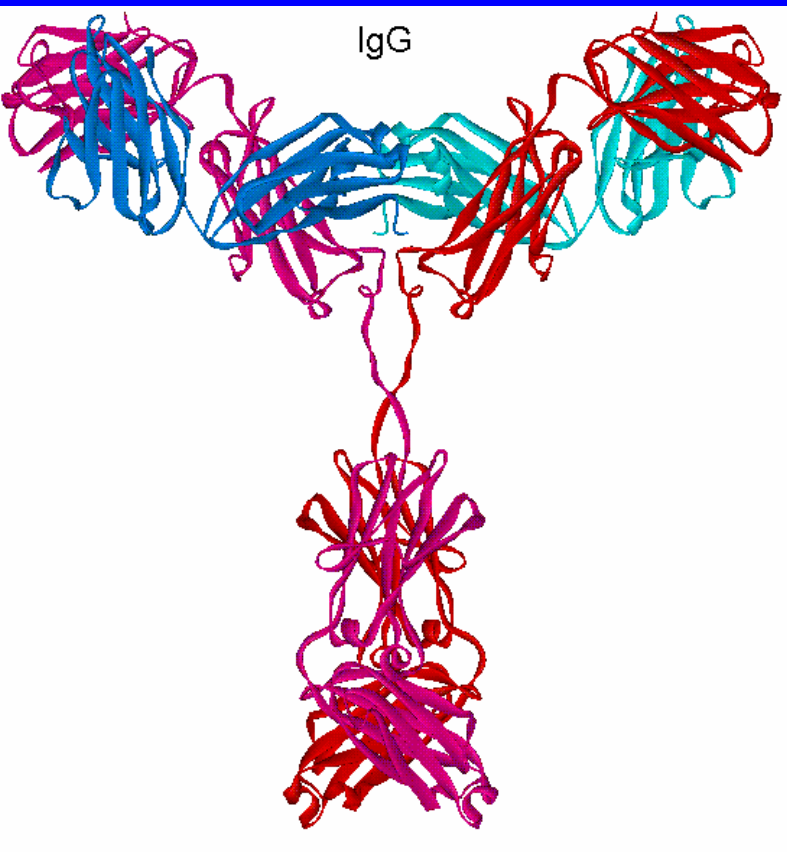


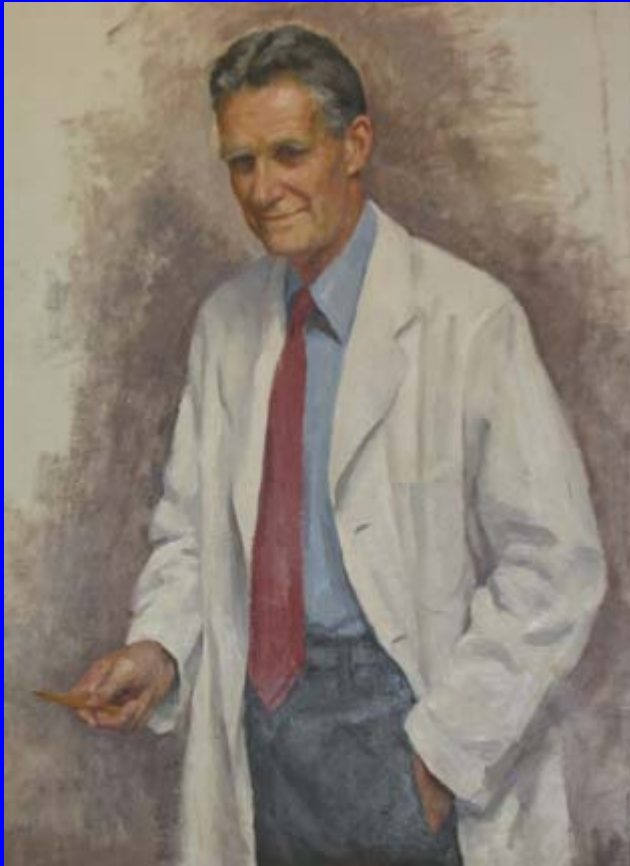
# What my Illness Taught Me About Health (The Role of the Immunoglobulins)



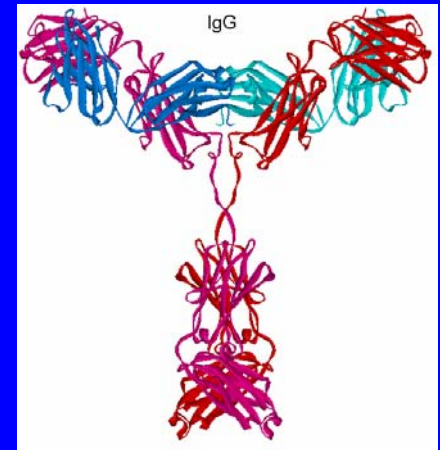
Allen R. Dyer, M.D., Ph.D.  
dyer@etsu.edu  
<http://faculty.etsu.edu/dyer>

# Charles Janeway, M.D.

**Father of Clinical immunology**



- **Pediatrician-in-chief at Boston Children's Hospital for 30 years**
- **Described**  
    **“A gamma globulin emia”**  
    **in children susceptible to**  
    **infections**



# **Patient: ARD**

- **Aug, 1997 - First symptoms: chin numbness**
- **Jan, 1998 - Rib tenderness**
- **March, 1998 - diagnosis: Multiple Myeloma**
- **March - June: 3 rounds of low-dose chemo**
- **July-Sept: Bone Marrow Transplant**

# Differential Diagnosis of Chin numbness/pain

- Multiple sclerosis
- Brain tumor
- Trigeminal neuralgia
- Herpes zoster
- Infection - neuritis
- Infection - systemic
- Cancer
- Functional
- Zebras







# **The law of parsimony**

**Par'si-mo'ny -**

**Unusual or excessive frugality.**

**Adoption of the simplest assumption in the interpretation of data**

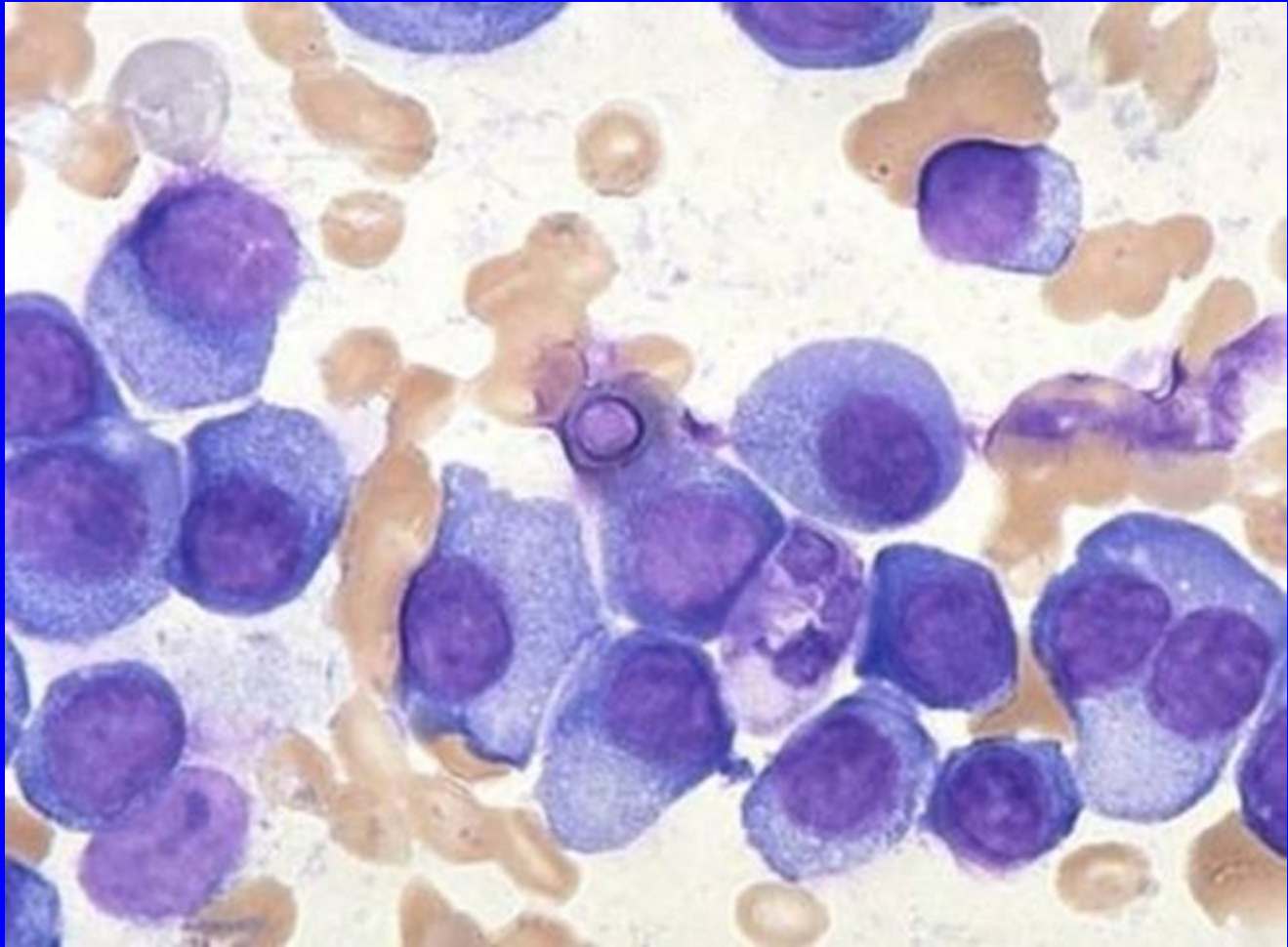
# Investigative Findings

**Serum immunofixation revealed an IgA-kappa monoclonal gammopathy.**

**Bone x-rays revealed radiolucent lesions within the skull, ribs, clavicles, right ischium, and right mid-humerus. The left 5th rib was fractured.**

**A bone marrow biopsy showed a slight increase in overall cellularity (70%)**

**A fine needle aspirate of the left 7th rib revealed in-filtration with atypical plasma cells.**

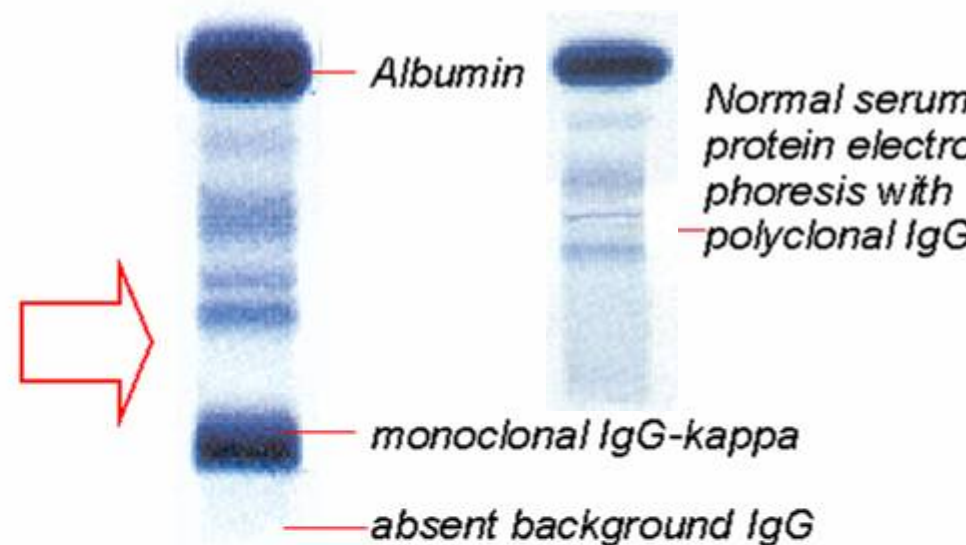




# Acquired immunodeficiencies



*Bone marrow of a patient with multiple myeloma is replaced with malignant plasma cells, some of which are binucleate & multinucleate. Normally, the malignancy involves a single plasma cell clone.*



*The malignant plasma cell clone produces a single immunoglobulin isotype with identical antigen receptors. Hence, in multiple myeloma, the ability to produce a diverse group of antibodies is impaired, & the patients become unusually susceptible to infection with extracellular organisms*

# Genetics

**Cancer is a genetic illness:  
It is not necessarily a hereditary  
illness.**

# Laboratory Results

|   |  |
|---|--|
| <b>CBC</b>                                | <b>Mild normochromic, normocytic anemia (H/H 11, 34)</b>       |
| <b>Erythrocyte sedimentation rate</b>     | <b>Markedly elevated (107mm/hr)</b>                            |
| <b>Serum biochemistries</b>               | <b>Mildly elevated calcium (10.3 mg/dL)</b>                    |
| <b>Serum protein electrophoresis SPEP</b> | <b>Mild polyclonal elevation in gamma globulin (2.3 gm/dL)</b> |
| <b>Quantitative immunoglobulins</b>       | <b>IgA hypergammaglobulinemia (1,880 mg/dL)</b>                |
| <b>Immunofixation</b>                     | <b>Monoclonal IgA-kappa paraprotein</b>                        |

# Lab results (cont.)

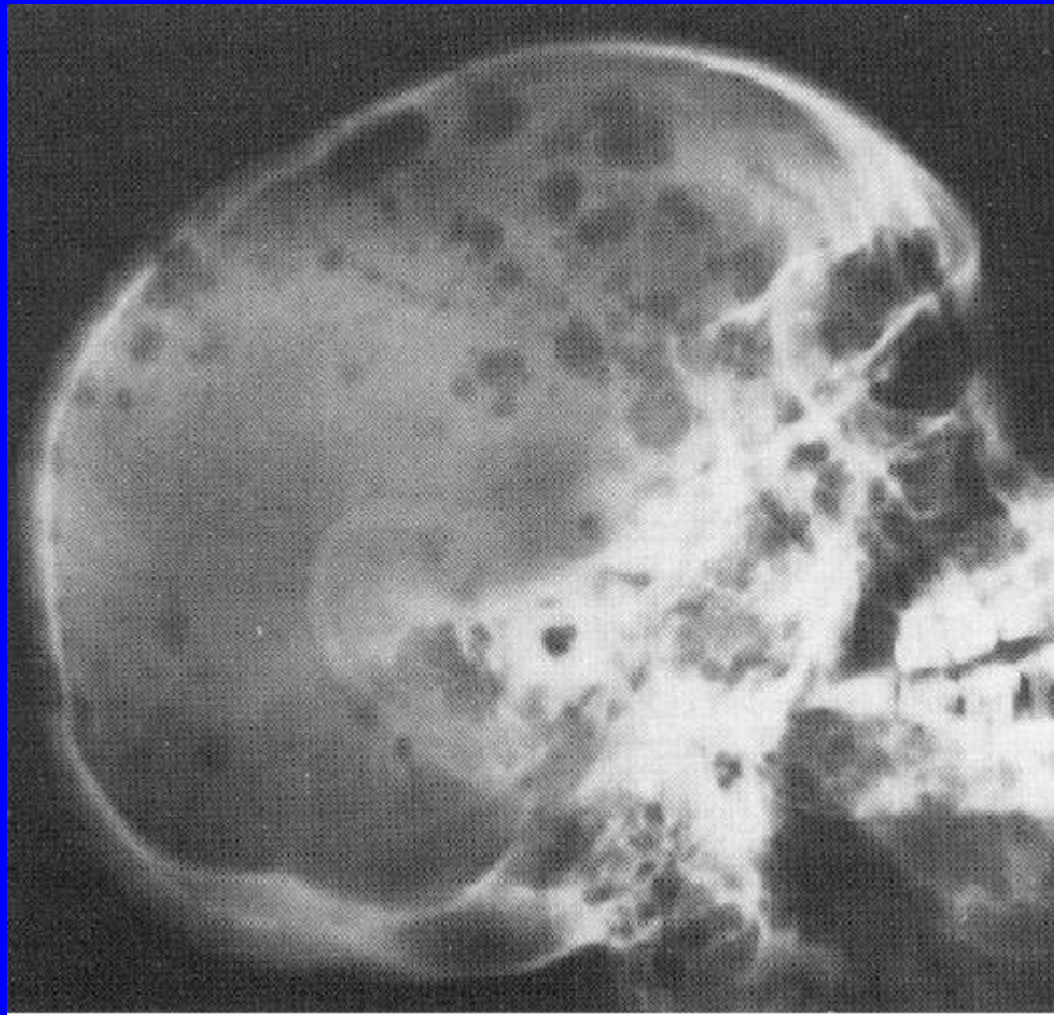
|   |                               |
|---|-------------------------------|
| <b>Serum interleukin -6</b>                 | <b>Absent</b>                 |
| <b>Urine protein electrophoresis (UPEP)</b> | <b>No protein in urine! 😊</b> |

# Myeloma Staging System

| <b>Creatinine Level</b> | <b>STAGE</b> | <b>Median Survival</b> |
|-------------------------|--------------|------------------------|
| <b>A &lt;2mg/dL</b>     | <b>IA</b>    | <b>61 months</b>       |
| <b>B &gt;2mg/dL</b>     | <b>IIA,B</b> | <b>55 months</b>       |
|                         | <b>III</b>   | <b>15 months</b>       |

## **β-2 microglobulin**

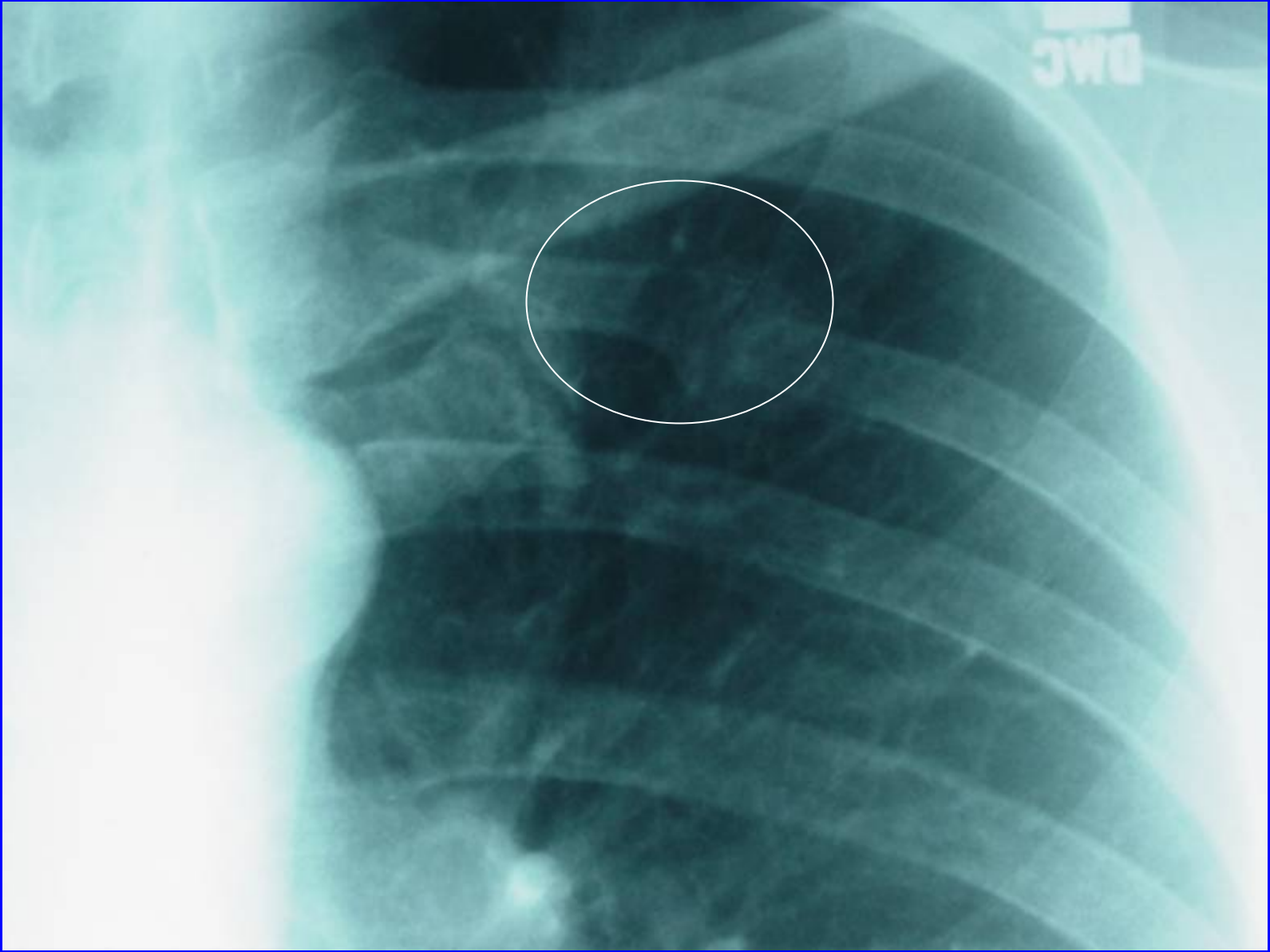
|                      |           |                  |
|----------------------|-----------|------------------|
| <b>&lt;0.004gm/L</b> | <b>I</b>  | <b>43 months</b> |
| <b>&gt;0.004gm/L</b> | <b>II</b> | <b>12 months</b> |



**Myelomatosis involving the skull**

# Pathologic Fracture and Lytic Lesions in Multiple Myeloma

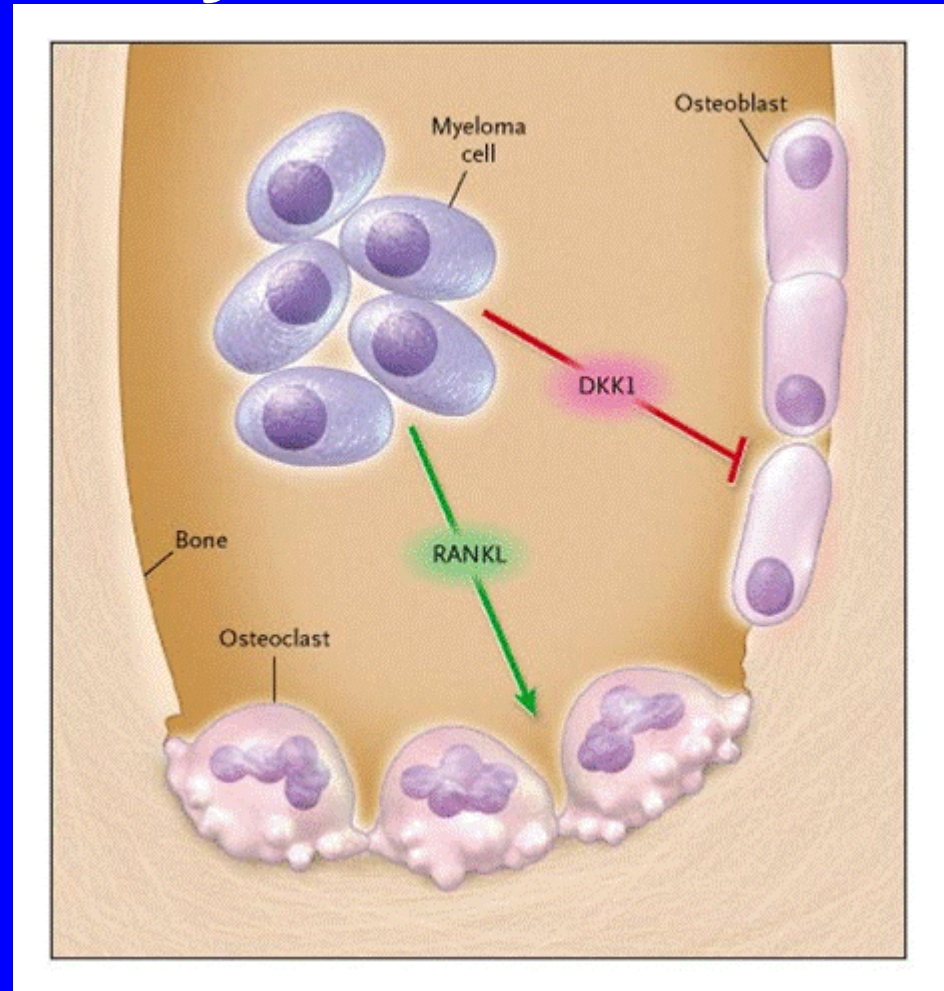






# Formation of Osteolytic Lesions in Multiple Myeloma

Myeloma cells secrete at least two molecules that modulate the bone microenvironment in a manner favorable to tumor growth. Receptor activator of nuclear factor *k*-B ligand (RANKL) acts to stimulate osteoclast formation and activity leading to bone erosion, whereas dickkopf1 (DKK1) appears to inhibit osteoblasts, thus preventing repair of the lesions.



Glass, D. A. et. al. N Engl J Med December 25, 2003



The NEW ENGLAND  
JOURNAL of MEDICINE

# Pathogenesis and Clinical Manifestations

| <b>Clinical finding</b>                   | <b>Underlying Cause</b>             | <b>Pathogenic Mech</b>                       |
|---|-------------------------------------|--|
| <b>Hypercalcemia,<br/>Fractures, pain</b> | <b>Skeletal destruction</b>         | <b>Osteoclast<br/>Activating Factors</b>     |
| <b>Renal failure</b>                      | <b>Light chain<br/>proteinuria</b>  | <b>Tumor products:<br/>OAF, DNA</b>          |
| <b>Anemia</b>                             | <b>↓production<br/>↑destruction</b> | <b>Inhibitory factors<br/>Autoantibodies</b> |
| <b>Infection</b>                          | <b>Hypogamma-<br/>globulinemia</b>  | <b>↓production<br/>↑IgG catabolism</b>       |
| <b>Neurologic Sx</b>                      | <b>Cord compression</b>             | <b>M globulins</b>                           |
| <b>Bleeding</b>                           | <b>↓clotting factors</b>            | <b>Tumor products</b>                        |



# **ANTICOAGULATION IN DEEP VEIN THROMBOSIS**

**Risk of Clot/thrombus vs. Risk of Bleed**

**Rule vs. Therapeutic principle**

**Complicating factors**

- Cancer**
- Steroids**
- Impending surgery**
- ? Underlying coagulation disorder**

# Playing the odds

**Informed consent: 1998**

**1-3 % change of death from treatment**

**(down from 10-15 %)**

**30% chance of complete cure**

**---**

**Duke Myeloma protocol: 1997-2002**

**n = 85**

**40 % still living**

**3 doing well**

# Stem cells harvested

Stem cells frozen



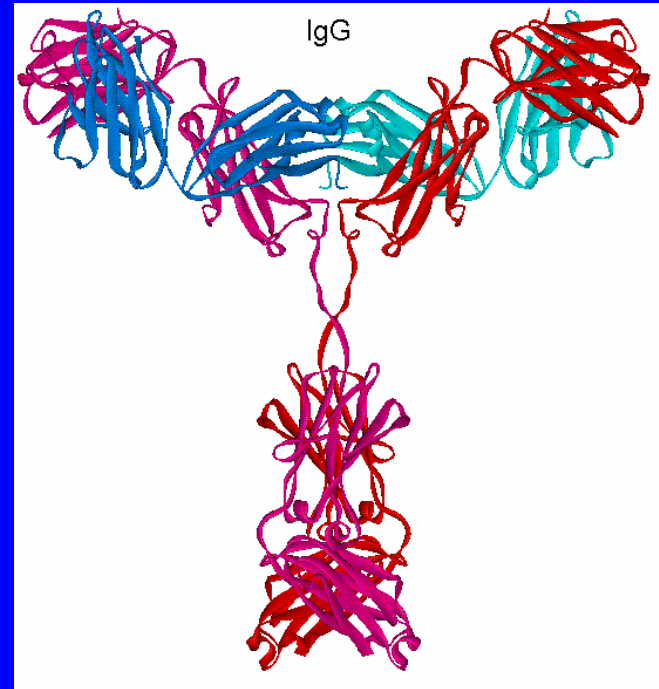
Patient given high doses of chemotherapy



Stem cells thawed

Stem cells infused back into the patient





**Charles (“Charlie”) Janeway, Jr. 1943-2003**  
**“Father of Innate Immunity”**  
**“How the Body Recognizes Foreign Invaders”**

# **Factors involved in Healing**

- **1. Education - accurate information**
- **2. Positive attitude**
- **3. Reducing stress**
  - **Relaxation**
  - **Exercise**
  - **Diet**
- **4. Eliminating Negative Beliefs and Emotion**
  - **Eliminate Anger, Rage, Fear, Guilt**
  - **Forgiveness**
  - **Problem Solving**
  - **Goal setting - creating positive future goals**
- **5. Positive visual imagery - commands and instructions to the body**

# Lance Armstrong



**1996 - age 25 -  
diagnosed with Testicular cancer  
(metastases to stomach, lungs, brain)**

**2005 - age 34 -  
wins 7th Tour de France**

# Allen Dyer



**1998 - age 52  
diagnosed with MM**

**2005 - age 60  
2nd Tour de France  
Ascention of Mt. Ventoux**



# Possible explanatory factors

- CHEMOTHERAPY
- Attitude                      Community
- Spirituality                      Love/Family support
- Prayer - Meditation
  
- Mind over matter                      *Mountain climbing*
- Environment                      *Hanging out with Buddhists*
- EXERCISE                      FUN
- Diet                      Genes                      Laughter

# **Explanatory factors (cont.)**

## **Luck**

**Good Fortune**

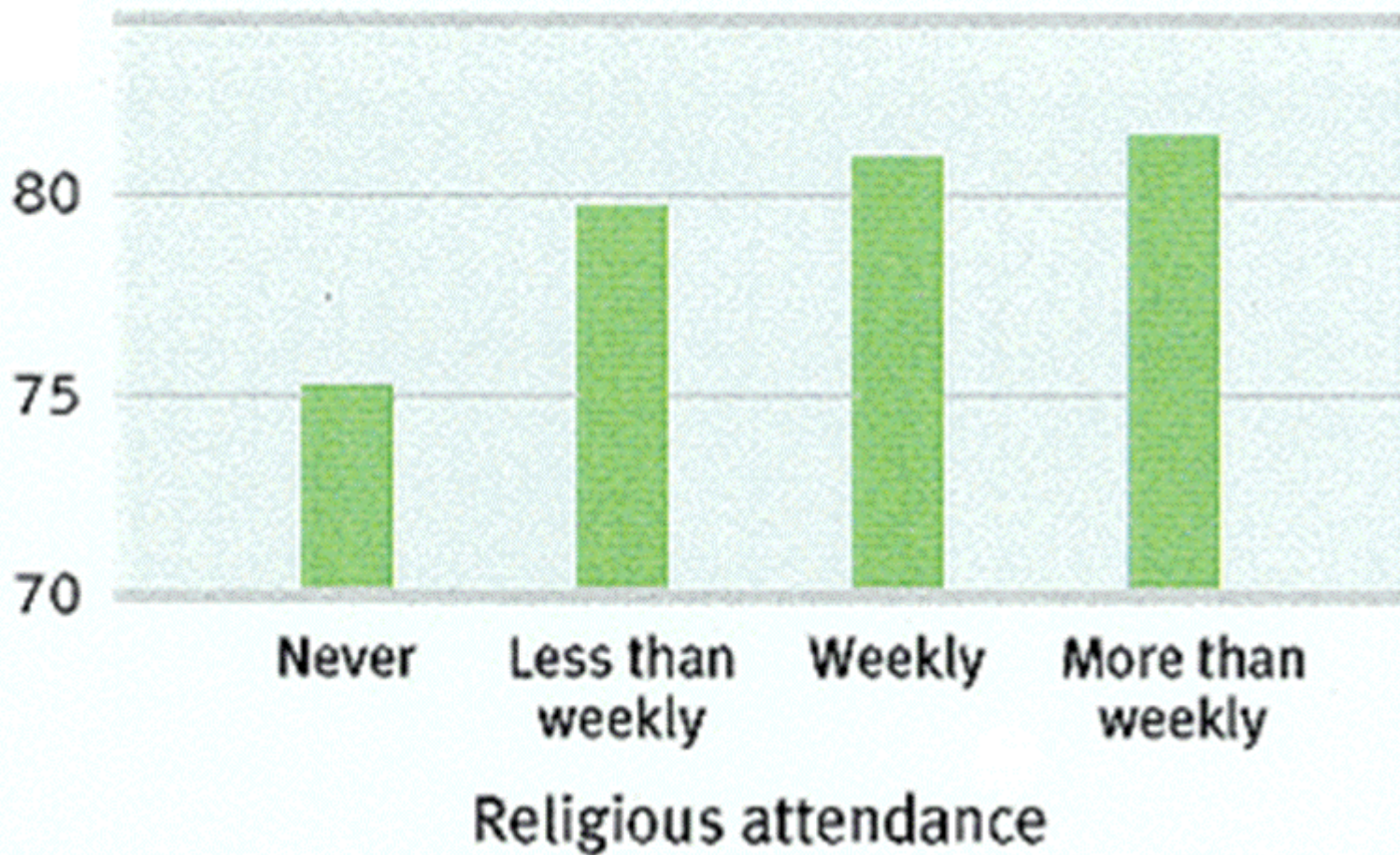
**Blessing**

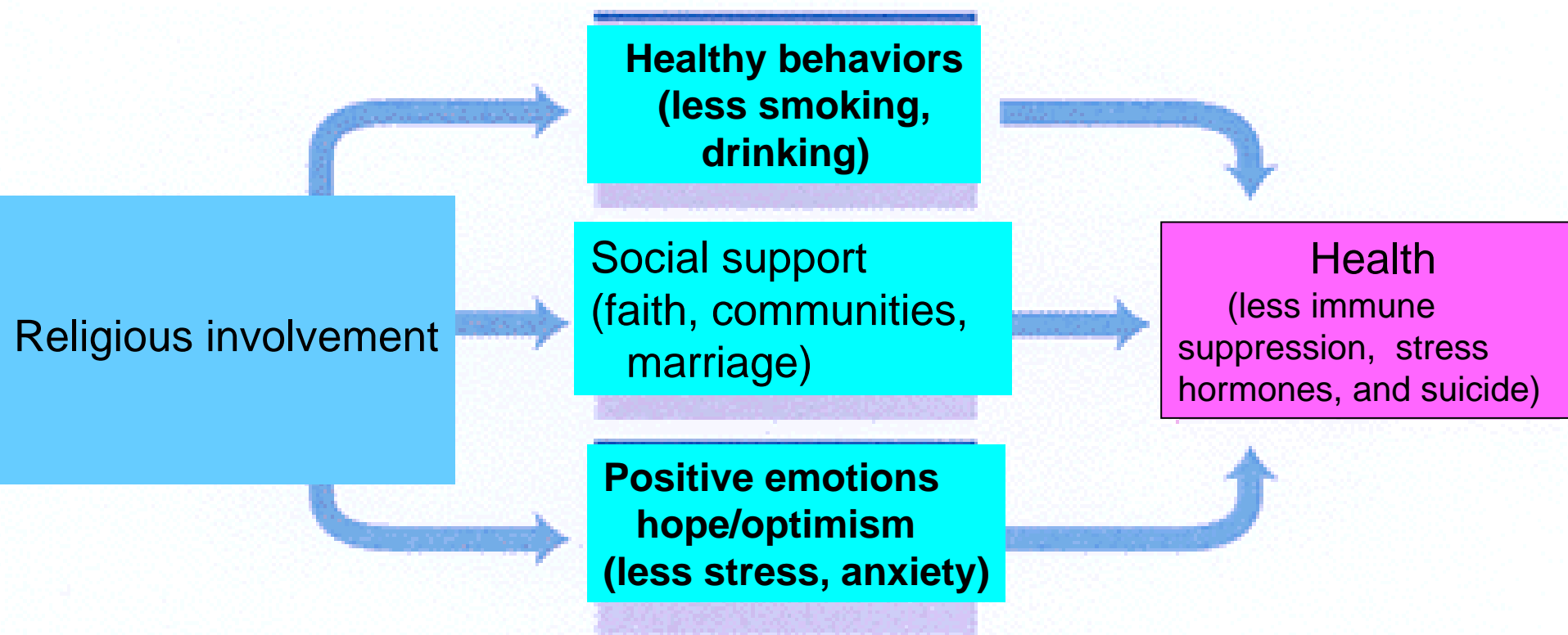
**Randomness  
Indeterminacy**

# Exercise and Cancer

- **Exercise improves immune function, lymph flow, and detoxification**
- **Helps regulate blood sugar levels**
- **Relieves both depression and anxiety**
- **Physical activity has also been shown to improve tolerance to chemotherapy.**
- **Fitness level prior to treatment helps endure the rigors of treatment.**

Life expectancy





Religious involvement

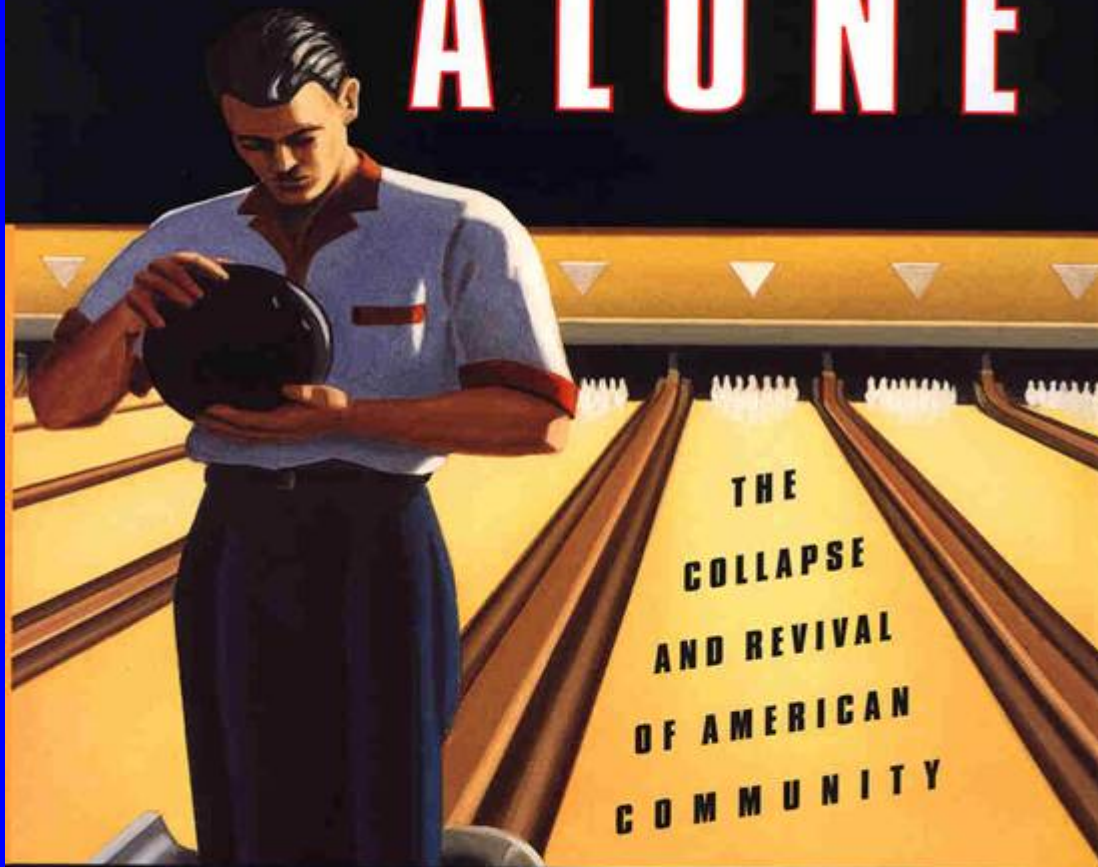
**Healthy behaviors  
(less smoking,  
drinking)**

**Social support  
(faith, communities,  
marriage)**

**Positive emotions  
hope/optimism  
(less stress, anxiety)**

**Health  
(less immune  
suppression, stress  
hormones, and suicide)**

# BOWLING ALONE



THE  
COLLAPSE  
AND REVIVAL  
OF AMERICAN  
COMMUNITY

Robert D. Putnam

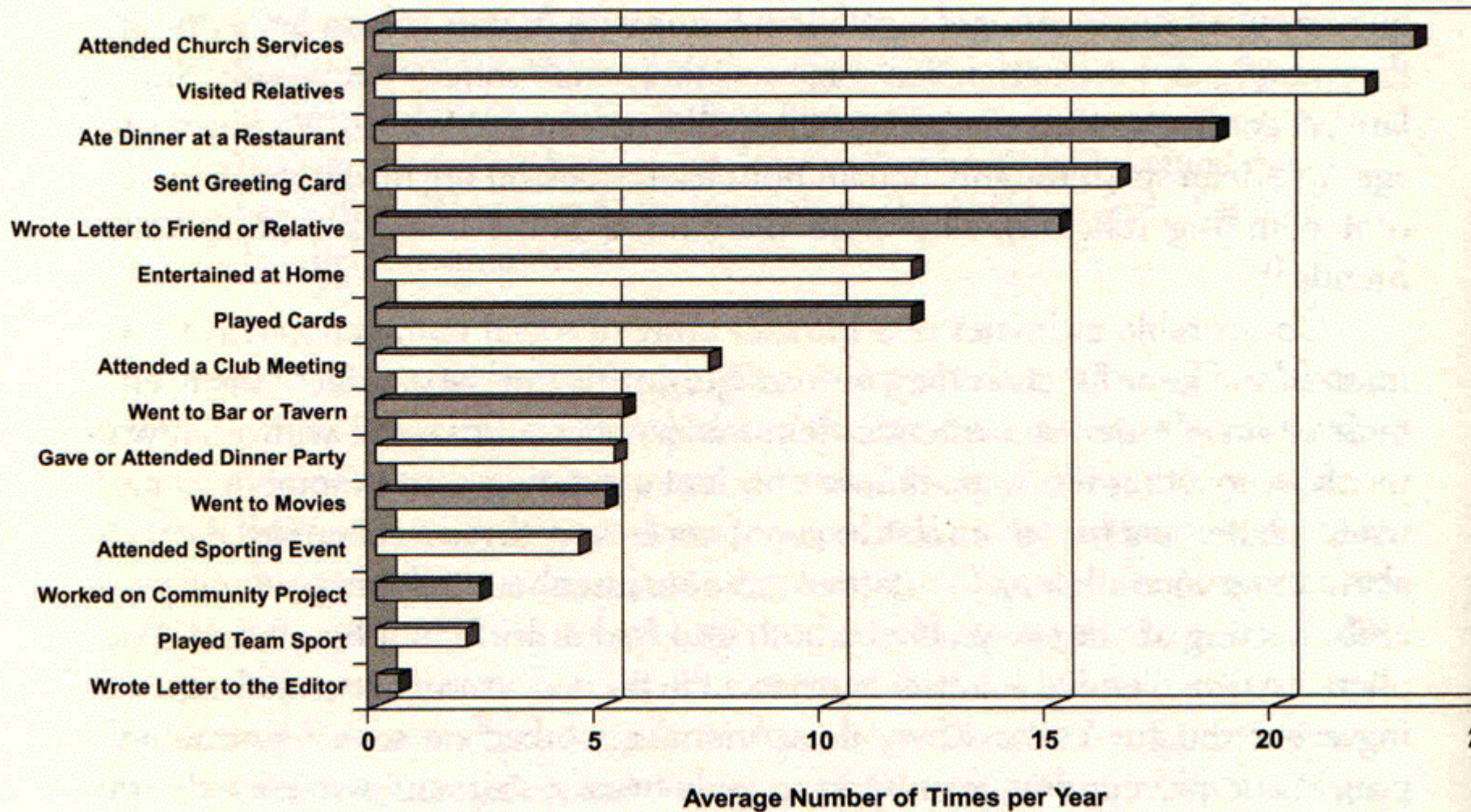


Figure 17: Frequency of Selected Formal and Informal Social Activities, 1975–1998

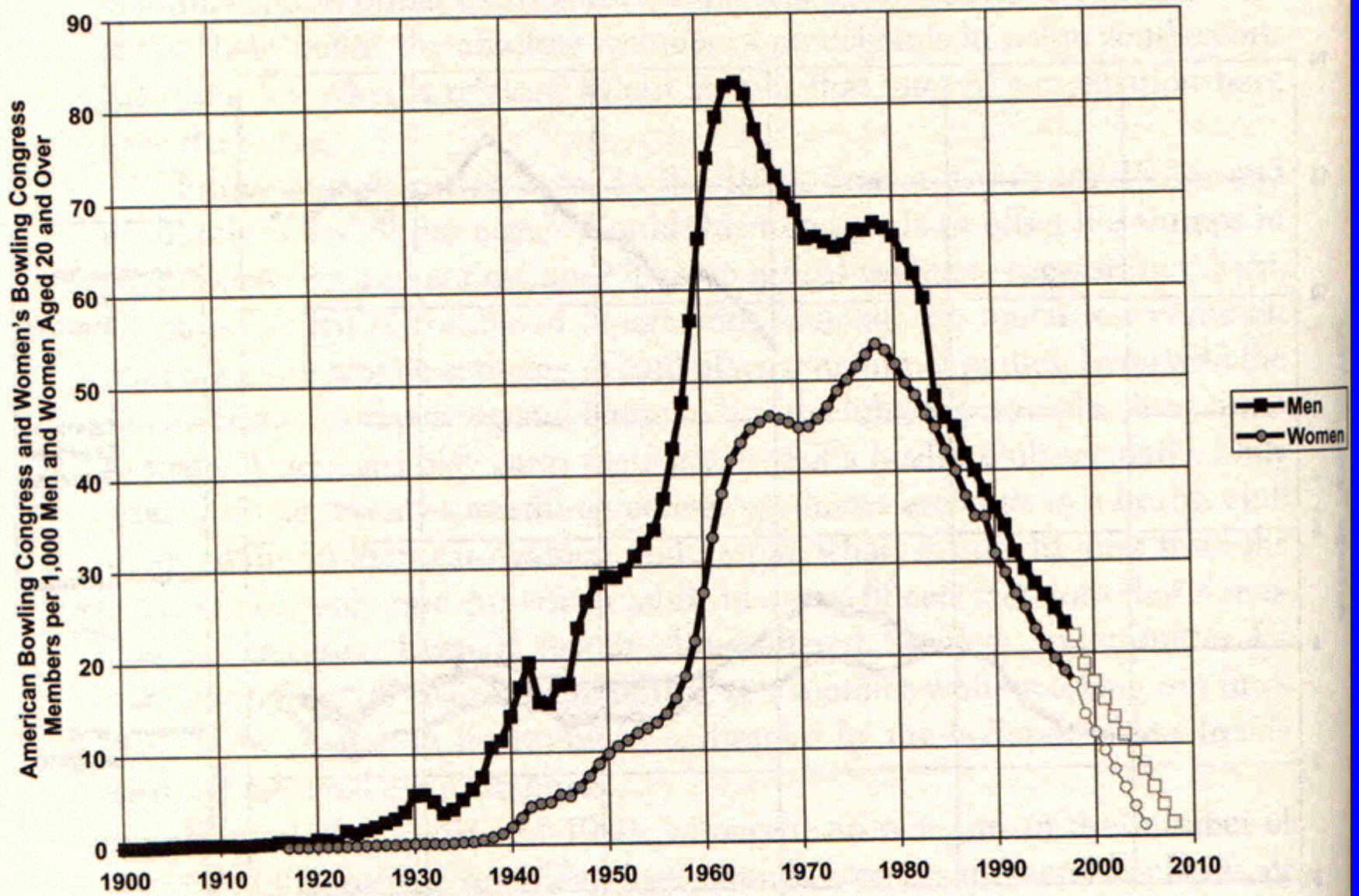


Figure 26: The Rise and Decline of League Bowling



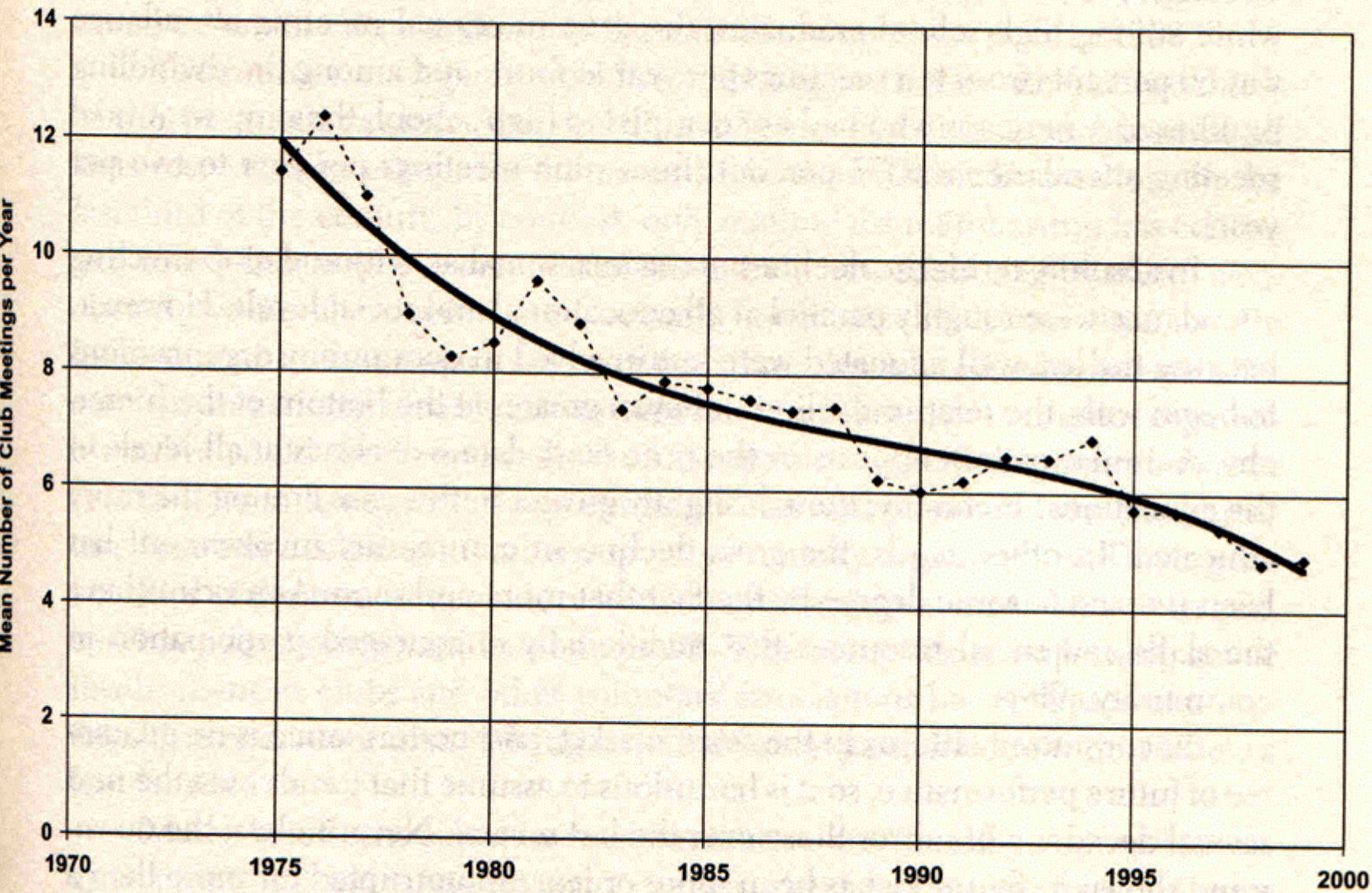


Figure 11: Club Meeting Attendance Dwindles, 1975–1999

United Way Giving, 1920–1997

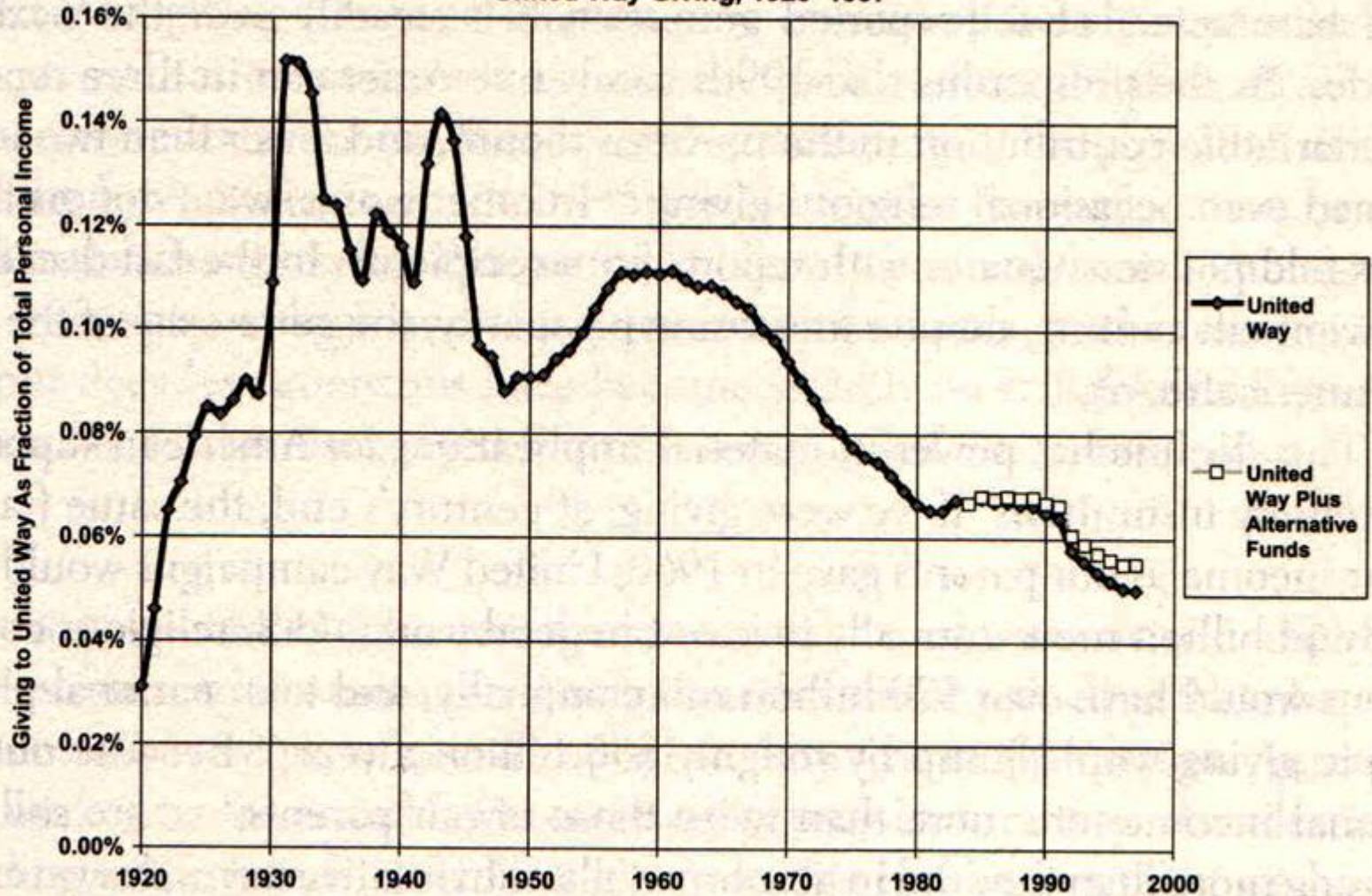


Figure 32: Trends in Protestant, Catholic, and United Way Giving, 1920s–1990s

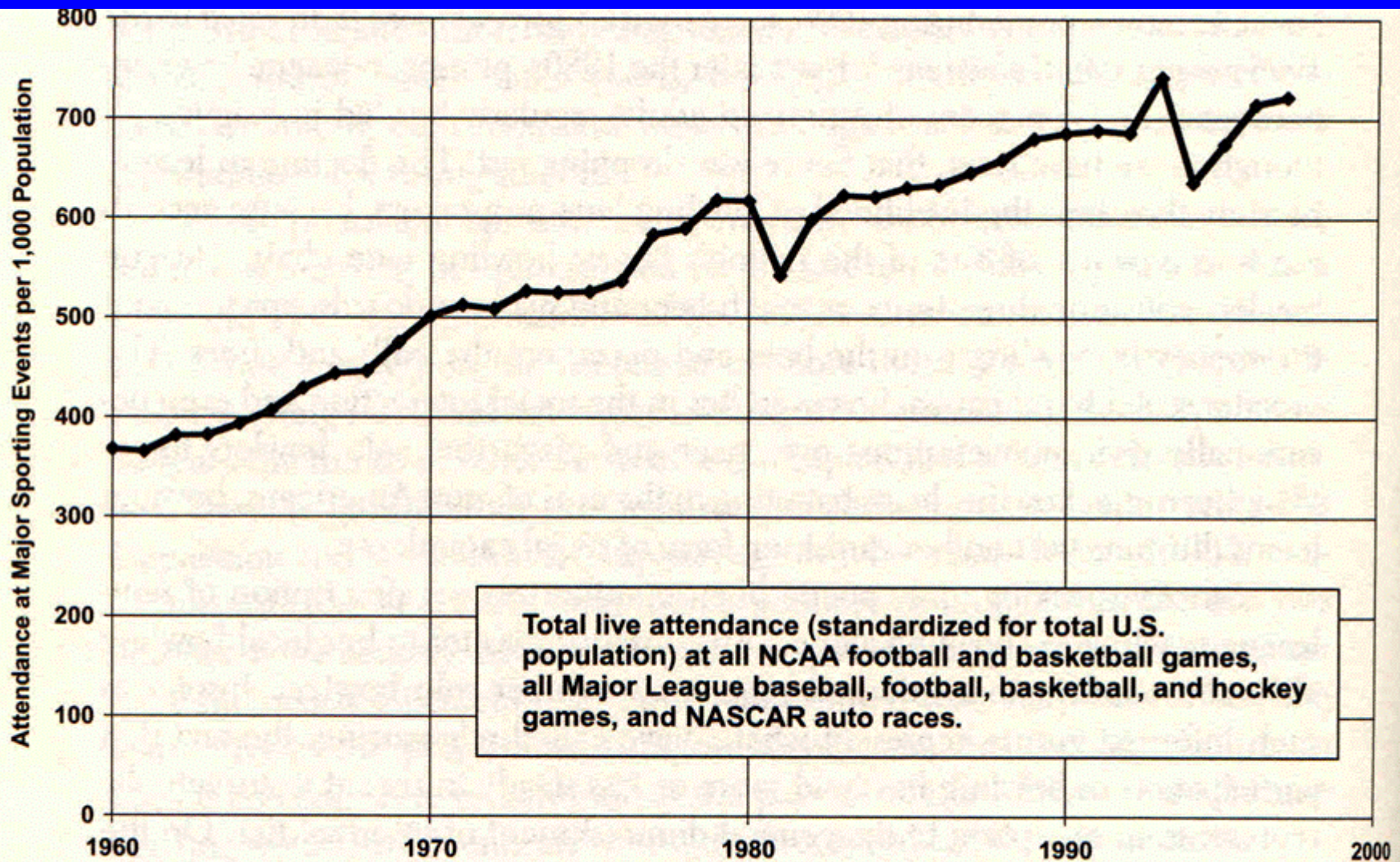


Figure 27: The Growth of Spectator Sports, 1960–1997

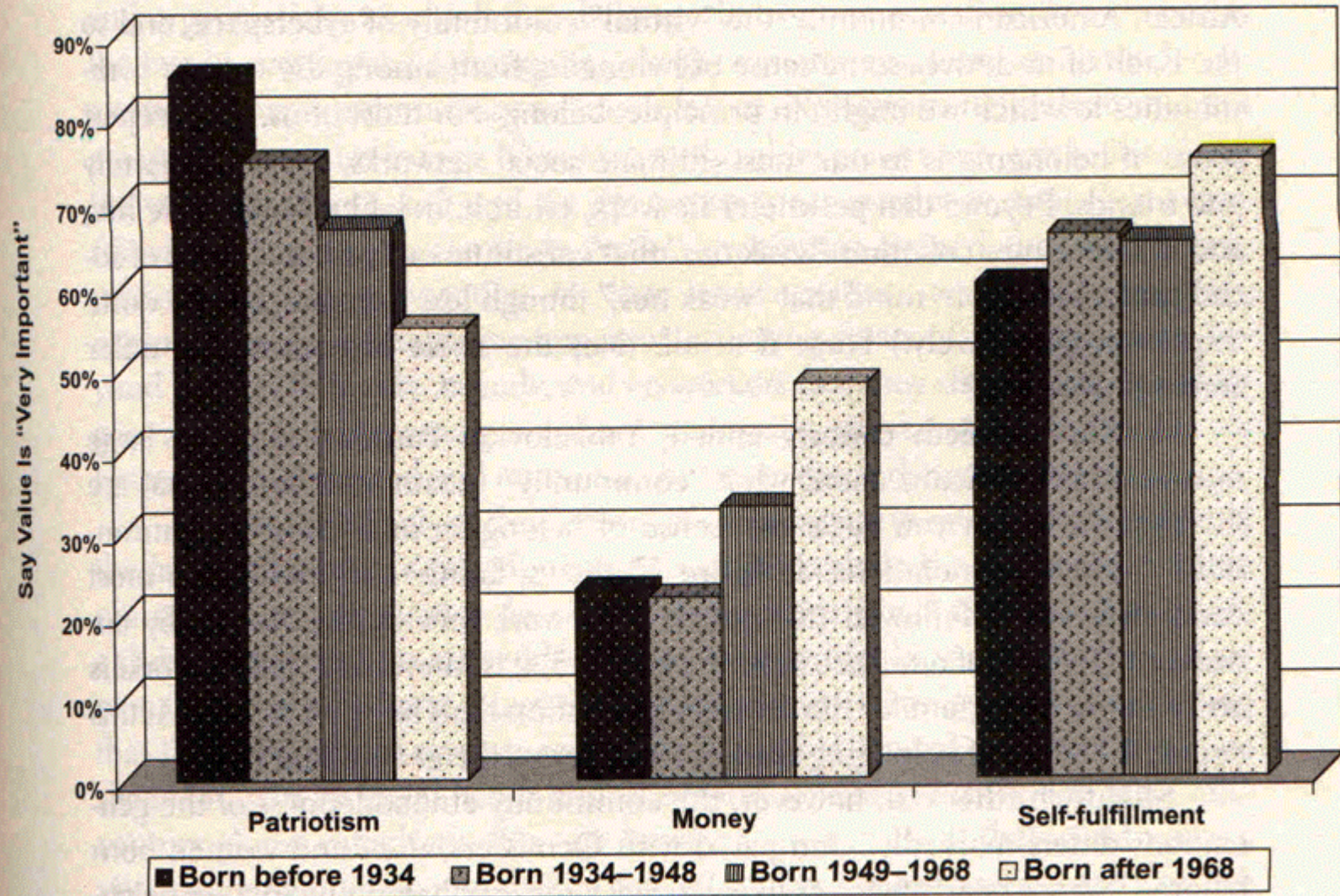


Figure 75: From Generation to Generation, Patriotism Wanes, Materialism Waxes

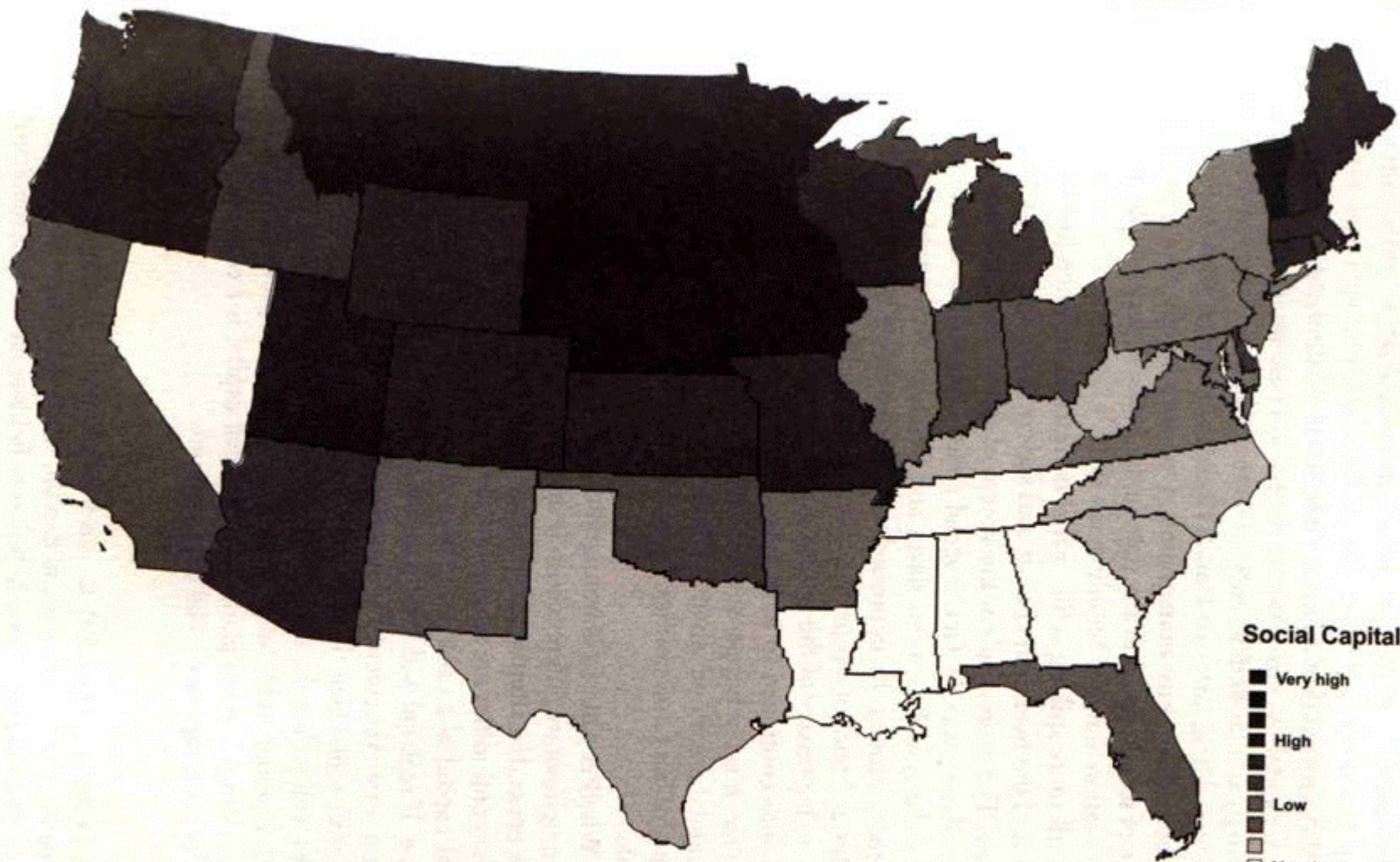


Figure 80: Social Capital in the American States

**Table 4: Measuring Social Capital in the American States**

| <i>Components of Comprehensive Social Capital Index</i>                  | <i>Correlation with Index</i> |
|--|-------------------------------|
| <b>Measures of community organizational life</b>                         |                               |
| Served on committee of local organization in last year (percent)         | 0.88                          |
| Served as officer of some club or organization in last year (percent)    | 0.83                          |
| Civic and social organizations per 1,000 population                      | 0.78                          |
| Mean number of club meetings attended in last year                       | 0.78                          |
| Mean number of group memberships   | 0.74                          |
| <b>Measures of engagement in public affairs</b>                          |                               |
| Turnout in presidential elections, 1988 and 1992                         | 0.84                          |
| Attended public meeting on town or school affairs in last year (percent) | 0.77                          |
| <b>Measures of community volunteerism</b>                                |                               |
| Number of nonprofit (501[c]3) organizations per 1,000 population         | 0.82                          |
| Mean number of times worked on community project in last year            | 0.65                          |
| Mean number of times did volunteer work in last year                     | 0.66                          |
| <b>Measures of informal sociability</b>                                  |                               |
| Agree that "I spend a lot of time visiting friends"                      | 0.73                          |
| Mean number of times entertained at home in last year                    | 0.67                          |
| <b>Measures of social trust</b>  |                               |
| Agree that "Most people can be trusted"                                  | 0.92                          |
| Agree that "Most people are honest"                                      | 0.84                          |

# Mortality is lower in high-social-capital states

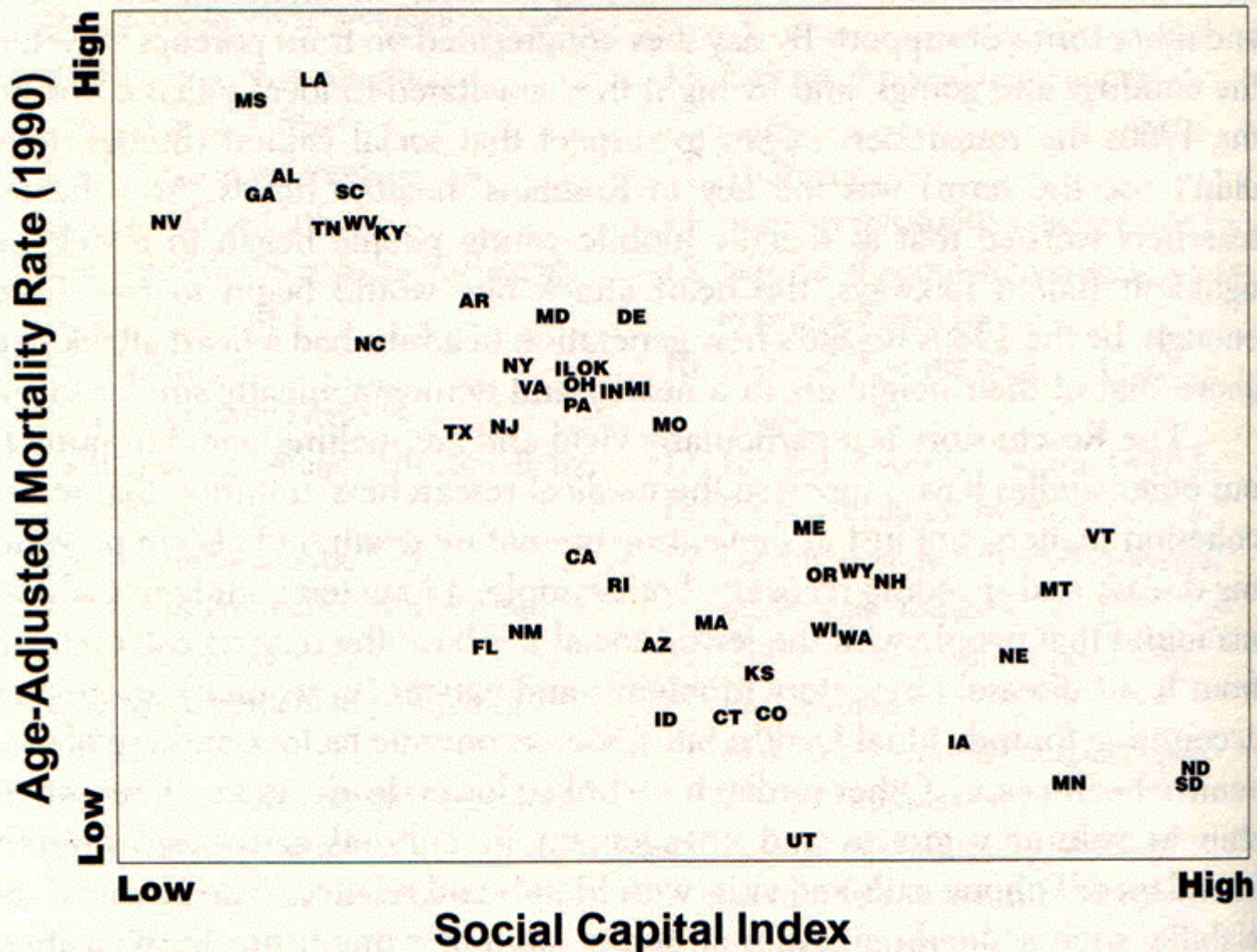


Figure 86: Health Is Better in High-Social-Capital States

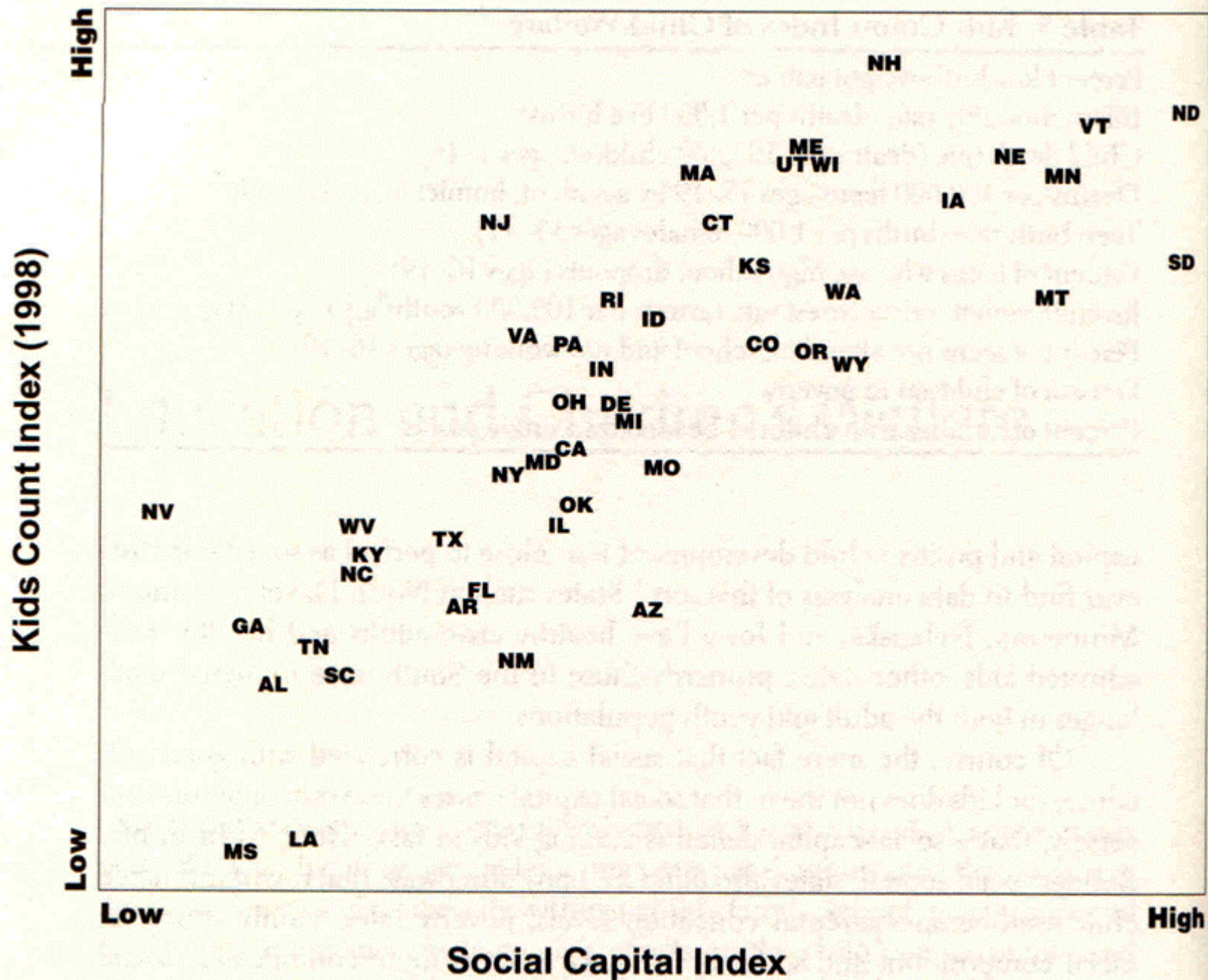


Figure 81: Kids Are Better Off in High-Social-Capital States



Index of Educational Performance (1990-96)

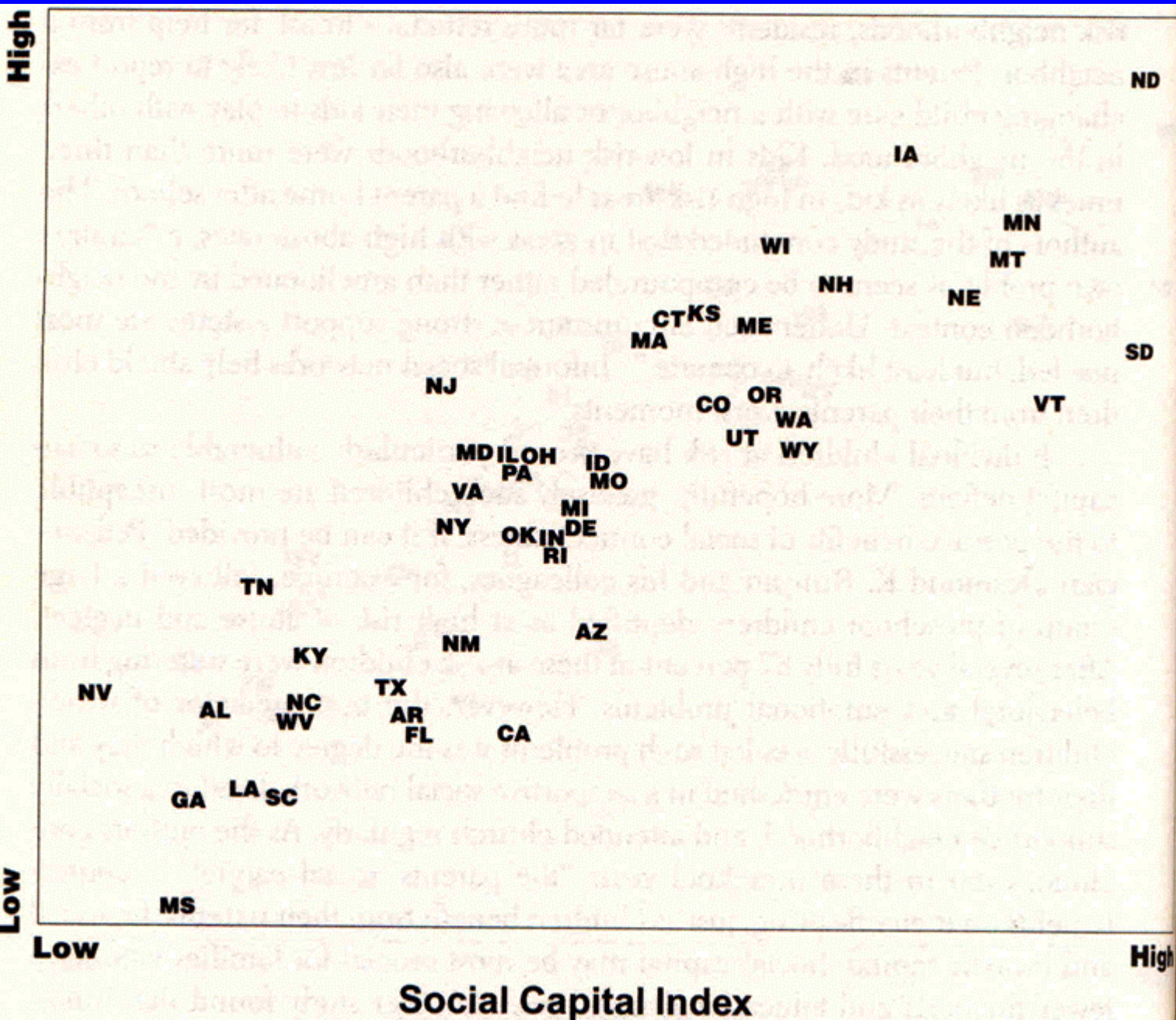
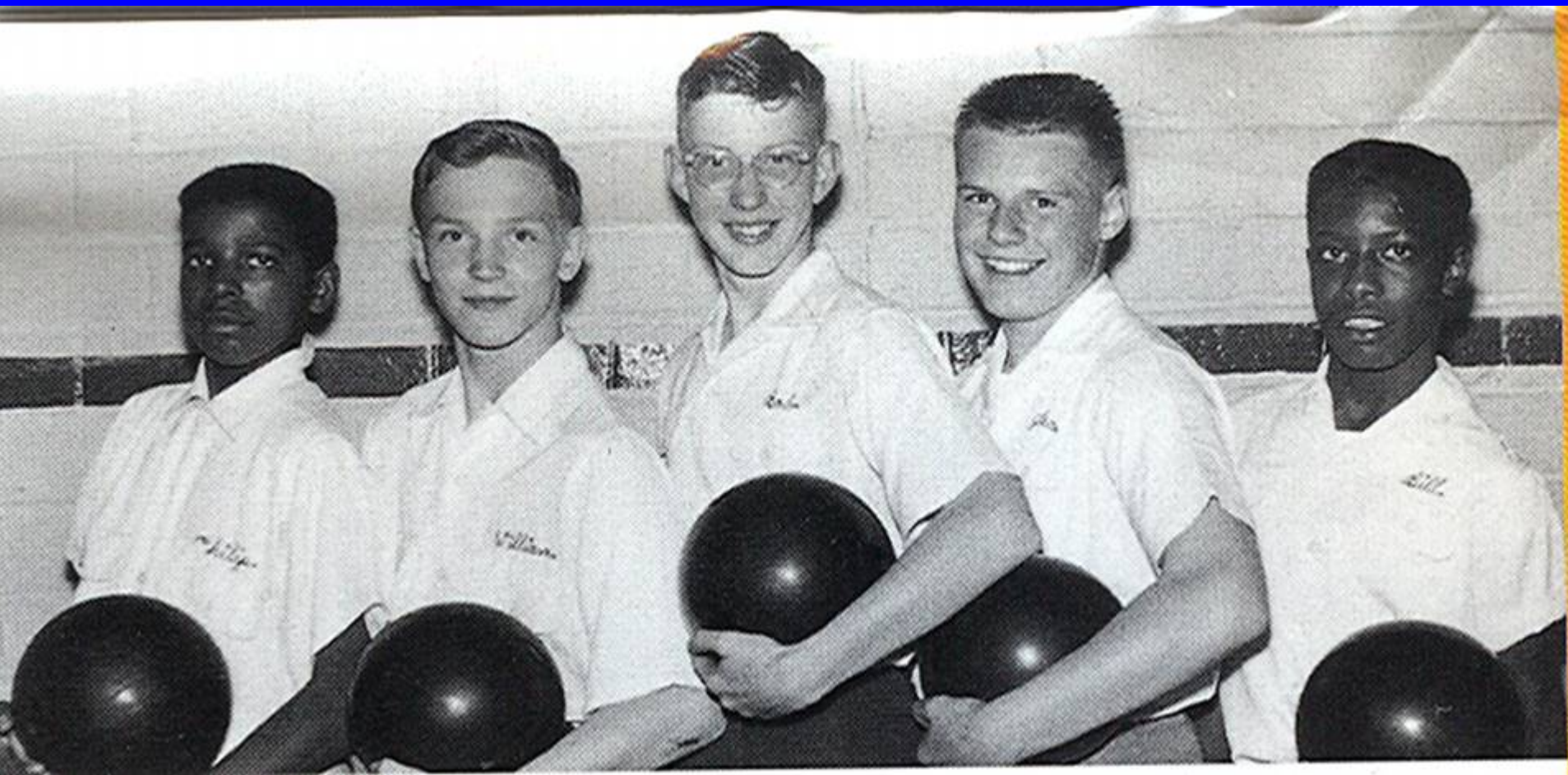


Figure 82: Schools Work Better in High-Social-Capital States

# So What?

- **Social capital operates through psychological and biological processes to improve individuals' lives.**
- **People whose lives are rich in social capital cope better with traumas and fight illness more effectively.**



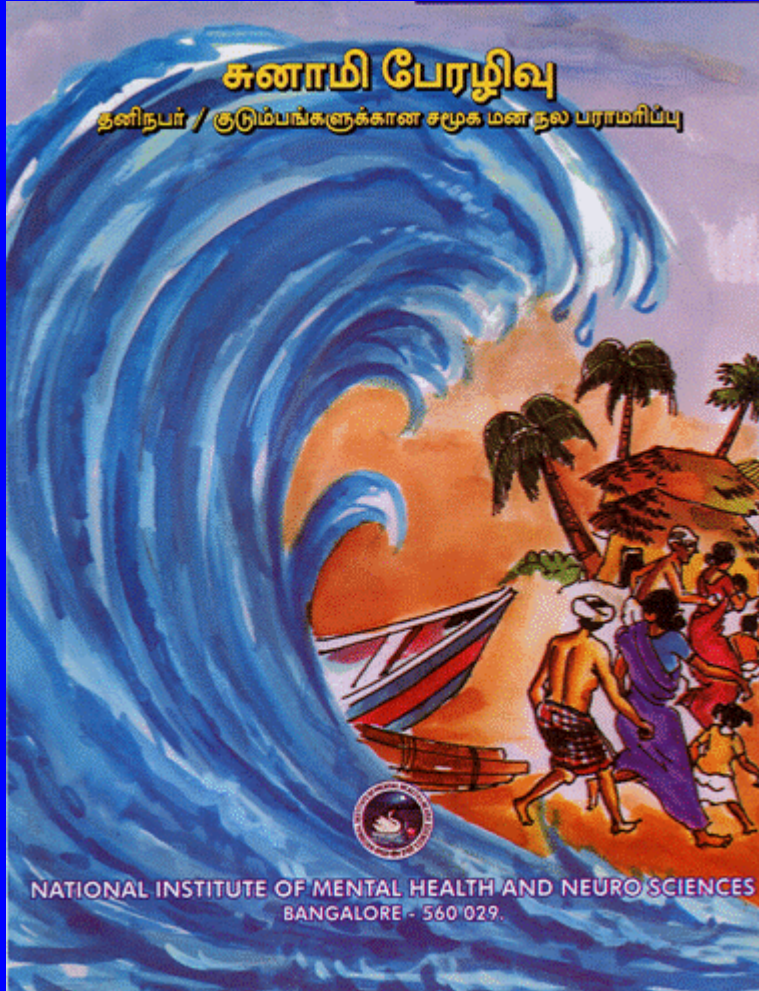
# **Psycho Neuro Immunology**

## **PNI**

- **The study of the link between psychological states and the functioning of the nervous system.**
- **The study of the interactions among the mind, immune system, and the neurological system that modulate susceptibility to disease or its progression**

# In the Wake of the Tsunami

- PsychoSocial Care of Disaster Victims



**Tsunami Survivors**



*P. Sabarinathan, 9 years, IV standard at  
Government Middle School, Akkaraipettai*

*'I am very scared to sleep. I get nightmares.  
I want to play with friends all the time so that I feel better.'*



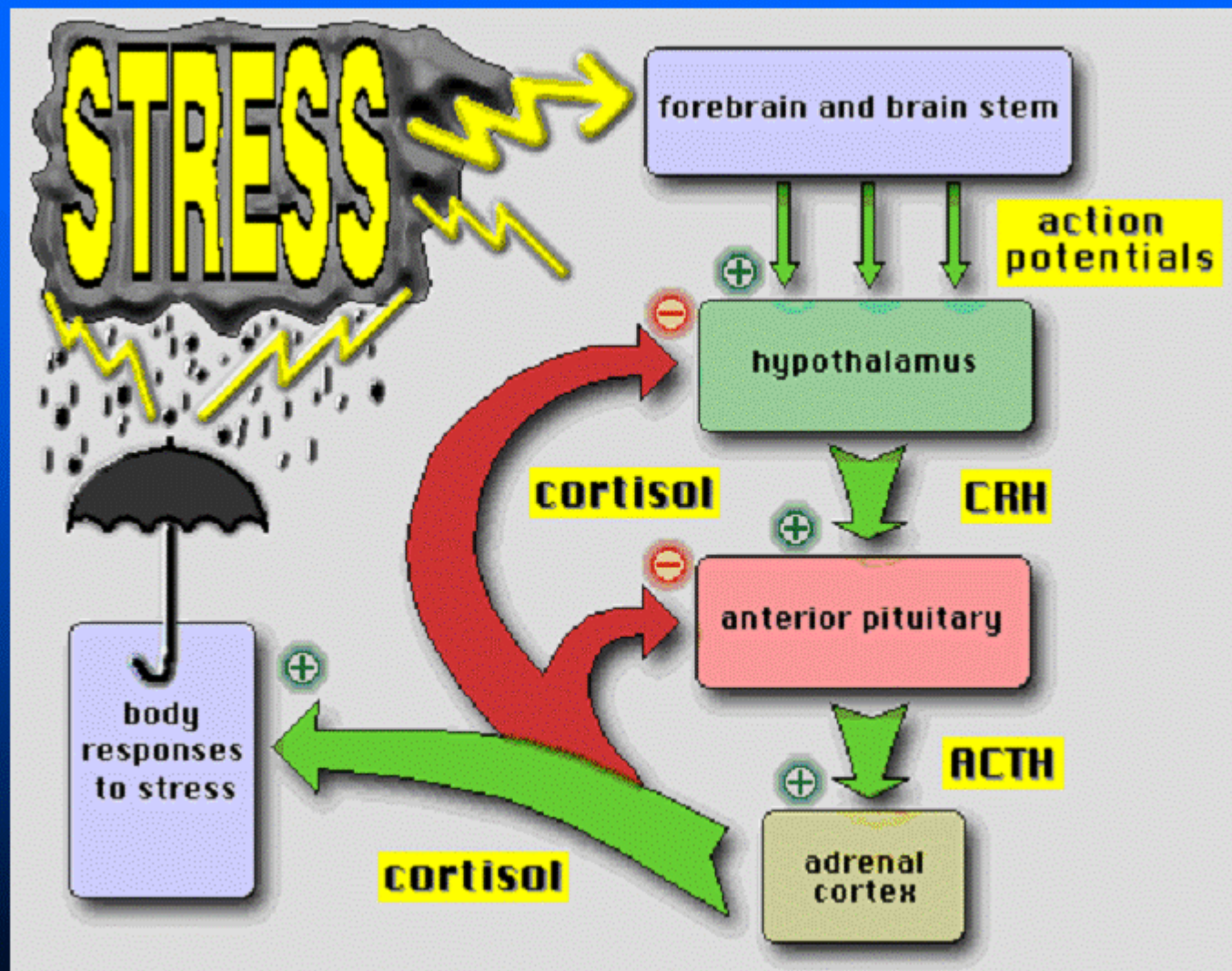




# Factors involved in healing

- CHEMOTHERAPY
- Attitude                      Community
- Spirituality                      Love/Family support
- Prayer - Meditation
  
- Mind over matter                      *Mountain climbing*
- Environment                      *Hanging out with Buddhists*
- EXERCISE                      FUN
- Diet                      Genes                      Laughter

# Stress and the Immune System



# Stressor Events

## Cataclysmic Disaster

- Effecting multiple people at the same time
  - Earthquake, war, terrorism

## Post-traumatic

- Re-experience of stress event as a dream or flashback
  - War experience
  - Childhood abuse

## Personal

- Major life event that have immediate effect but fade with time

## Background

- Daily irritating events

## Uplifting

Positive events that make one feel good

# Conditions with mind-body connections

Angina

Cardiac arrhythmias

Allergic skin reactions

Anxiety

Depression

Asthma

Herpes

Cough

Constipation

Diabetes

Ulcers

Fatigue

Hypertension

Infertility

Insomnia

N and V during pregnancy

Nervousness

All forms of pain: backaches, headaches  
abdominal pain, muscle pain, joint aches  
postoperative pain, neck, arm, and leg  
pain

Postoperative swelling

Premenstrual syndrome PMS

Arthritis

\* Side effects of cancer

\* Side effects of AIDS

# The Stress of Adjusting to Change

|                                   |     |
|-----------------------------------|-----|
| Death of Spouse                   | 100 |
| Divorce                           | 73  |
| Marital separation                | 65  |
| Jail term                         | 63  |
| Death of close family member      | 63  |
| Personal injury or illness        | 53  |
| Marriage                          | 50  |
| Fired at Work                     | 47  |
| Marital reconciliation            | 45  |
| Retirement                        | 45  |
| Change in health of family member | 44  |
| Pregnancy                         | 40  |
| Sex difficulties                  | 39  |
| Gain of new family member         | 39  |
| Business readjustment             | 39  |
| Change in financial state         | 38  |

# The Stress of Adjusting to Change

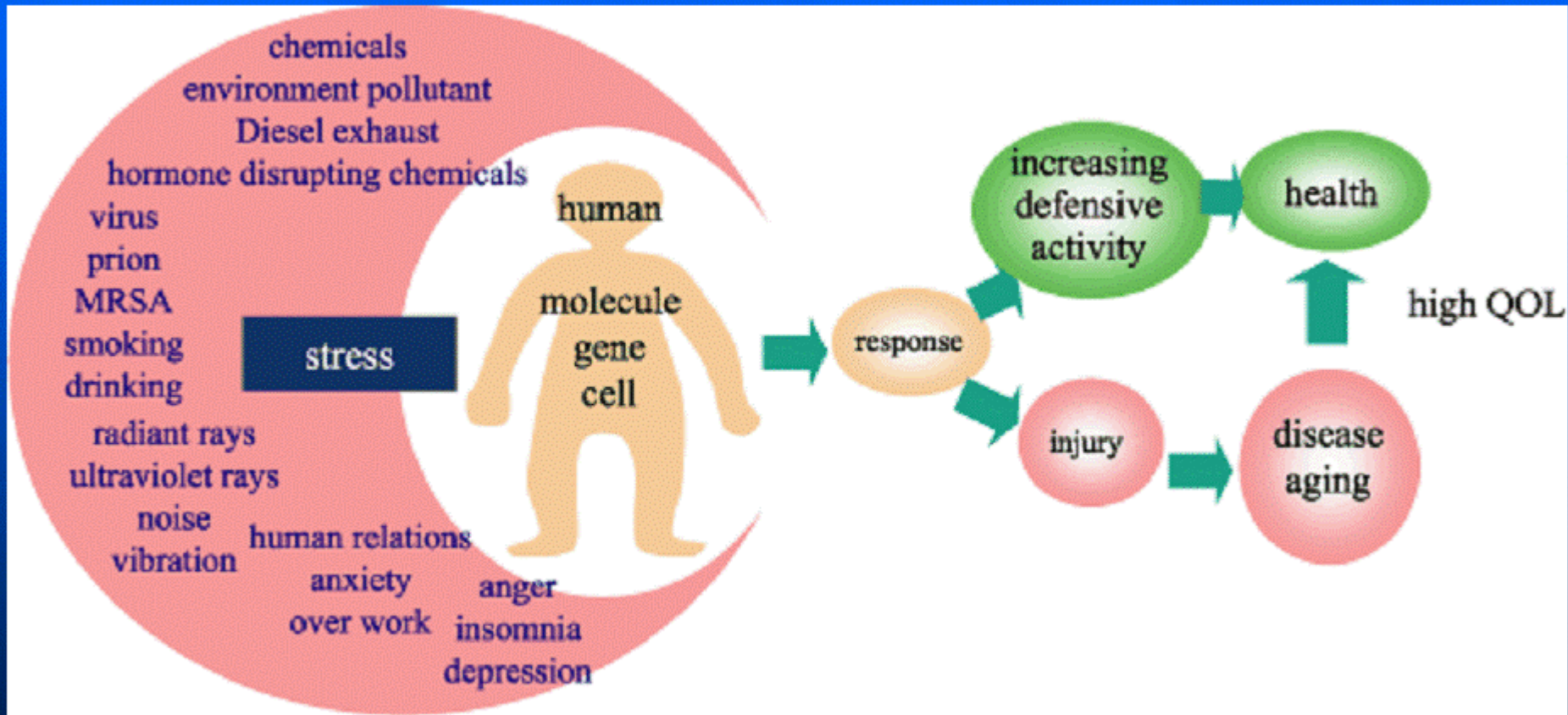
|  |    |
|--|----|
| Death of Close Friend                        | 37 |
| Change to a different line of work           | 36 |
| Change in number of arguments<br>with spouse | 35 |
| Mortgage over \$10,000                       | 31 |
| Foreclosure of mortgage or loan              | 30 |
| Change in responsibilities at work           | 29 |
| Son or daughter leaving home                 | 29 |
| Trouble with in-laws                         | 29 |
| Outstanding personal achievement             | 28 |
| Wife begins or stops work                    | 26 |
| Begin or end school                          | 26 |
| Change in living conditions                  | 25 |
| Trouble with boss                            | 23 |
| Change in residence, school                  | 20 |
| Vacation, Christmas                          | 12 |
| Minor violation of the law                   | 11 |

# Hassles

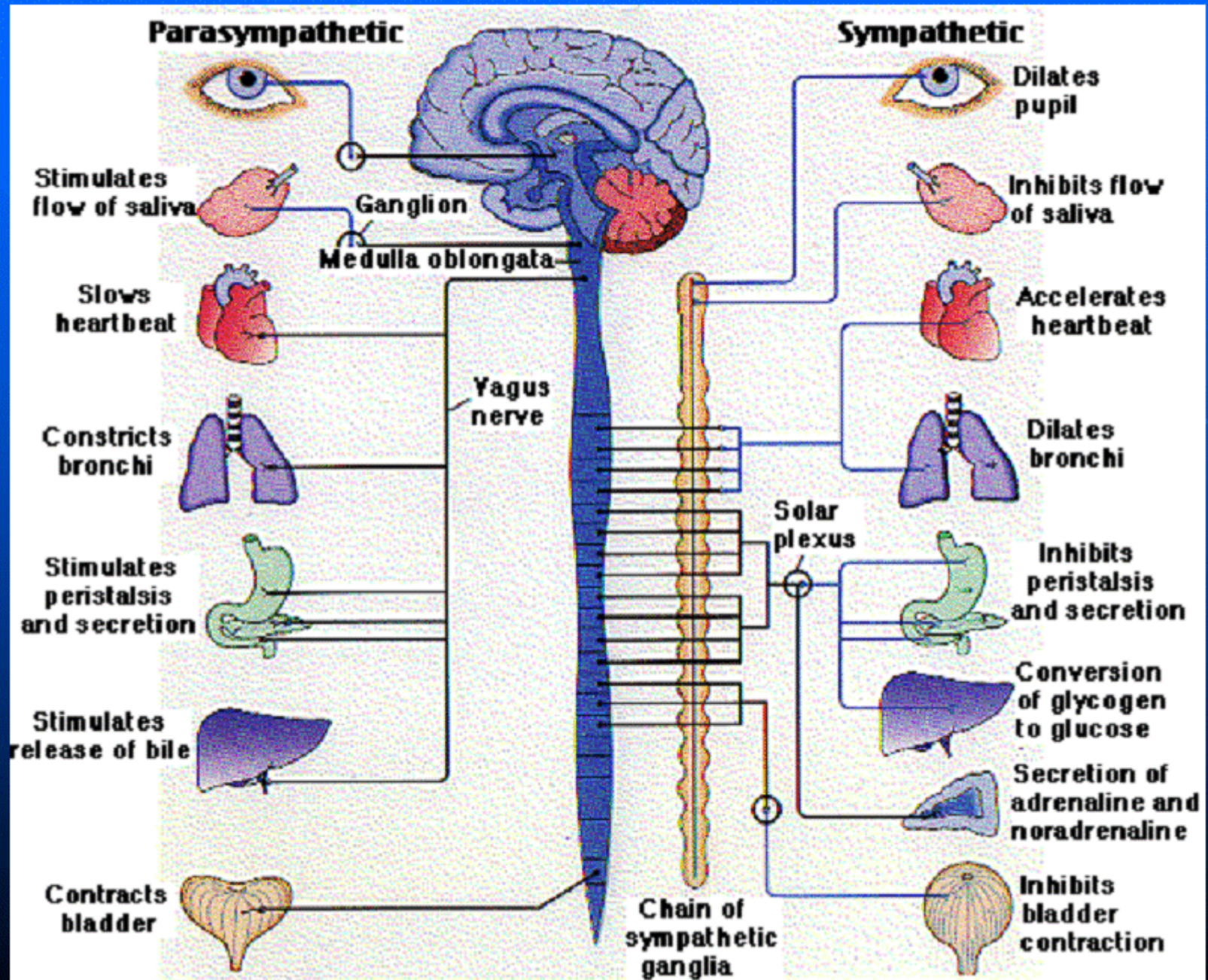
Misplacing or losing things  
Troublesome neighbors  
Concerns about owing money  
Too many responsibilities  
Planning meals  
Having to wait  
Being lonely  
Too many things to do  
Too many meetings  
Gossip  
The weather  
Difficulties with friends  
Difficulties with getting pregnant  
Auto maintenance  
Filling out forms  
Unchallenging work  
Problems with your lover

# Uplifts

Getting enough sleep  
The weather  
Not working (e.g. on vacation)  
Getting into good physical shape  
Quitting smoking  
Sex  
Spending time with family  
Shopping  
Making a friend  
Looking forward to retirement  
Being complimented  
Going someplace that 's different  
Giving love  
Being "one" with the world  
Flirting  
Having good ideas at work  
Socializing







# FIGHT or FLIGHT

## NOTICEABLE EFFECTS

PUPILS DILATE  
MOUTH GOES DRY  
NECK + SHOULDER  
MUSCLES TENSE  
HEART PUMPS FASTER  
CHEST PAINS  
PALPITATIONS  
SWEATING  
MUSCLES TENSE  
FOR ACTION  
BREATHING FAST  
+ SHALLOW -  
HYPERVENTILATION  
OXYGEN NEEDED  
FOR  
MUSCLES

## HIDDEN EFFECTS

BRAIN GETS BODY  
READY FOR ACTION  
ADRENALINE  
RELEASED FOR  
FIGHT/FLIGHT  
BLOOD PRESSURE  
RISES  
LIVER RELEASES  
GLUCOSE TO PROVIDE  
ENERGY FOR MUSCLES  
DIGESTION SLOWS -  
OR CEASES  
SPHINCTERS CLOSE -  
THEN RELAX  
CORTISOL RELEASED  
(DEPRESSES THE  
IMMUNE SYSTEM)

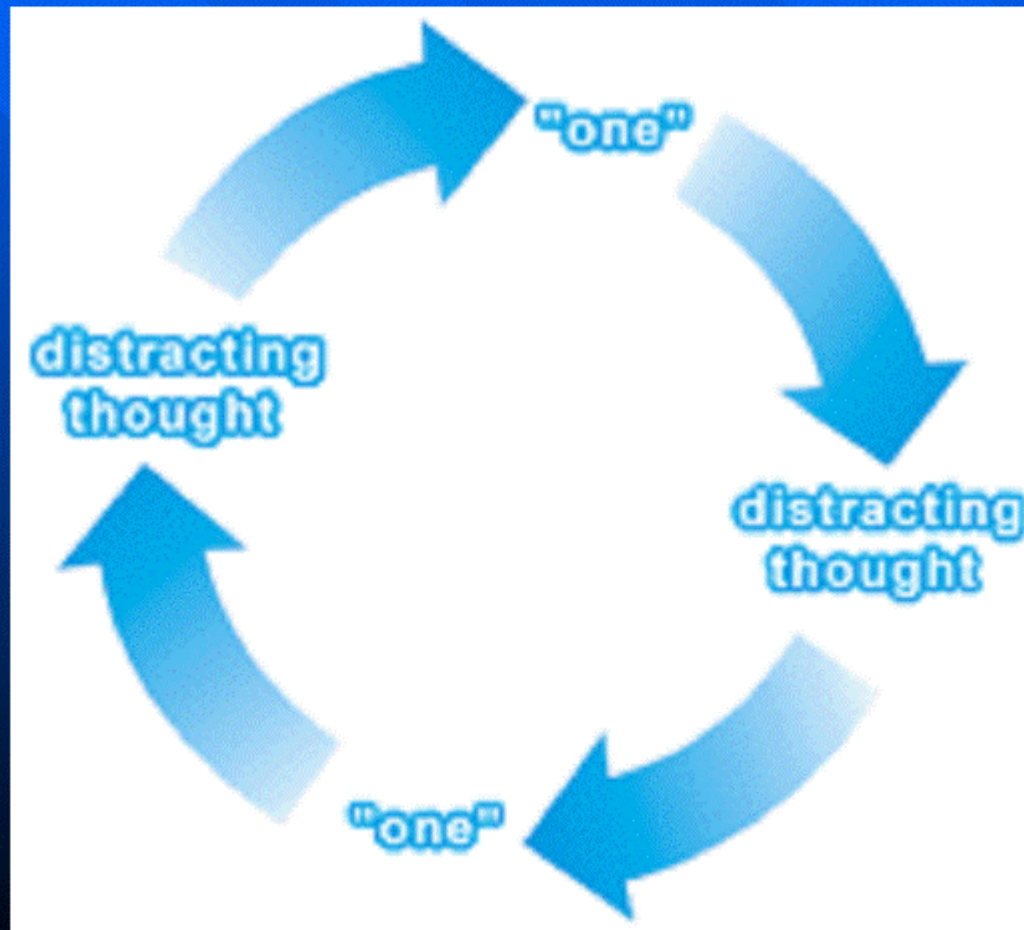
F. Hedges



# **Non-pharmacologic approach to anxiety**

- **Deep breathing**
- **Progressive muscle relaxation**
- **Guided imagery**

# The Relaxation Response






**CLASSIFICATIONS OF MANOVIKAR (MENTAL DISORDERS)**

1. MANODHISTHITA MANOVIKARA : EMOTIONAL (NEUROTIC) DISORDER  
 2. UBHAYADHISTHITA MANOVIKARA : DUAL TYPE MENTAL DISORDERS  
 SHAREERAMANODHISTHITA MANOVIKARA : BODY - MIND TYPE PSYCHOLOGICAL DISORDERS.  
 B. MANASHAREERADHISTHITA MANOVIKARA : MIND - BODY TYPE PSYCHOLOGICAL DISORDERS (SOMATISED NEUROTIC CONDITIONS).

**MANODHISTHITA MANOVIKARA : EMOTIONAL (NEUROTIC) DISORDERS**

|             |                |          |              |       |         |
|-------------|----------------|----------|--------------|-------|---------|
| ABHYASUYA   | : JEALOUSY     | KRODHA   | : ANGER      | LOBHA | : GREED |
| MOHA        | : INFATUATION  | KAMA     | : PASSION    | SHOKA | : GRIEF |
| VISHADA     | : LASSITUDE    | BHAYA    | : FEAR       | MANA  | : PRIDE |
| DAINYA      | : HELPLESSNESS | MATSARYA | : HOSTILITY  |       |         |
| MADA        | : ARROGANCE    | HARSHA   | : JUBILATION |       |         |
| CHITTODVEGA | : ANXIETY      | IRSHA    | : ENVY..     |       |         |

**SOURCE - AYURVEDIC TEXTS**





“Milt, I’m beginning to think that your illness is a disharmony of life energy”