A Personal Journey into New and Emerging Infectious Diseases

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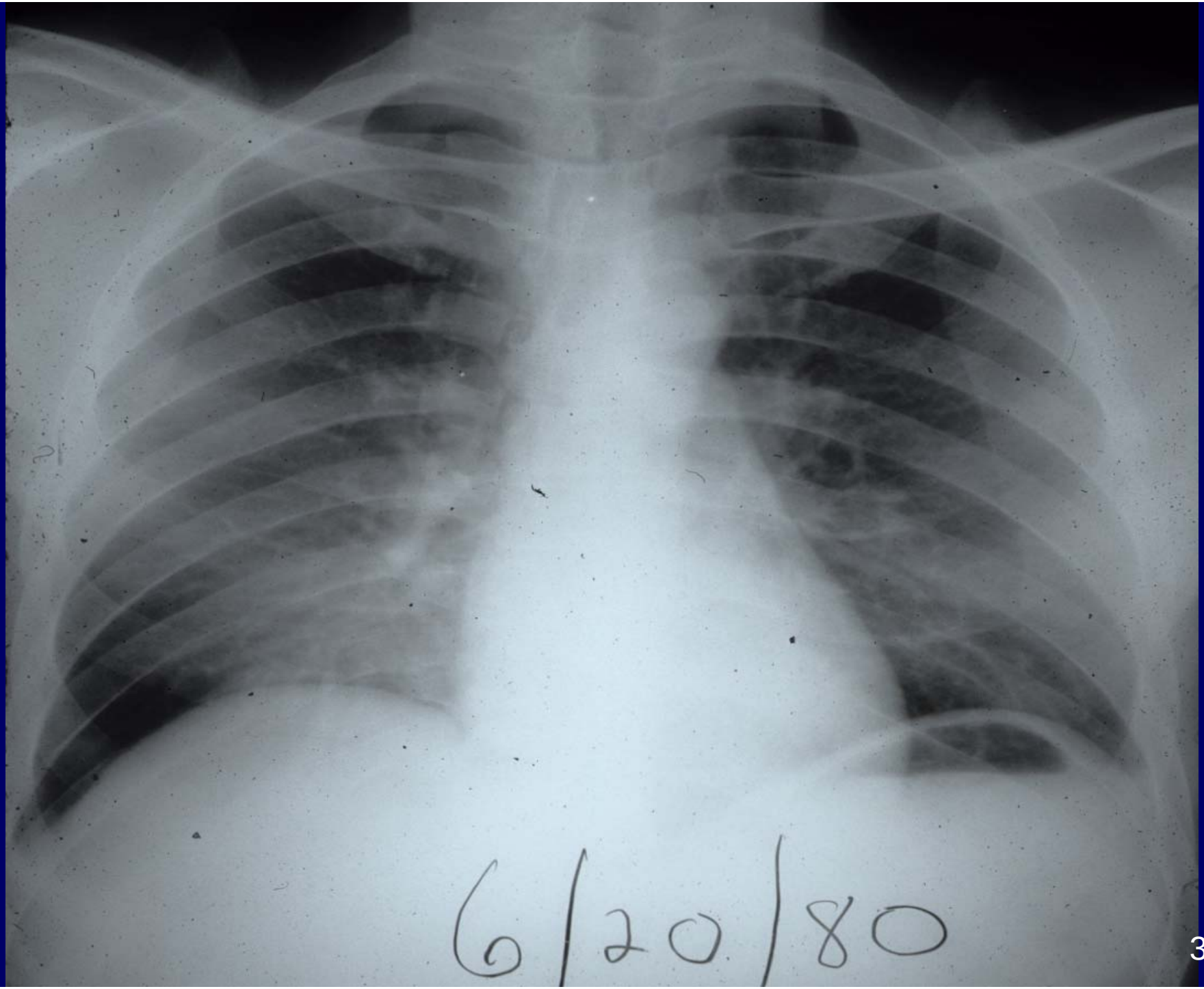
Disclosures

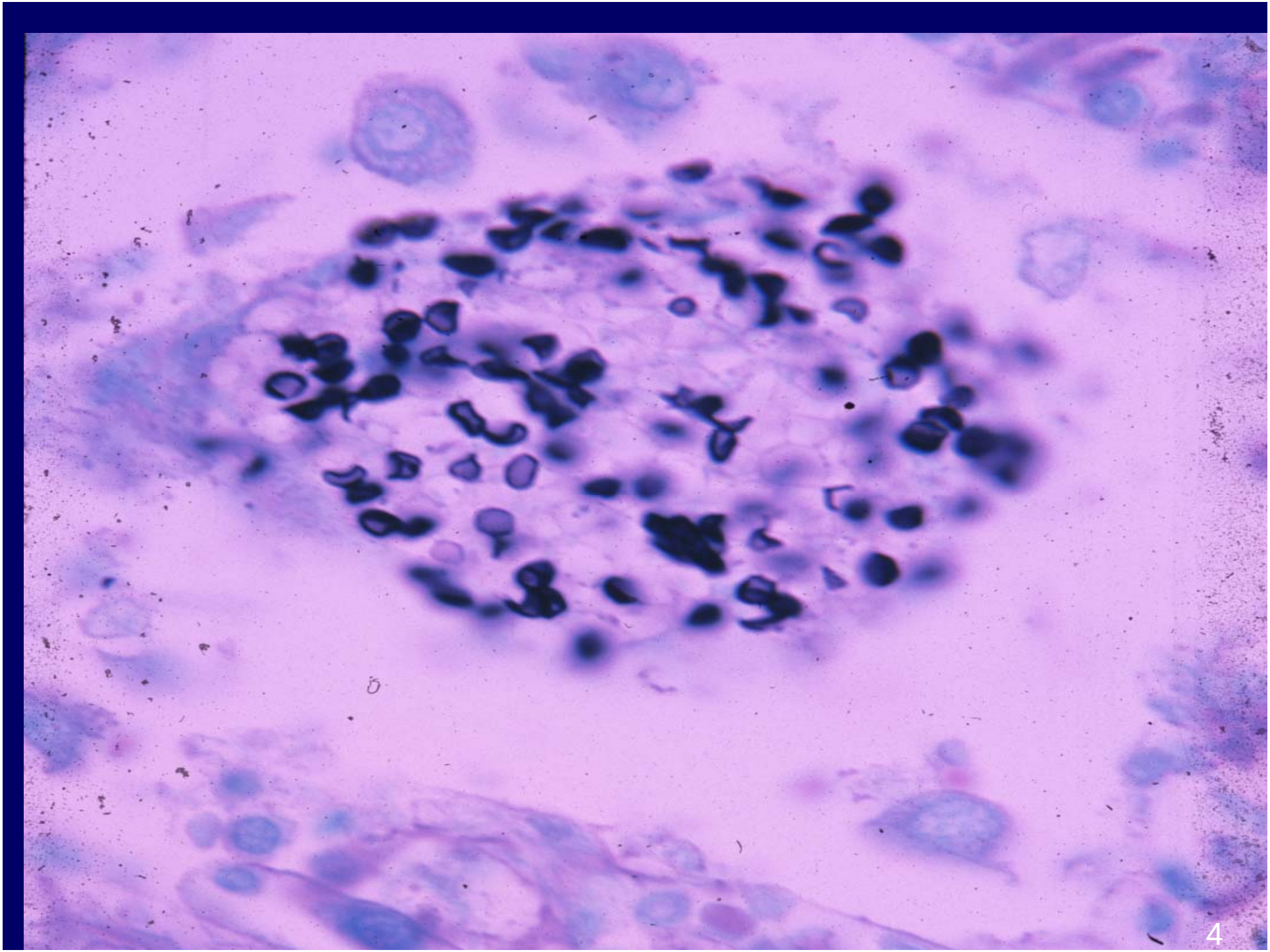
- Research grants from Immunetics, Inc., BioRad, and possibly from Biopeptides
- Educational grants to NYMC to support ID grand rounds from Merck and AstraZeneca, possibly Pfizer
- Former part owner of Diaspex, a company no longer in existence
- Equity in Abbott
- Expert witness in malpractice cases involving Lyme disease

"THE WAR AGAINST INFECTIOUS DISEASES HAS BEEN WON."
WILLIAM H. STEWART.
U.S. SURGEON GENERAL
(1969)

Courtesy of Donald Rumsfeld

- Known Knowns
- Known Unknowns
- Unknown Unknowns





Pneumocystis carinii Study Group

Head Investigator

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Investigators

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Jeffrey B Greene, MD	New York University Medical Center
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Susanna Cunningham–Rundles, PhD	Memorial Sloan-Kettering Cancer Center

11 Males With P. carinii Pneumonia

Avg. Age	33 yrs.	(range 27- 40 yrs.)	
Race	White-5	Black-4	Hispanic-2
Social Hx.	Drugs-6	(heroin, methadone, cocaine)	
	Homosexual-6		
	Alcohol-1		

SUMMARY OF IMMUNOLOGIC STUDIES

Cellular Enumerations

B- Lymphocytes (surface Ig^+)

T- Lymphocytes (sRBC rosettes)

Monocytes (latex ingestion)

Functional Studies

HUMORAL

Serum immunoglobulins

ABO-Isohemagglutinins

Tetanus Toxoid AB's

Diphtheria Toxoid AB's

Pneumococcal vaccine response

CELLULAR

Skin-Testing

In-vitro Lymphoproliferation
- -mitogens
- -antigens
- -allogeneic cells

MONOCYTIC

Anti-Toxoplasma Assay

Original Articles

Prophetic Words

October 1981

"With the appearance and identification of increasing numbers of KS in young homosexuals, I suspect that we are now observing the tip of the iceberg. We may well be seeing the evolution of a new syndrome of epidemic proportions." Alvin Friedman-Kien. J Am Acad Dermatol 1981;5:468-71.

Questions regarding AIDS

1. Is it transient?
2. What causes it? How widespread?
3. If infectious, old or new pathogen?
4. If infectious, how transmitted?
5. If infectious, is there a latent period and if so, how long is it?

Explanations for AIDS

1. Nitrites +/- contaminants
2. Contamination in the “baths”
3. Antigen overload from infections
4. Sperm on rectal mucosa
5. Mutation of CMV or EBV
6. “Erik”

AIDS was new, not newly appreciated

- PCP without prior immunodeficiency
- Increased incidence of KS among young patients in 1979 based on tumor registry data
- Evaluation of requests to CDC for pentamidine
- Review of post-mortem exams of 168 NYS prisoners 1/77-10/81 with reexamination of lung tissue in selected cases

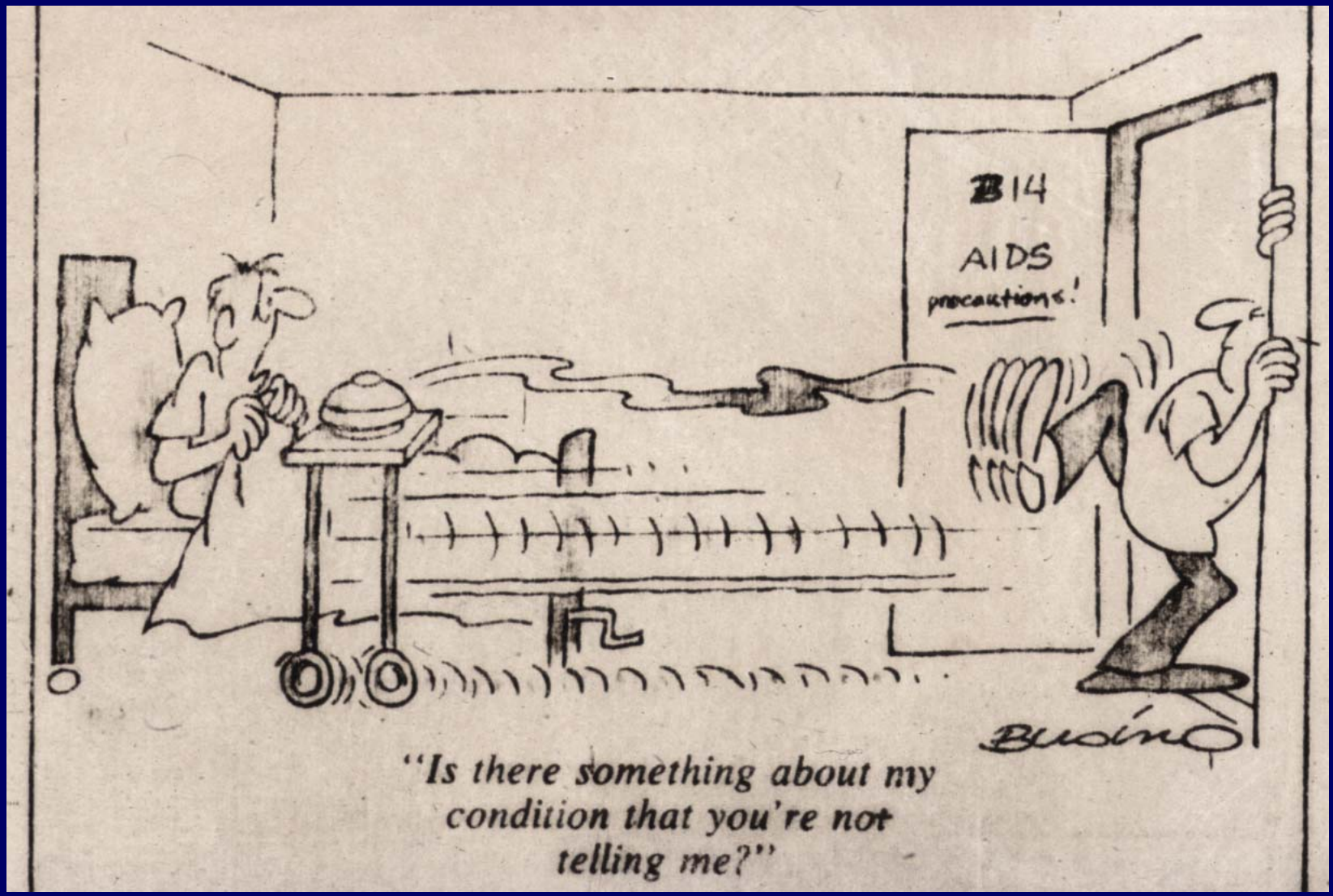
Wormser GP, et al. Ann Intern Med 1983;98:297-303

Evidence early on suggested a long incubation period

- No known iv drug use within an average of 22.6 months in prisoners with AIDS whose risk was ivdu
- Recognition of unexplained lymphadenopathy and/or leukopenia some time prior to onset of PCP
- Cases with single or limited exposure; or a case cluster
- Wormser GP, et al. Ann Intern Med 1983;98:297-303; Hanrahan JP et al. JID 1984;150:263-266

Fundamental observations that preceded the discovery of HIV

- Biochemical assay for reverse transcriptase -1970 (Temin and Baltimore)
- Growth of T lymphocytes in culture– T-cell growth factor (IL-2)- 1976 (Gallo)
- Identification of CD4 and other CDs – 1975-9 (Millstein and Kohler; Reinherz et al)
- Antiinterferon serum – 1979 (Barre-Sinoussi and Montagnier)



Sweat Study

- HIV cultures
  - Peripheral blood + in 39/50 (78%)
  - Sweat – None positive (0/50)
  - Controls – Both negative
- PCR for DNA and RNA
  - Sweat – None positive 0/39)
  - Control – Negative (0/1)

Wormser GP, et al. JID 1992;165:155-8

People vs Eaves, No. E032424 (Cal. App. 4 Dist.)

- 8/20/03
- A California appeals court affirmed that someone charged in a criminal complaint can undergo mandatory HIV testing if his/her sweat comes into contact with a peace officer.

AIDS/HIV Statistics (2006)

Global

- **~ 40 million living with HIV**
- **~5 million newly infected per year**
- **~ 3 million AIDS deaths per year (~20 million in total)**

USA

- **>1 million living with HIV (~25% undxed)**
- **>500,000 deaths in total**

A Passing Thought

How do we know that another infectious agent has not already infected the general population with long-term devastating consequences?

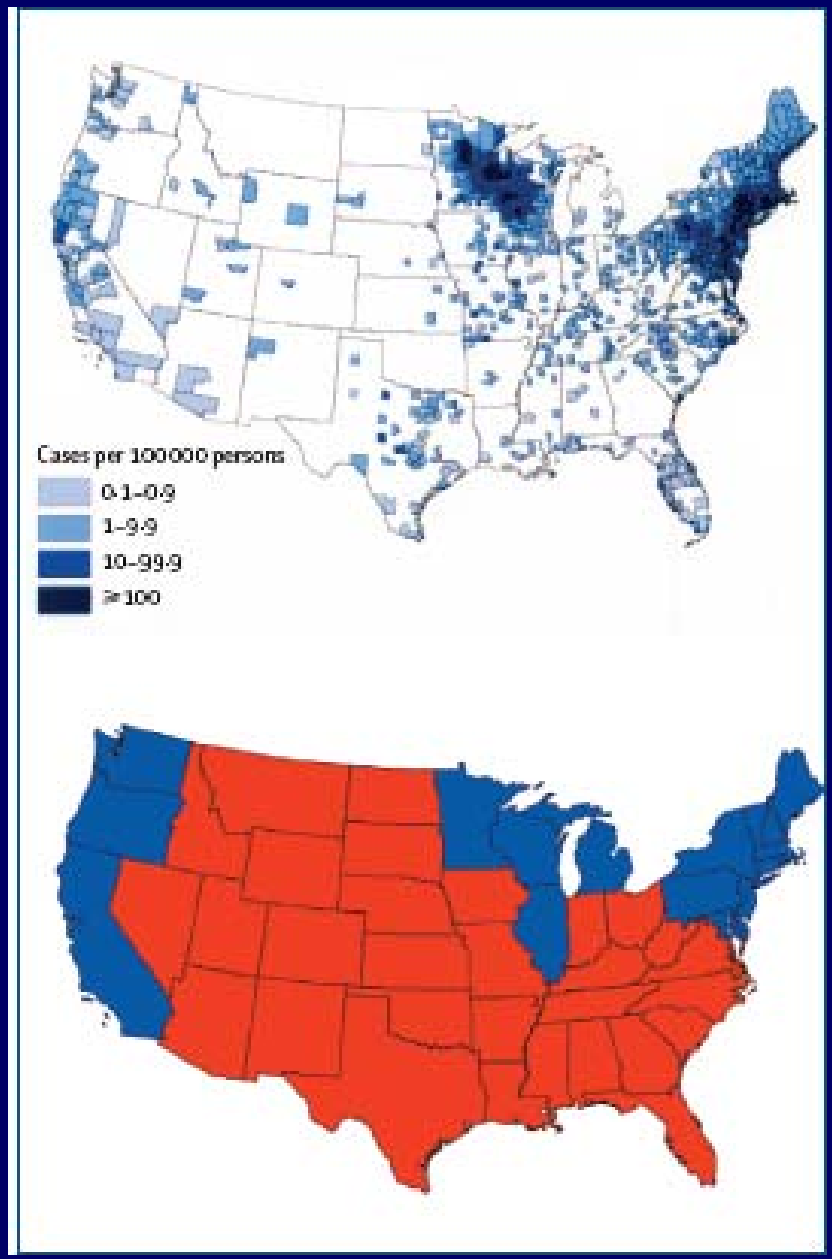
Lyme Disease – General Comments

- Caused by a spirochete known as Borrelia burgdorferi
- Transmitted by certain Ixodes species ticks
- Most common vector-borne infection USA
- A characteristic rash known as erythema migrans is the most common manifestation
- Other manifestations may involve the joints, nervous system and heart

Lyme Disease in the US 1993-2002

New York	28.6%	Wisconsin	3.6%
Connecticut	18.8%	Maryland	3.6%
Pennsylvania	15.4%	Rhode Island	3.5%
New Jersey	12.2%	Minnesota	2.2%
Mass	4.4%	Delaware	0.9%

CDC. MMWR 2004;53:365-369



Erythema Migrans in the South

- *Ixodes scapularis* < 0.5% infected with Bb and rarely bite humans
- Lyme serologies and cultures for Bb negative
- Often follows bite of *Amblyomma americanum* tick, which is not a competent vector of Bb
- ~ 2% infected with *Borrelia lonestari*

Erythema Migrans-Like Skin Lesions in the South

- Southern Tick Associated Rash Illness (STARI)
- Masters Disease

Case History

- 74 y/o African American man from NYS evaluated on 5/24/99
- Travel to MD 5/6, then to NC 5/7-5/18; returned to MD 5/18-5/20
- Noticed attached tick on 5/15 but did not remove it; noticed rash 5/20

Case History

- Temp 98.3˚F
- 19x11 cm erythematous skin lesion on RLQ of abdomen with an attached tick; 2nd skin lesion 4x3 cm LUQ
- CBC- WNL; LFT's WNL except Alk Phos=142 u/l
- Resolved with 14d doxycycline

Evidence for *Borrelia lonestari*

- ***FlaB*** **gene PCR product in both tick and skin**
- **PCR product in tick and skin identical**
- **PCR product nearly identical to *B. lonestari* but different from other borrelia**

JID 2001;183:1810-4

STARI (MO) VS EM (NYS): Microbiologic Results

Test	STARI	EM	P value
Skin GlpQ PCR	0/22	ND	
Skin 16S RNA	0/20	ND	
Skin culture +	0/20	89/142 (63%)	<.001
Seropositive acute or conv	0/25	107/143 (75%)	<.001

Wormser GP, et al. CID 2005;40:423-8

STARI – Outstanding Questions

1. What is the etiology?
2. Is it caused by an infectious agent?
3. Are there several different causes?
4. Are there extracutaneous manifestations?
5. What is the optimal treatment?

Thank You

Figure 3. Lone Star Tick and Its Geographic Distribution[16]

Approximate geographic distribution of *Amblyomma americanum* in the United States.

Lyme Disease in the South 1993-2002

Virginia	1,164*	Tennessee	323
Texas	733	Oklahoma	290
North Carolina	709	West Virginia	237
Missouri	552	Kentucky	209
Florida	492	Arkansas	117

*Cases

CDC. MMWR 2004;53:365-369

Comparison of Missouri (n =21) vs. NYS (n = 101) EM Cases 2001-2003

	Mo	NYS	P value
Tick bite	85.7%	19.8%	<0.001
Symptoms	19.0%	76.2%	<0.001
Fatigue	19.0%	57.4%	0.002
>1 EM	4.8%	26.7%	0.042
Sx 3 mos post rx	0%	21.3%	0.037

Wormser GP et al. Clin Infect Dis 2005;41:958-65

Would you eat cookies prepared by an AIDS patient?

Survey reveals harmful attitudes among professionals