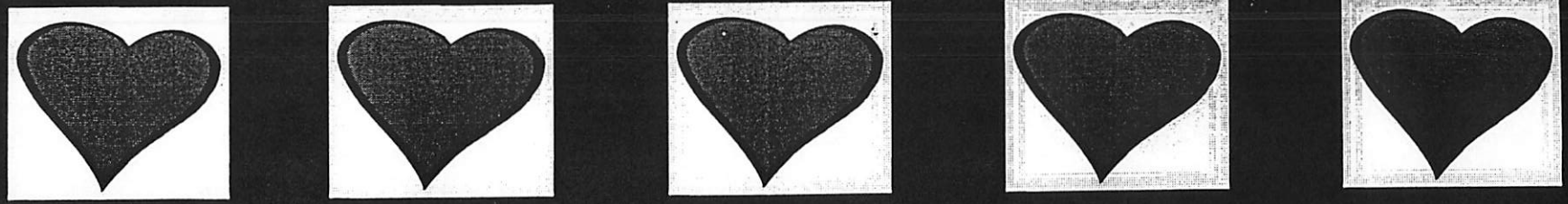
PEDIATRIC

PREVENTATIVE

CARDIOLOGY



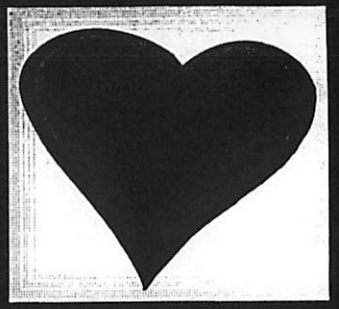
Pediatric Preventive Cardiology

Margaret M. Samyn, MD FAAP, FACC

University of Florida

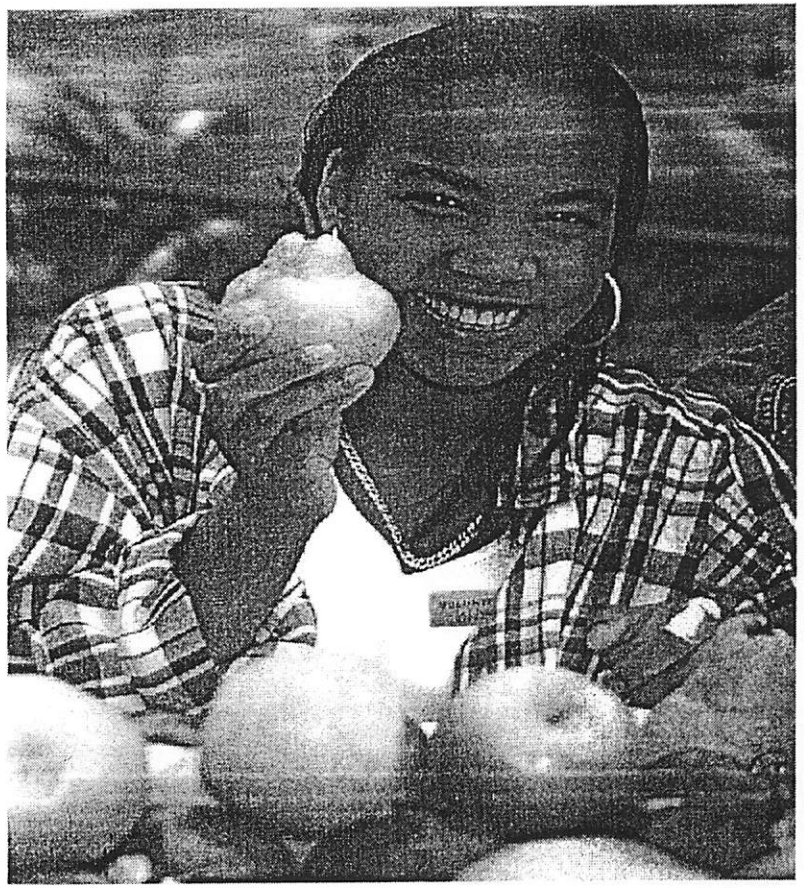
Clinical Associate Professor

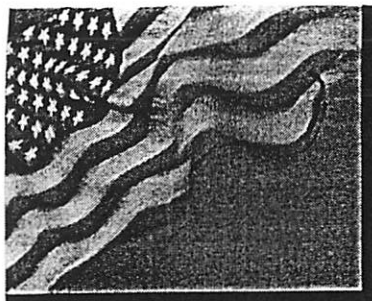
Agenda



- Scope of the Problem
- Precursors for CAD in Childhood
- AHA Guidelines for Hyperlipidemia Tx

The Scope of the Problem





Cardiovascular Disease

AHA 2002 Heart & Stroke Statistical Update,
Dallas, Texas

61.8 Million Americans with CV disease

- 50 Million – Hypertension
- 44.2 Million - Obesity
- 41.3 Million – Hypercholesterolemia
- **12.6 Million – Coronary heart disease**
- 4.8 Million - CHF
- 4.6 Million – Stroke

- **1 Million – Congenital cardiovascular defects**
  40,000 babies born with congenital heart disease

Cardiovascular Disease
The Leading Cause of Death for All Males & Females

What is atherosclerosis?

- Affects medium & large arteries throughout the body.
- Inflammation and cellular & lipid (fat) accumulation within vessel walls, leads to eventual luminal narrowing (artery stenosis).
- Prevents good oxygenated blood delivery to tissues.
- While initially asymptomatic, symptoms progressively occur as luminal narrowing combines with acute thrombotic (clotting) events.

Autopsy evidence: "Clogged arteries" begin in childhood as arteries w/ fatty streaks.

Role of LDL & HDL Cholesterol

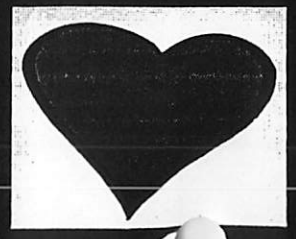
LDL

- Synthesizes cell membranes & steroid hormones
- Generates foam cells of early atherosclerosis
- * **2/3 removed by liver; 1/3 by scavenger pathways**

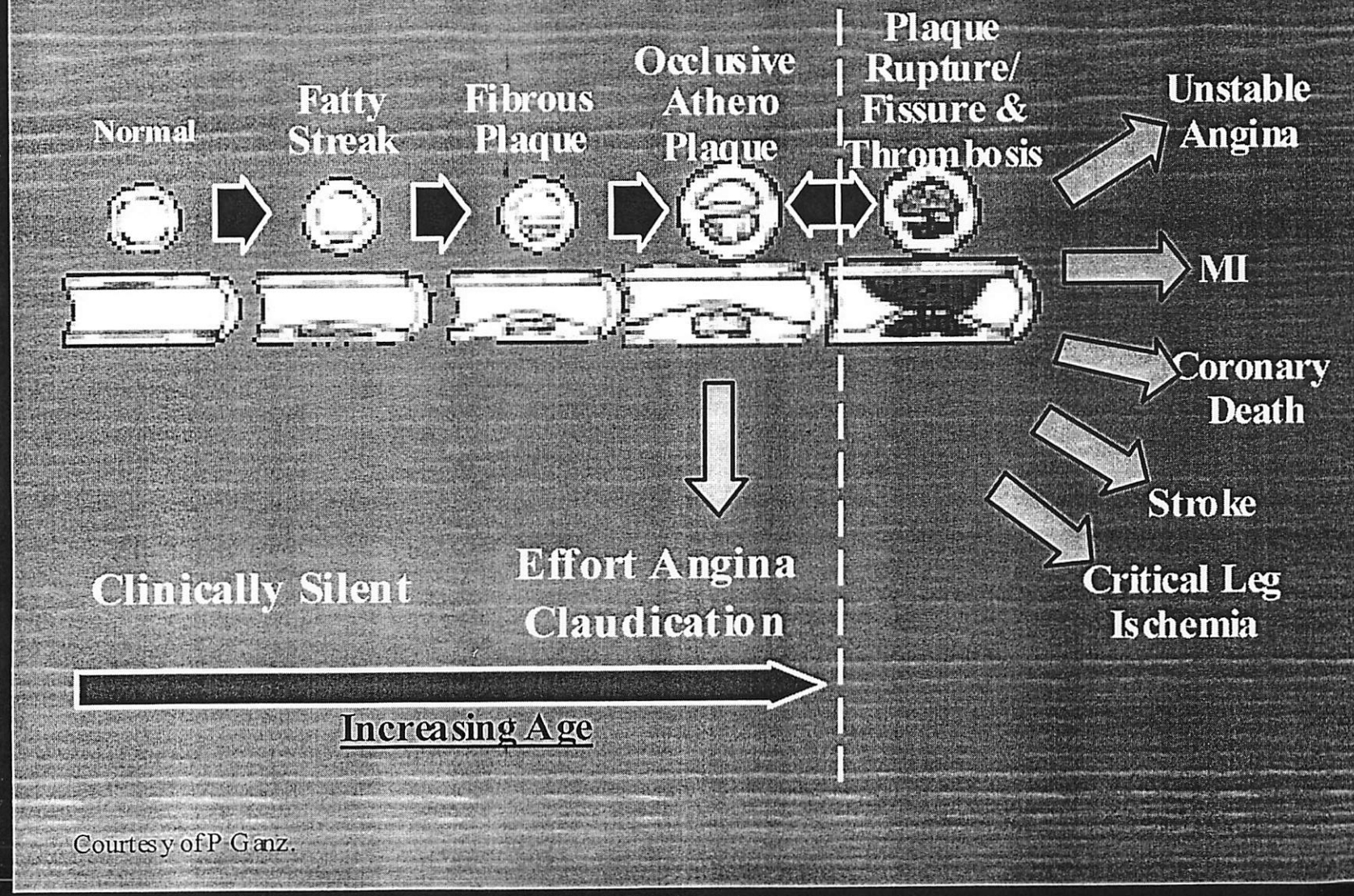
HDL

- Involved in reverse cholesterol transport
- Acquires more cholesterol

  (esterified using Lecithin Chol. Acyl Transferase - LCAT)
- Exists as multiple subtypes (HDL 1 - 5)
- > 60 = protective and < 40 = low

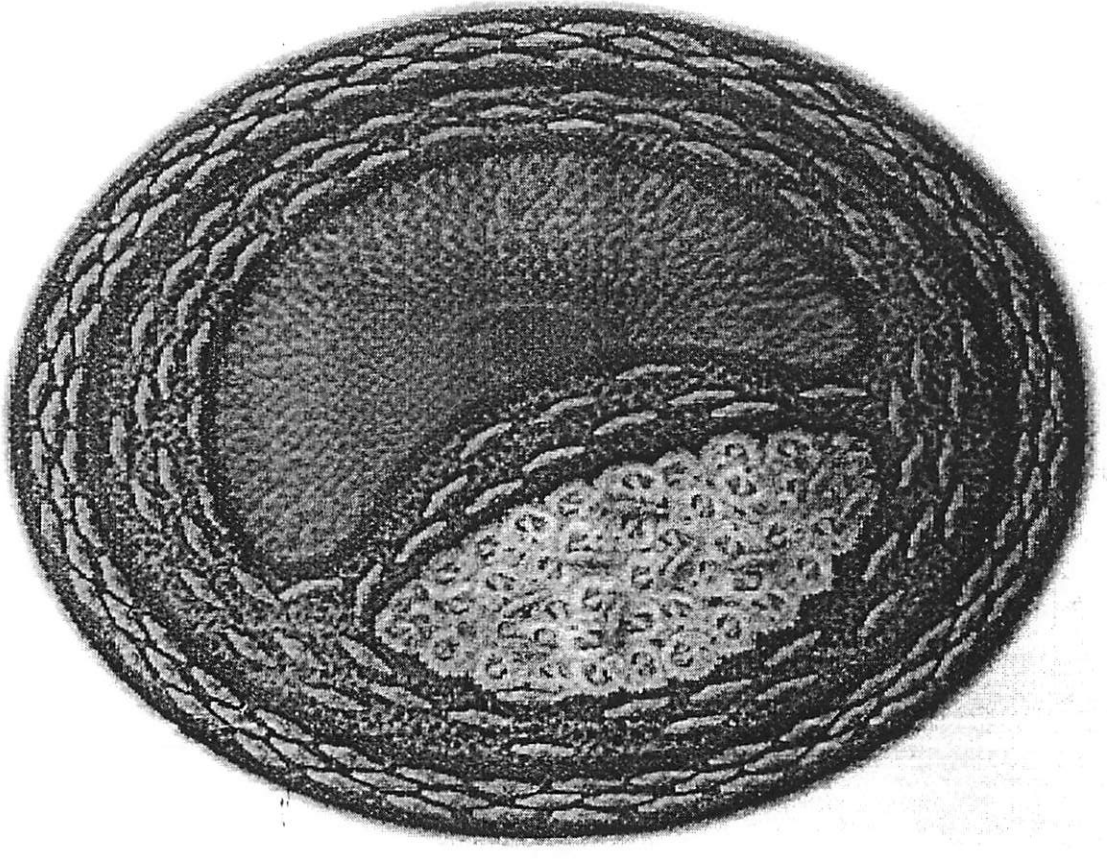


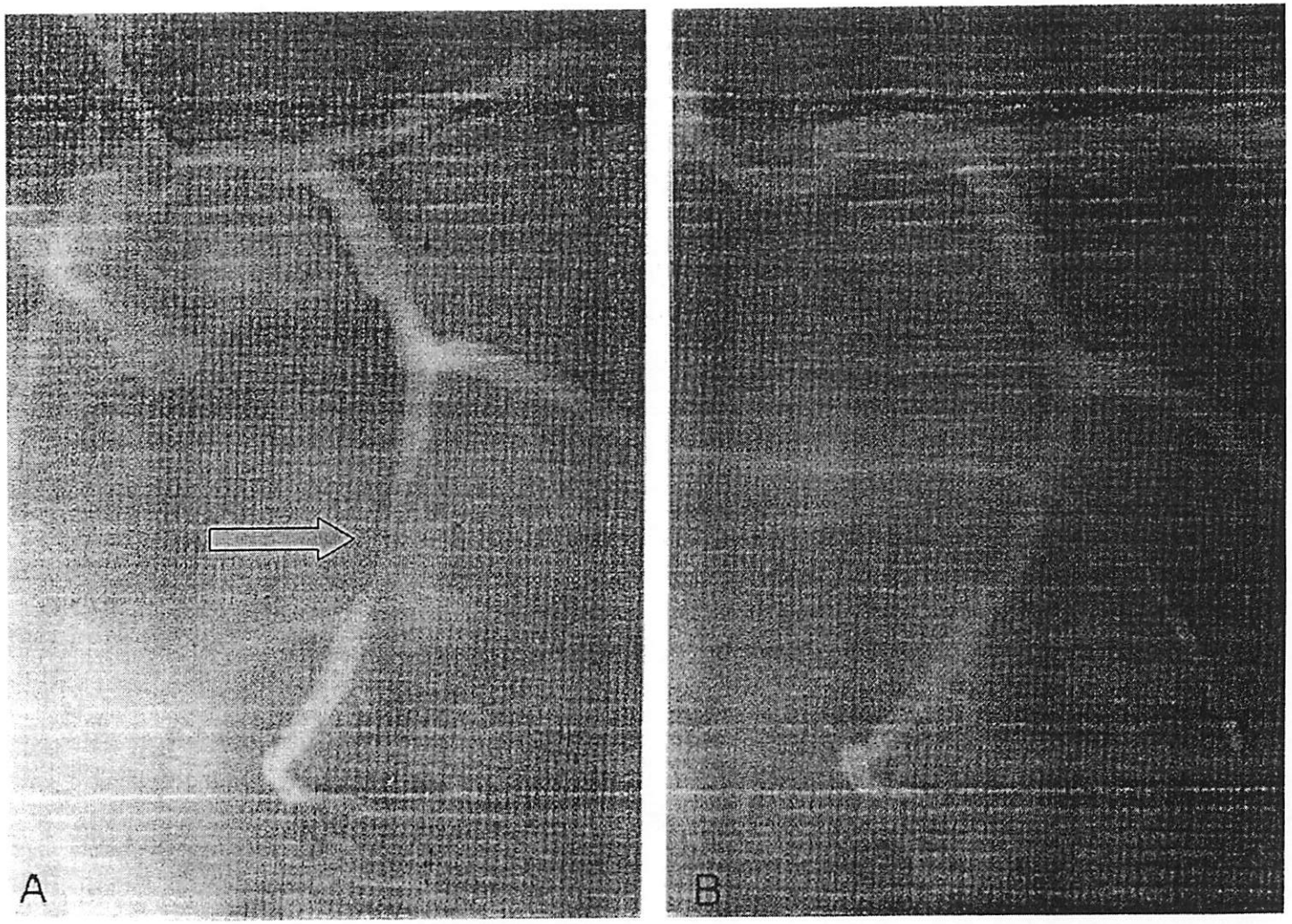
Atherosclerosis: A Progressive Process

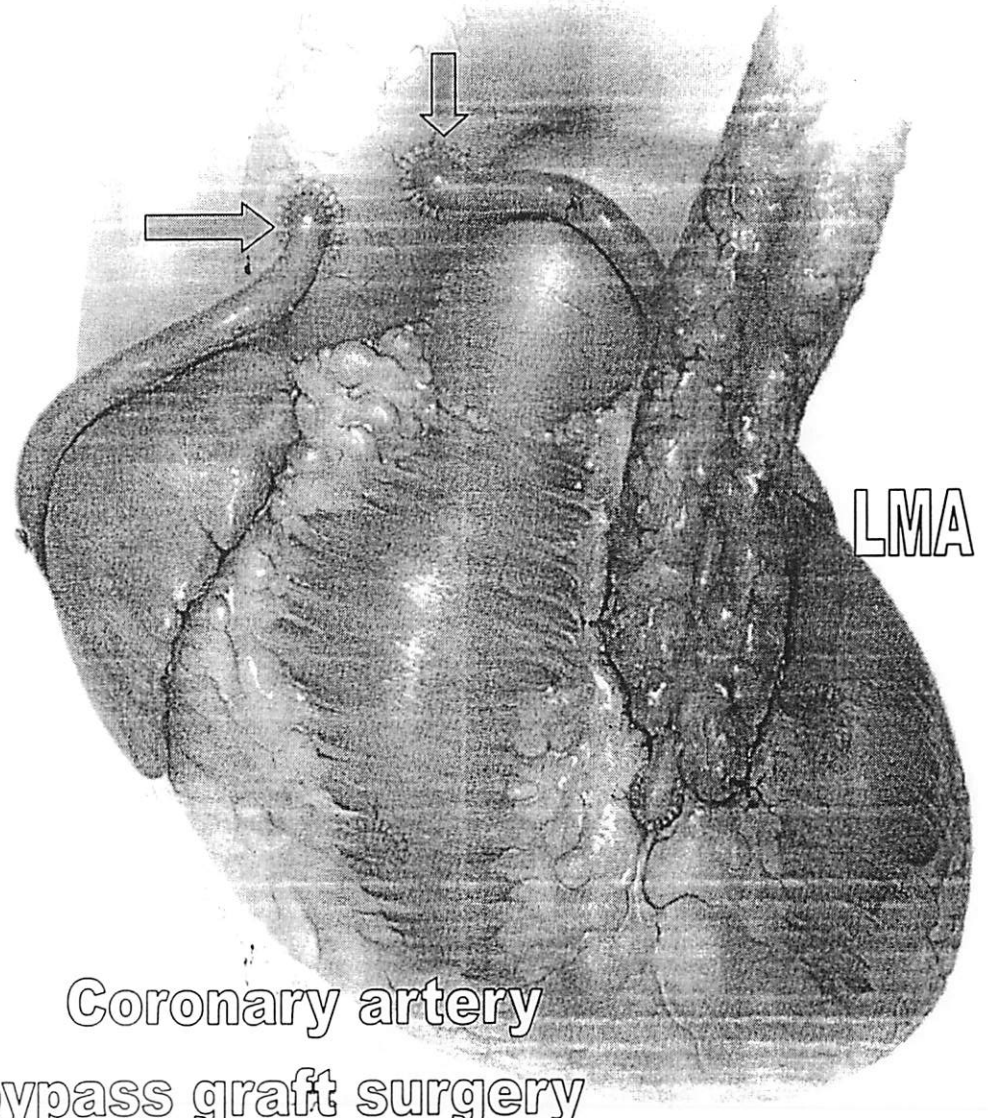


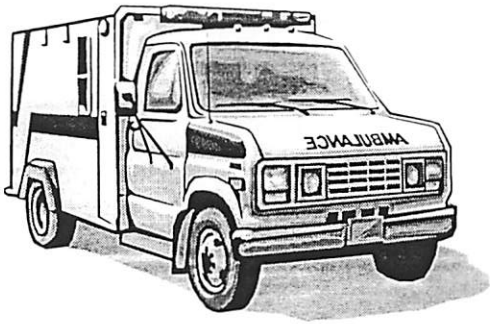
Courtesy of P Ganz.

Atherosclerosis




A
B

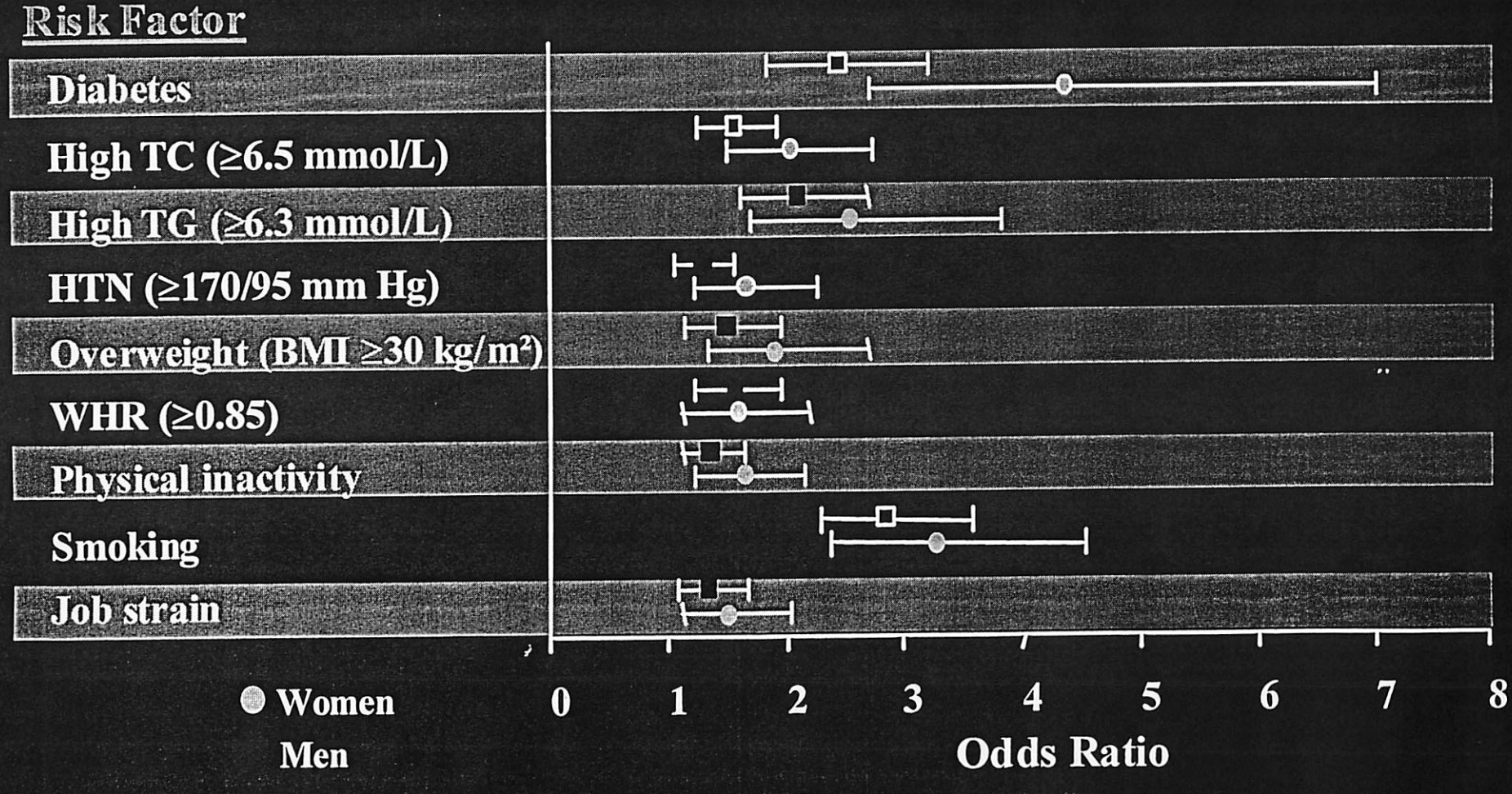

LMA
Coronary artery
bypass graft surgery



Manifestations of Atherosclerosis

- **Coronary Artery Disease (CAD)**
  - Angina (chest pain of myocardial ischemia)
  - Myocardial Infarction ("Heart attack")
- **Cerebral Vascular Disease (CVD)**
  - Transient Ischemic attacks (TIA)
  - Stroke
- **Peripheral vascular disease (PVD)**
  - Intermittant claudication
  - Rest pain (leading to limb loss)

SHEEP: Risk Factors for Nonfatal MI in Men and Women

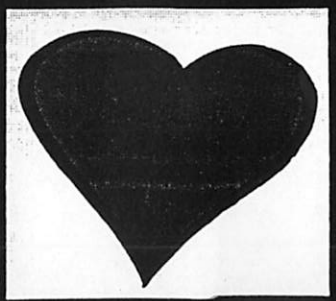


SHEEP=Stockholm Heart Epidemiology Program.

Reuterwall C et al. *J Intern Med.* 1999;246:161-174.

Risk Factors for CAD

- Lipids ⇑ LDL, ⇑ triglycerides, or ⇓ HDL
- HTN
- Diabetes
- Smoking
- Family History
- Age
- Obesity (> 95% for wt)
- Physical inactivity

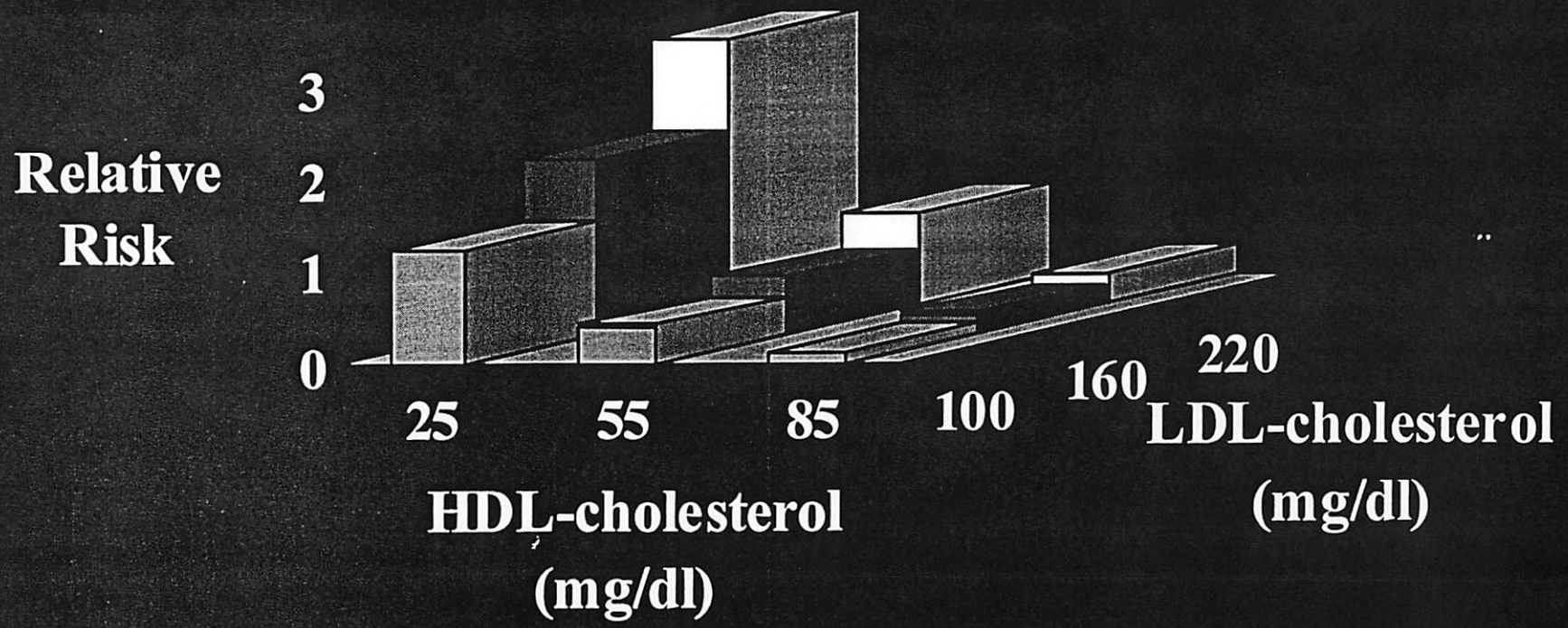


Friedwald Formula

LDL = Total cholesterol - HDL -TG/5

* Invalid if TG > 400 mg/dl

Relative Risk of Coronary Heart Disease In 4 Years



21 - 37% of patients with CHD have isolated low HDL

The Muscatine Heart Studies: Coronary Calcification Study

Study Design:

- Biennial School Surveys conducted in Muscatine Iowa from 1971 - 1981 (children age 8 to 18 yrs)
- 197 men & 187 women had CV risk factors measured in childhood (≅ 15yo) & 2x as adults with CT @ 2nd visit

Results:

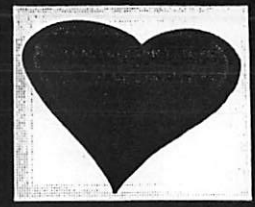
- Prevalence of coronary artery calcifications:

  31% in men 10% in women

Conclusions:

- **⇑BMI, ⇑ BP, & ⇓ HDL strongest association with coronary calcification (known biomarker of CAD)**

The Muscatine Heart Studies
Intimal Medial Thickness



Study Design:

- 182 men (M) & 136 women (W) (age 33 - 42), returned to U of Iowa for carotid Duplex US
- Determine mean of 12 measurements of maximal IMT & compare to Coronary Artery Calcification (CAC)

Results:

- CAC existed: 27% M & 14% W
- IMT ave: 0.788 mm(SD 0.127) M & 0.720(SD 0.105) W

Conclusions:

- **CAC was significantly associated with ⇑ IMT**
- **Risk factors for ⇑ IMT:**
  ⇑ LDL & smoking (M) & ⇑ LDL & ⇑ systolic BP (W)

The Bogalusa Heart Study

Study Design:

- Long term epidemiologic study of CV risk factors in Louisiana population (age 2 - 39 yo; begun in '70s)
- Autopsy Study (93/204) with autopsy & survey data
- re: ante mortum CV risk factors

Conclusions:

- Extent of aorta & coronary artery with fatty streaks & fibrous plaques ⇑ significantly with age in people dying of non cardiac causes.

- ⇑ BMI, total cholesterol, LDL & TG and
  ⇓ HDL *strongly* associated with lesions.

Biomarkers for CAD Assessment

- CPK MB & troponins:
  ⇑ BL levels correspond with ⇑ mortality at 30 days

- CRP: Correlation between inflammation & atherosclerosis
  0.05 mg/ dL normal & > 0.21 3x ⇑ MI Risk

- Lp_a: ⇑ level means ⇑ risk of ischemic heart dz.

- Fibrinogen: ⇑ level ⇑ death from premature CAD

- Homocysteine: > 15.8 nM/dL, then 3 x ⇑ risk of MI

This is an area of active pre clinical & clinical research.

AHA Guidelines for Cardiovascular Health Promotion for All Children and Adolescents

- Diet
  - Address overall healthy eating pattern
  - Attain appropriate weight
  - Attain appropriate lipid profile
  - Attain appropriate blood pressure

- Physical Activity
  - Be physically active *every* day
    - at least 60 min/ day moderate to vigorous aerobic activity; for teens may add resistive training
  - Reduce sedentary time
    - television, computer, video games, telephone time should be no more than 2 hours/ day

- Smoking
  - No new initiation of cigarette smoking
  - No exposure to environmental smoke
  - Complete cessation for those who smoke

AHA Guidelines for Identification of Children and Adolescents at High Risk of CVD

General assessment:

- Family History
- Education: risk factors

* Specific Risk Assessment:
  Level of Concern
- Lipids
- Blood pressure
- Body Size

Pediatric Lipid Guidelines

HDL <35 and TG > 150 are concerning.

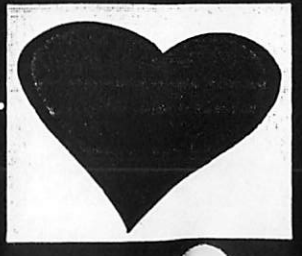
	Total	LDL
Desired	< 170	< 110
Borderline	170 - 199	110 - 129
High	≥ 200	≥ 130

Risk Assessment: Who do you screen?

- Children whose parents/grandparents have:
  - premature CAD (≤ 55years) by angiography
  - premature event: MI, angina, sudden cardiac death, cerebral vascular dz, or PVD

- Children whose parent with total cholesterol ≥ 240
- Children whose family history is not known & who may have other risk factors for CAD

* *Children should be over 2 years of age for screening.*



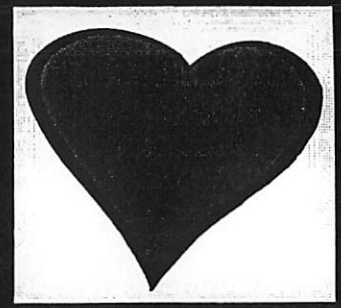
Initial Cholesterol Screening in Local Pediatrician's Office

Child's CAD
Risk Assessment

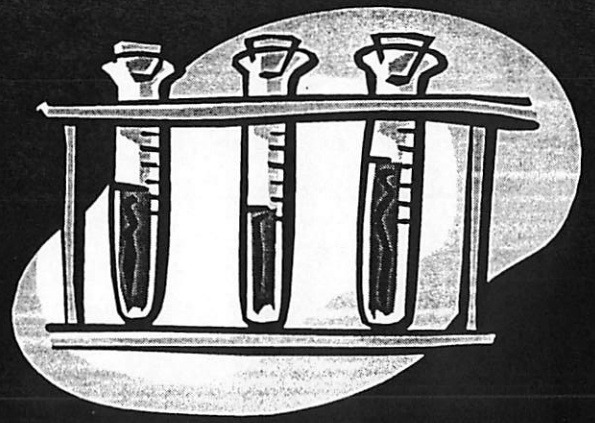
Parental High Cholesterol >240	Positive Family History
Measure Total Cholesterol (Acceptable <170 . . . ck in 5yrs Borderline 170 - 199 . . . repeat High > 200 . . . do lipoprotein analysis)	Do lipoprotein analysis Fasting profile (Total chol, HDL, TG, & LDL)

Refer to PPCC if fasting profile remains abnormal

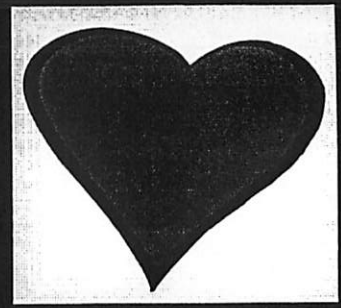
Initial Work Up Labs



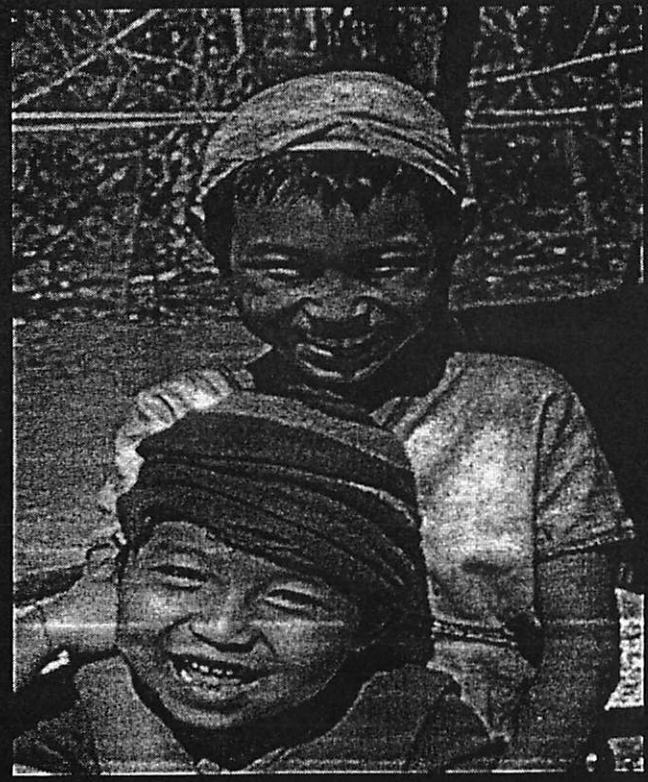
- Fasting cholesterol profile
- Electrolytes including calcium
- BUN/ Cr
- Fasting glucose
- UA
- Total Protein & Albumin*
- LFTs*
- TSH/ Free T4*



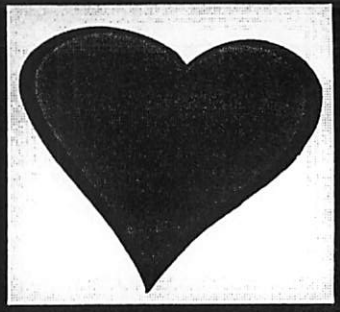
Secondary Causes of Hypercholesterolemia



- Hypothyroidism
- Nephrotic syndrome
- Chronic liver disease
- Dysglobulinemia
- Cushing's syndrome
- Hyperparathyroidism
- Acute intermittant porphyria



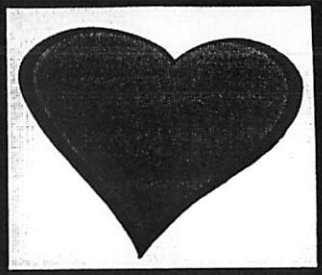
Secondary Causes of Hypertriglyceridemia



*Non fasting profile
*Obesity
Alcoholism
DM
Estrogen Use
CRF
Cushing's syndrome
Glucocorticoid use
B Blocker use
Diuretic use

Hypopituitarism
Hypothyroidism
Pancreatitis
Dysglobulinemia
Glycogen storage dz
Lipodystrophy
Pregnancy
Stress
Uremia
Acute intermittant porphyria

Pediatric Preventative Cardiology Clinic Work up of Hyperlipidemia



Do Lipoprotein Analysis
10 -12 hour fast

Acceptable LDL	Borderline LDL	High LDL
<110 Repeat & Average <110	110 -129 Repeat & Average 110 -129	>130 Repeat & Average >130
Repeat Analysis in 5 years Provide education on recommended diet & risk factor reduction	Risk factor advice Step One Diet Reevaluate in 1 year	Clinical evaluation (H&P, labs to r/o secondary causes) Screen all family members

1st return in 6 - 12 weeks*
with 2nd return visit in 12 weeks**

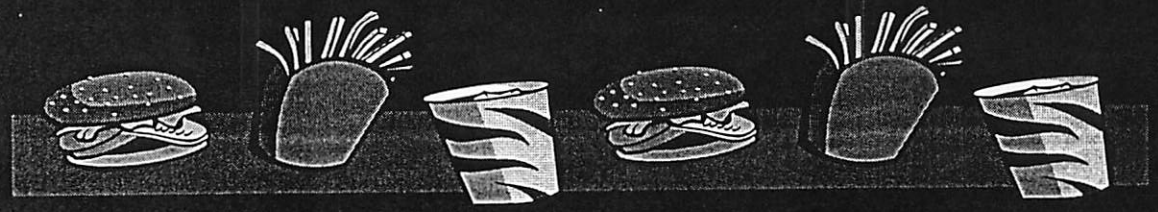
American Heart Association Diets

* No restriction of fat or cholesterol if <2years old.

(Advance to Step Two if no significant results in 3 months)

Step One Diet	Total Fat ≤ 30%	Sat Fat 8 – 10 % (<10% poly unsat fats)	**Cholesterol < 300 mg/dL**
Step Two Diet	Total Fat ≤ 30%	Sat Fat < 7% (<10% poly unsat fats)	**Cholesterol < 200 mg/dL**

Actual Fat Intake by US Children



- 35% calories from fat
- 14% sat. fat
- 193 - 296 mg/ day of cholesterol

US Dept of Agriculture 1987-88

- 34% calories from fat
- 12% sat fat
- 270 mg/day of cholesterol

Nat'l Health & Nutrition Exam 1994

When should drug therapy be considered?

Goal: LDL < 160 mg/dL (< 130 better)

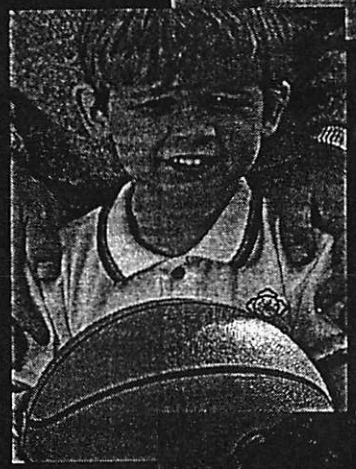
For diabetics, LDL < 100 mg/dL

- Children > 10 years old
- After 6 - 12 mo of diet/exercise tx
- LDL cholesterol remaining ≥ 190
- LDL cholesterol ≥160 plus:

1. Positive family hx (<55 CAD)

<u>or</u>

2. Child has 2 risk factors for CAD



Goal for other Lipids

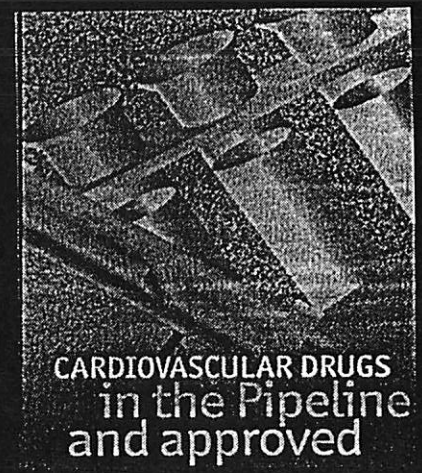
- Fasting TG $\leq$ 150 mg/dL
- HDL > 35 mg/dL

- Interventions typically involve lifestyle changes

- increase aerobic activities
- decrease intake of simple sugars (e.g. soda pop & sweets)
- no pharmacologic intervention unless TG > 400 *

*(*Look for secondary causes)*

Key Lipid Lowering Drugs for Children



1. Bile Acid Sequstrants*

2. Nicotinic Acid

3. Fibric Acid Derivatives

4. HMG Reductase Inhibitors (Statins)*

Bile Acid Sequestrants

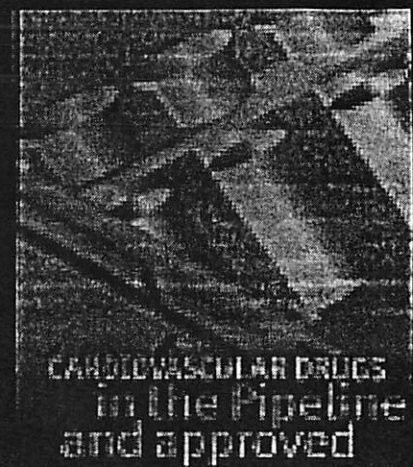
- Used if young patient
- Used if low risk for CAD

Contraindicated if:

1. **Elevated TG exists**
2. **Using certain drugs:**

   digoxin, warfarin, thyroxine, thiazides, B blockers (decreases their absorption)
3. *** Take care to give vitamins**

Nicotinic Acid



- Recommended for Tx elevated TG
- ASA 30 min prior - decreases side effects
- Side effects:
    1. Flushing
    2. Potentiates anti HTN drugs
- Exercise caution with:
    1. Diabetics
    2. Statins - hepatitis & myopathy ⇑
- Special formulation:
    Niaspan (KOS) slow-release niacin

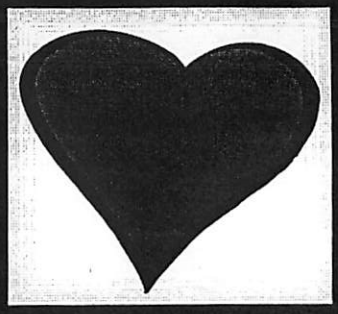
Fibric Acid

- Treatment for increased TG
- GI side effects
- Potentiates oral anticoagulants
- May cause myopathy if given with a statin

HMG Reductase Inhibitors (Statins)

- Block HMG CoA step in the acetylation of cholesterol to cholesterol esters
- Includes: atorvastatin, simvastatin,etc.
- *Liver functions studies be checked @ baseline, 6wks, and then q 6 mo.
- *Effective means of birth control essential
- *Transient myalgias

HDL-C : What's available

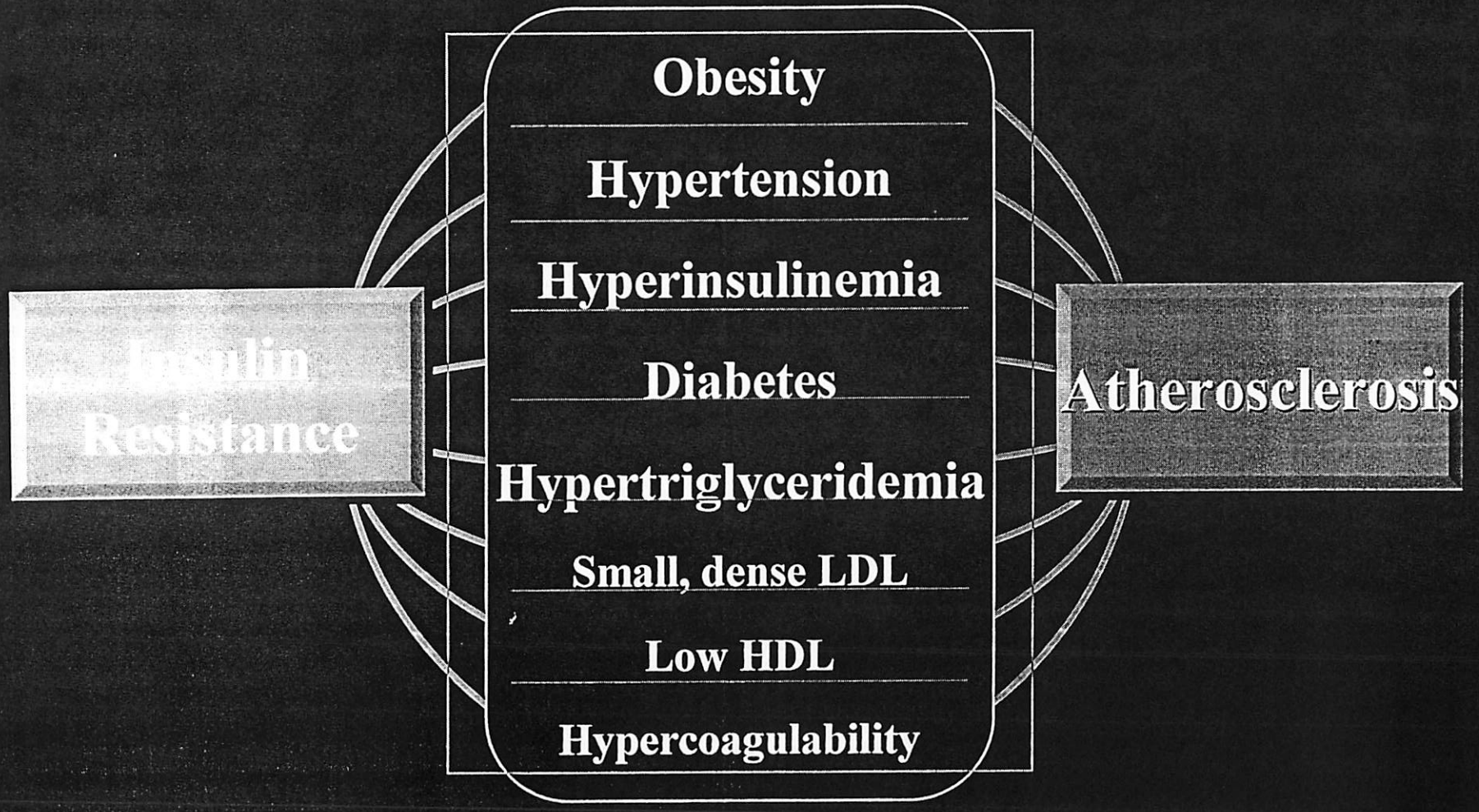


- Sequestrants - 3-5%
- Nicotinic acid (niacin) - 15-35%
- Fibrates - 10-15%
- Statins - 5-15%

Exercise can raise HDL in the pediatric population.

Metabolic Syndrome: Precursors Seen in Childhood

(JAMA Jan. 16, 2002)



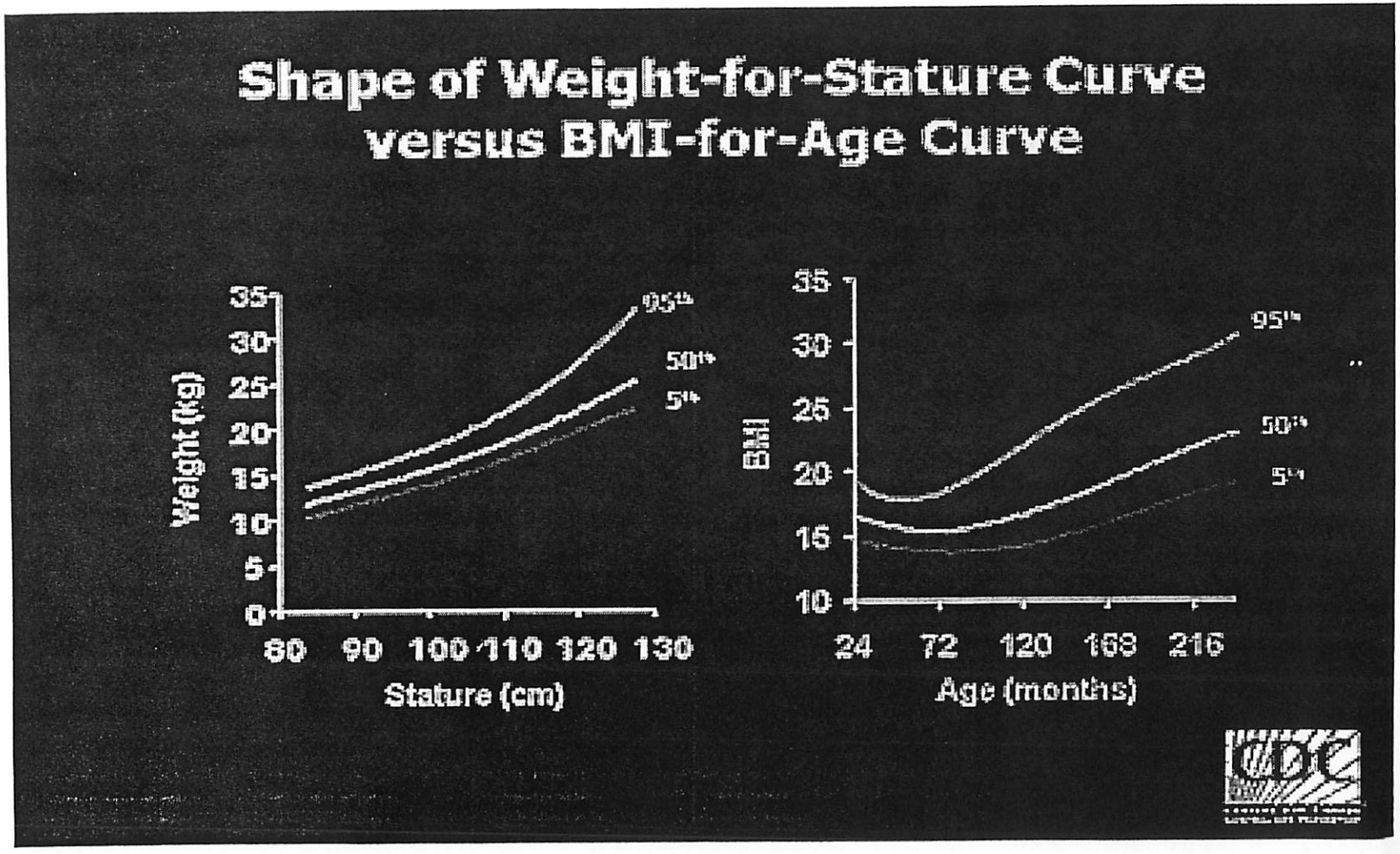
Definition of Obesity

AHA Scientific Statement. *Circulation* 106 (1): 143, 2002

American Heart Association broad definition:

" . . . a level of being overweight that is associated with adverse physical or psychological health problems."

Traditional vs. "New"



Body Mass Index (BMI)

- Recommended for clinical assessment
- Calculated as: weight (in kg)/ height (in m)^2
- CDC published age & sex specific BMI norms
- Physicians calculate BMI if child has height or weight > 75% for age & sex
- Crossing BMI percentiles = risk for obesity

*Adults: Overweight if BMI 25 – 29. Obese if > 30.

**Children/teens: "At risk," if @ 85th to 94th BMI percentile & if > 95%, obese.

Causes of Obesity

- Complex interplay of genetics & environment exists.

  65 – 80% heritability of body fat distribution & height.

- *Occasionally* secondary causes* exist like:

  Hypothyroidism
  Prader Willi Syndrome
  Cushing Disease*

**Usually such syndromes involves poor growth in height too & distinct phenotypes (physical characteristics).*

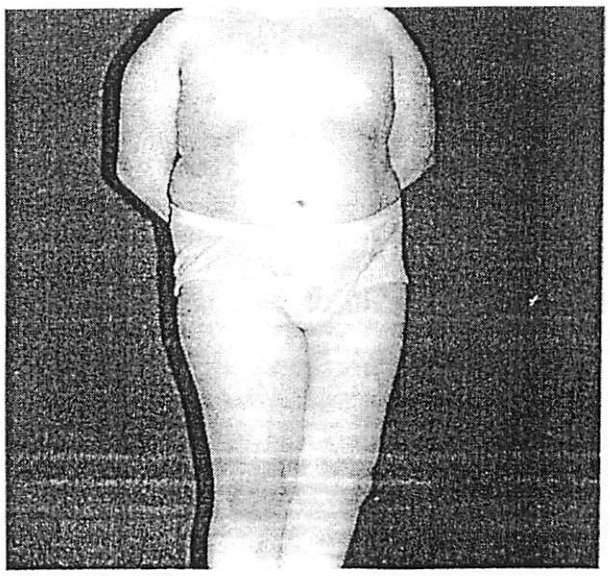
Co – morbidities Associated with Childhood Obesity (1)

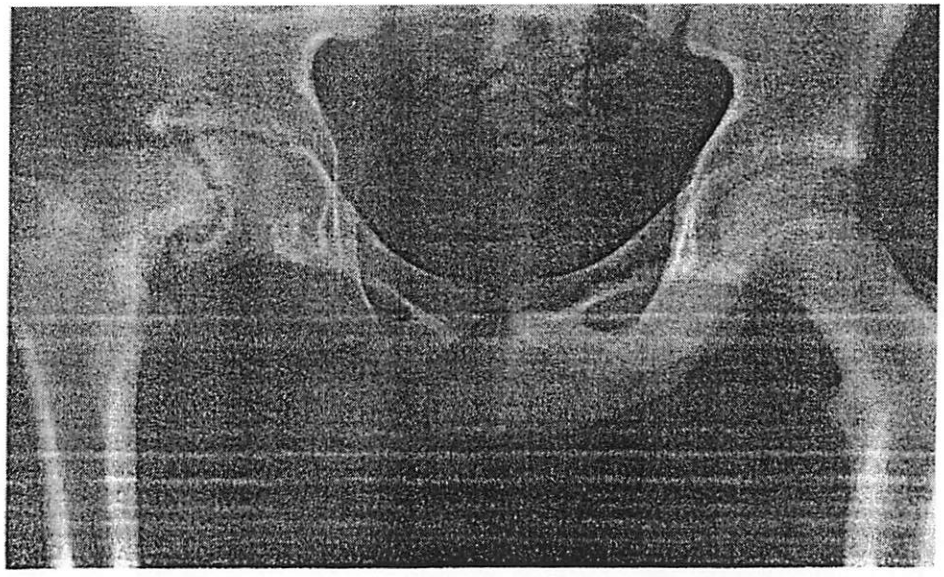
- Cardiovascular*:
  - Hypertension (High BP)
  - Lipid disorders
    - (⇑ total chol, LDL or triglycerides, ⇓ HDL)
  - Premature atherosclerosis

- Respiratory :
  - Poor ventilation (occasionally apnea)
  - Pickwickian syndrome

Co – morbidities Associated with Childhood Obesity (2)

- Orthopedic:
  - Slipped capital femoral epiphysis*
  - Blount's Disease (affects tibia)
  - Legg – Calve - Perthes Disease



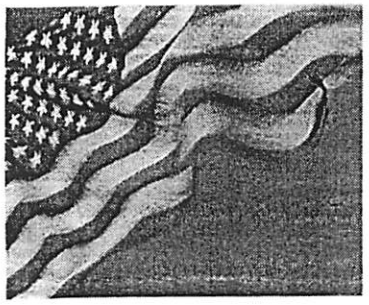


Co – morbidities Associated with Childhood Obesity (3)

- Endocrinologic:
  - Glucose intolerance (pre diabetic state)
  - Type II Diabetes
  - Dysmenorrhea
  - Polycystic Ovary Disease

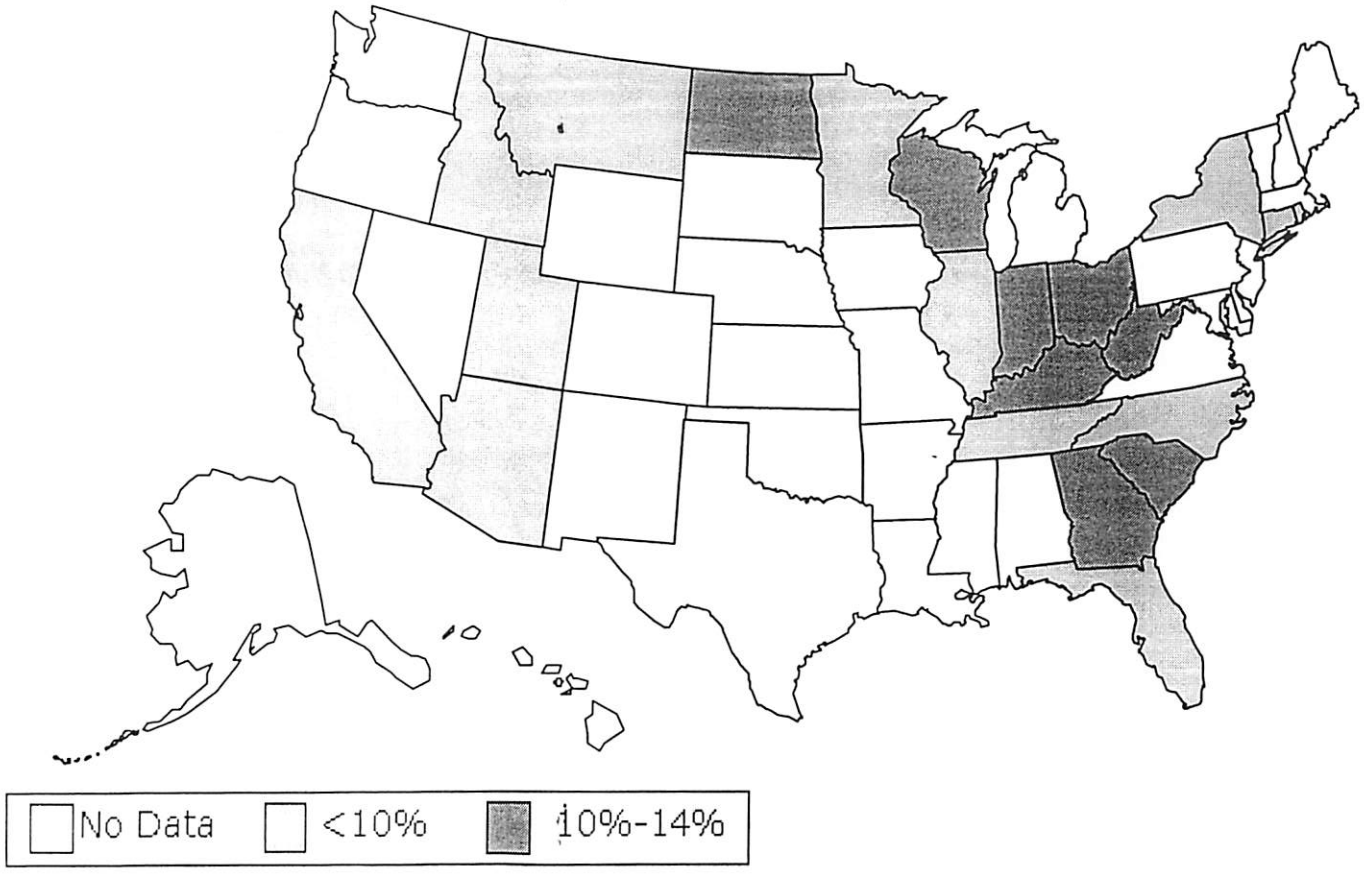
- Psychiatric:
  - Depression
  - Bulemia nervosa

- Dermatologic:
  - Furunculosis
  - Acanthosis Nigricans

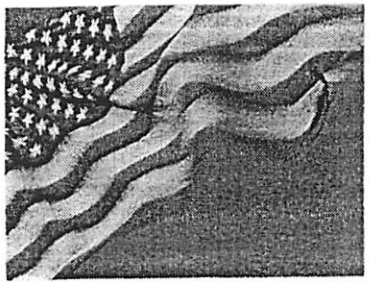


Obesity Trends* Among U.S. Adults in 1985

(*BMI ≥30, or ~ 30 lbs overweight for 5'4" woman)

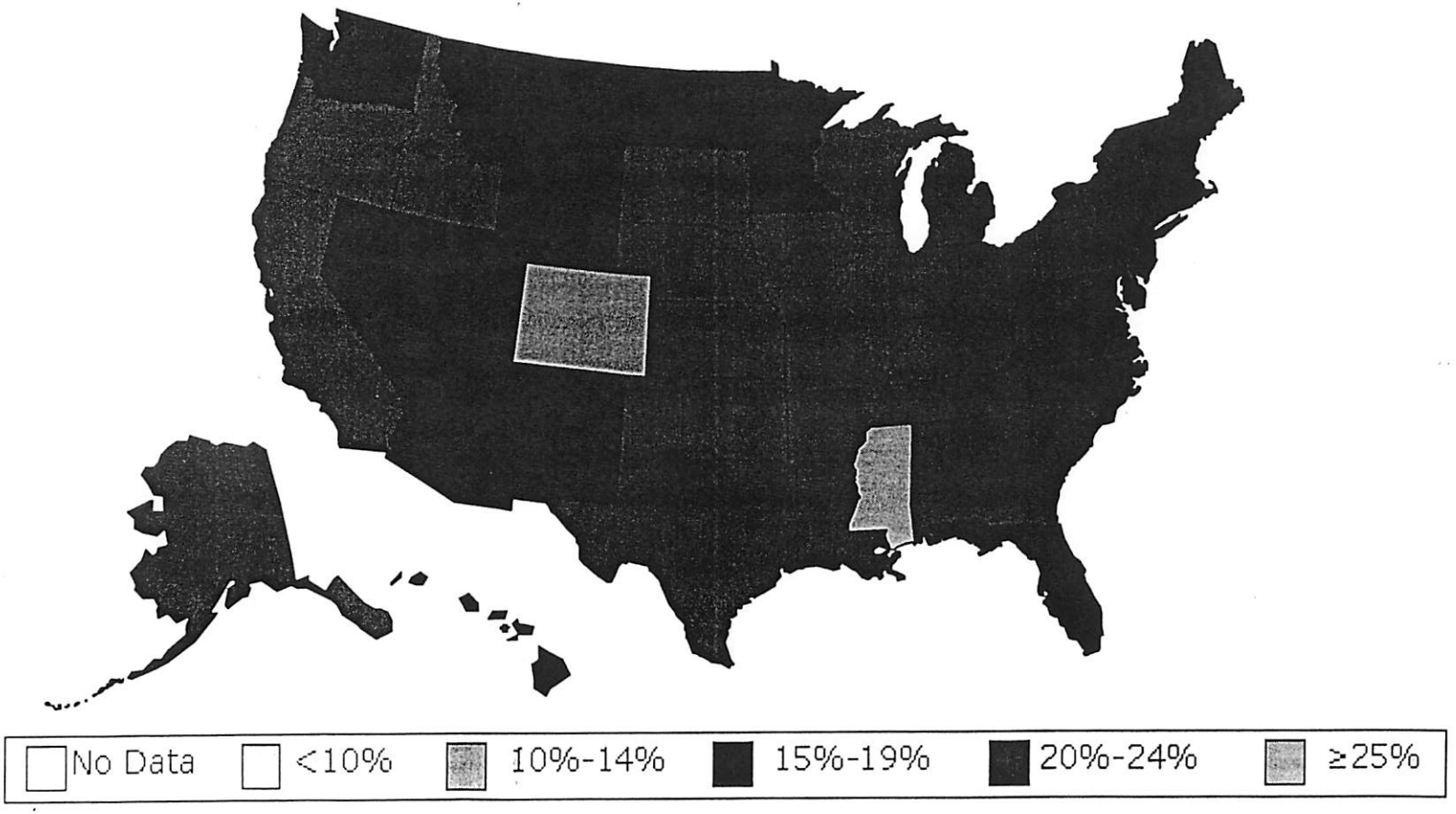


Source: Mokdad A H, et al. *J Am Med Assoc* 1999;282:16, 2001;286:10.

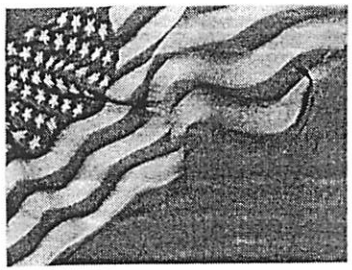


Obesity Trends* Among U.S. Adults in 2001

(*BMI ≥30, or ~ 30 lbs overweight for 5'4" woman)



Source: Mokdad A H, et al. *J Am Med Assoc* 1999;282:16, 2001;286:10.



National Pediatric Statistics

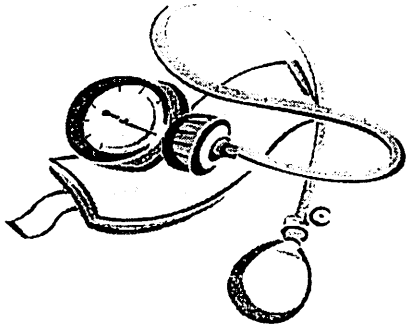
www.CDC.gov

- 70 Million (2000):
  US infant, children, teen population

- Overweight (1999 – 2000):
  10% age 2 – 5y
  15% (~ 9 M) age 6 – 15y*
  **triple the proportion in 1980*

- ⇑ chol. (> 200 mg/dL):
  10% (7 M) of 12 – 19 y.o

- High BP: *Add Stats*



Strong Correlation Between Obesity & Hypertension

- Rosner et. al.:
  Pooled data 8 large US epidemiological studies (N = 47,000 children).

  Irrespective of race, gender, or age,
  the risk of having ⇑ BP was significantly <u>higher</u> for kids in <u>upper deciles of BMI</u> than in lower deciles.

- Bogalusa Heart Study:
  Odds ratio 4.5 for developing systolic HTN &
  2.4 for diastolic HTN, if youngster overweight.

Consequences of Hypertension:

End Organ Damage

- Heart:
  - Accelerated CAD (e.g. chest pain or heart attack)
  - Cardiac hypertrophy (wall thickening)
  - Heart failure
- Kidneys
  - Renal dysfunction or failure
- Eyes
- Brain
  - Decreased cognitive function with aging
  - Stroke

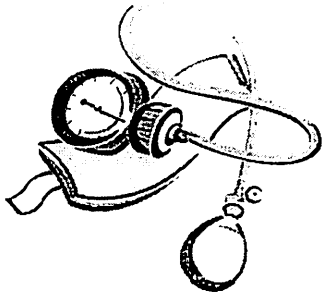
Comprehensive Therapy for Obese Patients

- Ultimate Goal: ⇓ morbidity & mortality.
- Focus on "heart healthy" lifestyle.
- Protect youngster's self esteem.
- Do not focus on achieving "cosmetic body."

Multidisciplinary Team Approach

- Members: Family*, pediatrician, sub specialist (endocrinologist or cardiologist), dietician, exercise physiologist, & sometimes a mental health professional.
- Address cardiac risk factors (BP, lipids, etc.).
- Set specific goals: exercise & food choices
- Follow up frequently with *trusted* care giver.

** Schools could play a role.*



Monitor Blood Pressure (BP)

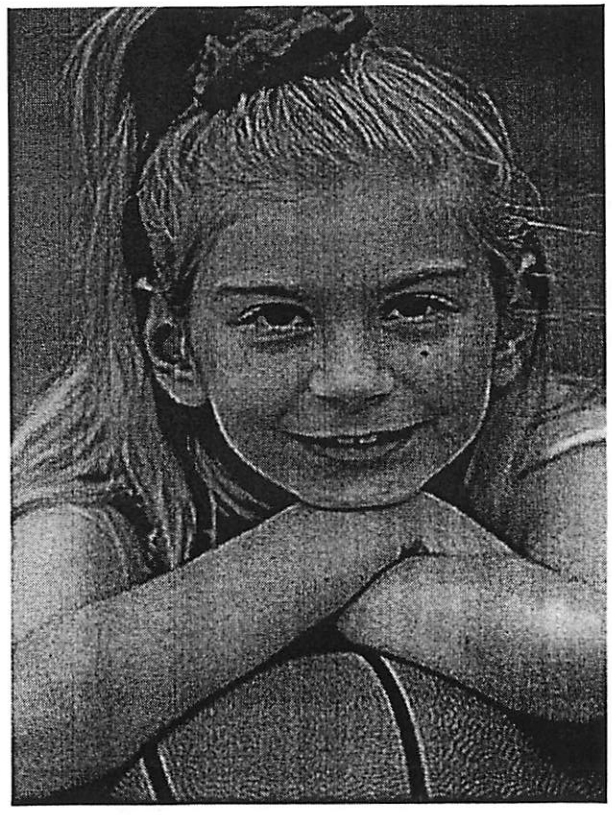
- E.g. 100/70 systolic/ diastolic BP
- American Heart Association charts give normal BP for males & females, listed by age & height %.
- Measuring BP is part of the normal physical exam.
- Refer to specialist, <u>if elevated BP 3 visits</u>, when taken with proper size BP cuff, while child *relaxed*.

Regular Pediatric Aerobic Physical Activity

*Goldberg & Samyn. A method for preventive cardiology in children. *Progress in Pediatric Cardiology* 12 (2001)155 –160.

- Fun & entertaining
- "Healthy:"

  Enhances weight loss
  ⇓ blood pressure
  ⇓ atherosclerotic risk*
  Raises HDL
  ⇓ LDL



- Sets pattern, creating "habit" for adult life.

More Intensive Therapies

- Weight reduction:
  - Enrollment in Weight Watchers (teens)
  - Summer camp for weight reduction
  - Hospitalization for weight reduction
  - Gastric bypass surgery (rare)

- BP Control & Lipid Therapy

  If exercise does not successful after ~ 6mo, consider anti HTN and cholesterol lowering medications*.

  (*usually child over 10 y.o. for cholesterol lowering meds).

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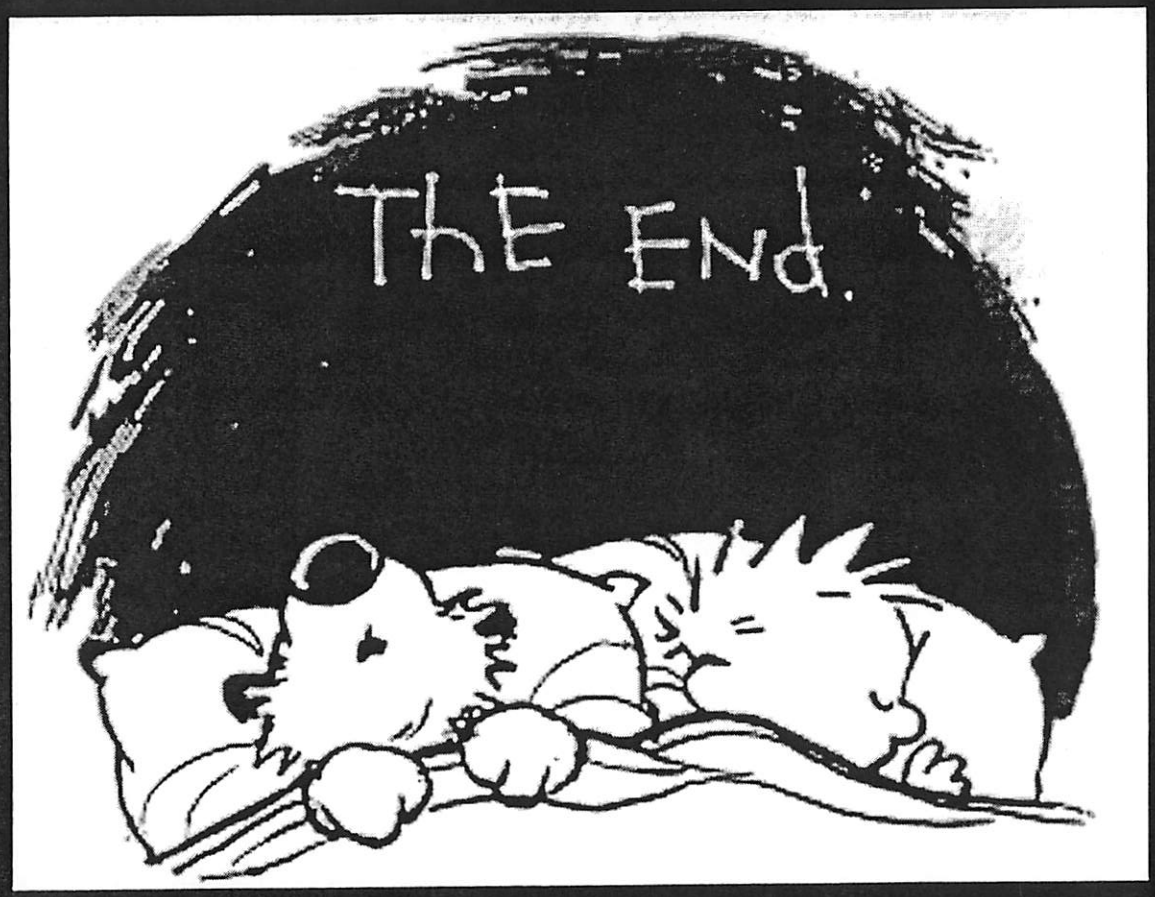
THE END.