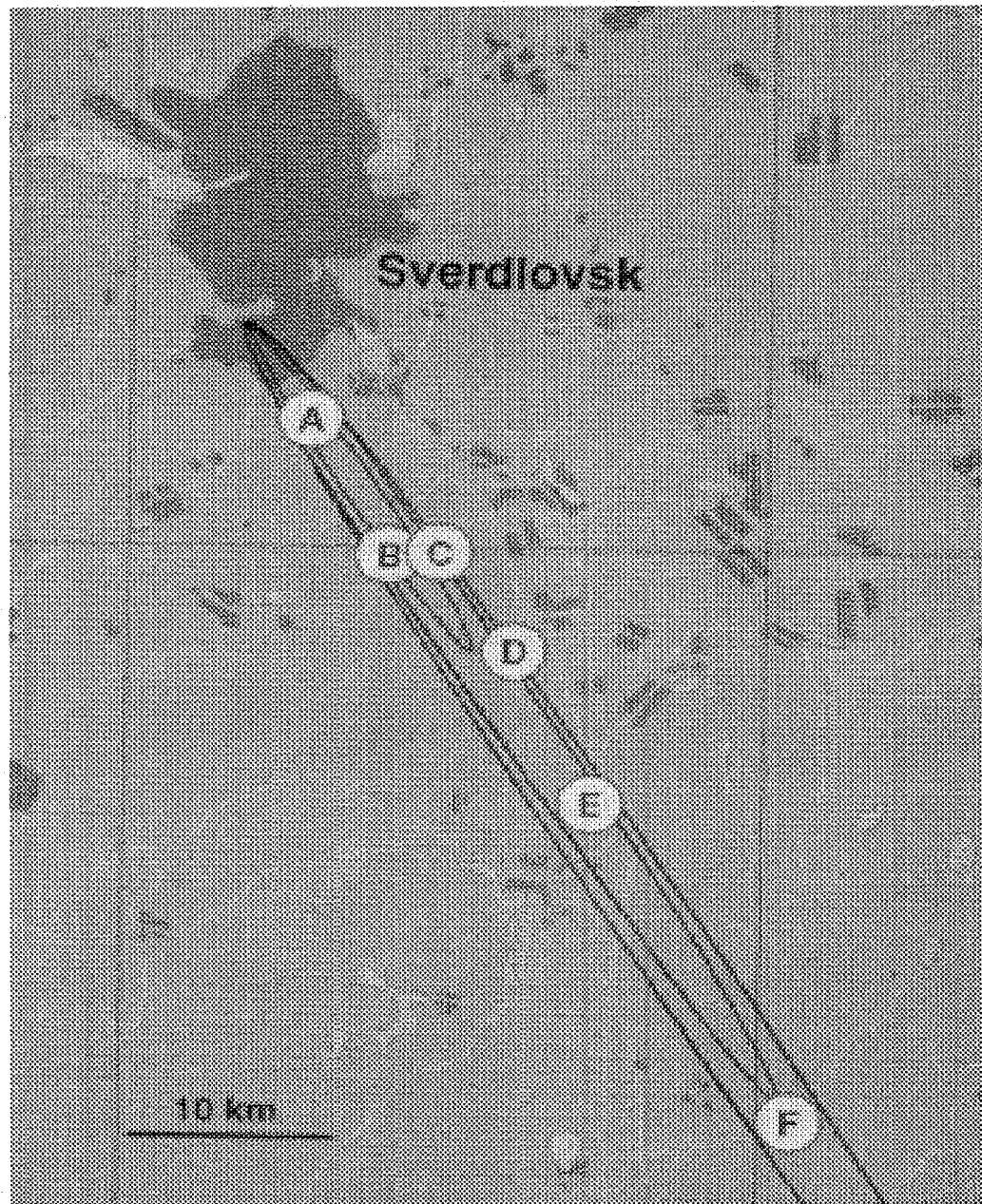


**Anthrax Clinical Disease and Epidemiology**

Martin Hugh-Jones, D.V.M.

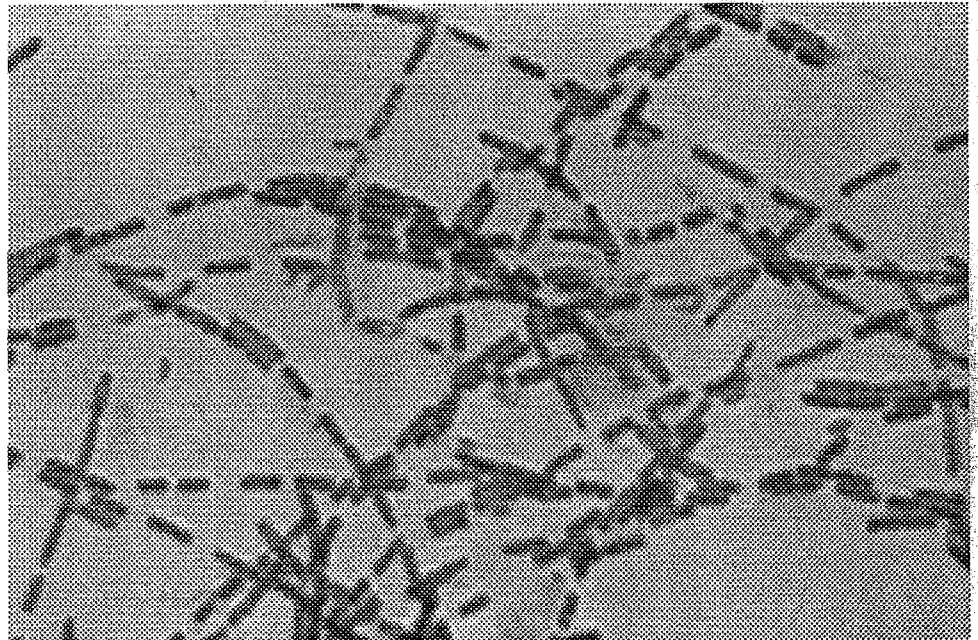
# ANTHRAX

Epidemiology 101



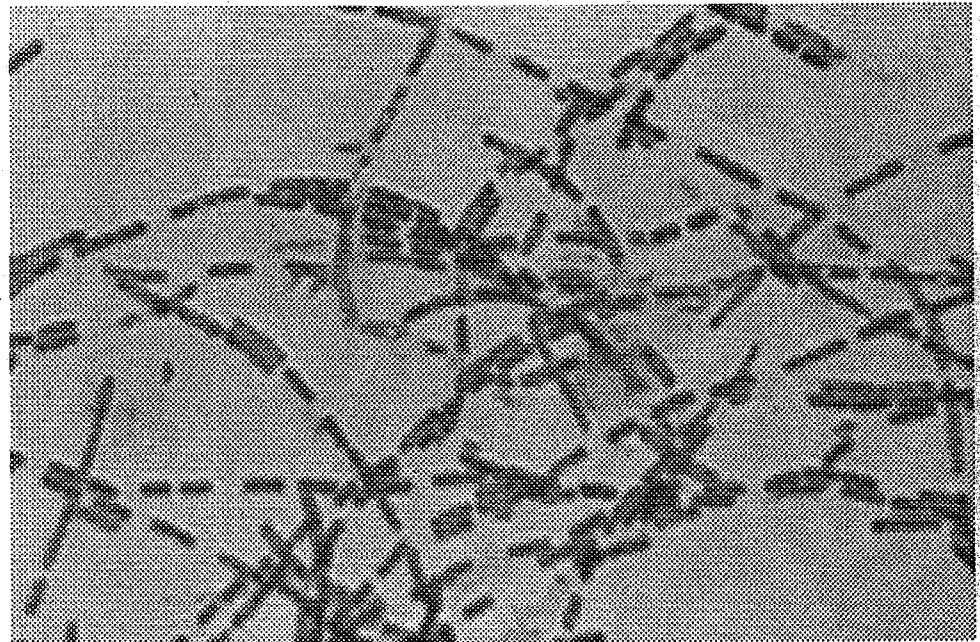
# *Bacillus anthracis*

- Disease known for thousands of years.
- Organism first described in mid-1800s
- Used as proof of Henle's postulates by Koch.
- First vaccines developed by Greenfield and Toussaint; public demonstration by Pasteur in 1881.
- Livestock and human vaccines.



# *Bacillus anthracis*

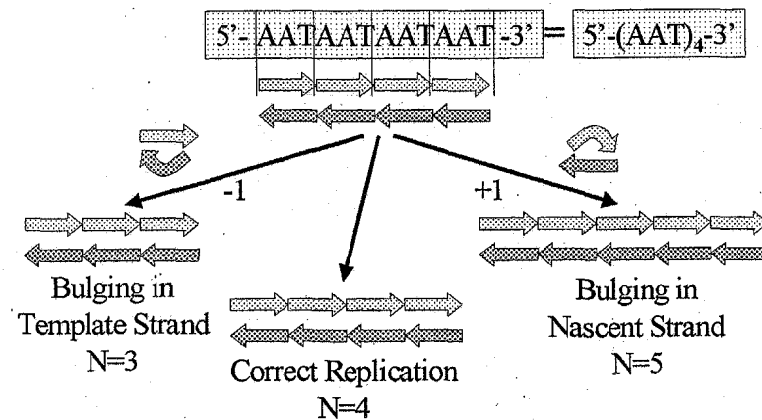
- Aerobic, sporeforming, Gram-positive capsulated rod
- It survives by killing.
- The spore has a capacity to survive in the environment for decades.
- It is a junior relative of *B. cereus/thuringensis*.
- Pathogenicity depends on two plasmids, pX01 & pX02.



## *B. anthracis*

- PCR analysis utilizes Variable Number Tandem Repeats ... these are repetitive sequence motifs.
- Eight VNTRs are presently used: *vrrA*, *vrrB1*, *vrrB2*, *vrrC1*, *vrrC2*, CG3 and one for each plasmid; 35 more are under development.
- Used rather like bar-codes.

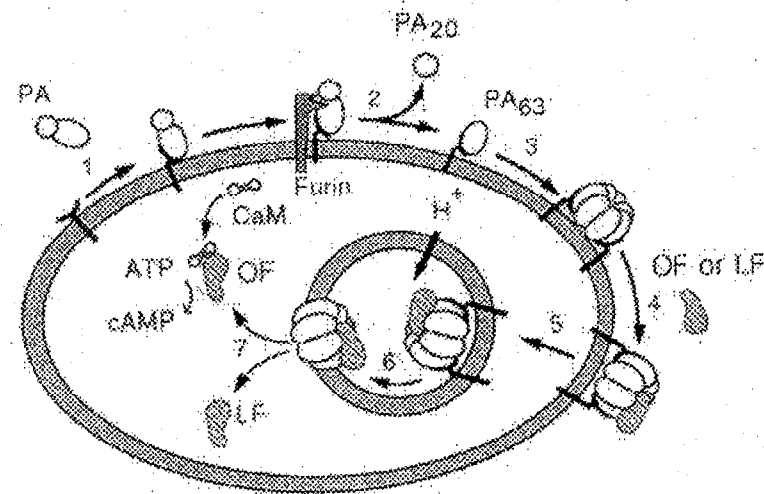
### VNTR Polymorphism





# Toxin production

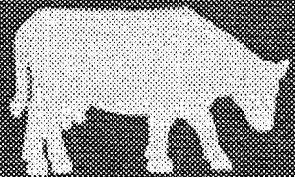
- Protective antigen (PA) binds to host cell receptor
- Furin cleaves and releases PA<sub>20</sub>
- PA<sub>63</sub> forms a heptamer
- The toxin enzymes bind to PA<sub>63</sub>
- Receptor-mediated endocytosis
- Endosome acidification leads to membrane insertion of PA<sub>63</sub>
- Translocation of toxic enzymes into the cytosol; LF, lethal factor; OF, oedema factor



*Nature* (1997) 385:833-838



CLINICAL  
ANTHRAX (1)



**PERACUTE**

FOUND DEAD

Bloody discharge from  
mouth, anus, and vulva.

ALIVE, FEVERED

muscular tremor, dyspnoea,  
congested mucosae and  
sudden collapse within  
1-2 hours.

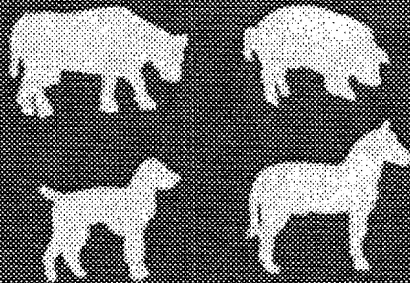


CLINICAL  
ANTHRAX (2)

PERACUTE



ACUTE



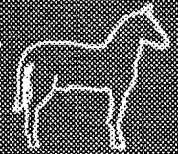
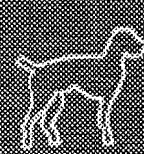
DEPRESSED, LISTLESS,  $<42^{\circ}\text{C}$   
Respiratory, mucosae, cardiac and  
enteric signs; Abortion; Pharyngeal  
and Laryngeal edema in pigs and  
dogs: ventral edema in other species  
Death  $<36\text{ H}$  Ruminants,  
 $<76\text{ H}$  Horses.

CLINICAL ANTHRAX (3)

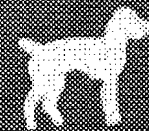
PERACUTE



ACUTE



'HYPOACUTE'



CUTANEOUS LESIONS

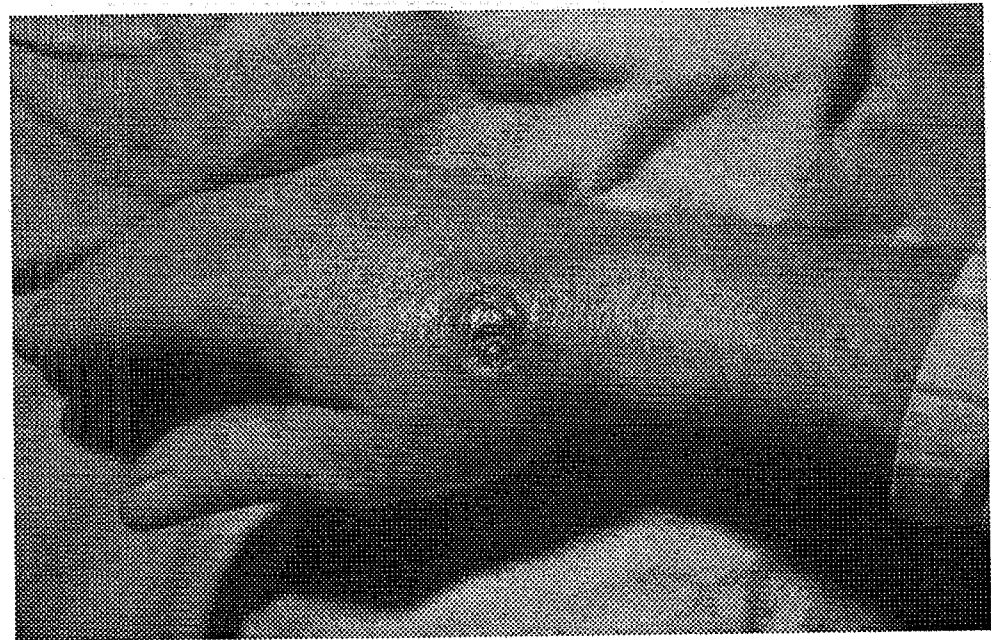
Haemorrhagic edema spreading to dependant parts.  
Seldom fatal with treatment

INTERNAL LESIONS

Pharynx, Larynx, intestinal wall, mesenteric lymph node or spleen.  
Seldom fatal

# Cutaneous anthrax

- This is a pathognomonic skin lesion ... with a raised vesiculated edge, inflamed, and with a black base to the ulcer, e.g., *charbon*, 'Siberian ulcer'.

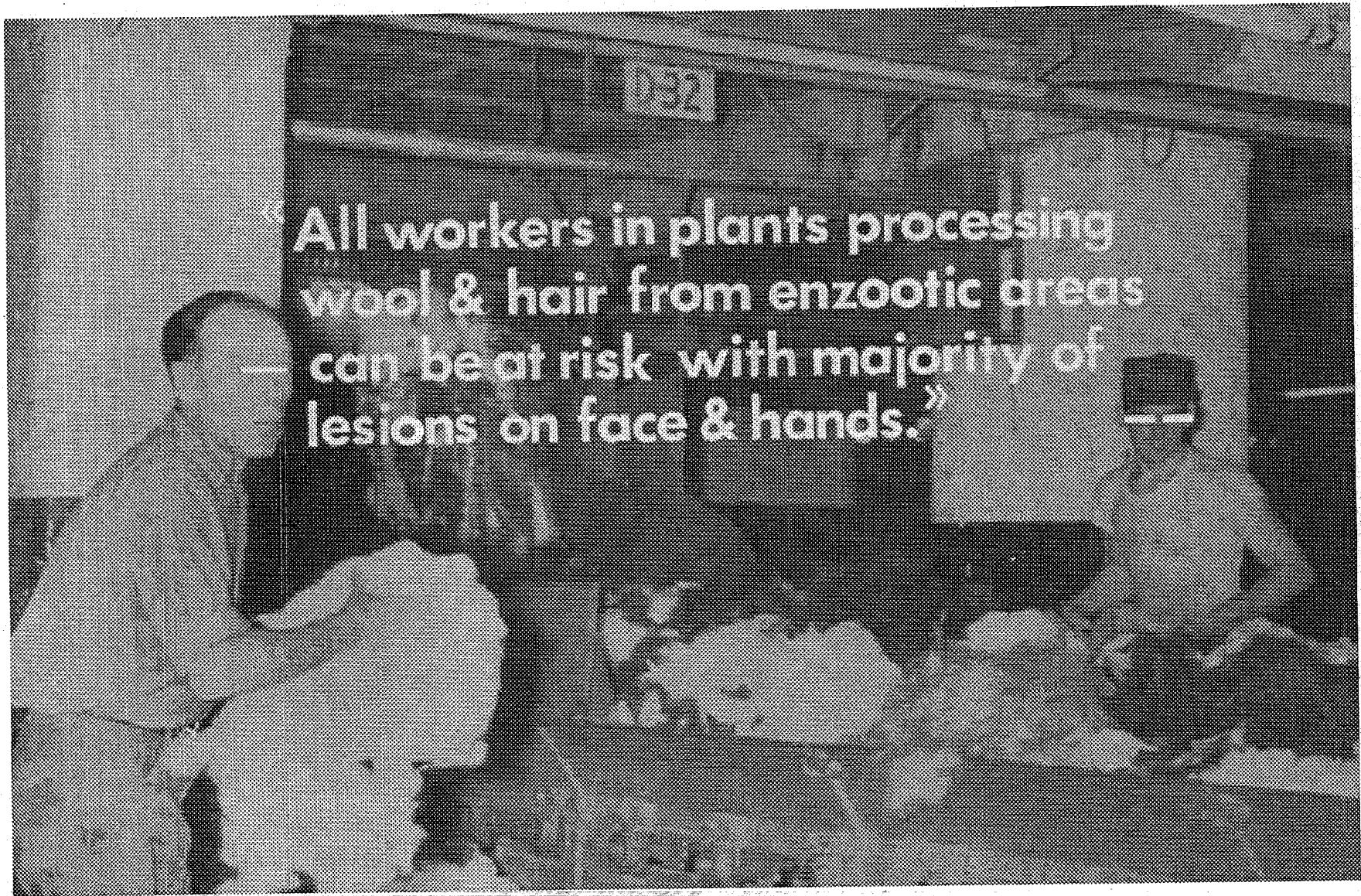


# Cutaneous anthrax

- This postman had borrowed his son's woolen scarf; the son worked in a bone meal plant.
- Without prompt treatment, it carries a 10% case fatality rate.



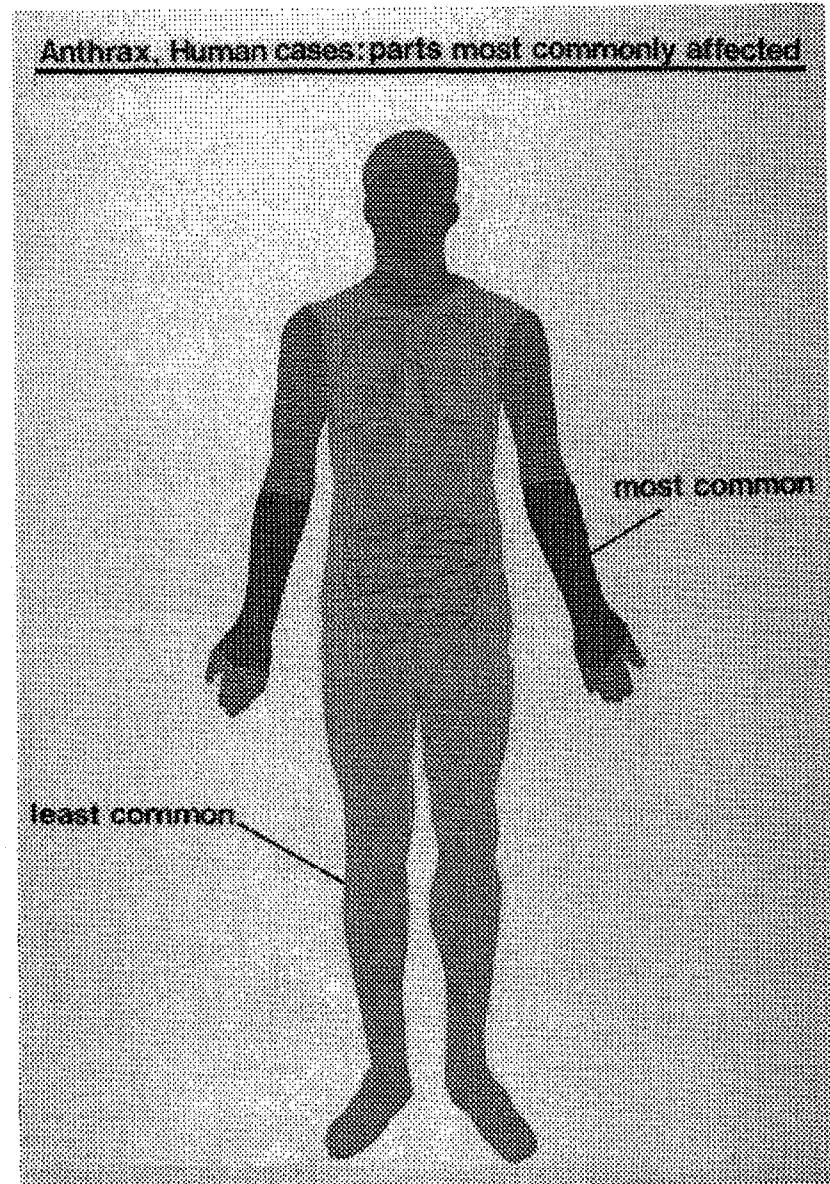




« All workers in plants processing wool & hair from enzootic areas — can be at risk with majority of lesions on face & hands. »

# Cutaneous anthrax

- Cutaneous lesions follow occupational exposure.
- Usually seen in men after butchering an affected cow; or from handling hides, especially sun-dried hides; or from carrying contaminated building insulation.
- Also following insect bites.



# PULMONARY



ABRUPT ONSET  
"Sick and Chilled"

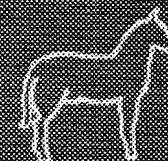


Cyanosis, Dyspnoea,  
rapid heart beat, feeble  
pulse, profuse sweating,  
possibly enlarged lymph  
nodes and spleen.  
FATAL WITHIN 3 DAYS.

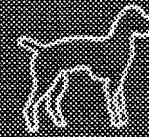
PERACUTE



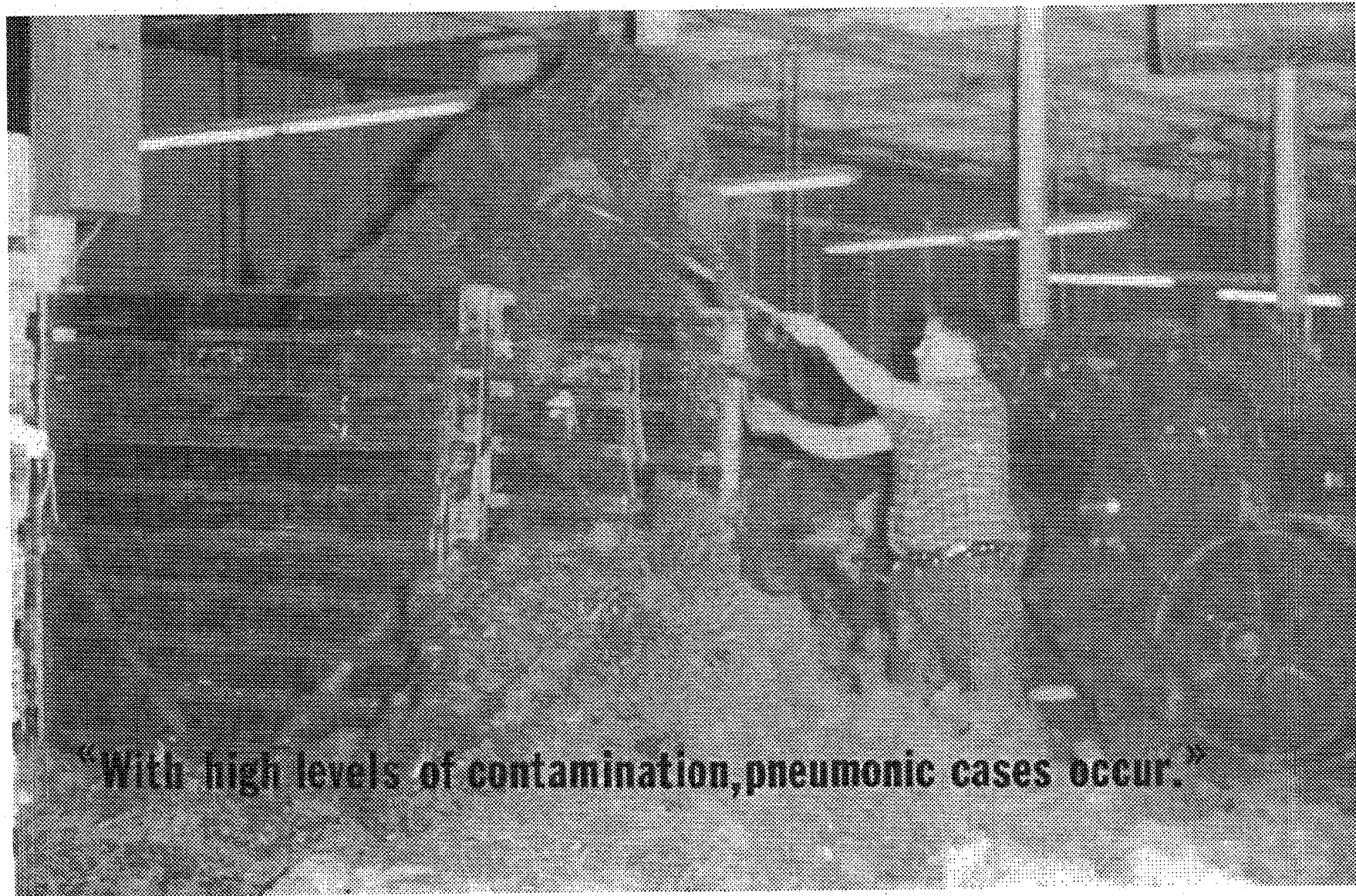
ACUTE



HYPOACUTE







**“With high levels of contamination, pneumonic cases occur.”**

CLINICAL ANTHRAX

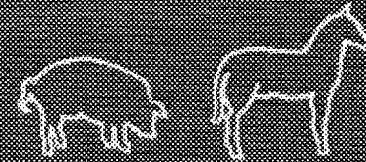
PERACUTE



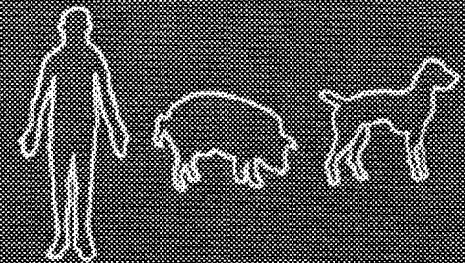
GASTROENTERIC



ACUTE



HYPOACUTE



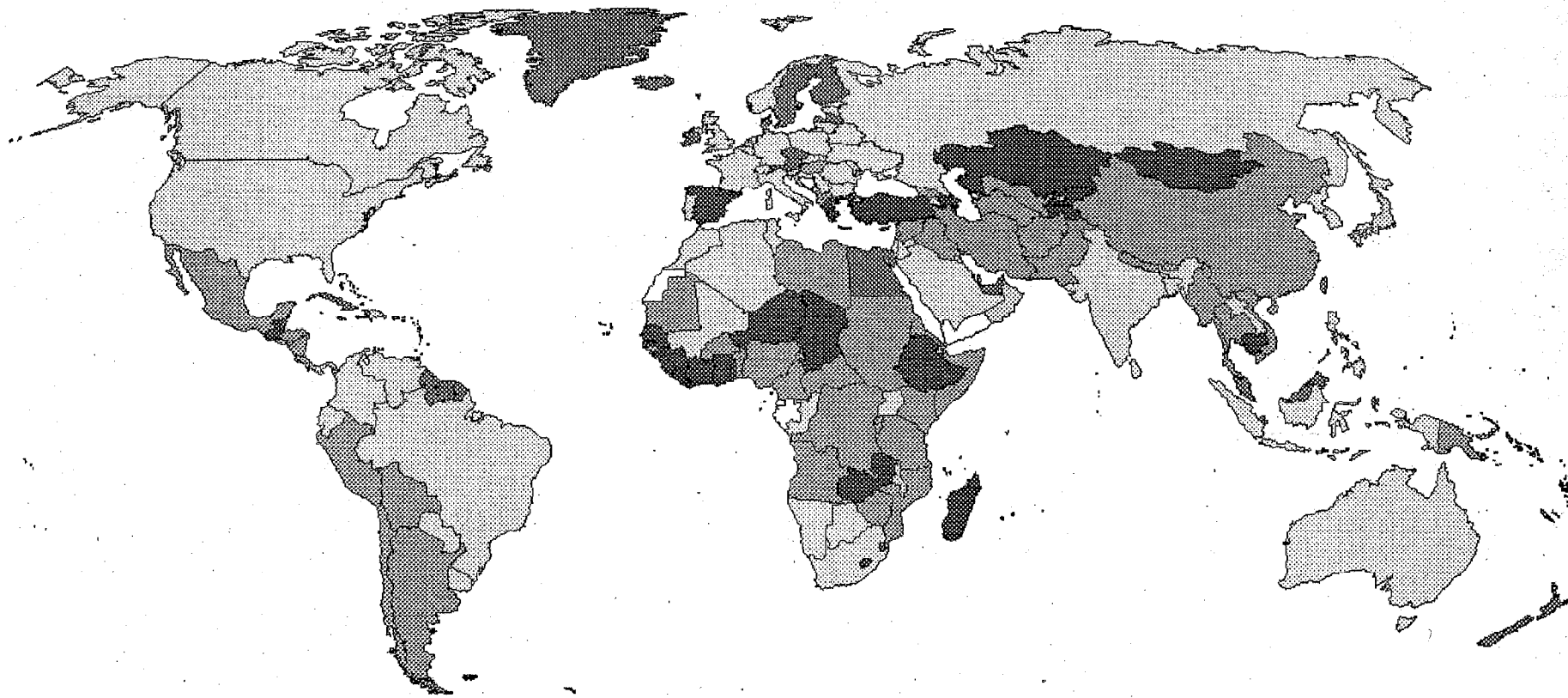
- Onset usually 2-5 days after eating contaminated food
- Nausea, fever, malaise, abdominal pain, bloody vomiting & diarrhea
- Often fatal even with treatment

# Gastroenteric anthrax

- Seen only in poor, developing countries with food shortages or inadequate veterinary inspection – recent cases in SubSahelian Africa, Central Asia, Russia, India & Thailand.
- Usually have concurrent cutaneous cases from butchering the affected animal or handling the infected meat.
- Probable frequency: one outbreak per 64 infected animals eaten.



# Anthrax status, 1998



□ Not reported



Sporadic



Endemic



Hyperendemic



Possibly free

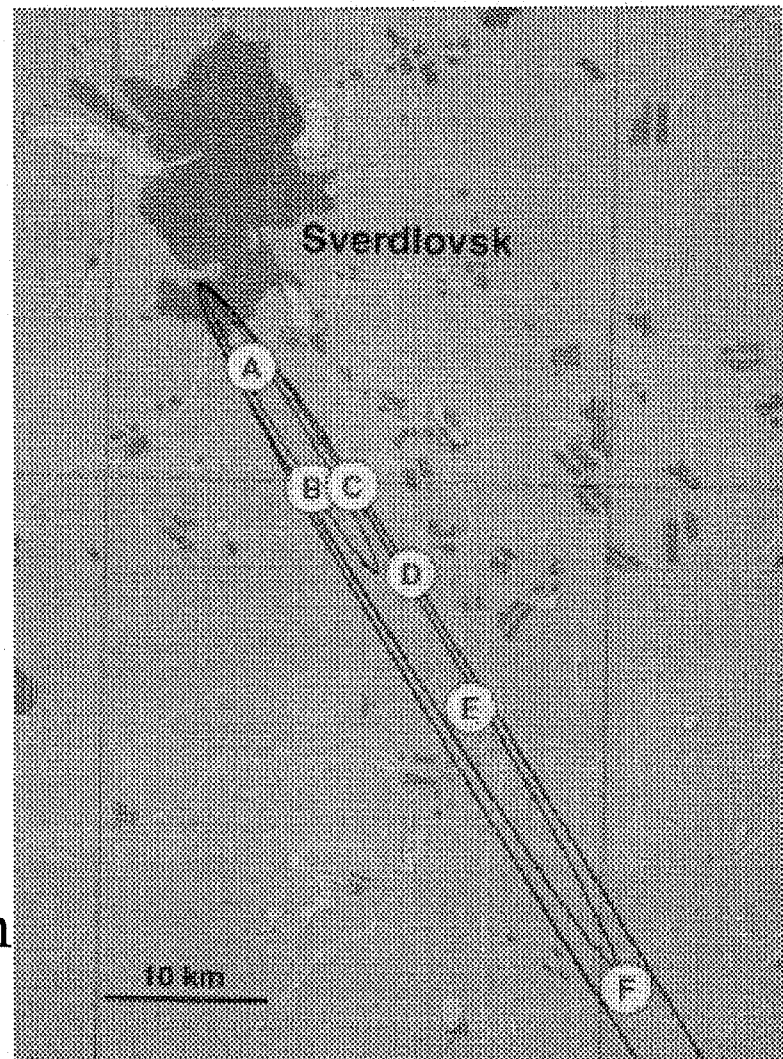


Free ( $\geq 8$  years  
without cases)



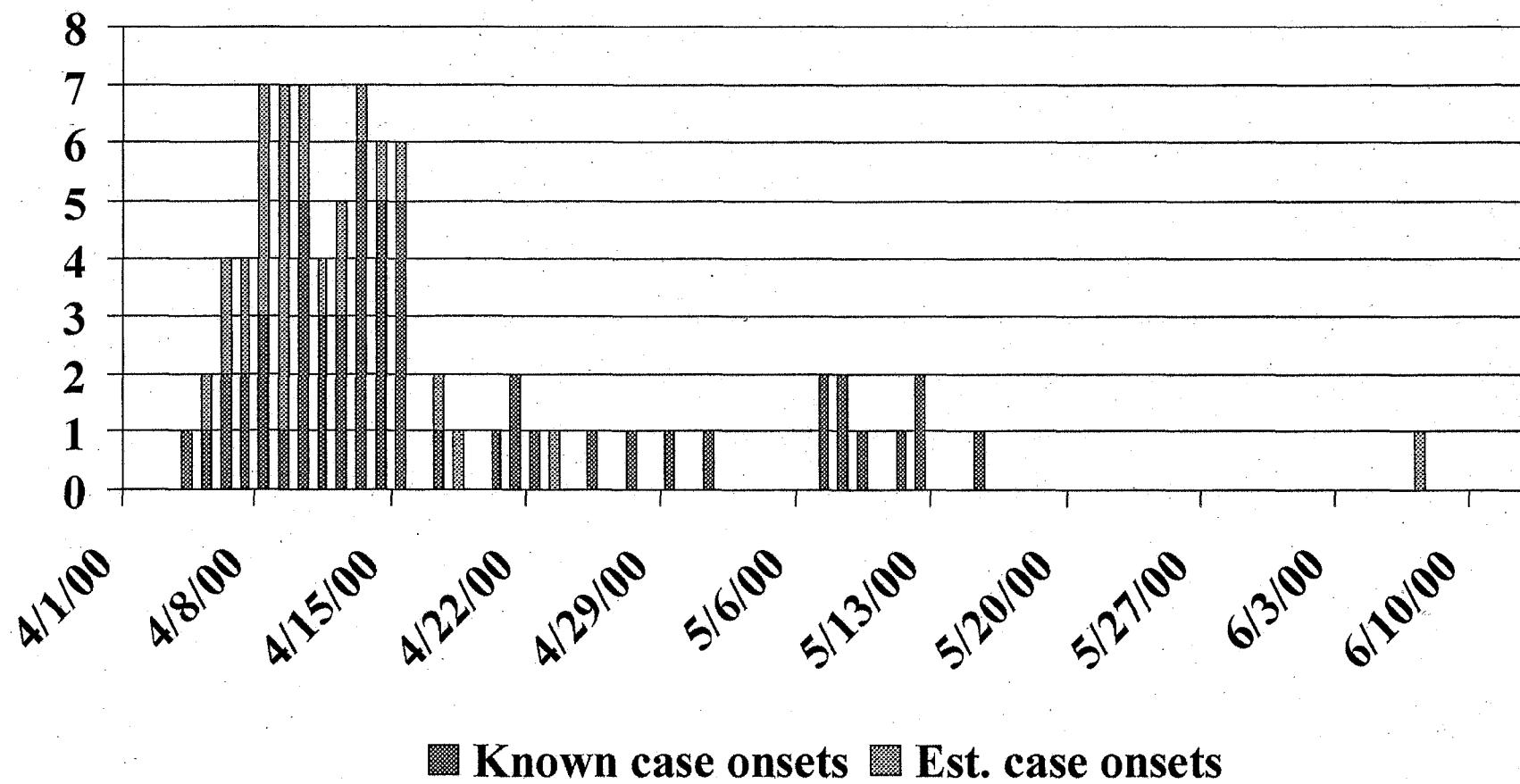
# Sverdlovsk incident (1979)

- ◆ 120 to >400 became ill, 75 died (at least, probably ~ 90)
- ◆ Soviet officials initially reported that outbreak was due to contaminated meat
- ◆ Autopsy findings of hemorrhagic mediastinitis
- ◆ Infection later linked to an aerosol leak from a nearby biologic weapons facility operated by the Soviet army
- ◆ Lines of equal dosage based on northerly wind pattern

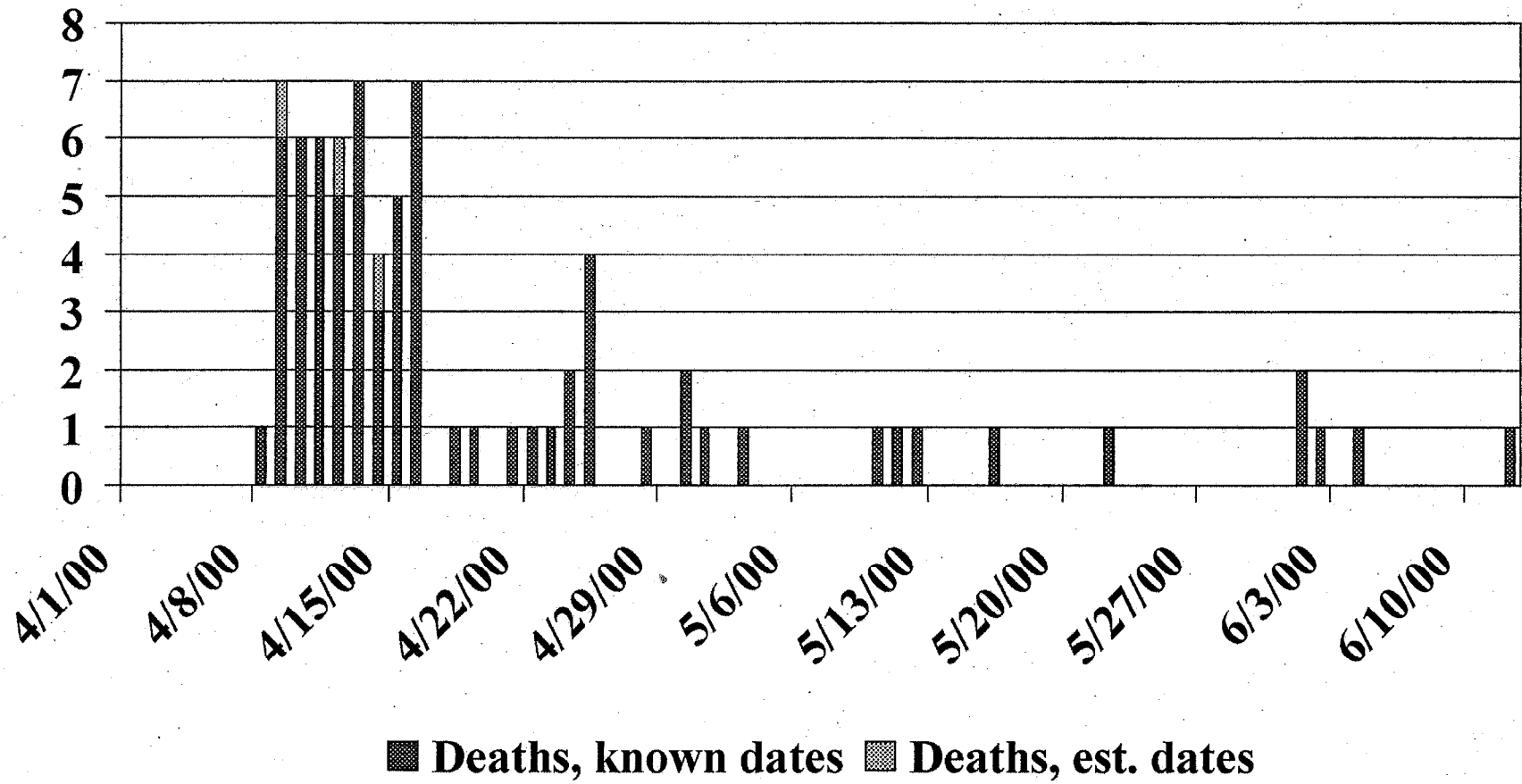


Meselson et al, *Science*, 1994

# Sverdlovsk: Anthrax case onsets

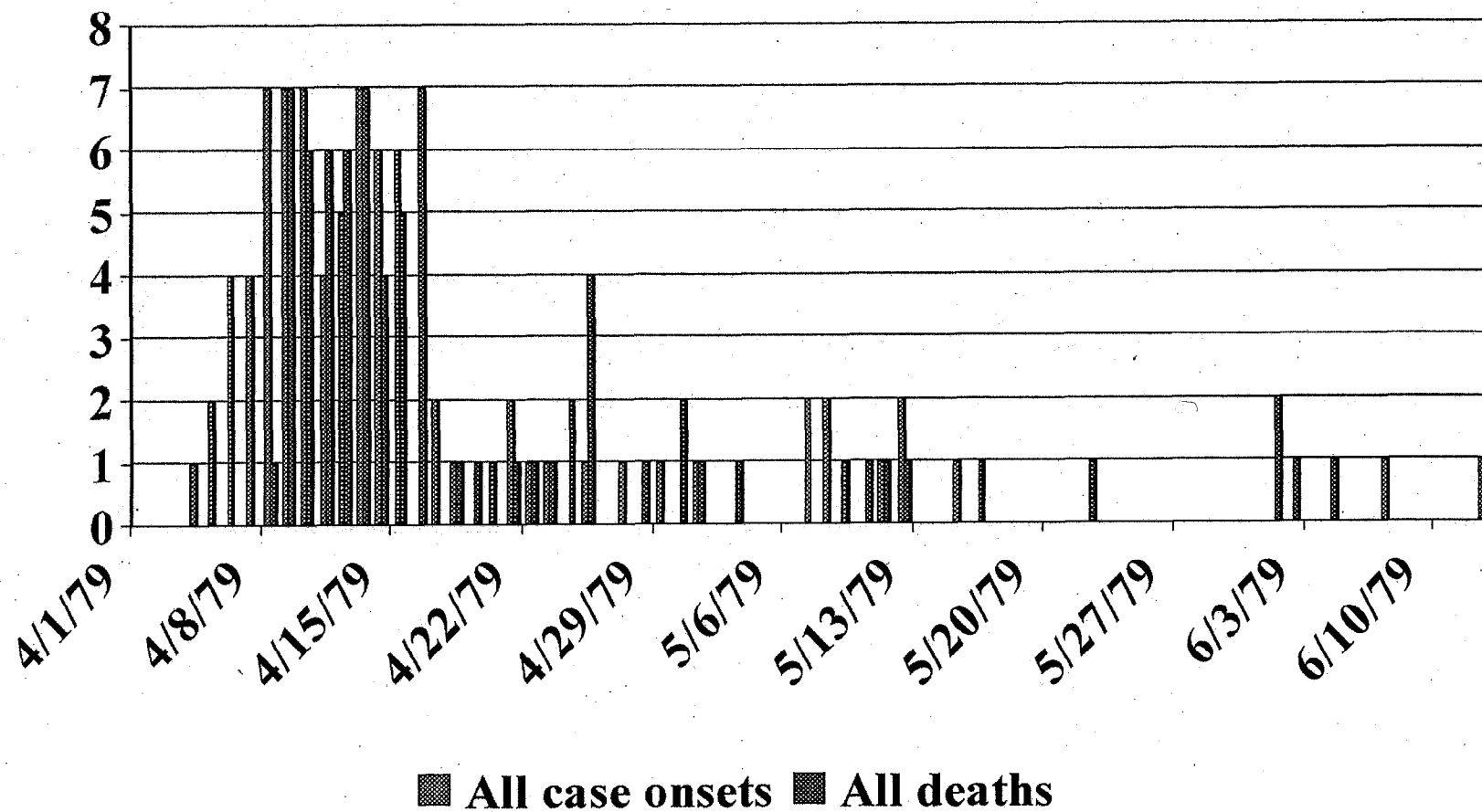


# Sverdlovsk: Anthrax deaths

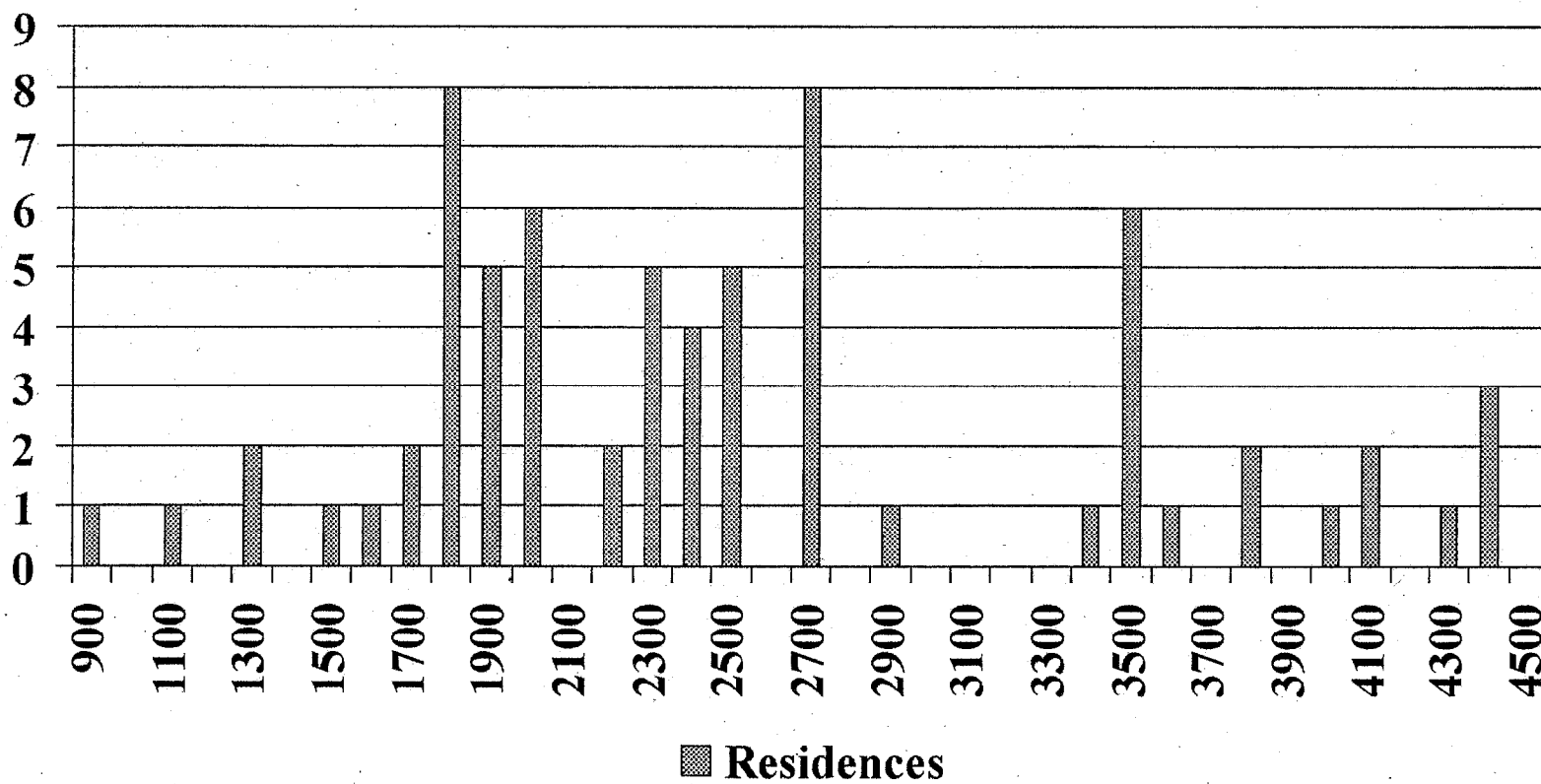




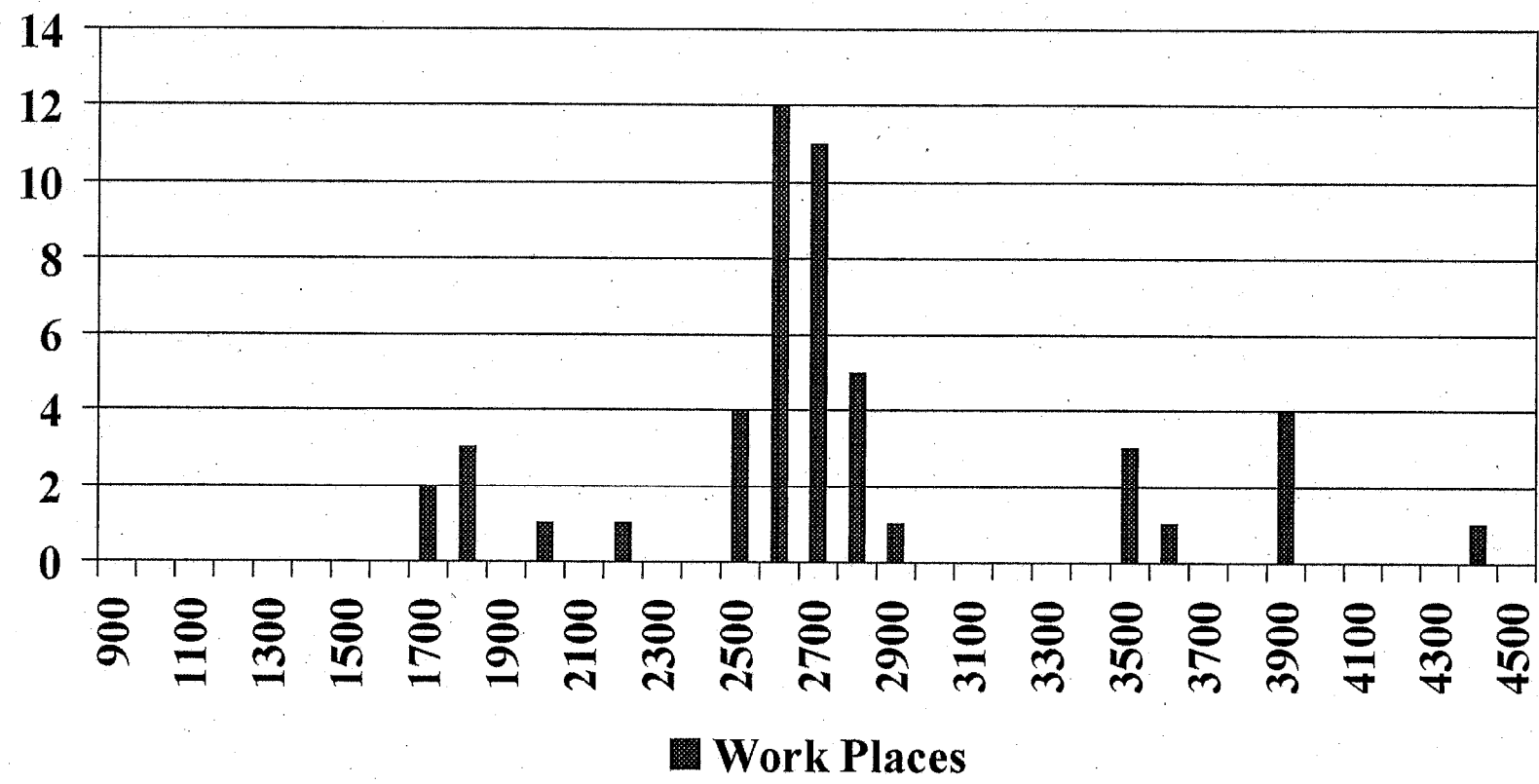
# Sverdlovsk: Case onsets & Deaths



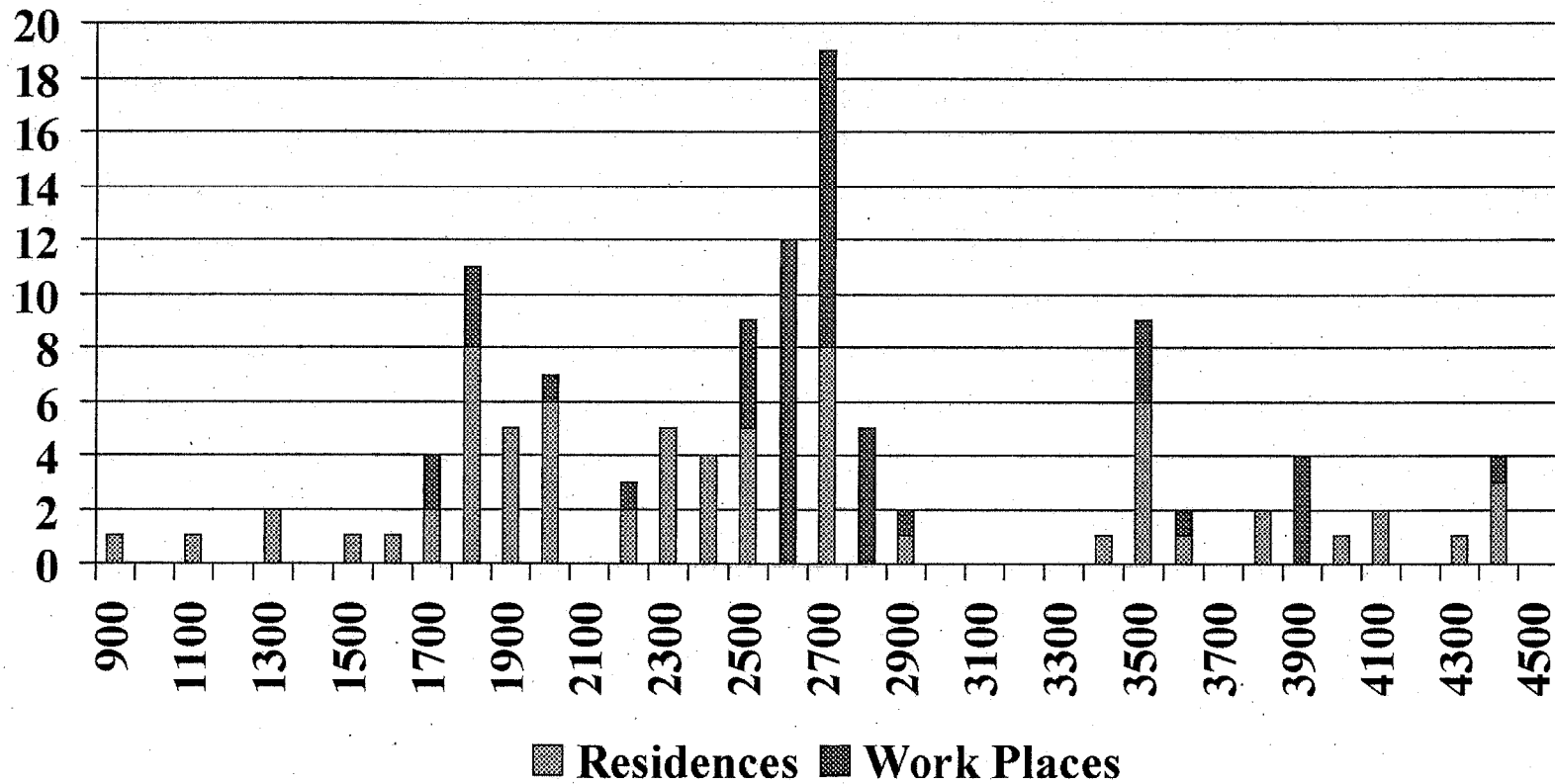
# Sverdlovsk: Residence distances (m) from source



# Sverdlovsk: Work place distances (m) from source



# Sverdlovsk: All distances (m) from source



# Antibiotic resistance & sensitivities

Sample Id	P	VA5	VA30	CIP	SXT	CZ30	E15	TE30	CC2
A0850	S	4	R	<b>R</b>	12	8	8	8	9
A0856	S	R	6	<b>10</b>	R	10	6	8	6
A0867	S	R	5	<b>11</b>	R	12	R	R	5
Kudu '93	S	3	R	<b>6</b>	R	12	6	9	6

Kudu '93 is our routine reference strain. The others were the three  $\gamma$ -phage resistant samples in our Italian collection (n=53).

**P** Penicillin; **VA** Vancomycin 5 & 30 $\mu$ g; **CIP** Ciprofloxacin 5 $\mu$ g; **SXT** Sulfathoxazole 23.75 $\mu$ g & Trimethoprim 1.25 $\mu$ g; **CZ30** Cefazolin 30 $\mu$ g; **E15** Erythromycin 15 $\mu$ g; **TE30** Tetracycline 30 $\mu$ g; **CC2** Clindamycin 2 $\mu$ g