

## Infectious eschars

Jeannette Guarner, MD  
Department of Pathology and Laboratory Medicine  
Emory University

## Definition (Wikipedia)

- ▶ An **eschar** (from the Greek word *eschara* (scab) ) is a slough or piece of dead tissue that is cast off from the surface of the skin, particularly after a burn injury, but also seen in gangrene, ulcer, fungal infections, necrotizing spider bite wounds, and exposure to cutaneous anthrax.

## Index Case

October 3, 2001.

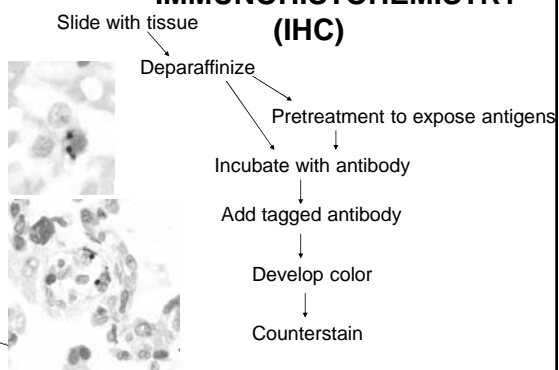
- ▶ BT investigation was started by CDC and other local and federal authorities when *Bacillus anthracis* was isolated from cerebrospinal fluid.
- ▶ Patient, a photographer that worked for a newspaper in Florida, started 2 days earlier with fever, fatigue, sweats, and altered mental status.

## Case Definition

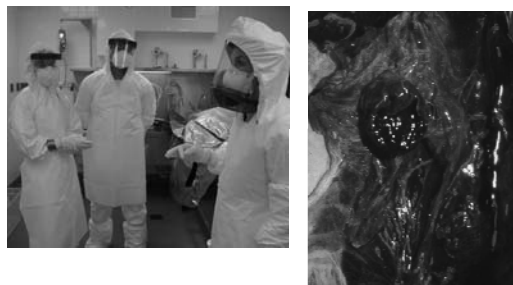
Patient with clinical disease compatible with cutaneous, gastrointestinal or inhalational anthrax with

- *B. anthracis* isolated from the affected site, or
- at least 2 other tests positive for *B. anthracis* (PCR, serology, or immunohistochemistry – IHC).

## IMMUNOHISTOCHEMISTRY (IHC)



Patient died October 5, an autopsy is performed to determine the route of transmission of anthrax.



Guarner et al. Am J Pathol. 2003;163:701

## Second case

Concomitant to index case:

- ▶ Mailroom worker from the same newspaper with pneumonia.
- ▶ Patient had persistent bilateral pleural effusions.
- ▶ Cultures were negative.
- ▶ Anthrax antigens in pleural fluid by CDC's IHC.
- ▶ Anthrax nucleic acids in pleural fluid by CDC's PCR confirmed the diagnosis.

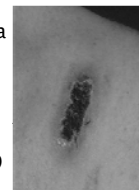
## The history gets more complicated...

September 25, 2001 in New York City:

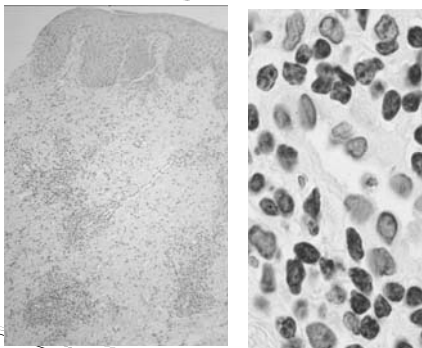
- ▶ Secretary working at NBC developed a cutaneous lesion.
- ▶ She received antibiotics.
- ▶ Cultures of lesion not obtained.

October 12, 2001:

- ▶ Culture and PCR of biopsy obtained 9 days after treatment: negative for *B. anthracis*.
- ▶ IHC on biopsy shows anthrax antigens.
- ▶ Serology eventually confirmed IHC result.



## Histopathology

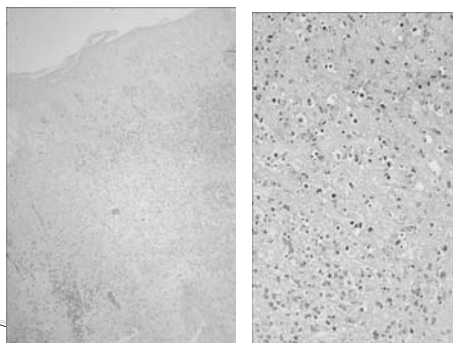


## Laboratory Results: skin cases

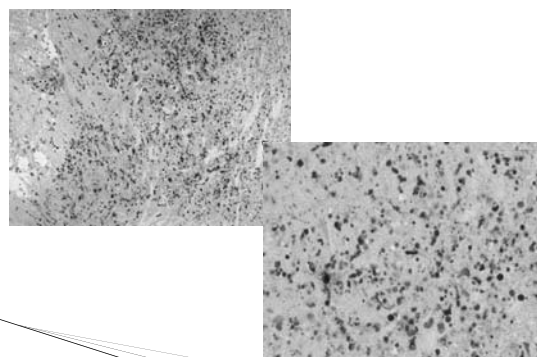
Case	IHC	Culture	PCR	Serology
1	Positive	Negative	Negative	Reactive
2	Positive	Negative	Positive (blood)	NA
3	Positive	Negative	Negative	Reactive
4	Positive	Negative	Positive (fixed skin)	Reactive
5	Positive	Positive (blood)	Negative	Reactive
6	Positive	Negative	Negative	Negative
7	Positive	Negative	Positive (frozen skin)	Reactive
8	Positive	Positive (wound swab)	Negative	Reactive
9	Negative	Negative	Negative	Reactive
10	Negative	NA	Negative	Reactive

Shieh et al. Am J Pathol. 2003;163:1901

## Histopathology



## Immunohistochemistry of skin lesions



### Special stains

	Positive with Gram stain	Positive with silver stains (Steiner or Warthin Starry)
Inhalational anthrax	3/8 (37.5%)	6/8 (75%)
Cutaneous anthrax	2/10 (20%)	5/10 (50%)

### Factors for cutaneous anthrax

- History of:
  - slaughtering or caring for animals,
  - meat processing, or
  - performing crafts with animal products
- Lesions occur in:
  - hands, fingers, and arms, (60 to 90%),
  - face or neck (6 to 30%)

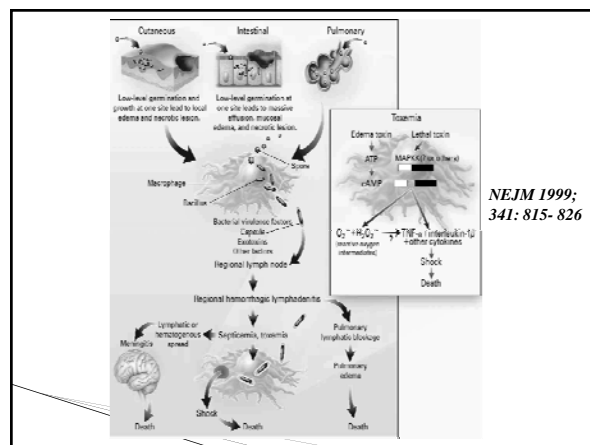
### 7 month old with a cutaneous lesion

1<sup>st</sup> painless, pruritic erythema,

48 to 72 hours: papule or multiple vesicles accompanied by local inflamed edema.

1 week: painless ulcer with a black center=eschar

(JAMA. 2002;287:869-874)



### 134 skin biopsies sent for possible anthrax:

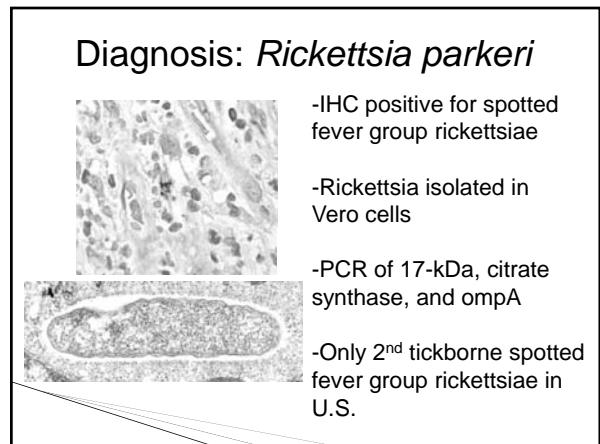
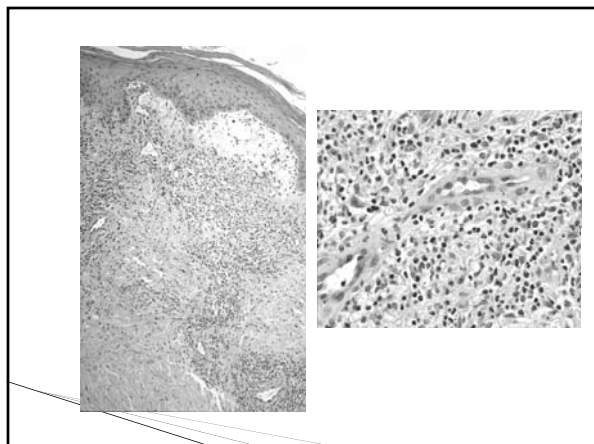
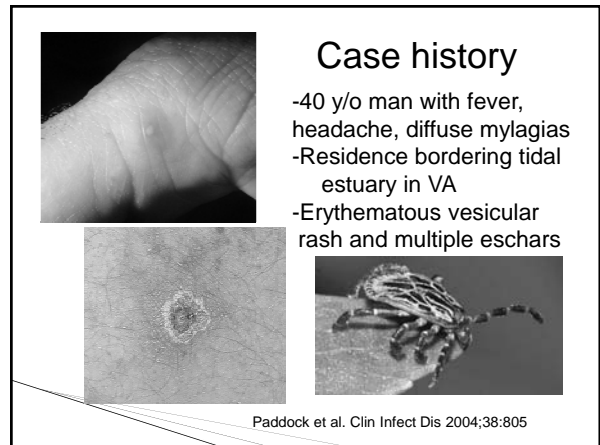
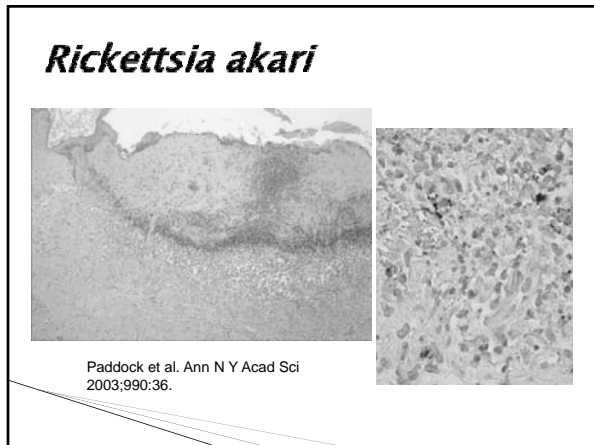
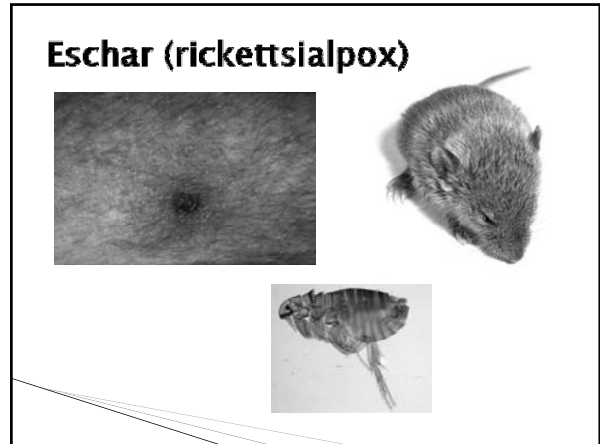
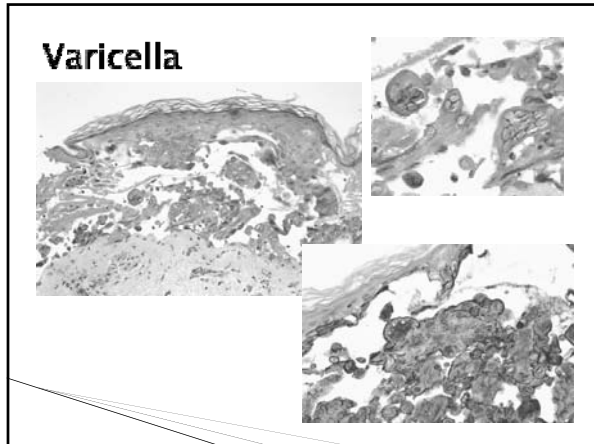
- 8 cases positive for *B. anthracis* using IHC:
  - Variable quantities of bacillary fragments and granular antigens.
- 2 probable anthrax cases (only serology+)
- Other diagnosis found using IHC:
  - 9 cases with Varicella-Zoster
  - 4 cases with Rickettsiapox
  - 3 cases with Herpes simplex
  - 1 case with spider bite
  - 1 case with squamous cell carcinoma

### Spider bite (brown recluse)

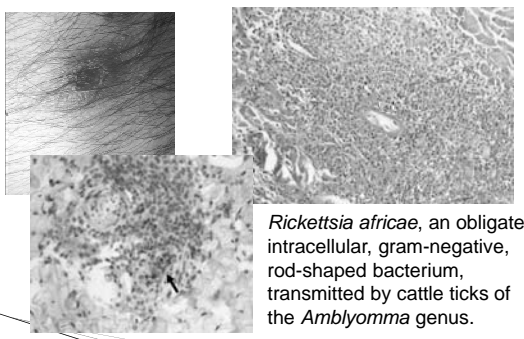
-7 month old child with rapidly appearing eschar, minimal edema

-Afebrile, WBC 23K, Gram stain unrevealing

-Mother works in laboratory where anthrax is studied extensively

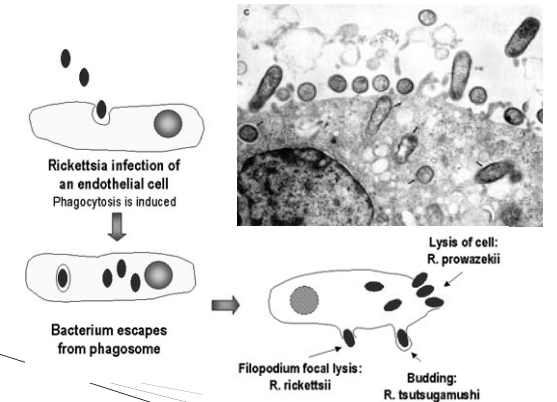


### African tick bite fever



*Rickettsia africae*, an obligate intracellular, gram-negative, rod-shaped bacterium, transmitted by cattle ticks of the *Amblyomma* genus.

Lepidi et al. Emerg Infect Dis 2006;12: 1332



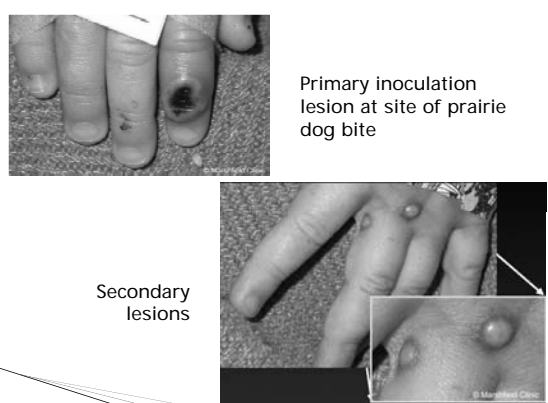
Rickettsia infection of an endothelial cell  
Phagocytosis is induced

Bacterium escapes from phagosome

Lysis of cell: *R. prowazekii*

Filopodium focal lysis: *R. rickettsii*

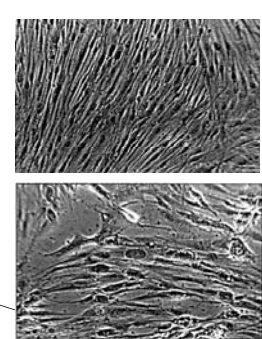
Budding: *R. tsutsugamushi*



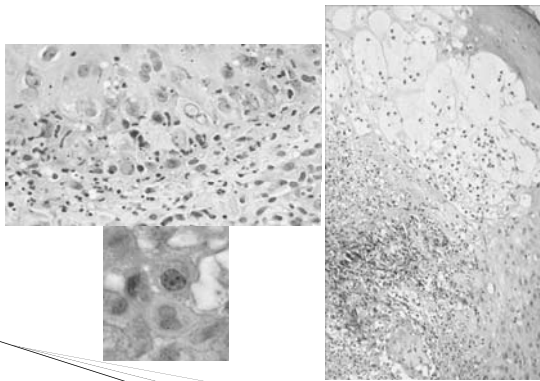
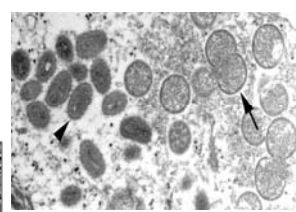
Primary inoculation lesion at site of prairie dog bite

Secondary lesions

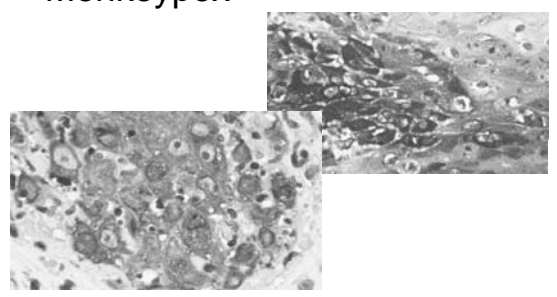
### Viral culture

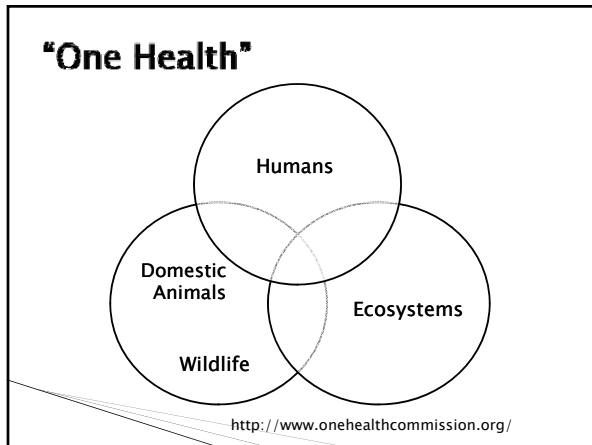
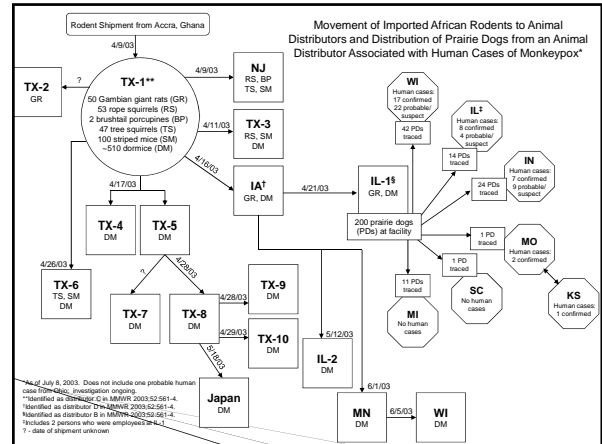


### Electron microscopy



### Monkeypox





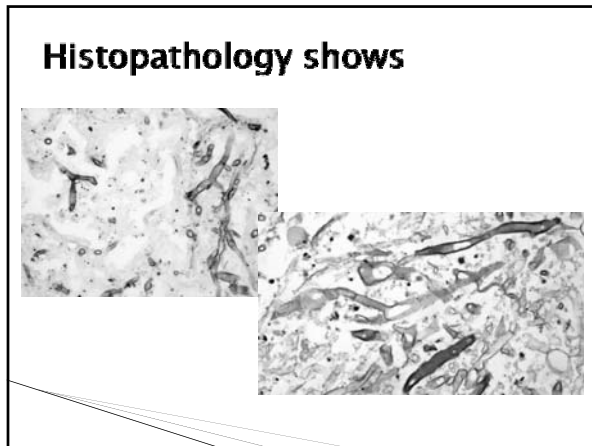
"A robust public health system— in its science, capacity, practice, and through its collaborations with clinical and veterinary medicine, academia, industry and other public and private partners—is the best defense against any microbial threat."

2003 IOM Report



**Case**

- ▶ A 5 years old girl with ALL.
- ▶ WBC count of 10,000.
- ▶ During the second week of induction she developed two red lesions over medial aspect of left forearm that in a matter of days expanded and turned black.
- ▶ Three antibiotics (ceftazidime, amikacin and vancomycin) were started, but with no improvement.



*Mucorales* genera

**Description:** Non-pigmented (hyaline), pauciseptate ribbon-like hyphae with right angle branching.

**Diagnosis:** Non-pigmented (hyaline), pauciseptate hyphae.

**Comment:** The morphology is consistent with *Mucorales* genera; however, *Aspergillus* spp. and other septated hyaline hyphae can sometimes have this morphology.

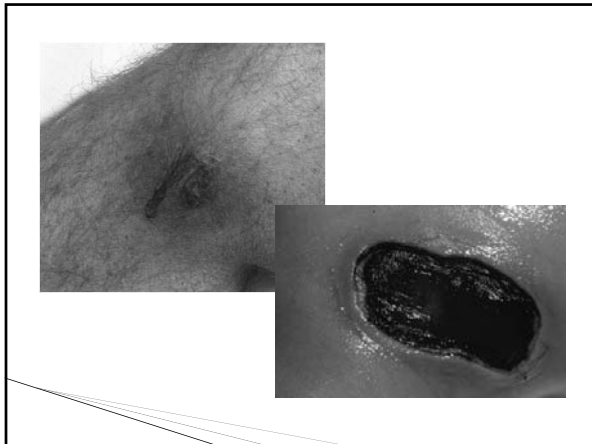
### *Mucorales* genera

The diagram shows two views of a sporangium (A and B) with labels: Sporangium, Apophysis, Columella, Columella, Apophysis, Sporangiospore, Sporangiospore, "Foot Cell", Rhizoids, and Rhizoids.

*Mucorales* genera

Cutaneous	<u>Angioinvasion</u> by hyphae with consequent <u>necrosis or hemorrhage</u> of surrounding tissue; inflammation if present is frequently <u>suppurative</u> , less common granulomatous, but varies depending on immune status	Necrotic (black) skin lesion in immunosuppressed patients
Rhinocerebral	Similar to that described for cutaneous disease	Particularly frequent in diabetic patients, but can occur in any immunosuppressed patient
Pulmonary	Similar to that described for cutaneous disease	Multiple pulmonary nodules and pleural effusions in immunosuppressed patients
Invasive disease	Similar to that described for cutaneous disease	Risk factors include cancer chemotherapy and stem cell transplantation

- ▶ Diagnosis requires biopsy:
  - One portion for culture
  - The second part for histopathology
- ▶ Prompt amphotericin B therapy should be administered due to the rapid spread and mortality rate.
- ▶ Surgical removal.

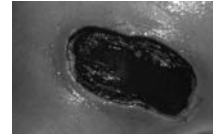


**Hematogenous spread of fungemias**

- ▶ Neutropenic patient
- ▶ Nodular lesion->central hemorrhage-> necrotic ulcer
- ▶ *Mucolales* or *Aspergillus*
- ▶ Vascular invasion, necrosis & scant inflammation

**Ecthyma gangrenosum**

- ▶ Neutropenic patient
- ▶ Painless nodular lesion->central hemorrhage-> necrotic ulcer
- ▶ *Pseudomonas aeruginosa* or other gram -negative bacteria
- ▶ Necrotizing vasculitis & scant inflammation



▶ Hematogenous spread of fungemias

▶ Ecthyma gangrenosum

Goolamali et al. Clin Exp Dermatol. 2009;34:180

**Mechanisms that give rise to eschars:**

- ▶ Vascular: rickettsial diseases, fungal infections
- ▶ Damage to epidermis: herpes, monkeypox
- ▶ Damage to the dermis: anthrax toxins, spider bites

