Allergy Division

- 2.5 years
- Start up package
  - Research technician salary
  - Budget for laboratory
    - Tissue culture hood, incubator, columns for protein separation, 2D gel electrophoresis, frequency generator for exposing cells, [oscilloscope, etc, from home]
- Awarded 2 of 12 grant applications
- 50% pay cut

"You'll be back in Emergency Medicine within two years. Some people have it in their blood."

Tony Harmon, MD
Emergency Physician
Washington Hospital Center

Allergy Division

- A preliminary study of the SCID-hu mouse as a model for atopy.
- In situ hematopoesis
  - Stem cells appear in the peripheral blood during the late phase of bronchospasm in the allergic asthmatic rabbit.
- Reactive upper airways dysfunction syndrome (RUDS): A form of irritant rhinitis induced by a chemical exposure

Allergy Division

- Allergy to Crops
  - Prevalence of skin test reactivity to corn smut and other basidiosphores in an agrarian district.
- Irritant sensitivity in a allergy clinic population
- Rhinolaryngoscopy findings in multiple chemical sensitivity syndrome
- Occupational allergy to gypsy moth larva exoskeleton among entomology laboratory workers.

Clinical Enigma: Sensitivity to Chemicals

- Multiple Chemical Sensitivity Syndrome
  - Chemicals of diverse classes
  - Symptoms involve multiple organ systems
  - Often acquired after acute chemical exposure
- Chemicals
  - Tobacco smoke
  - Furnace fumes
  - Perfumes, fragrances
  - Vehicle exhaust
  - Organic solvents
  - Irritant gases, SO2, Cl
  - pesticides
  - Etc.

Opposition to Chemical Sensitivity

- No possible mechanism [clinical enigma]
- No objective evidence of disease [clinical enigma]
- Strong opinion makers
  - Close ties to commercial interests
- Position Statements
  - AMA, AAAI, CA Medical Society
  - "Patients are crazy, doctors are quacks."
- Physicians lost their licenses
- Researchers stopped efforts to understand this disorder
- Unprecedented Attack on victims of an illness

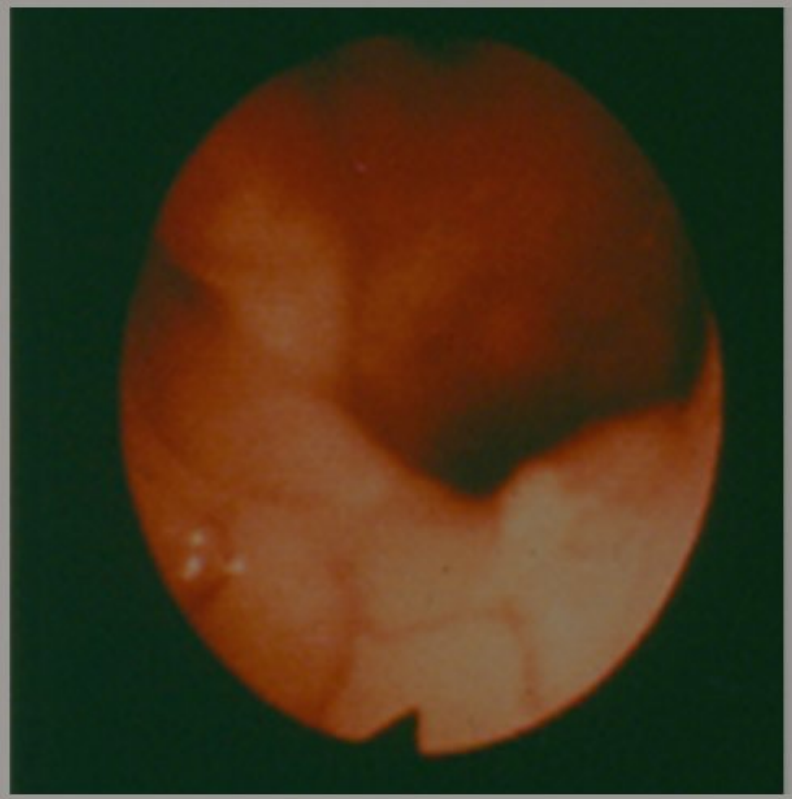
Rhinolaryngoscopic Examination of Patients with the Multiple Chemical Sensitivity Syndrome

WILLIAM JOEL MEGGS
Department of Emergency Medicine
Division of Clinical Toxicology
CRAWFORD HARALSON CLEVELAND, JR.
Department of Medicine
Section of Allergy/Immunology
School of Medicine
East Carolina University
Greenville, NC 27858-4354

No objective evidence of disease [clinical enigma]

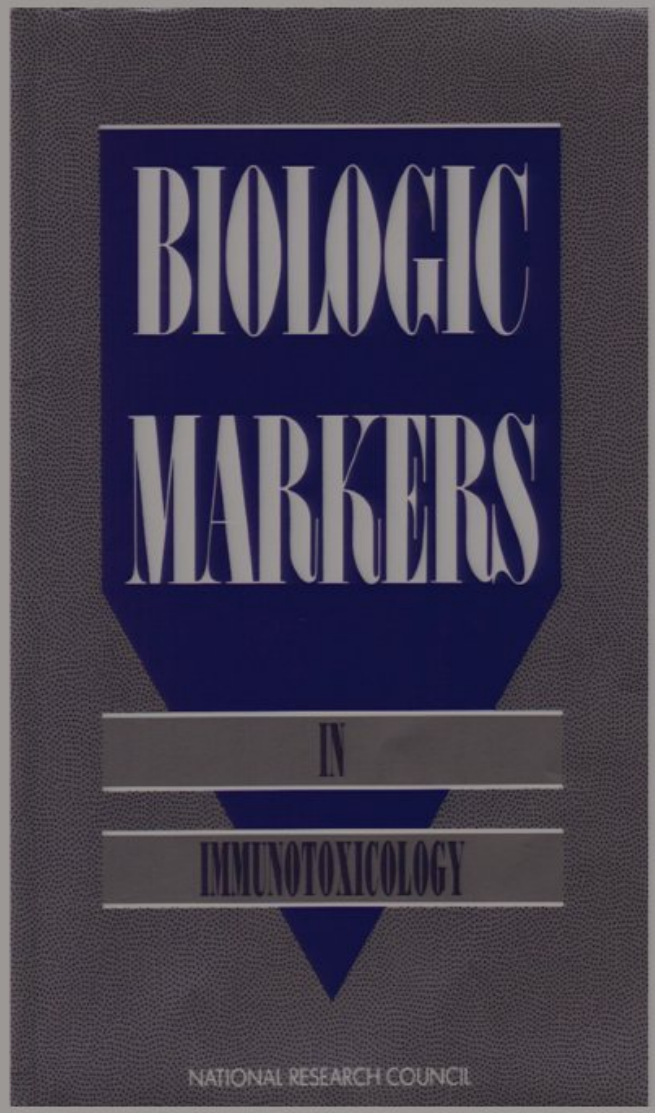
Biopsy with chronic inflammation, lymphocytic infiltrates

RUDS = Reactive Airways Dysfunction syndrome



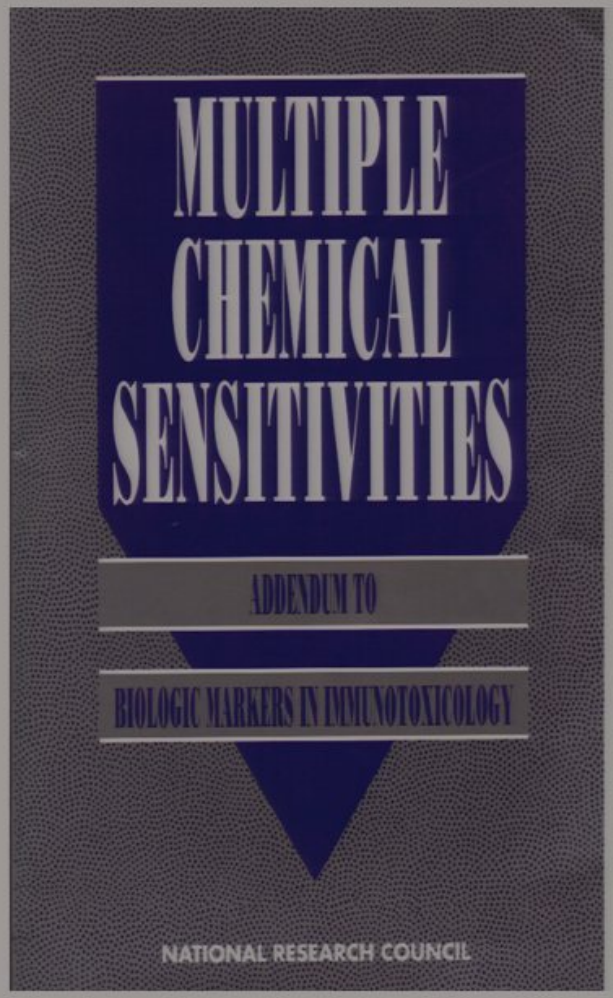
National Academy of Sciences

- Subcommittee on Immunotoxicology
- Co-authored book, *Biomarkers of Immunotoxicology*



National Research Council

- Broad based participation
- Consensus reached
- Research recommendations
- Secretary
- Topic shelved



Allergy Division Reorganization

Clinical Division

Meggs & Dr. A

Research Division

Dr. B & Dr. C

Allergy Division Reorganization

Clinical Division

Meggs & A $$$$

Research Division

B & C $$

"Your problem was that you made too much money in the clinic"

Penalize productivity.
Milk your cash cows for all you can.

Allergy Division Reorganization

Clinical Division

Meggs & A. $$$$$$$$

Research Division

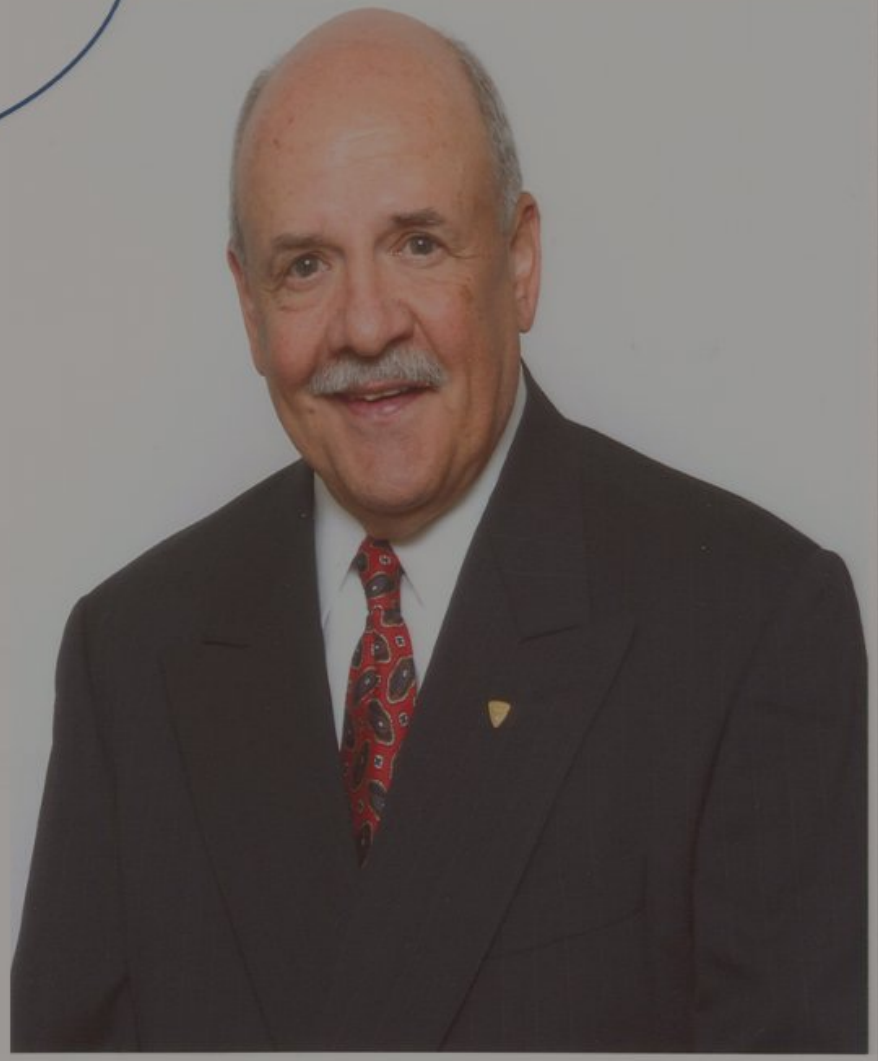
B & C 0

"Your problem was that you made too much money in the clinic"

Penalize productivity.

Milk your cash cows for all you can.

Come work for me

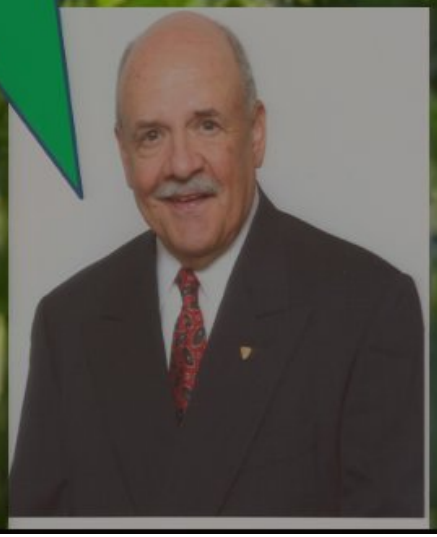


E.. Jackson Allison, III
Chair, Department of
Emergency Medicine
1980-1992

“But Jack, I already work for you.”

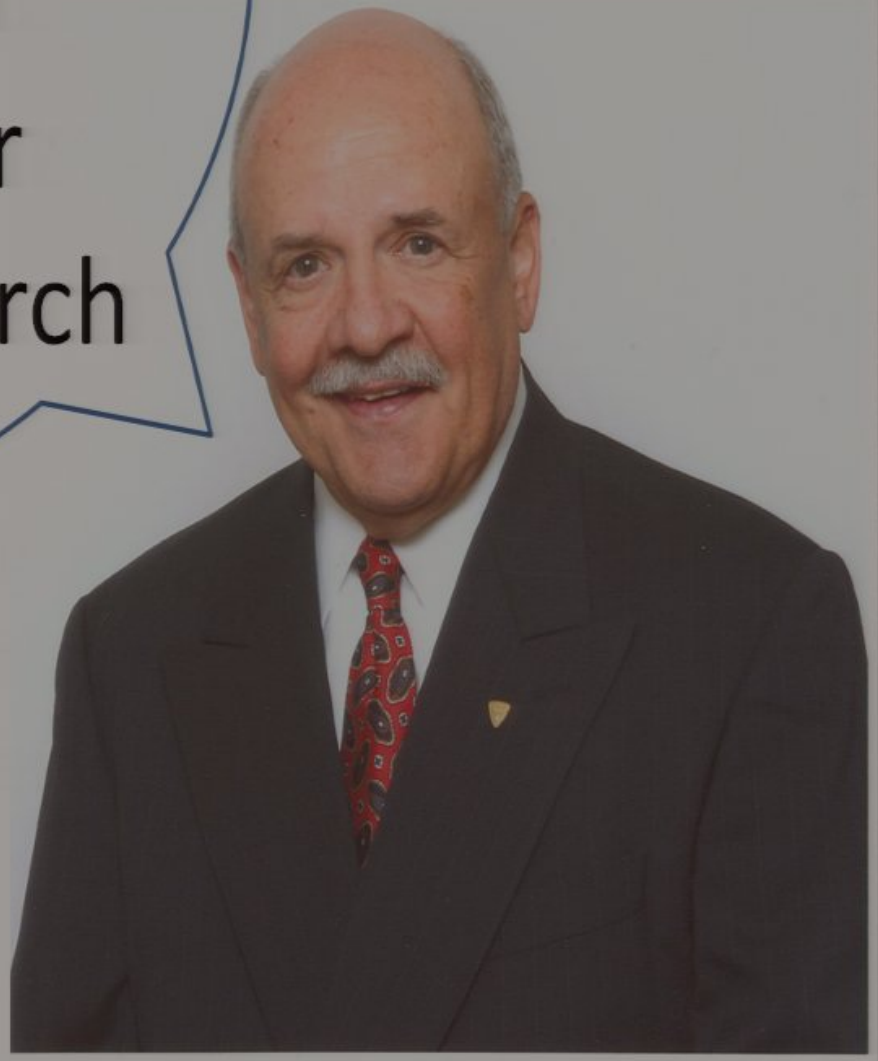
- ME: “Dr. Allison has offered me to work part-time in the ED for X$/hour.”
- Chair: “Good! Their practice plan can pay my practice plan.”
- ME: “Perhaps we can capture some of the money for lab supplies, tech salary, etc.”
- CHAIR [angrily]: “Their practice plan Will pay my practice plan and you will never see a cent of the money.”

I'm going to have me a:
Department of Emergency medicine
Emergency Medicine Residency
Air medicine service
EMS division
Research division
Etc,. etc,. etc.



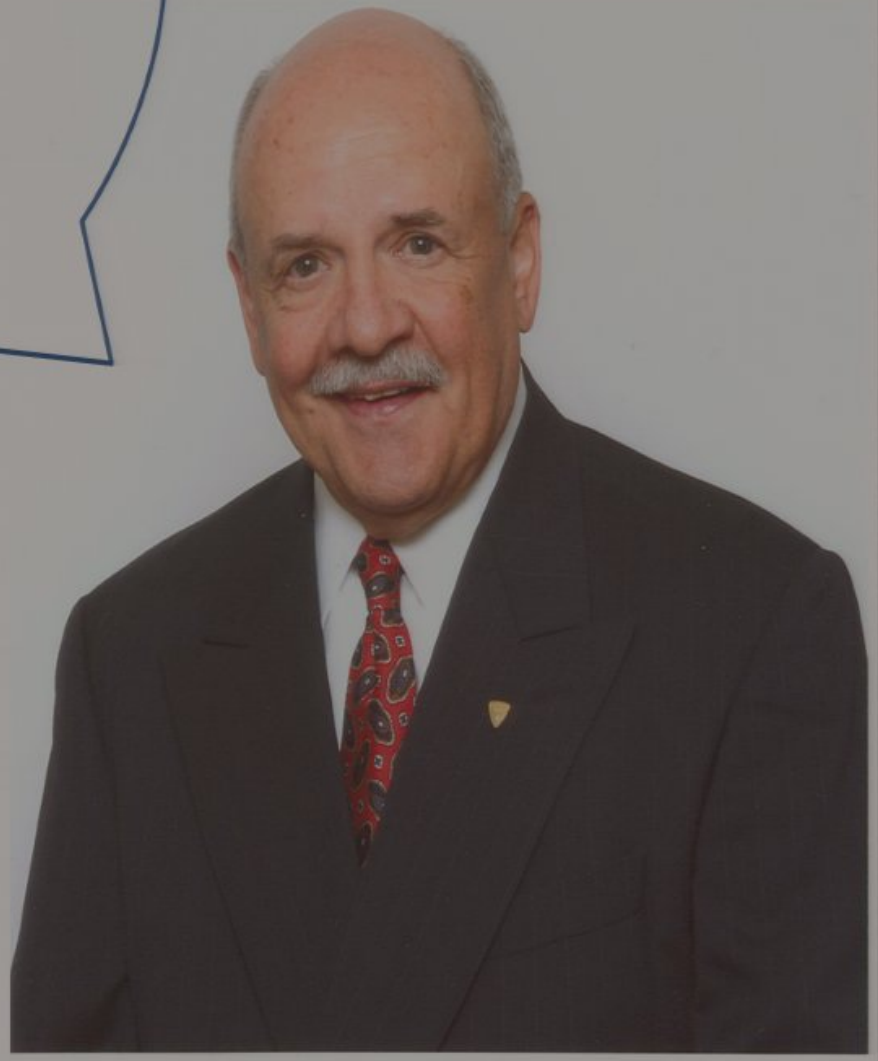
You can do anything you want for your clinical research

E.. Jackson Allison, III
Chair, Department of Emergency Medicine
1980-1992



Toxicology Fellowship

E.. Jackson Allison, III
Chair, Department of
Emergency Medicine
1980-1992



Medical Toxicology

- Approved as subspecialty, 1992, 2 yr fellowship
- Dr. Allison wanted some but none existed
  - Grow our own
- Faculty development
  - Two physicians, ½ & ½, 4 years
  - Leased apartment
  - Airfare and per diem
- Toxicology Boards, 1996

Prevalence and Nature of Allergy and Chemical Sensitivity in a General Population

WILLIAM J. MEGGS
KATHLEEN A. DUNN
Department of Emergency Medicine
RICHARD M. BLOCH
Department of Psychiatry
PEGGY E. GOODMAN
Department of Emergency Medicine
East Carolina University School of Medicine
Greenville, North Carolina

ANN L. DAVIDOFF
Department of Geriatric Medicine and Gerontology
Johns Hopkins University School of Medicine
Baltimore, Maryland

Table 1.—Frequencies of Allergy and Chemical Sensitivity in a General Population

	Allergic		Not allergic		Total	
Population	*n*	%	*n*	%	*n*	%
Chemically sensitive	172	16.9	163	16	336	33
Not chemically sensitive	186	18.3	498	48.9	685	67
Total	365	35	662	64		

Table 2.—Agents Cited as Producing Symptoms of Allergy and Chemical Sensitivity

Agent producing allergy	n*	%†	Agent producing chemical sensitivity	n*	%†
Pollens, general	177	49	Perfumes	108	32
Tree pollen	109	30	Pesticides	85	25
Dust	94	26	Cigarette smoke	83	25
Grass pollen	91	25	Fresh paint	57	17
Ragweed pollen	62	17	Gasoline	33	10
Cats	45	12	Automobile exhaust	31	9
Dogs	30	8	Cigar smoke	12	4
Foods	22	6	Other	112	34

*Number who reported symptoms from exposure to the agent.
†Percentage of individuals reporting allergy or chemical sensitivity that also reported symptoms from the agent.

Table 9.—Allergy and Chemical Sensitivity Reported by Those Who Also Reported Asthma

	Allergy		No allergy		Total	
Population	n	%	n	%	n	%
Chemical sensitivity	19	51	8	22	27	73
No chemical sensitivity	5	14	5	14	10	27
Total	24	65	13	35	37	100

Prevalence and Nature of Allergy and Chemical Sensitivity in a General Population

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Total	365	35	662	64		

Epidemiology of Chemical Sensitivity

State	Prevalence	Seriously affected
NC	30%	4%
CA	15.9%	7%
NM	15%	
GA	12.6%	4%
USA	11.3%	2.5%
Sweden	30%	

There is no possible mechanism to explain chemical sensitivity

Research Article

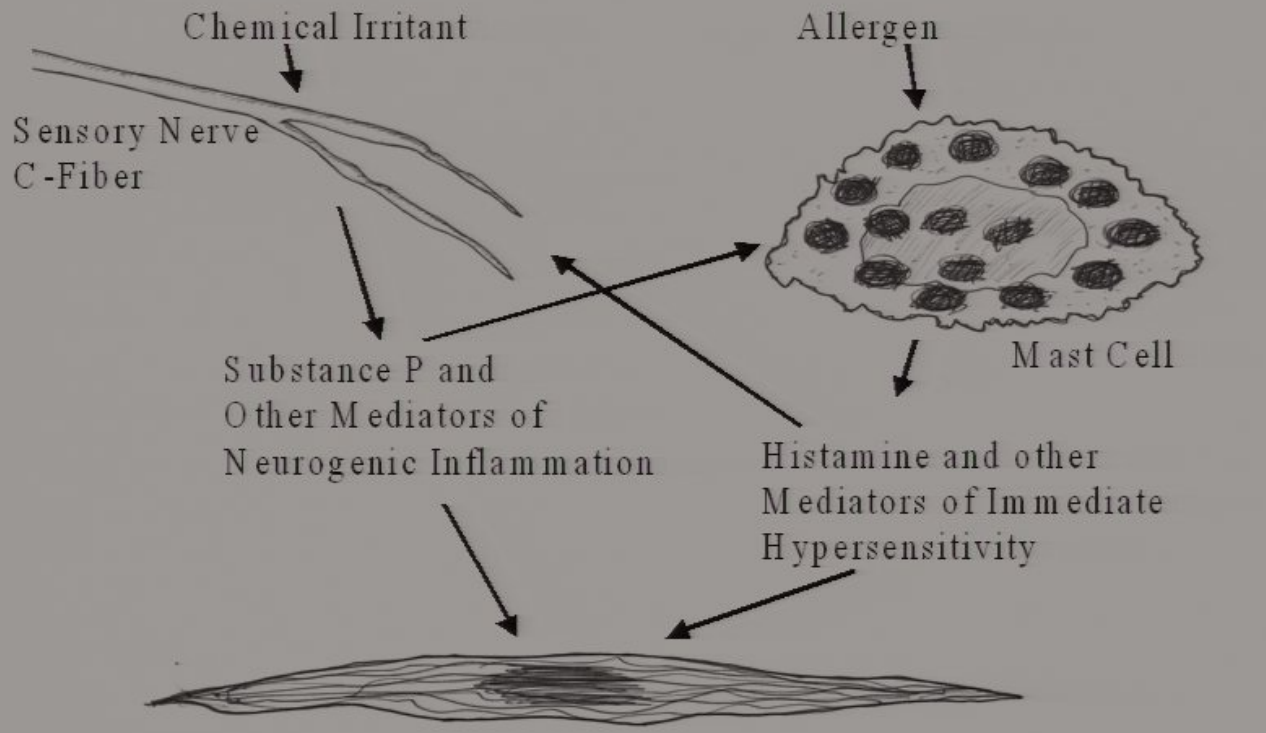
Neurogenic inflammation and sensitivity to environmental chemicals.

W J Meggs
Department of Emergency Medicine, East Carolina University School of Medicine, Greenville, NC 27858

Environ Health Perspect. 1993 August; 101(3): 234–238.

Crossover Network

- Nerve fibers have histamine receptors
- (some) Mast cells have substance P receptors



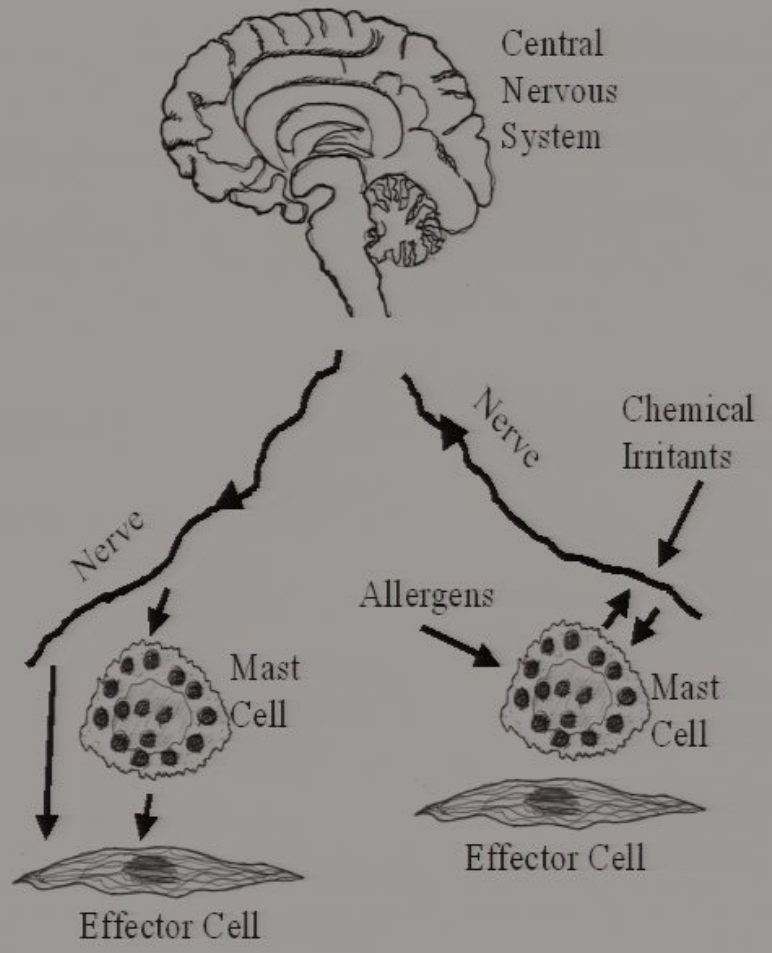
Neurogenic Switching: A Hypothesis for a Mechanism for Shifting the Site of Inflammation in Allergy and Chemical Sensitivity

William J. Meggs

Department of Emergency Medicine, East Carolina University School of Medicine, Greenville, NC 27858 USA and New York City Poison Center, New York, NY 10016 USA

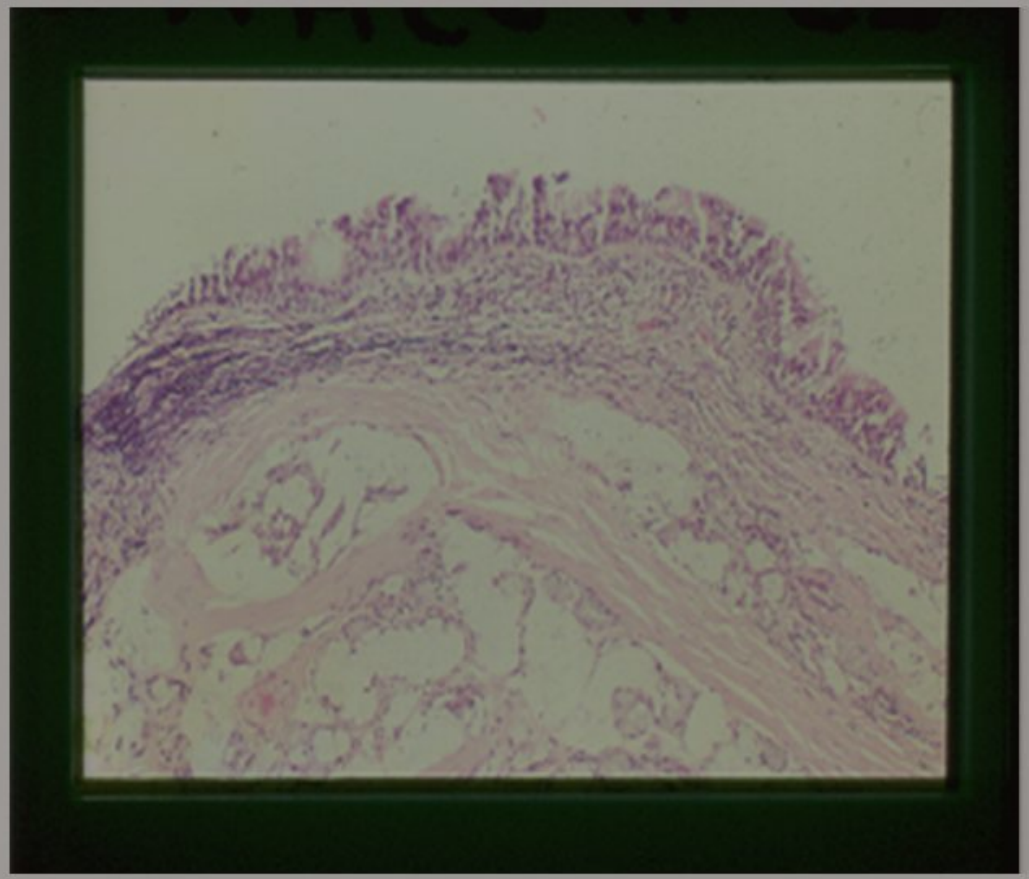
Neurogenic Switching

- The site of inflammation can be switched from the site of stimulation
- Occurs in both allergic and irritant airway inflammation
- May play a role in many disease processes



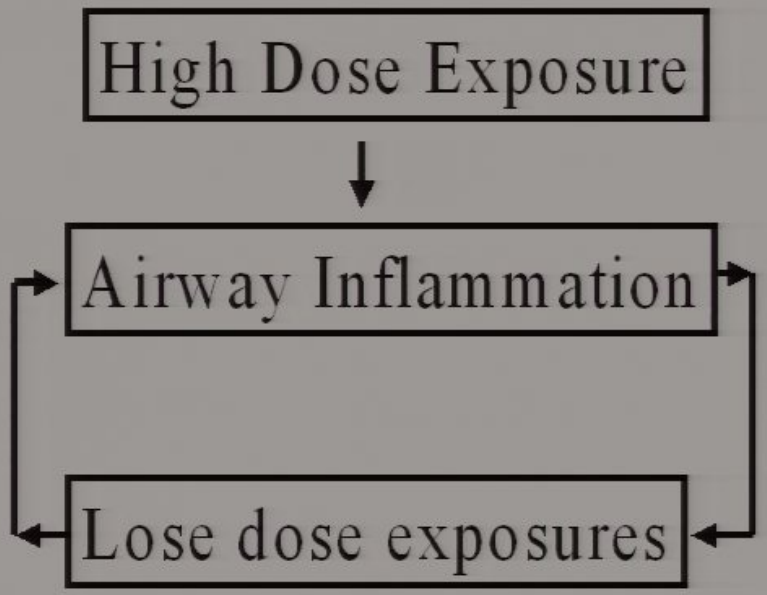
Irritant Rhinosinusitis: Pathological Features

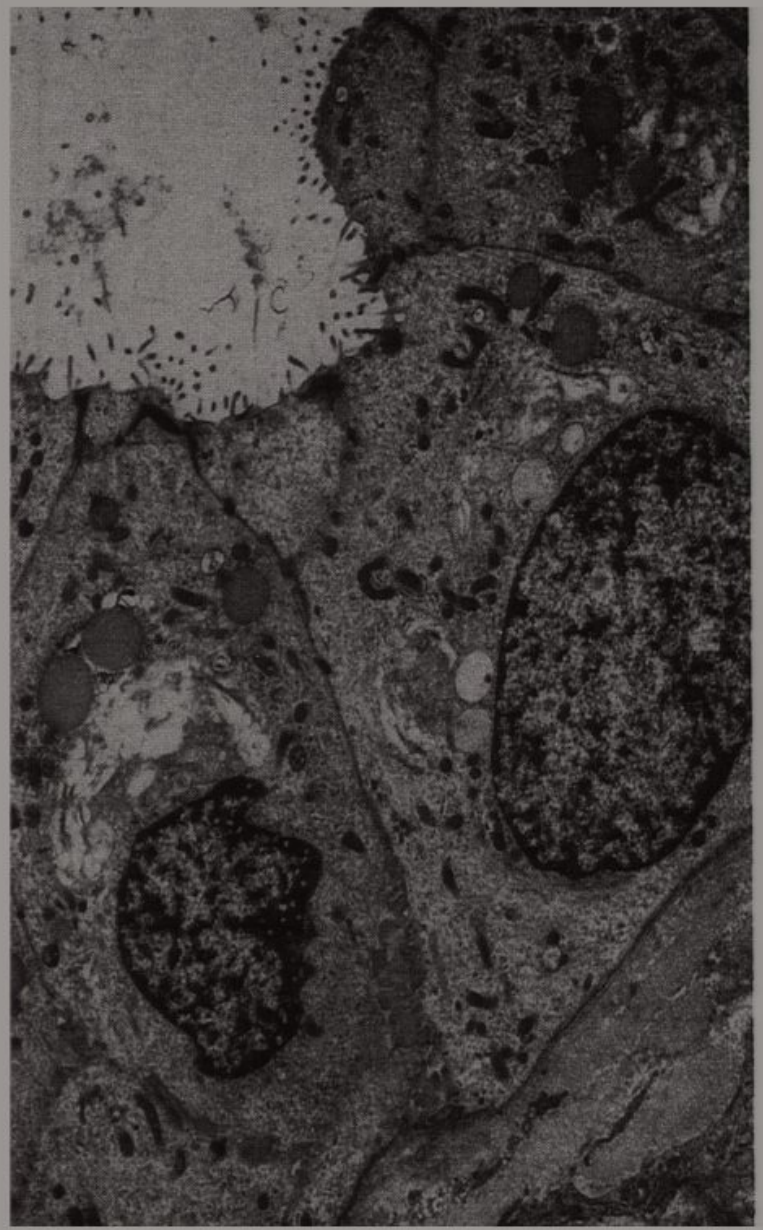
- Chronic inflammation with lymphocytic infiltrates
- Glandular hyperplasia
- Basement membrane thickening
- Nerve fiber proliferation
- Desquamation of the respiratory epithelium
- Defects in tight junctions

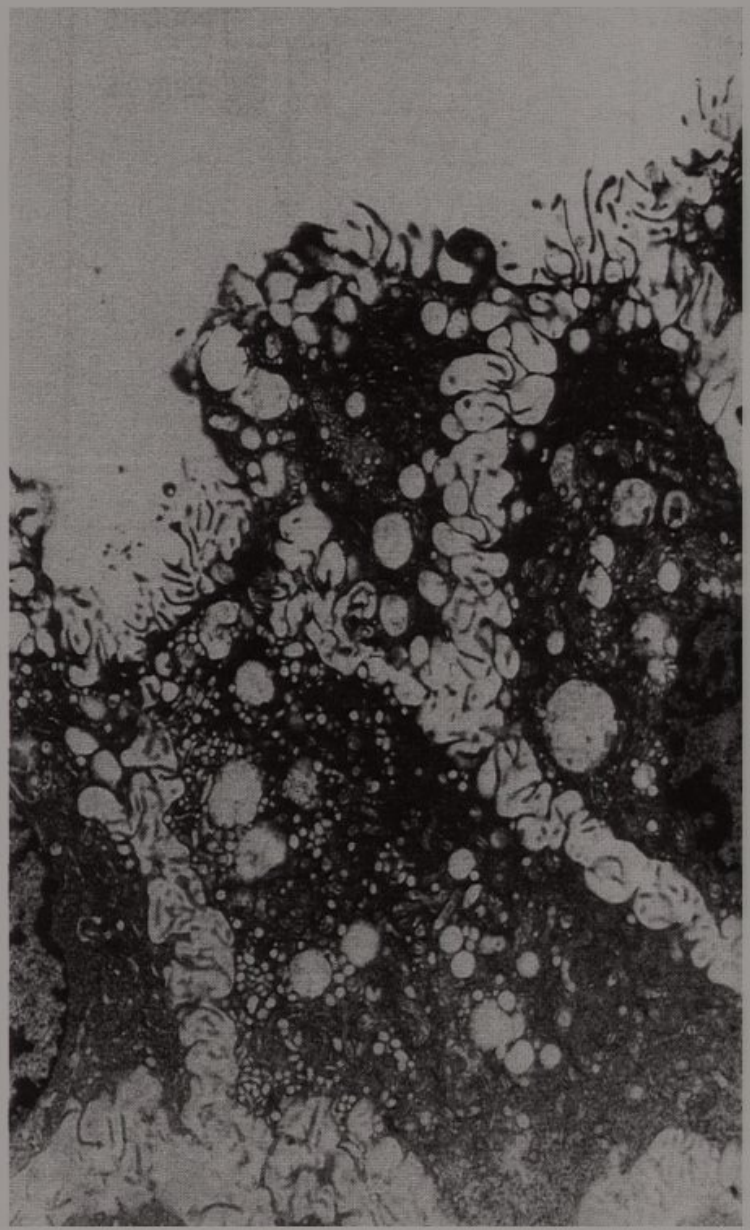


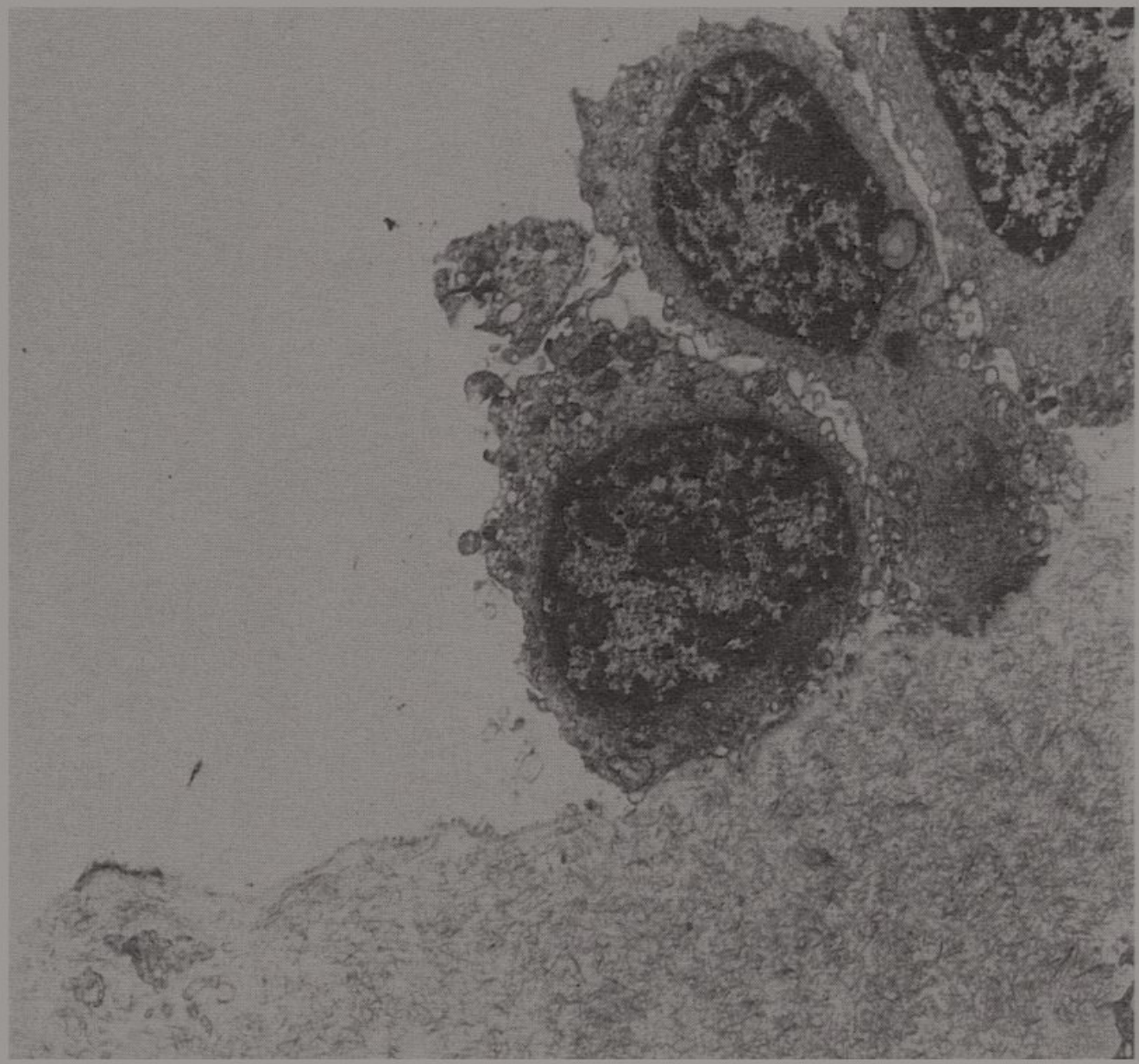
Induction Mechanism

- Positive feed back loop
- Induction exposure produces neurogenic inflammation



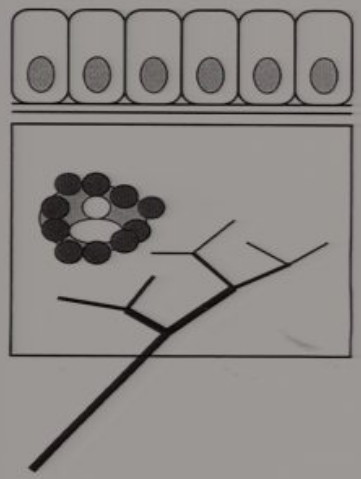






End Organ Sensitization

A



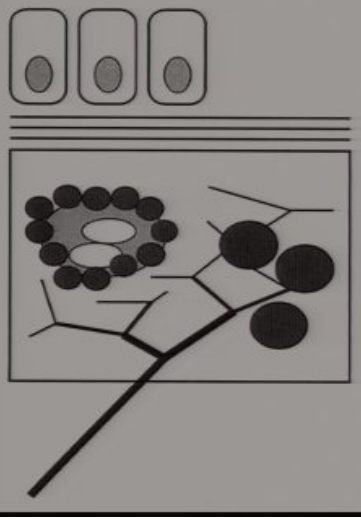
Respiratory epithelium

Basement membrane

Glands

Sensory nerve fibers

B

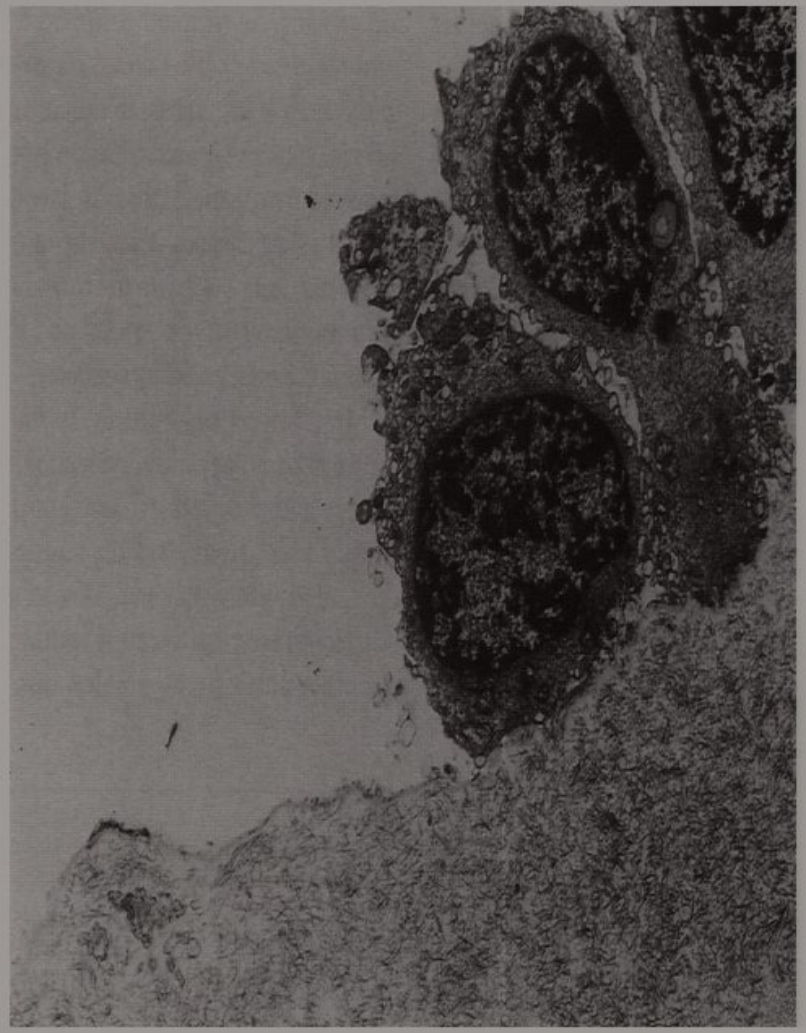


Respiratory epithelium: tight junction defects and desquamation

Basement membrane: thickening

Glands: hyperplasia lymphocytic infiltrates

Sensory nerve fibers: proliferation

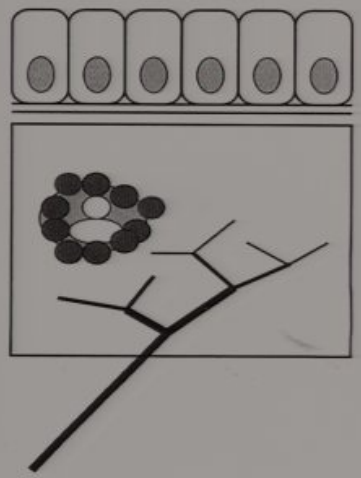


Clinic Disaster

- Leased space from Department of Medicine
- Pay hourly overhead
- Very successful
- Go somewhere else.

End Organ Sensitization

A



Respiratory epithelium

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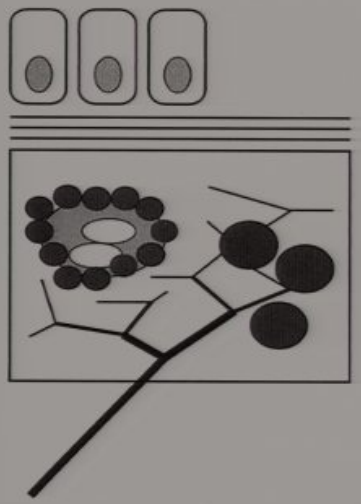

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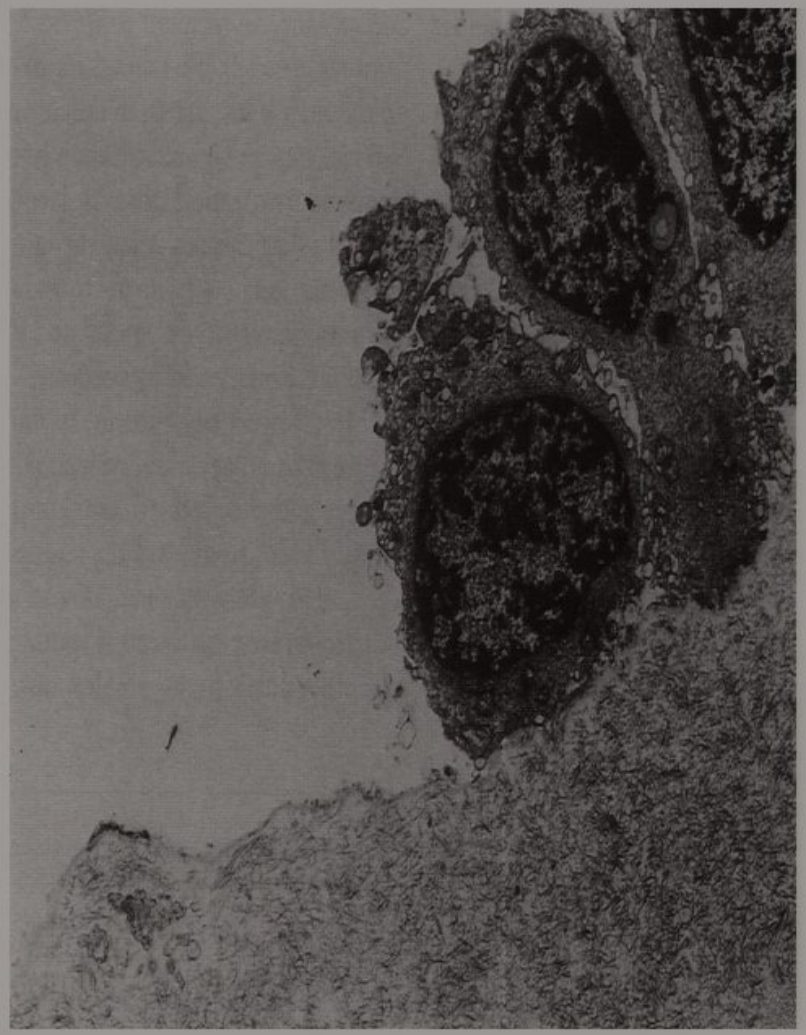

Clinic Disaster

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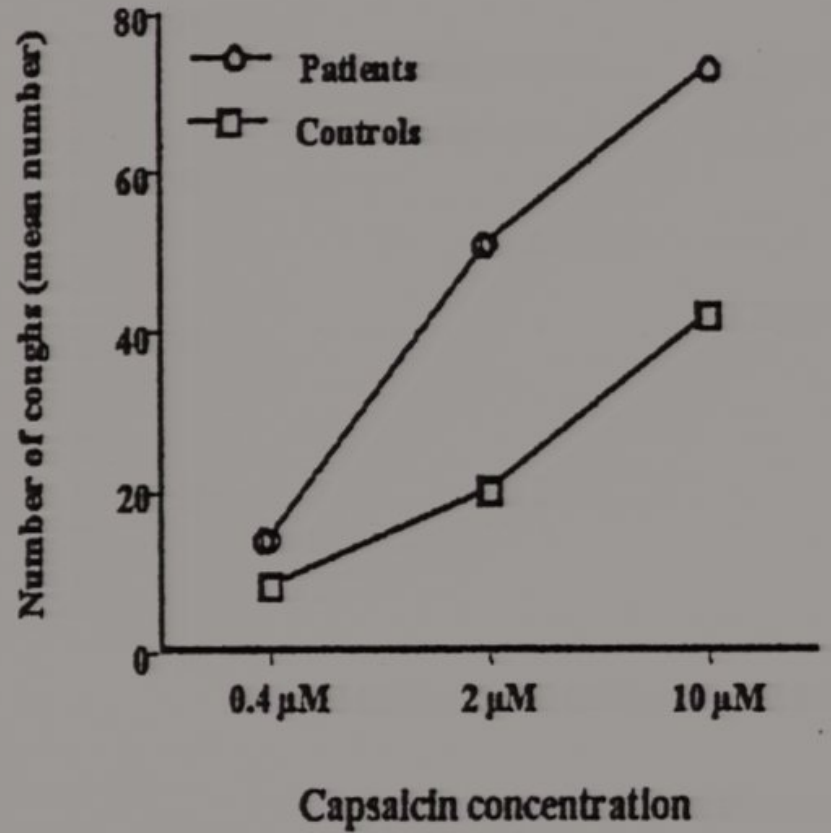
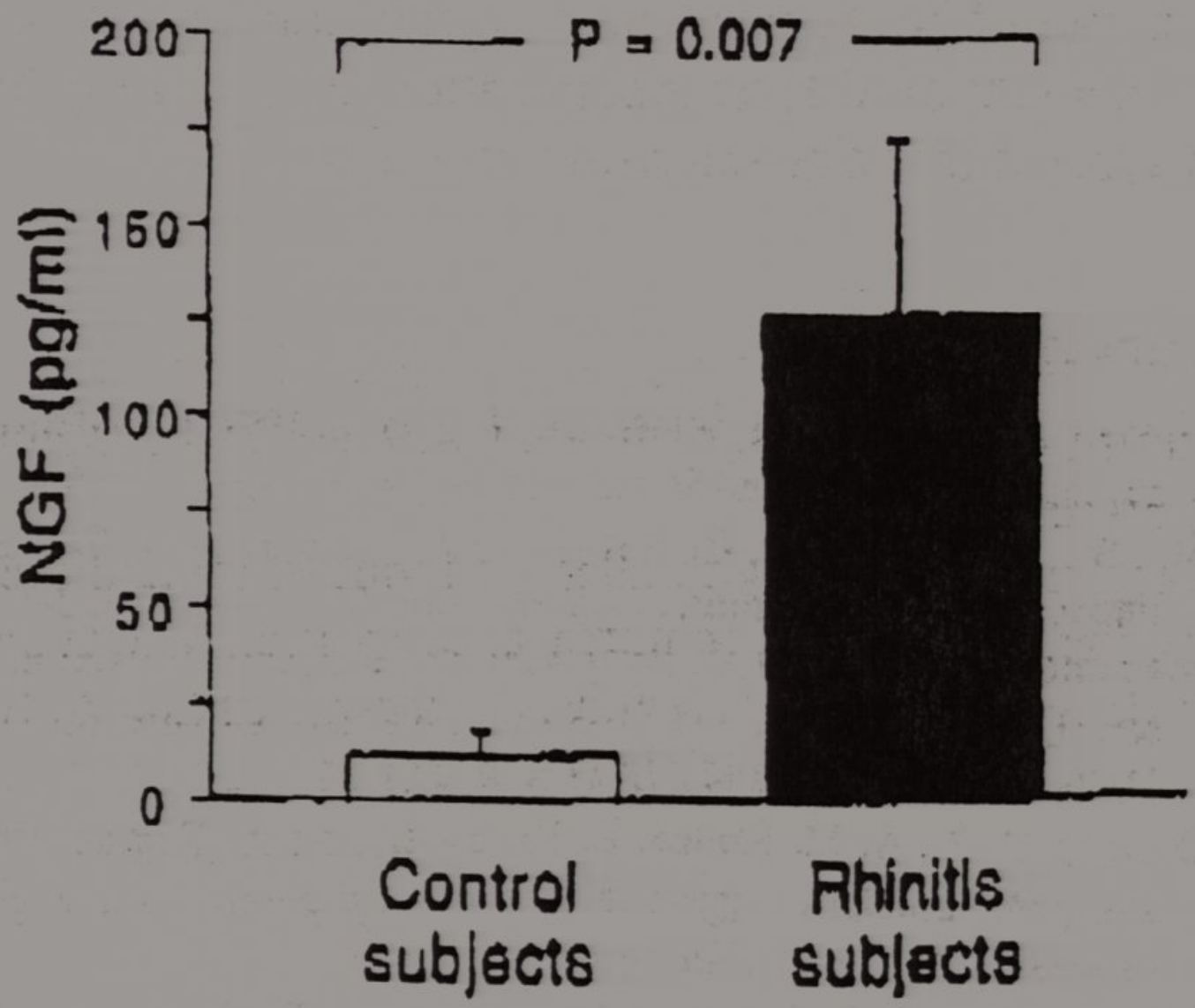
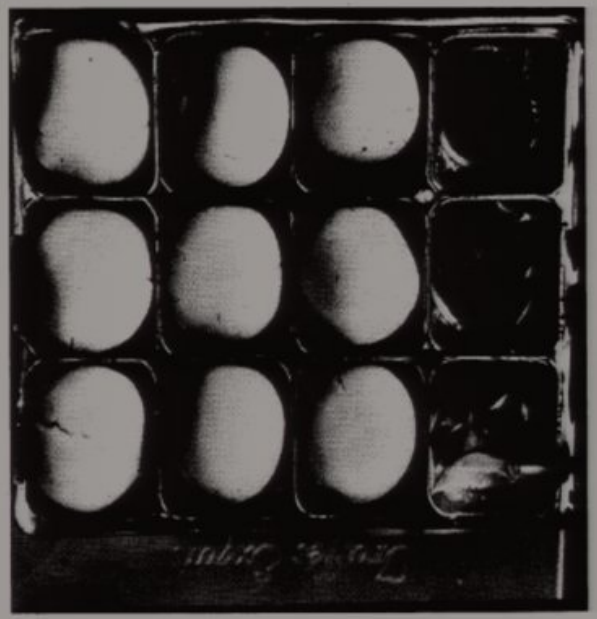
Millqvist Capsaicin inhalation cough test in patients with "Sensory Hyper-reactivity"





Sanico et al.
Am J Respir Crit Care Med. 2000 May;161(5):1631-5.

Case of the Poisoned Candy



Meggs WJ, Cahill-Morasco R, Shih RD, Goldfrank LR, and Hoffman RS. Effects of Prussian blue and N-acetycysteine on thallium toxicity in mice. *J Toxicol Clin Toxicol* 1997;35:163-166.

Verified safety & efficacy of Prussian Blue in controlled study in mice.

The Case of the Poisoned Tea

MMWR

CDC

March 24, 1995 / 44(11);193-195

Anticholinergic Poisoning Associated with an Herbal Tea New York City, 1994

Reported by: WJ Meggs, MD, R Weisman, PharmD, RS Hoffman, MD et al.

Lead Poisoning from Bullets

Meggs WJ, Gerr F, Aly MH, Kierena T, Roberts DL, Shih R, Kim HC, and Hoffman RS. The treatment of lead poisoning from gunshot wounds with succimer (DMSA). *J Toxicol Clin Toxicol* 1994;32:377-385.

Case of the Poisoned Heroin

MMWR

Scopolamine Poisoning among Heroin Users -- New York City, Newark, Philadelphia, and Baltimore, 1995 and 1996

1994 Woodstock Music Festival

- Drugs of abuse survey
- Laboratory Confirmation of Drug Use

Epidemiology of Substance Abuse at the 1994 Woodstock Music Festival

- Average age was 25 years (range 12 to 55 years)
- 54% male, 46% female
- 98% Caucasian
- 54% reported using alcohol
- 50% reported tobacco

Epidemiology of Substance Abuse at the 1994 Woodstock Music Festival

- 65% reported using at least one illicit drug at festival
- 62% reported using marijuana
- 19% reported using LSD
- 3.3% reported using Cocaine
- 2.7% reported using amphetamines
- 2.2% reported using Heroin
- 1% reported using PCP

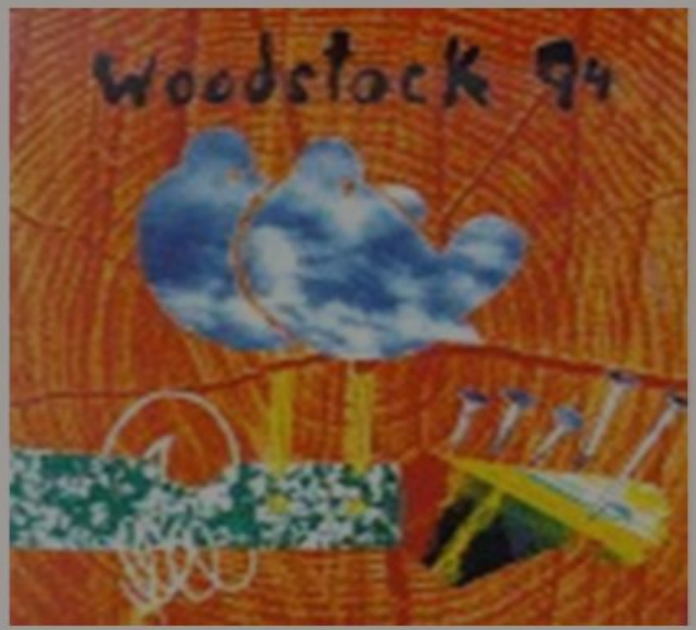
Source: WJ Meggs et al, Clin Tox 1995;33:503.

Laboratory Confirmation of Substance Abuse at the 1994 Woodstock Music Festival

- Subjects
  - Attendees at festival
  - Need for critical treatment or evaluation
  - Medical toxicology evaluation
  - Obtainable urine specimen

Laboratory Confirmation of Substance Abuse at the 1994 Woodstock Music Festival

- 39% of samples contained ethanol
- 84% of samples contained another substance
- 74% contained THC
- 26% contained LSD
- 13% contained PCP
- 13% contained opioids



Source: DeRoos et al. Clin Tox 1995;33:502.

CLINICAL PRACTICE

Trends in Emergency Department Utilization, 1988–1997

WILLIAM J. MEGGS, MD, PHD, THOMAS CZAPLIJSKI, RN, MS, NICHOLAS BENSON, MD

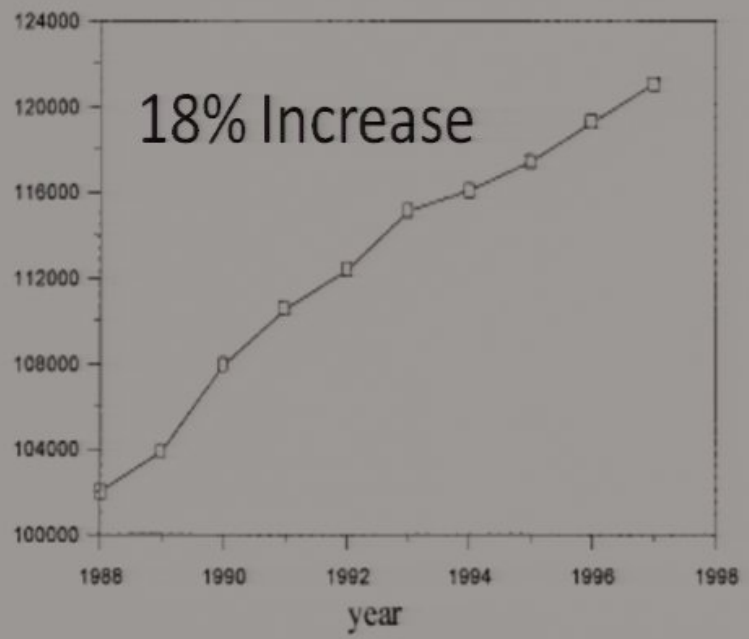


Figure 1. Population of Pitt County, North Carolina, from 1988 to 1997.[12–14]

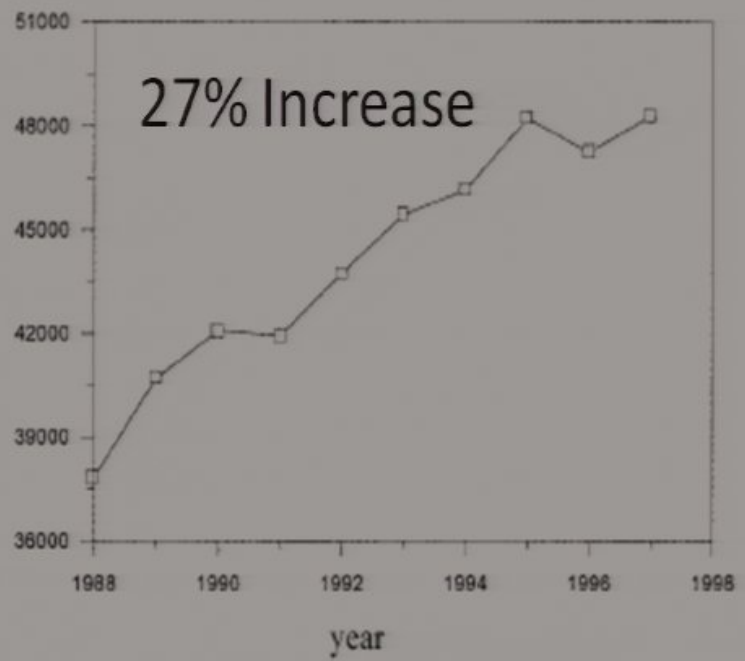


Figure 3. The number of ED visits at the study hospital from 1988 through 1997.

144, 000
74% increase

Figure 3. The number of ED visits at the study hospital from 1988 through 1997.

168,421
38% increase

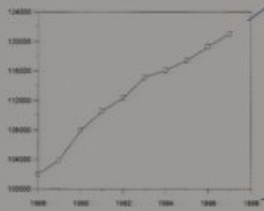


Figure 1. Population of Pitt County, North Carolina, from 1988 to 1997.[9–14]

2011

Common Wisdom:

Emergency Department visits are increasing because

People have no where else to go.

Common Wisdom:

Emergency Department visits are increasing because

People have no where else to go.

Scientific Fact:

Growth is coming in higher triage categories.

That is, Americans are older & sicker.

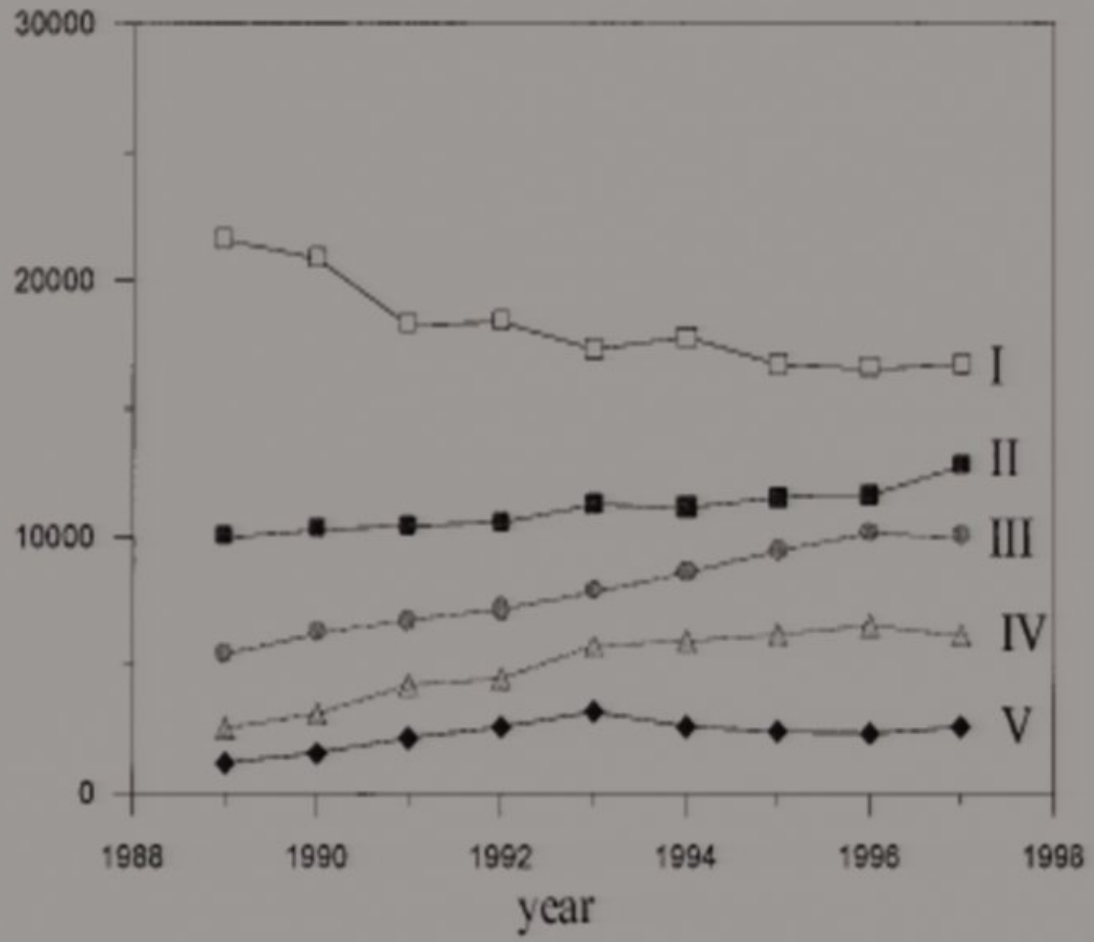
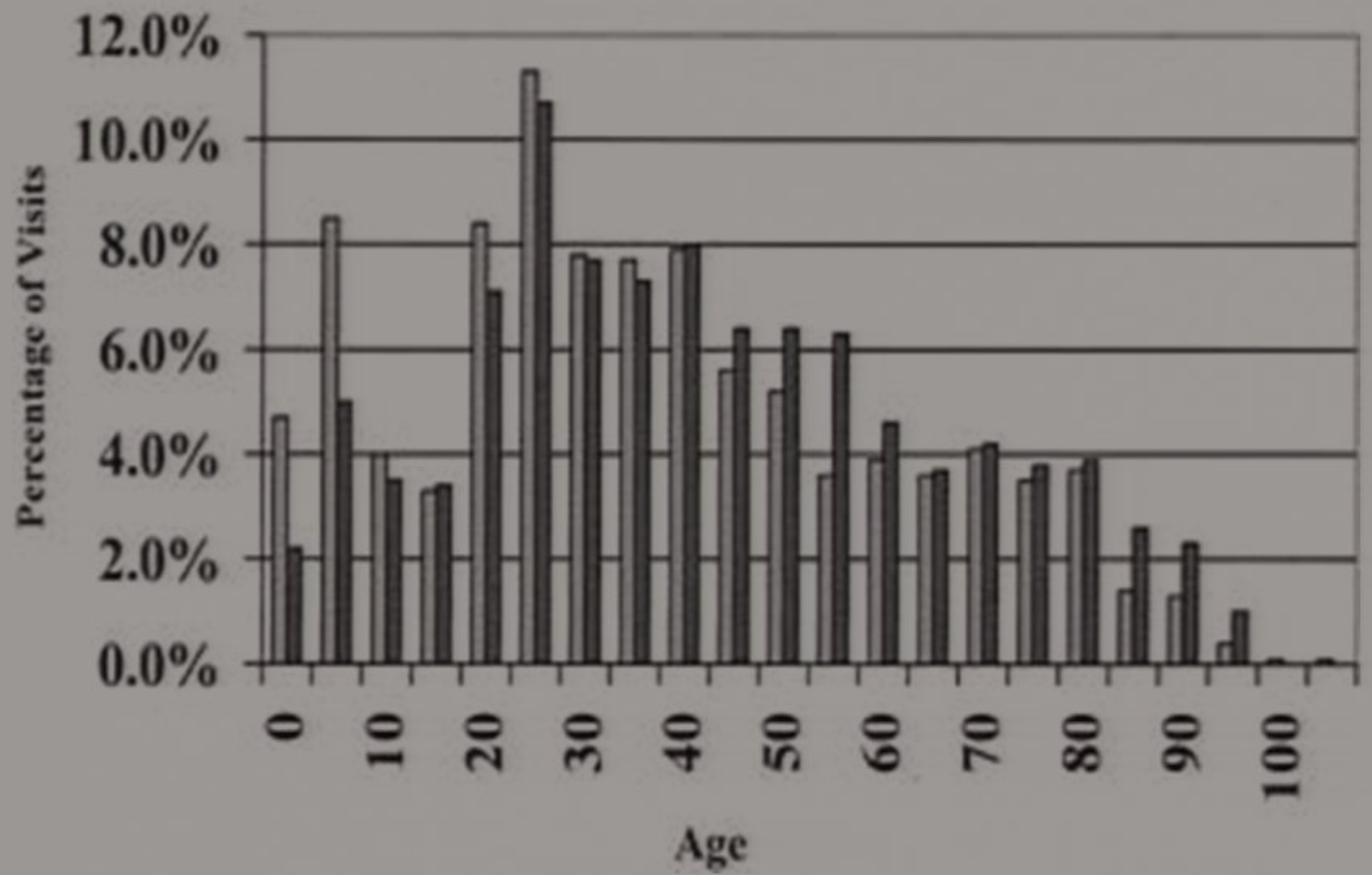


Figure 5. Number of visits for each of five triage categories, 1988 to 1997. Triage category I is the least urgent, while category V is the most urgent.

Follow Up Study: Enigma = Why???

The American Journal of Emergency Medicine **20***(7):583-7* (2002)
ED utilization: the effect of changing demographics from 1992 to 2000.
Timothy Reeder, Elizabeth Locascio, Jody Tucker, Thomas Czaplijski, Nicholas Benson, William Meggs

retrospective chart review
2-week period in both 1992 & 2000
rural, tertiary medical center.
ED visits increased 28.6%
county population increased 16.1%) ($P < 0.005$).
Average age: 35.2 yrs to 40.1 yrs (95% CI, 3.34 to 6.45).
Patients over 80 years increased by 83%,
Patients over 90 years 138%.
Admission rate: 21.9% to 25.6% ($P < 0.005$).
Medicare patients: 17.9% to 23.6% ($P < 0.005$).
Increased age, increased acuity, limited access to primary care contributed to increased ED demand in this study.



Average age: 35.2 yrs to 40.1 yrs (95% CI, 3.34 to 6.45).

Patients over 80 years increased by 83%,

Patients over 90 years 138%.

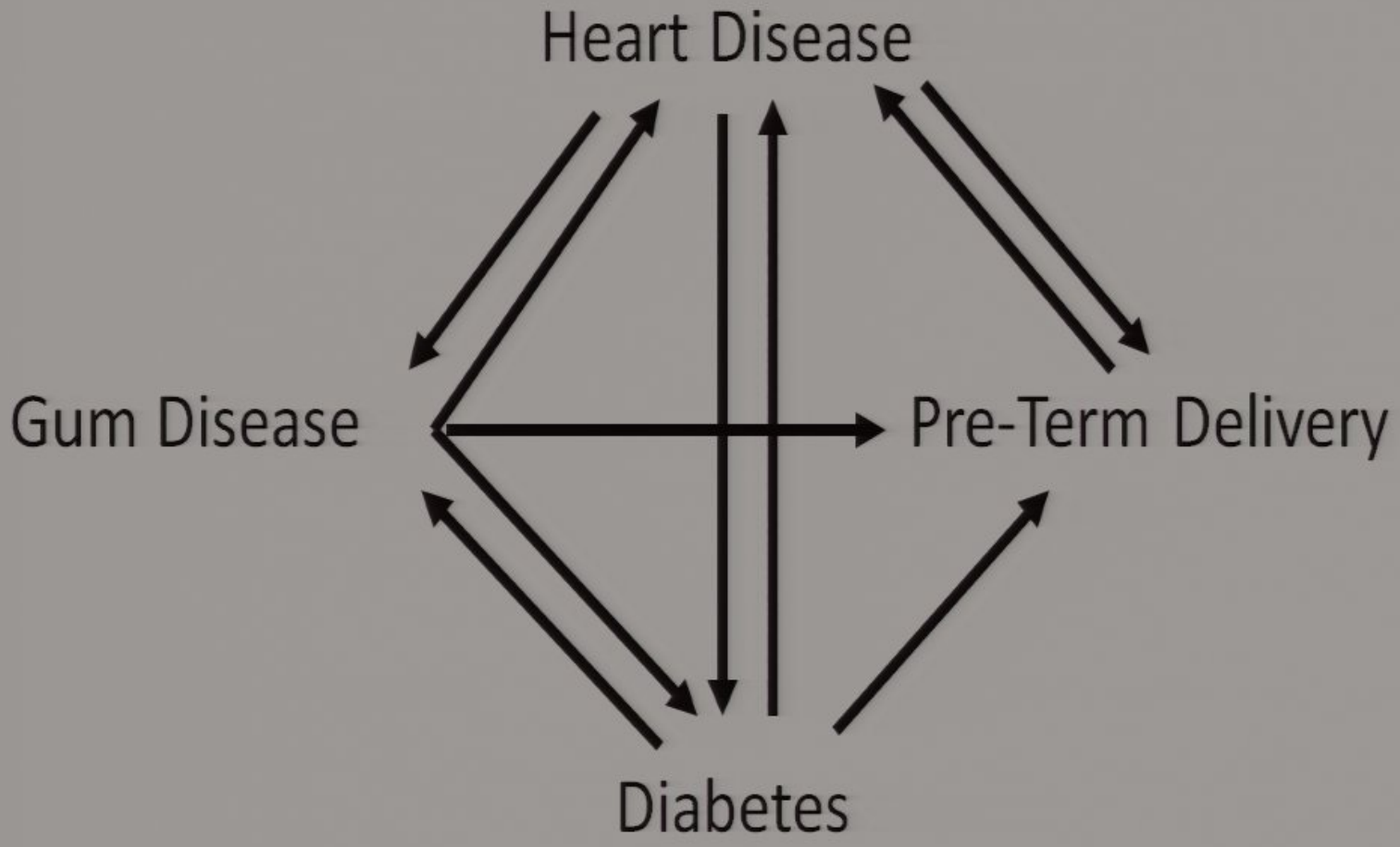
Change in Disease Prevalence Between 1992 and 2000

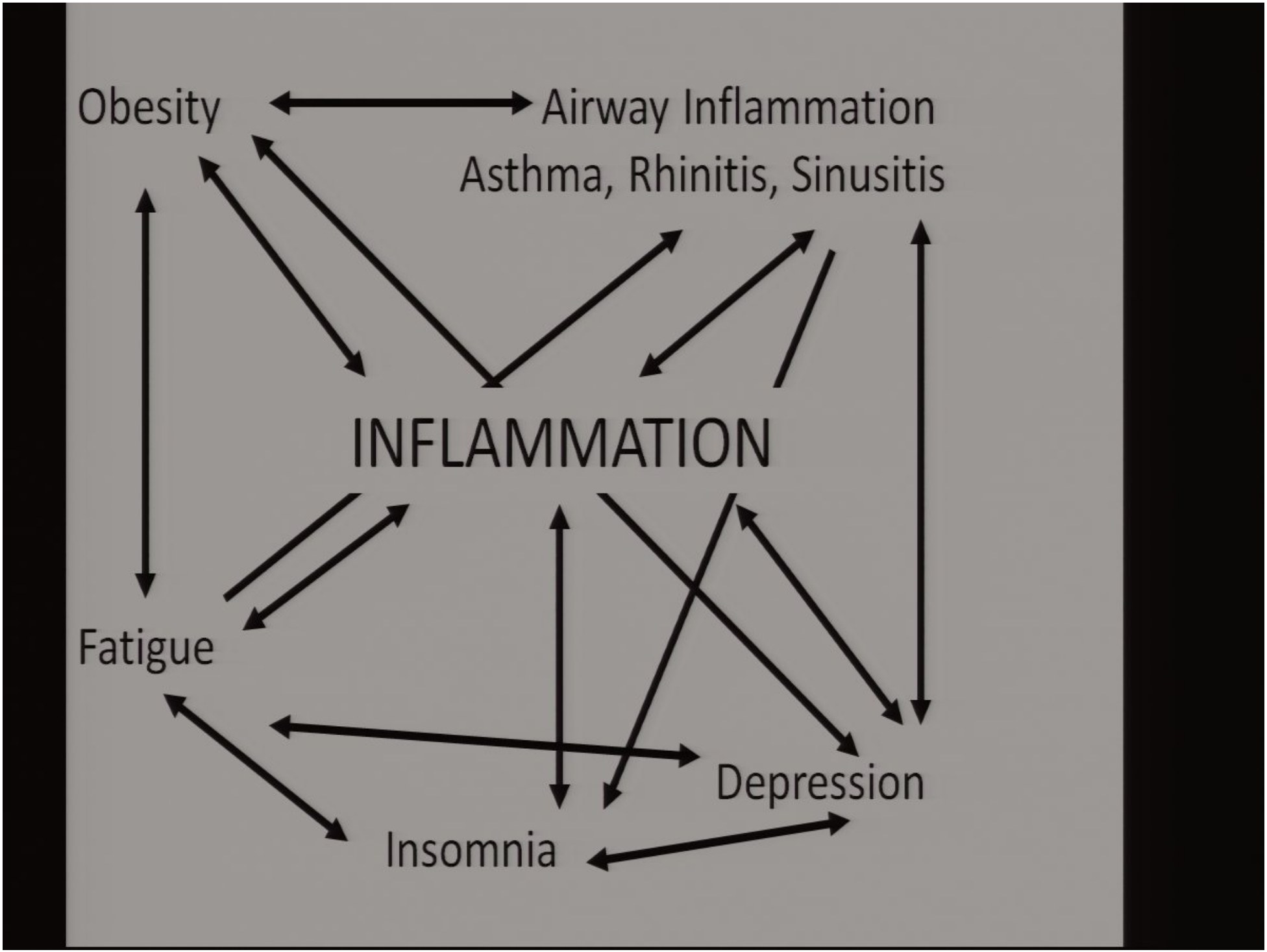
Past History	1992 (%)	2000 (%)	Chi square
Diabetes	7.2	11.5	.00002*
Reactive airway disease	4.6	6.2	.044*
Coronary artery disease	10.8	8.6	.030*
Hypertension	11.2	23.1	<.000001*
Cancer	2.5	3.8	.044*
HIV	0.5	0.5	.824
Mental illness	3.3	6.1	.0002*
COPD	2.3	2.2	.992
End-stage renal disease	3.0	2.8	.801
Strokes	2.3	4.2	.003*
Cong. heart failure	0.9	2.6	<.000001*

Los Angeles county health official warns medical center overcrowding is worsening.

The Los Angeles Times (3/22/2011, Lin) "LA Now" blog reported that Dr. Mitchell H. Katz, "The new chief of Los Angeles County's public hospital system said Tuesday that overcrowding is worsening at County-USC and Harbor-UCLA medical centers -- a situation he is concerned will continue to deteriorate even after the federal healthcare reform law is implemented in 2014." Dr. Katz' statement came as "new data shows that overcrowding at County-USC, the county's flagship public hospital northeast of downtown, is worsening again after a brief improvement late last year." Last month, the wait was "12 hours and 11 minutes, up from 10 hours and 34 minutes in December."

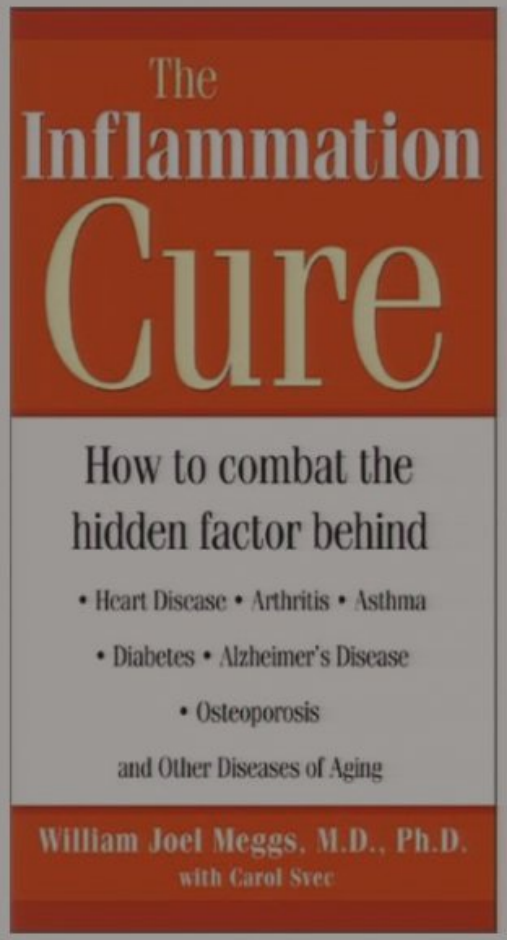
The Inflammation Connection




Obesity
Airway Inflammation
Asthma, Rhinitis, Sinusitis
INFLAMMATION
Fatigue
Depression
Insomnia

Inflam-Aging
Planned obsolescence
Inflammation is biological
mechanism to degrade
our bodies as we age.

The Inflammation Connection



- Diet & Nutrition
- Home & Workplace
- Life-style
- Mind-body
- Drugs: When all else fails

Favorably reviewed in New York Times & Library Journal

Hit top 100 best seller lists

The Inflammation Cure Cookbook

By

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ECU Nutrition/Dietetics Professor

William Joel Meggs, MD, PHD
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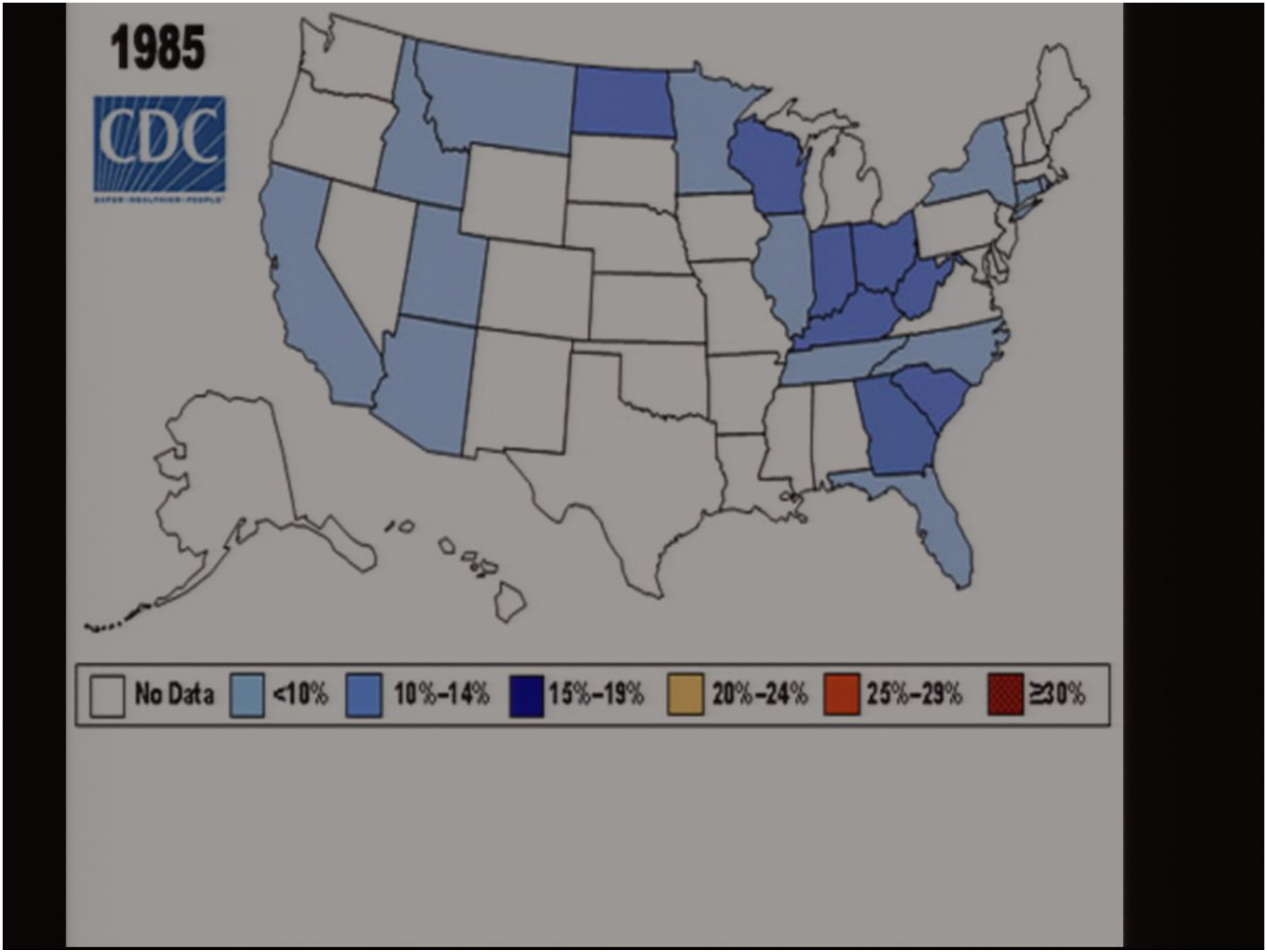
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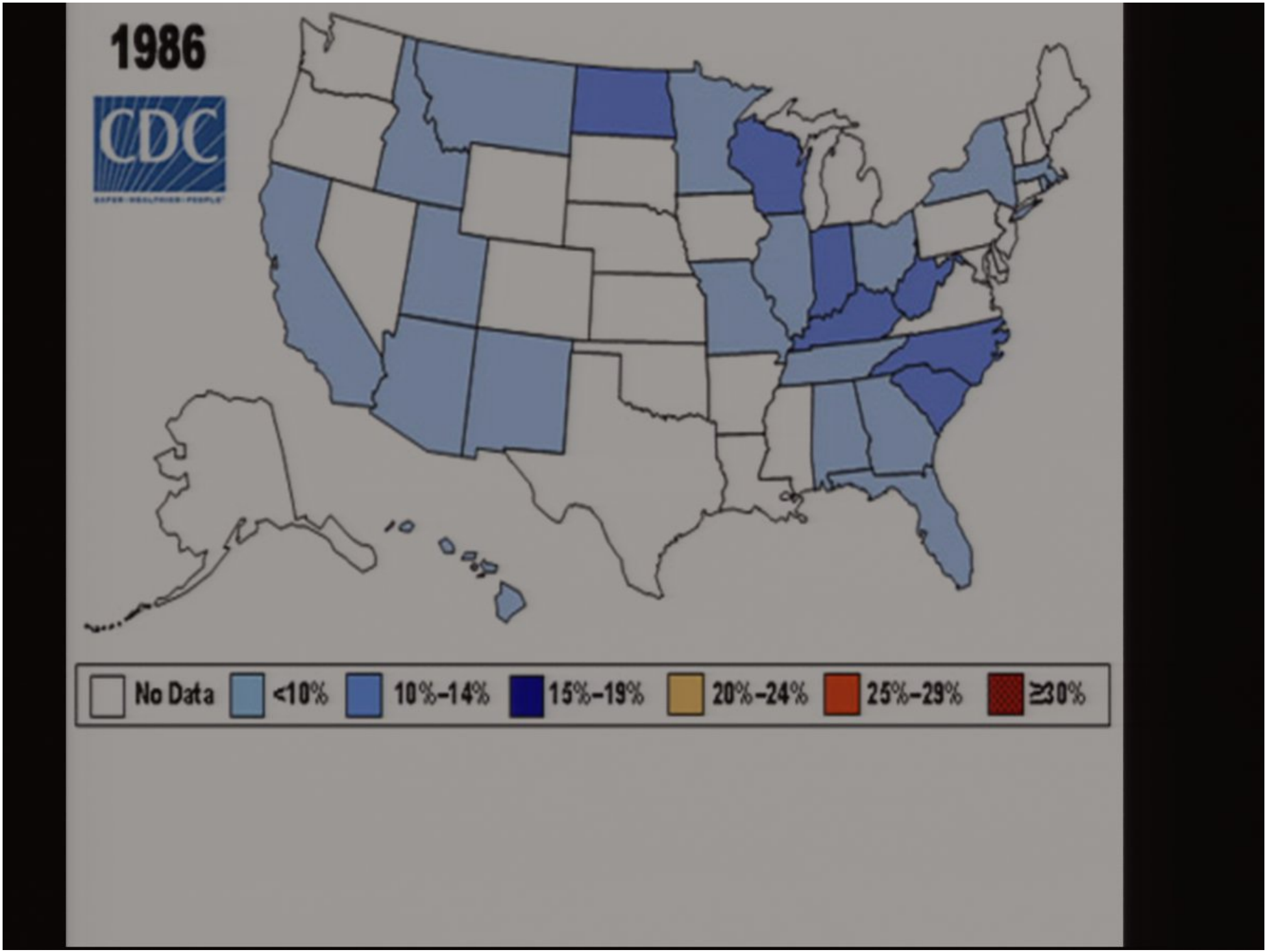
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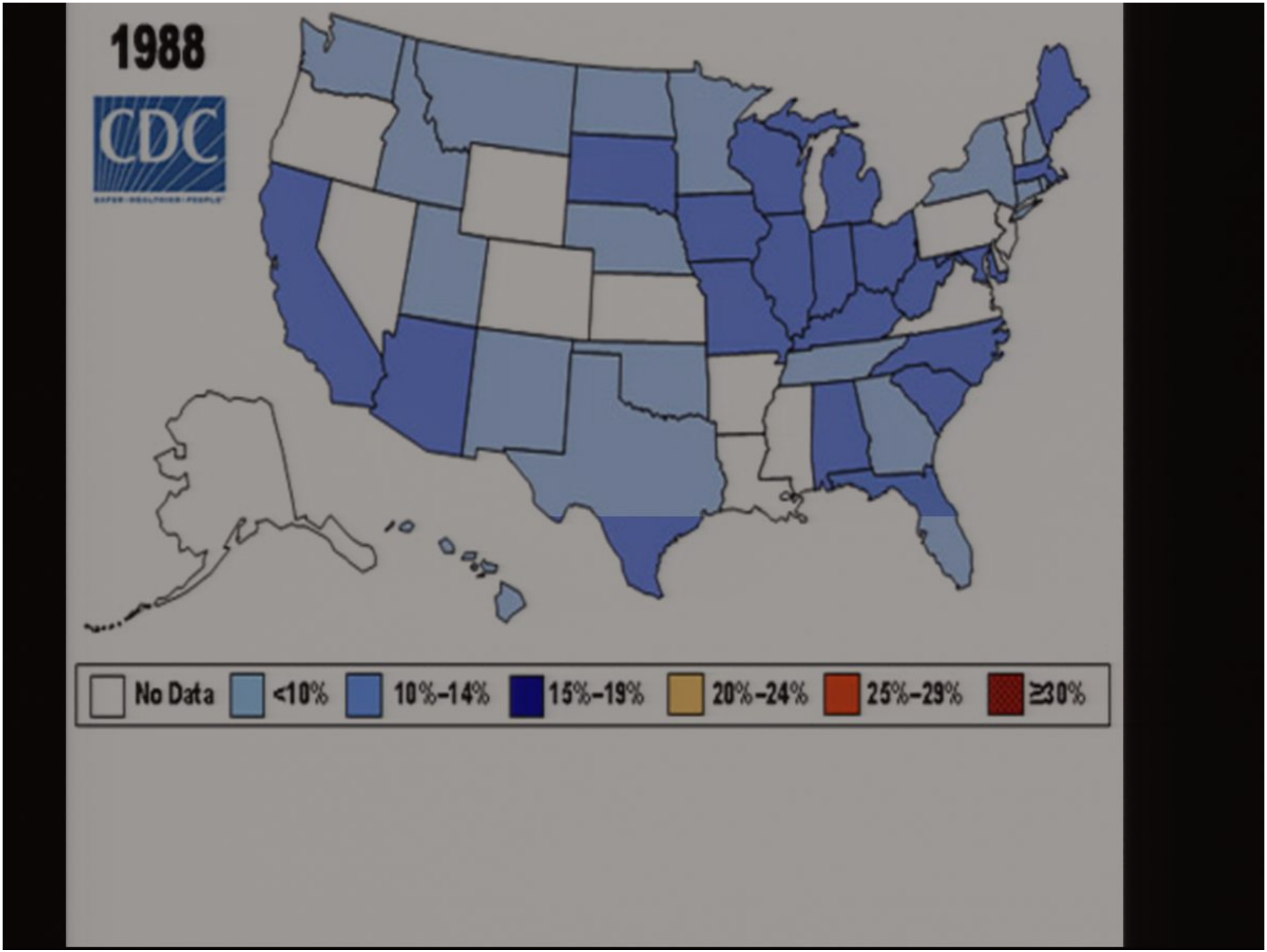
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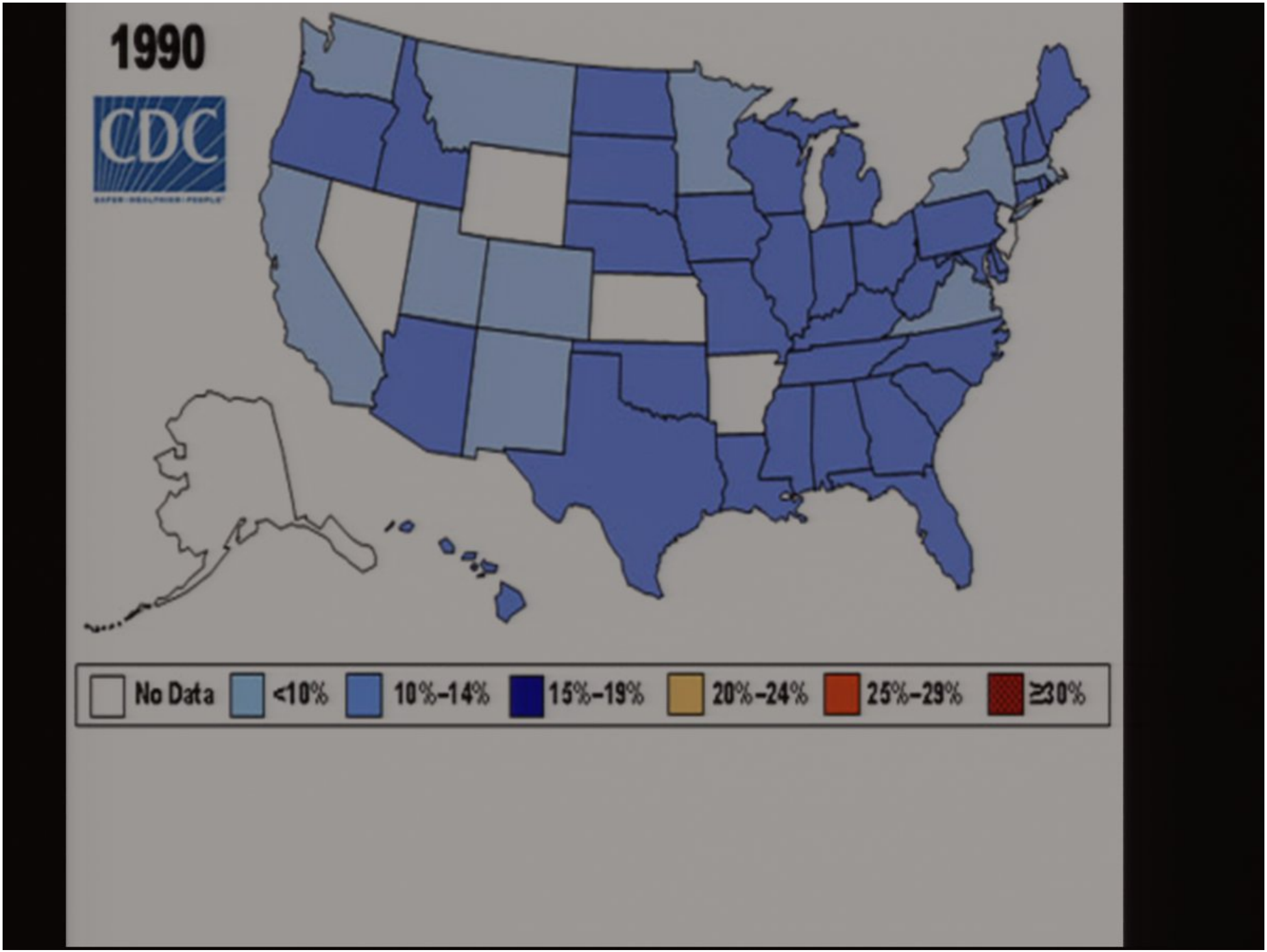
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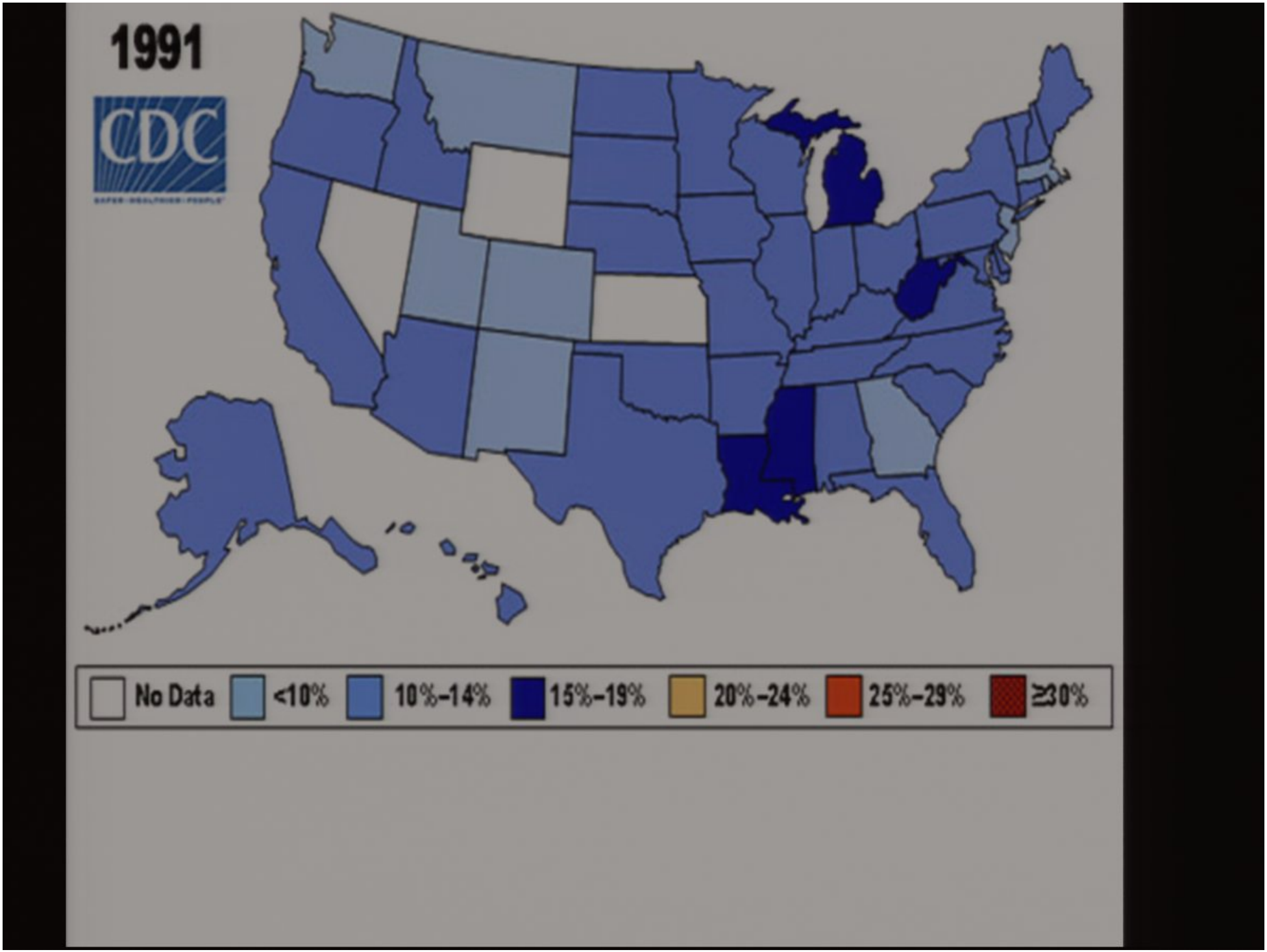
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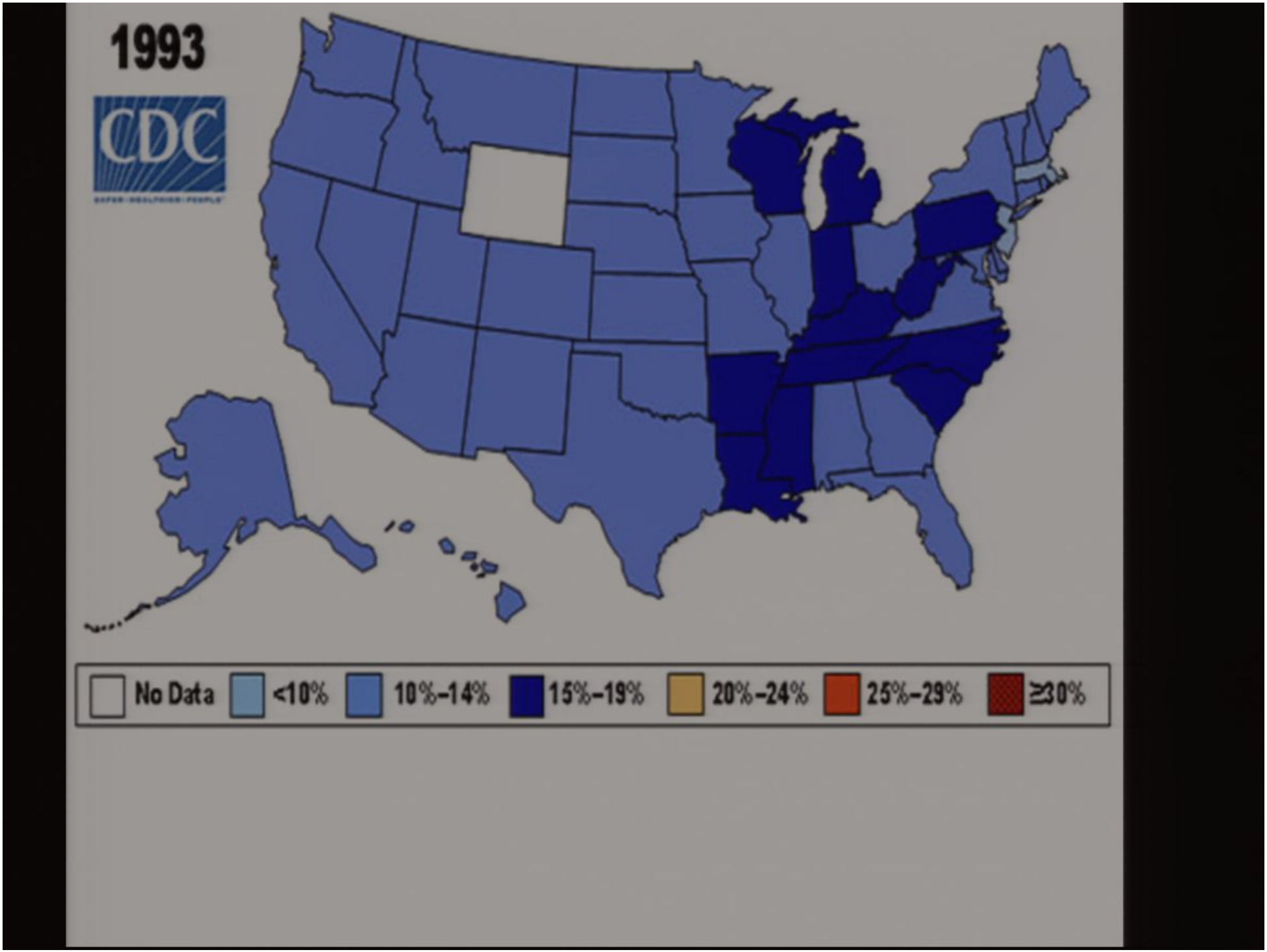
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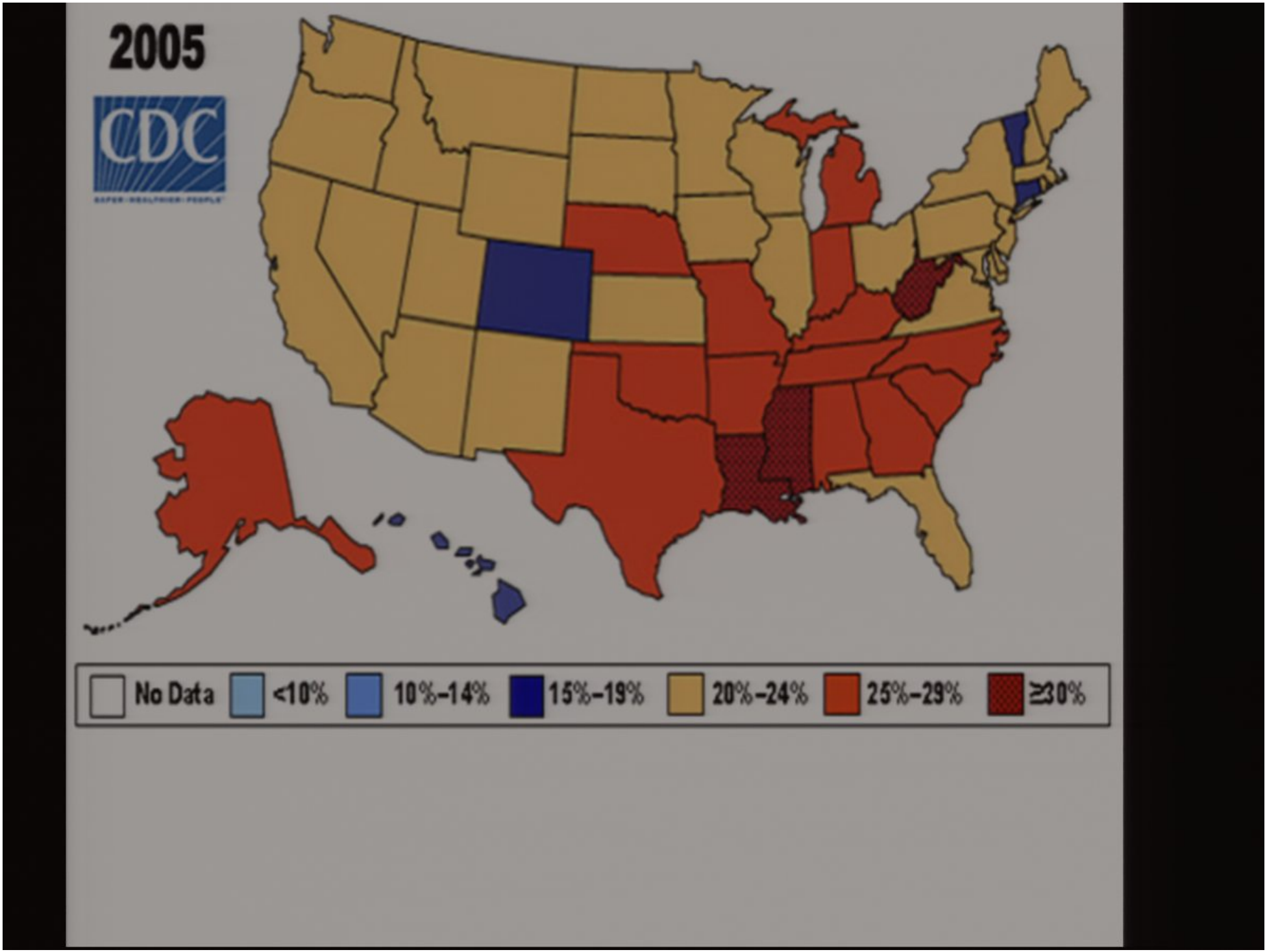
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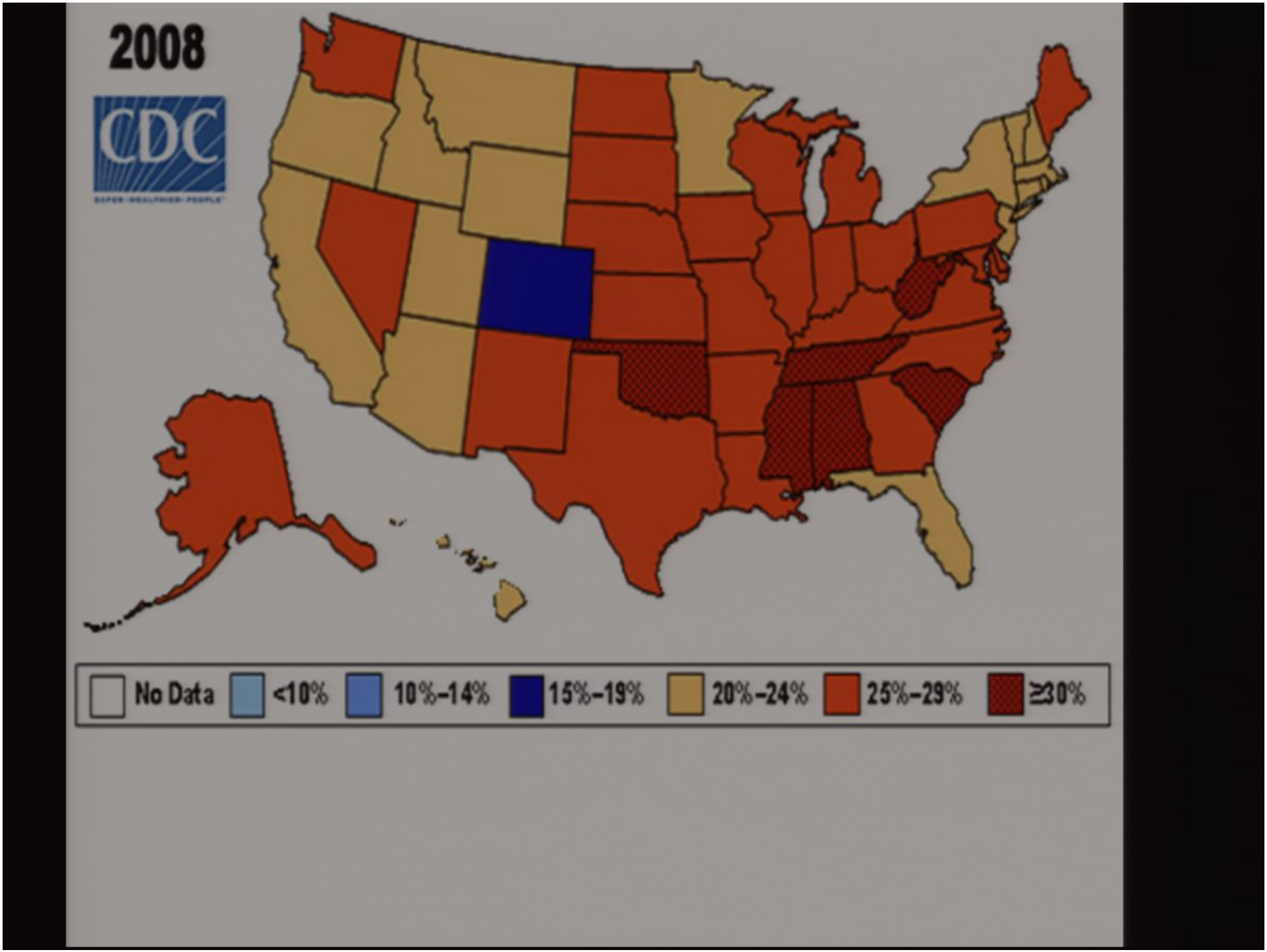
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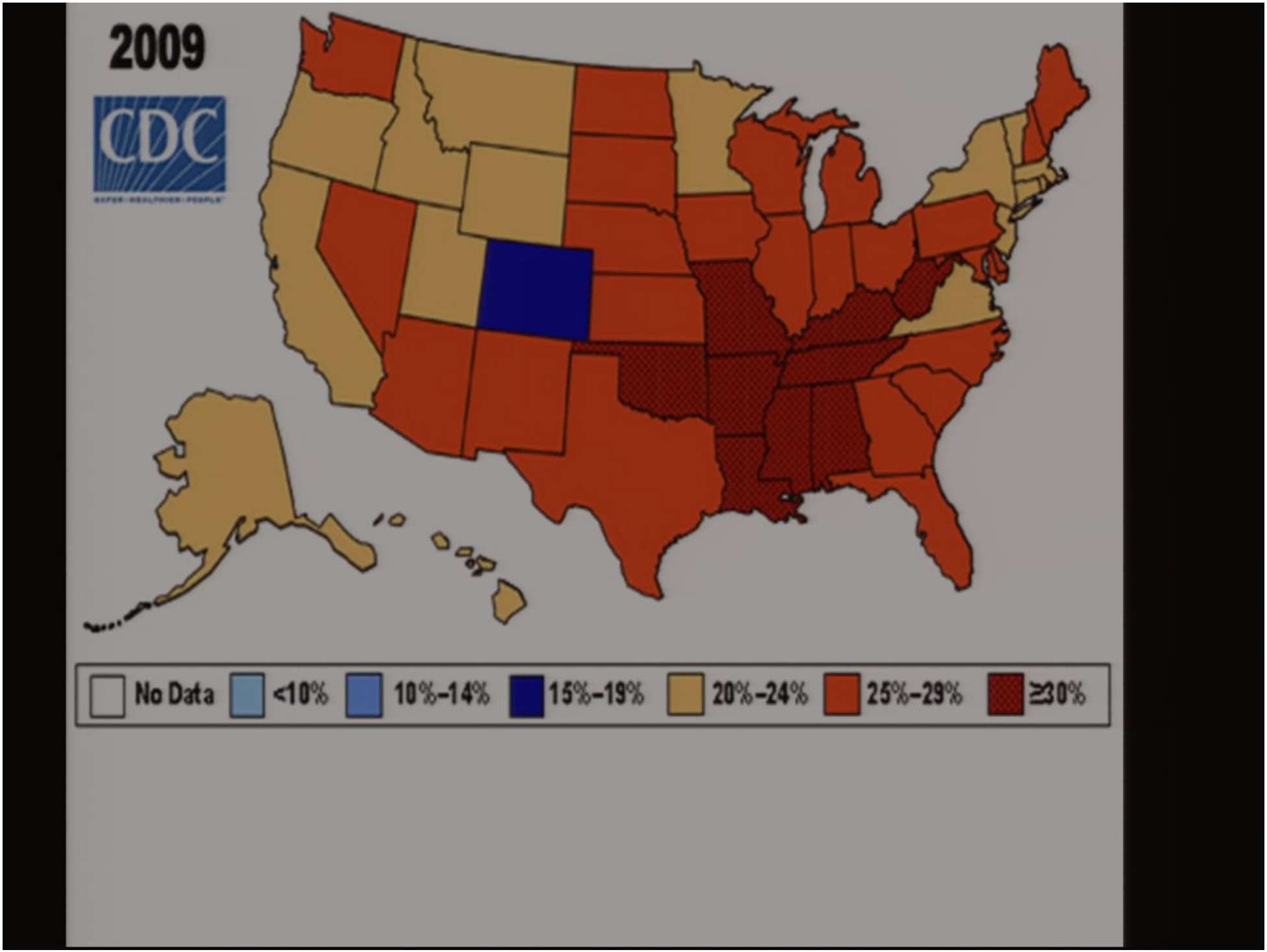
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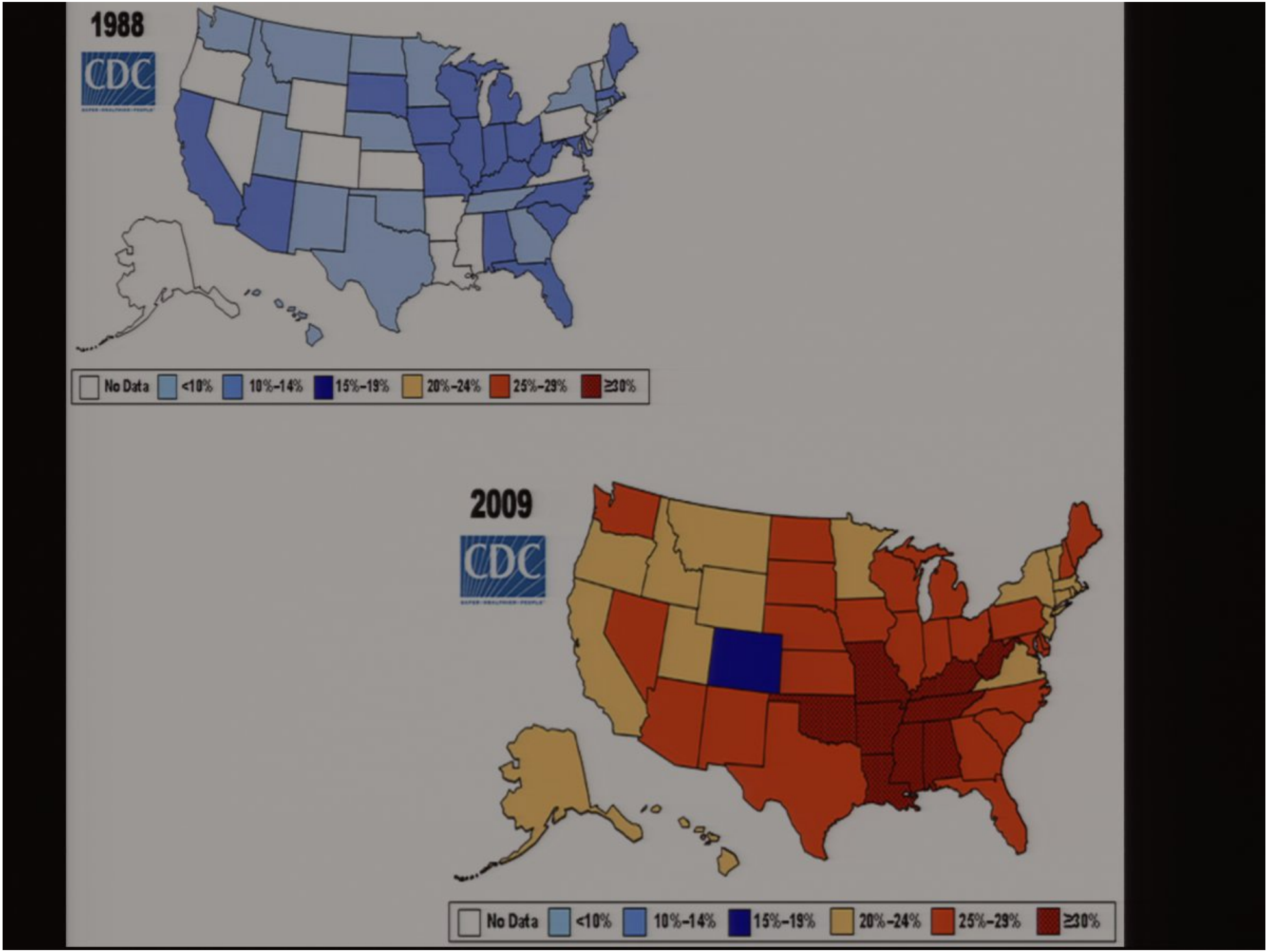
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Acute Toxicity

Exposure to chlorpyrifos at doses of 1 mg/kg and 5 mg/kg daily for 3 months did not produce any acute toxic effects in Long Evans mice.

Reference Memory

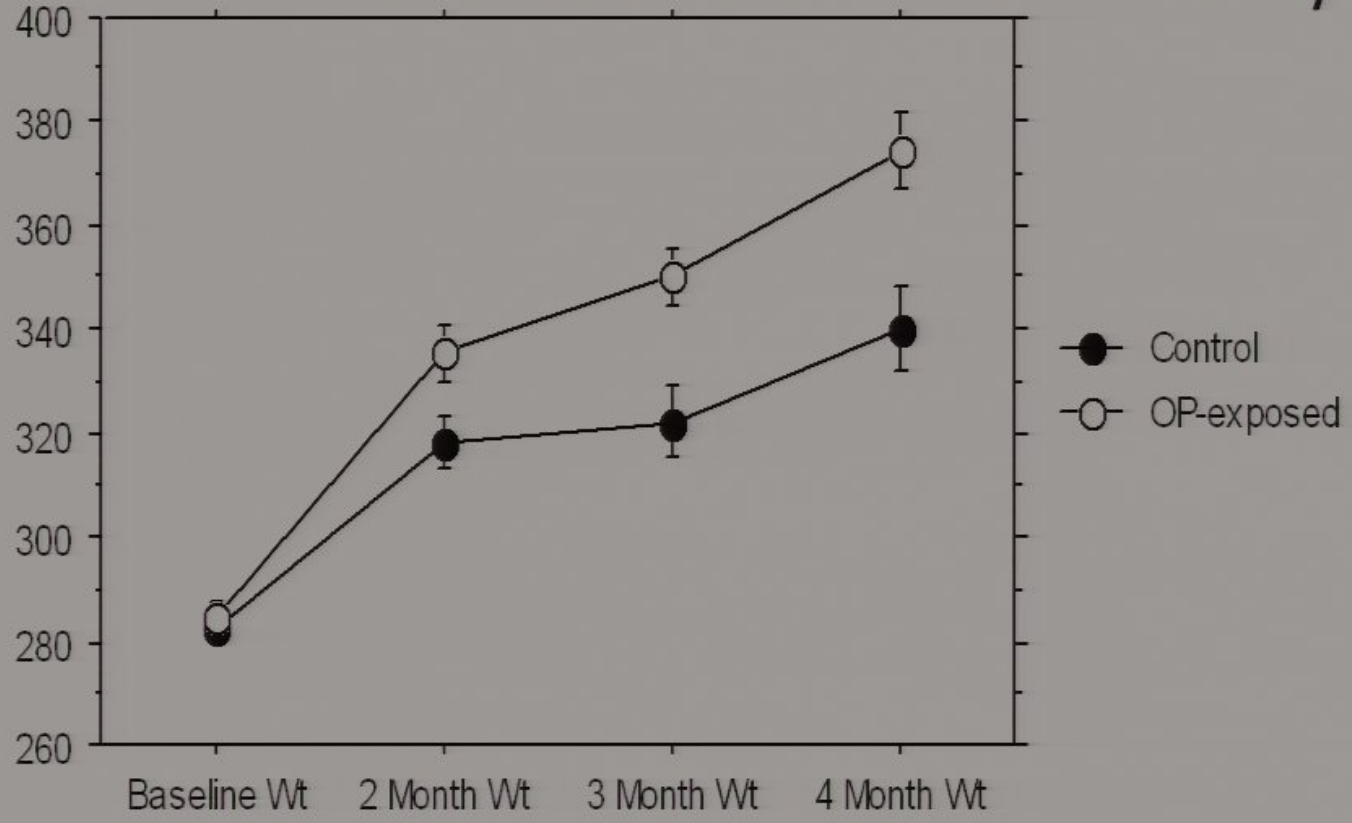
There were no significant differences in reference memory at 0, 1 and 3 months between the groups.

Working Memory

At three months, there were significantly significant impairments in working memory in group III relative to Groups I and II, with p-values of 0.047 and 0.049 on two trials.

Obesogens:

environmental chemicals that induce obesity



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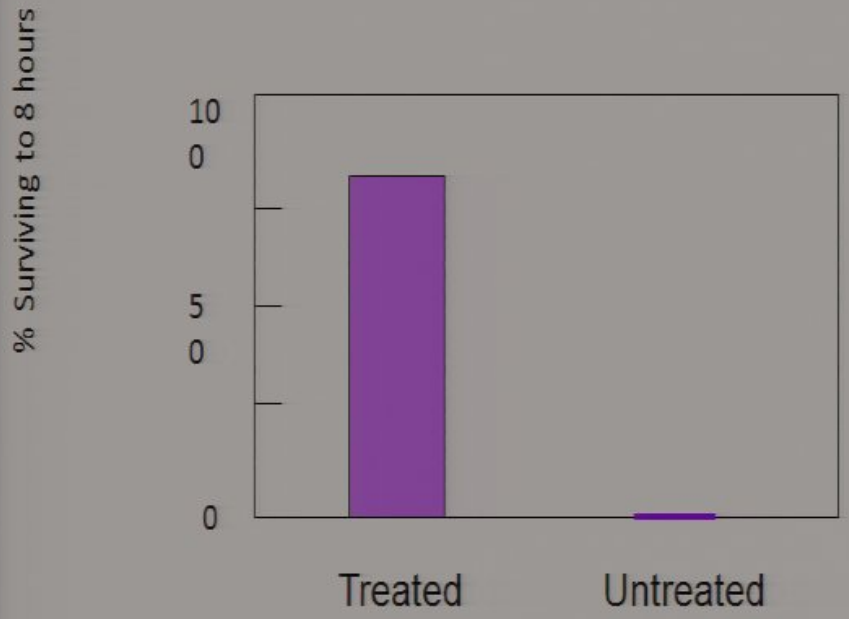

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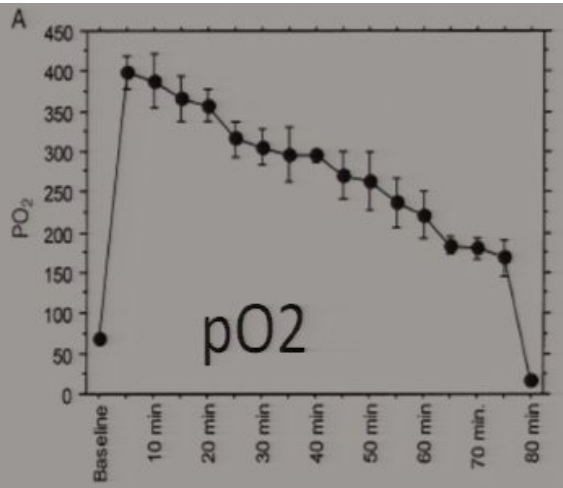

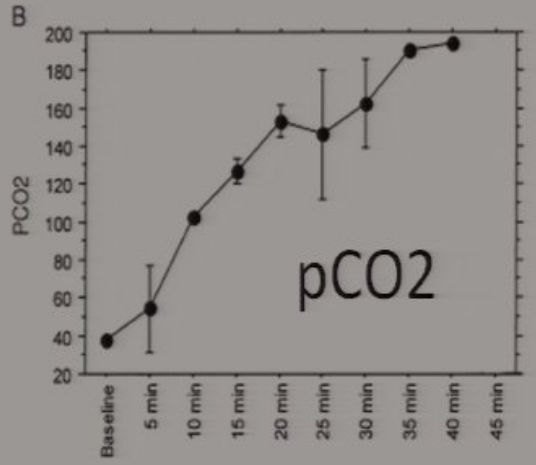

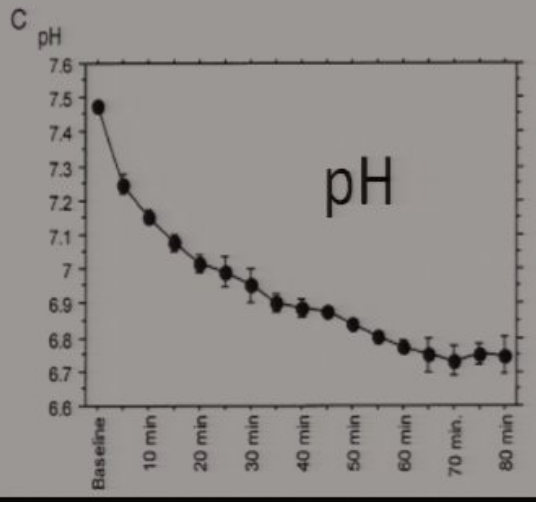

American Journal of Emergency Medicine (2005) 23, 864–867

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Accepted 31 May 2005

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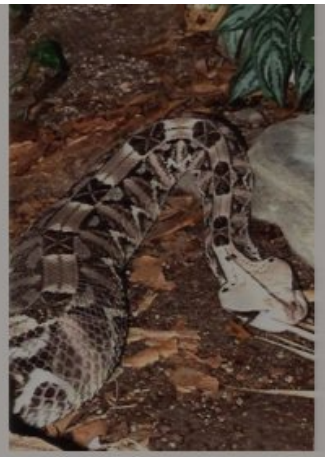

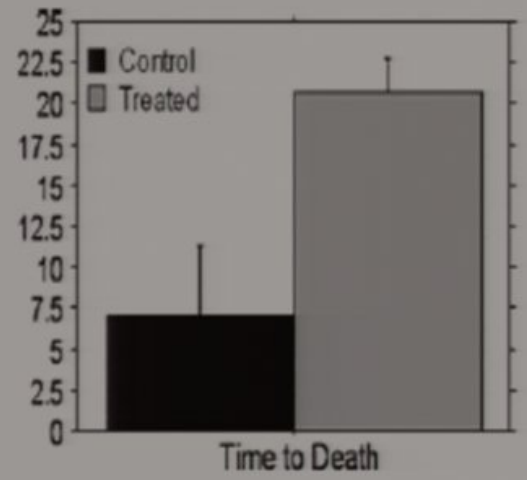

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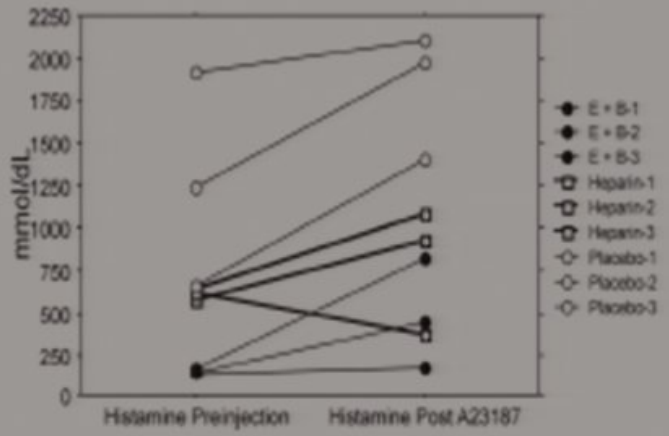

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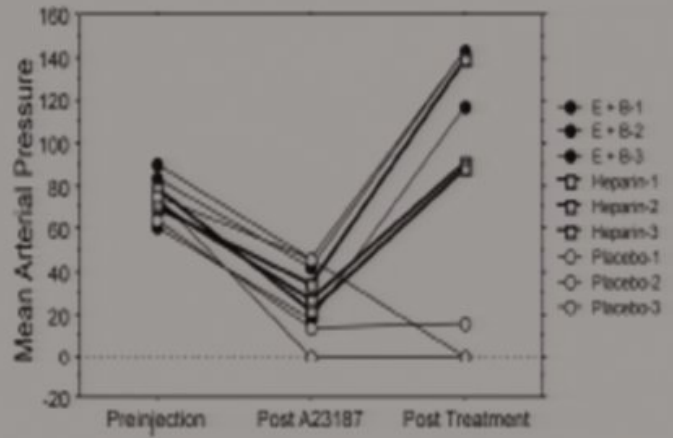

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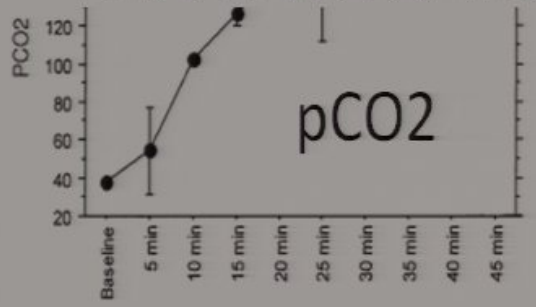

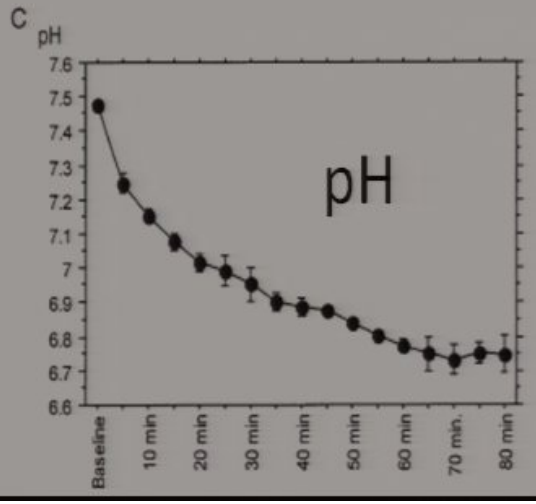

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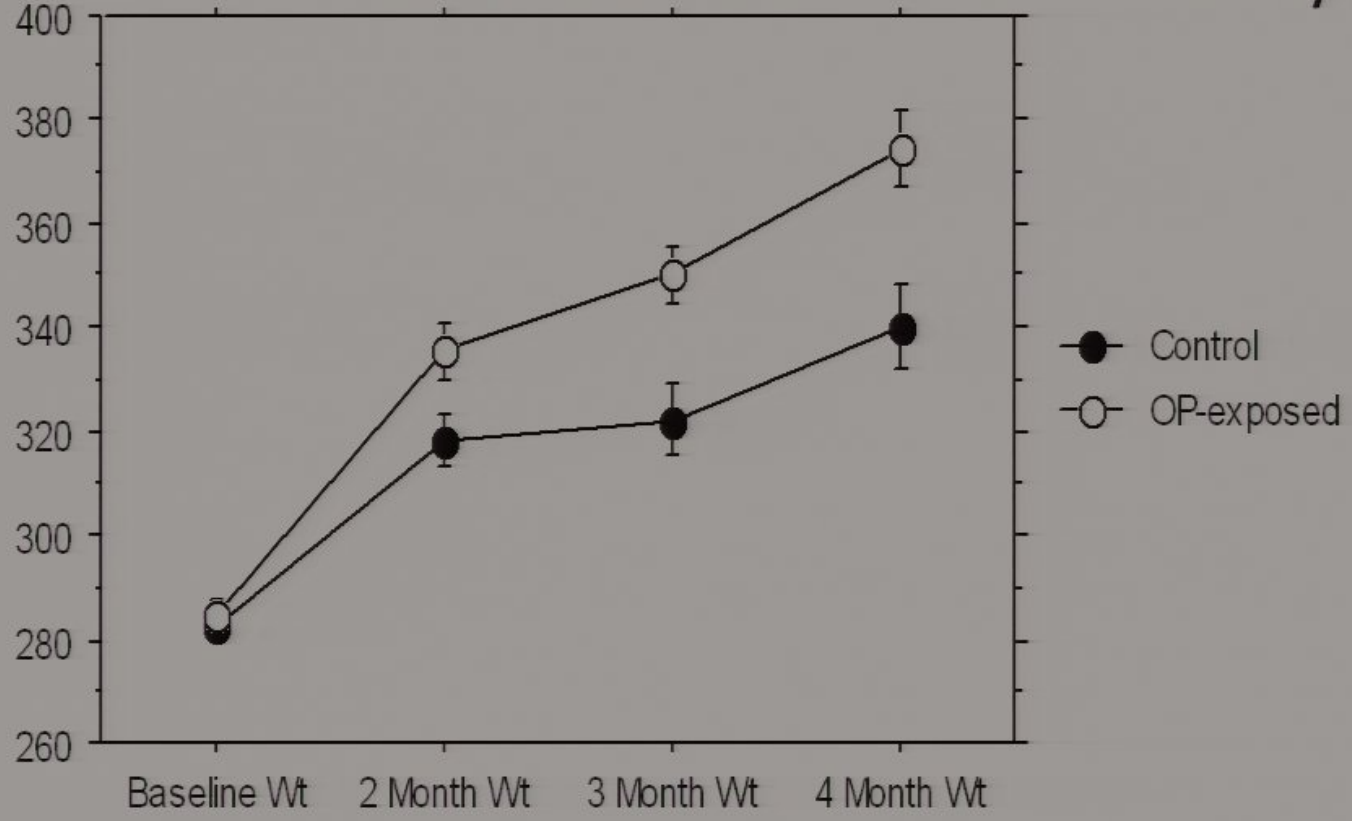

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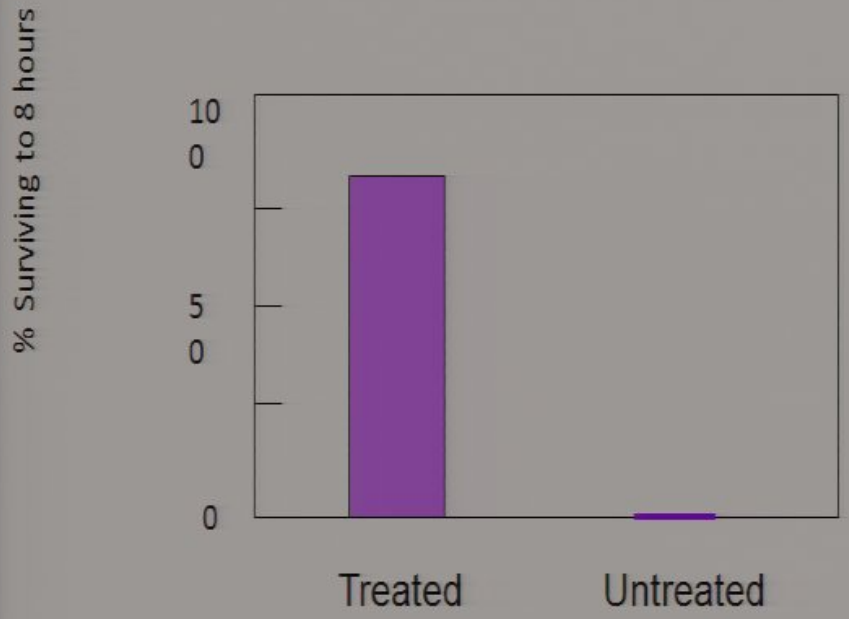

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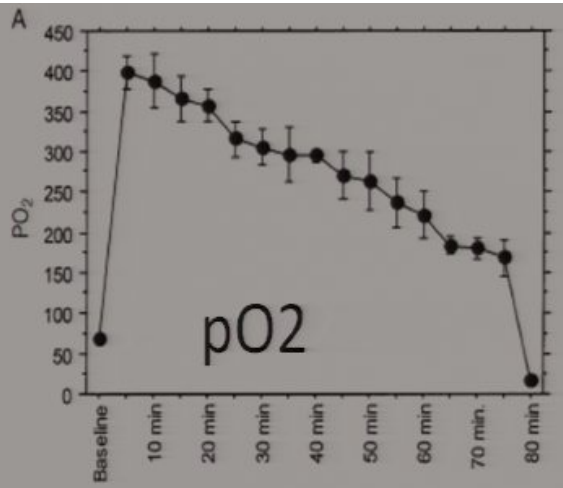

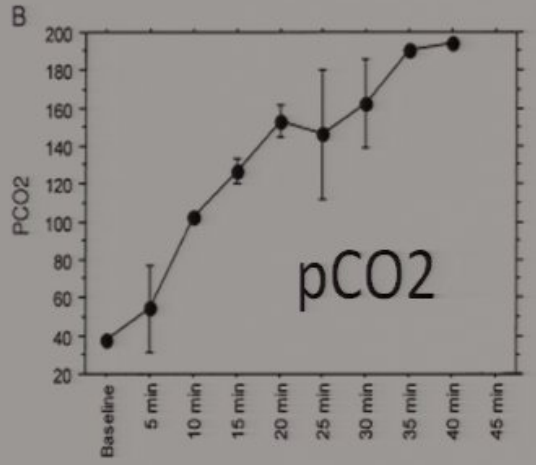

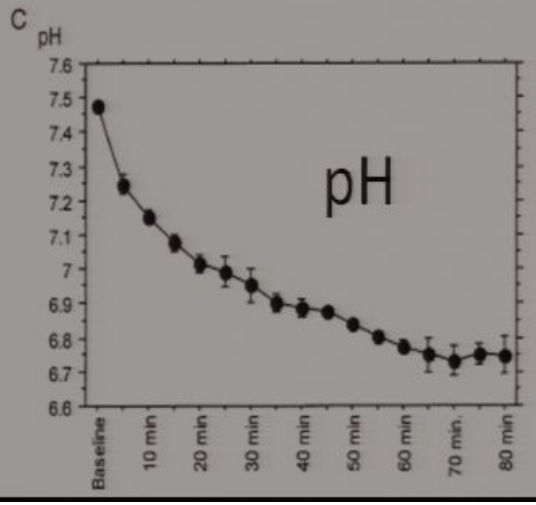

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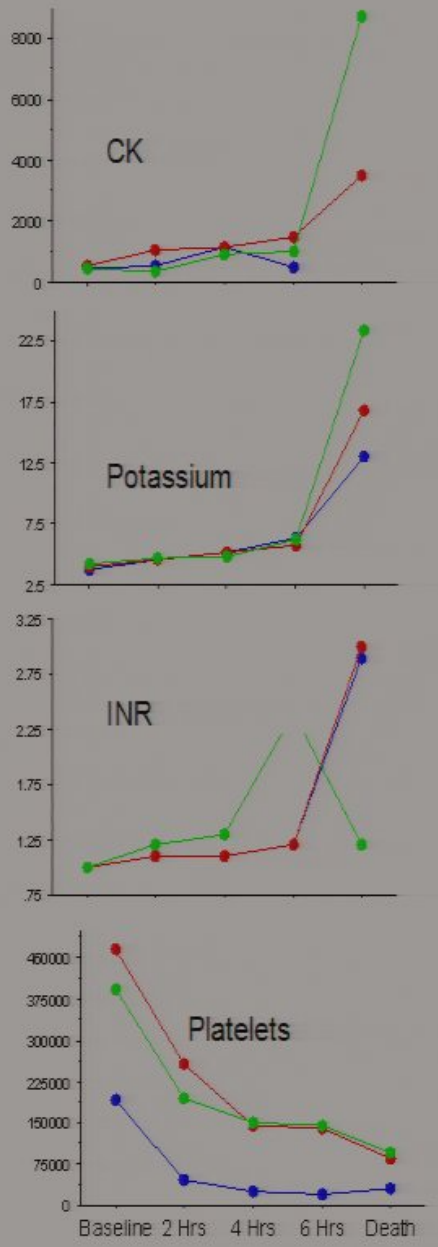
Results

- Survival to 24 hours
- Treatment group
  - 100% survival to 24 hours
- Control group
  - 0% survival to 24 hours
  - Time to death 13.68 ± 3.42 hours
- Chi-square p-value = 0.014

Venom Lysis syndrome

- Rattlesnake venom
- Precipitous fatalities
- Marked destruction of tissue
- Elevated potassium
- Cardiac dysrhythmias
- Similar to tumor lysis syndrome



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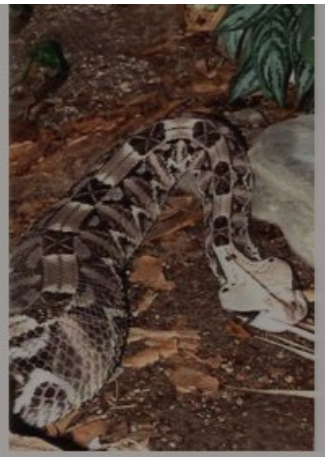

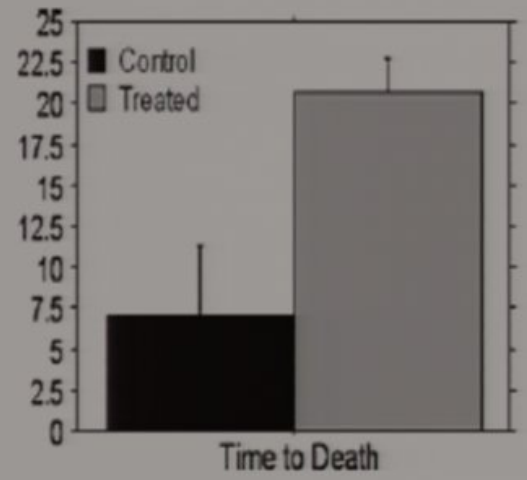

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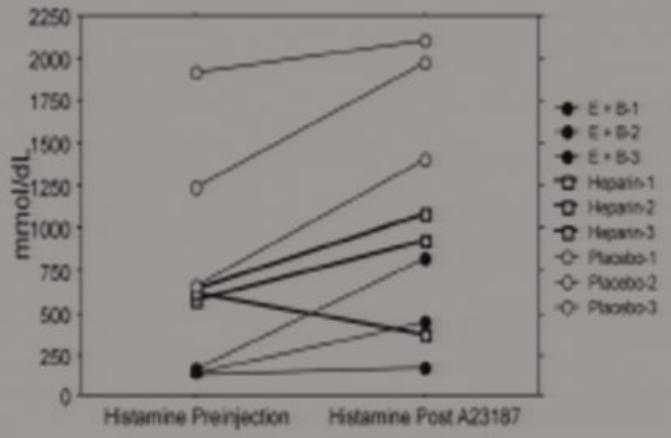

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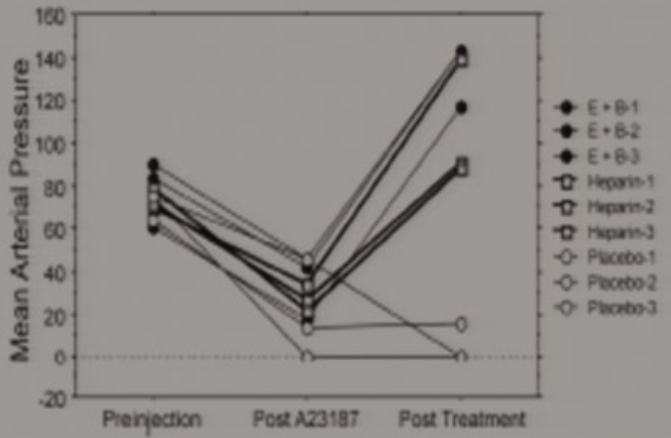

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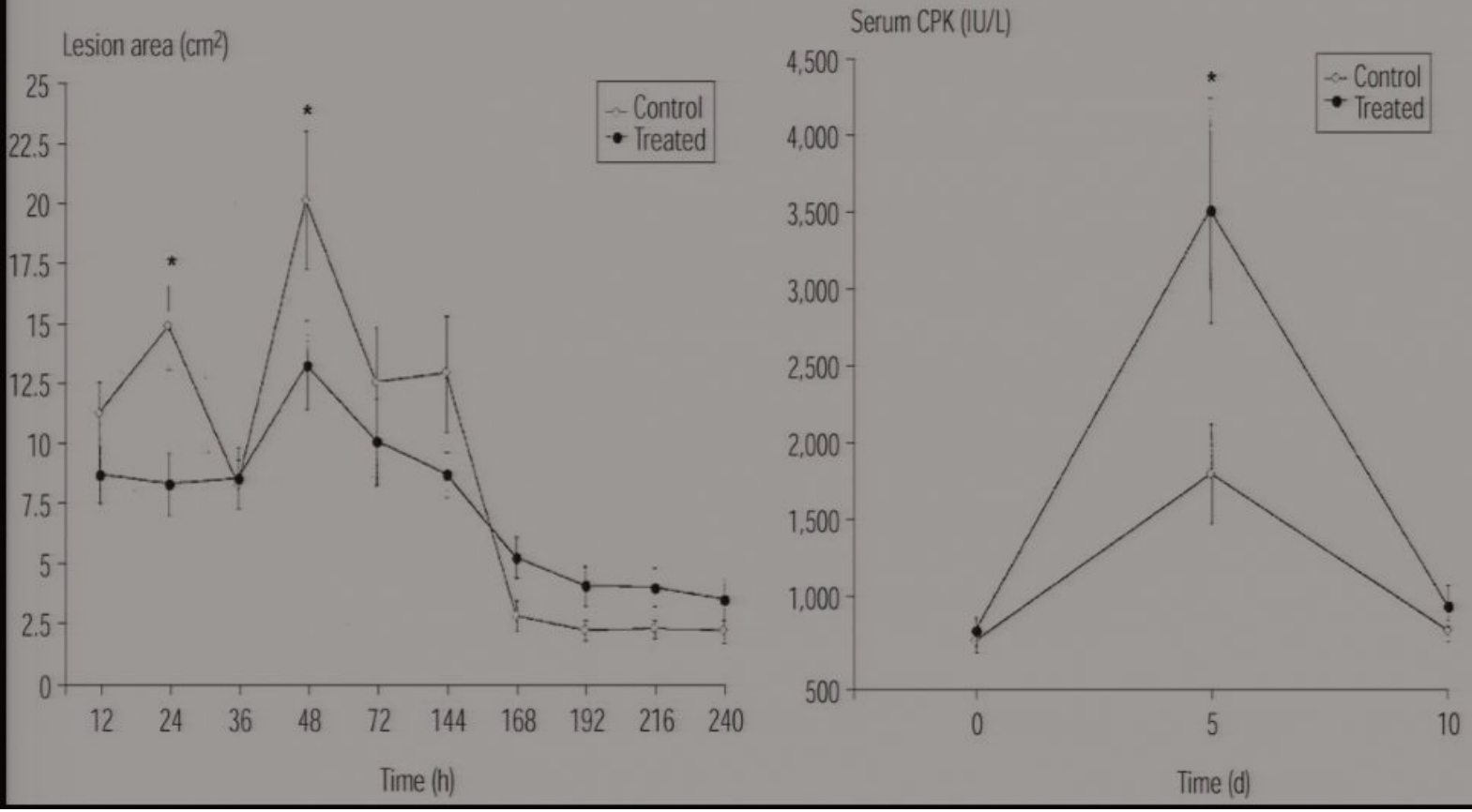
Annals of Emergency Medicine – 2001;37,

Lowry BP, Bradfield JF, Carroll RG, Brewer KL, Meggs WJ.



Clinical Toxicology, 43:383–384, 2005
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ISSN: 0731-3810 print / 1097-9875 online
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LETTER TO THE EDITOR

Fallacies in the Refutation of Causality

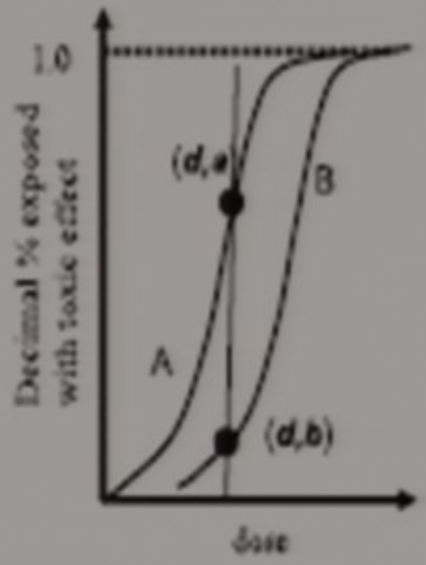

FIG. 1. A poisoning with two effects A and B has two seperate dose response curves that can be used to calculate the probabilities of getting both, one, or neither effect at a given dose.

Toxin affects two organ systems

Two distinct dose-response curves

a = % with effect A

b = % with effect B

P (A not B) = a(1 – b)

P (B not A) = b(1-a)

P (A and B) = a x b

Oral treatment of organophosphate poisoning in mice.

- Football stadium
- 70,000 participants
- Terrorist

- Crop duster filled with OP insecticide or nerve gas
- Who is going to stock 300,000 doses of IV/IM antidote and give 140,000++ injections?

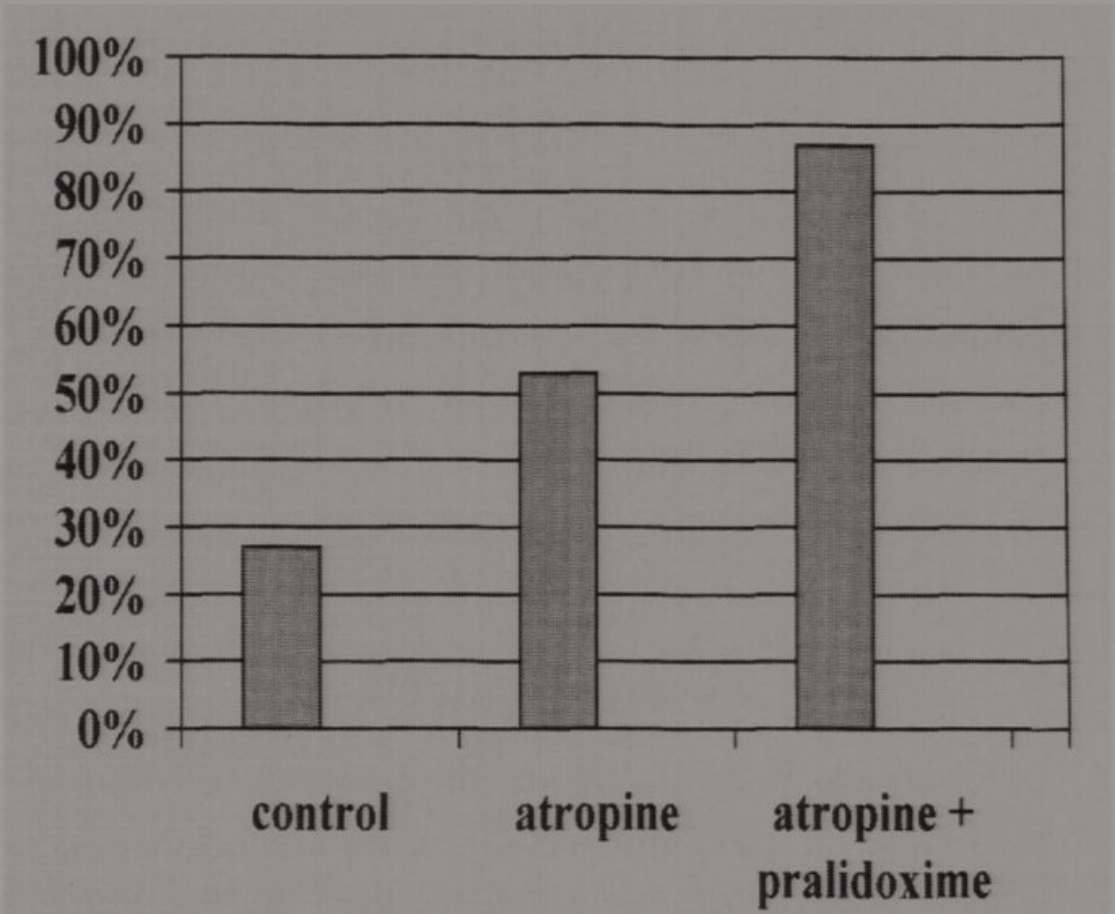

Figure 1. Percentage survival for mice treated by oral gavage with saline, atropine, and a combination of atropine and pralidoxime.

Oral Treatment of Organophosphate Poisoning in Mice

Bradford J. Bowls, MD, Jack M. Freeman Jr., MD, James A. Luna, MD, William J. Meggs, MD, PhD

Clearance of metformin by hemofiltration in overdose.

- Metformin, drug of choice for type 2 diabetes
- Increasing overdoses
  - Therapeutic misadventure
  - Intentional overdoses by adults
  - Unintentional by small children
- Cleared by kidney machine

Emergency Department hemodialysis in a case of severe ethylene glycol poisoning.

Highest level ever recorded
Minimal Toxicity

Treatment of Wide Complex Tachycardia

ACLS newly recommended a drug called amiodarone to treat wide complex tachycardia

Overdoses of tricyclic antidepressants cause wide complex tachycardia treated with sodium bicarbonate

What happens if you treat a tricyclic antidepressant overdose with amiodarone?

Safety verified.

Digoxin + Calcium = Stone Heart

1920's dog data

ACLS recommendation

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Enigma: digoxin + calcium

Digoxin overdose causes elevated potassium.

Elevated potassium is treated with IV calcium

Opps! We didn't know the patient was on digoxin.

Safety of treating elevated potassium with calcium in digoxin overdose verified

Clinical Enigma

Hydrofluoric Acid Poisoning

Low calcium & magnesium

Cardiac toxicity

Treat with calcium & magnesium

J Med Toxicol. 2007 Jun;3(2):45-51.

Limited efficacy of calcium and magnesium in a porcine model of hydrofluoric acid ingestion.

Coffey JA, Brewer KL, Carroll R, Bradfield J, Meggs WJ.

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Future

- Gulf War Illness
- Antidotes to prevent chronic neurological sequela to sarin poisoning
- Fundamental problem of physics
- 3 books on word processor
- Notebook of inventions