

**Human Pathology Inhalational Disease**

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Note: The following copies of Dr. Walker's slides may not be in the same order that Dr. Walker presents them at the Advisory Committee meeting.

# Quantitative pathology of inhalational anthrax

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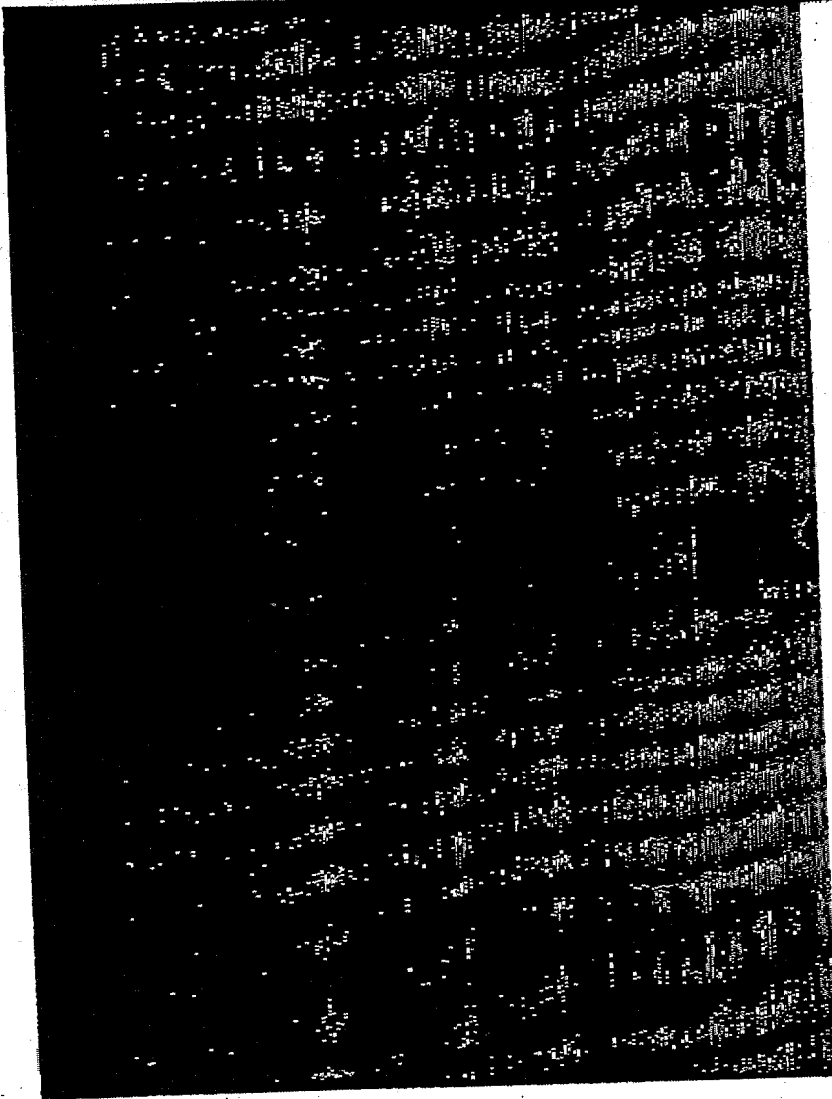
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# BIOHAZARD

The Chilling True Story of the Largest Covert  
Biological Weapons Program in the World—Told from  
the Inside by the Man Who Ran It

KEN ALIBEK  
WITH STEPHEN HANDELMAN

PLANTING THE SEEDS  
OF DEATH

JUL-27-00 THU 06:11 PM DEPT OF PATHOLOGY

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P.02

**Compound 19 was the Fifteenth Directorate's busiest production plant. Three shifts operated around the clock, manufacturing a dry anthrax weapon for the Soviet arsenal. It was stressful and dangerous work. The fermented anthrax cultures had to be separated from their liquid base and dried before they could be ground into a fine powder for use in aerosol form, and there were always spores floating in the air. Workers were given regular vaccinations, but the large filters clamped over the exhaust pipes were all that stood between the anthrax dust and the outside world.**

**On the last Friday of March 1979, a technician in the anthrax drying plant at Compound 19, the biological arms production facility in Sverdlovsk, scribbled a quick note for his supervisor before going home. The note read:**

**“Filter clogged so I’ve removed it.  
Replacement necessary.”**

**After each shift, the big drying machines were shut down briefly for maintenance checks. A clogged air filter was not an unusual occurrence, but it had to be replaced immediately.**

**Lieutenant Colonel Nikolai Chernyshov, supervisor of the afternoon shift that day, was in as much of a hurry to get home as his workers. Under the army's rules, he should have recorded the information about the defective filter in the logbook for the next shift, but perhaps the importance of the technician's note didn't register in his mind, or perhaps he was simply overtired.**



**When the night shift manager came on duty, he scanned the logbook. Finding nothing unusual, he gave the command to start the machines up again. A fine dust containing anthrax spores and chemical additives swept through the exhaust pipes into the night air.**

**Several hours passed before a worker noticed that the filter was missing. The shift supervisor shut the machines down at once and ordered a new filter installed. Several senior officers were informed, but no one alerted city officials or Ministry of Defense headquarters in Moscow.**

## Forty-two patients with inhalational anthrax in Sverdlovsk in 1979

No.	Age/ Sex	Onset	Date of		Identification of <i>Bacillus</i> <i>anthracis</i> by	
			Admis- sion	Death	Cul- ture	Hist- ology
1.	42/M	4/7/79	4/10/79	4/10/79	+	+
2.	67/M	4/7/79	4/8/79	4/9/79	ND	?
3.	68/F	4/8/79	4/9/79	4/10/79	+	+
4.	38/M	?	4/8/79	4/8/79	ND	ND
5.	47/M	?	?	4/12/79	+	+
6.	68/M	4/9/79	?	4/13/79	-	+
7.	25/F	4/10/79	4/12/79	4/13/79	+	+
8.	66/F	4/10/79	4/13/79	4/13/79	+	+
9.	50/M	4/12/79	4/13/79	4/13/79	-	+
10.	65/M	4/10/79	4/13/79	4/14/79	-	+
11.	48/M	4/11/79	4/13/79	4/14/79	-	+
12.	42/M	?	4/13/79	4/14/79	+	+
13.	40/M	?	?	4/14/79	+	+
14.	52/M	?	?	4/14/79	+	+
15.	37/M	4/12/79	4/13/79	4/15/79	-	+
16.	32/M	4/10/79	4/13/79	4/15/79	-	+
17.	52/M	4/13/79	4/14/79	4/16/79	-	+
18.	68/F	?	4/16/79	4/16/79	-	?
19.	71/F	?	?	4/15/79	-	+
20.	58/F	4/15/79	?	4/25/79	-	-

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## Forty-two patients with inhalational anthrax in Sverdlovsk in 1979

No.	Age/ Sex.	Onset	Date of		Identification of <i>Bacillus</i> <i>anthracis</i> by	
			Admis- sion	Death	Cul- ture	Hist- ology
21.	42/F	?	4/13/79	4/17/79	-	+
22.	49/M	?	4/16/79	4/16/79	+	+
23.	43/M	4/14/79	4/15/79	4/16/79	-	+
24.	68/F	4/14/79	4/22/79	4/30/79	-	-
25.	44/M	4/15/79	?	4/18/79	+	+
26.	49/M	4/15/79	?	4/19/79	+	+
27.	46/M	4/15/79	?	4/21/79	+	+
28.	50/F	4/17/79	4/21/79	4/25/79	-	+
29.	45/M	?	?	4/22/79	-	+
30.	39/M	4/20/79	?	4/23/79	+	+
31.	42/M	4/21/79	4/23/79	4/24/79	-	+
32.	42/M	4/21/79	4/24/79	4/24/79	+	+
33.	48/M	4/22/79	?	4/24/79	+	+
34.	33/M	4/25/79	?	5/3/79	-	?
35.	32/M	?	4/28/79	4/28/79	+	+
36.	55/M	4/27/79	5/1/79	5/1/79	-	+
37.	33/M	4/29/79	4/30/79	4/30/79	+	+
38.	43/M	5/4/79	5/6/79	5/10/79	-	?
39.	25/M	5/7/79	5/12/79	5/12/79	+	+
40.	30/M	5/9/79	?	5/10/79	+	+
41.	29/M	5/12/79	5/15/79	5/16/79	-	+
42.	?/M	?	?	6/15/79	+	+

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# Quantitative microscopic findings in inhalational anthrax

## Epidemiologic, clinical and general pathologic observations

	n	mean
Age (years)	40	46.13±1.99 (range 25-71)
Gender	41	Males 33, females 8
Antibiotic therapy (hours)	22	16.61±5.85
Incubation period (days)	30	16.07±1.80
Duration of clinical illness (days)	30	3.85±0.41
Duration of hospitalization (days)	37	0.96±0.27
Overall interval from exposure to death (days)	41	19.54±1.93 (range 6-69)
Post-mortem interval (hours)	36	18.82±2.94
Volume of bilateral pleural fluid (ml)		1776±177
Vasculitis & capillaritis		81%
Vasculitis only		73%

# Criteria for quantification of tissue concentrations of *Bacillus anthracis*

0	<i>Bacillus anthracis</i> / 25X objective field	= 0
< 1	<i>Bacillus anthracis</i> / 25X objective field	= 1
1 - 10	<i>Bacillus anthracis</i> / 25X objective field	= 2
11 - 100	<i>Bacillus anthracis</i> / 25X objective field	= 3
101 - 500	<i>Bacillus anthracis</i> / 25X objective field	= 4
501 or more	<i>Bacillus anthracis</i> / 25X objective field	= 5

## Criteria for quantification of tissue concentrations of inflammatory cells

0	cells / 25X objective field	= 0
>0 - 10	cells / 25X objective field	= 1
11 - 25	cells / 25X objective field	= 2
26 - 100	cells / 25X objective field	= 3
> 100	cells / 25X objective field	= 4

# Criteria for quantification of other parameters

0	=	Absent	=	
1/2	=	Minimal	=	Present, but barely evident
1	=	Mild	=	Clearly present, but probably pathophysiologically insignificant
2	=	Moderate	=	Present and significant
3	=	Marked	=	Prominent, but without destruction of the organ architecture
4	=	Severe	=	Prominent with organ architecture destruction



## Quantitative microscopic findings in mediastinum & peribronchial soft tissue in inhalational anthrax

	n	mean	
<i>B. anthracis</i> burden	37	1.375±0.269	(54%)
Fibrin-rich edema	37	2.146 ±0.179	(92%)
Low-pressure hemorrhage	37	2.274 ±0.170	(95%)
High-pressure hemorrhage	37	1.368 ±0.244	(60%)
Neutrophils	37	1.061 ±0.153	(81%)
Mononuclear cells	37	0.702 ±0.112	(76%)
Lymphangitis	37	1.472 ±0.236	(65%)

# Quantitative microscopic findings in lung in inhalational anthrax

	n	mean	
<i>B. anthracis</i> burden	35	1.39±0.28	(49%)
% <i>B. anthracis</i> , intravascular		56.88±10.18	(range=0-100; median=80)
% <i>B. anthracis</i> , intraalveolar		16.75±6.67	(range=0-95; median=6)
Bronchopneumonia, severity	41	0.515±0.113	(49%)
Intraalveolar exudate:	35		
Transudate		0.986±0.187	(60%)
Fibrin		0.950±0.202	(46%)
Hemorrhage		1.300±0.218	(66%)
Neutrophils		0.297±0.096	(37%)
Macrophages		1.136±0.161	(71%)
Lymphocytes		0.314±0.145	(17%)

# Quantitative microscopic findings in lung in inhalational anthrax

	n	mean	
<b>Interstitial exudate</b>	<b>35</b>		
<b>Transudate</b>		<b>1.243±0.132</b>	<b>(86%)</b>
<b>Fibrin</b>		<b>0.772±0.142</b>	<b>(57%)</b>
<b>Hemorrhage</b>		<b>0.943±0.153</b>	<b>(65%)</b>
<b>Neutrophils</b>		<b>0.315±0.090</b>	<b>(43%)</b>
<b>Macrophages</b>		<b>0.657±0.126</b>	<b>(54%)</b>
<b>Lymphocytes</b>		<b>0.449±0.161</b>	<b>(29%)</b>

# Quantitative microscopic findings in lung in inhalational anthrax

	n	mean
<b>High pressure hemorrhage (0 to 5 scale)</b>		78%
<b>Hemorrhagic diathesis</b>		71%
<b>Capillaries:</b>	<b>35</b>	
<b>Congestion</b>		<b>2.043±0.200 (91%)</b>
<b>Capillaritis</b>		<b>0.889±0.174 (57%)</b>
<b>Vasculitis</b>		<b>0.514±0.154 (65%)</b>
<b>Lymphatic vessels</b>		
<b>Dilatation</b>		<b>1.386±0.178 (74%)</b>

## **“Pneumonia” in Cases of Fatal Inhalational Anthrax**

- **Hematogenous anthrax pneumonia**
- **Retrograde lymphangitic pneumonia**
- **Anthrax pneumonia (possibly associated with impaired clearance of bacilli owing to pneumonia)**

**Notes: Respiratory insufficiency is greatly due to atelectasis (compression by pleural effusions, etc.).**

**There was only one case of aspiration pneumonia.**

**Pulmonary edema and nosocomial pneumonia did not appear to be major factors.**

## Quantitative microscopic findings in the meninges in inhalation anthrax (n=29)

<i>B. anthracis</i> burden	2.297±0.344	(79%)
Transudate	0.759±0.152	(59%)
Fibrin	0.901±0.159	(83%)
Low-Pressure Hemorrhage	1.239±0.221	(90%)
High-Pressure Hemorrhage	0.603±0.240	(21%)
Neutrophils	0.524±0.142	(55%)
Macrophages	0.478±0.104	(55%)

# Mechanisms of Death in Inhalational Anthrax

Mechanism	Primary Mechanism of Death	Contributory Mechanism of Death	
		Major	Minor
Atelectasis, due to pleural fluid, ascites and diaphragmatic elevation	16 (39%) <sup>a</sup>	19 (46%) <sup>b</sup>	
Hemorrhagic meningoencephalitis	14 (34%)	3 (7%)	2 (5%)
Pneumonia	2 (5%)	11 (27%)	3 (7%)
Septicemic shock	1 (2.5%)	21 (51%)	9 (22%)
Other	2 (5%)		
Uncertain	6 (15%)		
Chronic pulmonary disease		12 (29%) <sup>c</sup>	4 (10%) <sup>d</sup>

## Footnotes

a - including pleural gelatinous edema and 6 cases with diaphragmatic elevation due to hemorrhagic ascites, peritoneal or retroperitoneal gelatinous edema.

b - including pleural gelatinous edema and 2 cases with diaphragmatic elevation due to hemorrhagic ascites, peritoneal or retroperitoneal gelatinous edema.

c - including 4 cases of severe pulmonary hemosiderosis (arc welder's disease), 6 cases of chronic obstructive pulmonary disease (bronchiectasis, centroacinar emphysema, interstitial fibrosis and pulmonary arteriosclerosis), one case of asbestosis-silicosis and one case of pulmonary alveolar proteinosis.

d - including 2 cases of significant, not severe, pulmonary hemosiderosis (arc welder's disease), 1 case of chronic obstructive pulmonary disease, and one case of pulmonary silicotuberculosis.

# Effect of Antibiotic Treatment on Fatal Inhalational Anthrax

	<u>Treated</u>	<u>Not Treated</u>
Postmortem culture of <i>B. anthracis</i>	5/22 (23%)	15/18 (83%)
Histologic detection	12/22 (55%)*	18/18 (100%)

\* Patients treated for <21 hours had incomplete clearance of bacilli.