attachments are compressed and need to be "Unzipped" before they can be read. I have constant problems with this compression, so be patient if there is trouble.

Comments are welcome.

END

To: Barbara RING <ring@fas.harvard.edu>
Subject: Japanese Anthrax & other matters. (fwd)

Matthew Meselson
Department of Molecular and Cellular Biology
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---------- Forwarded message ----------
Date: Wed, 26 Dec 2001 12:40:05 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: Japanese Anthrax & other matters.

Dear Dr Meselson:

Thank you for your kind comments while reviewing your emails. I will certainly keep you on my forwarding list and feel honored you desire it. I believe you will find a long one from 12/8 on the meteorology of the Oct 9 Trenton mailings that may be of interest. If you don't, let me know. I have been having trouble with my internet provider, and things may have gotten lost in the ether.

The "unidentified man" I mentioned was taken from the March 1993 Proc Natl Acad Sci article by Ambromova et al that presented the pathology of the Sverdlovsk cases. It noted a case #42, found dead and autopsied on 6/15 but with histologic preservation that suggested he had not been dead for very long (hours). I assume this corresponds with your "number *" unidentified man of table 1 the Science article, as the source was presumably Ambromova's autopsy files.

Please let me know when you will be in LA in January. I make the trip from Newport Beach to LA at least once a week to use the medical libraries there. At any rate, it is not a long drive by Southern California standards, and my time is very flexible. If you have time I would be delighted to meet with you. The Japanese documents you asked about in your emails are quite bulky and have color illustrations, and although I have electronic copies of them I can share, they are best first seen in paper form, as seeing them first on a computer screen is rather confusing. And I believe I have one of the only two paper copies extant, as the original (which apparently was unique) has "gone missing" in the federal archive system, and the electronic copy in the Federal system, although complete, is so poorly documented that it is unusable without access to a paper copy.

The manuscripts that Dr. Harris and I have prepared that deal with the Japanese anthrax series were reviewed informally by Drs David Walker, Martin Hugh-Jones, and Mark Wheelis, who were quite supportive that they be submitted for publication, and the MSs are currently under consideration by

Emerging Infectious Diseases, the CDC journal. That means that they are officially "in embargo" as far as any further public release of their contents is concerned, but if you will treat them as a private correspondence I would be happy to share them with you, and I would be grateful for your comments. I will attach them to this email as "attachments." I have a lot of trouble sending such attachments, because AOL compresses them and they need to be "uncompressed" or "unzipped" to be read. This often makes a new folder of uncompressed files that needs to be opened. The files are MS WORD files. If you cannot open them, let me know and I will mail or fax you paper copies.

The papers, particularly the second one, will address your question regarding large particle size aerosols and inhalation anthrax. Briefly, Yes, I think such inhalations were common, and I think evidence of this can be seen in US and British cases, and are quite prominent in the Japanese series. Dr. David Walker's comments would lead me to believe he agrees.

The papers were written nearly a year before the current anthrax outbreak, so bear in mind they were written with the anticipation that bioterrorist agents and delivery systems would be like the Aum cult or the wet aerosol Iraqi weapons of the Gulf War era, rather than the current highly sophisticated dry preparation. The MSs were only slightly modified in light of early data from the current outbreak. Indeed, I need to revise the papers to include the current outbreak's autopsy results (which includes a predominantly pneumonic process in one treated victim, I believe). Because future attacks may indeed be "less sophisticated" than the rather unusual outbreak we are facing, I think these papers still make a quite important contribution to inhalation anthrax pathophysiology.

Best regards,

Martin Furmanski MD
Newport Beach, CA

 Unsophisticated AnthraxIE+.sit

To: Barbara RING <ring@fas.harvard.edu>
Subject: Re: Los Angeles Visit (fwd)

Matthew Meselson
Department of Molecular and Cellular Biology
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---------- Forwarded message ----------
Date: Fri, 28 Dec 2001 01:28:23 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: Re: Los Angeles Visit

Dear Dr. Meselson:

Thursday, January 17 would be fine for me. Either late morning or afternoon would be fine. As I said my time is flexible and it is no trouble for me to make the drive to the Hollywood area. Let me know the details. Also let me know how much time you have, as I can talk about the historical and pathological features of BW longer than anyone can tolerate, and I don't want to overstay my welcome. I would like to show you the Japanese documents, and perhaps some of the low-dose, downwind studies from this recent outbreak.

I am delighted that Dr. Guillemin will be accompanying you. I am of course familiar with her excellent account of the Sverdlovsk investigations, "Anthrax." Does your trip to darkest Hollywood indicate discussion of "movie rights?" I always describe her book as a real-life Michael Crichton novel: a group of brilliant scientists with different specialties are brought together as a team, and visit a strange place to investigate an extraordinary, sinister but very important event. Mix in the spies, satellite photos, secrets, anthrax, Yeltsin and the end of the Cold War and you've got quite a story to "pitch."

Will Dr Guillemin be meeting with us? I ask because in March I am planning a field trip to China to interview survivors and witnesses to some of the Japanese BW attacks from the 1940s, and my wife, who has professional training in structured interviews, will be a participant in that trip. If Dr Guillemin will be there, Virginia may want to tag along and pick her brain a little for pointers on doing BW survivor and witness interviews.

I will fax the papers tonight to your fax #. I am sending my single-spaced version to save on the length of the fax. If you would prefer double-spaced, I can do that. There are two formal papers, 15 and 18 pages in length, and an ethical justification regarding the use of this scientific data, derived from crimes against humanity, that is 6 pages in length.

Mark Wheelis was kind enough to fax me a copy of your 1995 ASA Newsletter article, but I do not have the current revision nor the Canadian DRES report on the B. globigii studies, and I would appreciate copies of both of them. Email is fine. I also have a dedicated fax number if that is easier: 949-675-5315.

My phone number here is 949-675-5155 in case you need to contact me once you are in LA. LA has a multitude of area codes, so be sure and use the 949 if you call from Hollywood.

Best regards,

Martin Furmanski MD
Newport Beach, CA

PS: Your time is probably tight, but if you want a break from the "tinsel town" aspect of being in LA, there is a really excellent exhibit at the Getty Center Art Museum, "Objects of Wonder" which has a fascinating collection of scientific, natural historical and technical artifacts from the 17th, 18th, and 19th centuries. One of my sons works there at the Getty Research Institute, and can get passes if you desire to spend a pleasant morning or afternoon "on the hill."

ThermoAnderson.com

Spoke c̄ Canadians Dr Ho
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no viable < 2.5μ.
1) another run comparable. time of flight HVAC off.
wash off Dich of sampler.
(Dichot 4x slit c̄ sonication. not on scope.) fig 5

10μ = 10^3 in aggr

Slit Sampler
fig 2 1.5 avg = 200/l × 10 min = 20,000 × 10 l/m
0.1 avg = 20/l × 10 min = 2,000 × 10 l/m

Aerobiologia 13:301-312 (2001) James Ho
Charac. Biol Aerosols.
Aerosol 2.5-4.0 μ has 4.5 viable/particle.
Dry BG powder (same) into H_2O, diluted, Hudson nebulizer,
10 mg/ml. fluid.
Electrostatic depn. none > 10μ.

Canister 1.5 ~ 10^7 × 500
0.15 ~ 10^6 ca 500

Particle c̄ 500 spores ca

$\int dt \stackrel{?}{=} 200/l \times 10 \times 10 = 2 \times 10^4$ dose

Aggregates Guinea Pigs
Chino Feb 28.

(949) 675 5315

3 mm/sec
× 600 = 1800 mm
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$\left(\frac{1.5}{r}\right)^3 = \frac{1}{500}$

8μ $\left(\frac{r}{1.5}\right)^3 = 500$

To: Barbara RING <ring@fas.harvard.edu>
Subject: Re: Los Angeles Visit (fwd)

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---------- Forwarded message ----------
Date: Sun, 30 Dec 2001 13:17:38 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: Re: Los Angeles Visit

Dear Dr Meselson:

How delightful to have a mother still living, and below the Griffith Park Observatory at that. Possessing such a treasure in such a place suggests to us that your family must have an unusually long history in Los Angeles. Virginia's grandfather was born in Hollywood in 1890 and attended Los Felix Elementary school, so their old family home was not far away in that venerable neighborhood.

2 PM on Thursday Jan 17 would be fine for us.

Thank you for your kind words regarding the Japanese Anthrax papers. But they have not yet been rescued from obscurity: we are still awaiting word from EID, the CDC journal. The papers are over a year old and were in 2001 rejected from the annual Human Rights issue of the Journal of American Medical Association, based apparently largely upon two reviewers' concerns that they would be too embarrassing to the Japanese and US governments and medical associations.

I would greatly appreciate the original Sverdlovsk pathology papers, particularly the English translations, as I have no Russian language skills and no easy source of obtaining translations. The Russian originals would also be welcome, as having the primary source data is always a goal. If you could send copies in advance, it would allow me to look them over before our meeting, and save us the complications of copying them during the visit. My fax number is 949-675-5315, or you can mail them to me at my address: 333 East Bayfront, Newport Beach, CA 92662.

I certainly would be most interested in looking over the 35 mm slides of the Sverdlovsk pathology. Since I wrote the paper you have, David Walker's group published additional material, and there is, tragically, new pathological material from the recent US outbreak. So the paper really needs some updating to include this new data, and access to more data from Sverdlovsk would be most welcome.

Best regards,

Martin Furmanski MD

To: Barbara RING <ring@fas.harvard.edu>
Subject: Re: Canadian report (fwd)

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---------- Forwarded message ----------
Date: Wed, 2 Jan 2002 04:09:30 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: Re: Canadian report

Dear Dr. Meselson:

Well, 1932 is still early times when it comes to LA; earlier than my family, which, like so many others, saw So Cal during WWII, and was seduced by the weather after a lifetime of Chicago winters (or worse). Through the tangled web of life my wife turns out to have been born in Manhattan, and although raised in LA, spent many summers in northern New Jersey as a girl, so perhaps your wife will not get too bored hearing old Angelenos talking about the Red Cars! Virginia's parents met at Art Students League in New York. She has splendid memories of throwing pennies into the fountain (now, alas, gone) at the Metropolitan Museum of Art and remembers well the 1964 World's Fair. The LA side of her family moved several times, to Eagle Rock and then to what was then the wilds of the San Fernando Valley, so I think you probably didn't meet her, but her grandfather faithfully attended the Los Feliz Elementary School Alumni Picnics every summer until he was too ill in the 1960s.

Having Federal Express leave the parcel is just fine: we have a secure place and prefer that to having to chase the package down if we happen to be out.

I received the Canadian report in good order and read it with great interest. Let me give you some quick comments.

First, please pardon my editorializing.

It is a tragedy that such an important piece of work so obviously and directly applicable to terrorist anthrax releases did not find its way to the CDC in time to influence the early management of the areas of the postal system at risk. But it also would have needed information about sophisticated dry spore anthrax agents to be truly useful. I think all of us in the purely civilian, "open literature" community assumed that a terrorist release would be wet aerosol, based upon the conventional wisdom that only the US and USSR had developed dry spore agent. The open literature sources

had stated that even the Iraqi program, despite having equipment for dry spore production, had not used this equipment, and that all the production and the warhead fills were wet slurry in character. The conventional wisdom, as codified by the Johns Hopkins group, also stated that re-aerosolization was NOT expected to be a problem, based upon US military studies. It is rather dismaying to find that the US and Canadian military had full knowledge of dry spore behavior, including knowledge about and possession of re-aerosolizing sophisticated dry spore preparations, yet did not share this, even as a worse-case contingency, as a closely held non-public informational matter with people at the CDC with security clearances. USAMRIID has stated they only worked with wet aerosols, who was keeping secrets from whom?

If the whole US BW effort is supposed to be about defense, and the prime target of anthrax releases are civilian populations (the US military being protected, at least in theory, by the [troubled] anthrax vaccination program) , how come nobody at DOD told the CDC about these potential anthrax agent preparations and their potential risks and potential behaviors?

As I will explain below, the knowledge of (or, perhaps, the acknowledgment of) the existence of such sophisticated anthrax preparations is of paramount importance, because as it stands, the Canadian interpretation has some serious flaws. If only the agent preparation that Dugway provided them is considered, their conclusions about delivery of many multiples of an LD50 is NOT persuasive. The demonstration of the danger of opening letters IS important. But it is particularly with sophisticated Daschle/Keahny agent, that this is so.

Well, now a technical analysis of the Canadian study.

The simulant preparation provided to Suffield by Dugway does not seem to be nearly as sophisticated as the Daschle/Leahy agent. Its particle size appears to be quite considerably larger. The Canadians do not state any specific parameters, except to say that 99+% were captured by the first stage of their filters, which they state places the particles in the range of "2.5 to 10 microns." But because the coarsest filter that they used captured essentially all particles, 10 microns appears to be an arbitrary upper limit. In fact it was much larger.

There is a lot of data that can be deduced from their charts, which give time/concentration plots of the release in their aerosol chamber with the recirculating system operating. Since this is a good approximation of the "stirred chamber" settling time parameter of aerosols, a mean particle diameter and distribution can be estimated.

If one looks at the first, second and third halving times of the release, one can get a very rough idea of the overall particle distribution curve of the agent. The best data is in Figure 5, and shows the decay curve of the aerosol over 10 minutes. The overall shape shows the rapid initial rise and a rapid initial decline, and then a slower decline to a level of only about 6% of the peak concentration at 10 minutes. This is the curve of an aerosol with a large component of particles over 10 microns and very few under 10 microns. If one plots sequential halving times, one finds a first half life of about 18 seconds, and second half life of 180 seconds, and a third half live of 205 seconds. In the 3 meter high Suffield chamber 70 micron diameter particles have a half life of 18 seconds. Similarly 20 micron particles

have a half life of 180 seconds. The behavior of the Canadian aerosol is that which would be expected of an aerosol with about 50% of its particles 70 microns in diameter, and the remainder about 20 microns, with very few under 5 microns. The 6% of particles remaining at 10 minutes is what would be expected with all of the 70 micron particles cleared after 33 half lives, and 12% of the original 50% component of 20 micron particles remaining after 3 half lives. There is no "persisting tail" to indicate that a longer-lived, smaller particle component was present. 5 micron particles have a half-life in a stirred 3 meter high chamber of 42 minutes, and 3 micron particles a half life of 2 hours. Particles of these sizes would not have decayed measurably in the 10 minute test period.

Data Source?

The indication that the Canadian aerosol was composed of large aggregates of spores rather than single spores, a comment the Canadians themselves make, is independently supported by the discrepancy between their impingement-derived concentration numbers and their filtration-derived concentration numbers. They provide both information for run 92, in Figure 5 and table 1. The peak impingement concentration (their ACPLA) is 80 cfu/liter. Yet the filtration-derived cfu/liter (which because of disaggreagtion during washing and plating may indicate the total number of spores more accurately than impingement, which counts aggregates as a single cfu) indicated 8,000 cfu/liter. This 100 fold difference can be easily explained by spore aggregates, for a 20 micron particle has well over 1,000 the total volume of a single spore. There is plenty of room.

An anthrax aerosol compromised of 70 and 20 micron particles, without a significant component under 5 microns will not be effective in causing inhalation anthrax. To extrapolate from the number of such particles trapped by a filter in a protective mask or other sampling device, and to use the LD50 derived from under 5 microns single spore preparations is NOT valid. The charts show no indication that there was any significant component under 5 microns, so it probably accounted for less than 1%, so the LD50s would need to be increased at least by a factor of 100. Since the Canadians used 2500 as a "worst case" LD50, using a more moderate number would increase the factor by another 4X, to 400. This makes their 0.1 mg release about a 1 LD50 exposure or less, and their 1.0 mg exposure under 7 LD50s. It does not change the discovery that opening letters is dangerous with anthrax powder inside, but it changes the overall risk IF the powder is what Dugway sent them.

These more moderate exposure numbers and large particle exposures are interesting if one applies them to the exposures from the Florida and New York letters mailed on Sept 18. The photo editor in Florida apparently handled the letter over his computer keyboard, and was nearsighted, so got his face up close to the paper. The Florida mailroom worker's exposure is not known, but there were many other people working in and passing through the rooms with the photo editor and the open letter. There were no other cases, although no one was taking antibiotics until after the index cases were recognized, and many other exposed workers had positive nasal swabs for anthrax spores. And in New York no one developed inhalation anthrax, despite similar letter-opening exposures and no protective antibiotics. It all suggests a large-particle rich, small particle poor release, similar to the Canadian study's Dugway agent, or for that matter, the Goat Hair mills. (or an unpublished Japanese series with only cutaneous disease),

I do not know if it is known to investigators whether the Sept 18 Florida/New York letters had similar, coarse agent or whether they had the

more sophisticated "Daschle/Leahy" agent that was somehow degraded before release. I have read conflicting reports regarding this. But it sure acted like the large-particle Dugway/Canadian agent.

Importantly, as far as potent Dashle/Leahy agent is concerned, the Canadian work, as alarming as it is, may underestimate the risk from the more sophisticated agent, because it presumably forms few and smaller aggregates, and is more persistent in the air. The "spike and decay" pattern produces a reduced integrated dose, compared to the persistently high concentration of small particle aerosols. A release of 5 micron particles in Figure 5 would have hit 80 and stayed there for the whole 600 seconds. Considering this, immediate prophlaxtic antibiotics must work very well, or there would have been some "breakthrough" cases in the Senate Office Building, if persons really received thousands of LD50s, which seems likely.

Thank you very much for sending me this paper. The fact that the aerosol seems to be predominantly large-particle is much like the wet Japanese aerosols of my paper with Dr. Harris that you have. I was able to knock off the above analysis rapidly because I have been thinking about large-particle exposures in small chambers because of the Japanese exposures, and the same principles apply to the Canadian study. It is interesting that the photo editor in Florida died with ascities, as did at least one postal worker. These facts suggest some of the features of the Japanese cases. I need to get more detailed autopsy information on these current cases.

By the way, is this Canadian report a public document? Need I keep it confidential in any way?

We are looking forward to your visit to LA

Martin Furmanski MD

Date: Tue, 8 Jan 2002 14:24:51 -0500 (EST)
From: "Matthew S. Meselson" <msm@wjh.harvard.edu>
To: Barbara RING <ring@fas.harvard.edu>
Subject: Reports Received (fwd)

Matthew Meselson
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---------- Forwarded message ----------
Date: Thu, 3 Jan 2002 16:31:15 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: Reports Received

Dr. Meselson:

The Russian Sverdlovsk Pathology translations arrived in good order. Many thanks: I will examine them closely and offer any impressions after a good study.

Do you have an email address for Dr. Kournikakis (or anyone else) at the Canadian Defense Research Establishment at Suffield? They have a nice website but they do not include a directory of email addresses. I really need to contact him about the "Risk Assessment of Anthrax Threat Letters" paper, as his aerosol plots are really quite inconsistent with his conclusions. I need to clarify some details about his experimental setup and inquire about other information he might have but did not include in the published paper before I conclude his analysis is erroneous.

I heard both you and a representative of Suffield on NPR yesterday, talking about the study, so I guess it is OK to talk about the specific details in paper you sent me. Please let me know if it needs to be kept confidential, however.

I am looking forward to meeting you come the 17th.

Best regards,

Martin Furmanski MD

To: Barbara RING <ring@fas.harvard.edu>
Subject: Re: Canadian Study (fwd)

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---------- Forwarded message ----------
Date: Fri, 4 Jan 2002 11:16:04 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: Re: Canadian Study

Dr Meselson:

Thank you for the contact information for Suffield.

I spent a day going over the report again. I think there are two likely possibilities:

1. Through a malfunction of a single instrument they erroneously got data that the aerosol was restricted to the 2.5 to 10 micron range. In this scenario, the aerosol particle size was really much larger. In this case it would have been like the Florida and New York releases, and their alarming calculations of hundreds or thousands of LD50s were erroneously high.

2. Due to an error in experimental design, the slit samplers they employed were insensitive to aerosols under 10 microns. In this scenario, the time/concentration plots that they present represent only the biologically insignificant "fallout" of an otherwise very biologically active small-particle aerosol. In this case their time/concentration curves offer a false impression that the aerosol was relatively short-lived, when in reality it would have been highly persistent (at least 80% at 10 minutes, rather than 6% that their decay curves show).

I have emailed Dr Kournikakis at Suffield. We will see what his thoughts are.

Regards,

Martin Furmanski

Date: Tue, 8 Jan 2002 12:42:57 -0500 (EST)
From: "Matthew S. Meselson" <msm@wjh.harvard.edu>
To: Barbara RING <ring@fas.harvard.edu>
Subject: New Canadian study data (fwd)

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---------- Forwarded message ----------
Date: Tue, 8 Jan 2002 10:24:06 EST
From: Martinfurmanski@aol.com
To: msm@wjh.harvard.edu
Subject: New Canadian study data

Dr. Meselson:

Another elegant theoretical speculation assassinated by an ugly piece of data.

I received from Dr Ho at Suffield a very nice plot of particle size performed by a dual-channel combined photoelectric and time of flight aerosol particle size analyzer that confirms the Canadians' assessment that their letter-release, Dugway-origin BG aerosol really was limited to particles smaller than about 8 microns. This plot, done on a later run with slightly different conditions, showed an even more rapid decay than their published data. Dr. Ho feels that this rapid decay is due to very marked electrostatic sequestering of the aerosol on the walls of the chamber in the very low humidity conditions of Alberta in the winter. It is interesting that Bill Patrick said recently in an interview that the Daschle/Leahy agent was very pure and manufactured to a fine diameter, but had NOT been made electrostatically neutral. I don't know if this statement is accurate, but if it is the case, then it looks like Dugway sent Suffield BG agent that was quite similar to the Daschle/Leahy anthrax agent. Perhaps those with security clearances already know that and that's why they are taking the Canadian data so seriously in pushing to get vaccine released from the rather scant military stockpile for the civilian follow-up program.

yes

Talking with Dr. Ho at Suffield has been quite useful, however, and he has referred me to some of his published papers, which I need to get in the next few days. Some of his thoughts and data have given me a new viewpoint in thinking about why the existing anthrax dose/response curves are as odd and contradictory as they seem to be. I hope to get these ideas together for our meeting next week.

?

We are looking forward to meeting you and Dr. Guillemin next week.

Best Regards,

Martin Furmanski