

# INFLAMATION AND CANCER

NANIALEI GOLDEN, M.D., F.A.C.R.O.

RADIATION ONCOLOGY MEDICAL DIRECTOR, HEALTH FIRST CANCER SERVICES ASSISTANT PROFESSOR, UNIVERSITY OF CENTRAL FLORIDA COLLEGE OF MEDICINE





#### PROTO-ONCOGENE

- A normal gene that mutates and can give rise to cancer.
- Thousands of proto-oncogenes





#### INFLAMATION

- The Good, The Bad, and the Ugly
- Inflamation is the immune system's response to various insults
- The Good Protective
- The Bad Overstimulation is pathologic
- The Ugly If excessive, major scar tissue





#### THE GOOD

- Inflamation is the immune system's response to various insults
- Protective
  - Pain limits further damage
  - Clear bacteria and other pathogens





#### THE GOOD

- After cancer surgery, immune cells converge to stimulate healing
- High numbers of "Tumor Infiltrating Lymphocytes" (TIL's) conveys a protective effect with better outcomes
  - CD3+ IM, CD8+ CCN





#### THE BAD

- Inflamation can lead to overstimulation of the immune system and lead to other diseases
- Inflamation associated with:
  - Cancer
  - Obesity
  - Heart disease
  - Stroke
  - Autoimmune disorders (Lupus, Celiac Dz)





#### THE BAD

- Excessive inflamatory conditions:
  - Asthma
  - Chronic bladder infections
    - Squamous Cell Carcinoma
  - Inflamatory Bowel Diseases
    - Ulcerative Colitis
    - Crohn's Disease





#### THE UGLY

- Excessive inflamation leads to scar tissue.
- But it's not scar tissue you can see from the outside.





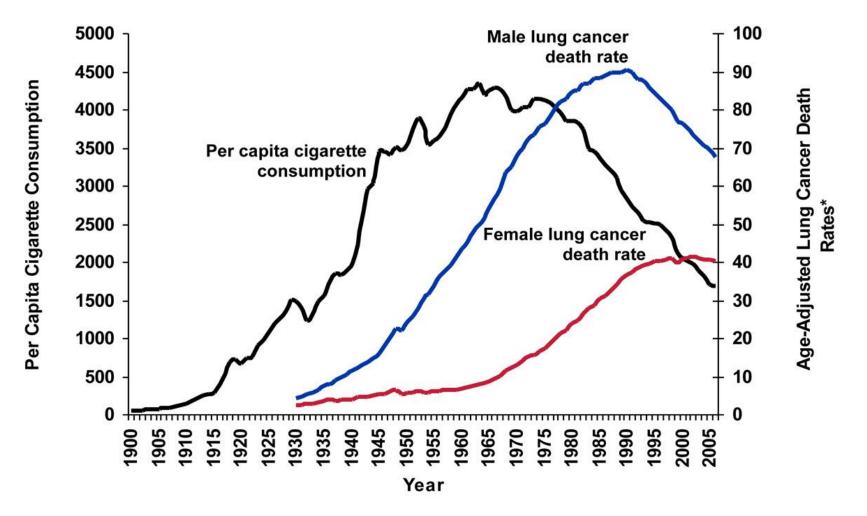
#### **SMOKING STATISTICS**

- 20% OF AMERICANS ARE SMOKERS
- # 1 RISK FACTOR FOR CANCER
  - ->1/3 OF 500,000 US CANCER DEATHS
- # 2 RISK FACTORS
  - OBESITY, PHYSICAL INACTIVITY
  - 1/3 OF 500,000 US CANCER DEATHS
- THUS ~2/3 OF CANCER DEATHS ARE POTENTIALLY PREVENTABLE



#### Tobacco Use in the US, 1900-2006



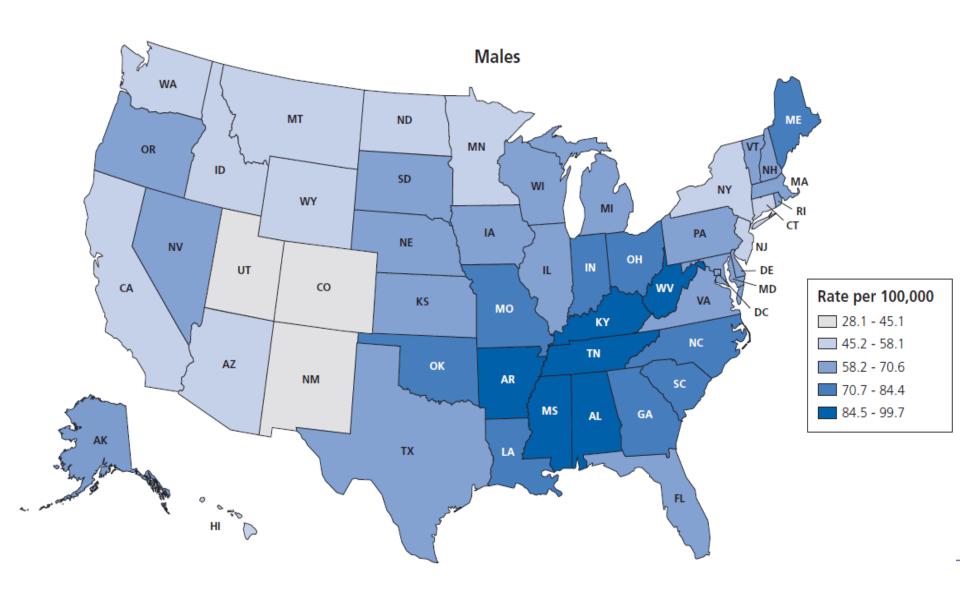


\*Age-adjusted to 2000 US standard population.

Source: Death rates: US Mortality Data, 1960-2006, US Mortality Volumes, 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2009. Cigarette consumption: US Department of Agriculture, 1900-2007.

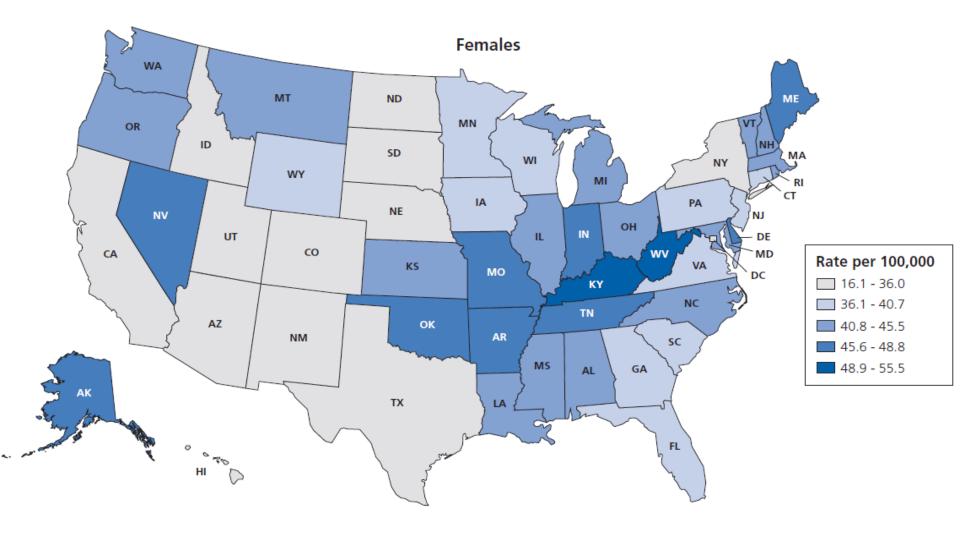


#### Geographic Patterns in Lung Cancer Death Rates\* by State, US, 2005-2009



#### Geographic Patterns in Lung Cancer Death Rates\* by State, US, 2005-2009









#### PROTO-ONCOGENE

- Lung cancer and COPD (emphysema) are related.
- Both strongly associated with tobacco.
- COPD doubles the risk of lung cancer.
- c-Src is mutated with cigarette smoke
- Inflamatory chemicals create a chain reaction
  - MMP-9, -12, cathepsin G, K, IL-17, TNF-α, MCP-1 and KC
- Creates environment conducive to cancer.



## **WE'VE COME** A LONG WAY, **BABY!!**

According to repeated nationwide surveys,

# **More Doctors** Smoke CAME than any other cigarette!

Dectors in every branch of medicine were asked. What cigarette de you smake?" The brand named most was Camel!

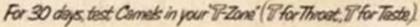
You'll supp Canada he she some consum no mante alternate name chase. Comella have thel, total management, purch after purch; and s. flat or economiched by one without expension Make this avenible year hander only Cample for 10 days and use now well Carrely places your tosse, been well they well Free through as your much associa. Was II we have supresselve a experience can be?

#### THE DOCTORS' CHOICE IS AMERICA'S CHOICE!













#### FLORIDA OBESITY STATISTICS

- ADOLESCENTS BMI
  - 15% OVERWEIGHT
  - 11% **OBESE**
- ADULTS BMI
  - 38% OVERWEIGHT
  - **-24% OBESE**

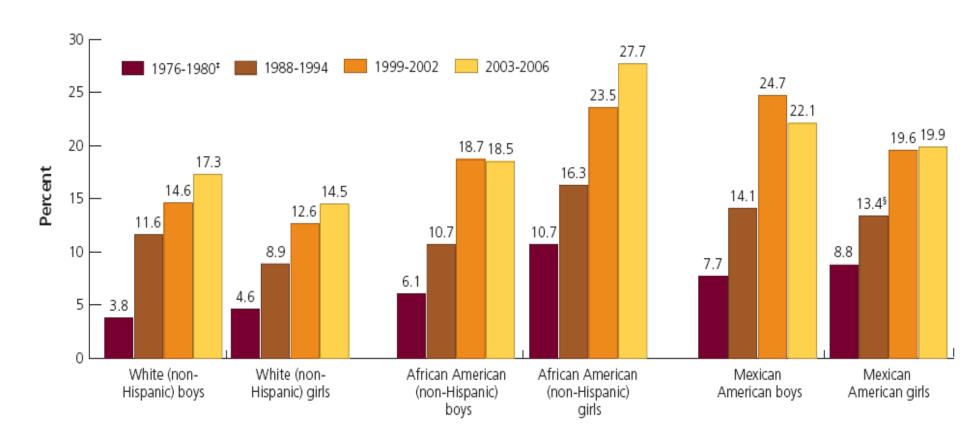


Height	Body weight (pounds)			
(feet, inches)	Overweight*	Obese <sup>†</sup>	Extremely Obese <sup>‡</sup>	<b>BODY MASS</b>
6′4″	205	246	328	
6′3″	200	240	319	INDEX
6′2″	194	233	311	
6′1″	189	227	302	
6'0"	184	221	294	
5′11″	179	215	286	<ul> <li>OVERWEIGHT</li> </ul>
5′10″	174	209	278	- BMI 25-29.9
5′9″	169	203	270	— DIVII 23-23.3
5′8″	164	197	262	
5′7″	159	191	255	ODECE
5′6″	155	186	247	<ul> <li>OBESE</li> </ul>
5′5″	150	180	240	- BMI 30-39.9
5'4"	145	174	232	
5′3″	141	169	225	
5'2"	136	164	218	• EVT OBESE
5′1″	132	158	211	• EXT OBESE
5′0″	128	153	204	− BMI >40
4'11"	124	148	198	——————————————————————————————————————
4′10″	119	143	191	——————————————————————————————————————



## **ADOLESCENT OBESITY**

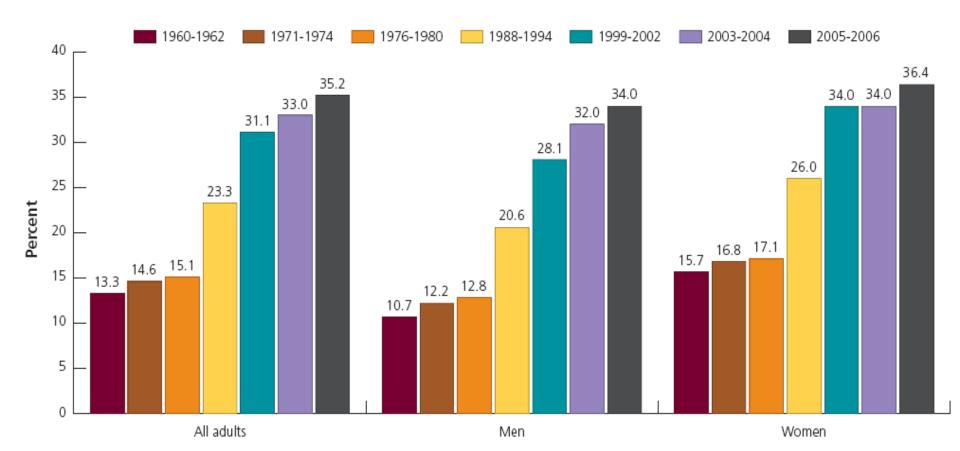
Figure 2A. Obesity\*, Adolescents 12-19 Years, by Gender & Race/Ethnicity†, US, 1976-2006





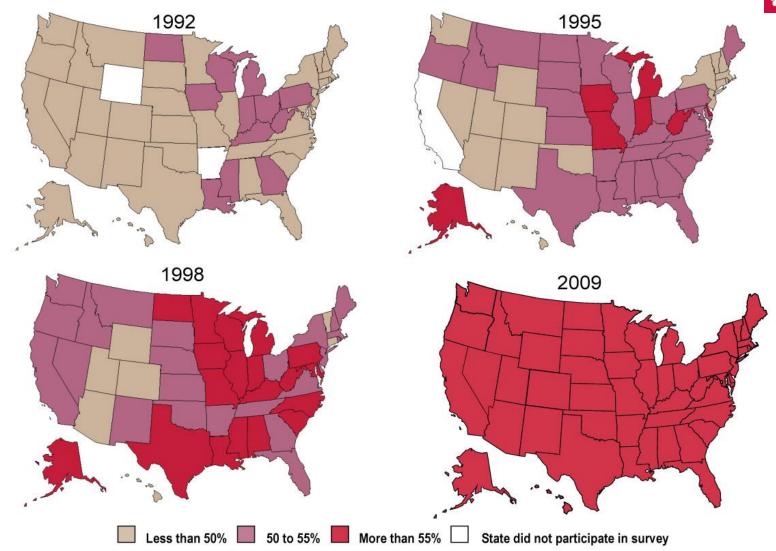
## **ADULT OBESITY TRENDS**

Figure 2B. Obesity\*, Adults 20-74 years, by Gender, US, 1960-2006<sup>†</sup>

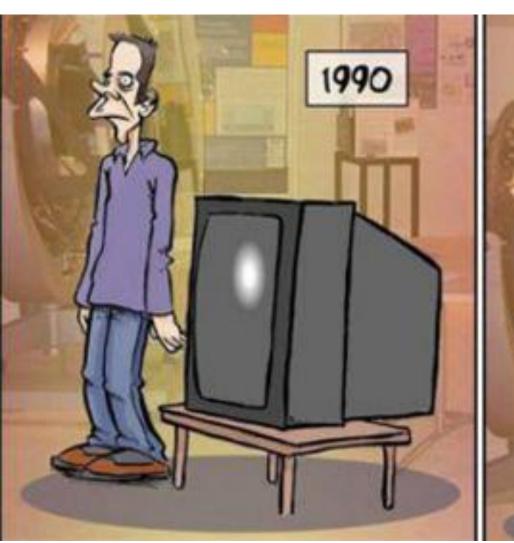


## Trends in Overweight\* Prevalence (%), Adults 18 and Older, US, 1992-2009





\*Body mass index of 25.0 kg/m<sup>2</sup>or greater. Source: Behavioral Risk Factor Surveillance System, CD-ROM (1984-1995, 1998) and Public Use Data Tape (2004-2009), National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 2010.









#### **OBESITY AND CANCER**

- Inflamation can lead to overstimulation of the immune system and lead to other diseases
- Clear association
  - Breast
  - Colon
  - Endometrium
  - Esophagus
  - Kidney





#### **OBESITY AND CANCER**

- RISK OF CANCER INCREASED FOR
  - PANCREAS
  - GALLBLADDER
  - THYROID
  - OVARIAN
  - CERVIX
  - MULTIPLE MYELOMA
  - HODGKIN'S LYMPHOMA
  - AGGRESSIVE PROSTATE CANCER





#### **OBESITY AND CANCER**

- Surgery for morbid obesity
  - Reduced mortality from diabetes, heart disease and cancer.

Obesity is considered a low grade inflamatory disease





#### **DIABETES**

- Glucose rises, insulin rises to surpress
- Chronically elevated glucose overwhelms and insulin can't keep up
- Leads to Metabolic Syndrome
  - Increase risk for heart disease
  - Increases risk for cancer through growth factor stimulation





#### METABOLIC SYNDROME

- Risk factors that increase risk of heart disease, stroke and cancer
- Having 3 of 5 diagnostic for Met. Syndrome
  - Large waistline (apple shape)
  - High Triglycerides (or being on meds for it)
  - Low HDL (the good cholesterol)
  - High Blood Pressure (or being on meds for it)
  - High fasting blood sugar





#### **APPLE SHAPE**

- Fatty deposition in the abdomen is a greater risk for heart disease than on the hips (pear shape).
- Chemicals released by abdominal fat are different than those in other parts of the body.





#### HIGH TRIGLYCERIDES

- Fat that is circulating in the blood stream
- Patients think that because they are on medication that their risk is back to baseline but that is false.





#### LOW HDL

- HDL helps remove cholesterol from the arteries.
- You can have totally normal LDL, cholesterol, and triglyceride levels but a low HDL increases risk of heart disease.





#### HIGH BLOOD PRESSURE

- Elevated pressure in the arteries causes damage. The damage incites an inflamatory response. That is what leads to the plaque build-up that clogs arteries
- Clogged carotid arteries increases risk of stroke
- Clogged heart arteries causes heart attacks





#### HIGH FASTING BLOOD SUGAR

 Mildly high glucose may be an early sign of diabetes.





## **METABOLIC SYNDROME**

- One study estimated that 25% of US population has it.
- You don't have complete control.
- Genetics plays a role.
  - Triglycerides, low HDL are familial
- BUT for most overweight/obese adults, weight reduction and a healthy lifestyle will lower BP and glucose, many can stop meds and reduce risk.





#### ROLE OF PLATELETS

- Platelets are what allows our blood to clot
- They have a direct relationship with inflamation through interaction with immune cells and endothelial cells.
- Damage to the lining of arteries causes platelets to recruit other cells that eventually leads to atherosclerosis.





#### **MODIFIERS**

- Aspirin and Cyclooxygenase(COX)-2 inhibitors (like Celebrex)
  - Blocks certain inflamatory pathways
  - Protective against heart disease
  - ASA has some protection for colon cancer
- Side effects
  - Bleeding, stomach ulcers





#### **BACTERIA**

- Infection stimulates an immune response
- Bacterial endocarditis linked to oral health
- Gut microbes linked to certain GI cancers





#### **HEALTHY LIVING**

- There is no food, pill, herb, liquid, or other concoction that is currently known to selectively attract the "good" immune cells and block the "bad".
- Be skeptical of products that "work with your immune system" or "boost your immune system"





#### LIFESTYLE RECOMMENDATIONS

- POSTMENOPAUSAL WOMEN
- CALCIUM 1,200-1,500 mg/d
- VITAMIN D 800U/d
- WEIGHT-BEARING EXERCISE
- MODERATE ALCOHOL USE
  - >1 DRINK / DAY
- SMOKING CESSATION





#### **HEALTHY LIFESTYLE**

- EAT LOTS OF FRUITS, VEGGIES, & WHOLE GRAINS
- EXERCISE REGULARLY
- MAINTAIN HEALTHY WEIGHT
- USE SUNSCREEN
- AVOID TANNING SALONS
- AVOID TOBACCO PRODUCTS
- WEAR YOUR SEATBELT
- ALCOHOL AND DRIVING DON'T MIX AND NEITHER DO CELL PHONES





# Cancer Services



Dr. Nani Golden